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Identify precisely all drugs and chemicals used, including generic name(s), dosage(s) and route(s) of administration. Do not use patients' names, initials or hospital numbers. Include numbers of observation and the statistical significance of the findings when appropriate.

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Present your results in logical sequence in the text, tables and illustrations. Do not repeat in the text all the data in the tables or illustrations, or both: emphasise or summarise only important observations in the text.

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Acknowledgements:
Acknowledgements of general support, grants, technical assistance, etc., should be indicated. Authors are responsible for obtaining the consent of those being acknowledged.

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Rampal L, Liew BS, Choolani M, Ganasegeran K, Pramanick A, Vallibhakara SA, et al. Battling COVID-19 pandemic waves in six South-East Asian countries: A real-time consensus review. Med J Malaysia 2020; 75(6): 613-25.

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Ministry of Health Malaysia. Press Release: Status of preparedness and response by the ministry of health in and event of outbreak of Ebola in Malaysia 2014 [cited Dec 2014]. Available from: http://www.moh.gov.my/english.php/database_stores/store_view_page/21/437.

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Original Articles

CONTENTS Page

Evaluating factors associated with paediatric cochlear implant outcome in four cochlear implant satellite centres in Malaysia

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ABSTRACT

Introduction: Many factors are associated with cochlear implant (CI) outcomes and various methods of assessment for auditory and speech performance outcomes in CI are available globally. The objective of this study is to identify factors relating to CI outcomes in paediatric population that suits local context.

Materials and Methods: A total of 18 factors consisted of variables which emphasise on audiological, CI service team, speech therapy, and family-related factors. These factors were then retrospectively analyzed among CI recipients. The outcome measurements of categorical auditory performance II (CAP-II) and speech intelligibility rating (SIR) were used to individually study each factor. Kruskal–Wallis H Test and Fisher Exact Test used with *p*-value <0.05 were considered significant.

Results: There were significant associations between post-CI CAP-II with type of hearing loss, hearing aid usage per day and mode of communication, attention, attending audiology and speech session, and siblings. For post-CI SIR, hearing aid usage per day, attention, mode of communication, attending audiology and speech session, initiatives, and siblings were statistically significant.

Conclusion: The factors affecting the outcome of CI are dynamic. Some of the factors have demonstrated to be associated with the auditory and speech outcome in CI recipients while some factors failed to replicate similar findings. Further prospective research may refine the outcome of individual factors.

KEYWORDS:
Cochlear implant; factors; candidacy; outcome

INTRODUCTION

Cochlear implant (CI) has been the choice for treatment for both bilateral and unilateral severe to profound sensorineural hearing loss (SNHL). The application in paediatric population has significantly improved speech production and perception outcome.[1–3] In selecting the appropriate candidate, it requires an assertive tool that evaluates the biographic and audiologic factors that may affect the outcome and the success of the auditory and speech performance. Hellman et al.[4] designed the Children's Implant Profile (ChIP) in 1991. This tool uses 11 factors to determine suitability for cochlear implantation. This ChIP has been globally adopted for the past 25 years but evolution and expansion of science and knowledge in cochlear implantation have necessitated many implant centres to modify the tools in accordance to the local needs such as Children's Hospital of Philadelphia Children Implant Profile (CHOPChIP) and Great Ormond Street Hospital Children Implant Profile (GOSHChIP).[5,6]

The selection criteria for CI involve multidisciplinary approaches. Establishing an ideal assessment tool is difficult because the decision-making for CI is complex and influenced by many factors.[7] Although the existing ChIP is a good assessment apparatus in forecasting various factors that affecting the CI outcome, inconsistencies in decision-making are noted when it is applied to our population. Therefore, Hospital Sultan Ismail Cochlear Implant team had listed down factors that might affect the outcome of CI (Table I). There were a total of 18 factors identified and each factor was rated from a scale of 1 to 3. The scoring system was adapted from Edwards et al.[6] who divided the score into three categories; those who are suitable to be implanted, 50% suitable for implantation, and not favourable for CI. The scoring system were as follows; those who score 18–30 is suitable for CI, those with a score of 31–42 should be considered for CI based on individualized justifications, while those with a score of 43–54 is not favourable for CI.

The main aim of this study is to identify factors that are relevant to the local population and current timeline. These factors were then assessed categorically by means of post-CI categorical auditory performance II (CAP-II) and speech intelligibility rating (SIR).

MATERIALS AND METHODS

Data collection

Hearing-impaired children who successfully underwent CI in

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Table I: The Hospital Sultan Ismail Cochlear Implant Profile (HSIChIP)

Factor	Item	Score		
		1	2	3
Audiological factors:				
1	Age of diagnosis	< 1 year old	1 to 2 years old	> 2 years old
2	Age of hearing aid fitting	< 1 year old	1 to 2 years old	> 2 years old
3	Expected age to be implanted	6 months to 2 years old	2 to 3 years old	3 to 5 years old
4	Hearing aid usage per day	Consistent (>8 hours)	Persistent (4–8 hours)	Rarely (<4 hours)
5	Type of hearing loss	Severe to profound bilaterally	Only one ear profound with residual hearing at the other ear	Dead ear bilaterally
Cochlear implant team services factors:				
6	Hospital/ Surgeon availability	Within 50km	50–100km	>100km
7	Speech therapist	Consistent and committed	Frequent changes of speech therapist	Limited or no trained speech therapist service
Speech therapy factors:				
8	Behaviour	Cooperative	Easily distracted	Poor attention and not cooperating
9	Attention (Based on Reynell Attention Scale)	5 to 6	3 to 4	1 to 2
10	Mode of communication	Verbal	Gesture with some verbal	Predominantly gesture
Family factors:				
11	Family involvement	Both parents involved	Only 1 caretaker or parents involved seemed involved but with great attention	One caretaker involved but lack consistency and involvement
12	Attending audiology and speech session	Consistently attending	At least absent few times	Absent most of the time
13	Initiatives	Proactive and willing to spend time and money for child benefit	Not proactive but follow diligently	No initiative at all
14	Siblings	≥ 3	2	1
15	Household income	> RM5000	RM3000 to RM5000	< RM3000
16	Working parents	One of the parents has stopped working to focus on the child rehabilitation	Only one is working while another is house bound	Both working and are not willing to stop for the child benefit
Variables				**n (%)**
17	Marriage	Healthy and happy	Still together but thinking of separation or had separated before	Divorced or married to different partner
18	Language spoken	Malay	Malay and others	Others

Table II: Categories of auditory performances II (CAP-II) and speech intelligibility rating (SIR)

CAP-II	Score	Categories
	0	No awareness of environmental sounds or voice.
	1	Awareness of environmental sounds.
	2	Response to speech sounds.
	3	Identification of environmental sounds.
	4	Discrimination of speech sounds without lip reading.
	5	Understanding of common phrases without lip reading.
	6	Understanding of conversation without lip reading.
	7	Use conversation with known speaker.
	8	Follows group conversation in a reverberant room or where there is some interfering noise, such as classroom or restaurant.
	9	Use of telephone with an unknown speaker in unpredictable context.
SIR	**Score**	**Categories**
	1	Connected speech is unintelligible. Pre-recognizable words in spoken language (primary mode of communication may be manual).
	2	Connected speech is unintelligible. Intelligible speech is developing in single words when context and lip-reading cues are available.
	3	Connected speech is intelligible to a listener who concentrates and lip-reads within a known context.
	4	Connected speech is intelligible to a listener who has little experience of a deaf person's speech.
	5	Connected speech is intelligible to all listeners. The child is understood easily in everyday contexts.

Table III: The characteristics of the subjects

Age (month), (mean ± SD)	41.8 ± 28.40
Gender	
• Male	39 (45.9%)
• Female	46 (54.1%)
Race	
• Malay	52 (61.2%)
• Chinese	26 (30.6%)
• Indian	7 (8.2%)
Pre-CI CAP-II (mean ± SD)	1.71 ± 1.438
Post-CI CAP-II (mean ± SD)	4.78 ± 1.340
Pre-CI SIR	
• Poor	76 (89.4%)
• Good	9 (10.6%)
Post-CI SIR	
• Poor	45 (52.9%)
• Good	40 (47.1%)

Table IV: The relationship between HSIChIP factors with pre- and post-CI CAP-II and SIR

Factor	Items	*p* value	
		Post-CI CAP-II†	Post-CI SIR‡
Audiological factors:			
1	Age of detection	0.122	0.066
2	Age of hearing aid usage	0.300	0.515
3	Expected age to be implanted	0.175	0.062
4	Hearing aid usage per day	0.025	0.033
5	Type of hearing loss	0.026	0.625
Cochlear implant team services factors:			
6	Hospital/ Surgeon availability	0.820	0.405
7	Speech therapist availability	0.843	0.733
Speech therapy factors:			
8	Behaviour	0.460	0.156
9	Attention	**<0.001**	**0.001**
10	Mode of communication	**0.002**	**0.013**
Family factors:			
11	Family involvement	0.488	0.469
12	Attending audiology and speech session	**0.044**	**0.017**
13	Initiatives	0.078	**0.039**
14	Siblings	**0.036**	**0.029**
15	Household income	0.209	0.346
16	Working parents	0.924	0.543
17	Marriage	0.175	0.202
18	Language spoken	0.184	0.554

CAP-II: Categorical of auditory performance II; CI: cochlear implant; SIR: speech intelligibility rating.
†Kruskal–Wallis H test, ‡Fisher Exact Test, statistically significant with p-value <0.05.

Malaysian government hospitals from 2008 until 2018 were recruited retrospectively from four CI satellite centres. The inclusion criteria included all children less than 18 years old with severe to profound SNHL bilaterally who were enrolled in the CI candidacy evaluation program by the National CI Committee. Bilateral or reimplantation of CI was not included in this study. Defaulters or deceased subjects were also excluded. All data were retrieved from subjects' medical records and CI database.

Measurement outcomes

Categorical auditory performance II (CAP-II) and speech intelligibility rating (SIR) were used as tools to measure the outcome of CI in this study. Each factor was analysed using the post-CI of the CAP-II and SIR. CAP-II is used to assess the auditory perception ability of patients with hearing impairment, as depicted in Table II.[8] In addition, SIR determines the speech intelligibility of patients with hearing impairment as illustrated in Table III.[9] The CAP-II and SIR were routine outcomes measurements for all CI candidate under National MOH CI programme. Post-CI CAP-II and SIR scores were evaluated by the same dedicated audiologist and speech therapist after 2 years of the CI surgery.

Ethical approval

Ethical approval from Malaysian Research Ethics Committee (MREC) has been obtained and registered with the National Medical Research Register (NMRR-20-649-53756).

Statistical analysis

A descriptive analysis was conducted for this research. Kruskal–Wallis H test was used to analyze the data obtained for the CAP-II outcome. The statistical significance test standard was at $p<0.05$. On the other hand, SIR was

categorized into poor (score 1-2) and good (score 3-5). Therefore, Fisher Exact Test was conducted to analyze the data for the outcome of SIR. Each of the factors was categorized into four main themes which comprised of audiology, CI team services, speech therapy, and family factors. The relationship between these factors and the outcome were analysed using the tests stated above.

RESULTS

In this study, 85 hearing-impaired children were included, which comprises 45.9% males and 54.1% females. Malay, Chinese, and Indian comprised of 61.2%, 30.6%, and 8.2%, respectively. The mean age ± standard deviation of the children at the time of CI surgery was 41.8 ± 28.40 months old. The mean CAP score ± standard deviation prior to CI was 1.71 ± 1.438, and it increased to 4.78 ± 1.340 after 2 years of CI surgery. Furthermore, only 10.6% of children with good SIR before CI and the percent were improved to 47.1% after 2 years of CI surgery. The characteristics of the subjects are outlined in Table III.

There were statistically significant differences observed in post-CI CAP-II for six factors which were hearing age usage per day (p=0.025), type of hearing loss (p=0.026), attention (p<0.001), mode of communication (p=0.002), attending audiology and speech session (p=0.044), and siblings (p=0.036). The other factors appeared to be not statistically significant (p>0.05) (Table IV).

Following Fisher's Exact Test analysis, there were statistically significant differences in post-CI SIR for six factors which were hearing aid usage per day (p=0.033), attention (p=0.001), mode of communication (p=0.013), attending audiology and speech session (p=0.017), initiatives (p=0.039), and siblings (p=0.029). The relation between post-CI SIR with other factors was not statistically significant in this study (p>0.05) (Table IV).

DISCUSSION

In this study, we attempted to identify preoperative candidacy factors befitting our local patients. For more than 13 years, the National MOH CI Programme was using CHOPChIP as one of the CI candidacy assessment tools.[5] However, some of the factors seem unsuitable to Malaysian context. So far, more than 400 children with hearing impairment had successfully received CI through this program.[10]

In this study, some factors mentioned in previous ChIP were maintained as these factors still hold true during pre-CI assessment. Previous ChIP included chronological age as one of the important factors. Similarly, age was emphasized in this study. Literature had shown that infants who received CI demonstrated better speech development as compared to older children.[11,12] In agreement, Gaurav et al.[13] reported that implantation below age of 5 years is preferable as the effects of auditory rehabilitation show promising results. Responding to this matter, the MOH had introduced the Universal Newborn Hearing Screening Programme (UNHS) and High Risk Newborn Hearing Screening Programme (HRNHS) in many Malaysian hospitals. However, these factors were not statistically significant in our analysis. Perhaps it was contributed by the low implementation of hearing screening at the moment.[14]

In agreement with previous CHOPChIP and NChIP, children's behavioural and attention issues were given priority. Children with attention deficit hyperactivity disorder with concurrent hearing impairment has less favourable outcome post-CI as these children have decreased ability in auditory, language, speech, cognition, motor, and communication skills.[15] Although hearing-impaired children with additional disabilities demonstrated some benefit from early CI, there is an issue in tackling the behavioural problems with greater parental stress.[16] Thus, pre-CI evaluation and counselling are important to facilitate family adaptation and also shape realistic expectations following CI.

Conducive family environment between parents and siblings was strongly related to social and cognitive development of children with hearing impairment.[17] Family factors form integral part of healthy family structures. The previously established ChIP also reported similar findings.[5] It has become evidence that family factors such as compliance in attending the audiology and speech session, parents' initiatives on home-based programme, and presence of siblings are important in predicting the speech development as shown in this study. Although family involvement, working parents, and marital harmony were unable to replicate similar results, we strongly believe that these factors are important based on our experience. In accordance with the previous analysis on CHOPChIP, some of the family factors did not represent a significant association with the speech outcome.[5] Dynamic family patterns might reflect the ambiguity of the results. Therefore, the ultimate decision should be individualized. In our opinion, it is strongly recommended that family environment should be thoroughly evaluated prior to CI and this commitment should be continuously monitored post-implantation as well.

Although the provision of CI is fully or partially funded by the government or third party, the long-term expenditures are fully borne by the family.[18] This is the reason why this factor is included in our analysis. A local study by Umat et al.[19] mentioned that parents of children with CI expressed their concern on financial support. Another study reported lower socioeconomic background associated negatively with the outcome post-CI surgery, such as poorer compliance to follow-up appointments, higher rates of complications postoperative, and lower chances of sequential bilateral cochlear implantation.[20]

Criticism may arise on the importance of spoken language. This factor indicating candidate who speaks in Malay language is favourable as compared to other languages. Multiracial and multiethnic population are unique features in Malaysia. There are multiple spoken languages and dialects used. As Malay language is the most commonly spoken language in this country, the speech rehabilitation using this language is widely available. This is important to ensure the continuity of rehabilitation as well as for the school placement later on.

These study limitations pertain to methodological issues, which may cause bias to the study findings. First, the CI outcome was analyzed by recruiting subjects retrospectively in which most of the subjects had undergone thorough assessment during National CI Programme. Secondly, subjects who have failed the initial candidacy and not implanted were not included and assessed in our study. Another limitation in this study is inter-rater variability in CAP-II and SIR was not assessed in this study. It is because the CAP-II and SIR were routine assessments and the data were extracted from subjects' medical records and CI database. For quantitative studies, limitations may include small sample size, which may limit the validity that affects the generalisability of the findings. Perhaps bigger sample size in multicentre studies in prospective manner will yield more significant results.

CONCLUSION

Upon scrutiny of each factor associated with paediatric CI outcome, the study finds that some of the factors appeared to be associated with the audiological and speech outcome among CI subjects. On the contrary, some of the factors failed to show statistically significant correlations. Hence, it can be inferred that the factors contributing to CI outcome are complex. Based on these findings, we are optimistic to develop our own Hospital Sultan Ismail Cochlear Implant Profile (HSIChIP) in future research. Future research will be directed towards content validation of the HSIChIP and its applicability in our local setting.

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ORIGINAL ARTICLE

Aquatic disaster activation plan and tactic: The natural history and management conceptual framework of aquatic disasters

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ABSTRACT

Introduction: In the past decades, water-related disasters had been accounted for about three-quarters of all-natural disasters worldwide. Asia is the most affected region with more than 45% of fatalities and more than 90% of the victims affected by aquatic disasters. Aquatic events progress differently and rapidly as compared to inland disasters. Thus, apart from additional equipments and trained aquatic rescuers, aquatic disaster operation requires specific strategies and tactics.

Materials and Methods: This qualitative study was conducted using mixed methods involving the Delphi method and decision-conferencing approach. Two rounds of open-ended questionnaires were sent to subject matter experts from rescue agencies that involved in aquatic disaster rescue and management. Feedback from the panel was reviewed, the natural history of different aquatic disasters was appraised, and the decision-analysis model on the command, control and management of aquatic disaster was developed. The model was then reassessed through an iteration process at decision-conferencing among the expert panel until the final framework was accepted by all members of the panel.

Results: The fast progression of aquatic disasters with multiple hazards on the scene and unique technical challenges of the operation increase the risk of rescuers to become victims themselves. The developed conceptual framework, namely Aquatic Disaster Activation Plan and Tactic (ADAPT), was found able to guide rescuers in risk assessment, judgment, and response in aquatic disasters based on strategies and tactics for different phases along the natural history of aquatic disasters.

Conclusion: With realistic scenario-based training and drills, ADAPT can be the blueprint in aquatic disaster management. It is designed to facilitate rescue agencies and organizations in preparing and executing the technical aquatic rescue operations safely, according to the resources available and the capability of the respective rescue organization.

KEYWORDS:
Aquatic disasters; conceptual framework; decision-analysis model; natural history; risk assessment

INTRODUCTION

Aquatic disasters had occurred more frequently in recent years. Millions of people worldwide had endured various aquatic catastrophic events with thousands of deaths as well as damages to infrastructures and the environment. Malaysia has had its share of major aquatic disasters. A National Security Council decree, Directive No. 20, dictates on preparation, response, and management of disasters.[1,2] Despite having a well-organized incident management system, the rescue operation and management at the scene of aquatic disaster were not well defined.

Due to the fluidity of the water, events in water tend to progress by the minutes. The window period to save lives is narrow. The situation at first hour differs from that of few hours later, the aim and response to the same event also differ with time. Even if the direct injury from the aquatic disaster was not life-threatening, the victim was still threatened with the risk of drowning and hypothermia. Besides that, managing aquatic disasters requires distinguished rescue personnel, equipment, and strategies. Slight error in judgment during the response to aquatic disaster could spell catastrophe, risking lives, and resulting collateral damages. Understanding the progression of aquatic disasters and guidance to an efficient response could minimize the destruction effect and facilitate faster recovery of the affected communities. Thus, the study objective is to appraise the natural history of aquatic disaster and to develop a framework that guides the response and coordination of mass casualty aquatic rescue.

MATERIALS AND METHODS

This study adopted a mixed methods approach (Figure 1) which involved the Delphi method and decision conferencing approach.[3] It was conducted from March 2019 until March 2020. First, the researchers assembled a panel of local experts in aquatic disaster management. The members of the panel consisted of commanding officers assigned by agencies from the Special Malaysia Disaster Assistance and Rescue Team (SMART), National Disaster Management Agency (NADMA), Malaysia Civil Defence Force (MCDF), Malaysian Maritime Enforcement Agency, Fire and Rescue Department of Malaysia (MMEA), representatives from the local life-saving societies, lecturers in emergency medicine of local

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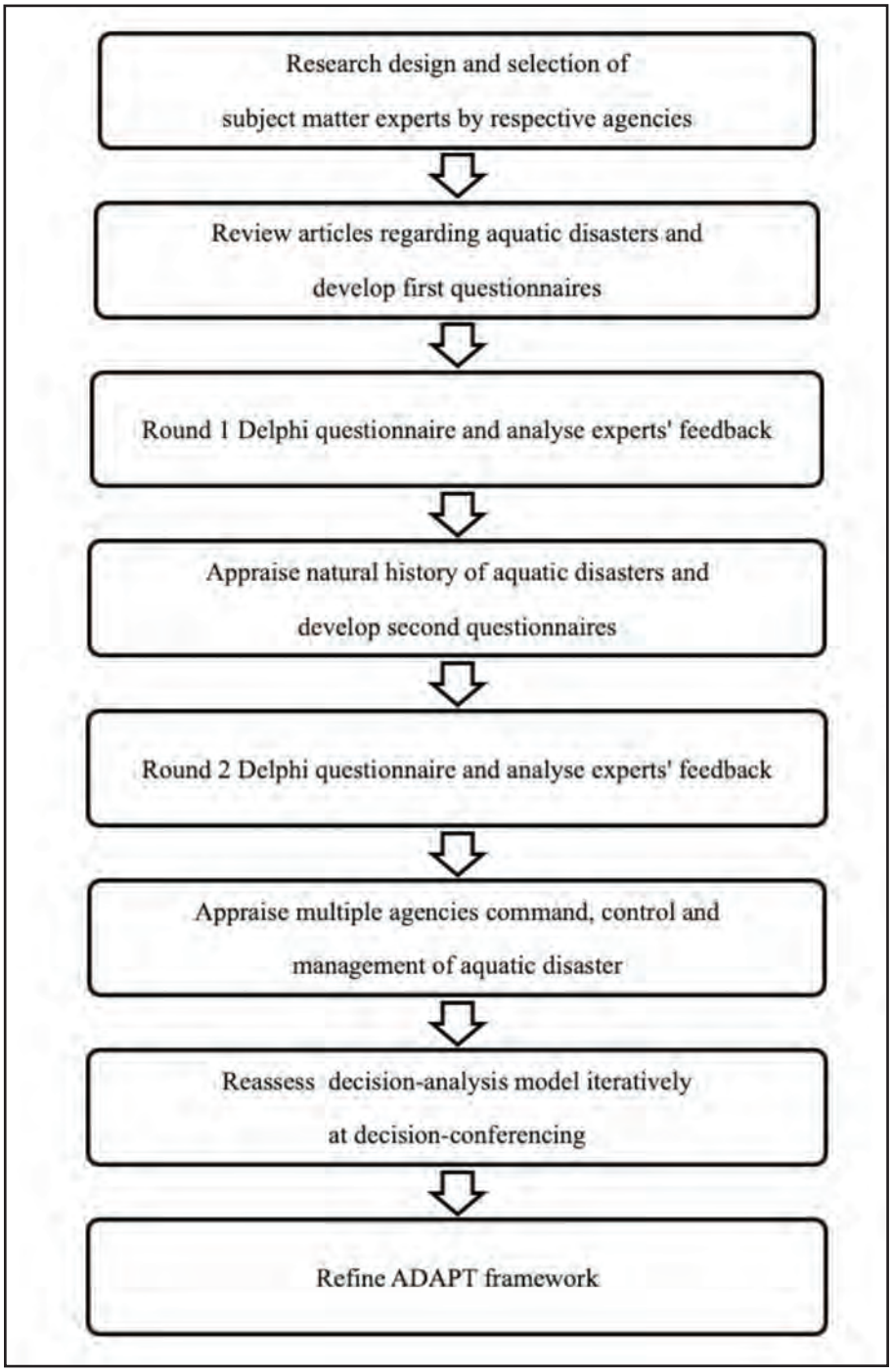

Fig. 1: Schematic diagram of ADAPT framework development methodology

universities, as well as emergency physicians from the National Heart Institute and the Ministry of Health of Malaysia (Table I). The experts had 7–35 years of experience in aquatic rescue and disaster management.

To develop the first round Delphi questionnaire, the researchers did a search and reviewed articles regarding previous aquatic disasters that occurred in Malaysia.[3-5] After risk assessment with geographical factors and climate in consideration, articles on aquatic events occurred in other countries that could possibly happen in Malaysia were also reviewed. The aquatic disasters reviewed were grouped into the following types: Storm and flood, tsunami, dam accident, watercraft accident or capsized, jetty collapse, offshore oil rig accident, aircraft accident into costal water, and mass refugee boat drift. Based on the scenarios described in the articles, a set of open-ended questions were designed to foster an understanding about natural history of different aquatic disasters, the magnitude of the events, and their destructive impact.

Table I: Representation of subject matter expert panel

Agency/Organization	Number of representative
National Security Council	1
National Disaster Management Agency and Special Malaysia Disaster Assistance and Rescue Team	1
Malaysia Civil Defence Force	5
Malaysian Maritime Enforcement Agency	3
Fire and Rescue Department of Malaysia	5
Ministry of Health Hospital	2
School of Medical Science, Universiti Sains Malaysia	1
Sultan Ahmad Shah Medical Center, International Islamic University Malaysia	1
Life Saving Society of Malaysia	5
Total	24

Table II: Comparison of general characteristic and principle of management between inland disaster and aquatic disaster

Characteristic/ Principle of management	Inland Disaster	Aquatic Disaster
Onset of incident	Onset is often unexpectedly without any warning.	Usually warning of the incident is detectable via surveillance systems. Anthropogenic aquatic incidents may occur more abruptly.
Accessibility to incident site	More accessible. Depending on the terrain, generally accessible by vehicle on road or by air. Bystanders and rescuers are ready to be recruited to assist at incident site.	Relatively less accessible. Incident site is accessible with watercrafts on water and by air. Rescuers trained in aquatic rescue are recruited to response at site of the aquatic incident.
Topography of the incident site	Physical features at inland incident site are relatively static, if progression occurs; it tends to happen in stages.	Physical features at aquatic incident site changes continuously due to fluidity of water and constant currents.
On scene risk	Low to moderate risk on scene depends on the nature of the disaster once scene safety is established via risk assessment and risk management.	Being in water on scene is high risk for drowning accident and environmental injuries. The risk is higher with additional environmental hazards.
Rescue window [a]	Within minutes to first 3 hours. (Platinum ten minutes and golden hour concepts)	Within seconds to minutes for victims who are not able to stay afloat on the water.
Principle of field triage	Victims are commonly triage according to the vital functions of respiration, circulation and mental status.	Victims are triage according to behavior in water to estimate their tendency of being submerged.
Search of victims	Victims often are static at the site of incident.	Victims are often being moved away from the site of incident by water flow and currents.
Principle of treatment on scene	Simple treatment to establish airway patency and stop bleeding.	Establish floatation for victims and retrieve them from water.

The first questionnaires were emailed to the subject matter experts to elicit individual views and responses. The responses from first-round questionnaire were analyzed and the aquatic disaster natural history was determined. The findings led to a framework for aquatic disaster management and the second round Delphi questionnaire was formulated and resent to the expert panel. The results from second questionnaires were analyzed by researchers to elaborate the role of rescue agencies as well as the command and control system in aquatic disasters. Both questionnaires were validated using face validation method by two emergency physicians with 13 and 20 years of experience, respectively, in emergency service and disaster management.

Subsequently,the experts had foregathered for decision-conferencing.[3] The decision-analysis model was presented to the panel and was reassessed iteratively with various aquatic disaster scenarios. Experts from multiple rescue agencies responded according to the framework and the coordinated response between agencies were elaborated and refined until the decision model was accepted by the panel.

RESULTS

The first round Delphi questionnaire addressed various aquatic disasters circumstances along the timeline. A common pattern of progression was observed, and the natural history of aquatic disasters was extrapolated and compared with inland disaster (Table II).

The 'physiology' of aquatic disasters comprises five distinctive sequential phases. The time lapse for each phase varies between the events and is dependent on the peculiarity of the situations. The discrete situations at different phases demand different directions and responses within a particular disaster. The phases and the appropriate response are being explained as follows (Table III):

Phase A - the "Alert" phase. This is the early phase or the pre-disaster period of an aquatic event during which the warning of a disastrous event is reported while the disaster has not yet actually happened. The objectives of management at this phase is to alert all agencies involved and the communities about the anticipated disaster, to take counteraction in preventing the incident from progressing into a full-blown

Table III: The description of general natural history and the aims of response to aquatic disasters

Phase	Features	Aim
A (Alert)	- Early phase during which the warning of a disaster is reported while the disaster has not actually happened.	(i) Taking counter-action to prevent the incident from progressing into a full-blown disaster; (ii) Taking necessary steps to minimize the destruction and loss of environment, infrastructures as well as human lives in the event of inevitable disaster.
B (Battle)	- Acute phase of the disaster. - The victims are either passing instantaneously from the impact of event or surviving temporarily with a high risk of mortality from life-threatening injuries and drowning if not being rescued within minutes.	(i) Battle to save lives, time is the essence; (ii) Intend to keep as many victims staying afloat as possible, to retrieve them out of the disaster zone, and to treat life-threatening injuries as quickly as possible.
C (Clear-up)	- The scene (disaster zone) is seemed "lifeless", no survivor is found during or after the acute phase of the disaster. - It can be due to either the high magnitude of the disaster resulting zero survivor; or all the survivors have been retrieved to safety; or all the survivors succumbed and drowned.	(i) Clearing the remains left by the disaster; (ii) The main task during this phase is to search and recover the bodies (corpses) and physical structures (e.g., airplane in plane crash or ship in shipwreck), followed by body and structures identification.
D (Dissolve)	- After the remains and physical structures are removed from the scene. - Decontamination is necessary if the disaster involves pollutants; omitted if no pollutant involved.	(i) Decontamination by containing, removing and cleaning pollutants to minimize exposure and negative effect to the population and environment; (ii) Dissolve the search and rescue mission ("stand-down") once all operations and efforts have completed.
E (Elevate)	- Usually take place after the aquatic disaster and its apparent impact had subsided. - The negative impact of disaster is elevated as the environment and communities return towards pre-disaster condition.	(i) Rebuild existent structures, infrastructures, and the society; (ii) Mitigate risks of aquatic disaster through education, training and drills, engineering, and construction; (iii) Law enforcement and execution in preventing risks from illegal activities.

Table IV: Model matrix for ADAPT framework which was used to summarize the tactics for different phases in various aquatic disasters that Malaysia is at risk

Aquatic disaster	Phase A	Phase B	Phase C	Phase D	Phase E
Flood/Typhoon					
Tsunami					
Dam overflow/failure					
Vessel capsized or accident					
Jetty collapse					
Mass refugees boat drift					
Offshore Rig Accidents					
Plane crash into sea					

disaster if possible, to take necessary steps in minimizing the destructive impact or loss of human lives, infrastructures as well as the environment if the imminent disaster approaches.

Phase B - the 'Battle' phase is the acute phase of the disaster. It marks the onset of the aquatic disaster and may last for hours. The force and magnitude of disastrous event peaks at this phase. The victims are either passing instantaneously from the impact of event or surviving temporarily but at high risk of mortality from life-threatening injuries and drowning if not being rescued within minutes. Surviving victims could be seen struggling to stay afloat, anchoring themselves to objects or structures, moving to higher platform, and performing other self-help gestures. The aim of response is to battle against time to save lives. The rescue operation intention is to keep as many victims staying afloat as possible, retrieving them out of the water or disaster zone, and treating life-threatening injuries as quickly as possible. Time is the essence in this phase.

Phase C - the 'Clear-up' phase occurs hours after the beginning of the disaster and may last for days or weeks depending on the complexity of the disastrous event. During phase C, the disaster zone is seemed 'lifeless' or motionless. No survivor is found during or after the acute phase of the disaster. It can either be zero survivors resulted from high impact and magnitude of the disaster, or all the survivors have been retrieved to safety with the remaining succumbed and drowned. The response in this phase intends to clear the remains left by the disaster. The main task is to search and recover the remains of the fatal victims and physical structures (e.g. airplane in plane crash or ship in shipwreck), followed by bodies and structures identification.

Phase D - the 'Dissolve' phase follows after the physical bodies and objects are being removed from the scene. The time period of transition into dissolution phase varies; generally, it is expected in few days to weeks after the occurrence of the disaster. Certain aquatic events (for example, oil rig accidents, watercrafts, or aircrafts accidents,

etc.) involve pollutants and contamination of the environment. In such instances, dissolution phase calls for decontamination of the contaminant. Agencies specialized in handling specific contaminant should contain, neutralize, and remove the pollutant to minimize the exposure and potential negative effect to the community and environment. After decontamination has completed, or in accidents that have no pollutant involved, providing all other search and rescue missions are completed, it is reasonable to dissolve operations and stand down at the aquatic disaster scene while recovery efforts are continued.

Phase E - the 'Elevate' phase ensues when the particular aquatic disaster and its apparent impact had subsided, about weeks to months down the progression of the event. It involves recovery effort to elevate the negative impact of the aquatic disaster and mitigation to return the environment and community to pre-disaster condition. It also reflects the elevation of the level of resilient against similar aquatic disaster in future. To achieve its aims, reconstruction of existent structures and infrastructures, mitigation of aquatic disaster through education, training and drills, engineering and construction, as well as relevant law enforcement and execution along with other mitigation measures are necessary.

DISCUSSION

The early warning system is a set of function in disaster risk communication and management. It aims at early detection, dissemination of information, prevention, and mitigation before disaster, as well as coordinating response and recovery during and after disaster.[6-8] According to ADAPT framework, Phase A involves risk surveillance and early warning is issued when disaster risk is present. The Malaysian Meteorological Department plays an important role in detecting natural aquatic disasters. It continuously monitors seismic waves, river and sea levels, weather and rainfall, earthquake in surrounding regions and tsunami threats. With quantitative precipitation forecasting, it provides reliable and accurate real-time flood warning and responses with adequate leadtime. In addition, the Drainage and Irrigation Department also provides forecast and early warning with Integrated Atmospheric and Radar Satellite Model-Based Rainfall and Flood Forecasting.

Since the tsunami in 2004, the National Tsunami Early Warning System was developed. Apart from monitoring earthquake and seismic wave, closed-circuit television cameras were installed in strategic locations to monitor for any threatening waves. Real-time data collected are transmitted through satellite for analysis. It also establishes connection for data with the US National Oceanic and Atmospheric Administration's Pacific Tsunami Warning Centre in Hawaii as well as the Japan Meteorological Agency in Tokyo.[8,9] It is able to alert the respective agencies and warns the country of possible tsunami occurring at surrounding oceans. The disaster threat is being alerted with sirens, Fixed-Line Disaster Alert System via telephone, short messaging systems, telefax, information and communication technology webpage and social networking media, mass media broadcasting system, as well as through public announcements.[8,9] In addition, the Government Integrated Radio Network is used for risk-communicate and coordinate management of disaster by multi-agency disaster responders.

Once the rescue agencies are alerted of an impending disaster, the Royal Malaysia Police and the Fire and Rescue Department of Malaysia are assigned to assess the risks and hazards on scene, as well as to estimate the magnitude of the probable disaster. As the disaster has not yet occurred during Phase A, the rescue agencies carry out surveillance of the risks and progression of the situation periodically. With unmanned aerial vehicles, rescue agencies may have a bird's-eye view of the situation without exposing to hazards on site. As the secretariat of disaster operation, MCDF sets up Disaster Operation Control Centre (DOCC) where risk communication and event reporting occur. DOCC and the operation are led by NADMA. After estimating the magnitude of impending disaster, DOCC identifies high-risk areas and considers opening the designated Disaster Relieve Centres. The communities may be instructed to evacuate to the relief centre by local authorities in coordination with the Royal Malaysia Police.[1]

In case of anthropogenic aquatic disasters, for example, dam failure, ferry accident, jetty collapse, mass refugees boat drift, and offshore rig accidents, often incident occurs unexpectedly and is reported by people nearby or those experiencing the unfortunate event via the Malaysia Emergency Response System hotline. The Royal Malaysia Police usually verifies the report about the event before initiating the aquatic disaster protocol. In imminent dam failure, for example, technical problem in the dam operation with the water reaches dangerous level; besides surveillance and evacuation planning, the dam operator should alert local authority regarding the dam water level and technical problem. Rescue agencies, dam engineer, and relevant technical experts should counteract the situation to prevent the incident from progressing into full-scale catastrophe. When the hazards are successfully elevated and the risks of the disaster resolve, the operation may stand down and mitigation plan for the disaster should be continued and strengthened. If the counter-measures are unsuccessful and disaster progresses, swift response and evacuation in Phase A could minimize the destructive impacts that follow.

Phase B is the zero hour, it begins at the moment the disaster actually happens. Disasters like tsunami, dam failure, watercraft accident, jetty collapse, offshore oil rig accident, aircraft accident in costal water, hit vigorously, leading to instantaneous destruction; while others, such as flood, mass refugee boat drift, have gradual course and peak after some time. In disasters with drastic course, as tsunami or dam failure, rescue agencies should ensure the safety of their officers and surroundings by carrying out surveillance from a safe distance even during Phase A. Ironically, rescue operation should not be carried out in the early minutes or hours during Phase B if the situation is perceived as likely to endanger the rescuers. Furthermore, the on-scene rescuers should retreat to safety if their position becomes unsafe with the progression of the event.

Rescue is only permissible when the situation is safe. Its timing varies among different disasters; it may be earlier in the gradual course disasters and latter in drastic course disasters after diminution of the disaster force. At this stage, rescue agencies actively search for victims. Search and rescue at coastal waters is led by the MMEA while that at inland waters is led by the Fire and Rescue Department of Malaysia. Other special search and rescue units, such as SMART, may be deployed to the scene to assist in the operation if necessary. The priority for rescue and retrieval is given to alive and injured victims. Fatal victims will be retrieved at Phase C after the retrieval of all living victims.

To complicate the matter, the window period to rescue in Phase B is particularly narrow. An average person can hold their breath for about 30–60 seconds before gasping for air instinctively. Thus, the concept of 'Platinum Ten Minutes' may not be appropriate, as struggling victims in water may perish within 60 seconds.[10] Hence, the rescue strategy in Phase B is to distribute buoyant aids to as many surviving victims, as soon as possible. When the victims are able to maintain buoyancy and respiration, it prolongs the rescue window period and increases the chance of survival. The victims are triaged according to the level of rescue urgency, retrieved, and treated for life-threatening injuries.[11] It cannot be stressed enough that timely response is utmost valuable to prevent fatal drowning. Rescue operation should be swift and in coordinated manner to do the greatest good for the greatest number.

With time, the scene becomes lifeless, marking the end of Phase B and the beginning of Phase C. It may be after the evacuation of all surviving victims leaving those who succumbed to injuries and drowning. It may also be when no survivor is found after thorough search at Phase B. During Phase C, rescue agencies continue the search and recovery of victims' bodies. The corpses and body parts are sent to forensic unit for identification and postmortem. The remains of vehicles and structures involved in the disaster are also recovered. The remnants of a plane crash and the shipwreck after a marine accident are important evidence for an investigation to determine the cause of accident and the preventive recommendations.

During search and recovery, it is essential for the rescuers to continuously monitor the risks and hazards brought by weather and water condition. Hazards such as storms, wind, limited light source and visibility at night, rapid water currents, and waves often threaten rescuers' safety and complicate the rescue when present. In contrast to the Phase B, the victim's outcome from search and recovery in Clear-up Phase is no longer time-dependent. Therefore, it is reasonable to defer search and recovery in Phase C when the condition is hazardous, and only to resume when the condition is favorable.

The term 'dissolve' describing Phase D has two connotations: 'dissolve' the pollutants, and 'dissolve' the operation. 'Dissolve' of pollutants, or in another word, decontamination is necessary in disasters that involve chemicals or pollutants, such as oil spill from drilling rig, nuclear power plant accident following earthquake and tsunami, etc. While Fire and Rescue Department of Malaysia serves as a rescue agency, the Department of Environment leads decontamination of oil spill or other pollutants; whereas the Atomic Energy Licensing Board is the leading agency in providing expertise and technical services in managing radiological, nuclear, or other hazardous material spillage. Efficient and timely decontamination minimizes detrimental effects on the environment, specifically to the marine plants, animals, as well as the communities. At the same time, Public Health officials survey for infectious disease outbreak and psychological health among the victims at Disaster Relieve Centres as well as the rescuers and frontliners. Nonetheless, decontamination sub-phase is omitted in disasters without any pollution or contamination.

Once decontamination process and other search and rescue missions are completed, the rescuers send reports to Evaluation Committees at DOCC to estimate losses and recovery from the disaster. DOCC may then summon 'dissolve' of the operation, all rescue agencies stand down and end the search and rescue mission. Despite the stand down of the rescue agencies on site, the recovery of the communities at the areas affected is ongoing, facilitated by the recovery agencies until the social, health, and economy functions of the communities return to the normal state.

Dissolving of the search and rescue operation marks the transition to Phase E. Besides focusing at elevating the destructive aftermath with recovery plans, it also intends to elevate the level of resilience and capability to withstand challenges of similar disaster thereafter. Aquatic disasters typically lead to large-scale destruction. Therefore, the recovery and mitigation work requires substantial efforts from the recovery agencies, governmental and non-governmental organizations (NGO) as well as the communities. Rubble and damaged structures need to be removed and disposed properly, while the standing buildings, infrastructures, and affected environment need to be cleaned. The Malaysian Public Works Department and the local authorities can pool their machines and resources to work together with NGOs and the local communities in cleaning and rebuilding houses and infrastructures. The victims are sent home once their homes are cleaned or rebuilt, and ready to be resided in.

Meanwhile, a 'post-mortem' examination on the aquatic disaster should be performed by surveying the affected area, inspecting the collected remains, and analyzing data to identify the cause and contributing factors of the disaster. The task force includes authority, relevant agencies, and the subject matter experts to produce a comprehensive report before formulating a mitigation plan. Holistic approach to risk mitigation is pertinent. Mitigation measures should include education and drills involving communities and governmental agencies, construction of structures that better withstand the forces of aquatic disasters, legislation processes, and law enforcement in regulating human activities.

Among other steps of mitigation, mangrove forests are found to be effective as a defense against the force of tsunami.[12] Thus, mangrove trees were planted for coastal protection and

research in that regards.[13] Apart from that, programs on preparation and response have been carried out among communities, one worth mentioning is the school-based tsunami education and development of evacuation plans and conducting drills, a project conducted by United Nations Development Programme in Malaysia in collaboration with the National Disaster Management Agency (NADMA) and the Ministry of Education.[2,14] Tabletop exercises and drills of different scales have also been carried out by rescue agencies. These on-going programmes enhance the nation's response and management of future disasters.

On the other hand, legislation and law enforcement are essential in prevention and mitigation of certain aquatic disasters by regulating human activities. For example, the forestry laws are intended to prevent illegal logging and forest clearing. With forests conservation, rainwater can be retained, preventing run-offs and further flooding. Besides that, the maritime laws help to reduce ferry or ship accidents by prohibiting overloading the watercrafts, and the risk of disastrous collapsing of jetty is also preventable with structures adhered to the building safety regulations. These laws and regulations must go hand-in-hand with stern enforcement and execution. The recovery efforts in Phase E may be ended when the environment and the communities have recuperated to normal state; however, the prevention and mitigation measures should be a continuous effort to prevent mainly anthropogenic aquatic disasters and strengthen the nation's resilience against aquatic disasters.

At any phase during aquatic disaster, if the situation overwhelms the national resources or expertise, the country may request and accept international aid through the National Security Council to assist the national disaster response.

STRENGTH AND LIMITATIONS

The anonymity nature of Delphi method enabled the exploration of ideas without socially induced bias; however, it is vulnerable to investigator bias on the synthesis and feedback process. On the contrary, the decision-conference method lacks anonymity, but expert panel in the same physical space can scrutinize the model framework for investigator's manipulation bias.[3,4] Thus, the mixed-method approach combining the two methods complements one another in the study. The ADAPT framework is developed from the consensual opinion of subject matter experts. Although it was examined repetitively, the framework has not been applied in actual disastrous situation. A full-scale drill is necessary to further test the framework. The endorsement of ADAPT follows 'all-or-nothing' rule. If adopted, all agencies should conform to the framework. Any disparity brings asynchronous and uncoordinated response that may result in confusion, conflict between agencies, discrepancy and overlapping roles, as well as wastage of resources. When all agencies and organizations have committed, drills are necessary to refine the multiple agencies response.

CONCLUSION

ADAPT is a conceptual framework of coordinated response against aquatic disasters for effective and efficient response. It is a universal framework to lay out technical details which include agencies involved, human resources and machinery supports, as well as specific taskforce and availability of aid necessary at each phase for any aquatic disaster (Table IV).

ADAPT may also be adopted by other non-rescue organizations. Corporate companies that are at risk of a particular disaster may develop an emergency action plan for their employees to guide their actions before, during, and after the aquatic disaster. Governmental organizations at local, district, state, and national levels can construct the contingency plan based on the hazards and scale of the possible disasters, as well as review resources allocated for managing the aquatic disaster at every level. Once ADAPT framework is developed, a tabletop exercise based on the framework should be carried out at each level and organization to evaluate the plan and explore the novel solution for possible unprecedented situations.

ADAPT is designed to complement the contemporary incident management system and serve as a platform for the development of an inclusive overall aquatic disaster management system. Not only it defines the disasters according to its constantly changing situation, it also serves as a guide to a systematic command, control, and coordination for multi-agency response to the rapidly progressing aquatic disasters. ADAPT may be as general as universal aquatic disaster management framework, or as unique as tailor-made emergency action plan considering the local culture and resources.

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ORIGINAL ARTICLE

Influence of oral health literacy on knowledge and attitude towards children's oral health among pregnant women in Malaysia

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ABSTRACT

Introduction: Health literacy is an independent predictor of health outcomes, including health knowledge and behavior. This study determined the influence of oral health literacy on knowledge and attitude towards children's oral health among pregnant women.

Materials and Methods: A total of 130 pregnant women (65 nulliparous and 65 primiparous or multiparous) attending Hospital Universiti Sains Malaysia for antenatal care who did not have any diagnosed cognitive disorders and could read and write in the Malay language participated in this cross-sectional study. A structured self-administered questionnaire was used to measure knowledge and attitude towards children's oral health, and the Malay version of the Oral Health Literacy Instrument (OHLI-M) was used to assess the oral health literacy of the participants.

Results: Multivariable linear regression analysis showed that older women and women with higher OHLI-M scores had higher mean knowledge scores than younger women (p=0.007) and women with lower OHLI-M scores (p=0.001), respectively. In addition, women with higher OHLI-M scores, women with higher mean knowledge scores, and women who had attended a talk about children's oral health were more likely to have higher mean attitude scores than women with lower OHLI-M scores (p=0.019), women with lower mean knowledge scores (p=0.006), and women who had never attended a talk about children's oral health (p=0.001).

Conclusion: Pregnant women's oral health literacy was positively associated with their oral health knowledge and attitude towards children's oral health. Strategies to improve the oral health literacy of pregnant women are indicated.

KEYWORDS:
Oral health; health literacy; knowledge; attitude; pregnant women

INTRODUCTION

Dental caries is one of the most prevalent chronic childhood diseases.[1] The Global Burden of Disease Study 2017 estimated that dental caries affect the deciduous teeth of more than 530 million children worldwide.[2] The global burden of dental caries has remained relatively unchanged over the past 30 years, although many countries have reported declining prevalence.[3] In Malaysia, caries prevalence in 12-year-old children and 5-year-old children is relatively high, despite the decline from 41.5% in 2007 to 33.3% in 2017 and from 76.2% in 2005 to 71.3% in 2015, respectively.[4-7]

Dental caries is largely preventable, and oral health literacy is a critical concept in oral disease prevention. Oral health literacy is the 'degree to which individuals have the capacity to obtain, process, and understand basic oral health information and services needed to make appropriate health decisions'.[8] Low or inadequate oral health literacy has been associated with poor oral health awareness and knowledge,[9,10] which may contribute to compromised oral health behavior and outcomes.[11,12]

Young children are incapable of taking care of their oral health. Hence, the responsibility lies with their parents or guardians. Parental oral health literacy has been demonstrated to be an important determinant of children's oral health.[13] The proposed explanation for this association is that parents with low oral health literacy may have limited knowledge about children's oral health or have difficulty understanding oral health care instructions, leading to poor adherence to preventive oral health behavior.[14] Nevertheless, the evidence was inconclusive due to the limited number of studies and methodological issues inherent in epidemiologic research,[15] indicating the need for further studies to strengthen the evidence.

Mothers play an important role in their children's health and development. A mother is also a child's first teacher and has the responsibility of passing health-related knowledge to her child and modelling appropriate health behaviors to the family.[16] Recognizing these roles, many health authorities worldwide, including Malaysia, developed specific oral health care programs for antenatal mothers to optimize their potential roles in improving the oral health status of their families.[17,18] The potential link between oral health literacy and oral health knowledge underlined the need to investigate this association in pregnant women. The findings will provide baseline information that can help restrategize the oral health care program for antenatal mothers aimed at improving the oral health status of children. In this study, we investigated the influence of oral health literacy on the knowledge and attitude of pregnant women towards children's oral health.

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MATERIALS AND METHODS

Study design and study population

This was a cross-sectional study of pregnant women attending the Obstetrics & Gynecology (O&G) Clinic at the Hospital Universiti Sains Malaysia (USM). Located in the state of Kelantan, northeast of Peninsular Malaysia, Hospital USM is a teaching hospital that supports the role of the Ministry of Health Malaysia to provide basic and specialized medical and health care services, including antenatal care, without charge to the public. Pregnant women at any gestational age, without any diagnosed cognitive disorders, who were able to read and write in the Malay language, were eligible to participate.

The sample sizes for all specific objectives of this study were calculated, and the largest affordable sample size was obtained from the objective of determining the oral health literacy of pregnant women using the formula to estimate a single mean with a 95% confidence interval (CI). The standard deviation of the mean oral health literacy score was estimated at 15.64 based on a study by Ramlay et al.[19] At a precision of 3.0, the largest affordable sample size of 104 was yielded. Anticipating a 25% non-response rate, a sample size of 130 was selected. Ethical approval for this study was obtained from the Universiti Sains Malaysia Human Research and Ethics Committee (USM/JEPeM/18110744).

Research tools

A new self-administered questionnaire was developed to measure knowledge and attitude towards children's oral health. The questionnaire was developed in Malay. The knowledge domain consists of 30 items to assess knowledge of the following: tooth development and eruption (two items), dental plaque (one item), dental caries and its risk factors (six items), foods and drinks with a high potential to cause dental caries (14 items), oral hygiene practice (four items), and fluoride in caries prevention (three items). The response format for the knowledge domain was close-ended options of 'true', 'false', and 'do not know'. Correct answers were given one mark, while the incorrect and 'do not know' responses received no mark. The total knowledge score can range from 0 to 30, with higher scores indicating better knowledge.

The attitude domain has 12 items to assess the following: importance of primary/permanent teeth (five items), oral hygiene practice (four items), feeding/dietary practice (two items), and dental visit (one item). Each item was ranked on a 5-point Likert scale of 1 (strongly disagree), 2 (disagree), 3 (neither agree nor disagree), 4 (agree), and 5 (strongly agree). Marks of 1 to 5 were given accordingly, except for the negatively worded attitude statements that were re-coded in the reverse direction so that a higher mark on each item indicated a better attitude. Thus, the total attitude scores can range from 12 to 60, with higher scores indicating a better attitude.

The pre-final draft of the questionnaire was tested on a convenience sample of 30 parents who brought their children to the Hospital USM Dental Clinic for treatment. Feedback was generally favorable and only minor technical editing was indicated. The time taken to complete the questionnaire was between 10 and 15 minutes. The questionnaire had a good internal consistency reliability coefficient, with a Cronbach's alpha of 0.795. The knowledge domain had an excellent internal consistency reliability coefficient, with a Cronbach's alpha of 0.943. However, Cronbach's alpha for the attitude domain was lower at 0.609, most probably due to the small number of items in the domain and the effect of three negatively directed items.

A validated Malay version of the Oral Health Literacy Instrument (OHLI-M)[19] was used to assess the oral health literacy of the participants, a factor hypothesized to be associated with knowledge and attitude of the pregnant women towards children's oral health. The instrument consists of two sections: a self-administered reading comprehension section and an interviewer-administered numeracy section. The reading comprehension section includes two passages, one on dental caries with 18 words omitted from the sentences and the other on periodontal disease with 20 omitted words. These 38 omitted words were the test items, and participants had to choose the correct answer from four possible choices given.

The numeracy section consists of a series of prompts: five prescription labels of medications frequently prescribed by dentists, one dental appointment card, and one printed post-extraction instructions. There were 19 test items in this section. Each correct answer was given one mark, and incorrect or missing answers were given no mark. The total score for the reading comprehension section was multiplied by 1.316 (50/38) and the total score for the numeracy section was multiplied by 2.632 (50/19). The total OHLI-M scores can range from 0 to 100. The score was categorized into three levels of oral health literacy: inadequate (0–59), marginal (60–74), and adequate (75–100), as recommended by Sabbahi et al.[20] who developed the original English version of the Oral Health Literacy Instrument (OHLI).

Additionally, a structured self-administered sociodemographic form was used to collect information on the demographic profile of the participants (age, highest education level, employment status, and monthly household income), number of children, last dental visit, and experience of attending a talk about children's oral health.

Data collection

To minimize selection bias, we stratified the study population by parity status and used non-proportionate stratified random sampling to obtain equal numbers of samples from the strata: 1) 65 pregnant women who had never given birth (nulliparous) or were pregnant for the first time (primigravida), and 2) 65 pregnant women who had given birth at least once (primiparous or multiparous). Potential participants who came for antenatal care appointment at the O&G Clinic were individually approached by the main author. Following the establishment of eligibility, systematic random sampling was used to select participants from each stratum. Women were informed of the importance, objectives, procedures, and other essential information regarding this study. Written informed consent was obtained from all women who agreed to participate. Further

instructions on how to complete the questionnaires were provided prior to the administration, which began with the self-administered questionnaires including the reading comprehension section of the OHLI-M, followed by the interviewer-administered numeracy section of the OHLI-M.

Statistical analysis

Data analysis was conducted using IBM SPSS software, version 24.0. Descriptive statistical analysis was performed to obtain the frequency and percentage of categorical variables and the mean and standard deviation of numerical variables. Factors associated with participants' oral health knowledge (mean knowledge score) and oral health attitude (mean attitude score) were determined at univariable and multivariable levels using simple and multiple linear regression analyses, respectively. The following independent variables were tested: age, highest education level, employment status, monthly household income, number of children, last dental visit, experience of attending a talk about children's oral health, and oral health literacy (OHLI-M score). In addition, the participants' mean knowledge score was tested as a potential factor associated with their oral health attitude (mean attitude score).

In multiple linear regression analysis, variables were selected using forward selection, backward elimination, and stepwise selection methods. Following the fit of the preliminary main effect model, the independent variables were examined for two-way interactions using the LR test and multicollinearity issues using the variance inflation factor (VIF) test. A VIF value of more than 10 indicated the presence of multicollinearity.[21] Residual plots were examined for linearity, normality, and equal variance to validate the regression model. Outliers were also identified; data points beyond +3.0 and –3.0 of standardized residuals were considered outliers.[22] The final model was presented with adjusted regression coefficients and 95% CIs, t-statistics, and p values. The level of significance was set at p value of less than 0.05.

RESULTS

Characteristics of participants

A total of 130 women (65 from each stratum) participated and completed the questionnaires, with a response rate of 100%. Table I shows the characteristics of the study participants. The ages of the participants ranged from 19 to 44 years, with a mean age of 30.3 years (SD=5.37). Most participants received at least post-secondary education (73.1%) and more than half (54.6%) were employed. Parity status of the women corresponded to the number of children. More than half (63.8%) had visited dentists within the past year, and slightly more than half (53.8%) had attended a talk about children's oral health. Slightly more than half of the participants had adequate oral health literacy (56.9%), followed by marginal (30.8%), and inadequate oral health literacy (12.3%). The mean OHLI-M score was 75.1 (SD=13.74), with the lowest score of 34 and the highest score of 97.

Knowledge towards children's oral health

Table II shows the knowledge towards children's oral health among the participants. Most women knew that a baby's mouth should be cleaned even though the teeth have not yet erupted (85.4%), that dental plaque can cause dental caries (93.1%), and that a child's teeth should be brushed twice daily (93.8%), particularly before bedtime (90.0%). Most participants also knew that a white spot on the tooth surface is an early sign of dental caries (86.9%), which can be prevented using fluoride toothpaste (87.7%), and they were aware of the appropriate amount of fluoride toothpaste to be used. With regard to caries risk, less than one-third of the women knew that children of mothers with caries are at risk of developing caries themselves (28.5%).

Most women knew that frequent intake of sugary foods (95.4%) and pooling of milk in the mouth (84.6%) could cause dental caries. However, most did not know that fruit juice (56.9%), white bread (60.8%), baby biscuits (44.6%), bananas (64.7%), and dried fruits such as dates (66.9%) and raisins (60.8%) have a high potential to cause dental caries. In addition, some (19.2%) erroneously thought that breast milk was highly cariogenic.

Attitude towards children's oral health

Table III shows the attitude of the participants towards their children's oral health. While more than half of the women agreed (strongly agree=23.1%, agree=34.6%) that permanent teeth will not last a lifetime, most participants had favorable attitude and agreed on the importance of baby teeth (strongly agree=40.0%, agree=53.1%) and the need to brush the newly erupted teeth (strongly agree=38.5%, agree=53.1%) at least twice daily (strongly agree=58.5%, agree=38.4%). Most women also agreed that they needed to bring their child for dental check-up before 1 year of age (strongly agree=30.8%, agree=43.1%).

Factors associated with knowledge towards children's oral health

The mean knowledge score was 19.9 (SD=4.18), with the lowest score of 7.0 and the highest score of 28.0. Table IV shows the results of the linear regression analysis of the factors associated with knowledge towards children's oral health among the participants. Multiple linear regression analysis showed a significant positive relationship between the OHLI-M score and mean knowledge score (p=0.001). A one-unit increase in OHLI-M score resulted in 0.09 unit increase in knowledge score (95% CI:0.04-0.14). In addition, older women had higher mean knowledge scores than younger women (p=0.007). A 1-year increase in age resulted in 0.18 unit increase in knowledge score (95% CI:0.05-0.30). With these two significant variables, the model explained 14.9% of the variance in knowledge score (R^2=0.149). The possible two-way interactions between the independent variables were not significant, and there was no multicollinearity issue. All model assumptions were met, and no outliers were detected.

Factors associated with attitude towards children's oral health

The mean attitude score was 48.1 (SD=4.99) with the lowest score of 34.0 and the highest score of 59.0. Table V shows the results of the linear regression analysis of factors associated with attitude towards children's oral health among the participants. Multiple linear regression analysis showed a significant positive relationship between mean OHLI-M and attitude scores (p=0.019). A one-unit increase in the OHLI-M score resulted in 0.07-unit increase in the attitude score (95%

Table I: Characteristics of participants (n=130)

Variable	Frequency (%)
Age (year)	30.3 (5.37)[a]
Highest education level	
No formal education/primary/secondary	35 (26.9)
Post-secondary	51 (39.2)
Tertiary	44 (33.9)
Employment status	
No	59 (45.4)
Yes	71 (54.6)
Monthly household income (MYR)	2500.00 (2650.00)[b]
Number of children	
None	65 (50.0)
At least one child	65 (50.0)
Last dental visit	
Never visited dentist	3 (2.3)
>2 years	20 (15.4)
1-2 years	24 (18.5)
<1 year	83 (63.8)
Ever attended oral health talk	
No	60 (46.2)
Yes	70 (53.8)
Oral health literacy level	
Inadequate	16 (12.3)
Marginal	40 (30.8)
Adequate	74 (56.9)

[a] Mean (SD)
[b] Median (IQR)

Table II: Knowledge towards children's oral health (n=130)

Variable	Frequency (%)		
	Correct	Incorrect	Do not know
Calcium intake during pregnancy helps in the formation of strong teeth	126 (96.9)	1 (0.8)	3 (2.3)
The first baby tooth will erupt at the age of 6–9 months	106 (81.5)	6 (4.6)	18 (13.9)
Plaque is a white layer containing bacteria that accumulates on tooth surface	121 (93.1)	2 (1.5)	7 (5.4)
Plaque can cause dental caries	121 (93.1)	0 (0.0)	9 (6.9)
Frequent intake of sugary foods can cause dental caries	124 (95.4)	0 (0.0)	6 (4.6)
Children are at risk of dental caries if they fall asleep with milk pooling in the mouth	110 (84.6)	5 (3.9)	15 (11.5)
Tooth decay can affect children below 2 years of age	84 (64.6)	12 (9.2)	34 (26.2)
Early sign of caries can be seen as a white spot on the tooth surface	113 (86.9)	3 (2.3)	14 (10.8)
Children of mothers with caries are at risk of developing caries themselves	37 (28.5)	44 (33.8)	49 (37.7)
Foods or drinks with high potential to cause dental caries:			
Formula milk	97 (74.6)	16 (12.3)	17 (13.1)
Breast milk	77 (59.2)	25 (19.2)	28 (21.6)
Fruit juice	56 (43.1)	39 (30.0)	35 (26.9)
Fortified drink	101 (77.7)	8 (6.2)	21(16.1)
White bread	51 (39.2)	43 (33.1)	36 (27.7)
Chocolate	113 (86.9)	7 (5.4)	10 (7.7)
Baby biscuits	72 (55.4)	29 (22.3)	29 (22.3)
Bananas	46 (35.3)	50 (38.5)	34 (26.2)
Dates	43 (33.1)	54 (41.5)	33 (25.4)
Peanuts	31 (23.9)	58 (44.6)	41 (31.5)
Sweets	119 (91.5)	7 (5.4)	4 (3.1)
Cheese	18 (13.8)	87 (66.9)	25 (19.2)
Raisins	51 (39.2)	44 (33.9)	35 (26.9)
Sticky dessert	105 (80.8)	7 (5.4)	18 (13.8)
A baby's mouth should be cleaned even though the teeth have not yet erupted	111 (85.4)	12 (9.2)	7 (5.4)
Dental plaque can be removed with toothbrushing	88 (67.7)	27 (20.8)	15 (11.5)
A child's teeth should be brushed twice daily	122 (93.8)	4 (3.1)	4 (3.1)
Brushing before bedtime is essential	117 (90.0)	9 (6.9)	4 (3.1)
Fluoride toothpaste can be used to prevent dental caries	114 (87.7)	5 (3.8)	11 (8.5)
Only a smear of fluoride toothpaste is needed to brush teeth of children below 3 years old	99 (76.2)	7 (5.4)	24 (18.4)
Only a pea size of fluoride toothpaste is needed to brush teeth of children above 3 years old	97 (74.6)	7 (5.4)	26 (20.0)

Table III: Attitude towards children's oral health (n=130)

Variable	Frequency (%)				
	Strongly agree	Agree	Neither agree nor Disagree	Disagree	Strongly disagree
Baby teeth are important	52 (40.0)	69 (53.1)	3 (2.3)	6 (4.6)	0 (0.0)
Carious baby teeth need not be given attention	8 (6.2)	13 (10.0)	8 (6.2)	66 (50.7)	35 (26.9)
Baby's teeth need not be given a good care as they will be replaced by permanent teeth	10 (7.7)	21 (16.2)	7 (5.4)	66 (50.7)	26 (20.0)
Premature loss of baby teeth due to caries can affect the normal eruption of the permanent teeth	41 (31.6)	61 (46.9)	19 (14.6)	9 (6.9)	0 (0.0)
Permanent teeth will not last a lifetime	30 (23.1)	45 (34.6)	19 (14.6)	34 (26.2)	2 (1.5)
A baby's mouth needs to be cleaned even though the teeth have not yet erupted	68 (52.3)	49 (37.7)	6 (4.6)	7 (5.4)	0 (0.0)
I need to brush my child's newly erupted teeth	50 (38.5)	69 (53.1)	6 (4.6)	5 (3.8)	0 (0.0)
I need to make sure my child brushes teeth at least twice daily	76 (58.5)	50 (38.4)	4 (3.1)	0 (0.0)	0 (0.0)
I need to supervise my child's toothbrushing	76 (58.5)	53 (40.7)	1 (0.8)	0 (0.0)	0 (0.0)
I need to encourage my child to drink from a cup by one year of age	27 (20.8)	59 (45.4)	25 (19.2)	19 (14.6)	0 (0.0)
I need to make sure my child does not take sweet and sticky foods	70 (53.8)	50 (38.5)	6 (4.6)	3 (2.3)	1 (0.8)
I need to bring my child for dental check-up before one year of age	40 (30.8)	56 (43.1)	25 (19.2)	9 (6.9)	0 (0.0)

Table IV: Factors associated with knowledge towards children's oral health (n=130)

Variable	Simple linear regression		Multiple linear regression		
	Crude *b* (95% CI)	*p* value	Adjusted *b* (95% CI)	t-statistics	*p* value
Age (year)	0.20 (0.07, 0.33)	0.004	0.18 (0.05, 0.30)	2.76	0.007
Highest education level					
No formal education/primary/secondary*					
Post-secondary/tertiary	0.68 (-0.95, 2.32)	0.410	-	-	-
Employment status					
No*					
Yes	1.18 (-0.27, 2.63)	0.109	-	-	-
Monthly household income (MYR)	0.00 (0.00, 0.00)	0.001	-	-	-
Number of children					
None*					
At least one child	1.74 (0.31, 3.16)	0.017	-	-	-
Last dental visit					
>1 year/never*					
≤1 year	-0.32 (-1.84, 1.19)	0.674	-	-	-
Ever attended oral health talk					
No*					
Yes	0.37 (-1.09, 1.83)	0.615	-	-	-
OHLI-M score	0.10 (0.05, 0.15)	<0.001	0.09 (0.04, 0.14)	3.56	0.001

*Reference category

Table V: Factors associated with attitude towards children's oral health (n=130)

Variable	Simple Linear Regression		Multiple Linear Regression		
	Crude *b* (95% CI)	*p* value	Adjusted *b* (95% CI)	t-statistics	*p* value
Age (year)	0.16 (0.00, 0.32)	0.044	-	-	-
Highest education level					
No formal education/primary/secondary*					
Post-secondary/tertiary	1.90 (-0.03, 3.83)	0.054	-	-	-
Employment status					
No*					
Yes	1.58 (-0.14, 3.30)	0.072	-	-	-
Monthly household income (MYR)	0.00 (0.00, 0.00)	0.004	-	-	-
Number of children					
None*					
At least one child	2.42 (0.73, 4.10)	0.005	-	-	-
Last dental visit					
>1 year/never*					
≤1 year	1.32 (-0.47, 3.12)	0.147	-	-	-
Ever attended oral health talk					
No*					
Yes	2.66 (0.98, 4.34)	0.002	2.75 (1.17, 4.34)	3.44	0.001
OHLI-M score	0.09 (0.03, 0.15)	0.004	0.07 (0.01, 0.13)	2.38	0.019
Knowledge score	0.37 (0.17, 0.57)	<0.001	0.28 (0.08, 0.48)	2.78	0.006

*Reference category

CI:0.01-0.13). Women with higher mean knowledge scores also had higher attitude scores (p=0.006). In particular, a one-unit increase in knowledge score resulted in a 0.28-unit increase in attitude score (95% CI:0.08-0.48). Another factor found to be significant was the experience of attending a talk about children's oral health. Women who had attended the talk had a higher mean attitude score than those who had not (p=0.001). In particular, the attitude score of women who had attended the talk was 2.75-unit higher than those who did not (95% CI:0.17-4.34). With these three significant variables, the model explained 19.7% of the variance in knowledge score (R^2=0.197). The possible two-way interactions between the independent variables were not significant, and there was no multicollinearity issue. All model assumptions were satisfied, and no outliers were detected.

DISCUSSION

Our findings provide evidence supporting the hypothesis that pregnant women with higher oral health literacy are more likely to have better knowledge towards children's oral health. These results are in agreement with those reported by Hom et al.[10] in North Carolina, United States, Vilella et al.[9,23] in Brazil, and Muralidharan et al.[24] in Pune, India. Additionally, we found that older women had higher mean knowledge scores than those who were younger, in agreement with other previous studies among pregnant women and mothers of newborn babies.[25,26] The positive association between the women's age and their oral health knowledge may be due to greater exposure to oral health information from previous experience attending to personal oral health care needs and problems, as well as others.

In this study, pregnant women with higher oral health literacy levels were also more likely to have favorable attitude towards their children's oral health. Previous studies on oral health literacy among pregnant women have not examined the influence of maternal oral health literacy on attitude towards children's oral health.[9,10,23,24] Hence, a direct comparison of this finding to previous studies could not be made. Our study also found that women who had attended a talk about children's oral health and had better knowledge about it were more likely to have favorable attitude towards the matter. These findings underline the benefits of oral health education for pregnant women and substantiate the importance of oral health education as an indispensable strategy in antenatal oral health programs to improve attitude, which has been shown to be an important predictor of preventive oral health behavior.[27]

Prevention of dental caries requires the recognition and reduction of risk factors. Most pregnant women in this study were aware that dental plaque is a white layer of bacteria that can cause dental caries. In addition, most participants could correctly answer most questions about tooth brushing and the use of fluoride in caries prevention and knew that a baby's mouth should be cleaned even though the teeth have not yet erupted. Although there is no evidence that pre-eruptive mouth cleaning can prevent dental caries, this practice is recommended by most professional dental organizations.[28]

Despite knowing that frequent intake of sugary foods can cause dental caries, a substantial percentage of the participants were not aware that some foods and drinks commonly given to children, including fruit juice, white bread, baby biscuits, bananas, dates, and raisins are cariogenic. In addition, some of the participants in this study incorrectly believed that breast milk has a high potential to cause caries. Breast milk has low cariogenic potential.[29] Current evidence indicates that breastfeeding does not increase the risk of dental caries.[30] Breast milk is considered the best food for infants due to its ability to provide complete nutrients and bioactive components needed for the first year of life, and the World Health Organization recommends that infants are exclusively breastfed for the first 6 months of life, with continuation of breastfeeding for 1 year or longer as complementary foods are introduced.[31] Nevertheless, appropriate preventive measures must be taken so that the benefits of breastfeeding are not jeopardized by the increased risk for caries due to improper feeding habit.[32] It is good to note that most women in this study were aware that children are at risk of dental caries if they fall asleep while feeding and the milk pools in the mouth.

Children whose mothers or primary caregivers have active caries are at high risk of having caries themselves, attributed to poor oral health behavior of the mothers or caregivers.[33,34] In this study, less than one-third of the participants knew about the link between the mother's caries experience and the child's risk for caries. Pregnant women should be aware that their oral health status is a strong predictor of their children's oral health status. In relation to the roles and protective nature of a mother, this awareness may positively influence women's personal oral health care behavior and how they care for their child's oral health.[16] Studies have shown that mothers or parents with good oral health behavior will transfer appropriate oral health beliefs, values, and habits to their children.[34,35]

Dental caries can be successfully reversed or treated during its early stages.[36] A non-cavitated white spot on the tooth surface is an early sign of caries, indicating loss of minerals from the enamel.[37] At this initial stage in the caries process, good plaque control with the use of fluoride dentifrice and topical fluoride application by dental professionals can arrest or reverse the caries progression by remineralization of the enamel surface.[36] Regular inspection of the teeth by mothers at home using the lift-the-lip technique to detect the lesion, followed by prompt dental visits for professional evaluation and/or management can prevent unnecessary complications.[38] Most women in our study knew that a white spot lesion is an early sign of caries.

Most pregnant women in our study had favorable attitude towards the importance of deciduous teeth and their care. However, it is important to note that more than half of the women agreed that permanent teeth would not last a lifetime. This misperception was common. A study in Iran reported that more than 70% of mothers of 9-year-old primary school children agreed that it is natural for people to lose all their teeth in old age.[39] The misperception that losing teeth is a natural consequence of the aging process is a fatalistic attitude. Mothers may communicate this erroneous belief to their children who will take on the values, resulting

in a continual lack of a perceived need for oral healthcare, including efforts to prevent oral diseases.

Our study adds to the growing body of evidence supporting the link between oral health literacy and oral health knowledge. We believe that our study is perhaps the first to report an association between maternal oral health literacy and attitude towards children's oral health, another important health-mediating variable that has not been examined in previous studies among pregnant women.[9,10,23,24] In this study, we used the OHLI-M, a functional oral health literacy instrument that was able to assess not only the ability of women to read and understand written information, but also to understand instructions requiring basic mathematical operations.[19,20] Most previous studies assessing the oral health literacy of pregnant women used the Rapid Estimation of Adult Literacy in Dentistry (REALD-30) instrument or its translated versions.[9,10,23,24] The REALD-30 measures the ability of a person to correctly pronounce a list of 30 oral health-related words arranged in increasing order of reading difficulty. The main drawback of the REALD-30 is that it evaluates only word recognition and reading skills that may not reflect the functional literacy of respondents.[8] In this study, in addition to controlling for the confounding effect of parity on the knowledge and attitude of the women at the study design stage using stratified sampling, multiple regression analysis was conducted to control the effects of other potential confounding variables including age, highest education level, employment status, monthly household income, last dental visit, and experience of attending a talk about children's oral health.

Nevertheless, this study has a limitation that relates to the inherent issue of using a self-administered questionnaire, which is a subjective outcome depending on the participants' motivation, honesty, memory, and ability to respond.[40] In addition, we could not establish a cause-and-effect relationship due to the non-temporal nature of the cross-sectional design used. This study was performed at a single hospital, which may compromise the extent to which the study results can be generalized to the larger population.

CONCLUSION

Our findings support the hypothesis that the oral health literacy of pregnant women is positively associated with their oral health knowledge and attitude towards children's oral health. These findings have important implications for strategies aimed at improving the oral health of children. Only slightly more than half of the pregnant women in our study had adequate oral health literacy. Hence, a well-planned program using well-designed and easy-to-understand oral health education materials is recommended. To ensure that women with lower oral health literacy will also benefit from the educational intervention, it is recommended that the readability and suitability of the oral health education materials be assessed accordingly prior to intervention.

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ORIGINAL ARTICLE

Understanding knowledge of hypertension among affected individuals in low-Income (B40) communities in Malaysia: The RESPOND study

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ABSTRACT

Introduction: Achieving optimal control of blood pressure is easier when those affected understand the risks and consequences of hypertension and the principles of management. It is particularly important in disadvantaged groups among whom blood pressure control is often poor. However, effective responses require evidence of the knowledge and beliefs of those affected. This was undertaken as part of a larger study of the therapeutic journeys followed by individuals living in B40 (bottom 40% by income) households in Malaysia, the Responsive and Equitable Health Systems-Partnership on Non-Communicable Diseases (RESPOND).This paper describes their reported knowledge of hypertension, health, and measures that can improve hypertensive control.

Materials and Methods:The communities were selected from rural and urban populations in four peninsular states (Selangor, Kelantan, Perak, and Johor). Following a multistage sampling approach, communities in each stratum were selected according to probability proportional to the size and identified based on national census data by the community and administrative registers. Households were randomly selected. Eligible individuals were those aged between 35 and 70 years old, self-reported or identified as hypertensive at screening. Informed consent was taken. A survey using validated questionnaires was conducted.

Results: The total number of respondents was 579. The mean age was 59.0 (95%: 58.4, 59.7) and more were women (71.5%) than men (28.5%). Regarding respondents self-reported level of hypertension knowledge, 2.9% reported having no knowledge at all, 80.1% had little knowledge, and 17.9% were very familiar. Among all respondents, 56.2% (95% CI: 50.7, 61.6) correctly answered at least four out of five objective knowledge questions.Almost all (91.5%) were aware that hypertension could cause a stroke. However, one-fifth believed it could cause cancer. Almost three-quarters said that people with high blood pressure generally felt well (72.1%) and recognized that they should not stop taking their medication (70.7%). Most of the respondents knew that people should take their medication even if they feel well (73.6%). Although more than half (66.0%) of the respondents rated their health as poor. Interestingly, most did not perceive themselves as having a long-term illness (95.0%).

Conclusion: This study provides reassurance that individuals with hypertension in disadvantaged communities in Malaysia have a relatively good understanding of hypertension. Further research should explore the challenges they face on their therapeutic journeys.

KEYWORDS:
Knowledge; Hypertension; Low income; B40; Malaysia; RESPOND study

INTRODUCTION

Hypertension is easily treatable with safe and effective drugs yet, almost everywhere, achieving control remains a challenge. In Malaysia, the 2019 National Health and Morbidity Survey, with almost 15,000 subjects,found that 30.0% (95% CI: 28.57, 31.50) of adults aged 18 and over had been diagnosed with hypertension or were found to have elevated blood pressure.[1] Another study, with over 11,000 subjects but restricted to those aged 30 and above produced a figure of 42% (95%CI: 40.9, 43.2),[2] while an analysis of earlier waves of the national survey found that 37.4% (95% CI:35.3, 39.5) of those with hypertension had achieved control.[3]

Conveying an understanding of what high blood pressure means and why it is important to reduce is an important part of the therapeutic process and those with such an understanding are more likely to achieve control.[4-6] Yet we lack detailed insight into the knowledge of Malaysians with hypertension and how this impacts on their self-management, which is so important in achieving control. One exception is a small study (n=110) in an urban area near the capital that found a relatively high level of knowledge, with almost 90% of patients knowing something and almost 60% knowing the target blood pressure levels.[4] There was also

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a relatively good understanding of common risk factors and consequences of poor control, including cardiovascular disease, stroke, renal failure, and memory loss but over half also believed, incorrectly, that cancer is associated with hypertension.[4] We also know that traditional and complementary medicines are used widely by those with hypertension in Malaysia.[7,8]

Malaysia is not unusual in having socio-economic inequalities in treatment and control of hypertension,[9,10] although they are narrower than in several otherwise comparable middle-income countries.[11] Research elsewhere has pointed to the importance of characteristics such as lack of education and unemployment.[12,13] Inequalities have long been on the political agenda in Malaysia, with the New Economic Policy, in operation from 1970 to 1990, having an explicit goal to eradicate poverty. However, the 9th Malaysian plan (2006–2010) recognized that progress had stalled. Indeed, it found that the income share going to the group labelled B40 (the poorest 40% of the population) had fallen while the M40 middle (40%) were receiving higher incomes. Consequently, the 10th Malaysian plan (2011–2015) shifted from targeting poverty as such to improve the lot of the B40 group. The 11th Malaysia Plan (2016–2020), went further, seeking to bring the living standards of those in the B40 closer to those of the M40.[14]

This has been associated with a range of health initiatives, including 'Mysalam' and 'PekaB40'. MySalam is a health insurance scheme providing a cash payment to those with one of 45 diagnoses and a daily payment while in hospital, initially limited to the B40 but now including the M40, while Peka B40 offers free health screening.[15] A newspaper reported that 13.8% of those screened in the PekaB40 initiative were found to have previously undetected hypertension.[16]

If further progress is to be made in narrowing inequalities in hypertension control in Malaysia, it will be important to understand the knowledge and beliefs of the most disadvantaged in society. In this paper, we report findings from a study conducted among those with hypertension living in low-income (B40) households in Malaysia.

MATERIALS AND METHODS

Data were collected within the 'Responsive and Equitable Health Systems – Partnership on Non-communicable Diseases' (RESPOND) Project, being undertaken in Malaysia and the Philippines. Unlike the surveys described earlier that offer wide coverage of the country, RESPOND has been designed to gain in-depth knowledge of the lived experience of those with hypertension living in low-income communities using a mix of quantitative and qualitative methods, with a particular emphasis on their therapeutic journeys. The protocol and detailed methodology have been published elsewhere.[17]

Definitions

At the time when the study was planned, those in the B40 category had a household income of less than RM3,855 (€832; US$932) (level set in 2014). The cut-off point has changed over time. Those in the B40 category can be found in urban and rural areas and the study design included communities in both settings. Urban and rural areas were defined according to the Malaysian Population and Housing Census 2000.[18]

Conceptual framework

Our conceptual framework illustrated in Figure 1draws on research and theory in three main areas. First, individual health-seeking behaviour is shaped by individual, household, community, societal,[19-21] and 'environmental'19 factors such as distance to facilities and affordability, which may lead to inequalities in care.[22] We consider both 'potential' (opportunity to use care that is available) and 'realized' access (actual use of services) in understanding health-seeking behaviour and addressing barriers to access. Second, characteristics of health systems influence utilisation,[23] including availability of trained staff, essential medicines, and effective management and oversight,[24] while recognizing that a simplistic cause-and-effect model may be unhelpful[25] because of failure to consider complexity (path dependency and feedback loops).[19] Third, we draw on ideas of 'people-centred' health systems,[26] whereby individuals with their multifaceted beliefs, motivation, and behaviour, operating in informal and formal ways.[27,28] We seek to operationalize the barriers that exist at the level of individuals, families, communities, the health system, and the broader environment, and then understand the interrelations and synergies that exist between them. We draw on insights from anthropology, sociology, and social psychology to understand health experiences and health seeking behaviour of individuals, families, communities as circumscribed by the stated and implicit socio-cultural norms and values of the communities and social networks rather than by purely individual decisions.[29-31]

To demonstrate, knowledge of hypertension is an individual-level factor that influences decisions and behaviors related to treatment initiation, medication adherence, and adoption of lifestyle, which then determine the likelihood of achieving blood pressure control and ultimately the risk of cardiovascular and other non-communicable diseases. Such knowledge is, in turn, influenced by other factors operating at multiple levels, such as one's education, household income, interactions with the health system, exposure to media, among many other things—each of which present potential barriers and opportunities to intervene to improve knowledge, blood pressure control, and population health.

Sampling method

The urban and rural B40 communities were selected using a multistage sampling approach. The first stage was a purposive selection of four states in Peninsular Malaysia, Selangor, Perak, Kelantan, and Johor, all larger states with a mix of urban and rural communities. The second stage was selection of 24 communities, 3 urban and 3 ruralfrom each of the four states. Communities in each stratum were selected according to probability proportional to size using sampling frames based on national census data by community and administrative registers. The third stage involved recruitment of 25 households from each community, randomly selected

using a random online generator. Nearby communities were substituted where it was not feasible to ensure high levels of engagement with the chosen communities. This could arise from lack of community support, security risk for study personnel, inaccessibility by usual means of transportation, poor internet connection, or the existence of ongoing activities that may affect hypertension treatment seeking behavior.

Study population

The study population comprised adults aged 35–70 years old with hypertension, living within B40 households that were expected to remain at the current address for at least 18 months from the date of screening, with either a self-reported history of hypertension (previously diagnosed whether on or off treatment) or found to have elevated blood pressure at screening. B40 households were identified by contacting the municipal council and district council offices to identify low-income communities. The leader of the housing area or village from the randomly selected communities were then contacted for the researchers to approach the families. The families were asked regarding total household income or whether they received government financial aid for low-income households. Those who fulfil the B40 criteria were invited to participate. The exclusion criteria were those with self-reported history of major chronic co-morbidities that required regular contact with the health system such as cancer or HIV and those who were planning to move within the next 18 months. High blood pressure on screening was defined as when the average of two blood pressure measurements > 140/90 mmHg (using an OMRON blood pressure recorder from the non-dominant arm while in a sitting position after at least 5 minutes rest).

Sample size estimation were calculated based on detecting urban and rural differences in hypertension treatment in a middle-income country with α=0.05 and power of 0.8 (two-tailed), which we had previously found was as large as 14 percentage points (42% urban and 28% rural). This would require a minimum sample of 600 hypertensive individuals across 12 urban and 12 rural communities.[17]

Study procedure and data collection process

A maximum of three attempts was made to contact identified households, with substitution of another randomly selected household if contact could not be made. When a household responded but refused to participate in the full study, simple demographics, risk factors, and CVD history were recorded. When an eligible household was identified and agreed to participate, all adults in the household were enumerated and initial data were collected using a household census form. Screening for eligibility was conducted and if more than one hypertensive individual was identified one was selected at random using a probability-based method and invited to participate. If none were present another household was selected. Those who agreed, were provided with a written informed consent and enrolled. A brief non-responder form was completed for those participants who refused, and substitute participants were asked. In addition, a household census questionnaire was completed with demographic information (number of individuals in the household, sex ratio, number of children, and relatives living in the household), tobacco use, level of education, and morbidities in all inhabitants of the household. Participants who agreed were asked to complete a pre-tested questionnaire within the home, which included socio-demographic details of the participants. The variables of interest in this study were participants' perception of their knowledge level, specific knowledge, health and illness perception, and activities for blood pressure control.

Measuring knowledge

We measured both the subjective and objective knowledge of hypertension of the participants. One item in the questionnaire measured subjective knowledge, and asked participants to rate their own knowledge of blood pressure, as having no knowledge vs. little knowledge vs. being very familiar. This was followed by five true or false statements to measure objective knowledge. The statements included 'high blood pressure can cause stroke', 'high blood pressure can cause cancer', 'people with high blood pressure generally feel well and do not notice that they have high blood pressure', 'People with high blood pressure can stop taking their medications when their blood pressure value is normal', 'people with high blood pressure only have to take their medication when they feel unwell.' These items are those used for the Prospective Urban and Rural Epidemiology study, a large ongoing international cohort study of CVD incidence, mortality and risk factors among more than 250,000 individuals across 21 low-, middle-, and high-income countries, including Malaysia;[32] and their use ensures comparability of our findings to the wider Malaysian and global context. We derived an overall objective knowledge level indicator, where participants were assessed as having good knowledge if they correctly answered at least four out of five objective knowledge questions.

Data analysis

Data were managed and analyzed using the Statistical Package for Social Science (SPSS) Version 27.0 (SPSS, Inc, Chicago, IL, version 27.0) and Stata Statistical Software Release 17 (College Station, TX: StataCorp LLC).[33] Descriptive analyses were used to report socio-demographic characteristics based on the levels of knowledge, detailed knowledge responses, health perception, and activities to control blood pressure. Normally distributed data were presented with means and standard deviations. Categorical data were presented as frequencies (n) and percentages (%).

The comparison of the socio-demographic characteristics and the level of knowledge on hypertension was analyzed using the chi-square test. The 95% confidence intervals (CI) were calculated for the prevalence of knowledge of consequences and management of hypertension. The comparison between self-rated health, long-standing illness, and activities limitation of the respondents and respondents' effectives of various interventions to control hypertension, and subjectively- and objectively assessed levels of hypertension knowledge were analyzed using the chi-squared test or the chi-squared test for trend, depending on the nature of the variables being compared. To control for the potential confounding effects of respondent characteristics, includingage, gender, education level, state, urban–rural location, case status, and marital and employment status, we adjusted these crude associations using ordered logistic regression models.

All analyses account for the multi-stage sampling approach through the application of probability-based sampling weights, calculated by taking the inverse product of i) the unconditional probability of selecting the mukim within the state, ii) the conditional probability of selecting household within the community, and iii) the conditional probability of selecting participant from all eligible residents within household. The significance level was set at a p-value <0.05.

Ethical considerations

Ethical approval was provided by the National Medical Research Register ID NMRR-17-2599-38713, the Research Ethics Committees at LSHTM (Ref: 12214),and Universiti Teknologi MARA (600-IRMI(5/1/6) REC/313/18). We followed the Ethical Guidelines for good research practice of the Association of Social Anthropologists of the UK and the Commonwealth (ASA) (Association of Social Anthropologists, 2011). The research protocol addressed key principles set out in Wellcome Trust guidance notes on conducting ethical research involving people in low- and middle-income countries.[34]

RESULTS

The final sample comprised 585 respondents who completed the survey, 6 (1.0%) of whom did not report their age and were excluded, leaving 579 adults remaining in the sample for this analysis, with a mean age of 59.0 (95%: 58.4, 59.7) years. There were more women (71.5%) than men (28.5%). This imbalance was expected and reflected working patterns. The small number of excluded observations due to missing data was not expected to bias the results, as a comparison of basic characteristics (i.e. gender, urban–rural location, state, awareness of diagnosis, education, marital,and employment) between those retained versus excluded from the analysis found no statistically significant differences.

Subjective self-reported levels of hypertension knowledge

Regarding respondents self-reported level of hypertension knowledge, 2.9% (17) reported having no knowledge at all of hypertension, 80.1% (464) had little knowledge, and 17.9% (98) were very familiar with hypertension. Table I reports the distribution of self-reported knowledge by selected respondent characteristics.Unsurprisingly, those previously diagnosed with hypertension were more likely to be very familiar with the condition than those who were newly identified during the study (p<0.001). Old cases had a higher percentage of familiar knowledge on hypertension than new cases (20.0% versus 1.6%).

There were also significant differences by age group (p=0.048). More respondents older than 50 years tended to be very familiar with the knowledge of hypertension than their younger counterparts. The other sociodemographic characteristics were not statistically significant. Those in Johor, in urban areas, having vocational and university levels of education, and married were more likely to be very familiar but this did not reach statistical significance (p>0.05).

Objective levels of hypertension knowledge

Table II provides further detail on what it is that people with different levels of knowledge actuallyknow. Almost all (91.5%) were aware that hypertension can cause a stroke. However, one-fifth believed it could cause cancer and over half did not know that it could not. Almost three-quarters of respondents said that people with high blood pressure generally feel well (72.1%) and recognized that people with high BP should not stop taking their medication (70.7%). Most of the respondents knew that people should take their medication even if they feel well (73.6%).

Among all respondents, 56.2% (95% CI: 50.7, 61.6) correctly answered at least 4 out of 5 objective knowledge questions. Table III reports the distribution of objective knowledge by selected respondent characteristics. Younger respondents tended to have better levels of knowledge than their older counterparts (p=0.001); and separated and married respondents tended to be more knowledgeable than single or widowed respondents (p<0.001).The level of objective knowledge also increased with education level; however, this did not reach statistical significance (p>0.05).

Self-reported health and subjective vs. objective levels of hypertension knowledge

More than half (66.0%) of the respondents rated their health as poor. Interestingly, most did not perceive themselves as having a long-term illness (95.0%). Among those who did, most perceived that their long-term illness limits their ability to care for themselves (52.1%), to participate in social activities (82.1%), and limits activities in other ways (88.9%).

The self-reported health of respondents stratified by subjective and objective levels of hypertension knowledge is reported in Table IV. Those who considered themselves to have a long-standing illness, disability or infirmity tended to self-report as being more knowledgeable of hypertension than those without (p=0.002). Other characteristics were not significantly associated with their subjective or objective level of hypertension knowledge.

After adjusting for potential confounding from age, gender, education level, state, urban–rural location, case status, and marital and employment status, self-rated health was not strongly associated with either subjective (aOR: 1.05, 95% CI: 0.78, 1.41, p=0.769) or objective (aOR: 0.94, 95% CI: 0.69, 1.28, p=0.689) levels of hypertension knowledge.

Perceived effectiveness of hypertension interventions and subjective versus objective levels of hypertension knowledge

A large majority of respondents perceived taking western medications (75.7%), reducing body weight (80.5%), taking less salt (87.0%), increasing physical exercise (84.9%), and reducing stress (86.5%) to be effective atcontrolling hypertension. Conversely, respondents most reported not knowing about the effectiveness of traditional medicines for hypertension (34.4%).

Table V shows the crude associations betweenthese perceptions andrespondents' subjectively and objectively assessed levels of hypertension knowledge. There was strong evidence for an association between perceived effectiveness of taking traditional medications and taking less salt and

Table I: The distribution of levels of knowledge of hypertension among the respondents (N=579)

	Nothing (n=17), n(%)	Little (n=464), n(%)	Very familiar (n=98), n(%)	*p* value+
State:				
Selangor	3 (4.1%)	54 (84.2%)	7 (11.7%)	0.165
Johor	1 (0.6%)	129 (78.0%)	35 (21.4%)	
Penang	2 (1.9%)	75 (84.9%)	12 (13.2%)	
Kelantan	11 (4.4%)	206 (78.8%)	44 (16.8%)	
Location				
Urban	12 (3.8%)	236 (76.1%)	62 (20.1%)	0.091
Rural	5 (1.8%)	228 (84.7%)	36 (13.4%)	
Cases:				
Old	13 (2.7%)	374 (77.3%)	97 (20.0%)	<0.001
New	4 (4.2%)	89 (94.2%)	1 (1.6%)	
Gender:				
Male	4 (2.5%)	124 (75.0%)	37 (22.5%)	0.242
Female	13 (3.1%)	340 (82.1%)	61 (14.8%)	
Age group:				
less than 50 years	2 (2.5%)	69 (92.9%)	3 (4.6%)	0.048
50–59 years	4 (2.2%)	161 (79.4%)	37 (18.4%)	
60 years and above	10 (3.5%)	234 (77.4%)	58 (19.1%)	
Educational status				
None	2 (3.9%)	44 (83.6%)	6 (12.4%)	0.361
Primary	3 (1.6%)	196 (81.1%)	42 (17.4%)	
Secondary	11 (4.0%)	216 (78.7%)	48 (17.4%)	
Vocational and University	0 (0.0%)	6 (75.8%)	2 (24.2%)	
Marital status				
Single	0 (0.0%)	11 (96.7%)	1 (3.3%)	0.136
Currently married	14 (3.3%)	325 (76.4%)	86 (20.2%)	
Widowed	1 (2.1%)	108 (88.4%)	11 (9.5%)	
Separated and divorced	0 (0.0%)	19 (98.1%)	1 (2.0%)	
Currently employed				
Yes	4 (2.6%)	117 (82.7%)	117 (82.7%)	0.777
No	13 (3.0%)	347 (79.2%)	788 (17.8%)	

+*p* value from chi-squared test adjusted for sampling design

Table II: Knowledge of consequences and management of hypertension (N=579)

	Prevalence (95%CI)
High BP can cause stroke:	
Yes	91.5% (95% CI: 88.7-93.7)
No	1.8% (95% CI: 1.0-3.0)
Don't know	6.4% (95% CI: 4.5-9.0)
High BP can cause cancer:	
Yes	19.1% (95% CI: 14.9-24.2)
No	28.0% (95% CI: 22.8-33.8)
Don't know	52.6% (95% CI: 44.3-60.7)
People with high BP generally feel well:	
Yes	72.1% (95% CI: 67.5-76.3)
No	19.6% (95% CI: 14.8-25.5)
Don't know	7.9% (95% CI: 5.3-11.7)
People with high BP can stop taking their medication:	
Yes	18.0% (95% CI: 12.3-25.5)
No	70.7% (95% CI: 64.8-76.0)
Don't know	11.0% (95% CI: 8.2-14.6)
People with high BP only have to take medication when they feel unwell:	
Yes	17.2% (95% CI: 12.6-23.0)
No	73.6% (95% CI: 69.6-77.3)
Don't know	8.9% (95% CI: 6.6-11.9)

Table III: The distribution of respondents correctly answering at least four out of five objective knowledge questions (N=579)

	n(%)	*p* value+
State:		
Selangor	30 (47.0%)	0.103
Johor	90 (54.7%)	
Penang	51 (57.6%)	
Kelantan	154 (59.0%)	
Location		
Urban	165 (53.1%)	0.074
Rural	161 (59.9%)	
Cases:		
Old	280 (57.8%)	0.197
New	46 (48.1%)	
Gender:		
Male	82 (50.0%)	0.237
Female	243 (58.7%)	
Age group:		
less than 50 years	48 (65.6%)	0.001
50 -59 years	123 (60.5%)	
60 years and above	154 (51.1%)	
Educational status		
None	17 (32.7%)	0.092
Primary	127 (52.3%)	
Secondary	175 (63.5%)	
Vocational and University	7 (79.1%)	
Marital status		
Single	5 (40.9%)	<0.001
Currently married	253 (59.3%)	
Widowed	52 (42.7%)	
Separated and divorced	16 (82.0%)	
Currently employed		
Yes	75 (52.9%)	0.868
No	251 (57.3%)	

+*p* value from chi-squared test or chi-squared test for trend (for age group and educational status)adjusted for sampling design

Table IV: Crude associations between respondents' self-reported health and subjective and objective knowledge of hypertension (N=579)

	Subjective knowledge level				Objective knowledge level	
	Nothing (n=17), n (%)	Little (n=464), n (%)	Very familiar (n=98), n (%)	*p* value+	n (%)	*p* value*
Self-rated health:						
Poor	1 (2.3%)	26 (79.2%)	6 (18.5%)	0.180	14 (41.7%)	0.305
Neither good nor bad	10 (5.9%)	126 (76.9%)	28 (17.2%)		98 (60.1%)	
Good	6 (1.7%)	311 (81.5%)	64 (16.8%)		213 (55.8%)	
Long-standing illness, disability, and infirmity						
Yes	1 (4.2%)	16 (54.2%)	12 (41.6%)	0.002	22 (77.0%)	0.060
No	16 (2.8%)	448 (81.4%)	86 (15.7%)		303 (55.1%)	
Limit the ability to care for oneself (n=33)	(n=1)	(n=18)	(n=14)	0.171		0.670
Yes	0 (0.0%)	8 (48.5%)	9 (51.5%)		13 (74.2%)	
No	1 (8.7%)	10 (60.5%)	5 (30.9%)		13 (80.2%)	
Limit the participation in social activities (n=33)	(n=1)	(n=18)	(n=14)	0.797		0.968
Yes	1 (5.1%)	15 (54.4%)	11 (40.6%)		21 (76.9%)	
No	0 (0.0%)	3 (53.7%)	3 (46.3%)		5 (77.7%)	
Limit the activities in any other way (n=33)	(n=1)	(n=18)	(n=14)	0.350		0.909
Yes	1 (4.7%)	17 (57.3%)	11 (38.0%)		23 (78.4%)	
No	0 (0.0%)	1 (24.3%)	3 (75.7%)		3 (75.7%)	

+*p* value from chi-squared test for trend and*chi-squared test adjusted for sampling design

subjectively assessed level of hypertension knowledge. Conversely, there was strong evidence for positive associations between objectively assessed level of hypertension knowledgeand the perceived effectiveness of all the listed activities for controlling hypertension, apart from taking traditional medication.

After adjusting for potential confounding from age, gender, education level, state, urban-rural location, case status, and marital and employment status, strong evidence for a positive association between subjectively assessed level of hypertension knowledge and perceived effectiveness of taking traditional medicationsonly (aOR: 1.32, 95% CI: 1.13–1.55, *p*=0.001). Regarding objectively assessed level of

Table V: Crude associations between respondents' perceptions on the effectiveness of activities for controlling hypertension and subjective and objective knowledge of hypertension (N=579)

	Subjective knowledge level				Objective knowledge level	
	Nothing (N=17), n(%)	Little (N=464), n(%)	Very familiar (N=98), n(%)	*p* value+	n (%)	*p* value*
Taking western (prescribed) medications:						
Effective	13 (80.5%)	341 (73.6%)	83 (84.7%)	0.064	266 (81.7%)	0.001
Sometimes effective and ineffective	2 (12.4%)	74 (16.0%)	9 (9.6%)		42 (12.9%)	
Ineffective	0 (0.0%)	14 (3.0%)	5 (5.7%)		12 (3.6%)	
Don't know	1 (7.1%)	34 (7.4%)	0 (0.0%)		6 (1.8%)	
Taking traditional medications:						
Effective	2 (14.8%)	101 (21.8%)	23 (23.3%)	<0.001	75 (23.1%)	0.086
Sometimes effective and ineffective	3 (21.1%)	97 (21.0%)	22 (23.0%)		78 (23.9%)	
Ineffective	6 (34.8%)	91 (19.7%)	32 (33.0%)		79 (24.2%)	
Don't know	5 (29.4%)	174 (37.5%)	20 (20.7%)		93 (28.7%)	
Losing bodyweight:						
Effective	11(65.0%)	373(80.4%)	82 (83.5%)	0.057	287 (88.2%)	<0.001
Sometimes effective and ineffective	2(10.1%)	31(6.7%)	9(8.7%)		20 (6.2%)	
Ineffective	0 (0.0%)	9 (2.0%)	1 (1.1%)		4 (1.3%)	
Don't know	4 (24.9%)	50(10.9%)	6 (6.6%)		14 (4.3%)	
Taking less salt:						
Effective	14 (82.7%)	398 (85.9%)	91 (92.9%)	0.043	300 (92.1%)	<0.001
Sometimes effective and ineffective	1 (5.6%)	23 (5.0%)	6 (5.7%)		16 (4.9%)	
Ineffective	0 (0.0%)	5 (1.0%)	1 (0.4%)		2 (0.8%)	
Don't know	2 (11.7%)	37 (8.1%)	1 (1.0%)		7 (2.3%)	
Increase physical exercise:						
Effective	14 (85.3%)	390 (84.2%)	87 (87.9%)	0.490	298 (91.5%)	<0.001
Sometimes effective and ineffective	1 (7.5%)	29 (6.3%)	6 (6.1%)		14 (4.4%)	
Ineffective	0 (0.0%)	4 (1.0%)	1 (0.4%)		2 (0.8%)	
Don't know	2 (11.1%)	4 (1.0%)	4 (4.5%)		11 (3.3%)	
Reducing stress:						
Effective	14 (85.0%)	399 (86.0%)	88 (89.2%)	0.532	300 (92.1%)	<0.001
Sometimes effective and ineffective	1 (7.9%)	24 (5.2%)	6 (5.7%)		14 (4.5%)	
Ineffective	0 (0.0%)	4 (0.9%)	2 (2.3%)		2 (0.8%)	
Don't know	1 (7.1%)	36 (7.9%)	3 (2.8%)		9 (2.7%)	

+*p* value from chi-squared test for trend and *chi-squared test adjusted for sampling design

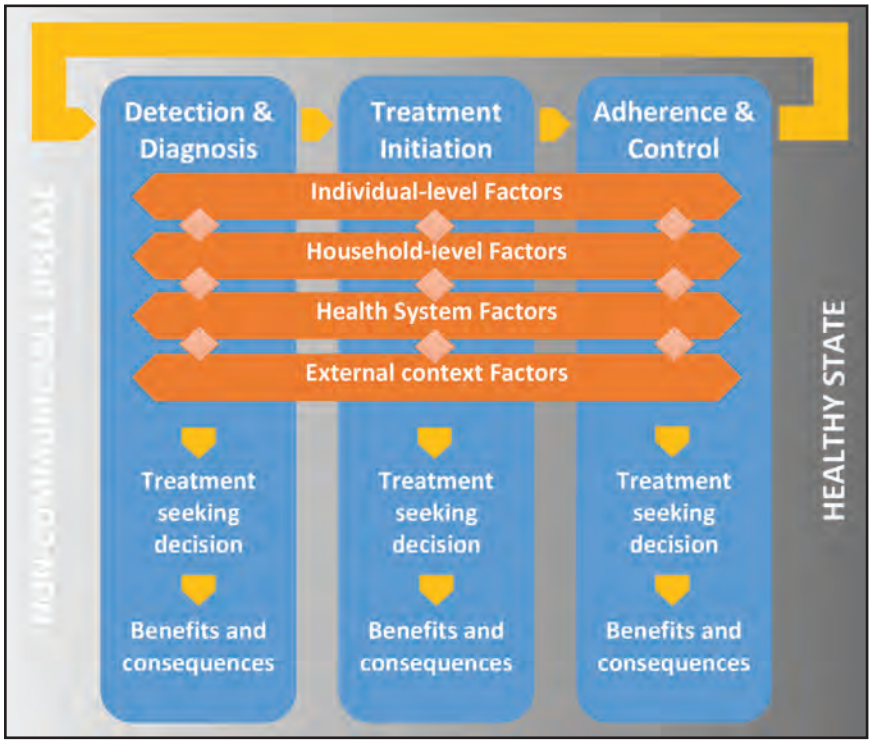

Fig. 1: Conceptual framework

hypertension knowledge, strong evidence remained for positive associations with the perceived effectiveness taking western medication (aOR: 2.28, 95% CI: 1.39–3.73, p=0.001), losing bodyweight (aOR: 2.82, 95% CI: 2.16–3.69, p<0.001), taking less salt (aOR: 2.56, 95% CI: 1.41-4.66, p=0.002),increasing physical exercise (aOR: 2.86, 95% CI: 1.63–5.00, p<0.001)and reducing stress (aOR: 2.62, 95% CI: 1.66–4.14, p<0.001), but not taking traditional medicine (aOR: 1.47, 95% CI: 0.91–2.39, p=0.118).

DISCUSSION

In these poor communities in Malaysia four out of five people with hypertension reported having little or no self-assessed knowledge of their condition. This was slightly better among those who had been hypertensive for longer and who were older, and therefore, more at risk from its consequences.

Yet, it is notable that, although self-assessed knowledge was low, their performance on the objective assessment of knowledge was better, withmore than half (56%) correctly answering at least four out of five of the related questions. This was consistent with other local studies that found hypertensive patients were relatively well informed of the risk factors and complications of hypertension,[4,35] but there is clear room for improvement. This study also reiterated that hypertensive patients were unsure about any link between hypertension and cancer, as most patients in our study responded that they did not know. In another study, patients believed that cancer was associated with hypertension, which is untrue.[4]

Most patients knew that people with high blood pressure cannot stop taking their medication (71%) and that they should take their medication despite feeling well (74%), However, there were still a quarter who were unsure or believed they did not need to take their medication if they felt well. The knowledge gap identified here is important because it could influence adherence to medication and blood pressure control. The overall rate of control among Malaysians on treatment is under 40% (30.7%[2] and 37.4%[3] in different studies). Inconsistencies in taking medication and doubting the role of medication are important factors in poor blood pressure control.[36]

Our study findings also highlight an important aspect of how hypertension is perceived:all respondents have high blood pressure and while 65.6% rate their health as poor, 94.4% do not describe themselves as having a long-term illness. Thus, hypertension appears not to be commonly viewed as a chronic condition, but rather as one that comes and goes – which is consistent with qualitative RESPOND study findings in the Philippines[37] – again, potentially affecting medication adherence. This could be due to the asymptomatic nature of those with high blood pressure, thus not equating it to feeling ill or having a long-term illness. This understanding is crucial when attempting to educate hypertensive patients on self-management and blood pressure control. It is important to acknowledge that hypertension may not cause symptoms and remain 'silent' for many years, while increasing the risk of devastating complications, such as heart disease or stroke. It is encouraging that hypertensive patients in these low-income communities identify western medications, losing weight, taking less salt, increase physical exercise, and reducing stress as effective means of controlling blood pressure. It is of particular interest that these positive perceptions of hypertension control measures appear to be supported by good levels of objective, and not subjective knowledge of hypertension, as suggested by the findings from our regression analyses. Consistent with findings from another study,[8] we also observed continued belief in traditional and complementary medication (TCM) as a means to treat high blood pressure. Again, our regression analyses provider further insight as a belief in the effectiveness of TCM for hypertension appears to be supported by high levels of subjective, and not objective knowledge of hypertension.

Malaysia has invested substantial resources in chronic disease management, with a Salt Reduction Strategy, a model of health care based on the Family Doctor Concept, Clinical practice guidelines for hypertension, and various community-based programs.[38] The 10-year National Strategic Plan for Non-Communicable Disease (NSP-NCD) introduced in 2016, explicitly seeks to improve health equity and to encourage people to adopt healthy lifestyles.[38] In light of our study's findings, the success of these policy outcomes could be enhanced by ensuring that related activities reach low-income groups, particularly those that aim to improve objective, rather than subjective knowledge of hypertension, and an understanding of the asymptomatic nature of this chronic condition.

An important consideration in interpreting our findings concerns their generalizability to other low-income communities in Malaysia, and in other LMICs more broadly. As mentioned previously, there were no notable differences in the characteristics of the 579 respondents included and 6 excluded in this analysis due to missing data; therefore, their exclusion is unlikely to bias our findings.Quality assurance measures conducted by the RESPOND study also show that the median household income, level of hypertension control, education, and employment observed in our sample are closely aligned with national data, which suggests that we have, indeed, sampled a suitable cross-section of hypertensive adults in low-income communities in Malaysia. However, several of the indicators presented that relate to respondents' hypertension knowledge and the perceived effectiveness health interventions may be affected by social desirability bias, where respondents may answer questions in ways that may be viewed favorably by others. We have taken steps to minimize this by interviewing respondents in their homes (rather than in clinical settings) and by interviewers trained in non-judgmental techniques. On the other hand, we accept that participants may have still considered the study as 'clinical' because it involved blood pressure measurement at enrolment.

CONCLUSION

This study provides some reassurance about knowledge of hypertension among some of the most disadvantaged communities in Malaysia. However, given that the rates of hypertension control across all populations nationally are low despite, further improvements in patient knowledge could support further and more equitable gains in

hypertension outcomes. It can be concluded that there is a gap between knowledge and action. The mere knowledge on activities that can control blood pressure does not necessarily lead to change for healthier lifestyle or compliance to medication. Recommendation can include better implementation of national policies that can reinforce the knowledge and stimulate lifestyle changes among individuals and communities. Yet, more research is needed, and other parts of this project will explore in more detail how the respondents conceptualize hypertension, for example, the role of the blood and other body systems[37] and the challenges they face on their therapeutic journeys,[39] issues already reported in the Philippines part of the project. Such insights, combined with the findings from this study, will help to inform strategies that aim to improve patient knowledge about hypertension, and ultimately, population levels of blood pressure control in ways that leave no one behind.

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ORIGINAL ARTICLE

The sensitivity and specificity of methylene blue dye as a single agent in sentinel lymph node biopsy for early breast cancer

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ABSTRACT

Introduction: Axillary lymph node dissection (ALND), although associated with significant morbidity, has been the standard procedure for axillary staging for breast cancer in many hospitals in Malaysia. The limited resources for radioisotope tracer and nuclear medicine service, coupled with insufficient number of trained surgeons, have been the major obstacles to perform sentinel lymph node biopsy (SLNB).

Materials and Methods: This study looks into the application of 1% methylene blue dye (MBD) as a single agent for SLNB and observes the outcome and any associated complication. Thirty-four patients with early breast cancer were enrolled. Two millilitres (ml) of 1% MBD was diluted with saline to a total volume of 5 ml. After induction of general anaesthesia, 3 ml of the diluted 1% MBD is injected subdermally at the upper outer quadrant of the breast followed by 5 minutes of massage. Sentinel nodes are identified as blue nodes or lymph nodes with a blue-stained lymphatic channel and were surgically removed. All patients then underwent tumour excision, either mastectomy or breast-conserving surgery, and ALND. The sentinel nodes were categorized to positive or negative for metastases and were compared with axillary lymph nodes for diagnostic value assessment.

Results: Identification rate of sentinel nodes was 91.2%. The mean number of removed sentinel nodes was 2 (SD=1) and the mean number of axillary nodes was 16 (SD=6). Sentinel node metastasis was found in 13 (41.9%) cases. There were two false-negative cases, resulting in a sensitivity of 86.7% (95%CI: 62.1-96.3). The negative predictive value of sentinel nodes to predict axillary metastasis was 88.9% (95%CI: 67.2-96.9). There were no complications observed.

Conclusion: Although inferior to the standard dual-tracer technique, the usage of MBD as a single agent in SLNB for early breast cancer still offers favourable accuracy and identification rate. With continuous training and improved surgeons experience, performing SLNB with blue dye alone is feasible in order to reduce the risks and morbidities associated with ALND.

KEYWORDS:
Breast cancer, sentinel lymph node biopsy, dye, sensitivity and specificity

INTRODUCTION

Breast cancer is one of the most common causes of cancer-related death worldwide. In 2012, 1.7 million cases of breast cancer were estimated by World Health Organization (WHO).[1] It accounts 25.1% of all cancers with standardized incidence rate of 43.1 per 100,000 and standardized mortality rate of 12.9 per 100,000.[2] In Malaysia, approximately 1 in 20 women will develop breast cancer in their lifetime with a higher incidence reported among Chinese followed by the Indians and the Malays.[3]

Over the years, the surgical treatment of breast cancer has developed substantially. It is known that the recurrence and survival rate in breast cancer are strongly dependent on the presence and extent of axillary lymph node involvement.[4] Breast-conserving surgery for early breast cancer has reduced the major morbidity of mastectomy and therefore, greater consideration is now placed on the method for axillary staging.[5] Conventionally, axillary lymph node dissection (ALND) is performed even for early breast cancer based on earlier reported evidence that it improves survival and reduces risk of recurrence.[6,7] However, ALND is associated with significant morbidity such as lymphoedema, numbness, limited mobility, stiffness, and seroma formation, as well as risk for vascular and brachial plexus injury.[4,8]

Many studies have proved that performing ALND for early breast cancer patients with clinically negative axillary nodes does not offer added benefit apart from subjecting patients for unnecessary morbidity and complication.[4,9-12] For that reason, sentinel lymph node biopsy (SLNB) has been performed and studied over the years as an alternative to ALND. Current literatures support the use of dual-tracer technique for lymphatic mapping in SLNB, using both radioisotope and blue dye, as it results in the highest identification rates of up to 90% to 98%.[13,14] On the other hand, the success rates for mapping with blue dye alone are slightly lower at between 83% and 93%.[13]

However, the non-availability of nuclear medicine service in many hospitals in Malaysia, coupled with limited resources for pre-operative lymphoscintigraphy and intra-operative radioisotope tracer have contributed to the difficulty in administering SLNB in Malaysia. Over the years, studies have been conducted to explore the possibility of performing SLNB using blue dye alone as a single agent. Few randomized

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studies showed that surgeons achieved equal results with favourable success rates when using blue dye alone compared with a combination of blue dye and radiolabelled colloid.[15] Due to its cheap cost, methylene blue dye (MBD) was more extensively studied for SLNB, especially in developing countries.[13,16-19] As the dye is readily available and affordable in Malaysia, this study aims to evaluate its sensitivity and specificity as a single agent in SLNB for early breast cancer.

MATERIALS AND METHODS

Study design

This cross-sectional study was conducted at Sarawak General Hospital, Kuching from January 2018 to June 2019. Convenient sampling was used to include all patients with early breast cancer who were admitted for an elective surgery.

Inclusion criteria

All patients diagnosed with breast cancer with tumour size of 3.0 cm or less, and negative ultrasound finding of axillary lymph nodes.

Exclusion criteria

Patients with no palpable breast lump, clinically palpable axillary lymph nodes, locally advanced tumour or large tumour more than 3.0 cm, inflammatory breast cancer, previous extensive surgery to the breast or axilla, previous neoadjuvant therapy, previous radiation therapy to the breast or axilla, pregnancy, prior history of allergy to blue dye, and patients who do not consent to be included in the study.

Sample size

This study aims to determine the sensitivity and specificity of MBD in detecting sentinel lymph nodes for biopsy. The prevalence of positive lymph node detection is estimated not less than 80%. Therefore, a minimum sample size of 39 subjects (including 31 subjects having the positive lymph node identification) will be required to achieve a minimum power of 80% (actual power = 80.7%) in order to detect a change in the percentage value of sensitivity from 0.70 to 0.90, based on a target significance level of 0.05 (actual = 0.048).[20]

Study tool and protocol

Demographic data were collected from the medical notes and interviews with the patients. Clinical data were obtained from the medical notes, mammogram and ultrasound reports, and the histopathology reports.

General surgeons with more than 5 years of experience in breast cancer surgery and have undergone training to perform SLNB participated in the study. Early breast cancer defines as stage I and IIA, or tumour size of T1 and T2 with negative regional lymph node metastasis.[15,21] However, for this study, we included only those with tumour size of less than 3.0 cm.[10,11]

SLNB was performed using a 1% MBD (LaboratoiresSterop, Belgium). Two millilitres (ml) of 1% MBD was diluted with saline to a total volume of 5 ml. After induction of general anaesthesia, 3 ml of the diluted 1% MBD was injected subdermally at the upper outer quadrant of the breast followed with 5 minutes of massage.[5,22] SLNB was then performed through a separate incision at the axilla. Sentinel nodes were identified as blue nodes or lymph nodes with a blue-stained lymphatic channel.[23] All patients subsequently underwent the planned surgery of either breast-conserving surgery and axillary clearance, or, mastectomy and axillary clearance.

The tumours, sentinel nodes, and the axillary lymph nodes were labelled separately. All specimens were fixed in formalin and sent for histopathological examination. The tumours were histologically classified according to the World Health Organization (WHO) Histological Classification of Breast Tumours.[1] Molecular subtypes were classified as luminal A (ER+ and/or PR+, HER2-, and histological grade either 1 or 2), luminal B (ER+ and/or PR+, HER2+; ER+ and/or PR+, HER2-, and histological grade 3), HER2 positive (ER-, PR-, HER2+), and triple negative (ER-, PR-, HER2-).[24,25] The sentinel nodes were categorized as positive or negative for metastases based on the histological evidence of metastatic carcinoma. The findings were compared with axillary lymph nodes for diagnostic value assessments.

Statistical analysis

The categorical data were presented as frequency and percentage. The numerical data were presented as mean and standard deviation in a normally distributed data, while for not normally distributed data, they were presented as median and interquartile range.

Analysis of the data was performed at 95% confidence interval (CI) using SPSS version 23.0 and OpenEpi online calculator (openepi.com). The false-negative rate was determined as false negative/(true positive + false negative). Sensitivity was measured as true positive/(true positive + false negative) while specificity as true negative/(true negative + false positive). The negative predictive value was calculated as true negative/(true negative + false negative) while the positive predictive value as true positive/(true positive + false positive).

Safety and ethical consideration

This study was approved by the National Medical Research and Ethics Committee (MREC) of the Ministry of Health, Malaysia with KKM/NIHSEC/P17-1694(16) and KKM/NIHSEC/P17-1694(18) as reference. All patients were given a patient information sheet and written informed consents were obtained.

The safety of patients was ensured and potential complications associated with the usage of blue dye such as allergic reaction and skin necrosis were constantly observed and monitored. The privacy and confidentiality of patients were always protected, and all data and personal information were kept classified.

Table I: Demographic and clinical characteristics of patients (n=34)

Characteristics	Value
Age, years old, mean (SD)	53 (11)
Race, n (%)	
Malay	14 (41.2)
Chinese	10 (29.4)
Iban	6 (17.6)
Bidayuh	4 (11.8)
Diameter of tumour, n (%)	
< 2.0 cm	17 (50.0)
2.0–3.0 cm	17 (50.0)
Site of tumour, n (%)	
Upper outer quadrant	20 (58.8)
Lower outer quadrant	8 (23.5)
Upper inner quadrant	5 (14.7)
Lower inner quadrant	1 (2.9)
Histology type, n (%)	
Invasive carcinoma of no special type	33 (97.1)
Medullary carcinoma	1 (2.9)
Molecular subtypes, n (%)	
Luminal A	16 (47.1)
Luminal B	11 (32.4)
HER2 positive	2 (5.9)
Triple negative	5 (14.7)
Surgery, n (%)	
Breast conserving surgery	16 (47.1)
Mastectomy	18 (52.9)

Table II: Identification of sentinel and axillary lymph nodes metastases (n=31)

	Axillary lymph nodes metastases	
	Yes	No
Sentinel lymph nodes metastases		
Yes	13	0
No	2	16

Table III: Diagnostic value of methylene blue dye in sentinel lymph node biopsy

	Value	95%CI
Sensitivity	86.7%	62.1 - 96.3
Specificity	100.0%	80.6 - 100.0
Positive predictive value	100.0%	77.2 - 100.0
Negative predictive value	88.9%	67.2 - 96.9

RESULTS

A total of 34 patients were included in the study with a response rate of 87.2% (34/39). The demographic and clinical characteristics of the patients are summarized in Table I.

The mean age of patients was 53 years old (SD=11) and the ethnic composition of the respondents was 41.2% Malay, 29.4% Chinese, 17.6% Iban, and 11.8% Bidayuh. Majority of the tumours were located at the upper outer quadrant of the breast (58.8%) and there was equal distribution in term of tumour size. Almost all the tumours were reported histologically as invasive carcinoma of no special type (97.1%) and luminal A was the most common molecular subtypes (47.1%). 18 patients (52.9%) underwent mastectomy while 16 patients (47.1%) had a breast-conserving surgery.

The study identified sentinel lymph node in 31 patients and therefore, the identification rate was 91.2%. The mean number of removed sentinel lymph nodes was 2 (SD=1) and the mean number of axillary lymph nodes was 16 (SD=6).

Among the 31 patients with identified sentinel lymph nodes, 13 of them (41.9%) were reported as positive for metastasis as shown in Table II. There were two false-negative cases and the false negative rate was calculated as 13.3%. As listed in Table III, the sensitivity of MBD to identify the sentinel lymph nodes was 86.7% (95%CI: 62.1, 96.3) with a negative predictive value of 88.9% (95%CI: 67.2, 96.9).

There were no allergic reaction or local inflammatory reaction at the injection site such as skin necrosis or ulceration. All patients had an uneventful post-operative recovery and were discharged well.

DISCUSSION

SLNB is considered the gold-standard treatment and has replaced ALND in the evaluation of axillary staging for early breast cancer. Despite the knowledge that ALND is associated with many risks and morbidities,[4,8,26] SLNB has not become a common practice among surgeons in Malaysia. Firstly, majority of patients with breast cancer in this country present late to the hospital, either in a locally advanced or advanced stage.[3] The other factors include the non-availability of nuclear medicine service in many hospitals in Malaysia, as well as the limited financial resources for the radioisotope tracer. In addition to that, many surgeons are not trained and credentialed to perform SLNB.

Several other developing countries like Malaysia are facing similar problems and therefore, studies have been conducted over the years to look at the possibility of performing SLNB using blue dye alone as a single agent. There have been many promising results with favourable identification rates and low false-negative rates.[13,18,22]

The response rate of this study was 87.2% as it did not achieve the target sample size of 39. However, the positive identification of sentinel lymph nodes in 31 patient fulfils the requirement of the study to achieve a minimum power of 80% for data analysis. The most obvious factor was the difficulty in recruiting patient with early breast cancer in the study hospital. Majority of breast cancer patients present late at a locally advanced or advanced stage. The effort to educate the public on awareness of screening and early detection should be continued and carried out on a frequent basis.

The mean age of patients was 53 years old with the youngest at 36 and the oldest at 73. Malay ethnicity composed the majority of patients in this study, followed by Chinese, Iban, and Bidayuh. Although previous data showed a higher prevalence of breast cancer among Chinese in Malaysia,[3] this difference might be due to higher Malay population (61.8%) compared to Chinese (37.3%) in Kuching, Sarawak which was the location of the study hospital.[27]

Consistent with other epidemiological data,[27] this study showed that the commonest breast cancer is the invasive carcinoma of no special type (97.1%) and the main molecular subtype is luminal A (47.1%). Sixteen patients (47.1%) underwent mastectomy while the other 18 (52.9%) opted for breast-conserving surgery. However, the decision for type of surgery was not made based on the size and the location of tumour. Rather, it was decided by the patients and the attending surgeons after the surgical options and subsequent treatment plan were explained in detail.

In overall, only 15 patients (44.1%) were lymph node positive for metastases. It means that more than half of them could have been spared from the risks and morbidities of ALND. This finding is consistent with other previous reports[4,9-12] and further accentuates the benefit of SLNB for early breast cancer.

The sentinel lymph nodes were identified in 31 patients, resulting in identification rates of 91.2%. It is lower than the standard dual-tracer technique with both radio labelled colloid and blue dye.[13,14] However, it is comparable with other similar studies that used MBD as a single technique in SLNB.[17-19,22] Most importantly, it surpasses the recommendation by the American Society of Breast Surgeons which stated that the sentinel lymph node identification should be above 85% in order to abandon axillary dissection.[15]

The age of the three patients with unidentified lymph nodes was 36, 65, and 66 years old, respectively. All three of them had tumour size of <2.0 cm with negative axillary lymph node metastases. Many factors were reported to be associated with the success or failure in identifying sentinel lymph nodes which include age, body mass index, tumour size, grade and location, as well as SLNB technique and surgeons experience. This study did not look at these associated factors in detail but the older age, small tumour size, and limited surgeons experience were in tandem with the findings from some of the studies.[29-31]

There were two patients with false-negative outcome, resulting in false-negative rates of 13.3%. It is higher than the average rates of 8.4%, and the recommendation by American Society of Breast Surgeons on acceptable false-negative rates to abandon axillary dissection should be 5% or less.[15] False-negative results are usually down to lack of experience and technical failures which may be avoidable.[14]

There are few possible reasons that this study did not achieve the recommended 5% false-negative rates. The numbers of sentinel lymph node harvested is one of the factors that influence the false-negative rates.[32-34] The mean number of two sentinel lymph nodes obtained in this study could contribute to the final result. Although it fulfils the minimum number of sentinel lymph nodes required for SLNB in breast cancer as suggested by other studies, they showed that the false-negative rates significantly decrease as the number of lymph nodes rises.[32-34] Hence, removing more than two sentinel lymph nodes in subsequent study or clinical practice may reduce the false-negative rates.

In both cases with false-negative result, the tumour was <2.0 cm in size and located at the lower outer quadrant. A previous study contradicts this observation, as they reported a significant increase in the false-negative rates for tumours located in the upper outer quadrant compared with other locations.[31] Surgeons' performance could also factor in the result. General surgeons involved in this study, although proficient in breast cancer surgery, have limited experience in SLNB. However, it has been reported that performing SLNB using blue dye demonstrates a short learning curve among experienced surgeons. Surgeons are advised to perform at least 20–30 cases before they can achieve the highest identification rate and lowest false-negative rates.[15,16]

As a result, the sensitivity and negative predictive value (NPV) in this study were 86.7% and 88.9%, respectively. It is lower compared to other studies that reported sensitivity as high as 91.7% to 94.0% and NPV as high as 90.0% to 96.1%.[22,35] A better outcome can be achieved in future by increasing the identification rates and reducing the false-negative rates.

There was no incidence of severe anaphylactic reaction in all patients. Although previous studies reported local inflammatory reaction with MBD, no complications were observed in this study. This could be due to the usage of diluted dye as recommended by previous literatures.[5,13,17]

The lower sensitivity and specificity of MBD as a single agent for SLNB shown in this study proves that the dual-tracer technique with radio labelled colloid and blue dye remains the gold standard in current clinical practice. However, in places with limited resources and expertise, this study has shown that performing SLNB with blue dye alone has favourable accuracy and identification rate to reduce the morbidity of ALND. Future studies and training should be designed to involve more general surgeons in the hope that SLNB will be practiced widely in future for the benefits of the patients.

CONCLUSION

Although inferior to the standard dual-tracer technique, the usage of MBD as a single agent in SLNB for early breast cancer still offers favourable accuracy and identification rate. With continuous training and improved surgeons experience, performing SLNB with blue dye alone is feasible in order to reduce the risks and morbidities associated with ALND.

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DISCLOSURE

None.

CONFLICT OF INTEREST

None.

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ORIGINAL ARTICLE

Clinical severity of COVID-19 with omicron variant predominance in relation to vaccination status, age, comorbidities- a single center in Selangor, Malaysia

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ABSTRACT

Introduction: Recently, the rapid surge of reported COVID-19 cases attributed to the Omicron variant of severe acute respiratory syndrome coronavirus (SARS-CoV-2) created an immediate concern across nations. Local information pertaining to the new variant of concern (VOC) is lacking. We aimed to determine the clinical characteristics of COVID-19 during a period of Omicron prevalence among patients hospitalised from February 1 to 21, 2022 at Sungai Buloh Hospital and to estimate the risks of disease progression presumably caused by this variant in association with gender, age, comorbidity, and vaccination status.

Materials and Methods: In this retrospective, single-centered, retrospective cohort study, all hospitalised adults with laboratory-confirmed COVID-19, aged 18 and above, were recruited from February 1 to 21, 2022. Clinical characteristics, investigations, and outcomes were assessed.

Results: A total of 2279 patients aged 18 years and above with laboratory-proven COVID-19 were recruited and analysed, excluding 32 patients owing to incomplete data. Majority of the study population had a mean age of 41.8 ± 17.7, was female-predominant (1329/2279, 58.6%), had completed a primary series of vaccination with a booster (1103/2279, 48.4%), and had no underlying medical conditions (1529/2279, 67.4%). The risk of COVID-19-related disease progression was significantly lower in hospitalised patients under the age of 50 who were female, had no comorbidity, and had completed two doses of the primary series with or without a booster. [respectively, OR 7.94 (95% CI 6.16, 10.23); 1.68 (1.34, 2,12); 2.44 (1.85, 3.22); 2.56 (1.65, 3.97), *p*< 0.001].

Conclusion: During the period of Omicron prevalence, a favourable outcome of COVID-19 was strongly associated with female gender, age below 50, a comorbidity-free condition, and having completed immunization. With this new observation, it could help improve public health planning and clinical management in response to the emergence of the latest VOC.

KEYWORDS:
Age, comorbidity, COVID-19, Omicron, severity, vaccination status

INTRODUCTION

Malaysia first reported COVID-19 cases on January 25, 2020[1] and has suffered great losses caused by COVID-19 pandemics up till now. The emergence of the alpha, beta, and delta severe acute respiratory syndrome coronavirus (SARS-CoV-2) variants of concern (VOCs) had previously been linked to new waves of infections that spread globally and resulted in high morbidity and mortality. The B.1.1.529 variant, better known as Omicron, has emerged as a new strain, first detected in South Africa on November 25, 2021.[2] The World Health Organization (WHO) declared it as the fifth variant of concern on November 26, 2021.[3] The presence of 37 mutations in the spike protein enhances the immune evasion, giving an advantage of greater infectivity compared with previous variants.[4,5] From January 24 to February 7, 2022, the main proportion of COVID-19 variants in Malaysia was predominantly Omicron (737/802, 92%) followed by Delta (65/802, 8%) (6). Subsequently, from February 7 to 21, 2022, the Omicron variant (1211/1231, 99%) gradually replaced Delta (20/1231, 1.6%).[6] On February 7, 2022, the Ministry of Health (MOH) declared that the new Omicron had replaced the Delta as the dominant strain in Malaysia.[7] In real-world conditions, the substantial surge of COVID-19 cases during the Omicron-variant encounter is straining the healthcare system. However, recent studies from the UK[8], Canada[9], South Africa[10,11], USA[12], and Sweden[13] described that the Omicron variant, though wildly transmissible, appeared less severe and deadly than the Delta variant in various age groups. Wolter et al. reported that the immunisation programme had significantly reduced the odds of hospital admission and severe disease for patients infected with the Omicron SARS-CoV-2 VOC compared with other SARS-CoV-2 variants during the same period, although reduced severity could be due to past infection.[10,14] To date, no local data was available to clearly delineate the clinical characteristics of the Omicron variant.

To guide the public health planning and response during the period of Omicron prevalence, we sought to study the clinical characteristics of COVID-19; to monitor the risks of hospitalised patients, according to age, sex , comorbidities, and vaccination status.

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MATERIALS AND METHODS

We conducted a retrospective cohort study of adults aged 18 and above who were hospitalised according to the admission criteria (Table I)[15], from February 1 to 21, 2022, during the period of near-universal spread of the Omicron variant in Malaysia, with laboratory-confirmed SARS-CoV-2 infection. During the period of study, Sungai Buloh Hospital was assigned as the primary referral hospital for COVID-19 in the Klang Valley. Cases were retrospectively followed up closely to February 21, 2022. However, cases were excluded if data was invalid or missing; or if subjects were pregnant. We linked data from two main sources: 1. Demographic and clinical data that were retrieved from clinical case notes recorded in electronic datasets of Sungai Buloh Hospital. 2. Vaccination data was obtained from the Malaysia Vaccine Administration System (MyVAS).

Definitions

SARS-CoV2 infection was defined as an individual who was tested positive using either a nasopharyngeal swab (NPS) or oropharyngeal swab (OPS) of rtPCR test for COVID-19, NPS COVID-19 GeneXpert or saliva/NPS RTK Ag for COVID-19.[15] Based on the COVID-19 Management Guideline by the Ministry of Health (Malaysia), each COVID-19 case was classified according to disease severity: stage I (mild)- "asymptomatic", stage II (mild-moderate)- "symptomatic without pneumonia", stage III (moderate)- "pneumonia without hypoxia", stage IV (moderate-severe)- "pneumonia requiring oxygen therapy", stage V (severe)- "critically ill".[15] All confirmed cases would be hospitalised if they fulfilled the admission criteria incorporated by the Ministry of Health, Malaysia.[15] Co-morbidity was described as one or more of the following conditions: diabetes mellitus, chronic cardiac disease, peripheral vascular disease, chronic renal disease, chronic pulmonary disease, malignancy, HIV, chronic liver disease, and stroke.[16,17] Individuals were considered as 1) not fully vaccinated, either they had not been vaccinated (unvaccinated) at all or only one dose of the primary series had been received (partially vaccinated) 2) fully vaccinated if two doses of primary series were administered, including Pfizer-BioNTech (Comirnaty®), Oxford-AstraZeneca (ChAdOx1-S ®) and Sinovac Biotech 3) up-to-date if one booster was received on top of two doses of primary series.[18-22] Cytokine release syndrome is defined as a systemic inflammatory response involving rapidly progressive pneumonitis requiring oxygen supply, with or without multi-organ failure.

Statistical analysis

Sociodemographic data, clinical characteristics, laboratory results, and clinical outcomes were analysed with SPSS version 26. Continuous variables were describe it as standard deviation, SD and interquartile range, IQR, whereas categorical variables as frequency and percentage. Group differences for numerical variables were analysed by using the Students' unpaired t test or Mann-Whitney test; whereas for categorical variables by using Chi-square or Fisher's exact test. The risk estimation was determined by using binomial logistic regression.

RESULTS

From February 1 to 21, 2022, about 81,738 Klang Valley residents aged 18 and above were diagnosed with COVID-19, of whom were 55319 (67.7%) patients aged 18–39, 20,360 (24.9%) aged 40–59, and 6059 (11%) aged 60 and above. Of the total patients, 2311 (2.8%) patients were hospitalised at Sungai Buloh Hospital. There were 32 hospitalised cases being excluded owing to incomplete data collection as they were still receiving inpatient care at our centre. The admission rate was higher in the elderly age group [447/6059 (7.3%)] compared with the middle age group [589/20360 (2.9%)] and the younger age group [1233/55319 (2.2%)].

Among 2269 hospitalised patients, the mean age was 41.8 (SD 17.7) [male: 44 (SD 18), female: 40 (17)]. The majority of hospitalised patients were female (1329/2279, 58.6%), of whom 779/1329 (58.3%) were aged 18–39 years old, 320/1329 (24.1%) aged 40–59, and 230/1329 (17.3%) aged 60 and above; whereas there were 940/2269 (41.4%) male patients who were hospitalised, of whom 454 (48.3%) were aged 18–39, 269 (28.6%) aged 40–59, and 217 (23.1%) aged 60 and above ($p < 0.001$). Of 2269 patients, 1529 (67.4%) had no medical conditions, 476 (21%) had at least one comorbidity, and 264 (11.6%) had two or more comorbidities. Of 1529 patients without coexisting illnesses, 1020 (66.7%) were young people aged 18–39. Half of the patients having two or more health conditions were the elderly (135/264, 51.1%). Of 2269 patients, 1103 (48.4%) had completed the primary series with one booster, 1050 (46.1%) received two doses of the primary series, 14 (0.6%) received only one dose of the primary series, and 102 (4.5%) were not vaccinated yet.

Table II illustrates the severity of disease among the study population in the inpatient setting, based on gender, age category, and the presence of comorbidities, vaccination status. Among 2269 hospitalised patients, 1919 (84.6%) presented with a mild-moderate degree of COVID-19 severity with no disease progression, of whom the majority were young (1173, 61.1%), female (1162, 60.6%) with no comorbidities (1377, 71.8%) and with the administration of a COVID-19 vaccine booster in addition to the primary series (988, 51.5%). Whereas, 350/2269 (15.4%) experienced COVID-19 disease progression, either at presentation or later during hospitalization, of whom the majority were male (183, 52.3%), elderly (185, 52.9%), and with at least one comorbidity (198, 56.6%). In accordance with the vaccination status, the proportion of patients who experienced COVID-19 disease progression was found to be higher among those with incomplete vaccination (36/116, 31%) compared with those who had completed the primary series without a booster shot (199/1050, 19%) and with a booster shot (115/1103, 10.4%).

Table III depicts the odds ratio of risk estimators in association with the disease severity of COVID-19 infection. Female gender, age less than 50 years old, absence of comorbidity, and completion of at least two doses of the primary series were found to be favourable predictors of milder COVID-19 disease. In constrast, the elderly group (age of 60 and above) and the hospitalised patients with at least two comorbidities and more, were at greater risk of experiencing disease progression of COVID-19 pneumonia,

Table I: The admission criteria for patients with the laboratory-confirmed diagnosis of COVID-19.[15]

Criteria for hospital admission of confirmed COVID-19 cases
1. Patients with the COVID-19 infection categorised as 3 to 5
2. Those found to be unstable with warning signs* after evaluation in COVID-19 assessment centres
3. Individuals with comorbidity that is uncontrolled, such as diabetic ketoacidosis, hypertensive emergency, unstable angina etc
4. There is no alternative outpatient dialysis for patients with underlying end-stage renal failure (ESRF) on regular dialysis, though the COVID-19 severity is mild or categorised 1 to 2.
5. Individuals who are immunocompromised**
6. Pregnant mothers in category 2 and higher
7. Pregnant mothers with a BMI of ≥35 kg/m^2 at booking
8. Pregnant mothers who are not fully vaccinated and have medical/obstetrics morbidities, regardless of the disease severity of COVID-19
9. Individuals who are unsuitable to be managed in an outpatient setting while on home quarantine

* Identified warning signs are protracted or worsening symptoms (including persistent cough, angina pectoris, malaise, pyrexia, gastrointestinal losses, anorexia, dyspnoea) and signs (such as confusion, reduced urine output, cyanosis, and oxygen saturation of less than 95%).

** Include solid or bone marrow transplant recipients, people with cancer undergoing active chemotherapy, cancers of the blood and bone marrow, primary immunodeficiency, HIV infected with low CD4 count and not on suppressive ART therapy, splenectomised individuals, on prolonged corticosteroids or other immunosuppressive agents

Table II: The proportion of patients hospitalised for COVID-19 from February 1 to 21, 2022 in relation to age group, comorbidities, vaccination status, and degree of COVID-19 severity

	CAT 1–3 at presentation, without disease progression N=1919		CAT 1–3 at presentation, with disease progression N=61		CAT 4–5 at presentation N=289		Total	*p* value
	n	%	n	%	n	%		
Gender								
Male	757	80.5	31	3.3	152	16.2	940	
Female	1162	87.4	30	2.3	137	10.3	1329	< 0.01
Age group								
18–39	1173	95.1	7	0.6	53	4.3	1233	
40–59	484	82.2	17	2.9	88	14.9	589	
≥ 60	262	58.6	37	8.3	148	33.1	447	< 0.01
Comorbidities								
0	1377	90.1	22	1.4	130	8.5	1529	
1	375	78.8	18	3.8	83	17.4	476	
≥ 2	167	63.3	21	8	76	28.8	264	< 0.01
Vaccination								
Up-to-dated	988	89.6	28	2.5	87	7.9	1103	
Fully vaccinated	851	81	27	2.6	172	16.4	1050	
Not fully vaccinated	80	69	6	5.2	30	25.9	116	< 0.01

with OR 3.26 (95% CI 2.45, 4.32) and OR 5.26 (95% CI 3.89, 7.11), respectively ($p < 0.001$).

DISCUSSION

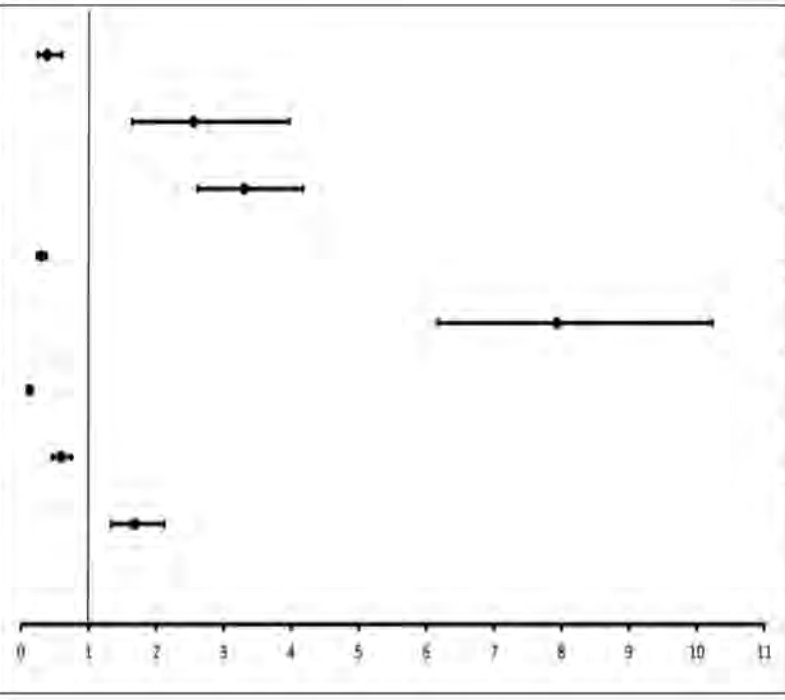
From February 1 to 21, 2022, during which Omicron appeared as the predominant circulating variant across the globe, we observed that a majority of hospitalised patients had not experienced COVID-19 associated severe deterioration. Consistent with earlier studies,[8-10,23,24] hospitalizations during the period of Omicron prevalence were strongly associated with a lower chance of ICU admission, mechanical ventilation, and mortality, compared with the Delta-variant encounter. As reported in the UK, the Omicron cases had a nearly 50% lower risk of hospitalisation and mortality than the Delta cases.[25]

Interestingly, there is evidence stating that the immune effect observed in Delta cases was less than that found in Omicron cases.[10,14] Recent studies suggested a paradigm shift in Omicron-variant tropism towards the upper respiratory tract, in comparison to previous VOCs including Delta and wild type, that had marked tropism for the lower respiratory tract.[26] Even though the Omicron mutations may increase transmissibility as a result of immune escape,[27] they lack the ability to replicate effectively in the lower respiratory tracts, sparing the lung parenchymal tissue and thus not causing severe disease when compared to the Delta variant.[28] Supported by one animal model,[28] reduced pathogenicity in the Omicron variant was observed, resulting in less severe disease involving lower respiratory tracts.

Gender differences are recognised as risk estimators impacting COVID-19 severity. It was reported that the morbidity and mortality rates were significantly higher among males compared with females. Interestingly, the crucial reason behind this observation is presumably related to immune response, hormonal differences, behavioural attitudes, and inflammatory markers.[29] Studies have shown that feminine hormones promote an appropriate immune response to COVID-19 infection and vaccines. Besides, there is a strong association between oestrogen and suppressed

Table III: The odd ratio of age groups, gender, comorbidities, and vaccination status in association with the disease severity of COVID-19

Factor	Predictors towards disease severity of COVID-19	OR (95% CI)	*p* value
Fully vaccinated status		0.39 (0.25, 0.61)	< 0.001
Unvaccinated status		2.56 (1.65, 3.97)	< 0.001
Presence of comorbidities		3.31 (2.62, 4.18)	< 0.001
Comorbidities free		0.30 (0.24, 0.38)	< 0.001
Age > 50		7.94 (6.16, 10.23)	< 0.001
Age < 50		0.13 (0.098, 0.16)	< 0.001
Female		0.595 (0.47, 0.75)	< 0.001
Male		1.68 (1.34, 2.12)	< 0.001



expression of angiotensin-converting enzyme-2 (ACE2) receptors, which are fundamental components of SARS-CoV-2 receptors as the keys to unlocking the doors of host target cells.[30,31] On the other hand, androgens enhance the gain entry of SARS-CoV-2 into host cells via ACE2 receptors, by upregulating the expression of transmembrane protease, serine (TMPRSS2) genes,[32] thus leading to increased susceptibility of males towards COVID-19 infection. Besides, men generally had a higher prevalence of high-risk exposures, for instance, smoking and alcohol consumption.

In line with other studies,[13] the risks of severe disease caused by Omicron variants were significantly higher in unvaccinated individuals aged 50 and older, especially those with multiple comorbidities. In our study, younger individuals without comorbidities barely reported severe complications caused by COVID-19. It is well-known that the risks of life-threatening conditions caused by COVID-19 increase with age, with older individuals being at higher stakes.[33] Up to 80% of COVID-19-related deaths occurred among individuals aged 65 and above, and they were 97 times more likely to die compared with individuals aged 18–29 years.[34] Furthermore, chronic illnesses are well known as the leading cause of mortality and morbidity in COVID-19 infection.[35]

In our study, there was a trend of having higher incidence and hospitalisation rate ratios among COVID-19 patients who had yet to complete their primary series of vaccinations in contrast to those who were fully vaccinated, with or without a booster. In line with one study conducted by Danza et al., the COVID-19 incidence and admission rates in Los Angeles County among unvaccinated patients were 3.6 and 23 times, respectively, higher than those who were fully vaccinated.[12] Furthermore, recent studies found that any individual who received an effective COVID-19 immunisation programme after a booster remains significantly protected against severe damage and even death caused by SARS-CoV-2 variants, including Omicron.[24,36] It can be explained by the post-vaccination T-cell response in cross-recognizing the Omicron variant, contributing to adequate protection against severe disease.[37,38] Jingyou et al. recommended that booster vaccines would help our immunity system consistently produce an adequate level of neutralising antibodies against the Omicron variant of SARS-CoV-2.[39]

LIMITATIONS

There are some limitations to our study. First, the genomic sequencing data was not available to determine the predominance of COVID-19 sub-variance in our studied group; nevertheless, the variant predominance trends presumably occurred during the study period. Second, the follow-up duration was short. A longer period of observation is desirable to determine the outcome. Third,the methodology of our study was constructed based on the adaptation of previous guidelines on COVID-19 vaccination before a newer version was launched officially on April 1, 2022.

CONCLUSION

In this retrospective cohort study conducted during the period of Omicron prevalence, we concluded that COVID-19 severity may potentially rise with age and in the presence of comorbidities, as well as among unvaccinated individuals. In

light of the high transmissibility of the Omicron variant leading to a substantial surge of COVID-19 cases, the enormous volume of hospitalisation may heavily strain the local healthcare systems. The availability of local data can help in fine tuning the limited local healthcare resources during the Omicron onslaught. Furthermore, this data could assist in informing programme managers on admission criteria to avoid unnecessary admissions that burden hospitals; identifying high-risk individuals to target interventions, for instance, completing vaccinations and avoiding high-risk exposures; and prognosticating which patients will suitably benefit from timely treatment with antiviral or monoclonal antibodies.

ETHICS APPROVAL

For this study, we have obtained an approval from the National Medical Research Register, Ministry of Health, Malaysia.

CONFLICT OF INTERESTS

None to declare.

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ORIGINAL ARTICLE

Subtenon implantation of wharton's jelly-derived mesenchymal stromal cells in retinitis pigmentosa

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ABSTRACT

Introduction: Retinitis pigmentosa (RP) is a clinically and genetically heterogeneous group of hereditary disorders in which there is progressive loss of photoreceptors and pigment epithelial function culminating in complete vision loss. Unfortunately, given the disease's devastating effects, it is untreatable and there is often little that can be done to improve visual outcomes in these patients. The lack of curative intervention creates a challenge in the management of RP and its progression. As such, the main goal is to slow down the apoptosis and loss of photoreceptors in order to delay visual deterioration.

Materials and Methods: We present two case illustrations of RP treated with WJ-MSC implanted in the deep subtenon space. Each patient underwent 4 sessions ranging from 1 to 3 months apart.

Results: At 3, 6, 9 and 12 months follow-up, the following were observed:(i) Both patients had no change in visual acuity and no further deterioration in vision or visual field.(ii) Optical coherence tomography showed a layer of hyperreflective material noted at the IO/OS junction area suggestive of a layer of new photoreceptors. The changes were noted in the macula and extramacular region for both patients.(iii) Both patients reported better discernment of colors and better vision at certain times during the day. (iv) No systemic or ocular adverse events were observed in the 12 month follow-up following the subtenon implantation of WJ-MSC.

Conclusion: Subtenon implantation of WJ-MSC appears to be a feasible and safe option to consider in delaying the progression of retinal degeneration and improving the quality of life affected by visual deterioration in patients with RP.

KEYWORDS:
Mesenchymal Stem Cells, Retinitis Pigmentosa, Subtenon implantation

INTRODUCTION

Retinitis pigmentosa (RP) is a group of hereditary degenerative disorder associated with retinal dystrophy of photoreceptors and an important cause of severe vision impairment. The degeneration of photoreceptors in RP is usually associated with gene mutations which maybe inherited as autosomal recessive (50–60%), autosomal dominant (30–40 %), or X-linked recessive. It has a very variable clinical course, and in the initial stages, the disease involves the destruction of the rod photoreceptors causing loss of night vision and progressive peripheral visual field loss, leading to tunnel vision. Further progression to later stages results in degeneration of cones leading to loss of central and colour vision followed by blindness at age 40–50 years.[1,2]

Part of the difficulty in treating RP is its complex and diverse genetic aetiology. While there are several different supportive treatments available, including supplementation with vitamin A and omega-3 fatty acids, or usage of neurotrophic factors and antioxidants, these therapies have often been shown to be ineffective, failing to address the root cause of the disease.[3]

Gene therapy has begun to show promising results for improving visual outcomes, as evidenced by new clinical trials like the one used to secure Luxturna's approval However, there are still several important challenges for gene therapies including its severely limited therapeutic target and extremely high cost.[4]

Consequently, scientific interest is particularly directed at restoratory therapy based on stem cells. The latter aims to recover cell density as well as to preserve the remaining retinal cells by improving intra/extracellular conditions.[6,7]

Mesenchymal stem cells are multipotent stromal cells with self-renewal and multi-differentiation abilities into various mesenchymal tissues, most notably bone, cartilage and adipose. Studies have also described the ability of MSC to differentiate into retinal progenitor cells, photoreceptors and retina neural-like cells whilst exerting neuroprotective and pro-regenerative effects via multiple paracrine factors.[5]

Özmert and Arslan recently reported the results of an open label, phase III clinical trial (NCT04224207) with WJ-MSCs. In this study, WJ-MSCs were implanted in the sub-tenon space in 32 patients (64 eyes) diagnosed with RP. In the 6-month follow-up period, a significant improvement in mean best corrected visual acuity (BCVA), outer retinal thickness values, mf-ERG results, and a decrease in the visual field mean deviation value were observed.[8]

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The authors did not observe any severe ophthalmic or systemic complication thus assuring its safety. An improvement in light perception and vision was observed 1 week after the treatment and no serious side effects were seen during that period.[8]

MATERIALS AND METHODS

This clinical study included four eyes from two patients attending the ophthalmology clinic of Shah Alam Hospital between November 2020 and November 2021. The study followed the tenets of the Declaration of Helsinki. The patients were informed about the details, aims, and the course of the study. Written informed consent was obtained from each subject before any of the study procedures or examinations were performed. The diagnosis of RP was established depending on the clinical history, ophthalmological findings, visual field (VF) test, optical coherence tomography(OCT), and electroretinography (ERG) test results of the patients.

The inclusion criteria were as follows: 1) a clinical diagnosis of RP confirmed by clinical history, fundus appearance, VF, OCT, and ERG; 2) subjects older than 18 years of age; 3) subjects who are able to do a reliable VF evaluation; 4) subjects who have at least 1-yearfollow-up results.

Patients with previous ocular surgery other than cataract extraction, ocular media opacities that would make the image quality insufficient for ocular imaging or affect the test results, coexisting ocular disease (e.g. retinal pathology other than RP, glaucoma, uveitis, strabismus, nystagmus), any other systemic disease (e.g., diabetes, neurological diseases, hypertension) that would have an impact on the results were excluded from the study.

A single experienced vitreoretinal surgeon (AO) performed all the surgical procedures and ophthalmic evaluations. Baseline ophthalmic evaluation of the patients included BCVA, applanation tonometry, slit lamp biomicroscopy, color fundus photography, OCT, VF, and ERG. Visual acuity was evaluated by using a Snellen chart at a distance of 3 m. OCT was performed using the Optovue (Optovue Inc, USA) with a standardized scanning protocol. VF examination was performed by (the Threshold 30-2 Humphrey VFby HFAII750 device (Carl Zeiss Meditec AG, Germany). ERG (ERG-Vision monitor, Monpack 3, Metrovision, France) Readings were recorded from each eye according to the International Society for Clinical Electrophysiology of Vision(ISCEV) guideline . All tests were performed with the same instrument and by the same technician.

Preparation of umbilical cord Wharton's jelly-derived mesenchymal cell

The WJ-MSC used in both patients were isolated from Wharton's Jelly of the umbilical cord that was collected from the single donor with the mother's consent and treated as follows:

The umbilical cord initially immersed in cord preservative solution was washed with 0.9% sodium chloride injection and soaked with filtered 70/75% medical grade ethanol for disinfection. After rinsing with 0.9% sodium chloride injection and measured by clamping and stretching both ends with hemostats, it was cut into 2–3cm small pieces. The Wharton's jelly was weighed, cut, washed, and centrifuged before seeding for culturing process in complete culture media. The cultured tissues are incubated in the CO_2 incubator with the parameters of 37°C, 5.0% CO_2, and 95% relative humidity. All cell preparation and cultivation procedures were conducted by Beike 23 Century International Stem Cell Laboratory, an MOH cGMP/cGTP accredited facility.

Culture expanded cells were cryopreserved at P4 using standard cryopreservation protocols until their use . Cells are characterized at the time of cryopreservation with flow cytometric analysis according to FDA and ISCT guidance to determine the expression of positive surface markers for CD90, CD73, CD105, CD29, ad negative for CD45, CD34, CD79a, CD14, and HLA-DR. Quality control analyses were carried for the following: mycoplasma analysis according to Ph.Eur2.6.7; endotoxin analysis were performed according to Ph.Eur 2.6.14. Microbial limit testing according to US-6.1, Sterility testing according to USP 7.1.

The average cell viability was over 90% and each patient received 10–11 million cells in 1.5 ml of electrolyte solution per eye.

Injection of WJ-MSC

A total of 1.5 ml of WJ-MSC suspension was injected into the subtenon space of each eye. The procedure was conducted under local anaesthesia with proparacaine hydrochloride drops (Alcaine, Alcon , USA) under sterile conditions. Subtenon injection using a 25 G subtenon curved cannula (BD, Visitec, UK) into the supero-temporal region was used for effective delivery of the 1.5ml of WJ-MSC. Post-operatively,Guttae maxitrol (neomycin + dexamethasone) eye drops were given qid for 1 week, oral Ibuprofen 200 mg three times a day for one week, and amoxycillin clavulonate 500 mg four times a day for three days.

RESULTS

Case 1

A 65-year-old Malay man known case of RP for more than 25 years with no prior history of mesenchymal stem cell (MSC) treatment . The current condition of both eye vision affects his daily living activities (DLAs) and his business.

Pretreatment assessment were done including, visual acuity, anterior and posterior segment slit lamp examination, color fundus and specific investigational test such as Automated visual field test, electrophysiology (Full field ERG and multifocal ERG) and OCT.

His vision was 1/60 and CF 1' for the right and left eye, respectively. He has both IOL implanted and had normal intraocular pressure. Both fundi showed typical RP changes minimally sparing the macula area. The visual field revealed a very constricted field in both eyes. Full-field ERG was not able to perform, and multifocal ERG showed an extinguished response in all fiverings in both eyes. His OCT revealed loss of the photoreceptor layer in all segments of both eyes.

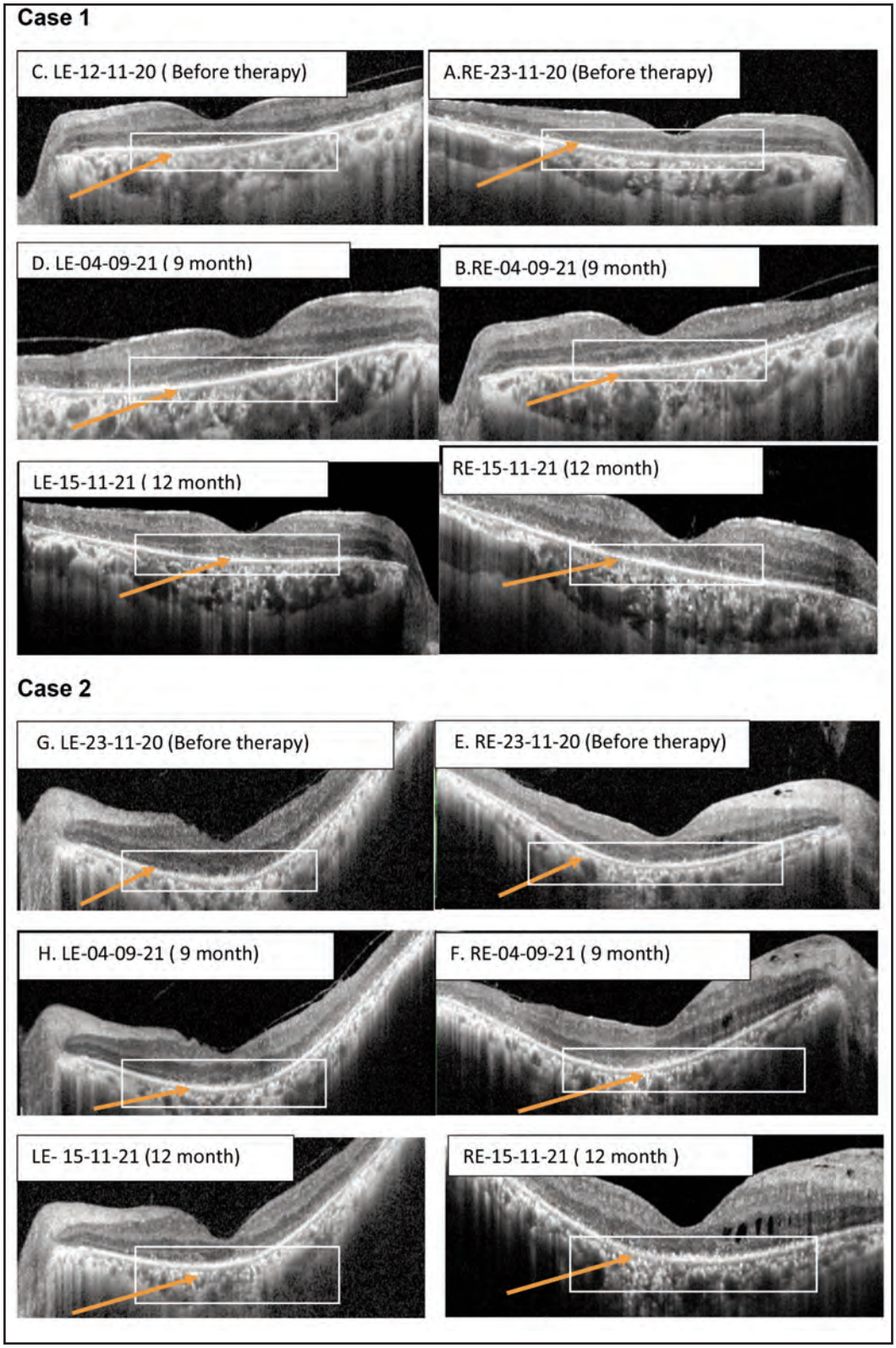

Fig. 1: OCT of Right Eye and Left Eye for both cases comparing the pre-treatment and 3rd and 4th post subtenon MSC implantations: (A,C &E,G): the OCT prior to MSC subtenon treatment- showing very minimal area of hyperreflectivity seen anterior to RPE layer.
(B,D& F,H): OCT after the 4th dose of MSC and post follow up at 9 and 12 month respectively; showing increased area of hyperreflectivity (orange arrow) at the interdigitation zone anterior to the RPE layer signifying possible regeneration of the outer segment of PRC.
The interdigitation zone is considered to be the contact cylinders formed by the apices of the RPE cells that encase part of the outer segment of the cones.

He underwent four sessions of WJ-MSC subtenon injection, which was carried out under aseptic technique. The injection interval was 4 weeks for the first three injections and 3 months for the fourth injection.

Post injection 9 months follow-up demonstrated no worsening in visual acuity charting and other slit lamp assessments. Subjectively patient reported ability to appreciate colors in more definite brightness and was also able to appreciate incoming vehicle while sitting at the passenger seat and able to read his handphone message much faster. The OCT findings noted an increase in hyperreflective material at the interdigitation zone layer of the photoreceptors cells (PRC) seen at the macula and extramacular region (Figure 1). After the third and fourth injection, a more definite hyperreflective layer can be seen on OCT. However, the central macula thickness did not show much increase in thickness.

Case 2
A 57-year-old Malay woman who was diagnosed with RP 20 years ago. She is currently coping with her job despite the progression of her tunnel vision which is gradually affecting her DLA. Her pretreatment assessment prior to WJ-MSC subtenon treatment revealed vision of 6/40 Ph 6/20 in the right eye (RE) and 6/30 Ph 6/20 in the left eye(LE). Both eyes had intraocular lens implanted and had normal intraocular pressure. Both fundi showed general RP changes with bony spicules, waxy pallor disc, and attenuated vessel in all four quadrants. Automated visual field showed bilateral grossly constricted field. Her ERG results were as expected,and revealed extinguished response in scotopic, photopic, and undetectable 30Hz flicker implicit time.

Her multifocal ERG response was reduced in all five rings in both eyes. OCT revealed the loss of PRC. She received a total of four sessions of subtenon MSC treatment with almost similar timing as case 1.

Post-treatment 9th and 12th month follow-up indicated her vision being maintained at 6/30 Ph 6/20 for both eyes. The OCT revealed a significant layer of photoreceptors with hyperreflective material at the interdigitation zone layer of the PRCs at macula and extramacular region(Figure 1).

Subjectively she claimed her vision is much clearer in the mornings, lasting a few hours until the afternoon. She was noted to be more confident and able to move faster at workplace as was observed by her staff and colleagues.

Post procedure, both patients received guttae maxitrol (neomycin + dexamethasone) four times a day for one week duration, T.Ibuprofen 200 mg three times a day for one week and T.amoxycillin 500 mg four times a day for three days to cover for the post-op inflammation and prevent infection.

DISCUSSION

Mesenchymal stem cells have been successfully isolated, cultured and expanded from several tissue sources including bone marrow, adipose tissue, amniotic membrane, dental pulp, umbilical cord blood and Wharton's jelly. They are considered as promising candidates for therapy to regenerate and repair degenerated retina cells in several retinal degenerative diseases.

In addition to this, it has been demonstrated in animal models that WJ-MSC can stimulate progenitor cells in the retina and elicit self repair mechanisms.[6] Such improvements could be largely due to the paracrine effects[7] of the implanted cells leading to a functional integration of grafted cells to substitute lost retinal photoreceptors or maintain their neuroprotective and neurotrophic effects to retain recipient functional photoreceptors.

For both of our cases, an increased area of hyperreflectivity demonstrated by OCT findings at the interdigitation zone layer of the PRCs was seen at the macula as well as extramacular region. This is likely attributed to the regeneration of the outer segment of the PRC which also coincided with subjective improvements in function as reported by both patients.

No further deterioration in visual acuity was observed and there were no serious adverse events or ophthalmic/systemic side effects reported during the 12 month follow-up.

To the best of our knowledge, there is no other clinical study in Malaysia using WJ-MSC application for RP. A similar study by Ozmert and Arslan from Ankara University , Turkey [9] reported efficacy and safety in their 6 month followup. We have followed up our cases for more than 12 months and thus far there is sustained improvement with no disease progression and with no adverse events demonstrating safety and efficacy of subtenon transplantation of WJ-MSC. However, long term followup is essential to evaluate the durability of the improved visual function and to determine when a booster treatment with WJ-MSC will be required.

CONCLUSION

We postulate that delivery of WJ-MSC by subtenon implantation in RP cases can induce repair and have significant immunomodulatory effects by inhibiting proinflammatory cytokines in the retinal microenvironment suppressing chronic inflammation and subsequent prevention of apoptosis.[5]

Although still far from routine clinical practice, regenerative stem cell-based therapies may become the standard means of treating severe retinal degeneration giving hope to those suffering from RP.

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Primary dysmenorrhoea among reproductive-age women at Kuala Selangor health clinic: Prevalence and factors associated

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ABSTRACT

Introduction: Primary dysmenorrhoea (PD) is a frequent gynaecological condition in adolescents and adult women worldwide, affecting their daily activity and leading to a lower quality of life. The purpose of this study is to determine the prevalence, severity, and factors associated with PD among reproductive-age women at Kuala Selangor Health Clinic.

Materials and Methods: This cross-sectional study used systematic random sampling at the Kuala Selangor Health Clinic from 3rd July to 29th September 2017. This study included 213 women between the age of 18 and 35 years old. The questionnaires consist of sociodemographic, lifestyle activities, and menstrual history components with Numerical Rating Scale (NRS) for menstrual pain as well as the Pictorial Blood Assessment Chart (PBAC) to quantify the blood loss during menstruation.

Results: A total of 210 women participated in this study with a response rate of 98.6%. The prevalence of PD was 60.5% with 13.4%, 75.6%, and 11.0% for mild, moderate, and severe in intensity, respectively. Nulliparous (OR: 5.1, CI: 1.508, 17.277, *p* = 0.009), first-degree family history of dysmenorrhoea (OR: 4.431, CI: 1.727, 11,368, *p* = 0.002), heavy menstrual blood flow (OR: 11.6, CI: 2.849, 47.53, p <0.001), and lack of regular physical exercise (OR: 14.037, CI: 5.161, 38.183, *p* < 0.001) were found as the significant association for PD. Meanwhile, having a short menstruation reduces the risk of PD during menstruation (OR: 0.04, CI: 0.004, 0.391, *p* = 0.006).

Conclusion: PD is prevalent among reproductive-age women. Physical exercise is a protective factor for PD, hence health care providers particularly those in primary care settings should regularly counsel and encourage women to be physically active.

KEYWORDS:
Primary dysmenorrhoea, reproductive-aged women, primary care, Malaysia

INTRODUCTION

Dysmenorrhoea is defined as pain during menstruation and is classified as either primary or secondary dysmenorrhoea (SD).[1] Primary dysmenorrhoea (PD) is a menstrual pain without any pelvic pathology that develops 1 or 2 years after menarche and can last up to 40 years. The pain is described as cramping or spasmodic located at the lower abdomen and radiating to the thigh's back or medial aspect. The pain started a few hours before or shortly after menstruation and lasted up to 48–72 h.[2] Secondary dysmenorrhoea is menstrual pain caused by an underlying gynaecological condition. The most common causes of SD are uterine fibroid, endometriosis, and adenomyosis.[1] The pain typically begins 1–2 weeks before menstruation and can last for a few days after menstruation has ceased.[1,2]

PD, which is more common than SD, has a significant impact on women's daily activities and quality of life. Studies have shown that PD causes work or school absenteeism,[3,4] limitations in social activities,[3-5] psychological disorders such as depression and anxiety,[6] and increased self medication.[4] The prevalence of PD ranges from 59 to 96 %[5,7–9] worldwide. In Malaysia, PD was found in 74–76% of adolescence[10,11] and 50–78% among university students.[3,12,13]

Several studies have found that some modifiable factors, including physical exercise and second hand smoker are significantly related to PD while other factors such as body mass index (BMI) and frequent fast food intake were not. Studies on the factors contributing to PD in Malaysia were limited to adolescent and university students with no studies conducted in the community. Previous local research found that race,[12] positive family history of dysmenorrhoea,[3,12] and lack of physical exercise[3] were all strongly linked with PD. However, Soe et al.[13] found a negative association between BMI, fast food intake, and physical exercise with PD.

In Malaysia, there are scarce studies on the factors contributing to PD, especially those not changeable. Other factors associated with PD, including occupation, parity, smoking, second-hand smoking, and attempting to lose weight, have yet to be studied in Malaysia. The purpose of this study was to determine the prevalence of PD among reproductive-age women, the severity of the disease, and the factors associated with PD.

MATERIALS AND METHODS

This was a cross-sectional study conducted from 3rd July 2017

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to 29th September 2017 at Kuala Selangor Health Clinic in Selangor, a state in Malaysia. The sampling frame was registered women with ages ranging from 18 to 35 years old who attended the out-patient clinic during the duration of the study. The inclusions criteria were reproductive-age women (18–35 years old) and understand the Malay language whereas participants who were pregnant, had a history of gynaecological diagnosis or surgery, had menstruation more than 6 months ago, presented to the clinic with an acute life-threatening illness, or had SD (exclusion by symptoms) were excluded from the study. Participants were asked if they had menstrual pain 1–2 weeks before menstruation and if it lasted until a few days after it stopped. If the response is yes, the participant was excluded because suspicious of SD.

A structured questionnaire in the Malay language was developed consisting of three sections namely sociodemographic, menstruation, and lifestyle. The first section covered socio-demographic characteristics such as age, race, occupation, parity status, and marital status. The second section of the questionnaire explored the participants' menstrual history, such as the age of menarche, regularity of menstrual cycle, blood loss during menstruation, duration of menstruation, and first-degree family history of dysmenorrhoea. Pictorial Blood Loss Assessment Chart (PBAC) was used to determine the blood loss during menstruation. The chart has been validated for menstrual blood loss[14-16] and reliable[15] with Cronbach α 0.7–0.8. The total scoring from the PBAC chart was categorised into > 100, 16–99, and < 15 for heavy, normal, and light menstrual blood loss, respectively. Participants were also asked whether they experienced PD with a yes or no format response. If the answer is yes, they need to answer the severity of the PD question using the Numerical Rating Scale (NRS). The tool was validated for measurement severity of pain for general acute pain[17] and reliable[18] with Cronbach α 0.8. The participant will rate their menstrual pain and the scoring of the marks of 1–3, 4–7, and 8–10 indicate mild, moderate, and severe in intensity, respectively. The third section of the questionnaires was used to determine the participants' BMI and their lifestyle activity such as smoking habits whether smoker, non-smoker, or second-hand smoker, regularity of practising physical exercise, frequent fast-food intake, and any attempt to lose weight. Height and weight were measured, and BMI was calculated during the interview. For the lifestyle questionnaire, the format answer was either yes or no. All the responses were self-reported by the participants.

The menstrual cycle was classified as regular if the participants had menstruation at regular intervals of 21–35 days from the last menstrual cycle.[19] For the duration of menstruation, less than 4 days, 4–8 days, and more than 8 days were categorized as short, regular, and prolonged duration, respectively.[20] Biological mother, sister, or twin was classified as first-degree family. A smoker is defined as who is currently smoking at least one tobacco product every day over a period > 1 month,[21,22] whereas a second-hand smoker is someone who is being exposed to another person's tobacco smoke (mainstream smoke and sidestream cigarette smoke) for at least 15 minutes every day on > 1 day/week.[23] BMI was calculated using the kg/m^2 formula, and the classification followed the Malaysia Ministry of Health.[24] Regular physical exercise was defined as a participant practising moderate-intensity physical exercise for more than 150 minutes per week or at least 75 minutes per week of high-intensity physical exercise.[25] The participant who took fast food more than once a month was categorized as frequent fast-food intake[26] meanwhile attempting to lose weight was defined whether the participant currently trying to lose weight in whatever method such as low carbohydrate diet, low-fat diet, low-calorie diet, consume slimming pills or supplements, involve in commercial slimming program, induced vomiting, or practising physical exercise.

Two Family Medicine Specialists performed content and face validity. Pretested among 30 women before the data collection was done at the same clinic. They were recruited using the same eligibility criteria with systematic random sampling one in four. Participants who were involved were included in the name list and were subsequently excluded during the actual data collection. No changes either questionnaire or flow of the study after the pretested research was done.

The sample size was calculated based on Pocock's formula with 80% power and significance level α at 0.05 with a 95% confidence interval. Based on the previous study,[9] 210 participants were required, with an estimated 90% eligibility and 80% response rate. After screening using eligibility criteria, participants were recruited using systematic random sampling one in four and were chosen according to the number series in the interval of 4 starting from number 3. The patient information sheet was given to the participant and written consent was obtained. The questionnaire was given to the participant and was using face to face interview method by the main researcher. Ten to fifteen minutes were required to complete the questionnaire. The completeness of the questionnaire was re-check at the end of the interview session. Completed questionnaires were stored in an envelope to maintain confidentiality. Participants with PD who had heavy menstrual bleeding were given an appointment in the outpatient clinic for further gynaecological assessment and examination.

The data were analyzed using Statistical Package for Social Sciences (SPSS) IBM version 22.0. A significant *p* value was set at <0.05 with a 95% confidence interval (CI). The characteristics of the participants, the prevalence of PD, and the severity of PD were described in descriptive analysis using percentages and frequency. Simple logistic regression (SLR) was used for univariate analysis. Significant independent factors associated with PD were included in multiple logistic regression (MLR) for further prediction contributing to PD. Multicollinearity was done before proceeding with MLR analysis, and the Hosmer–Lemeshow test was used to see the model's fit. The independent variables are age, race, parity, occupation, age of menarche, regularity of menstrual cycle, duration of menses, menstrual blood loss, family history of dysmenorrhoea, BMI, smoking, second-hand smoker, regularity of physical exercise, attempting to lose weight, and frequency of fast-food intake meanwhile the dependent variable is PD.

Table I: Sociodemographic, menstrual, and lifestyle characteristic of respondents (n = 210)

Variables	n	%	
Age (years)			Median:25.00
18–24	102	48.6	
25–29	56	26.6	
30–35	52	24.8	
Race			
Malay	134	63.8	
Chinese	10	4.8	
Indian	66	31.4	
Others	0	0	
Occupation			
Professional	27	12.9	
Non-Professional	111	52.9	
Unemployed	72	34.2	
Parity			
Nulliparous	144	68.6	
Parous	66	31.4	
Marital status			
Single	130	61.9	
Married	75	35.7	
Separated/divorce	5	2.4	
Age of menarche			
< 11 years old	33	15.7	
> 11 years old	177	84.3	
Menstrual cycle			
Regular	179	85.2	
Irregular	31	14.8	
Duration of menstruation			
Normal	189	90	
Short	12	5.7	
Prolong	9	4.3	
Menstrual blood loss (PBAC Scoring)			Median: 84.00
Normal	150	71.4	
Light	6	2.9	
Heavy	54	25.7	
Family history of dysmenorrhoea			
Yes	119	56.7	
No	91	43.3	
Body mass index (BMI)			
Normal	68	32.4	
Underweight	29	13.8	
Overweight	46	21.9	
Obese	67	31.9	
Smoking			
Yes	7	3.3	
No	203	203	
Second-hand smoker δ			
Yes	79	38.9	
No	124	68	
Regular physical exercise			
Yes	68	32.4	
No	142	67.6	
Frequent fast-food intake			
Yes	167	79.5	
No	43	20.5	
Attempting to lose weight			
Yes	81	38.6	
No	129	61.4	

δ= 203 respondents

Table II: The association between sociodemographic, menstrual, and lifestyle factors with PD among reproductive-age women (n=210)

Variables	No PD n (%)	PD n (%)	Crude OR (95% CI)	*p* value
Age (years)				
18–24	31 (30.4)	71 (69.6)	3.665 (1.82 - 7.38)	
25–29	20 (35.7)	36 (64.3)	2.880 (1.31 - 6.29)	
30–35	32 (61.5)	20 (38.5)	1	**0.001***
Race				
Chinese	7 (70%)	3 (30)	1	0.111
Indian	28 (42.4)	38 (57.6)	3.167 (0.75 - 13.33)	
Malay	48 (35.8)	86 (64.2)	3.181 (0.93 – 16.91)	
Occupation				
Professional	10 (37)	17 (63)	1	0.255
Non-Professional	39 (35.1)	72 (64.9)	1.086 (0.45 – 2.60)	
Unemployed	34 (47.2)	38 (52.8)	0.657 (0.26 – 1.63)	
Parity				
Nulliparous	43 (29.9)	101 (70.1)	3.614 (1.96 – 6.64)	
Parous	40 (60.6)	26 (39.4)	1	**< 0.001***
Age of menarche				
< 11 years old	10 (30.3)	23 (69.7)	1	0.241
> 11 years old	73 (41.2)	104 (58.8)	1.614 (0.72 – 3.59)	
Menstrual cycle				
Regular	65 (36.3)	114 (63.7)	2.428 (1.11 - 5.27)	**0.025***
Irregular	18 (58.1)	13 (41.9)	1	
Duration of menstruation				
Normal	72 (38.1)	117 (61.9)	1	**0.040***
Short	9 (75)	3 (25)	0.205 (0.054 - 0.78)	
Prolong	2 (22.2)	7 (77.8)	2.154 (0.43 - 10.65)	
Menstrual blood loss (PBAC Scoring)				
Normal	76 (50.7)	74 (49.3)	1	**< 0.001***
Light	4 (66.7)	2 (33.3)	0.514 (0.09 - 2.88)	
Heavy	3 (5.6)	51 (94.4)	17.459 (5.21 - 58.4)	
Family history of dysmenorrhoea				
Yes	27 (22.7)	92 (77.3)	5.452 (2.98 – 9.95)	**< 0.001***
No	56 (61.5)	35 (38.5)	1	
Body mass index (BMI)				
Normal	27 (39.7)	41 (60.3)	1	0.546
Underweight	8 (27.6)	21 (72.4)	1.729 (0.67 - 4.46)	
Overweight	20 (43.5)	26 (56.5)	0.856 (0.40 - 1.8)	
Obese	28 (41.8)	39 (58.2)	0.917 (0.46 - 1.8)	
Smoking				
Yes	2 (28.6)	5 (71.4)	1.660 (0.31 - 8.76)	
No	81 (39.9)	122 (60.1)	1	0.551
Second-hand smoker δ				
Yes	19 (24.1)	60 (75.9)	3.158 (1.69 - 5.89)	
No	62 (50)	62 (50)	1	**< 0.001***
Regular physical exercise				
Yes	51 (75)	17 (25)	1	**< 0.001***
No	32 (22.5)	110 (77.5)	10.312 (5.24 - 20.26)	
Frequent fast-food intake				
Yes	58 (34.7)	109 (65.3)	2.610 (1.31 - 5.17)	
No	25 (58.1)	18 (41.9)	1	**0.006***
Attempting to lose weight				
Yes	33 (40.7)	48 (59.3)	0.921 (0.52 - 1.62)	
No	50 (38.8)	79 (61.2)	1	0.775

1= Reference group. *= p <0.05 significance association. δ= 203 respondents. OR= Odds Ratio. CI= Confidence Interval.

RESULTS

Out of 210 women (98.6% response rate) who participated in this study, 127 (60.5%) of them have PD. Based on the NRS, among the PD group, 17 (13.4%), 96 (75.6%), and 14 (11%) had mild, moderate, and severe pain, respectively.

Sociodemographic, menstrual, and lifestyle characteristic

The median age of the participant was 25 years old. The majority of the participants were Malay (63.8%) followed by Indian (31.4%) and Chinese (4.8%). Most of them were nulliparous (68.6%). The median age of menarche in this study was 12 years old. Majority of the participants attained menarche at the age of >11 years old (84.3%), regular menstrual cycle (85.25%), and had normal menstrual blood flow (71.4%). For BMI, 13.8%, 32.4%, 21.9%, and 31.9% were underweight, normal weight, overweight and obese, respectively. Only 3.3% of the participants were found as smokers, whereas 38.9% were identified as second-hand

Table III: Multivariate analysis of independent factors associated with PD among reproductive-age women

Variables	Adjusted OR	95% CI		*p* value
		Lower	Upper	
Age (years)				
18–24	1.558	0.408	5.956	0.517
25–29	3.404	0.884	13.106	0.075
30–35	Ref			
Parity				
Nulliparous	5.104	1.508	17.277	**0.009***
Parous	Ref			
Menstrual cycle				
Regular	2.979	0.900	9.855	0.074
Irregular	Ref			
Duration of menstruation				
Normal	Ref			
Short	0.040	0.004	0.391	**0.006***
Prolong	0.283	0.023	3.535	0.327
Menstrual blood loss (PBAC Scoring)				
Normal	Ref			
Light	0.342	0.015	7.704	0.5
Heavy	11.636	2.849	47.533	**0.001***
Family history of dysmenorrhoea				
Yes	4.431	1.727	11.368	**0.002***
No	Ref			
Second-hand smoker				
Yes	1.961	0.741	5.187	0.175
No	Ref			
Regular physical exercise				
Yes	Ref			
No	14.037	5.161	38.183	**<0.001***
Frequent fast-food intake				
Yes	2.623	0.826	8.333	0.102
No	Ref			

Ref= Reference group. *= p <0.05 significance association. OR= Odds Ratio. CI= Confidence Interval
Hosmer and Lemeshow test suggested model good fit for data. $\chi 2 = 6.155$, p= 0.630
Cox and Snell $R^2 = 0.502$, Nagelkerke $R^2 = 0.679$

smokers, and many of them practice sedentary physical activity (67.6%) and frequent fast-food intake (79.5%). The findings are shown in Table I.

Factors Associated with PD

Univariate analysis using SLR found age, parity, family history of dysmenorrhoea, regularity, duration and menstrual blood loss, second-hand smoker, regular physical exercise, and frequent fast-food intake were significant factors associated with PD as shown in Table II. Further analysis using MLR found null parity, heavy menstruation, positive family history of dysmenorrhoea, and lack of regular physical exercise as the significant association for PD, which is shown in Table III. Women who had a short duration of menstruation were found lesser probability to have PD.

DISCUSSION

The prevalence of PD among reproductive-aged women at Kuala Selangor Health Clinic was 60.5% (n=127). When compared to the local research among university students,[3,12,13] the outcome prevalence of PD ranged from 50.9% to 78%. There is no comparable local study with a similar age group in the community setting to our investigation. However, in a survey conducted by Amini et al.[27] in a community setting in Indonesia, the prevalence of PD was 62.5%, which is not significantly different from our findings. Other studies were done in the community setting with similar age groups in South Korea,[28] Turkey,[29] and Iran[30] found that the PD prevalence is in the range of 58.8% to 63.6%.

Among our participants who had PD, three-quarters (75.6%) had moderate pain followed by mild (13.4%) and severe pain (11.0%). The findings were similar to those of local studies by Jaiprakash et al.[12] and Soe et al.[13] However, the researchers used different tools to determine the intensity of the pain, which is the Verbal Multidimensional Scoring System. Meanwhile, Shamsunarnie et al.[3] discovered disparities in pain assessment scores while using similar methods as in this study although majority of their participants had mild pain. The differences in pain perception could explain the findings and threshold among the subjects studied. Furthermore, pain perception is possibly influenced by the background, lifestyle, and culture of the women.[5]

This study discovered that parity is a significant factor leading to PD with nulliparous women are 5.1 times more likely to have the disease compared to the parous group. However, we are unable to compare our findings to those of local studies. However, our results were similar to previous studies by Heilemeskel et al.[9] and Patel et al.[31] in which nulliparous women are more likely to have PD. Multiparous women were assumed to be less prone to PD due to pudendal nerve compression and stretching during delivery, resulting in pelvic floor neuropathy.[32]

Heavy menstruation was found to be a significant factor contributing to PD. Our finding is consistent with Habibi et al.,[5] which also used PBAC as a tool to quantify menstrual blood loss. It was postulated that women with heavy menstruation had a high level of prostaglandin F2A and E2, which increased uterine activity and caused uterine hypoxia and pain.[33,34] Our findings contradict with a local study by Shamsunarnie et al.[3] although they did not specify the instruments for quantifying blood losses in their research. A first-degree family history of dysmenorrhoea was also discovered to be a risk factor for PD. The findings were consistent with those of other research conducted around the world.[3,5,7,9,12,35] They were seen to have a similar lifestyle since they stayed together[12] and they learned their behaviour in the family.[35]

Women with shorter menstruation were found to be lesser probability to have PD. The level of prostaglandin synthesis and release was low in women with brief menstrual cycles.[33] Our findings differ from Sahin et al.[7] who discovered no link between menstrual duration and PD. However, their definition of menstrual duration is different whereby less than 2 days, 2–7 days, and more than 7 days are considered short, regular, and prolonged menstruation, respectively.

Physical exercise was found to be a modifiable associated factor for PD. Women who do not exercise regularly are 14 times more likely to develop PD, and our findings are consistent with other studies.[3,36] Intervention studies by Ortiz et al.[37] and Mahvash et al.[38] found that regular physical exercise can lower the severity of PD and can even cure it. It was postulated that the endorphin hormone released during physical exercise could inhibit pain perception and improve mood among the exercisers.[38]

Other modifiable factors, such as second-hand smoking and frequent fast-food consumption, were unrelated to PD. Regarding second-hand smokers, the findings are different from those of Amini et al.[27] and Chen et al.[39] Both studies, however, did not define second-hand smokers clearly including the frequency and the duration of tobacco smoke in the surroundings. Even though more than three-quarters of our sample group consumed fast food regularly, we discovered no evidence of a link between this factor and PD. Our finding is matched with a local investigation by Soe et al.[13]

The impact of PD on the study population was not investigated in this study, which was regarded as a limitation of the study and suggested for future research. However, a previous local study discovered that PD has a significant impact on women's lives, such as class absenteeism and interfering with daily activities.[3]

STRENGTH AND LIMITATION

This is the first study of PD in a community setting among Malaysian women. This survey had a broader scope than the earlier local studies, which were more focused on adolescent and university students. Our findings revealed that PD is still a widespread issue among reproductive-aged women.

Our study has a few drawbacks. The findings of our study were unable to reflect reproductive-age women in Malaysia because our participants came from a single government primary health clinic in Malaysia, the majority of whom were Malay, and the location was in a semi-urban area. Thus, the generalization of the finding was limited. Besides that, the diagnosis of PD and SD was based on symptoms and was not supported by a gynaecological examination and ultrasound due to financial constraints. Furthermore, the participants in this study answered the question by self-reporting, which has a high possibility of recall bias.

It is recommended that in the future, large-scale research is to be conducted in a variety of settings such as a community setting or a primary care clinic as well as the impact of PD towards women. The findings will be more diverse and may be extrapolated to a larger population.

CONCLUSION

The prevalence of PD in this study was 60.5% and three-quarters of them (75.6%) reported having moderate pain. This study showed that null parity, positive family history of dysmenorrhoea, menorrhagia, and lack of exercise are the risk factors for PD. Meanwhile, it was discovered that having a short duration of menstruation was a protective factor. Therefore, health care providers, particularly those in primary care, should encourage women to engage in regular physical activity to reduce the prevalence and severity of PD.

ETHICAL APPROVAL

Approval was obtained from the National Medical Research Registry (NMRR-16-1832-32450), Medical Research & Ethics Committee of the Ministry of Health Malaysia (MREC), and Research & Ethics Committee of UPM (JKEUPM). All participants volunteered and gave their consent before taking part in this study.

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CONFLICT OF INTEREST

The authors involved in this study declare that there was no conflict of interest.

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ORIGINAL ARTICLE

Comparative study on the evaluation of patient's satisfaction on esophagogastroduodenoscopy and colonoscopy between a pre-filled and standard hand-written consent form in Hospital Kuala Lipis

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ABSTRACT

Introduction: Informed consent is the patient's self-determination authorization of a choice made by themself before any intervention is performed by the health care provider. It should be a structured process that includes the disclosure of relevant procedural information, benefit, risk, and other treatment option.

Materials and Methods: An open-label static group comparison experimental design was conducted in a single-centred study starting from April 2021 until January 2022 among patients who were going for OGDS and Colonoscopy at Hospital Kuala Lipis. The patients were stratified by 2-by-2 randomization to either the standard hand-written pre-filled consent forms. The satisfaction was assessed using Gastrointestinal Endoscopy Satisfaction Questionnaire version 2. The difference in the satisfaction was analyzed using multifactorial ANOVA.

Results: The percentage score of satisfaction on the endoscopic procedure using pre-filled was significantly higher than standard form consents (mean difference: 18.36 (95%CI: 14.15, 22.58)) and the effect size was large (partial ή = 0.399). The difference in percentage score of satisfaction was associated with gender (p = 0.003) and medical officers' years of working experience (p < 0.001).

Conclusion: The pre-filled consent form fulfils the ethical and legal aspects of the informed consent process and should be used in endoscopic and other invasive procedures in Malaysia. It is suggested that a formal training, exposure to course in communication skills, breaking bad news on patient consent among junior doctors need to be taken to improve patients' satisfaction of the endoscopic procedure to make them more satisfied.

KEYWORDS:
Patient's satisfaction, esophagogastroduodenoscopy, colonoscopy, pre-filled consent form, standard hand-written consent form

INTRODUCTION

Informed consent has evolved over the past decades from an ethical concept to a legal principle. It is constructed on the ethical principles of respecting patients' autonomy and self-determination to empower them in making their own decisions. Taking consent for any procedure is not just about taking signature from patients on the consent form, but it is a decision-making process involving a competent person who fully understands the procedure and the possible complication that may occur and makes a decision without coercion.[1] It also has a mutual connection and trusts in-between clinician and patient with patient's autonomy being the main concern. Furthermore, it is a legal duty of healthcare professionals to obtain valid consent from patients as required by the Malaysian Medical Council.[2] Material risks relevant to the patient should be informed for the patient to make an informed decision. The more risk of the procedure, the more disclosure of information must be done.[3] A valid and complete consent form must include the detail of the process of the procedure, associated risks, how the procedure will be performed, post-procedure management, and other alternative options. The information must also include any benefit, risk, and procedure limitation, any tissue sampling, image recording, and presence of a supervisor for the trainee to perform any invasive procedure.[4]

The consent form was introduced back in 1900 by Major Walter Reed for his clinical trial to search for the cause of yellow fever infection.[5] It was then legally decided in the courts in the case of *Mohr v Williams* [1905] 104 N.W. 12, *Pratt v Davis* [1906] 79 N.E. 562, *Rolater v Strain* [1913] 137P. 96 and *Schloendorff v Society of New York Hospital* [1914] 105 N.E. 92.[6] The principles of the judgement were for respecting patients' autonomy in making decisions. It also emphasizes the duty of healthcare professionals to give complete information regarding the procedure, which covers both the ethical and legal duties.[7] The consent documentation consists of two parts: the consent form and the patient information sheet. The content of these documents must be in layman terms

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without any medical jargon. It also must be complete, simple, and easy to understand.[1]

Endoscopy (esophagogastroduodenoscopy (OGDS) and colonoscopy) is a procedure in which the gastro-intestinal tract (GIT) is viewed through a lighted, flexible tube with a camera at the end (endoscope). The upper endoscopy is an inspection of the upper part of the GIT (from esophagus to small intestines) that can be viewed by a thin flexible tube inserted through mouth. Whereas the colonoscopy is an inspection of the entire large bowel (from the distal rectum to the cecum) that can be viewed by a flexible tube inserted through the rectum. OGDS and colonoscopy are the two endoscopic procedures that contain a pre-filled consent form, which is routinely being used in Ministry of Health (MOH) hospital. The standard form of consent, which is the older version of the informed consent form requires the doctor to concurrently explain and write all the detailed information before the patient signs it. There are possibilities that the information may be inadequately explained as the doctor may be rushing to complete all the procedures while filling up the consent form. The information might also be missed and below the professional standard. Besides, the information retention might also be affected by the person taking the consent itself.[8]

The information contained in the pre-filled consent form was created and validated by a group of experts in endoscopic procedures in the General Surgery fraternity, which included all the information necessary for these two procedures. There are a few reasons to support the use of a pre-filled consent form. Examples include the lack of experience and knowledge, especially in junior doctors taking consent, time constraints in government hospitals, missing important information, and lack of awareness on the importance of documentation in the consent form. These factors depict that a pre-filled consent form is better to gain patients' understanding and satisfaction.[9] Importantly, using a standard blank form consent form with the potential of lack of disclosure and information in the consent may lead to patients' misunderstanding and confusion regarding the procedure.[10] Inadequate information may also lead to patients' dissatisfaction if the outcome is not as expected.[3]

Medical negligence is a major challenge in several countries, including Malaysia.[11] It has been a significant concern in recent years, as the number of claims has risen in Malaysia. Issues with informed consent may have contributed to the rise in medical negligence cases in the country and worldwide.[12] Disclosure of information is a core component of informed consent[13] and should include material risks, other alternative options, and legal requirements of adequate information given to patients.[14] The major concern with information disclosure is that patients do not receive adequate information as they are supposed to.[15] These can lead to patients' poor understanding and knowledge regarding the procedure. More importantly, this may lead to medical litigations due to a lack of information during the informed consent process. The pre-filled consent form appears to fulfil the inadequacy of the standard consent form.

By using a pre-filled consent form, it will standardize the information given and minimize information retention.[8] It will also assist the doctor to disclose the information according to the professional standard as there is a significant variation of disclosure between junior and senior doctors.[9] This variation of disclosure was based on the person's experience and knowledge.[16] Therefore, this pre-filled consent will reduce the variability and insufficient information experienced in the standard hand-written form concerning legal disputes for poor documentation.

There is also a gap between the standard consent form and pre-filled consent in terms of the patient's satisfaction. Certain factors are associated with the satisfaction of both these pre-filled and standard hand-written consent forms, such as lack of experience and knowledge especially among junior doctors on taking consent, time constraints (especially in government hospitals), missing to include important information, and lack of awareness regarding the significance of documentation in the consent form. These factors indicate that a pre-filled consent form will improve the patient's understanding and satisfaction. The lack of disclosure and information in the consent may lead to patient misunderstanding and confusion regarding the procedure. Inadequate information may also lead to patient dissatisfaction if the outcome deviates from the original plan. Hence, this pre-filled consent form will improve patients' understanding and satisfaction with the informed consent process and the procedure. Therefore, this study was conducted to evaluate patients' satisfaction with the pre-filled consent form and standard hand-written consent form on the endoscopic procedure of OGDS and colonoscopy.

MATERIALS AND METHODS

An open-label static group comparison experimental design was conducted in a single-centred study starting from April 2021 until January 2022. The study population involved patients who were going for OGDS and colonoscopy at Hospital Kuala Lipis from November 2021 until January 2022. Screening of the patients was performed in an outpatient general surgical clinic. The eligible patients were identified and briefed about the research purpose and objectives. The patients were recruited only by the principal investigator to reduce the inter-reliability issue. The patients' information sheet containing brief information about the study and the procedure was given to the patients. Informed consent was obtained from the patients before starting the data collection. There was no blinding in this study.

Sampling Method

Simple random selection (SRS) was used to enroll patients from Hospital Kuala Lipis, who were scheduled for OGDS and colonoscopy. The patient was consented and met the eligibility criteria. The research continued the recruitment until the required sample size was attained.

Randomization

A stratified 2 by 2 block randomization was applied in this study. First, it was stratified into the method of endoscopy (OGDS and colonoscopy). Then 2 by 2 block randomization was applied to obtain an equal number of patients in each

group (group A: pre-filled and group B: standard hand-written (standard) consent forms).

Intervention
There were two consent forms used in this study:

1) *Standard Handwritten Consent Form*
   This consent form was used officially by the Ministry of Health, Malaysia. It has two pages. The first page was about the details of the patient's name, address, procedure and signature of the patient's or next of kin, healthcare provider, witness, and translator if needed. Meanwhile, the second page is about the procedure information. This page was intentionally left bank, requiring the healthcare provider to fill up this page before or while explaining to the patient. The patient or the next of kin was then required to sign both pages of the consent form.

2) *Pre-Filled Consent Form*
   This form was the same as the standard handwritten form with additional procedure names and detailed information, specific for a particular procedure. The healthcare provider must provide a detailed explanation before the patient or next of kin signs it.

The main framework of the standard handwritten and pre-filled consent form is the same as in a standard MOH consent form but both of these forms have a few differences. The main difference in the pre-filled consent form is that the information for the specific procedure has been written in the form compared to the standard handwritten form which is empty. The other difference is that the standard consent form can be used in all procedures; however, the pre-filled consent form has specific information based on the procedure. For example, the pre-filled consent form for endoscopy can be used only for endoscopy procedures, not for another type of invasive procedure.

Assessment
The outcome of this study was the patient's satisfaction score on the endoscopic procedure of the consent form. The score has been assessed using the Gastrointestinal Endoscopy Satisfaction Questionnaire (GESQ) version 2.17. It was developed by Hutchings, Cheung[17] with high internal consistency. It consists of 21 items with four domains, which are skills and hospital (seven items; Cronbach's $\alpha = 0.83$), pain and discomfort during and after endoscopy (four items; Cronbach's $\alpha = 0.84$), information before endoscopy (five items; Cronbach's $\alpha = 0.80$), and information after endoscopy (five items; Cronbach's $\alpha = 0.76$). Item 15 has a dichotomous option (yes and no), items 3, 13, and 14 are presented using 3-point Likert scales, whereas the remaining items have 5-point Likert scales. Eight items (items 1 to 8) were used to assess the patient's satisfaction. All items were assessed before the patients were discharged from the hospital in both groups. All the items were summed up and divided by the number of valid responses. The score was then transformed to the range 0–100 using the formula: ([score-lowest possible/score range] × 100).

For this analysis, the lower score depicts lower satisfaction. Notably, the score was calculated if the patient responded to at least 50% of the questions. If patients had completed fewer than 50% of the questions, it is considered missing. The approval to utilize the questionnaire, "Gastrointestinal Endoscopy Satisfaction Questionnaire" (GESQ), was obtained from the original author, Professor Hayley Hutchings on 5th May 2021 via official email: h.a.hutchings@swansea.ac.uk

Method of Data Collection
A face-to-face interview was employed for the assessment using GESQ. Five medical officers in General Surgery Department in Hospital Kuala Lipis were selected to collect the data. Their working experience ranged from 1 to 5 years, familiar enough with the procedure of endoscopy, assisted and performed many endoscopies guided by the specialist. A briefing on how to conduct the assessment has been done to reduce the inter-rater reliability among the interviewer.

Duration of Participation
The respondent was only approached once for this study, and the questionnaire took between 15 and 30 minutes to be completed.

Statistical Analysis
The collected data were initially entered into the Microsoft Excel (2019) spreadsheet and transferred to the Statistical Package for Social Sciences, version 24 for analysis. The descriptive statistics were presented using mean and standard deviation for normally distributed numerical data while either median and interquartile range were presented for non-normal distributed numerical data. Categorical data were presented in the form of absolute number and their corresponding percentages. The score of the satisfaction for the pre-filled and standard hand-written consent forms was presented using mean and standard deviation.

The comparison of the respondents' percentage satisfaction scores for the pre-filled and standard consent forms based on socio-demographic characteristics was analyzed using one-way ANOVA. The satisfaction score on the endoscopic procedure for the pre-filled and standard hand-written consent forms was compared using multifactorial analysis of covariance (MF-ANOVA) to adjust for other variables of interest such as type of procedure, patients' age, gender, race, education, occupation and experience of doctor taking the patient's consent.

Approval of The Study
This study was approved by the Medical Research & Ethics Committee, Ministry of Health Malaysia on 13 September 2021 (NMRR-21-1622-61046) and the Universiti Teknologi MARA Research Ethics Committee (REC/12/2021 MR/926).

RESULTS

A total of 156 patients were invited to this study. However, only 130 patients were involved in this study. Four patients declined to participate, whereas 22 had already had endoscopic procedures. The overall response rate was 85.5%. The characteristics of the patients who received the standard and pre-filled consent forms are shown in Table I.

Table I: The characteristics of the patients who received the Standard and Pre-filled consent forms

Variable	Consent Form		Total, N = 130, n (%)	*p* value[a]
	Prefilled, N = 65, n (%)	Standard, N = 65, n (%)		
Gender:				
Male	34 (52.3)	35 (53.9)	69 (53.1)	0.860
Female	31 (47.7)	30 (46.2)	62 (46.9)	
Race:				
Malay	29 (44.6)	28 (43.1)	57 (43.8)	0.971
Chinese	24 (36.9)	23 (35.4)	47 (36.2)	
Indian	9 (13.8)	11 (16.9)	20 (15.4)	
Orang Asli and others	3 (4.6)	3 (4.6)	6 (4.6)	
Age:				
Less than 40	15 (23.1)	13 (20.0)	28 (21.5)	0.303
40–59	35 (53.8)	29 (44.6)	64 (49.2)	
60 and above	15 (23.1)	23 (35.4)	38 (29.2)	
Educational level:				
Primary	10 (15.4)	9 (13.8)	19 (14.6)	0.086
Secondary	43 (66.2)	52 (80.0)	95 (73.1)	
Tertiary	12 (18.5)	4 (6.2)	16 (12.3)	
Occupation:				
Professional	10 (15.4)	4 (6.2)	14 (10.8)	0.176
Non-professional	23 (35.4)	26 (40.0)	49 (37.7)	
Not working	5 (7.7)	3 (4.6)	8 (6.2)	
Housewife	27 (41.5)	29 (44.6)	56 (43.1)	
Pensioner	0 (0.0)	3 (4.6)	3 (2.3)	
Procedure:				
OGDS	33 (50.8)	32 (49.2)	65 (50.0)	0.861
Colonoscopy	32 (49.2)	33 (50.8)	65 (50.0)	
Doctor's experience who assesses the patients				
Less than 1 year	14 (21.5)	17 (26.2)	31 (23.8)	0.136
1–2 years	15 (23.1)	18 (27.7)	33 (25.4)	
2–3 years	10 (15.4)	16 (24.6)	26 (20.0)	
More than 3 years	26 (40.0)	14 (21.5)	40 (30.8)	

[a]Variables with a $p < 0.05$ are considered significant. Statistical test: Chi-square test.

The majority of the respondents were male (53.1%), Malay (43.8%), aged between 40 and 59 years old (49.2%), having secondary educational qualification (73.1%), housewives (43.1%), and medical officers with working experience of 3 years and above (30.8%). An equal number and proportion of respondents were subjected to the OGDS and colonoscopy procedures. Among those who received the pre-filled consent form, most of them were males (52.3%), Malay (44.6%), aged between 40 and 59 years old (53.8%), having secondary education (40.0%), housewives (41.5%), having OGDS procedure (50.8%) and medical officers with working experience of 3 years and above (30.8%). Meanwhile, for those who received the standard consent form, the majority of them were males (53.9%), Malays (43.1%), aged between 40 and 59 years old (44.6%), having secondary education (80.0%), housewives (44.6%%), subjected to colonoscopy procedure (50.8%), and medical officers with 1–2 years working experience (27.7%). Comparisons between the socio-demographic characteristics of those who received the pre-filled and standard consent forms showed that none of the variables was statistically significant ($p > 0.05$). Thus, it can be concluded that both groups are comparable.

The respondents' mean percentage scores of satisfaction on the endoscopic procedure for the standard consent form was 70.15% ± 12.56 and for the pre-filled consent was 91.31% ±13.72. The comparison of percentage scores of satisfaction of the pre-filled and standard consent forms in between-group based on the respondents' socio-demographic characteristics are shown in Table II.

In the pre-filled consent form group, there were no statistically significant difference in the percentage score of satisfaction between gender ($p = 0.462$), race ($p = 0.114$), age group ($p = 0.627$), educational level ($p = 0.758$), occupation ($p = 0.655$), and procedure ($p = 0.604$). However, there was a statistically significant difference in the percentage score of satisfaction between years of medical officer's experience ($p < 0.001$). In the standard consent form group, there were no statistically significant difference in the percentage score of satisfaction between gender ($p = 0.497$), race ($p = 0.479$), age group (p$p = 0.983$), educational level ($p = 0.713$), occupation ($p = 0.229$), and procedure ($p = 0.495$). However, there was a statistically significant difference in the percentage score of satisfaction between years of medical officer's experience ($p = 0.004$).

The comparison of the percentage score of satisfaction on endoscopic procedure between standard and pre-filled consent form is shown in Table III while controlling for other variables (sex, age (in category), race, education level, occupation, procedure (OGDS and colonoscopy), and doctors' years of experience.

A significant difference in the percentage satisfaction score was observed between the pre-filled and standard consent

Table II: Comparisons of the respondents' percentage satisfaction scores for the pre-filled and standard consent forms based on socio-demographic characteristics

	Consent form					
	Pre-filled			Standard		
	N	Percentage score (Mean ± SD)	*p* value	N	Percentage score (Mean ± SD)	*p* value
Gender						
Male	34	92.43 ± 10.67	0.462	35	71.14 ± 14.70	0.497
Female	31	90.08 ± 14.72		30	69.00 ± 9.59	
Race						
Malay	29	91.03 ± 13.45	0.114	28	70.71 ± 13.52	0.479
Chinese	24	90.04 ± 13.08		23	69.56 ± 11.57	
Indian	9	97.78 ± 6.67		11	67.27 ± 10.09	
Others	3	77.78 ± 4.33		3	80.00 ± 20.00	
Age						
Less than 40	15	93.33 ± 9.75	0.627	13	70.39 ± 15.06	0.983
40–59	35	91.50 ± 14.07		29	69.83 ± 12.57	
60 and above	15	88.83 ± 12.35		23	70.44 ± 11.57	
Educational level						
Primary	10	89.25 ± 13.54	0.758	9	68.89 ± 14.53	0.713
Secondary	43	91.22 ± 13.40		52	70.00 ± 12.52	
Tertiary	12	93.33 ± 9.84		4	75.00 ± 10.00	
Occupation						
Professional	10	96.00 ± 8.43	0.655	4	70.00 ± 11.55	0.229
Non-Professional	23	90.00 ± 14.46		26	69.04 ± 14.97	
Not working	5	90.50 ± 9.42		3	86.67 ± 11.55	
Housewife	27	90.83 ± 13.13		29	69.83 ± 9.77	
Pensioner	0	-		3	66.67 ± 11.54	
Procedure						
OGDS	33	92.12 ± 11.11	0.604	32	69.96 ± 13.22	0.495
Colonoscopy	32	90.47 ± 14.31		33	71.21 ± 11.99	
Doctor's experience						
Less than 1 year	14	85.71 ± 16.51	<0.001*	17	62.35 ± 5.34	0.004*
1–2 years	15	86.83 ± 10.20		18	70.28 ± 12.18	
2–3 years	10	85.25 ± 15.74		16	71.25 ± 10.24	
More than 3 years	26	99.23 ± 3.92		14	78.21 ± 16.60	

Statistical test: one-way ANOVA.
*Statistically significant at $p < 0.05$.

Table III: Multivariate analysis of the percentage satisfaction score between respondents that received the pre-filled and standard consent forms

Source	Type III Sum of Squares	df	Mean Square	F	Sig.[b]	Partial Eta Squared	Observed Power
Corrected model	20454.815[a]	17	1203.224	9.269	<0.001*	0.585	1.000
Intercept	139321.939	1	139321.939	1073.310	<0.001*	0.906	1.000
Consent	9671.450	1	9671.450	74.507	<0.001*	0.399	1.000
Sex	628.919	1	628.919	4.845	0.030*	0.041	0.588
Age	11.006	3	3.669	0.028	0.762	0.001	0.052
Race	207.070	2	103.535	0.798	0.994	0.014	0.055
Education Level	705.155	4	176.289	1.358	0.453	0.046	0.183
Occupation	13.744	1	13.744	0.106	0253	0.001	0.412
Procedure	4884.477	3	1628.159	12.543	0.745	0.251	0.062
Doctor experience	70.907	2	35.453	0.273	<0.001*	0.005	1.000
Error	14538.262	112	129.806				
Total	882262.500	130					
Corrected Total	34993.077	129					

[a]R Squared = 0.585 (adjusted R squared = 0.521)
[b]Significant value is $p < 0.05$
[c]Mean difference of the score of satisfaction between-group: 18.36 (95% CI: 14.15, 22.58)
Statistical analysis: Multifactorial ANOVA (GLM).

Table IV: The comparison of the percentage satisfaction score between respondents that received the pre-filled and standard consent forms based on the significant findings

Variables	Percentage score (95%CI)	Mean difference [a] (95% CI)	*p* value [b]
Sex			
Male	86.35 (78.44, 94.26)	7.47	0.030
Female	78.88 (69.80, 87.95)	(0.73, 14.21)	
Doctor experience			
Less than 1 year	75.03 (66.82, 83.25)	Post hoc test	< 0.05
1–2 years	81.31 (72.81, 89.82)		
2–3 years	81.64 (72.59, 90.69)		
More than 3 years	92.47 (83.75, 99.98)		

[a]Based on estimated marginal means
[b]Adjustment for multiple comparisons: Bonferroni

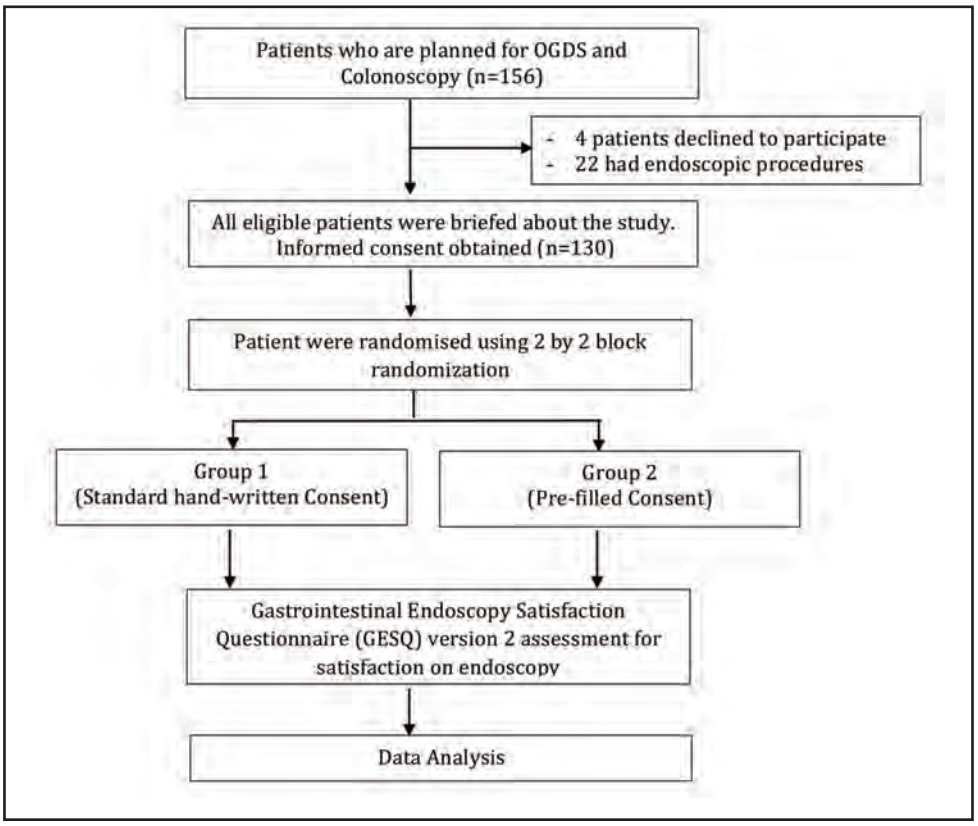

Fig. 1: Flowchart of the study

form groups (F (1,112) = 74.507, $p < 0.001$). The percentage score of satisfaction on the endoscopic procedure using pre-filled was higher than standard form consents (mean difference: 18.36 (95%CI: 14.15, 22.58)). The effect size was large (partial ή = 0.399) and the power was 100.0%. Additionally, two variables were also found to be significant: gender ($p = 0.030$) and years of medical officer's experience ($p < 0.001$). The difference in percentage score of satisfaction was associated with gender ($p = 0.003$) and medical officers' years of working experience ($p < 0.001$).

The comparison of the percentage of satisfaction on the endoscopic procedure between standard and pre-filled consent forms for the significant findings is shown in Table IV. There was a significant difference for the gender group ($p = 0.03$). The percentage satisfaction score of males was significantly higher than that of females (mean difference = 7.47; 95% confidence Interval [CI]: 0.73, 14.21). The medical officer with working experience of 3 years and above recorded a higher percentage satisfaction score compared to those with less than 1 year [mean difference = 17.44; 95% CI: 9.65, 25.23), $p < 0.001$], those with 1–2 years [mean difference = 11.16; 95% CI: 3.52, 18.80), $p = 0.001$], as well as respondents with 2–3 years working experience [mean difference = 10.83; 95% CI: 2.78, 18.89, $p = 0.003$].

In the comparison between unadjusted and adjusted analysis, the difference in the percentage satisfaction score

decreased from 21.15 (95% CI: 16.76, 25.54) to 18.36 (95% CI: 14.15, 22.58). Likewise, the effect size decreased from 41.6% to 39.9%. However, in terms of respondents' satisfaction, the impact of giving the pre-filed consent was large enough compared to administering a standard consent form.

DISCUSSION

In this study, the pre-filled consent form enhanced patients' satisfaction significantly when compared to the standard consent form ($p < 0.001$). Based on the socio-demographic characteristics, gender and the medical officer's years of working experience have a significant impact on patients' satisfaction with the pre-filled against standard consent forms.

It also showed that males had higher satisfaction scores compared to females ($p = 0.030$). It could be that the female patient required more information and explanation before they can be satisfied. The nature of females is that they will usually ask more questions than the male patient.[18] It also depends on the doctor's gender in giving the informed consent. On meta-analysis review done by Roteret al.[19] found that female doctors have better communication skills, disclose more information, and more engagement in between female patients. A study carried out by Wolosker et al.[20], found that there was no significant difference in a predicting factor for procedure satisfaction observed in both genders. However, few studies have reported that satisfaction may affect a gender if the procedure is executed by the same gender. For example, a female endoscopist working on a female patient[21] or in a single-gender environment where all the staff is of the same gender.[22] As the study only evaluated patient satisfaction based on validated GESQ questionnaire, other factors that influence patient's satisfaction, such as the language used when obtaining consent, the use of medical jargon, the patient's privacy when obtaining consent and the standardization of how doctors obtaining the consent, were not explored.

In this study, the medical officers' working experience had a significant impact on patient satisfaction with informed consent ($p < 0.001$). Studies have shown that patients are more satisfied when they are attended by an experienced doctor.[23] This is supported by a study conducted by Shiwani and Gosling[24] demonstrated that consent information differs depending on one's level of experience. Senior doctors usually will have better explanation in disclosing information while obtaining informed consent because of the experience they have in communication with patients which involves their role in paying full attention, listening, allowing questions, affirming concerns, a sense of shared responsibility, and trust than the junior doctors have.[25]

There was no statistical difference found for the race in both consent forms. A similar conclusion was also reached in a study by Spodik et al.[26] in the association between race and satisfaction in endoscopic procedures. The researchers concluded that there was no evidence of racial prejudice or a difference in cultural knowledge between the pre-filled and standard consent forms. The age group also found no significant difference in the satisfaction scores in both forms. However, previous studies showed that younger generations are more prone to feel unsatisfied with the informed consent forms than the older generations.[27] Borello et al.[28] reported that age has no effect on a patient's understanding and satisfaction concerning informed consent. The level of education also did not affect the difference in the satisfaction scores ($p = 0.453$). This result was consistent with a previous study in which education level did not influence patients' satisfaction with informed consent.[29] Additionally, a high educational degree is not predictive of effective health literacy.[30]

The patient should be informed before he or she decides, as those procedures may involve risks and complications that are unpredictable to the patient.[31] In addition, the patient may experience anxiety and mental symptoms, which is a natural human reaction when confronted with such life-or-death decisions.[32] The pre-filled consent form must contain complete information for patients to exercise their rights and autonomy according to their best interests. To justify a patient's autonomy in decision-making, the doctor must establish that the patient fully understands and acknowledge the consent completely. According to the study, patients failed to recall all of the information presented. Patients tended to be more focused on high expectations in the outcome rather than comprehension of other anticipated complications. Akkadet al.[33] demonstrated that most patients in their study interpreted consent as a legal and administrative necessity, not knowing that they had rights to other treatment options.

For a patient to decide, he must rely on the doctor who gives the information he believes. If the pre-filled informed consent is more structured with the complete information needed for the patient to decide, it will make the patient feel more secure and comfortable with the doctor. This also promotes the doctor to patient's relationship.[34] It will lead to firm decision-making without any hesitation and coercion. Also, the patient will be certain that his or her autonomy is secured from any form of abuse, deception, or mistreatment.[35] From the doctor's view, it will lead to a good impression and motivation to perform any procedure without hesitation. However, it might also lead to medical paternalism if the patient has too much trust in the doctor's decision. Informed consent can protect the patient from any harm and preserve confidentiality.[36]

It is necessary to consider a patient-specific approach when obtaining comprehensive informed consent. It integrates clinical and socio-cultural information about patients. Additionally, these approaches vary in terms of the complexity of the procedure. The riskier the procedure, the more complicated the informed consent process becomes. However, it should act as a guide on how informed consent should be obtained. By using the pre-filled consent form, all the standard information regarding the procedure will be available. This will make the informed consent process more systematic and comprehensive. Also, the pre-filled consent form should comply with MMC guidelines.[37] It includes the patient's capacity, the use of comprehensive language, voluntary participation without coercion, adequate time for discussion, the opportunity for a second opinion, and the presence of a witness or someone who can translate into the patient's native language.

The pre-filled consent form should comply with MMC guidelines[38] and may protect the doctor from liabilities in medical malpractice, provided the standard of care and duty of disclosure which is consistent with the acknowledged body of medical opinion and case law. Following the MMC consent guidelines 2016, under provision 12, all doctors are not authorised to get consent from patients unless they have the credentials and have been granted privileges by the head of the department.[37] This is to ensure that only qualified and experienced doctors have the authority to get permission and execute any operation. Consequently, it will safeguard the doctors from medical malpractice due to their competency in obtaining informed consent.

Experts across several subspecialties prepared it to standardise the inadequacy of consent processes in Malaysia. It also obligates the disclosure of information and warning of any particular material risk before obtaining consent.[38] No treatment can be performed without the patient's valid informed consent.[31] The disclosure should be made easy to enable the patient to make a final decision. Four preconditions are to be met before any doctor can take the consent include : i) the establishment of the doctor–patient relationship where the doctor who is performing any invasive procedure must meet the patient before the procedure; ii) all information regarding the nature of the procedure, benefit, alternative procedures, and complication must be explained to the patient; iii) the estimated duration of hospitalization must be made known to the patient, and iv) the prerequisite must be satisfied so that valid informed consent can be obtained from patients. Failing of any disclosure may be interpreted as a failure in the standard of care. This guideline also permits the use of any prepared information such as a pre-filled consent form for improved understanding and patient satisfaction on informed consent.

It is recommended to use the pre-filled consent form in other invasive procedures. The usage of this form can be forwarded to high authorities such as the Ministry of Health and Malaysian Medical Council so that it can be legally applied across Malaysia. Future studies could explore the satisfaction of doctors and the legal implications in using this pre-filled consent form, as well as assess if the information content is in line with the legal standard of informed consent.

Some limitations were found in this study. This study only focused on the pre-filled consent form for the endoscopy procedure as this procedure is routinely performed and easy to recruit the required number of participants. Other factors such as understanding and recalling information were not discussed. Secondly, the study was conducted using quantitative methodology only. It would be recommended to proceed with a qualitative approach to understand further the benefit of a pre-filled consent form.

CONCLUSION

The pre-filled consent form fulfills the ethical and legal aspects of the informed consent process and should be used as a standard consent form in endoscopic and other invasive procedures in Malaysia. It is suggested that a formal training, exposure to course in communication skills, breaking bad news on patient consent among junior doctors need to be taken to improve patients' satisfaction of the endoscopic procedure.

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CONFLICT OF INTEREST

All authors declare that there is no conflict of interest.

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Hospital healthcare utilisation among older adults admitted to a university hospital in the last months of life: A retrospective observational study

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ABSTRACT

Introduction: Health needs increase in older age. This translates into higher healthcare utilisation and expenditure compared to any other age group. Much of this is driven by frailty and multimorbidity. Many older people spend their last days in hospital. The aim of this study was to explore the utilisation of healthcare services among older adults admitted to a university hospital in the last 6 months of life.

Materials and methods: Patients aged 70 years and over who died on medical wards of a university hospital in 2019 were included based on a stratified sampling approach using three categories. The categories were which medical ward the patient was admitted under, ICD-10 reported cause of death, and gender. The proportion of patients distributed across all three categories was calculated and 200 patients out of 472 deaths in that year were randomly selected to ensure mirrored proportion distributed across these three categories. Data on demographics and healthcare utilisation were collected. Healthcare utilisation parameters included clinical encounters, radiological investigations, and medical procedures undergone.

Results: The median age was 83 years with more women (51%) than men. Septicaemia was the commonest cause of death (24.5%), followed by pulmonary disease (21.0%), and cardiovascular disease (19.5%). In the last 6 months before death, median inpatient stay was 9 days. The median number of Emergency Department and outpatient attendance was one episode, respectively, and number of radiology was four investigations. Over one-third of patients had multiple hospital admission. During the terminal admission, the median inpatient stay was 6 days. 45% had a nasogastric tube in-situ. Antibiotics used during the last 24 hours of life and polypharmacy (≥5 medications) were high at 74.5% and 82.5%, respectively. 7% of patients received cardiopulmonary resuscitation.

Conclusion: This study has provided descriptive evidence of hospital care delivered in the last months of life. The majority had contact with a healthcare team prior to their terminal admission. Many during their terminal admission had healthcare procedures, investigations, antibiotics, and issues of polypharmacy during this time. With an aging population, how care is organised and delivered is important in promoting good care in their later years.

KEYWORDS:
Aged, geriatric, hospital, end of life, palliative

INTRODUCTION

The health condition among older adults deteriorates with increasing age. This was much driven by multimorbidity and frailty.[1-3] This is associated with increased healthcare utilization.[3-5] In one study using Norway's public health registries which captures data for much of its entire population, those aged 65 and over utilised almost half of the total cost allocated to healthcare despite only representing 15% of the population.[5] This indicated that older people in this country accounted for the greatest amount of one country's healthcare costs.

Malaysia is seeing huge growth in its ageing population. The 60 years and over age group has seen the largest growth compared to any other age category.[6] In 2021, 7.4% of the population was aged 65 years and above, a rise from 7.0% the year before.[7] By 2040, it is estimated that this proportion will rise to 14.5%.[8] Additionally, the life expectancy at birth of the population has progressively increased and is now 73.2 years for men and 78.3 years for women.[9] With greater longevity comes higher morbidity and increasing use of healthcare services, which ultimately increases health expenditure.[10,11]

Studies have reported that a significant amount of hospital healthcare resources are consumed at the patient's end of life (EOL).[12] In the United States, up to 25% of the healthcare budget was spent on care in the last year of life.[13] This expenditure was on average at least five times higher than in other years of life.[14] Much of this was associated with care delivered within an acute healthcare setting.[13-15]

Over half of all deaths in Malaysia occur in hospitals.[16] However, how healthcare is utilised in hospital at the latter stage of life among older Malaysians has not been reported. This study aims to report on the utilisation of healthcare in hospital and the preceding 6 months of life among older people admitted to a university hospital in Malaysia.

MATERIALS AND METHODS

The retrospective observational study was conducted at an urban 1600-bedded university hospital. The hospital's

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Table I: Characteristics of patients (n=200)

Characteristics	Number (%)
Age (median, IQR) years	83 (9.0)
Gender	
Male	98 (49.0)
Female	102 (51.0)
Polypharmacy, n (%)[a]	165 (82.5)
Race (count, %)	
Malay	42 (21.0)
Chinese	126 (63.0)
Indian	25 (12.5)
Others	7 (3.5)
Cause of death	
Cerebrovascular accident	11 (5.5)
Cardiovascular disease	39 (19.5)
Pulmonary disease	42 (21.0)
Sepsis	49 (24.5)
Malignancy	39 (19.5)
Gastrointestinal/hepatic disease	7 (3.5)
Others[b]	13 (6.5)

[a]Polypharmacy, ≥5 medication
[b]Advanced renal failure, advanced dementia/ parkinsonism, abdominal aortic aneurysm rupture.

Table II: Healthcare utilisation during the terminal admission

	Total (n = 200)
Inpatient bed days, median (IQR)	6 (8.0)
Radiological studies during admission, median (IQR)a	3 (2.0)
Procedures during terminal admission, n (%)	
Nasogastric tube	91 (45.5)
Central venous catheter	9 (4.5)
Intercostal drain insertion	3 (1.5)
Non-invasive ventilation	44 (22.0)
Invasive mechanical ventilation	12 (6.0)
Antibiotics in the last 24 hours, n (%)	149 (74.5)
Specialist palliative care consultations (n, %)	43 (21.5)
Cardiopulmonary resuscitation, n (%)	14 (7.0%)

[a]Plain radiographs, ultrasound, computerised tomography, magnetic resonance imaging, dual energy x-ray absorptiometry, or positron emission tomography

medical records department provided a list of all deceased inpatients aged 70 years and over from 1 January 2019 to 31 December 2019 who died in any medical ward.

Data on patient demographics and healthcare utilisation were collected during the terminal hospital admission as well as the preceding 6 months using hospital electronic health records. Healthcare utilisation parameters included clinical encounters (inpatient bed days, emergency department (ED) attendances, and outpatient visits), radiological investigations (plain radiographs, ultrasound, computerised tomography, magnetic resonance imaging, dual energy X-ray absorptiometry and positron emission tomography), and medical procedures underwent (nasogastric tube, central venous catheter, chest tube insertion, non-invasive, and invasive mechanical ventilation). Data on EOL care delivered (deprescribing, antibiotic use, symptom-relieving medication, and specialist palliative consultation) were also collected. Polypharmacy was defined as ≥ 5 medications.[17] Non-beneficial medication use that should be considered for deprescribing was based on previously reported research studies.[18-21] These medications included statins,[18,20] vitamins, and mineral supplements.[21] Cause of death was based on the ICD-10 recorded cause by the Medical Records Department.

Over the study period, 472 patients passed away on the medical wards. A sample of 200 patients, representing 42.4% of total deaths provided a 95% confidence interval for a proportion of ±8.9%, a value deemed acceptable to meet the aim of this study with the resource available. The sample was selected via a two-step process. Firstly, the study population was stratified into three categories based on the medical wards the patient was admitted under (clinical team overseeing care), ICD-10 reported cause of death, and gender. The proportion of patients distributed across all three categories was calculated. Next, 200 participants were then selected randomly using Microsoft Excel RAND function to ensure equal proportion distributed based on what was calculated in the previous step. This process would have minimised selection bias for the patients included in this study. For example, if out of all the 472 deaths consisted of 10% of patients who were male that died due to sepsis on the geriatric medicine ward, then of the 200 participants in this study's cohort, 10% (20 patients selected at random) would mirror this criteria. Data were also collected by a single researcher using an agreed data collection tool which would have minimised any data extraction bias during this stage.

Findings were presented as numbers and percentages for categorical data and either median with interquartile range (IQR) or mean with standard deviation (SD) based on the parametric distribution of the data using Kolmogorov-Smirnov test. Missing values will be regarded as missing, and analysis will be performed on available data. All analyses were performed using SPSS version 26. This study received ethics approval from local Medical Research Ethics Committee (reference number: 2020525-8673).

RESULTS

Among the 200 patients, the majority were female and of Chinese ethnicity, and participants had a median (IQR) age of 83 (9) years (Table I).

During the terminal hospital admission, the median (IQR) number of hospital bed days was 6 (8) days. During the last 24 hours, patients were still on a median (IQR) of 8 (5) drugs. Many remained on vitamin and mineral supplementation (97/200 patients, 48.5%) and lipid-lowering therapy (70/200 patients, 35.0%). Table II summarises the key aspects of healthcare utilisation during the terminal admission.

In the preceding 6 months, the median (IQR) number of emergency department presentation and outpatient visits was 1 (1.0) episode, respectively. 72/200 patients (36%) had another hospital admission in the preceding 6 months, spending a median (IQR) of 9 (11) days. Five patients received specialist palliative input prior to their terminal admission.

DISCUSSION

This study has reported on the pattern of hospital healthcare utilisation by those aged over 70 who died in a Malaysian university hospital. More than half of the deceased spent at least 9 days in hospital and had either one emergency or outpatient visit in the preceding 6 months. Over one-third had also been admitted previously, spending almost 2 weeks in hospital. Most of them required radiological investigations, invasive procedures, antibiotics and had multiple medications that were continued up till the time of their death, some of which were non-beneficial.

This is the first study looking into healthcare utilisation among older adults in the last 6 months of life in the Malaysian hospital setting. The data reported represent those who passed away in the Department of Medicine, as participants were recruited across the different medical subspecialties. The stratified sampling method was followed by a randomised selection and minimised possible selection bias. The sample was also as representative as possible of all those aged 70 years and above that passed away in 2019. By extrapolating this study's sample to the total 472 patients that died in that year, it is possible to estimate that the overall healthcare utilisation by this older group of patients would be over 4200 inpatient bed days, 470 outpatient visits, 1800 radiological tests, and 210 nasogastric tube insertions.

However, there were limitations associated with this study. Important factors that could have influenced healthcare utilisation were not analysed, such as frailty, disability morbidity, and illness severity. This would support targeting attention on factors associated with either high or low healthcare utilisation. Actual healthcare cost was not calculated and should feature in future studies. Additionally, this study's findings were from a single urban hospital which limits its generalisability to other setting. Malaysia's healthcare system consists of both public and privately funded healthcare providers delivered across urban and rural areas at the primary, secondary, and tertiary levels. Additionally, by its retrospective design, data accuracy, and reliability were entirely dependent on clinical notes and records obtained from the hospital electronic health record system. The accuracy of the ICD-10 coded cause of death provided by medical records may not necessarily reflect the true cause of death as these would often be entered by non-clinical coders. Death may also be a result of multiple factors yet only described as a single cause in death certificates and the coding system. Other aspects of healthcare usage such as blood investigations, oxygen tubing, and dressings, for example, were also not captured within this study. This study was also unable to conclude if the healthcare utilised was deemed appropriate or not. Foreseeable deaths due to underlying chronic illnesses and sudden, unexpected deaths will be treated very differently. Moreover, as data were limited to this hospital's electronic medical records, this study was unable to comment on the healthcare utilisation that could have been accessed in other healthcare facilities.

High healthcare utilisation among older people in hospital in the last year of life has previously been reported.[13] In this study, several medical procedures and treatments contributed to the overall healthcare utilisation. Almost half of the patients had a nasogastric tube in-situ during the terminal admission. This echoes findings from a study done previously in this same hospital.[22] Bypassing the swallowing mechanism and delivering food directly into the stomach tends to be the typical approach in people with swallowing difficulties, or with poor oral intake due to either an acute or chronic illness. However, this carries problems such as aspiration pneumonia, diarrhoea, and local trauma.[23,24] Hence, whether nasogastric tube insertion and feeding should be done requires an individualised approach, an awareness of local cultural context and supported by clinical frameworks.[25-27] Besides that, 28% of the patients required ventilatory support with either non-invasive or invasive mechanical ventilation during the last 6 months of life. Supported ventilation, similar to nasogastric tube feeding, also requires an individualised decision-making process to balance the goals of care and risk-benefit in the context of one's overall prognosis. Both procedures require trained personnel to initiate and monitor the care delivered.

This study also demonstrated that almost three-quarters of all patients received antibiotics up till the last 24 hours of life. Such high usage has also been described in other cohorts.[28] Infection is common and represents the terminal event in chronic conditions, such as dementia and frailty.[29,30] Antibiotics have been reported to be frequently prescribed empirically in end-of-life care situations based on signs and symptoms without confirmatory imaging studies or laboratory tests.[31,32] This study only reported whether patients were receiving antibiotics and did not explore the indication

or appropriateness for the treatment. There is a fine balance between active treatment which may still be beneficial for a reversible illness that entails a burden of treatment, against maximising comfort and minimising aggressive interventions for the dying.

Polypharmacy towards the end of life was a significant finding. Many older adults would have chronic illnesses necessitating the need for a number of medications.33 However, as the chronic disease progresses towards its terminal stages, or when there is an irreversible acute illness, deprescribing needs to be part of the person's care. Guidance on prescribing and deprescribing in older people such as STOPP/START and Beers criteria, as well as those more specific to palliative care to support deprescribing in end of life can support more person-centred prescribing.[34-37] Prescribing focus towards the end of life should be on anything that relieves distressing symptoms, provide comfort and optimise quality of life.

This study was not meant to determine if the healthcare utilisation was appropriate and beneficial or not. Clinicians work in a challenging environment to ensure that healthcare is delivered in the patient's best interest, i.e. to reverse what is reversible and to provide comfort when it is irreversible. Many of the patients included in this study did have a healthcare contact prior to their terminal hospital admission. Although each healthcare contact could be for very different reasons, it may also be possible that they were for a similar condition to their eventual hospital admission. The high overall healthcare use than could be a sign of chronic disease progression. Thus, each healthcare contact may represent an opportunity to consider how future care should be directed and individualised for the patient in the form of advance care planning (ACP).[38] ACP can set clear goals and care plans which could include decisions on artificial hydration and nutrition, preferred place of death, medication appropriateness, ceilings of treatment, and the extent of investigations.

This study has set the scene on what happens towards the end of life among older adults admitted to hospital. Further research to understand how healthcare decisions are made at this stage would provide insight into what clinicians deemed appropriate and how that decision was made. Besides that, risk stratification to determine characteristics and factors associated with high healthcare usage would allow clinician and stakeholders to focus efforts to better support care during this vulnerable period. A better understanding of this would allow better organisation of care and the delivery of high-quality end-of-life care services to address the healthcare needs of an expanding aging population. There is an emerging evidence that within our local context factors such as frailty and care need requirements were associated with higher healthcare utilisation.[11,39] Further work needs to build on this to provide a clearer picture that is relevant to our local healthcare system.

CONCLUSION

This study has reported on the hospital healthcare utilisation among older adults admitted to hospital in the preceding 6 months before their passing. The majority had contact with a healthcare team prior to their terminal admission. During their terminal admission, many had healthcare procedures, investigations, antibiotics used, and issues of polypharmacy during this time. With an aging population, how care is organised and delivered is important in promoting good care in their later years.

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ORIGINAL ARTICLE

A quality improvement project: Reducing bloodstream infection by improving adherence to the care bundle of peripheral vascular catheters at the COVID-19 treatment centre

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ABSTRACT

Introduction: During the COVID-19 pandemic, bloodstream infection (BSI) rates were substantially rising in Sungai Buloh Hospital (HSB). It is believed that the COVID-19 pandemic has had an adverse impact on BSI incidence caused by contaminated periphery vascular catheters (PVCs). The study's objective is to reduce the BSI rates in HSB by improving adherence to the PVC care bundle via the Plan-Do-Study-Act (PDSA) approach.

Materials and Methods: A quality improvement (QI) project was employed over four months, from June to September 2021, during the COVID-19 pandemic in HSB. All adults hospitalised for COVID-19 with intravenous lines were subjected to data collection. A baseline audit was conducted to study BSI incidence from April to May 2021. Implementation was carried out by PDSA cycles and data on BSI rates per 100 admissions was described using a monthly run chart.

Results: At baseline, the BSI rate per 100 admissions was 5.44 before implementing our QI project. Initial changes via PDSA cycles did not bring significant improvements to BSI rates and a rising trend in BSI rates was observed after two PDSA cycles. Further audits identified the problem of non-compliance with the practice of aseptic non-touch technique (ANTT) and a lack of effective leadership in implementing the PVC care bundle. The third PDSA cycle focused on adopting practical leadership skills among senior clinicians to ensure compliance with the prevention bundle and to encourage the use of ultrasound guidance for difficult line insertion. After the third PDSA cycle, the BSI rate per 100 admissions was reduced from 6.41 to 4.34 ($p < 0.05$). The BSI rates continued to decline down the line for another five months.

Conclusion: Through QI initiatives, the risk of BSI can be significantly reduced.

KEYWORDS:
COVID-19, BSI, PDSA, QI

INTRODUCTION

With the global emergence of COVID-19, Sungai Buloh Hospital became the main COVID-19 treating centre in the Klang Valley from January 2020 onwards. Of note, all wards in HSB [including all general wards, intensive care unit (ICU), day care unit, day-care surgery unit, casualty ward, and the old hospital extension (also known as the *"Pusat Kawalan Kusta Negara"* (PKKN) (National Leprosy Centre)] were expanded to accommodate the sharp increase in the daily intake of patients with COVID-19. To meet the high demand for critically ill COVID-19 patients desperately requiring intensive care beds, critical care services in the ICU setting were augmented in the cardiac care unit, burn unit, and operation theatre. In general wards and ICU, the ratio of healthcare worker to patients was 1:6 and 1:1, respectively. The cohort of patients hospitalised to HSB were mainly the laboratory-confirmed COVID-19 cases with severe pneumonia and those with a high risk of potential deterioration.

In general, inpatient care often requires peripheral vascular catheters (PVCs) for intravenous (IV) administration of fluids, medications, blood products, or contrast media. However, PVCs may come with undesirable complications, such as phlebitis, catheter-related bloodstream infection (BSI), and extravasation leading to cellulitis or abscess formation. As COVID-19 cases surged daily in 2021 and with healthcare systems stretched by the COVID-19 pandemic, there was also a gradual surge of BSI. As experienced by other centres during this unprecedented period, BSI became a global issue due to the adverse impacts caused by the COVID-19 pandemic.[1-3] The severity of COVID-19 infection, prolonged hospital stays, use of steroids or immunomodulators, and a lack of adherence to infection control (IC) practices have contributed to a higher rate of nosocomial BSI and contaminated blood cultures.[4] Interestingly, BSI incidence was reported to be significantly higher in hospitalised individuals with COVID-19 compared with those without COVID-19.[4]

The BSI is suspected when one or more pathogens are obtained from cultured blood samples, possibly related to peripheral or central lines.[5] Having implemented a QI project using the Plan-Do-Study-Act (PDSA) approach, there was an improvement in adherence to care bundle targeted to reduce venous catheter-related BSI,[6] followed by improved BSI rates.[7] The main concepts in QI include: educating relevant staff on adherence to the PVC care bundle, developing measures to improve compliance with the bundle, plotting outcome data

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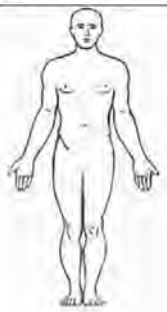
Table I: The assessment form of PVC care bundle used in HSB

Peripheral Vascular Catheter, PVC Daily Assessment	Name: Age: IC: MRN: Diagnosis: Comorbidity: ☐Stroke ☐CCF ☐ESRF ☐CA ☐RVD
Date of Admission:	Date of Insertion:
Size of PVC	☐ Blue (22G) ☐ Pink (20G) ☐ Green (18G) ☐ Grey (16G)
Reason of Insertion ☐ Transfusion	☐ Fluid ☐ TPN ☐ Intravenous medication(s) ☐ Others (SPECIFY) :
Site of Insertion (Circle "R", right or "L", left) ☐ Hand R / L ☐ Wrist R / L ☐ Forearm R / L ☐ Antecubital fossa R / L ☐ Others (SPECIFY) :	 PLEASE MARK THE SITE OF INSERTION WITH CIRCLE(s)
Reason of removal ☐ No longer required ☐ Poorly complied with HII* ☐ VIP** ⩾ 2 ☐ Others (SPECIFY) :	

INSERTION DATE	D1 (Date:)	D2 (Date:)	D3 (Date:)	D4 (Date:)
VIP score				
REMOVED (Y/N)				

HIGH-IMPACT INTERVENTION, HII of PVC*

1. Hand hygiene (hand washing before and after assessing PVC, with hand gloves).
2. Skin cleaning with 2% chlorhexidine or 70% alcohol.
3. Using sterile, transparent dressing. The dressing should be immediately changed if it is soiled or loose.
4. Recording PVC on the assessment form and medical record.
5. Scrub the hub with a 70% alcohol swab while using PVC.
6. Daily assessment of PVC (aseptic non-touch technique) with the visual infusion phlebitis (VIP) tool. Remove the PVC if one of the indications as stated above is fulfilled.

Visual infusion phlebitis score, VIP**

Score	**0** Absent	**1** 1 of following	**2** 2 of following	**3** > 2 of following
Pain	No	slight near IV site	pain near IV site	pain along cannula path
IV site	Healthy	Slight redness near intravenous site	Erythema swelling	Erythema induration
Venous cord	Not palpable	Not palpable	Not palpable	Palpable
Result	No phlebitis	Possible phlebitis	Early phlebitis	Medium stage of phlebitis
Action	Observe PVC	Observe PVC	Re-site PVC	Re-site PVC Consider antibiotics

CA, cancer; CCF, congestive cardiac failure; D, day; ESRF, end stage renal failure; G, gauge; HII, high-impact intervention; IC, identification card; IV, intravenous; PVC, peripheral vascular catheter; RVD, retroviral disease; TPN, total parenteral nutrition; VIP, visual infusion phlebitis; Y/N, yes/no

Table II: The PDSA cycles executed from June to September 2021 in HSB

	First PDSA cycle (June–July 2021)	Second PDSA cycle (July–August 2021)	Third PDSA cycle (August–September 2021)
PLAN	To promote hand hygiene and create a safe work environment in the setting of isolation wards, in line with the guidelines established by the Ministry of Health	To reintroduce the concept of PVC care bundle to healthcare workers	To promote the adoption of a good leadership style among senior healthcare providers in executing the PVC care bundle
DO	1. To emphasise the importance of adherence to the PVC care bundle by routinely using the PVC care checklist (Table I) for every individual on PVC. 2. To promote hand hygiene and avoid reusing, decontaminating, or utilising single-use medical gloves for an extended period 3. To prepare each cubicle of isolation wards with hand hygiene devices and instrument trolleys equipped with a complete set of tools essential for effective cannulation under the ANTT technique.	1. To educate care providers on the PVC care bundle via video presentations, pictorial guidelines, and posters. 2. To promote compliance with the checklist of PVC care bundle through the teaching materials	1. To encourage senior clinicians to act as role models in implementing strict PVC care bundle. 2. A set of standard questions was developed to help senior clinicians supervise the junior doctors and nurses during the ward round (Table III). 3. To encourage senior clinicians to assist junior doctors with difficult line placement using ultrasound guidance
STUDY	All wards, including ETD and ICU, were supplied with instrument trolleys. However, the qualitative experience revealed that most healthcare providers, especially junior doctors and nurses, were unsure how to execute an effective ANTT.	The BSI rates remained unsuppressed. In addition, qualitative experience revealed that full compliance with the PVC care bundle was still not achieved due to the new staff entry and a lack of supervision.	A reduction in the BSI rates was achieved. Adherence to PVC care bundle was sustained.
ACT	We proceeded with the implementation of the next PDSA.	The next PDSA cycle was discussed and executed.	Regular audits were continued.

Table III: Relevant questions for leaders to evaluate the PVC care during ward round during the third PDSA cycle

1. How many intravenous cannulas are there at a given time?
2. Where is the intravenous cannula site?
3. Why is the intravenous cannula required?
4. Does the healthcare provider practise ANTT during the procedure?
5. Does the healthcare provider do daily inspection, cleaning/scrubbing hubs, and dressing on the patient's intravenous cannula?
6. Have any complications from intravenous cannula arisen?

over the study period, and studying the effectiveness of these interventions. We aimed to reduce the BSI rates over four months by addressing flawed IC practices and improving compliance with the ANTT in maintaining PVCs among patients admitted for COVID-19.

MATERIALS AND METHODS

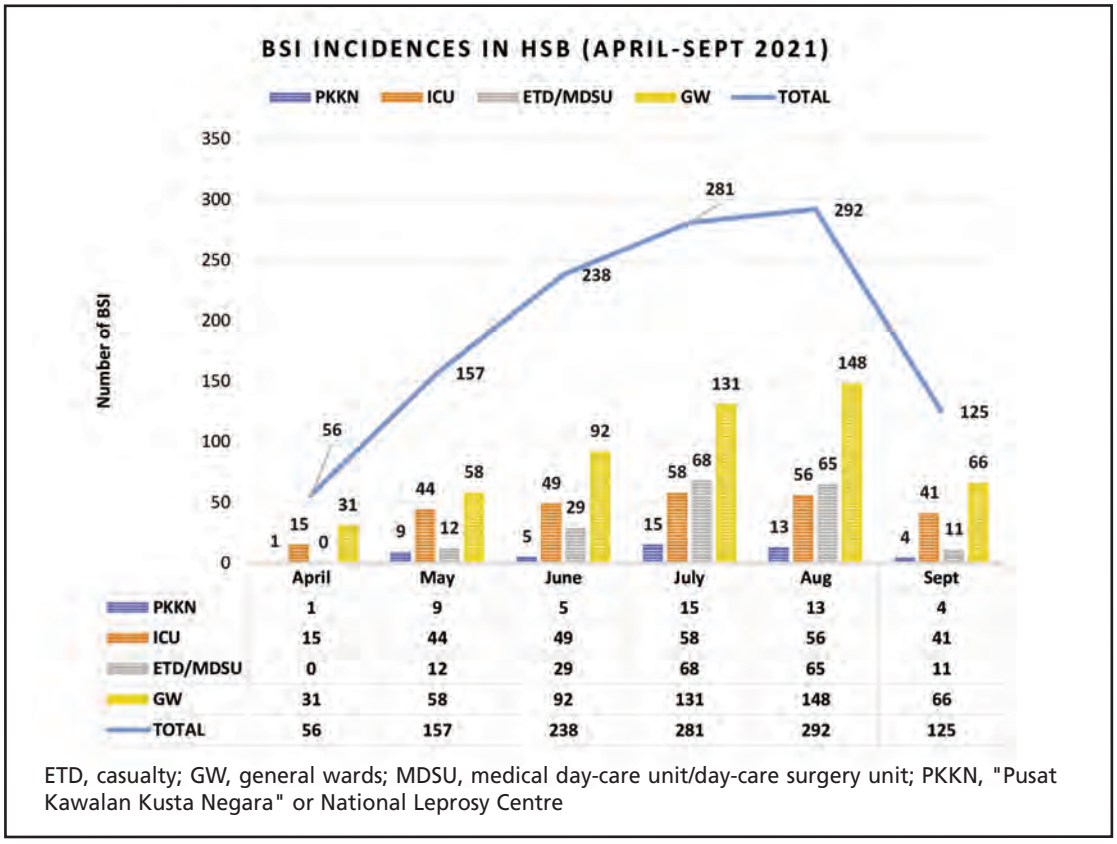
A multidisciplinary team was created, comprising of clinicians, ward nurses, the infection control unit, and microbiologists. The interventions were implemented from June to September 2021 at all wards, including the emergency and trauma department, general wards, ICU, and PKKN. From April to September 2021, all adult patients admitted to HSB who required IV cannulation were recruited. The PVC care bundle was based on local PVC guidelines for preventing PVC complications, and its implementation was ensured with the help of a PVC assessment form (Table I).[8-11] The outcome measure of this QI project was the BSI rates. An initial audit of 3-month BSI incidence was conducted to establish a baseline. Implementation of monthly PDSA cycle was described in Table II.

Data Interpretation and statistical methods

The incidence of BSI was described in numerical value. In contrast, the BSI rate was calculated in percentage with a formula of (total number of BSI per month/total number of admissions per month x 100 admissions). The data was analysed using SPSS version 26. The *p* value was measured using a paired student t-test, and its value of less than 0.05 was considered statistically significant.

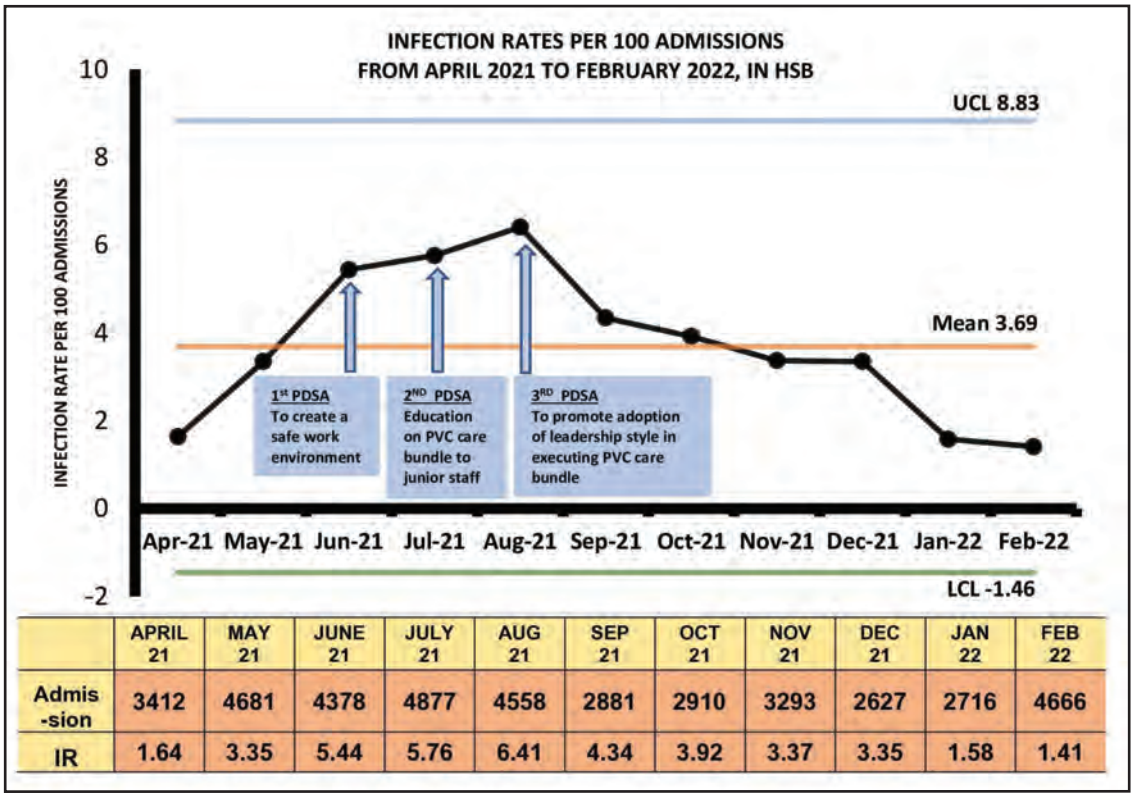
RESULTS

The PDSA cycles described in Table II were implemented over four months, from June to September 2021, to improve the BSI rates. All the healthcare workers were briefed about the guidelines in Tables I and III.



ETD, casualty; GW, general wards; MDSU, medical day-care unit/day-care surgery unit; PKKN, "Pusat Kawalan Kusta Negara" or National Leprosy Centre

Fig. 1: The number of BSI incidence in HSB from April to September 2021



	APRIL 21	MAY 21	JUNE 21	JULY 21	AUG 21	SEP 21	OCT 21	NOV 21	DEC 21	JAN 22	FEB 22
Admis -sion	3412	4681	4378	4877	4558	2881	2910	3293	2627	2716	4666
IR	1.64	3.35	5.44	5.76	6.41	4.34	3.92	3.37	3.35	1.58	1.41

Fig. 2: The trend of the BSI infection rates per 100 admissions in HSB from April 2021 to February 2022

From April to September 2021, 24,787 patients required hospitalisation at HSB (Figure 2). A baseline of BSI incidence and rate from April to May 2021 was studied (Figure 1 and 2). All plot points (Figure 2) were within the control limit range [mean 3.69, upper control limit of 8.83, lower control limit of –1.46]. Before the intervention, the BSI rates were on the rise, with a monthly increment of 40–50%. During the four months of intervention, challenges were encountered during the initial implementation of interventions and new PDSA approaches were applied to reduce the BSI rates. As shown in Figure 2, the infection rates per 100 admissions declined after the third PDSA cycle, from 6.41% to 4.34% ($p < 0.05$). At the end of interventions by September 2021, the total number of BSI cases at HSB significantly dropped off 57.2% from the peak of 292 in August 2021 ($p < 0.05$). This reduction was sustained for half a year following the completion of the QI project through the continuous effort and coordination between treating clinicians, ward nurses, and the infection control unit.

DISCUSSION

In conjunction with the local guidelines on managing the COVID-19 pandemic, infection prevention and control standards were adapted to prevent the transmission of nosocomial COVID-19 infections and maintain the integrity of environmental hygiene.[12] However, one of the challenges in sustaining existing infection control practices posed by the COVD-19 pandemic was the massive increase in demand for healthcare systems, which was characterised by the shortage of workforce and personal protective equipment (PPE) caused by the staggering numbers of COVID-19 cases.[13] As a result, compliance with infection control practices had decreased.

Our first PDSA cycle aimed to improve the quality of PVC care in understaffed and overcrowded wards and to promote environmental infection prevention and control in the healthcare setting. The PPE and instruments for PVC maintenance were stockpiled consistently to address shortages. Procedure trolleys with a complete set of instruments necessary for intravenous line insertion and maintenance were prepared and made readily available in each isolation room to promote easy access and compliance.[14] In addition to decontamination prior to use, the trolleys were cleaned every week, after each use, or when soiled. Next, increasing hand hygiene devices at the isolation facilities promoted compliance with hand hygiene practice. Rykkje et al. reported that increased hand rub availability improved hand hygiene compliance.[15] Additionally, the World Health Organisation (WHO) guidelines on hand hygiene in health care strongly recommend that hand hygiene devices must be readily available at the point of care.[16] However, this earlier initiative did not significantly impact BSI rates. We postulated that the primary contributory cause involved behavioural factors among healthcare providers. Thus, the next PDSA cycle was undertaken.

The following PDSA cycle in our study raised awareness among healthcare workers, especially untrained ones, about the importance of adherence to PVC care bundle and ANTT. As a general rule, the PVC care bundle is a collection of evidence-based interventions that, when grouped, are proven to reduce BSI rates and improve patient care outcomes significantly.[6] Agreed by experts in infection control,[8,10,17,18] there are several essential aspects to the PVC care bundle, which are to first consider the requirement of catheter insertion by referring to the PVC checklist, secondly assess the necessity of inserted lines daily, appropriately maintain PVC care by applying the concept of ANTT, and consider the prompt removal of unnecessary PVC. Recognised internationally as an essential clinical competency in healthcare, ANTT is a standardised framework of infection prevention measures to protect patients from nosocomial infections.[19-21] Of note, implementing ANTT during intravenous line insertion and maintenance is critical in avoiding infections.[22]

In our study, we speculated several factors contributing to non-compliance with the PVC care bundle and ANTT, notably lack of knowledge of their importance and inconsistent implementation, especially by new untrained staff. Hence, attention was focused on improving the education and training programmes to enhance compliance with infection prevention and control practices, including hand hygiene, donning and doffing of PPE, ANTT, and appropriate ways of venous cannulation in the setting of a quarantine facility. As suggested by other studies,[22,23] simulated teaching programmes involving posters and videos were proven effective. Continuous education helps healthcare providers, especially new staff, develop essential skills in intravenous line insertion and maintenance.[21,22,24] Additionally, onboarding education has been proven to effectively improve role clarity and equity of care.[22,25] Nevertheless, despite these emphases, our aim to reduce BSI rates was unmet even after the execution of the second PDSA cycle. Thus, we next focused on the component of leadership to facilitate behavioural change.

Notably, a lack of competency in leadership could contribute to BSI.[26,27] In other words, leadership is the key to eliminating BSI.[28] Involvement of leadership helps engage every healthcare provider in the same ward to handle PVC more effectively. When ward leadership is emphasised, every staff member in the ward plays a pivotal role in the PCV care bundle. In our third intervention, every ward specialist and consultant were empowered as leaders to educate their subordinates about the PCV care bundle and enforce the execution of PVC care in the ward. Successful leadership strengthens the IPC culture by providing tangible support to team members, listening meticulously to workforce concerns, and actively engaging staff in IPC.[27] With the participation of these leaders in the improvement plans, PVC preventive efforts materialise into organisational priorities and related processes, leading to good outcomes.[29]

Patients with difficult PVC access are often subjected to multiple attempts by cannulation and are more likely to experience treatment delays, high-risk vascular procedures, and infection.[30] To overcome this challenge, ultrasonography (USG)-guided venous cannulation was implemented, and it was shown to significantly reduce mechanical complications and infection rates.[17,31,32] Furthermore, timely utilisation of USG guidance for PVC helps clinicians obtain precise

vascular cannulation[33] in one go and avoid unnecessary central venous catheter placement,[34] which provides a safe outcome and reduces financial impact. In our study, the use of USG performed by senior clinicians for difficult placement of intravascular cannulation led to a good outcome. Besides, senior clinicians and experienced technicians were assigned to inculcate junior staff with the skill of obtaining vascular access via USG guidance. Development of didactic and hands-on training was found effective in achieving competency for frontliners in establishing USG-guided PVC insertion.[35]

Our findings demonstrated that the implementation of PDSA cycles was fundamental in identifying shortfalls and designing improvement initiatives to increase good adherence with PVC care bundle. After regular evaluation of each PDSA cycle, an eventual improvement in the adherence of the PVC care bundle reflects a successful QI project. In the PDSA initiative, in our case, the multidisciplinary approach helped explore various potential reasons for higher BSI rates and identify any deficiencies. This teamwork approach allowed us to brainstorm solutions from different angles, including nursing care and infection control practices. In addition to implementing the PVC care bundle, regular meetings and educational sessions proved effective and vital during the initiative. Furthermore, it was found effective in implementing and sustaining change by promoting teamwork, welcoming feedback from all staff, stimulating knowledge sharing in the workplace, and measuring the outcomes of interventions.

LIMITATION

One major confounder to the findings of this project is that there was a significant reduction in the number of admissions by September 2021. As it is readily agreed, infection control practices tend to be compromised when admissions are numerous and healthcare systems are stretched; the reverse is true. Nevertheless, although the number of admissions had declined during this time, the number of healthcare workers had also decreased. Thus, the "healthcare worker-patients" ratio did not vary significantly during these months. Secondly, all studied cases were inclusive of blood culture contamination (BCC), primary and secondary BSI. Worthy of note, primary BSI is often related to central or peripheral venous lines in place at the time of or within two days prior to infection onset, whereas secondary BSI results from an infection derived from another body site.[5] Interestingly, BCC is reflective of poor compliance with ANTT[36], and this issue has been addressed in our study. Further study of these findings is warranted.

CONCLUSION

This study demonstrates that all quality improvement (QI) initiatives require timely reviews via PDSA cycles, and not all changes will result in improvement. Teamwork and effective leadership are recognised as a substantial core of QI to deal with behavioural change among healthcare providers.

The development of leadership skills is essential to implement behavioural changes while facing challenges, especially during this unprecedented time. With leadership in place, it allows the healthcare organisation to build a strong IC team and develop a sustainable IC programme. Complications of intravenous lines can be caused by a lack of knowledge among junior staff. In certain circumstances of difficult line insertion, using ultrasound guidance can prove superior and strategic.

ETHICS APPROVAL

Approval of this study was obtained from the National Medical Research Register, Ministry of Health, Malaysia.

COMPETING INTERESTS

None to declare.

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Outcomes of traumatic brain injury in the patient of 60 years and above: a single centre retrospective study

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ABSTRACT

Introduction: The elderly is at risk for traumatic brain injury (TBI), but local data on their morbidity and mortality outcomes was lacking. This study aims to assess the outcome in mortality and functional outcome, Glasgow Outcome Scale (GOS) and factors associated with poor outcomes in patients with TBI more than 60 years old.

Materials and Methods: This single centre retrospective cohort study was carried out involving patients age 60 years old and above with TBI between June 2018 to May 2021. The mortality and GOS at hospital discharge, 30th day, and 90th day of trauma were analysed. The simple logistic regression (SLR) and multiple logistic regression (MLR) were performed to determine factors associated with poor outcomes and mortality.

Results: A total of 248 patients were analysed. The mean age was 67.5 ± 6.31 years. 156 (62.9%), 26 (10.5%), and 66 (26.6%) had mild, moderate, and severe TBI, respectively. The overall mortality rate was 9.7% and the median(IQR) GOS score were 4(2); p<0.001 at hospital discharge, 30th day and 90th day. There was significant difference in GOS outcomes after 90 days $\chi 2(2) = 136.76$ p<0.001. Upon MLR, there was a significant association of polytrauma, Adj. OR 11.04 (2.503–48.711); p < 0.002 and TBI severity: moderate TBI, Adj. OR 71.44(13.028–391.782); p < 0.001 and severe TBI, Adj OR 2533.51 (213.050–30127.644); p<0.001 towards poor outcome. However, only severity of TBI: moderate TBI, Adj. OR 19.48 (1.899–199.094); p=0.012 and severe TBI, Adj OR 26.42 (2.864–243.722); p=0.004 is associated with mortality.

Conclusion: Polytrauma and moderate-severe head injury are associated with poor outcomes and moderate-severe head injury is associated with high mortality.

KEYWORDS:
traumatic brain injury, older age, mortality

INTRODUCTION

Traumatic brain injury (TBI) is regarded as one of the major causes of death and disability worldwide with increased risk in elderly patient.[1] According to Malaysian Institute of Road Safety Research (MIROS), total number of road accidents had increased approximately 15% from 2010 to 2013. For moderate to severe TBI survivors, the injury may cause long-standing deficits that interfere with independent living, reduced, level of functioning and restrictions on activities.[2] The incidence of TBI among elderly is increasing, with an increase in fatality rate.[3,4]

In Norwegian study, increasing age, reduction in presenting GCS and type of injury is associated with increased risk of in-hospital mortality.[4] The meta-analysis by McIntyre et al found among the elderly identified those elderly patients with comorbidities who presented with severe TBI have increased mortality rate.[4,7] Furthermore, the mortality was nearly twice as high among very old (>74 years) patients, compared to patients between 65 and 74 years.[5] In Canada, the long-term outcome and proportion of patients discharged with outpatient rehabilitation therapy are increased with advancing age.[6] This may be attributed to the consequences of biological ageing as well as chronic disease prevalence thus rendering the elderly more prone to complications.[7,8]

As for local data, Mazlan et al.[9] found fewer young adult patients with good functional outcome as compared to other studies. Ang BH and colleagues found very elderly (age >75 years) had doubled mortality rate as compared to those younger.[10] However, there were no studies determining the factors associated with poor functional outcome post TBI. This study aims to provide a comprehensive global picture of the outcomes of TBI in elderly patients who are subcategorized under mild, moderate, and severe. Its primary objectives are to determine the mortality rates and functional outcomes after TBI and factors associated with mortality and poor functional outcome in elderly patients.

MATERIALS AND METHODS

Study Design, Inclusion, and Exclusion Criterias

This a single centre retrospective cohort study involves all TBI cases referred to and managed in Hospital Universiti Sains Malaysia from June 2018 until May 2021. The study was approved by the Human Research Ethics Committee of USM (USM/JEPeM/21110739). All elderly patients with the age of 60 years old or more presented with TBI were included in the

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study. Those patients who defaulted clinic follow-up at 3 months' post-injury were excluded from the study.

Method of Research
Comprehensive details of all patients' admission characteristic from the case folders which comprises the patient demographics (age, gender, race), various aetiologies of brain injuries (traffic, fall, others), polytrauma, Glasgow Coma Scale (GCS) on admission, severity of TBI (mild, moderate, and severe), Computer Tomography (CT) findings (extradural haemorrhage (EDH), subdural haemorrhage (SDH), contusion, subarachnoid haemorrhage (SAH), others) and Glasgow Outcome Score (GOS), and mortality at hospital discharge, at 30 days and 90th day of trauma was studied and recorded.

Data Collection
The patients' registration number was obtained from data registry from general ICU, surgical ICU, trauma ICU and neuro ICU, wards and neurosurgery clinic. The registration number and the patient's particulars were traced using Hospital Universiti Sains Malaysia, Hospital Information System (HIS) via Patient Information Database and Eletronic Medical Record; LIFELINE. Subsequently, the case folders were traced from Medical Record Unit, (Level G and Level 1, Blok D, Hospital Universiti Sains Malaysia) and related data were obtained and recorded. The CT images and reports were reviewed from Radiology Information System and Picture Archiving & Communication System (RIS-PAC) via link https://pacszfp2.usm.my/zfp Hospital Universiti Sains Malaysia, Kubang Kerian.

Outcomes Measurement
We measured the primary outcome(mortality) and secondary outcome (poor functional outcome) based on the Glasgow Outcome Scale (GOS). The GOS score classifies patient functioning into five categories; and for reporting outcomes in clinical studies purposes, the GOS score is usually dichotomized into "good functional outcome" (5: Mild or no disability and 4: Moderate disability) and "poor functional outcome" (3: severe disability, 2: vegetative state and 1: death) outcomes.[11] The factors associated with the mortality and poor functional outcome were studied. Identified factors include age, gender, race, aetiology of TBI, polytrauma, GCS at presentation, and CT scan finding. The Mortality and Glasgow Outcome Score (GOS) at hospital discharge at 30 days and 90th day of trauma was reviewed.

Statistical Analysis
For statistical analysis, categorical data was presented as frequency and percentage while numerical data was presented as mean and standard deviation (SD) or median and Interquartile range (IQR). We applied simple logistic regression (SLR) tests in the univariate analysis. All variables in the univariate analysis were selected for the multivariate analysis. A forward, backward, and manual method were used to determine our final model. Then, we used multiple logistic regression test to analyse the multivariate analysis. All assumptions for the tests were met. Variables comparison with p-value less than 0.05 is considered as significant. The data were analysed using SPSS software version 26.

RESULTS

Demographic and Baseline Data of Patients
A total of 248 patients fulfilled the criteria and the mean age of the TBI patients were 67.5 years, with majority sustained traffic injury (77.8%). Of the 248 patients, 156 (62.9%), 26 (10.5%), and 66 (26.6%) patient had mild, moderate, and severe TBI, respectively. 66.1% of the patient recovered with good GOS score at 3 months' post TBI. 9.7% of the patient died at hospital discharge and no additional mortality after hospital discharge to 3 months' post TBI. Patient demographic and clinical features are summarized in Table I.

Outcomes of patients
There was a statistically significant difference in GOS outcomes after 90 days $\chi^2(2) = 136.76$ ($p<0.001$). Post hoc analysis with Wilcoxon signed-rank tests was conducted with a Bonferroni correction applied, resulting in a significance level set at $p<0.017$. Median (IQR) of GOS outcome at discharge, 30 days and 90 days were 4 (2), 4 (2), and 4 (2), respectively. Also, there were significant differences between GOS at discharge and GOS after 30 days ($Z = -7.75$, $p<0.001$) or GOS at discharge and GOS after 90 days ($Z = -9.33$, $p<0.001$) or GOS at 30 days and GOS at 90 days ($Z = -5.20$, $p<0.001$). Table II summarizes the GOS comparison.

Factors Associated with Poor Outcome
There was a significant association of aetiology of TBI (Crude OR 5.54, 95% CI:2.23–13.56), $p<0.001$), polytrauma (Crude OR 5.54, 95% CI: 2.23–13.56), $p<0.001$), GCS level (Crude OR 0.27, 95% CI: 0.180.41), $p<0.001$), moderate TBI (Crude OR 145.44, 95% CI: 29.02–729.07), $p<0.001$), SDH (Crude OR 0.23, 95% CI: 0.13–0.43), $p<0.001$), and SAH (Crude OR 0.06, 95% CI:0.010.28), $p<0.001$) with poor outcomes. The rest were not significant and the factors and results for the SLR were summarized in Table III.

In the multivariate analysis, first we selected all variables for the selection process. The variables were processed by forward LR, backward LR, and manual methods to achieve a parsimonious model for the study. The final model consisted of polytrauma and TBI severity only. Polytrauma has a significant association with poor GOS outcome. A patient with polytrauma has 11.04 likelihood of poor GOS compared to non-polytrauma patient (Adj 95% CI (2.5048.71), $p=0.002$) when TBI severity was controlled (Table IV). TBI severity has a significant association with poor GOS outcome. A patient with moderate level of TBI has 71.44 likelihood of poor GOS compared to mild level patient (Adj 95% CI (13.03-391.78), $p<0.001$) when polytrauma was controlled. Also, a patient with severe level of TBI has 2533 likelihood of poor GOS compared to mild level patient (Adj 95% CI (213-30127), $p<0.001$) when polytrauma was controlled.

Factors Associated with Mortality
There was a significant association of polytrauma (Crude OR 16.40, 95% CI: 4.73–56.86), $p<0.001$), mortality (Crude OR 0.68, 95% CI: 0.59–0.79), $p<0.001$), moderate level TBI (Crude OR 36.91, 95% CI: 4.11–331.36), $p=0.001$), and severe level TBI (Crude OR 58.13, 95% CI: 7.56–446.81), $p<0.001$) and mortality among the patients. The rest were not significant and the factors and results for the simple logistic regression were summarized in Table V.

Table I: Patients characteristics and clinical features (n=248)

Variable		N	%	Mean	SD
Age				67.53	6.31
Gender	Male	189	76.2		
	Female	59	23.8		
Race	Malay	223	89.9		
	Chinese	18	7.3		
	Other	7	2.8		
Etiology	Traffic	193	77.8		
	Fall	54	21.8		
	Others	1	0.4		
Polytrauma	Yes	88	35.5		
	No	160	64.5		
GCS				11.62	4.17
TBI Severity	Mild	156	62.9		
	Moderate	26	10.5		
	Severe	66	26.6		
Scan Finding	Contusion	72	29.0		
	EDH	17	6.9		
	SDH	134	54.0		
	SAH	25	10.1		
GOS	Good	164	66.1		
	Poor	84	33.9		
Mortality	Alive	224	90.3		
	Death	24	9.7		

Table II: GOS Comparison at hospital discharge, 30 days and 90 days

Variable	At Discharge	30 Days	90 Days	
	Median (IQR)	Median (IQR)	Median (IQR)	*p* value*
GOS	4 (2)	4 (2)	4 (2)	<0.001

Table III: Factors associated with poor outcomes using SLR (n= 248)

Variables		Crude Odd Ratio (OR)	95% CI		
			(Lower,	Upper)	*p* value[a]
Age		1.02	0.978	1.062	0.376
Gender	Male	1.51	0.791	2.882	0.211
	Female	1			
Race	Malay	0.40	0.086	1.812	0.232
	Chinese	0.15	0.021	1.048	0.056
	Other	1			
Aetiology	Traffic	5.53	2.263	13.558	<.001
	Fall and Others	1			
Polytrauma	Yes	35.11	16.831	73.222	<.001
	No	1			
GCS		0.27	0.182	0.410	<.001
TBI Severity	Mild	1			
	Moderate	145.44	29.015	729.071	<.001
	Severe	5005.00	445.989	56167.354	<.001
Scan Finding	Contusion	1			
	EDH	0.50	0.171	1.463	0.206
	SDH	0.23	0.127	0.430	<.001
	SAH	0.06	0.014	0.284	<.001

[a]Simple Logistic Regression

Table IV: Factors associated with Poor outcome using MLR (n=248)

Variables		Adjusted OR	95 % CI		
			(Lower,	Upper)	*p* value*
Polytrauma	Yes	11.04	2.503	48.711	0.002
	No	1			
TBI Severity	Mild	1			
	Moderate	71.44	13.028	391.782	<.001
	Severe	2533.51	213.050	30127.644	<.001

* Multiple Logistic Regression
Constant = - 5.06
Forward LR, Backward LR, and manual method were applied
No multicollinearity and no interaction
Hosmer Lemeshow test, *p* value= 0.821
Classification table 96.4.0% correctly classified
Area under Receiver Operating Characteristics (ROC) curve was 98.7 % (*p*<0.001)

Table V: Factors associated with mortality using SLR (n=248)

Variables		Crude Odd Ratio (OR)	95 % CI (Lower,	Upper)	*p* value*
Age		1.04	0.977	1.103	0.231
Gender	Male	1.63	0.533	4.966	0.392
	Female	1			
Race	Malay	2.76	0.357	21.362	0.331
	Chinese and Other	1			
Etiology	Traffic	7.31	0.964	55.372	0.054
	Fall and Others	1			
Polytrauma	Yes	16.40	4.732	56.856	<.001
	No	1			
GCS		0.67	0.589	0.778	<.001
TBI	Mild	1			
	Moderate	36.91	4.110	331.362	0.001
	Severe	58.13	7.561	446.807	<.001
Scan Finding	Contusion	1			
	EDH	1.32	0.323	5.467	0.694
	SDH	0.56	0.223	1.376	0.204
	SAH	0.00	0.000	.	0.998

*Simple Logistic Regression

Table VI: Factors associated with mortality using MLR (n=248)

Variables		Adjusted OR	95 % CI (Lower,	Upper)	*p* value*
Polytrauma	Yes	3.21	0.790	13.047	0.103
	No	1			
TBI	Mild	1			
	Moderate	19.48	1.899	199.094	0.012
	Severe	26.42	2.864	243.722	0.004

* Multiple Logistic Regression
Constant = - 5.257
Forward LR, Backward LR and manual method were applied
No multicollinearity and no interaction
Hosmer Lemeshow test, *p* value= 0.335
Classification table 90.3.0% correctly classified
Area under Receiver Operating Characteristics (ROC) curve was 85.8 % (p<0.001).

In the multivariate analysis, first we selected all variables for selection process. The variables were processed by forward LR, backward LR and manual methods to achieve a parsimonious model for the study. The final model consisted of polytrauma and TBI severity only. TBI severity has a significant association with poor GOS outcome. A patient with moderate level of TBI has 19.48 risk of mortality compared to mild level patient (Adj 95% CI (1.90–199.10), *p*=0.002) when polytrauma was controlled. Also, a patient with severe level of TBI has 26.42 risk of mortality compared to mild level patient (Adj 95% CI (2.86–247.72), *p*=0.004) when polytrauma was controlled. However, polytrauma has no significant association with mortality when TBI severity was controlled.

DISCUSSION

This study is a 3-year retrospective study of TBI sustained in 60 years old and above. The study assesses functional outcome of patient with GOS, as well as the mortality rate of the patient. Old age is recognised as a poor prognostic factor for mortality and morbidity with slower rates of functional and cognitive recovery.[11-13] There is a lot of prognostic factors which may influence the functional outcome of the patient.

In this study, polytrauma is associated with poor GOS. The associated injury to other system beside cranial injury complicated the functional recovery. Polytrauma patient especially those with open wound and long bone fracture are prone to get coagulopathy which will complicate the condition of the cranial injury. For patient with polytrauma especially to the chest causing pneumothorax, patient will be prone for chest infection and prolonged ventilation. Thus, it will hamper the recovery of the patient. The severity of TBI also influence the functional outcome of the patient. We found that moderate and severe TBI are associated with poor GOS. Functional outcome of all-severity and moderate-severe TBI in older patient is well studied and generally associated with poor functional outcome.[14] There is one small study that shows 80% of mild TBI patient with age more than 65 years old has good GOS.[15] Older adults when compared to younger patients with similar injury severity usually has a better initial GCS.[16] However, extra care need to be given also to old patients with initial mild head injury as their clinical condition might deteriorate abruptly. CT scan findings of SDH and SAH are significantly associated with poor GOS. Subdural haemorrhage, contusional bleed, and intracerebral hematoma are more common intracranial haemorrhage for older adults with TBI. Mechanism of injury for TBI for older adults are commonly due to fall. Thus, less commonly having

skull fracture and EDH. SDH and SAH are common, mainly due to brain volume reduction approximately by 6–11% by 60–80 years of age.[17] Hence, as the brain volume decreases, the volume of subdural space increases as well as the mobility of the cerebral hemisphere.

Mortality post TBI for older adults is high, and it is reported to be as high as 70–80%.[18,19] There is actually a lot of factors influencing the mortality rate, which are aggressive resuscitation, good premorbid health and independent prior to injury.[20,21] In our study, polytrauma as discussed previously in functional outcome is associated with high morbidity but not mortality. Severe and moderate TBI is associated with high mortality rate. It is reported that mortality post TBI among older adults is high especially for severe TBI patients. Despite that mild TBI patient should be paid attention to as well. There is reported old adult patient to present initially with good neurological condition initially but later on deteriorated to severe and moderate TBI within 48 hours. CT scan findings however does not have any association with high mortality, as compared to functional outcome.

LIMITATIONS AND RECOMMENDATIONS

As with all other studies, this study also has some limitations. This is a relatively small population study from only one local neurosurgical institution. Therefore, it is recommended that future prospective and multicentre study to be conducted with longer observation periods to evaluate the long-term outcome of the elderly post-TBI.

CONCLUSION

Moderate to severe head injury are associated with poor functional outcome and high mortality rate. In contrast, polytrauma was associated with poor functioning outcome but not mortality. Thus, optimising cerebral resuscitation, preventing secondary insult, and vigilance critical care is essential in reducing the mortality and improving the outcome of elderly with TBI.

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ORIGINAL ARTICLE

Correlation between blood pressure and lung function in Malaysian adult population

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ABSTRACT

Introduction: The correlation between pulmonary function and hypertension remains ambiguous. This study therefore determined the relationship between pulmonary function and hypertension among adult subgroup in Malaysia.

Materials and Methods: Data for this study were obtained from an ongoing Prospective Urban Rural Epidemiology-Rural Urban Study (PURE RUS) , which is a prospective cohort study done by MARA University of Technology (UiTM) Medical Faculty research team to track risk factors, changing lifestyles, and chronic diseases in rural and urban population. The inclusion criteria included: Malaysian citizen, age 18–80 years, not on any anti-hypertensive agents, and able to perform lung function test. 1640 participants satisfied the criteria and were recruited in this study.

Results: From the studied population, males comprised 43.5% of them and female comprised 56.5%. A significant inverse relationship was found between pulmonary function and systolic blood pressure in both sexes measured by forced vital capacity (FVC) and Forced Expiratory Volume in 1 second (FEV1). A substantial inverse relationship was also found between pulmonary function and age, and there was a profound positive association between blood pressure and age. No major disparities were significant in pulmonary function between hypertensive and age-matched normotensive participants.

Conclusion: Even though a substantial inverse relationship was evident between systolic blood pressure and pulmonary function, its precise clinical importance needs to be further explored particularly when age can influence both pulmonary function and blood pressure. Clearly, the impact of age has to be removed before FVC can be used as a prognosticator of hypertension.

KEYWORDS:
Pulmonary function, blood pressure, hypertension

INTRODUCTION

Hypertension is one of the main risk factors for cardiovascular, cerebro-vascular, and renal diseases.[1] About 4.5% of the global disease burden has been estimated to be caused by hypertension and it is prevalent in many developing and developed countries around the world.[2] Based on the national prevalence of hypertension in Malaysia is 32.7% for residents aged 18 years and older.[3] This is higher than that reported in the United States (28% in 2010).[4]

An inverse correlation between pulmonary function and blood pressure has been found in few research. Baseline forced vital capacity (FVC) was noted to be inversely correlated to probability of developing hypertension, and this correlation was not affected by weight, blood pressure, age, and cigarette smoking.[5] A strong inverted correlation between FVC and the probability of developing high blood pressure has also been described in another study.[6] These two studies established that FVC is a valuable prognosticator of further development of high blood pressure. An earlier study in China reported a reverse correlation between pulmonary function and blood pressure in the Chinese population but the relationship was very weak.[7] A study in Germany, on the other hand reported that hypertension and the consumption of beta blockers, are strongly linked with reduced pulmonary function in the German population of adult.[8] In contrast, another research, also in Germany, found that hypertension in blend with antihypertensive medications and not high blood pressure itself may possibly be linked with reduced pulmonary function in the overall mature population.[9] A more recent paper from Korea concluded that hypertension might be linked with an augmented deterioration in FVC, and high blood pressure medications might reduce the rate of deterioration in healthy subjects who have no symptom.[10] The precise reason/s for the differences in the findings and in the strength of the link between pulmonary function and hypertension in these researches is unclear. It is possible the differences might be due to the differences in race, regions, or study methodologies used. Association between hypertension and pulmonary function in a community-based setting has also not been well investigated in Malaysian population. Hence, the objective of this analysis is to explore if there is any significant association between hypertension and pulmonary function in the Malaysian adult population. Given that Malaysia is a multi-racial society, the findings in this study might alter the perception on the association between hypertension and pulmonary function. This study also attempts to look at age and sex as the confounding

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factors that may or may not affect the inverse relationship between hypertension and pulmonary function.

MATERIALS AND METHODS

Study Design

Data for the analysis of correlation between pulmonary function and blood pressure were derived from an ongoing PURE RUS study. This study is a prospective cohort study done by UITM Medical Faculty research team to trace changing risk factors, lifestyles, and chronic disease in rural and urban settings. It is a continuing 15-year longitudinal and cross-sectional study, commenced in 2008. Baseline lung function data of adult men and women, rural and urban, from east and west Malaysia were collected. The inclusion criteria consisted of: Malaysian citizen, aged 18–80 years, not on any anti-hypertensive (anti-HPT) medications and able to perform lung function test. An overall of 1640 subjects matched the standard criteria and were enrolled in this study.

Ethical Consideration

Consent had been received from all subjects during the recruitment for the PURE RUS to the usage of their data for other related studies. The usage of the data for this study analysis was endorsed by Universiti Teknologi MARA (UiTM) Ethics Committee, which governs all studies involving humans by staff and students of the centre. Research Ethics Code (Rec): REC/UITM/2007(10).

Pulmonary Function

Pulmonary function tests were performed by qualified personnel involved in the research team. Pulmonary function was assessed via a portable Spirometer (Micro Medical Ltd.). Before the test, the correct procedure was demonstrated to all the participants by the assessor and the subjects were supervised throughout the tests. Spirometric measurements were recorded while the subject was standing, with at least one minute rest in between the repetitive measurements, and were done according to the American Thoracic Society (ATS) requirements.[11] The subjects completed at least three forced expiratory pulmonary function tests in order to acquire a minimum of two satisfactory and reproducible readings. The average of two best recordings was recorded. The parameters measured were FVC and forced expiratory volume in 1 sec (FEV_1). The most excellent results for FEV_1 and FVC were obtained and percent predicted values were determined based on Crapo et al.[12]. However, the predicted values were not used in the correlation, as the predicted value is consistently higher than the actual value.

Hypertension, Medical Treatments, and Other Factors

Blood pressure measurement was obtained from the right arm in a sitting position using an automated blood pressure recorder (Omron HEM-757).[9] Apart from that, anthropometric values, computer-assisted standardized feedback form and self-administered surveys on lifestyle and health-related aspects, medical history, and pulmonary symptoms were completed. Lung diseases such as asthma were established from self-reported physician's analysis. The smoking status (current, former, or never-smokers) was evaluated from patient's own self-assessment.

Statistical Analysis

Statistical analysis was conducted using statistical assessments contained in Statistical Package for Social Sciences (SPSS) Version 20.0 software. Measure of central tendencies, the frequency distribution, and measure of distribution were calculated. The normality of continuous data was confirmed by Kolmogorov-Smirnov testing. α=0.05 was set as the significant level. The normally distributed continuous data are shown as mean and standard deviation. The categorical data is presented in the form of absolute numbers and their corresponding percentage values. Pearson's correlation coefficient was applied to ascertain the relationship between systolic blood pressure (SBP), FEV_1, and FVC. Simple linear regression was used for univariate analysis for the association between independent variables and the outcome (FEV_1 and FVC). All significant variables in simple linear regression were adjusted for the confounding factor using multiple linear regressions.

RESULTS

Characteristics of the 1640 participants involved in this study are presented in Table I. Male participants were significantly older, had lower BMI, higher FEV_1, higher FVC, and higher SBP compared to female participants.

SBP had a significant negative correlation with FEV1 (r= -0.111, p<0.001) and FVC (r= -0.104, p<0.001) from the overall population, also in male and female subjects when correlated separately. However, no significant correlation was noted between diastolic blood pressure (DBP) and lung function (FEV_1 and FVC) in male and female subjects and the overall population (Table II).

The correlation between age and SBP is also noted to be statistically significant in which r=0.322, p<0.001. However, age and DBP are not statistically significant with r=0.023, p =0.347.

In the overall population, FEV_1 was significantly correlated with age (negative correlation), sex and BMI in simple and multiple linear regressions. However, it only correlated significantly with SBP (negative correlation) in simple linear regression (Beta[a] = -0.003). FVC was significantly correlated with age, sex, BMI, and SBP (negative correlation) in simple and multiple linear regression and it is only significantly correlated with DBP in multiple linear regression (Table III).

Following simple and multiple regression analysis, in males, FEV_1 had a significant negative correlation with age, and FVC had a weak negative correlation with age. In females, FEV_1 correlated significantly with age (negative correlation) and BMI in simple and multiple linear regressions, and only significantly correlated with SBP (negative correlation) and DBP in multiple linear regression (Table IV).

To minimize the influence of age, pulmonary function, and blood pressure were correlated in subjects aged 30–35 years. No significant correlation was evident between BP and lung function in this group (Table V).

Table I: Overall parameters comparing male and female participants of the study population

Parameter	Gender	N	Mean (SD)	Mean difference (95%CI)	*p* value
Age	Male	713	53.88 (9.79)	4.50 (3.55, 5.44)	<0.001*
(years)	Female	927	49.38 (9.50)		
BMI	Male	709	25.35 (4.64)	-0.89 (-1.37, -0.41)	<0.001*
(kg/m^2)	Female	922	26.34 (5.12)		
FEV_1	Male	713	2.41 (0.55)	0.58 (0.02, 0.53)	<0.001*
	Female	927	1.84 (0.43)		
FVC	Male	713	2.84 (0.68)	0.72 (0.66, 0.77)	<0.001*
	Female	927	2.12 (0.53)		
SBP	Male	712	136.52 (19.76)	3.92 (1.92, 5.92)	<0.001*
(mmHg)	Female	918	132.60 (20.9)		
DBP	Male	712	79.94 (11.54)	0.72 (-0.41, 1.84)	0.213
(mmHg)	Female	918	79.22 (11.46)		

* denotes statistically significant at α=0.05

Table II: Correlation between Blood Pressure (Systolic and Diastolic) and Lung Function in subject 18–80 years of age

		Correlation between SBP and:		Correlation between DBP and:	
		r	*p* value	*r*	*p* value
FEV	General	-0.111	<0.001*	0.015	0.550
	Male	-0.179	<0.001*	0.013	0.719
	Female	-0.197	<0.001*	0.016	0.637
FVC	General	-0.104	<0.001*	0.014	0.584
	Male	-0.187	<0.001*	0.100	0.785
	Female	-0.173	<0.001*	0.005	0.878

*Denotes statistically significant at α=0.05.

Table III: Factors associated with lung function (FEV1 and FVC) in 18–80 years old

Model for:	Variables	Simple linear regression (SLR)		Multiple linear regression (MLR)		
		Betaa(95%CI)	*p* value	Adjusted Betab (95%CI)	*p* value	R^2
FEV_1	SBP	-0.003 (-0.004, -0.002)	<0.001*	-0.001 (-0.002, 0.001)	0.088	0.483
	DBP	0.001 (-0.002, 0.003)	ns	-	ns	
	Age	-0.020 (-0.022, -0.017)	<0.001*	-0.026 (-0.028, -0.024)	<0.001*	
	Sex	0.576 (0.528, 1.868)	<0.001*	0.705 (0.664, 0.746)	<0.001*	
	BMI	0.010 (0.004, 0.015)	0.001*	0.008 (0.003, 0.012)	<0.001*	
FVC	SBP	-0.004 (-0.005, -0.002)	<0.001*	-0.003 (-0.005, -0.001)	0.046*	0.416
	DBP	0.001 (-0.002, 0.004)	0.584	0.003 (0.001, 0.007)	0.001*	
	Age	-0.019 (-0.022, -0.015)	<0.001*	-0.026 (-0.029, -0.023)	<0.001*	
	Sex	0.718 (0.659, 0.777)	<0.001*	0.847 (0.793, 0.901)	<0.001*	
	BMI	0.008 (0.001, 0.015)	0.029*	0.006 (0.001, 0.012)	0.030*	

[a] Crude regression coefficient;
[b] Adjusted regression coefficient; (Multiple linear regression with backward method. The model reasonably fits well. Model assumptions are met. There is no interaction between independent variables and muti-collinearity problem)
* denotes statistically significant at α=0.05

Table IV: Factors associated with lung function (FEV_1 and FVC) in Male and Female participants among 18–80 years old

Model for:	Variables	Simple linear regression (SLR)		Multiple linear regression (MLR)		
		Beta[a] (95%CI)	*p* value	Adjusted Beta[b] (95%CI)	*p* value	R^2
FEV_1	SBP	-0.003 (-0.007, 0.001)	0.159	-	ns	0.044
(Male)	DBP	-0.002 (-0.009, 0.004)	0.479	-	ns	
	BMI	0.008 (-0.009, 0.025)	0.345	-	ns	
FEV_1	SBP	-0.001 (-0.003, 0.001)	0.176	-0.005 (-0.007, -0.002)	0.001*	0.114
(Female)	DBP	0.003 (-.001, 0.007)	0.187	0.008 (0.002, 0.013)	0.005*	
	BMI	0.012 (0.002, 0.021)	0.028*	0.009 (0.001, 0.019)	0.049*	
FVC	SBP	-0.003 (-0.008, 0.002)	0.218	-	ns	0.012
(Male)	DBP	-0.006 (-0.014, 0.002)	0.148	-	ns	
	BMI	0.001 (-0.020, 0.020)	0.985	-	ns	
FVC	SBP	-0.001 (-0.004, 0.001)	0.356	-0.005 (-0.009, -0.001)	0.010*	0.115
(Female)	DBP	0.004 (-0.002, 0.009)	0.174	0.009 (0.002, 0.017)	0.015*	
	BMI	0.016 (0.003, 0.029)	0.017*	0.013 (0.001, 0.026)	0.047*	

[a] Crude regression coefficient;
[b] Adjusted regression coefficient; (Multiple linear regression with backward method. The model reasonably fits well. Model assumptions are met. There is no interaction between independent variables and muti-collinearity problem)
* denotes statistically significant at α=0.05

Table V: Correlation between Blood Pressure and lung function in 30–35 years old participants

	Systolic Blood Pressure (SBP)		Diastolic blood Pressure (DBP)	
	r	*p* value	*r*	*p* value
FEV	-0.239	0.098	-0.111	0.449
FVC	-0.274	0.057	-0.094	0.519

DISCUSSION

The evaluation of this population-based analysis confirms that raised systolic blood pressure is correlated with reduced lung function or *vice versa* (Table II). Predicted lung functions (FEV_1 % Pred, FVC % Pred) were not included in the results because the formulae available for prediction were not derived from the population under study and might therefore be inappropriate. Earlier studies on lung function in the Malaysian population found the actual FVC and FEV_1 values to be consistently lower in the Malaysian population when compared to the predicted values, with differences ranging from 5 to 49% depending on the formula used.[13,16] The main reason for this difference appears to be related to the population from which the data for the formulae were derived. In any case, the objective of this analysis is to assess and look for correlations between actual pulmonary function and blood pressure, hence predicted values were deemed not critical or necessary.

As a general comment on the data, as expected lung function values were significantly higher in the males than females (Table I). This is primarily due to the bigger build of males than that of females. Males have significantly higher mean systolic blood pressure than females (Table I). With regard to the findings on pulmonary function and blood pressure, they seem to be consistent with previous studies showing that blood pressure and lung function are in reverse association.[7,17,18] Whilst the precise reason for this link might not be evident, the interpretation of any link between blood pressure and lung function has to take into account the influence of age. Age has a positive and negative correlation with blood pressure and pulmonary function, respectively.[19-22] The data in Table III clearly demonstrated the influence of age on pulmonary function which shows a significant negative correlation between FEV_1, FVC, and age. Age and SBP are also significantly correlated with r=0.322. Age also revealed a very strong negative correlation with FEV_1 and FVC in males and females even when analysed individually (Table IV). The correlation is stronger in males than females, and the reason for this is unclear but it might be due to differences in the body frame between the two. There were no other factors that correlated significantly with lung function in males other than age. Significant age-related decline in FVC has been reported in Malaysian males where the average decline in FVC was found to be about 295 ml per decade between the age of 13 and 78 years. It was also interesting to note that although a substantial negative association was evident between blood pressure and pulmonary function and in the whole population, this association was not so evident when examined for just within a group aged 30–35 years (Table V). The objective of this brief analysis was to observe if the correlation between lung function and blood pressure was evident when the impact of age was minimised. The absence of any significant difference in this group could imply that the evident relationship between pulmonary function and blood pressure in normal individuals are more likely contributed by the age factor rather than the effect of pulmonary function on blood pressure or *vice versa*. The assumption might appear in contrast to previous reports, which postulated that lung function itself is one of the main factors that increase the risk of developing hypertension, independent of age.[5,6] Clearly the findings of this study do not confidently support the above postulation. The impact of age has to be removed completely to ascertain the relationship between blood pressure and pulmonary function. Substantial positive correlation is reported between small artery elasticity and forced vital capacity and with forced expiratory volume in 1 second in middle-aged to older free-living adult.[23] This has been proposed to be due to corresponding physiological paths for elastic changes in the vasculature and in pulmonary parenchyma, which happens with aging. Age related decrease in small artery elasticity would increase resistance and consequently pressure and decreased elasticity in the lung parenchymal tissue which would increase its resistance and consequently its expansion. It is therefore not surprising that a negative correlation exists between blood pressure and lung function when examined over a wide age range. The increment in blood pressure and reduction in lung function is not because they are interacting with each other, but mainly because they occur independently, in the same human body due to ageing process. The positive correlation between blood pressure and age have been shown in previous studies as well.[24-26]

There are varieties of other confounders which might also influence the correlation between hypertension and pulmonary function, such as gender and BMI. It is clear that gender and BMI is significantly correlated with lung function (Tables I and III), and BMI has significant effects especially to the female subjects (Table IV).

LIMITATION

Some limitation to our study would be procedural bias, which might lead to inadequate pulmonary function measurements. However, we believe that this possible bias is unlikely to greatly alter our findings. It is difficult to make a clear statement about the temporal sequence and causality between high blood pressure and lung function due to the cross-sectional study design of this analysis. Few prospective analysis pointed out that hypertension is a risk factor for declined pulmonary function, and yet others indicate diminished pulmonary function raise the probability of developing hypertension.[5-7,27] Thus, it is paramount to assess the temporal order, acute and chronic effects and the interconnection between pulmonary function and hypertension in prospective longitudinal analysis, while taking into consideration other confounding factors, such as cardio and respiratory co-morbids, smoking, occupation, and lifestyle.

CONCLUSION

Our observations are in line with previous findings demonstrating a reverse relationship between pulmonary function and blood pressure. However, this association is more age dependant and likely caused by the effect of age rather than the effect of pulmonary function on SBP or *vice versa*. However, these findings do not exclude the possibility of correlation between lung function and hypertension in lung disease but clearly the hypothesis needs more study.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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Parental control on handphone access and usage among Malaysian children

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ABSTRACT

Introduction: Parental control for a child's handphone access is important to ensure online safety. This study was to determine parental control on handphone access and the usage amongst Malaysian children.

Materials and Methods: A cross-sectional survey was conducted electronically between April 2017 and March 2018 among parents with children above 2 years of age, who owned a handphone. The 10-item questionnaire included questions about rules applied to the use of handphones, education on cybersafety, the characteristics and activities of their youngest children who had full-time access to a handphone, and parental perceptions of their children's usage of handphones. A total of 215 parents were included.

Results: From this, 92% controlled their children's handphones use by setting rules. The commonest rules were limiting the time of handphone usage (77%) and being aware of whom the child was communicating with (77%). The majority (94%) educated their children on cybersafety, and the commonest discussed topic was not to communicate with strangers (93%). The children's average age of first handphone ownership was 10.6 (SD: 3.6) years, and the use of the handphone averaged 17.4 (SD: 18.5) hours a week. Despite the rules and education provided, only a quarter of parents were confident of their children's capability to manage their own safety when using handphones (27%).

Conclusion: In summary, Malaysian parents did control their children's handphone usage.

KEYWORDS:
parental control; children handphone usage; cyberbullying; Malaysian children; rules and education online

INTRODUCTION

According to the United Nations International Children's Emergency Fund (UNICEF) estimates, approximately one in three internet users were children under 18.[1] Children could be seen clicking on keypads and swiping across electronic screens even before learning to speak. Less than 8% of those between the ages of 9–11 had followed the American Academy of Paediatrics guidelines on restricting media usage to less than 2 hours a day.[2] Electronic device usage among older children had been linked to obesity and other metabolic syndromes.[3] Taiwan reported that 15.2% of students were addicted to smartphones and owning a handphone, frequent gaming and low parental control were predisposing factors.[4] A 2014 nationwide telephone survey among 2401 users of handphones on all digital platforms in Malaysia reported that 12.5% of all handphone users were younger than 20 years and 34% of school-going children owned a handphone.[5] Results of a large-scale online survey of Malaysian secondary school children's view of the internet showed that more than 95% of school children in Malaysia use the internet.[6] Many school children expressed positive family values on their use of the internet and they followed rules set by parents. However, several school children also reported that their behaviours online were influenced by their peers, they experienced cyber-bullying, and there were inappropriate sexual activity online involving children.[6] Like subjected to sexual harassment on the internet, asked for intimate photographs or videos of themselves or sent such photographs or videos to someone over the internet.[6]

Since 2010, several studies have been conducted by public and private organisations locally on the impact of information and communication technology on children's rights and well-being. However, sources of such data were from the perspective of the children, and little appeared to be available about the views of parents. Therefore, the main objective of this study was to determine parental control on handphone access, the usage of handphones among children, the intention, and the actual usage of handphones given to children in Malaysia.

In this study, a handphone was a device that requires a sim card with internet access that could make calls and send or receive messages, images, videos, and other digital materials. Handphone ownership meant having their own handphones and not borrowing from others. Parental control was the method practiced by the parents to restrict their children's access to and use of handphones. Parents who practised at least one of the rules specified were considered to have some control of their children's handphone usage.

MATERIALS AND METHODS

This was a cross-sectional study conducted over 12 months, from April 2017 to March 2018. Malaysian parents with children aged 2–18 years were approached via social media

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platforms such as Facebook® and WhatsApp® to participate in an online survey. To encourage participation from the wider parental community, the researchers also disseminated the link of this survey to their paediatric colleagues working in the Malaysian Ministry of Health (MOH) and researchers in the Clinical Research Centre (CRC) Network, who were requested to share the study invitation with their contacts.

Inclusion criteria were Malaysian parents, regardless of marital status, who understood written English, Malay, or Mandarin and had children between the ages of 2 and 18 years, of which at least one possessed a handphone at all times. If more than one child in a household possessed a handphone at all times, the youngest child would be the main target of the survey. Parents who had any children with severe intellectual disabilities were excluded because our team would like to focus on typical family for this study.

2014 nationwide survey among handphone users in Malaysia reported that 40% of parents had "some amount of control" over their children's computer and internet usage.5 We calculated that a sample size of 256 participants was required (power of 90%, setting the alpha at 5% and the prevalence of 40% of Malaysian parents had control over their children's handphone use).

The questionnaire was developed and made available online via Google Form in three commonly used languages in Malaysia—English, Malay, and Mandarin. The questionnaires were developed by paediatricians. There was no reliability or validation done. In the forms, participants would first read a Participant Information Sheet that briefly explained the study. Parents who agreed to the consent statement would proceed to the next page of the questionnaire. Socio-demographic characteristics of the participants were first collected followed by the 10-item questionnaire. The questionnaires included the child's age of acquiring a handphone, the hours of usage per week, parental reasons for providing the handphone, and the commonest purpose for the use of handphones. We asked whether parental control was applied to handphone use and, if yes, the specific rules or restrictions chosen. We also asked whether parents educated their children on cyber-safety and, if yes, the topics provided. Parents' perceptions on whether their children followed the rules imposed were also evaluated. All questions were made compulsory for a successful submission of the questionnaire.

Survey responses were automatically recorded in a Google Sheet, which was downloaded and exported to SPSS v21.0 for analysis. Data analysis for this paper was purely descriptive. Continuous data were summarised as means with standard deviations if normally distributed, or medians and interquartile ranges if otherwise. Categorical data were presented as frequencies with percentages.

The study was approved by the Medical Research & Ethics Committee (MREC) of the MOH Malaysia ((6)KKM/NIHSEC/P17-729). All participants provided consent online prior to answering the questionnaire. No unique identifiers were collected and all participants remained anonymous. All collected data and responses were kept strictly confidential, and only the researchers had access to the online questionnaire and the database.

RESULTS

We received a total of 270 responses. Fifty-five of the respondents were parents whose children were allowed access to handphones but did not own them and hence were excluded. The subsequent analysis was based on 215 respondents, which was 84% of the target sample size.

Figure 1 compared parents' intentions of providing their children a handphone, and their children's actual use of the handphone. While communication was a joint purpose of owning a handphone, parents intended the handphone for reasons of safety or emergency contact (30.70%), while children primarily used the handphone for entertainment (59.26%).

Table I describes the socio-demographic characteristics of the parents who had participated and their children. Majority of the respondents were from social classes I and II and had less than 4 children. The average use of the handphone was about 2.5 hours a day.

198 out of 215 parents (92%) controlled their children's handphone usage by setting rules (Table II). Approximately half of the parents set between 9 and 12 rules. The five commonest rules set included limiting the time of usage, being aware of the person communicating on the other end, limiting the type of applications downloaded, and restricting the time spent online and place where handphone should be used. A small proportion (10%) of parents were unsure if their children followed the rules.

201 out of 215 parents (94%) stated that they educated their children on cyber-safety, out of which the majority (83%) discussed five or more topics with their children. The five commonest topics discussed included not communicating with strangers, not disclosing personal information, not sharing passwords, seriously considering before posting photos, and observing basic internet etiquette as in Table III.

When asked about their children's capability to manage their own cybersafety when using the handphone, only a quarter of parents (27%) were confident that this was possible (see Table IV).

DISCUSSION

Reasons cited by parents for providing a handphone to their children differ from their children's actual use of the handphone. A particular cause of concern was the use of entertainment, especially gaming and gambling. Instant messengers, gaming, and entertainment had shown to be strong predictors of smartphone addiction.[7] This should bring awareness to the community as it had a potential negative outcome.

The average age for a child's first handphone ownership was 10.6 years, which meant most of them were still in primary school. Our results were similar to the findings from a 2016

Table I: Socio-demographic characteristics of respondents and children[a]

Characteristics	N (%) n=215
Occupational class[b]	
Managerial, administrative, or professional (class I)	121 (56.3)
Intermediate managerial, administrative, and professional (class II)	59 (27.4)
Supervisory, clerical and junior managerial, administrative, and skilled manual worker (class III)	11 (5.1)
Semi-skilled and unskilled manual worker (class IV)	1 (0.5)
State pensioner, unemployed, housewife, or househusband (class V)	23 (10.7)
Number of children in the family	
1–2	85 (39.5)
3–4	96 (44.7)
5–10	34 (15.8)
Number of children in the family who owns a handphone	
1	99 (46.0)
2	62 (28.8)
3	32 (14.9)
4	6 (2.8)
5–10	16 (7.5)
Age of youngest child when he/she first owned a handphone (years), mean (SD)	10.6 (3.6)
Current age of youngest child who owns a handphone (years), mean (SD)	12.7 (4.0)
Number of hours per week the youngest child uses the handphone (hours), mean (SD)	17.4 (18.5)

SD: standard deviation
[a]Data presented are frequencies (percentages) unless otherwise specified.
[b]Office for National Statistics (ONS) 2010. Standard occupational classification 2010, Vol.3. The national statistics socio-economic classification: Rebased on the SOC2010 user manual, London, Palgrave MacMillan.

Table II: Rules set by parents on handphone usage[a]

Characteristics	N (%) n=198[b]
Number of rules practised	
1–4	33 (16.6)
5–8	76 (38.4)
9–12	89 (45.0)
Type of rules practisedc	
Limit time of total handphone usage	153 (77.3)
Knowing the person who is communicating with our children in any form	153 (77.3)
Limit type of applications	145 (73.2)
Limit time to go online, either using data or Wifi	145 (73.2)
Limit place of handphone usage	142 (71.7)
Confiscate child's handphone as a form of punishment	138 (69.7)
Check files (images and videos) that are downloaded into the device	133 (67.2)
Add your child into your network (Facebook®, social media)	129 (65.2)
Install applications (apps) to monitor/control child's online activities	128 (64.6)
Check in-coming private messages (e.g. email, Facebook®, Whatsapp®, Wechat®) content (text, images, videos, files, etc.) from time to time	124 (62.6)
Accompany child when using device	44 (22.2)
Other methods	73 (36.9)
Parent's perception if their youngest child follows rules set	
Yes	147 (74.2)
No	21 (10.6)
Do not know	20 (10.1)
I do not control my child[d]	10 (5.1)

[a]Data presented are frequencies (percentages) unless otherwise specified.
[b]n=17 did not set any rule and were therefore excluded from this analysis.
[c]Parents were allowed to select all relevant rules that were practised/applied.
[d]These parents had earlier indicated that they had imposed rules on their children but in response to this question, they denied any control over their children's handphone use.

Table III: Cyber-safety topics discussed with the children[a]

Characteristics	N (%) n=201[b]
Number of topics discussed	
1-2	17 (8.5)
3-4	17 (8.5)
5-6	100 (49.8)
7 and more	67 (33.3)
Parent's method(s) in educating their youngest child regarding cyber-safetyc	
Not to text people that you do not know	187 (93.0)
Never disclose personal information online	184 (91.5)
Not to share passwords with others except parents	179 (89.1)
Not to post photos of self or others without understanding the impact	172 (85.6)
Tell them about internet etiquette, like asking ourselves – 'should I really be posting this?' and 'will someone be hurt or offended by this post?'	166 (82.6)
Always log out from online accounts especially when using public computers	149 (74.1)
Other methods	89 (44.3)

[a]Data presented are frequencies (percentages) unless otherwise specified.
[b]n=14 did not provide any education and were therefore excluded from this analysis.
[c]Parents were allowed to choose all relevant methods that were used.

Table IV: Parent's perception about their children's capabilities to manage their own safety when using a handphone[a]

Characteristics	N (%) n=215
Yes	59 (27.4)
Maybe	89 (41.4)
No	40 (18.6)
Not sure	27 (12.6)

[a]Data presented are frequencies (percentages) unless otherwise specified.
[b]Parents were allowed to choose only one answer from the 4 options of Yes, Maybe, No, Not Sure

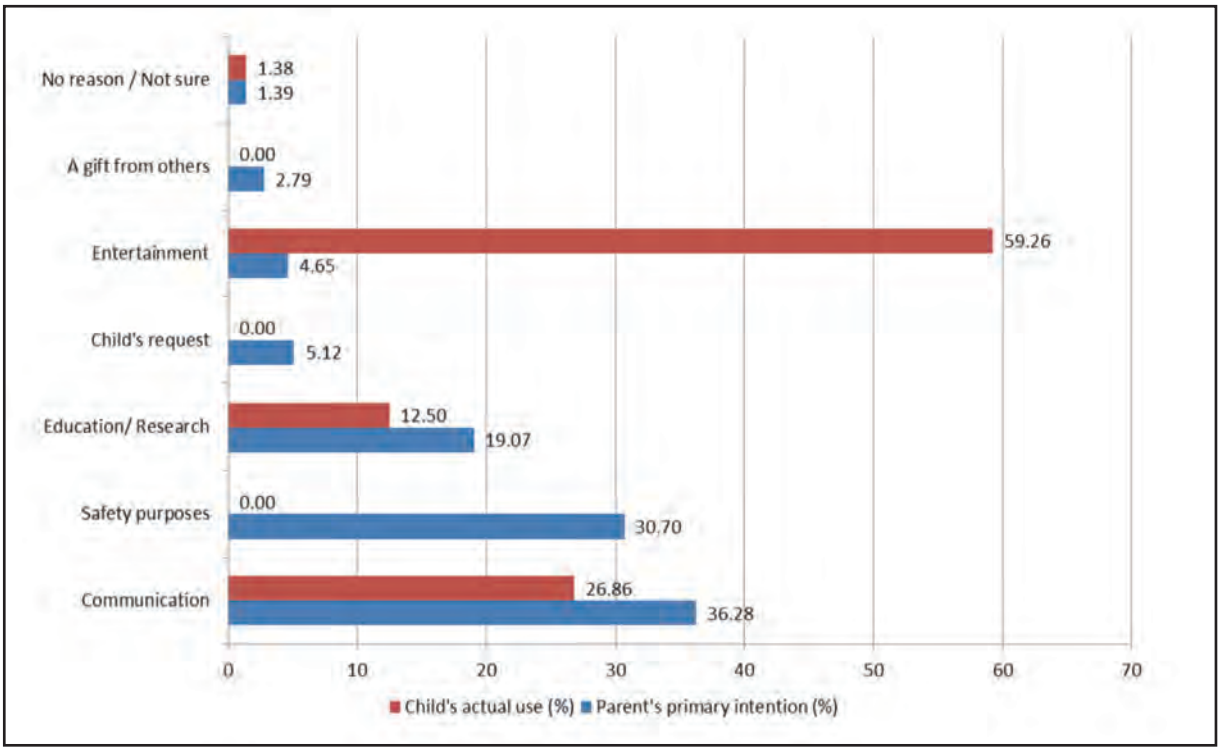

Fig. 1: Parent's intentions of providing their children a handphone and child's actual use of the handphone

Digital Trends Study in the United States where 500 women reported that the average age for a child getting their first smartphone was 10.3 years.[8] However, back in 2012, a survey done in Japan, India, Indonesia, Egypt, and Chile showed the commonest age for children to get their first handphone was 12.[9]

In the 2014 nationwide survey among users of handphones in Malaysia, the common methods of parental control include checking the content of their children's phone (73%), limiting their children's out-going calls (59%) and the length of conversation (47%), and confiscating the phone as a form of punishment (45%).[5] A survey on 249 parent-child pairs in the United States on technology rules and their perceived effectiveness reported that children were more likely to follow activity constraints, like boundaries set on specific technology activities (e.g., no Snapchat) than context constraints (e.g., no handphone at the dinner table).[10] These methods of control were similar to those reported by parents in our study, where limit the time of total handphone usage, type of applications, time spent online were commonly practiced.

In the United Kingdom, common strategies of parental safety mediation included explanation of the good and bad of websites, suggestions on safe internet use, providing help with difficult internet searches and asked not to disclose personal information online.[11] Our parents preferred to explain the exact method, like advising their children not to text people whom they did know and not to disclose personal information online.

A survey among Malaysian secondary school children further confirms that children do experience cyber-bullying, addiction, sexual harassments, and have been exposed to inappropriate language when they use the internet, and they may not have the capacity to mitigate such problematic situations or negative experiences.[6] As a result, only a quarter of parents in our study perceived their children to be capable of managing their own safety when using handphones despite the rules and education provided.

There were a few limitations to this study. Since the study was conducted via an online questionnaire, parents without regular access to the internet would not be able to participate, thus affecting the representativeness of the sample. As with any self-reported data, there was a potential for measurement bias as there might be deviation from the actual practices compared to those perceived. The use of electronic questionnaires had been shown to elicit truthful responses from participants as it was anonymous and could be done privately, but there was no possibility for clarifying ambiguous responses. For example, the parents that had earlier indicated that they had imposed rules on their children but in response to this question, they did not state any control being practised.

CONCLUSION

The majority of Malaysian parents controlled their children's handphone usage by setting rules as well as educating them on cybersafety. A wide range of rules and education topics were practised. Most parents perceived that their youngest children in the family followed the rules set by them. Despite the rules and education provided, many parents were still not confident that their children were able to manage their own safety when using handphones.

Lastly, there was a need for more research and evidence-based guidelines on protecting children's safety in the use of media devices. Future studies should also be expanded to include parents of children from marginalised settings to examine their perspectives of mediating their children's digital media use.

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DISCLOSURE STATEMENT

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ORIGINAL ARTICLE

A retrospective study of factors affecting mortality in patients with complicated intra-abdominal infection

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ABSTRACT

Introduction: Complicated intraabdominal infection (cIAI) is a widespread infection of intraabdominal organs and it has a high mortality rate. Patients might present with various factors affecting the prognosis of this condition. This study aims to analyze the various factors of cIAI patients and to find their association with mortality during the treatment in hospitals.

Materials and Methods: A cross-sectional retrospective single-center study was conducted between 2020 and 2021 using 265 patients' medical records at Dr. Soetomo General Hospital in Surabaya, Indonesia. Various data regarding patient factors at the time of admission were recorded and analyzed to find the association with mortality during treatment. Chi-square and logistic regression test were used to verify our hypothesis statistically.

Results: The patient factors in this study were predominantly male patients (65.3%), younger age (86.4%), cIAI caused by appendicitis (35.5%), and normal nutritional status (73.2%). The overall mortality rate during treatment in this study was 34.7%. Five factors were significantly associated with mortality in cIAI patients during treatment ($p<0.05$), which are: older than 65 years old (OR: 2.85; 95% CI 1.11–7.31), having comorbid disease (OR: 7.92; 95% CI 2.05–30.63), septic shock on admission (OR: 5.56; 95% CI 2.40–12.91), treatment duration more than 3 days (OR: 2.52; 95% CI 1.24–5.15), and SOFA score more than 2 points (OR: 12.14; 95% CI 2.70–54.72).

Conclusion: Patient factors including age, comorbid disease, septic shock on admission, treatment duration, and SOFA score were significantly associated with the incidence of mortality during the treatment in cIAI patients.

KEYWORDS:
Complicated Intraabdominal Infection, peritonitis, mortality

INTRODUCTION

Complicated intra-abdominal infection (cIAI) is a widespread infection of intra-abdominal organs that results in localized peritonitis, intra-abdominal abscess, and diffuse peritonitis. This condition has a substantial impact since it significantly increases morbidity and mortality.[1] The CIAOW global study states that 16% of cIAI patients fall into critical condition and 10% of cases die while receiving therapy.[2] The global AbSeS study noted that the cIAI global mortality rate was 29.1% and estimated to reach 40.3–54.9% if they fell into septic shock.[3] Sartelli et al.[4] revealed that when there is coexistence with sepsis, the mortality rate of cIAI increases from 1.2% to 4.4%, even reaching 67.8% in septic shock.[4] Epidemiologic data of cIAI in Indonesia at six reputable medical institutes identified 608 cases of cIAI over a 2-year period with a mortality rate of 16.6%.[5,6]

Intra-abdominal sepsis is a challenge in the surgery field, especially its management in developing countries. The survival rate of cIAI patients is influenced by various factors such as bacterial pathogenicity, prompt and adequate source control, appropriate antibiotic administration, and intrinsic risk factors of the patient.[7] Patient sepsis-related risk factors are strong predictors in assessing the mortality of cIAI patient.[8,9] Early detection of septic conditions and taking prompt action to prevent cIAI patients' progression into septic conditions will increase their survivability. Although there have been multiple publications of cIAI worldwide, current studies that describe the characteristics of cIAI patient factors and their association with mortality during treatment are still limited. This study aims to analyze the characteristics of various factors in cIAI patient and their association with mortality during treatment at one of health centers in Indonesia.

MATERIALS AND METHODS

Study design

A retrospective cohort study was conducted using data from medical records of patients who received treatment at our healthcare center, Dr. Soetomo General Hospital Surabaya, Indonesia, between 2020 and 2021. We searched for the association between patients' factors at the time of admission to our emergency department with the mortality during the treatment. This study was approved by the ethics committee in our hospital and all researchers have undergone a certified Good Clinical Practice course. All data used in this study were anonymous and information regarding patients' personal data was kept confidential.

Patient data and factors

We collected patient medical records in 2020–2021 by consecutive total sampling according to the following inclusion criteria: an Indonesian, men/women aged over 18 years, diagnosed with cIAI, or suffering from secondary/tertiary peritonitis, intra-abdominal abscess, and

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underwent source control surgery during hospitalization. Incomplete medical record data for analysis will be excluded from this study. Cases of primary peritonitis and pancreatitis were not analyzed.

The study recorded several factors of the patient present to the emergency department, including gender, age, referral/non-referral, etiology of cIAI, nutritional status, comorbid disease, septic shock event, immune status, time-to-treatment, duration of source control surgery, and Sequential Organ Failure Assessment (SOFA) score based on Sepsis-3 global criteria. We performed a binary classification of several factors to facilitate statistical analysis of the association to patient mortality at the end of treatment. The patient's age was classified into two classes, with those who are > 65 years classified as geriatric. The home address is recorded according to the patient's domicile to know whether the patient was referred or not (primary patient in our hospital). The nutritional status is divided based on the classification of body mass index into excess nutrition, normal, and undernourished groups.

Factors such as comorbid disease, septic shock status, and immune status at the time of admission to the emergency department were also recorded. A comorbid disease is defined as any disease which is not directly related to cIAI itself, that co-exists in the patient diagnosed with cIAI. Those diseases can be cardiovascular (hypertension, heart failure), lung (chronic obstructive pulmonary disease, acute respiratory distress syndrome), renal (chronic renal failure, acute kidney injury), liver (elevated liver function, hepatitis, cirrhosis hepatitis), and malignancy. This information was retrieved from the patient's medical record. The immune status was analyzed with the history taking. Immunosuppression is a condition when patients have a suppressed immune system such as chronic use of immunosuppressants, undergoing chemotherapy, or suffer from systemic disease involving a lymphatic (lymphoma) or immune system. Shock septic is evaluated based on patient condition at the time of arrival to our emergency department. We classified patient into the septic shock group if the Mean Arterial Pressure (MAP) was below 65 mmHg (with no vasopressor). Time-to-Treatment (days) is defined as time consumed from the onset of symptoms appear to the time when patient received treatment at our hospital. The duration of surgery is the time (minutes) required by the patient during source control surgery. SOFA scores are divided into two classes, with score of >2 considered as high-risk. Each patient was then monitored until the completion of their course of treatment and it was noted whether they had survived or not. This condition is listed as the patient's outcome.

Statistic analysis

Each data of patient factors will be presented in frequency. The mean, median, and standard deviation were calculated for each data with a ratio scale (age, duration of surgery, time-to-treatment, and SOFA score). Factor data of nominal and ordinal scale is analyzed for statistical association, while the outcome is analyzed with chi-square test. We aim to explore factors that are significantly associated with the incidence of mortality during treatment. The second stage of statistical test is to perform a Logistics Regression test on factors that are already proven to be associated in previous analysis. The significance value of this study was $p<0.05$. The study also calculated the value of Odds Ratio (OR) and 95% Confidence Interval (95% CI) on factors that were significantly related to patient mortality. All statistical tests was done using Statistical Package for Social Science computer application IBM SPSS Statistics for Windows version 25; IBM Corp., Armonk, NY, USA.

RESULTS

Characteristics of patient factors

During the period of data collection, 278 cIAI patients were obtained from a total of 2.330 surgical patients who presented to the emergency department of Dr. Soetomo General Hospital Surabaya, Indonesia. Thirteen cases were excluded due to incomplete data for statistical analysis, finally there 265 subjects who are eligible for this study. Table I presents the characteristics of cIAI patients in our study with the statistic value. We found that cIAI patients in this study were majority consist of males (65.3%), non-geriatric age (86.4%), patients with normal nutritional status (73.2%), and patient with normal immune status (92%). The average age of our participants was 42.6 years old (median 41±17.5 years).

We found that the ratio of referral and non-referral patients treated in this hospital was almost equal, with 52% of patients are referred from other hospitals. Appendicitis remains the most common cause of cIAI (35.5%), followed by gastroduodenal perforation (21.5%) as the second most common. Most of the cIAI patients had comorbidities (74%). There were 20.4% cases of cIAI with septic shock state. Sixty-one percent (61%) of patients came to our hospital after more than three days from the onset of symptoms appearance (median 3±2.85 days). Medical team usually need 155 minutes (median 150±65 minutes) to undergo a source control surgery in cIAI patient. Those surgery might act as a damage control surgery or as a single-stage definitive surgical procedure. We also found that 71.3% cases of cIAI were classified as a high-risk group based on SOFA scores, where multiple organ failure had occurred.

Statistical analysis for association

A two-stage statistical analysis was conducted in this study to evaluate the association of several patient factors at the time of admission to the hospital with the final outcome. The first stage of statistical test, which used a non-parametric Chi-square, is listed in Table I. There is a significant association ($p<0.05$) between patient factors and mortality during treatment, including age, referral/non-referral case, etiological diagnosis, comorbid disease, septic shock condition, time-to-treatment being longer than 3 days, and high-risk SOFA score.

Second stage of statistical test was carried out to rule out the influence of confounding factors of mortality (Table III). Logistics regression test showed a significant association ($p<0.05$) in several factors, namely age (OR 2.85; 95%CI 1.1–7.3), comorbid disease (OR 7.92; 95%CI 2.05–30.63), condition of septic shock at arrival (OR 5.56; 95%CI 2.40–12.9), Time-to-Treatment being longer than 3 days (OR 2.52; 95%CI 1.24–5.15), and SOFA score more than 2 points (OR 12.14; 95%CI 2.7–54.72).

Table I: Characteristics of participants and Chi-Square Test

Patient's Factors		Outcome		Total	*p* value
		Survived	Not survived		
Gender	Male	115	58	173 (65.3%)	0.577
	Female	58	34	92 (34.7%)	
Age	Non-Geriatric (< 65 years old)	159	70	229 (86.4%)	0.001
	Geriatric (> 65 years old)	14	22	36 (13.6%)	
Referral Case	Non-Referral case	93	33	126 (47.5%)	0.006
	Referral case	80	59	139 (52.5%)	
Etiology Diagnosis	Appendicitis	83	11	94 (35.5%)	0.001
	Gastroduodenal Perforation	30	27	57 (21.5%)	
	Jejunoileal Perforation	21	14	35 (13.2%)	
	Colon Perforation	16	22	38 (14.3%)	
	Hepatic Abscess	6	5	11 (4.2%)	
	Splenic Abscess	2	0	2 (0.8%)	
	Other Intraabdominal Abscess	5	3	8 (3%)	
	Intestine Anastomotic Leakage	3	5	8 (3%)	
	Others	7	5	12 (4.5%)	
Nutritional Status	Overweight	27	15	42 (15.8%)	0.989
	Normal	127	67	194 (73.2%)	
	Underweight	19	10	29 (10.9%)	
Comorbid Disease	No Comorbid Disease	66	3	69 (26%)	0.001
	Comorbid Disease	107	89	196 (74%)	
Septic Shock	No Septic Shock	161	50	211 (79.6%)	0.001
	Septic Shock	12	42	54 (20.4%)	
Immunity Status	Normal	162	82	244 (92.1%)	0,196
	Immunosuppression	11	10	21 (7.9%)	
Duration of Source Control Surgery	< 150 minutes	70	48	118 (44.5%)	0.068
	> 150 minutes	103	44	147 (55.5%)	
Time-to-Treatment	< 3 days	75	28	103 (38.9%)	0,040
	> 3 days	98	64	162 (61.1%)	
SOFA Score	Low Risk (<2)	74	2	76 (28.7%)	0.001
	High Risk (> 2)	99	90	189 (71.3%)	
Total Subjects		**173 (65.3%)**	**92 (34.7%)**	**265**	

Table II: Descriptive analysis of patient's factor

	Age (years)	Surgery Duration (minutes)	Time to Treatment (days)	SOFA score
Mean	42.59	155.19	3.52	3.71
Median	41.00	150.00	3.00	3.00
Std. Deviation	17.536	65.280	2.851	3.114
Minimum value	15	25	0	0
Maximum value	89	420	28	14

Table III: Logistic regression analysis of patient's factor associated with mortality

	Sig. (p)	Odds Ratio	95% CI	
			Lower	Upper
Age >65 years old	**0.030**	**2.846**	**1.109**	**7.306**
Referral case	0.128	-	-	-
Diagnosis	0.102	-	-	-
Nutritional status	0.834	-	-	-
Comorbid disease	**0.003**	**7.921**	**2.048**	**30.631**
Septic shock status	**0.001**	**5.560**	**2.395**	**12.905**
Immunity status	0.881	-	-	-
Duration of source control operation	0.211	-	-	-
Time to treatment	**0.011**	**2.521**	**1.235**	**5.145**
SOFA Score	**0.001**	**12.138**	**2.692**	**54.718**

DISCUSSION

Surabaya is one of the big cities in Indonesia with a population of 1% of national population. This city is the second largest city in Indonesia, following Jakarta as the capital city. Dr. Soetomo General Hospital had surgical emergency visits up to 1.800 cases annually (in 2021) with a bed occupancy rate of 85.47%. The prevalence of cIAI in this hospital is 12% of all surgical emergency cases.[10,11] This prevalence rate is close to the national prevalence rate of cIAI at 10%.[12,13] Therefore, our hospital is considered reliable to represent the characteristics of cIAI in general Indonesian society and along with other condition at the national level.

The statistics of gender, age, and etiological diagnosis found in this study revealed a similar frequency distribution to several previous global studies. CIAOW study in 2013 found that the amount of male patients was higher than female (62.3% : 38.7%). Lalisang et al.5 also found similar findings in Indonesian population with the ratio of 67.3% : 32.7%. Male gender seems to be more susceptible to cIAI compared to women; however, there is no literature that sexplains the rationale of gender as a factor. Majority of cIAI patients was in the non-geriatric age group (< 65 years old), with a median age of 41 years. Llorente et al16 in Spain, Abdel-Kader et al[14], and Inui et al[15] stated that subjects of cIAI patients in their study were between 30 and 50 years old. Perforated appendicitis is the most common cause of cIAI in all research data worldwide. This remains consistent in both developed countries in Europe and developing countries in Asia. As one of the national referral center hospitals, we get many referrals of cIAI cases across the nation for more advanced treatment. Our National Consensus of cIAI recommends that those with a high-risk and complex condition to be referred to a higher-level referral hospital, including ours. This will have an impact on the high number of referral cases for cIAI patients as the participants of our research.[2,4,5,12,14-8]

Comorbid disease, nutritional status, septic shock, and immune status were thought to have an association with mortality in cIAI patients. Llorente et al[16] explained that the proportion of cIAI patients was greater in the group of patients with few and mild comorbidities (Charlson Comorbidity Index/CCI 0-4). Llorente et al16 also mentioned that cIAI patients were predominantly have a normal nutritional status or normal body mass index. Obesity cases were found in 15.8% of cases of our study, comparable to Llorente's study with a frequency of 15.9%. The number of cIAI cases with septic shock in this study was slightly higher than the CIAOW global study, which was 13.1%. The presence of septic shock has been shown to significantly increase the risk of mortality from 5.1% to 36.6% compared with those patients who are clinically stable.[2,16,18]

On average, our participants seek medical treatment on the third day after the onset of symptoms, which according to the literatures are too late to get treated appropriately. Several factors that we found, such as recognition delay, financial/economy issues, and limited access to healthcare facilities in the remote area, were the reasons for the delay in managing patients. Majority of previous studies use the 24-hour time limit as the cut-off value for determining mortality risk. A similar study in our country, Puspitadewi et al[13], revealed only 31.4% cases of patients who came to the healthcare facilities within less than 24 hours since the symptoms onset. However, Llorente et al16 noted that there was >24 hours delay in surgery within 14.8% cases of cIAI.[13,16]

A total of 71.3% cases in our subjects had high SOFA scores on arrival (cut off >2). The presence of organ failure reflects of a life-threatening systemic infection according to the definition of sepsis in the Sepsis-3 criteria. The mortality rate of cIAI patients managed in this study was 34.7%, which is higher than the previous national and global studies. The single centre study of cIAI in Jakarta revealed a mortality rate of 20.9%, other multicentre study in our country showed a

mortality rate of 16.6%, the CIAOW global study in 2014 at 10.5%, while other global study in 2017 at 9.2%. Other literatures state that the mortality rate might actually vary within range of 23-38%.[4,5,7,12,19,20]

The two-stage statistical analysis (Chi-square and Logistic Regression) showed that patient factors such as age, presence of comorbid disease, septic shock condition, delay in time-to-treatment more than 3 days, and SOFA score >2 points were strongly correlated with mortality of cIAI patients during treatment ($p<0.05$). Based on statistics, those five factors, either related or independently associated regardless of their relationship with other factors, were able to affect the final outcome of cIAI patient treated in our hospital. Other factors that have been recorded have no effect on mortality.

Patients who are older than 65 years old are strongly associated with mortality during hospitalization (OR: 2.84; 95%CI 1.11–7.31). This finding is supported by various literatures that conclude that old age is a poor prognosis factor for cIAI patients. Higher risk of mortality in elderly can be explained by the inability of the body to handle stressor. Similarly, they are more susceptible to get sepsis and multiple organ failure due to the declining physiological function and disability to deal with stress. According to various scoring systems, age is considered as one of the poor prognostic factors in cIAI patients, although the age limit varies greatly within studies. The Manheimm Peritoneal Index (MPI) scoring system, WSES Sepsis Severity Score, and Calgary PIRO score are prognostic scoring systems for cIAI that utilize age with different cut-off point, where the patient's age is inversely correlated with the patient's survival.[16,17,21,22]

The presence of comorbid disease also increases the risk of mortality (OR: 7.92; 95% CI 2.05–30.63). Llorente et al[16] stated that the presence of comorbid disease affects the incidence of morbidity and mortality in cIAI patients significantly up to 90 days after infection. Comorbid diseases influence the occurrence of complications based on the Clavien-Dindo index. Comorbid disease should be measured by the Charlson Comorbidity Index (CCI) to predict its relationship with morbidity and mortality in cIAI patients. Up to 90 days of treatment, the greater the CCI value, the higher the rate of mortality and the Clavien Dindo's morbidity index. One of the limitations of this study is that we do not use CCI index system in assessing the presence of comorbid disease in patients, thereby the association analysis of comorbid disease cannot be carried out. This study also does not classify the types of comorbid diseases that affect mortality.[16]

The incidence of septic shock at the time of diagnosis is significantly associated with patient mortality during treatment (OR: 5.56; 95%CI 2.40–12.91). Similarly, Luo et al23 stated that the incidence of septic shock affected patient mortality up to 28 days of treatment in cIAI patients ($p<0.001$; OR 5.69 95%CI 3.31–9.77). Septic shock defined as a condition of cardiovascular organ failure characterized by the need for vasopressors to maintain arterial pressure above 65 mmHg accompanied by an elevated lactate levels above 2 mmol/L. This circumstance will have a consequence on peripheral tissues with significant hypoxia in the form of oxidative stress. The mortality rate in our patients with septic shock was quite high (77%), in contrast to Luo et al23 at 30.9%.[23] Patients with septic shock are usually failed to survive in late phase of intensive care. Literature explain that early death was secondary to the irreversible multiorgan failure associated with the underlying infection (82%) and the presence of mesenteric ischemia (6.4%). In the late phase, death mostly happened after a family decision to halt the treatment (29%) and the presence of nosocomial infection (20.4%).[24]

The duration of time from onset to treatment in patients are significantly influence the mortality of cIAI patients. There are a total of 61.1% of patients who seek for medical treatment after the third day of symptoms onset. The longer the time for patient to get treated, the lower the chance their survival (OR 2.52 with 95% CI 1.24–5.15). Several studies use a lower cut-off value of 24 hours for the treatment of cIAI. Delay in source control surgery is a major risk factor for patient mortality. The patient's survival rate is significantly decreased when the source control surgery is performed in more than 6–8 hours. Global experts suggest that source control surgery should be carried out as early as possible. However, there is currently no agreement on the exact time limit to carry out the surgery. Early surgery and adequate resuscitation are both critical factors that surgeons must consider to lower the morbidity and mortality rate. Major surgical procedures including intestinal resection or only percutaneous drainage under local anesthesia both can be performed in critically ill patients. Minimal interventions are still recommended to treat sepsis in critically ill patients. Delay of treatment in this study was influenced by several things, including patient knowledge, limited access to healthcare facilities, limited medical support, and other non-technical factors.[16,23,25]

Assessment of SOFA scores on arrival had a predictive value on patient mortality (OR: 12.14; 95%CI 2.69–54.72). SOFA score can be measured in cIAI patients who fall into a critical condition. This score can be applied in the intensive care unit for both non-surgical and surgical critical patients. Creatinine levels and level of consciousness by the Glasgow Comma Scale are both the strongest prognostic factors associated to the patient mortality. Despite the fact that there are various scoring systems recently in the assessment of mortality specifically for cIAI patients, SOFA score remains an accurate, easy-to-use, and objective tool for assessing patient's severity.[26,27]

Prolonged duration of source control surgery may result in poor survival rate, secondary to the declining immune defense mechanisms which lead to several morbidities. Immunosuppression conditions and delayed detection will also make the patient's condition worse.[28] There is no doubt that widespread infections in the bloodstream can raise morbidity and mortality by up to 31%. In addition, the duration of treatment and health costs will increase significantly.[29] The concept of adequate damage control surgery has been routinely applied to cIAI cases that are previously thought to have a high mortality risk. As has been discussed, understanding the risk factors of mortality may promote surgeons to perform simple procedure such as bedside percutaneous drainage in critically ill patients.[30]

Following a 48-hour period in which the patient's condition has improved, definitive surgery may be considered. When a one-step definitive management strategy is implemented right away in severe and critical cases, a high risk of mortality will increase.[5]

CONCLUSION

Several patient factors on arrival which are significantly associated with the incidence of mortality during treatment in the cIAI patients are being older than 65 years, presence of comorbid disease, septic shock, Time-to-Treatment longer than 3 days, and SOFA score higher than 2 points. This finding is consistent with the previous scientific literature as a predictor of mortality in the management of cIAI patients.

There are several limitations in this research. We did not collect microbiologic and antibiotic susceptibility data which also may affects the prognosis regarding source control management. We did not use the Charlson Comorbidity Index (CCI) to assess comorbid disease in our patients. This study did not analyze the confounding factors during patient care, such as the use supportive vasoconstrictor therapy during septic shock, use of ventilator as a respiratory support, perioperative fluid therapy, etc. Morbidity assessment using Clavien Dindo index may be carried out to assess its association within cIAI after the patient is discharged. Apart from the above description, patient mortality can also be predicted through other methods, such as the Acute Physiology and Chronic Health Evaluation II (APACHE II) scoring system, procalcitonin levels, and the Neutrophil-Lymphocyte ratio.[31]

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest and financial in the writing of this manuscript.

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ETHICAL CLEARANCE

This study was reviewed and approved by the Medical Ethical Committee of Dr. Soetomo General Hospital, Surabaya, Indonesia (Ref. No.: 0956/LOE/301.4.2/VII/2022) following the guidelines of the Declaration of Helsinki.

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Chronic suppurative otitis media and immunocompromised status in paediatric patients

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ABSTRACT

Introduction: The role of immunodeficiency in the development of chronic suppurative otitis media (CSOM), especially in paediatric populations, have yet to be fully elucidated. The purposesof this study is to investigate the association between immunocompromised status and CSOM among paediatric population in a tertiary hospital in Indonesia.

Materials and Methods: A cross-sectional study was performed by retrieving medical records of paediatric patients, with and without CSOM (age 0–18 years), visiting otorhinolaryngology (ENT-HNS) outpatient clinic in a tertiary hospital in Indonesia (2018-2020). We collected data on comorbidities causing immunosuppression such as HIV status, tuberculosis, and cancer.

Results: Among the 1018 included patients (50 immunocompromised children), HIV infection was the most common cause of immunodeficiency in the CSOM group (24 patients, 60%), and cancer in the non-CSOM group (10 patients, 100%). We found a significant association between immunocompromised hosts and CSOM (odds ratio 19.5 [95% confidence interval: 9.5–39.9], p<0.001).

Conclusion: Immunocompromised children with HIV, tuberculosis, or cancer may be more vulnerable to CSOM. Further research is required to explore the association between other immunocompromised conditions and CSOM in paediatric populations.

KEYWORDS:
Chronic suppurative otitis media, HIV, immunocompromised host, paediatrics, tuberculosis

INTRODUCTION

Chronic suppurative otitis media (CSOM), characterized by a persistent or intermittent discharge from the middle ear through perforated tympanic membrane, is a major cause of acquired hearing loss in children, afflicting more than half of the affected children. It is estimated that developing countries account for 90% of the global burden of CSOM, especially in Southeast Asia. Several factors may predispose children to CSOM, including poor living conditions, sanitation, and hygiene, as well as frequent and improper treatment of upper respiratory tract infections.[1] While immunocompromised patients are believed to be more vulnerable to chronic infections, the role of immunocompromised hosts either due to primary immunodeficiency, systemic comorbidities (e.g., HIV infection, cancer, diabetes, malnutrition), or immunosuppressive therapies, in the development of CSOM has yet to be fully understood.[2] Therefore, this study aims to explore the comorbidities causing immunocompromised state and investigate the association between immunocompromised status and CSOM among paediatric population in a tertiary hospital in Indonesia.

MATERIALS AND METHODS

A cross-sectional study was conducted by reviewing medical records of paediatric patients visiting the ENT-HNS outpatient clinic in a tertiary hospital in Indonesia between 2018 and 2020. The study protocol has been approved by the Health Research Ethics Committee, Faculty of Medicine Universitas Indonesia and Cipto Mangunkusumo National General Hospital (protocol number: 21-04-0376).

All paediatric patients aged between 0 and 18 years presenting to our outpatient clinic with CSOM or non-CSOM were included in the present study. CSOM was defined as a chronic ear infection characterized by a history of ear discharge lasting for more than two months and tympanic membrane perforation found on otoscopic examination. All types of CSOM such as tubotympanic (CSOM without cholesteatoma/safe type) and atticoantral (CSOM with cholesteatoma/dangerous type) were included in this study. Patients without any presence of tympanic membrane perforation were included in non-CSOM group. Data on the immune status of the patients were collected based on the diagnosis in the medical record. The immunocompromised status of the patients was categorized based on the comorbidity into tuberculosis, HIV infection, and cancer. The diagnosis of tuberculosis was based on the Indonesian National Guidelines of Tuberculosis,[3] and the diagnosis of HIV infection based on reactive immunoserological anti-HIV assays. All patients were included regardless on the disease type, disease status (e.g., WHO clinical stage or CD4 counts in HIV-infected patients, active or latent tuberculosis cases, or cancer stage), and treatment received. Due to data limitations, we were unable to record HIV markers such as CD4 counts and viral loads, as well as other immunocompromised conditions including primary immunodeficiency diseases, patients receiving

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Table I: Subject characteristics

Characteristics	Patients (n=1018)	%
Gender		
Male	583	57.3
Female	435	42.7
Age (years)		
0-5	711	69.8
>5-10	183	18.0
>10-15	89	8.7
>15-18	35	3.4
Non-CSOM	817	80.3
CSOM	201	19.7
Non-Immunocompromised	968	95.1
Immunocompromised	50	4.9

CSOM, chronic suppurative otitis media

Table II: Characteristics of immunocompromised patients

Comorbidity	CSOM	Non-CSOM	Total
HIV	24	0	24
Tuberculosis	6	0	6
Cancer	10	10	20
Total	40	10	50

CSOM, chronic suppurative otitis media; HIV, human immunodeficiency virus

Table III: Association between immunocompromised hosts and CSOM in the study population

	Non-immunocompromised	Immunocompromised	Total	*p* value	OR	CI 95%
Non-CSOM	807	10	817	<0.001[a]	19.5	9.5-39.9
CSOM	161	40	201			
Total	968	50	1018			

[a]Chi-square, statistically significant. CI, confidence interval; CSOM, chronic suppurative otitis media; OR, odds ratio

immunosuppressive therapy, organ recipients, malnutrition, and hematological diseases. All data were collected and analyzed using SPSS 23.0 (SPSS Inc., Chicago, IL).

RESULTS

A total of 1018 patients participated in this study (583 boys [57.3%] and 435 girls [42.7%]). More than half of the patients were aged between 0 and 5 years (69.8%), while only 3.4% were aged between 15 and 18 years (Table 1). During the study period, 201 CSOM patients (19.7%) and 817 non-CSOM patients (80.3%) visited our clinic (Table I). About 50 patients were immunocompromised (40 in the CSOM group and 10 in the non-CSOM group; Table II). Among the 40 immunocompromised children in the CSOM group, HIV infection was the most common cause of immunodeficiency (60.0%), followed by cancer (25.0%) and tuberculosis (15.0%). Meanwhile, all immunocompromised children in the non-CSOM group suffered from cancer. We found that an immunocompromised state was associated with a higher odd of CSOM (OR 19.5 [95% CI: 9.5–39.9]; p<0.001; Table III).

DISCUSSION

CSOM is a multifactorial disease involving complex interactions between the hosts, bacterial agents, and environmental factors. The present cross-sectional study sheds light on the role of immunity on the development of CSOM in paediatric patients, where immunocompromised children were found to be more vulnerable to CSOM. This indicates that both innate and adaptive immune system plays a vital role in the defense against CSOM pathogens.[4] In immunocompromised hosts, the innate and adaptive immune systems are unable to exert immune response against pathogens, resulting in pathogen escape and replication.[5]

In the present study, we found that more than half of the immunocompromised children in the CSOM group suffered from HIV infection. Our findings further reinforced Indonesia's position as one of the hotspots for HIV in the region, afflicting about 3200 children in 2020 alone.[6] Such condition may result from the destruction of CD4+ T cells by the HIV, thus resulting in diminished functional ability of CD4+ T cells to respond to infections leading to the acquisition of opportunistic infections including CSOM. Therefore, early detection and prompt antiretroviral treatment in these populations are paramount in preventing the development of opportunistic infections. In this regard, Hallbauer et al. suggest that patients presenting with chronic otorrhea should be evaluated for HIV and be promptly treated with antiretroviral therapy.[7]

Other comorbidities causing immunosuppression observed in our CSOM cohort were cancer and tuberculosis. Immunodeficiency in cancer may result directly from the invasion of the cancer cells to the bone marrow–halting the production and development of white blood cells[8], and indirectly from immunosuppressive therapies.[9] Meanwhile, immunosuppression in tuberculosis is mediated by immune

dysregulation involving regulatory T cells.[10] Altogether, these indicate that immunocompromised children with HIV infection, cancer, or tuberculosis should be closely monitored to prevent the occurrence of chronic infections including CSOM, which may result in debilitating complications leading to morbidity and poor quality of life.

This study is limited by the fact that other immunocompromised conditions such as primary immunodeficiency diseases, patients receiving immunosuppressive therapy, organ recipients, malnutrition, and hematological diseases were not considered due to data limitations. In addition, the cross-sectional design implies that causations between variables could not be explained. Further large, high-quality studies exploring the role of other immunocompromised conditions in the development of CSOM in paediatric populations are warranted.

CONCLUSION

In conclusion, our findings indicate that immunocompromised children with HIV, tuberculosis, or cancer may be at a higher odd of developing CSOM, suggesting that these populations should be closely monitored to prevent potential debilitating complications. Further research exploring the association between other immunocompromised conditions and CSOM in paediatric populations are warranted.

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ORIGINAL ARTICLE

Tracheal resection and reconstruction: A 3-year case series of 14 patients

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ABSTRACT

Introduction: Tracheal resection and reconstruction is one of the most challenging procedures and is seldom performed due to its complexity. Despite being a life-saving procedure, only a handful of centres are performing this procedure in Malaysia. We report our 3 years' experience in Hospital Kuala Lumpur performing tracheal resection and reconstruction in 14 patients.

Materials and Methods: Retrospective review of medical records of tracheal resection and reconstruction was performed from September 2018 till August 2021. Data that were extracted include demographic information, indication for surgery, intraoperative airway management, surgical approach, perioperative parameters, complications, and 1-year outcome.

Results: Fourteen patients with the mean age of 49.1 years underwent tracheal resection and reconstruction, consisting of 9 benign and 5 malignant diseases. Non-intubated airway approach was used in three patients. Transcervical surgical access was used in 10 patients whereas thoracotomy, video-assisted thoracoscopic surgery, and combination of thoracotomy, transcervical incision with manubrial split were used in 3 patients respectively. The mean length of trachea resected was 2.3cm, with the longest length of 4.5cm. All patients were extubated post-operatively except for one due to traumatic brain trauma. No anastomosis dehiscence was seen. We also did not see any post-operative stenosis and all the patients are alive.

Conclusion: Tracheal resection and anastomosis can be performed safely in complex stenosis and malignant tumours. Pre-operative planning with a multidisciplinary approach is vital to ensure a good outcome.

KEYWORDS:
Tracheal surgery, tracheal resection and reconstruction, tracheal stenosis, tracheal tumour

INTRODUCTION

The first recorded tracheal surgery was performed by Belsey in 1950.[1] Despite seven decades after its introduction, it remains as one of the most challenging procedures among surgeons. This is mainly due to the peculiar anatomy of the trachea, particularly its location both in the neck and mediastinum, length, structural rigidity, and blood supply.[2] The success rate of tracheal resection and reconstruction varies from 71 to 95% and the reported mortality rate is 1.2%.[3,4]

Though challenging, it is imperative for all thoracic surgeons to be competent in tracheal resection and reconstruction as it is a life-saving procedure. With the evolution of video technology, bronchoscopic intervention coupled along with surgery has achieved good outcomes for tracheal pathologies.

In this article, we report our early experience in tracheal surgery and its feasibility, safety, and short-term outcome. Tracheal resection and reconstruction was never performed in our unit before this.

MATERIALS AND METHODS

Medical records of all patients who underwent tracheal resection and reconstruction at the Thoracic Surgery Unit, Hospital Kuala Lumpur from September 2018 till August 2021 were reviewed retrospectively. All patients who underwent tracheal resection and reconstruction in Hospital Kuala Lumpur within the study period were included in this review. Descriptive analysis was performed. Informed consent for usage of clinical data was obtained from all patients in this study.

Patients' demographic information, indication for surgery, intraoperative airway management, surgical approach, perioperative parameters, and 1-year outcome were reviewed. No ethical approval was necessary as this was a retrospective observational study.

Perioperative preparations

Generally, all patients for tracheal surgery have undergone contrast-enhanced computed tomography scan (CECT) of neck and thorax with 3-dimensional (3D) reconstruction, bronchoscopy, and echocardiogram.

These patients would be reviewed by the anaesthetist for airway assessment, and subsequently referred to pulmonologist, ENT (ear, nose, throat), or thoracic surgeon. After the airway was secured either by emergent tracheostomy, debulking of tumour by rigid bronchoscopy or bronchoscopy-guided intubation, CECT neck, and thorax with 3D reconstruction were performed. These investigations

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enabled us to determine the site and distance of the tracheal stenosis or tumour from the vocal cord, carina, and the extent of circumferential involvement of the trachea along with extra tracheal involvement.

Anaesthetic technique
For patients with tracheal stenosis lumen sized 5.5mm and above and can be dilated, the airway was secured with an endotracheal tube (ETT) sized 6 passed beyond the stenotic segment. For stenosis not amenable for dilatation, ETT may either be placed above the stenosis, or a laryngeal mask airway used based on the patient's tolerability to lie flat. Once the trachea was transected distal to the lesion, a surgical field flexo-metallic ETT sized 7.5 was passed into the distal trachea.

All patients were subjected to total intravenous anaesthesia (TIVA) to prevent anaesthetic gas contamination during the intermittent opening of the airway during reconstruction. Remifentanil and propofol 1% were delivered by target-controlled infusion (TCI) using the Minto and Schnider model, respectively. The depth of anaesthesia was monitored using bispectral index between 40 and 60. TIVA was titrated to achieve spontaneous ventilation with minimal surgical field movement while always maintaining oxygen saturation above 95%. This enabled us to perform non-intubated tracheal resection in some of our patients. Extracorporeal membranous oxygenation (ECMO) was never used in our series.

After the surgery, an on-table bronchoscopy was performed to aspirate retained blood clots and to examine the anastomosis. The patients were aimed to be extubated immediately to prevent anastomotic complications.

Surgical technique
Approach to tracheal surgery was based on the location of the lesion. Cervical collar incision approach was used for patients with cervical tracheal lesion, with manubrium split if the lesion extends behind the manubrium. A right posterolateral thoracotomy or right video-assisted thoracoscopic surgery (VATS) approach was the method of choice for patients with mediastinal tracheal lesions. Depending on the length of resection, non-tension anastomosis can be achieved by releasing supra and infra laryngeal attachments, inferior pulmonary vein, and hilum. Anastomosis was achieved by long-absorbable monofilament 3/0 suture as described by Grillo.[5] Grillo's chin to chest suture was applied to all patients with the neck in a neutral position following skin closure to prevent neck extension.

Bronchoscopy was performed on post-operative day 5 to assess anastomotic integrity. The chin to chest suture was removed following bronchoscopy and soft cervical collar will be applied to maintain the neck in a neutral position. This collar will be maintained for a period of 6 weeks post-surgery. All patients underwent surveillance bronchoscopy at 1, 3, and 6 months after surgery for up to 2 years.

RESULTS

There were 14 patients who underwent tracheal surgery from September 2018 till August 2021. Out of the 14 patients, 6 (43%) were male and 8 (57%) were female with a mean age of 49.1 years old, ranging from 14–78 years old. The common presenting symptoms were dyspnoea (10 patients), stridor (3 patients), cough (2 patients), and haemoptysis (1 patient). Hypertension, diabetes mellitus, and bronchial asthma were the commonest comorbidities. However, those patients who were diagnosed with bronchial asthma were free from asthmatic attack after the tracheal resection and reconstruction. There were only three patients without any co-morbidity.

All patients that underwent tracheal resection had grade 2 (6 patients) and 3 (7 patients) Cotton Meyer's grading. One patient cannot be classified for stenosis due to acute tracheal tear secondary to trauma and was already intubated for cerebral protection. There were two patients presented with Karnofsky performance status scale of 50 while the remaining presented with the Karnofsky performance status scale of 90. (Table I) One of our patient required pre-operative debulking of tumour with rigid bronchoscopy to establish airway before undergoing definitive surgery.

The tracheal lesion requiring resection originated from the cervical trachea in six patients and mediastinal trachea in eight patients. All the primary tracheal tumours in our series were from the mediastinal trachea (Table II).

Various surgical approaches were used for tracheal resection and reconstruction. Most patients underwent surgery via transcervical approach (71%). The other approaches used were right thoracotomy, VATS, transcervical combined with right VATS and manubrial split and transcervical combined with right thoracotomy. The main aim during the reconstruction is to achieve non-tension anastomosis, which can be achieved by performing various release manoeuvres as described in Table III.

The intraoperative airway management was by intubated (11 patients) and non-intubated (3 patients) manner. The mean duration of surgery was 246.2 minutes (range 70-540 minutes) while the mean length of trachea resected was 2.3cm (range 1.0 - 4.5cm). The nearest resection of trachea from the carina was around 1cm. Only one patient (7%) was ventilated post-operatively and 10 patients required ICU/PACU admission with the mean stay of 1 day. The median duration of hospital stay was 9.5 days. Most frequent post-operative complication was dysphagia. One patient developed right vocal cord paralysis. There was no tracheal anastomotic leak as well as no mortality was observed. (Table IV)

There were five malignant tracheal tumours operated, and the average size of the tumour was 2.3cm (range 1.7-3.5cm). Out of the five patients, three patients (60%) had resected margin involved, which included two patients with papillary thyroid carcinoma where the tumour involved the thyroid cartilage. There was one patient who was pre-operatively diagnosed as granulomatous inflammation causing stenosis; with the final histopathological diagnosis of lymphoma. (Table IV)

DISCUSSION

Tracheal resection and anastomosis for both benign and malignant conditions are not widely performed, owing to the surgical complexity and complications involved. The success rate of tracheal resection is 89.5% and resectable malignant tracheal lesions stand a best chance of cure by surgical resection.[6,7] Post-intubation tracheal stenosis and malignant tracheal lesions were the main indications for tracheal surgery in our centre. There was no benign tumour of the trachea seen in our series, probably because endoscopic resection was already performed by the pulmonologist for such cases. These findings were similarly reported by Cordos et al, Marques P et al, and Hassan et al.[8-10]

The difficulty of the airway management in patients with tracheal lesions undergoing resection varies according to site and severity of the stenosis. All the patients in this cohort presented with symptoms of central airway obstruction with Cotton Meyer's grade 2 and 3. We advocate both intubated and non-intubated techniques of ventilation during tracheal resection. Intubated techniques are used in cases where at least an ETT sized 6.0 can be passed through the lesion. Alternatively, non-intubated technique is used in VATS tracheal resection and reconstruction to enable anastomosis to be performed without ETT interruption. Furthermore, the technique is used when ETT cannot be secured effectively in tight stenosis, which is located less than 3 cm from vocal cord. Non-intubated technique allows the patient to continue spontaneous ventilation with supraglottic airway assistance using laryngeal mask and TIVA. This method was described previously by Benedict et al.[11] and Liu et al.[12] With the advocation of non-intubated techniques, none of our patients required ECMO or cardiopulmonary bypass to perform complex tracheal resection and anastomosis.

The commonest surgical approach used for tracheal resection and reconstruction in this cohort was via the transcervical incision. The similar approach was also performed in some reported case series.[2] Transcervical incision can be used for benign tracheal stenosis resection as low as the T1 vertebra level. For lower stenosis near the carina, a sternotomy or right posterolateral thoracotomy can be the approach of choice. We have perfomed resection of mediastinal tracheal stenosis by a combination of right VATS and manubrial split, as well as a totally VATS tracheal resection. The manubrial split was performed to allow safe dissection of the severely adhered brachiocephalic artery to the crushed mediastinal trachea after trauma (Figure 1).

In cases of malignant tracheal lesions, the aim is to achieve clear resection margins and to remove as many paratracheal and precarinal lymph nodes as possible. If the tumour is located at cervical tracheal, transcervical approach is preferred.[12] However, if the tumour is at the mediastinal trachea, even at the level of T1 vertebra, a sternotomy, a right posterolateral thoracotomy or right VATS approaches can be used to ensure adequate tracheal mobilisation, good resection margin, and adequate lymph node clearance. In our series, we never used sternotomy to access the mediastinal trachea for malignant lesion. This is because of the surgeon's choice to avoid dissecting in between the major vessels (SVC, aorta, innominate vessels, and pulmonary artery) through a narrower quadrilateral space for radical lymph node dissection.[13] The advantage of using a trans-sternal approach is that the carina can be easily accessed. If need arises for left bronchial replacement to achieve extra tracheal length, it can be performed via the same incision.[14]

The length of trachea to be resected determines the extent of mobilisation. For cervical trachea lesions, all our patients underwent pretracheal fascia release, infralaryngeal, and precarinal dissection. For a resection of more than 3cm of cervical trachea, a supralarnygeal dissection was advocated as well. This will allow tension free anastomosis and reduce the risk of dehiscence. Despite the benefits, supralaryngeal release will cause dysphagia to the patient and may require to be on nasogastric tube feeding for 6 weeks after the surgery.[15,16] Tracheal mobilisation should be done mainly in the anterolateral aspect of the trachea, preventing dissection in the posterolateral plane to avoid disruption of the segmental tracheal blood supply.[17] None of our patients had pre or post-operative tracheostomy in the course of the management of tracheal stenosis as seen in other series.

For mediastinal trachea resection, laryngeal release has a minimal role in achieving extra tracheal remnant length.[18] Precarinal dissection, inferior pulmonary ligament dissection, and complete hilar release will provide extra length of around 1–2cm for mediastinal trachea anastomosis, especially near the carina. Three patients with mediastinal trachea resection with anastomosis near carina in our series underwent these mobilisation techniques with good outcome. In cases where around half the length of the trachea needs to be resected, the left main bronchus can be replaced on to the right bronchus intermedius to achieve greater remnant length.[5] Cervical flexion alone can reduce tension on the anastomosis by allowing descent of the cervical trachea into the mediastinum for up to 4cm.[19] Due to this, all our patients will be on chin chest suture post-operatively for 3–5 days until bronchoscopy is performed for anastomosis assessment. Neutral neck position is preferred. One must be cautious not to over flex the neck to avoid risking vertebral artery compression and stroke.[15]

The longest tracheal length resected in our series was 4.5cm for a patient with mediastinal tracheal squamous cell carcinoma. This patient underwent both transcervical approach and right posterolateral thoracotomy to achieve cervical, paratracheal as well as posterior carinal nodal clearance with anastomosis performed 1 cm from the carina. On-table frozen section of tracheal margin was sent to ensure tumour-free margin before anastomosis. The longest tracheal resected with successful reconstruction reported to date is 5.4cm by Mohsen et al.[19]

The complications we encountered were mainly related to dysphagia and lung collapse secondary to mucous plug. No anastomotic leak was seen. One patient with papillary thyroid carcinoma infiltrating the trachea and recurrent laryngeal nerve, developed left-sided vocal cord paralysis due to resection of the nerve. There was no mortality. In comparison with other published tracheal series, the complications seen in our series were lower.[3,4] This could be due to early referral by the primary team for surgical

Table I: Demographic characteristics

Parameters		Value
Age, years in mean (Range)		49.1 (14-78)
Sex, n (%)	Male	6 (43)
	Female	8 (57)
Presenting symptoms, n (%)	Dyspnoea	10 (71)
	Stridor	3 (21)
	Cough	3 (21)
	Reduced effort tolerance	2 (14)
	Hoarseness of voice	2 (14)
	Subcutaneous emphysema	2 (14)
	Odynophagia	2 (14)
	Haemoptysis	1 (7)
Comorbidity, n (%)	Nil	3 (21)
	Hypertension	7 (50)
	Diabetes mellitus	4 (29)
	Bronchial asthma	3 (21)
	Dyslipidaemia	3 (21)
	Ischaemic heart disease	1 (7)
	End stage renal failure/ CKD	2 (14)
	Paroxymal atrial fibrillation	1 (7)
	Chronic obstructive airway disease	1 (7)
	Endometrial carcinoma	1 (7)
	Hyperthyroidism	1 (7)
Cotton Meyer's Grading, n(%)	1	0
*One patient had acute tracheal	2	6 (46)
tear secondary to trauma without stenosis.	3	7 (54)
Karnofsky performance status Scale	90	6 (43)
	80	2 (14)
	70	3 (21)
	60	1 (7)
	50	2 (14)

Table II: Site of tracheal lesion with etiology

Site of lesion	Aetiology	No (n)
Cervical trachea	***Benign***	
	Tracheomalacia	2
	Traumatic tear	1
	Post intubation stenosis	1
	Malignant	
	Papillary thyroid carcinoma	2
	Total	6
Mediastinal trachea	Benign	
	Post traumatic stenosis	1
	Post intubation stenosis	4
	Malignant	
	Primary tracheal SCC[a]	1
	Primary tracheal adenocystic carcinoma	1
	Primary tracheal lymphoma	1
	Total	8

[a]Primary tracheal squamous cell carcinoma.

Table III: Surgical approaches

Variables	Types	Values
Surgical approach, n (%)	Transcervical	10 (71)
	Thoracotomy	1 (7)
	VATS[a]	1 (7)
	Transcervical combined with right VATS[a] and manubrial split	1 (7)
	Transcervical combined with right thoracotomy	1 (7)
Releasing manoeuvres, n (%)	Infrahyoid laryngeal release	13 (93)
	Suprahyoid laryngeal release	2 (14)
	Right hilar release	2 (14)

[a] VATS:video-assisted thoracoscopic surgery.

Table IV: Perioperative parameters

Variables	Total (n=14)
Airway management	
Intubated	11
Non-intubated	3
Duration of surgery, mean in minutes (range)	246.2 (70–540)
Blood loss, mean in mL (range)	185.7 (50–700)
Length of trachea resected, mean in cm (range)	2.3 (1.0–4.5)
Distance from vocal cords, mean in cm (range)	3.9 (1.0–8.4)
Distance from carina, mean in cm (range)	4.8 (1.0–8.0)
ICU/PACU[a] admission post operation, n (%)	10 (71)
Duration of ICU/PACU[a] stay, mean in days	1
Post op ventilation, n (%)	1 (7)
Duration of hospital stay, median in days (range)	9.5(4-29)
Post operative complications, n (%)	
Vocal cord paralysis	1 (7)
Dysphagia	3 (21)
Lung collapse due to mucous plug	2 (14)
Post op granuloma	1 (7)
Hospital acquired pneumonia	1 (7)
Anastomosis dehiscence	0
Post-operative mortality, n	0
Malignant lesions, n	5
Tumour size, mean in cm (range)	2.3 (1.7–3.5)
Margins involved, n (%)	
Yes	3 (60)
No	2 (40)

[a]ICU/PACU= Intensive care unit/post-operative acute care unit

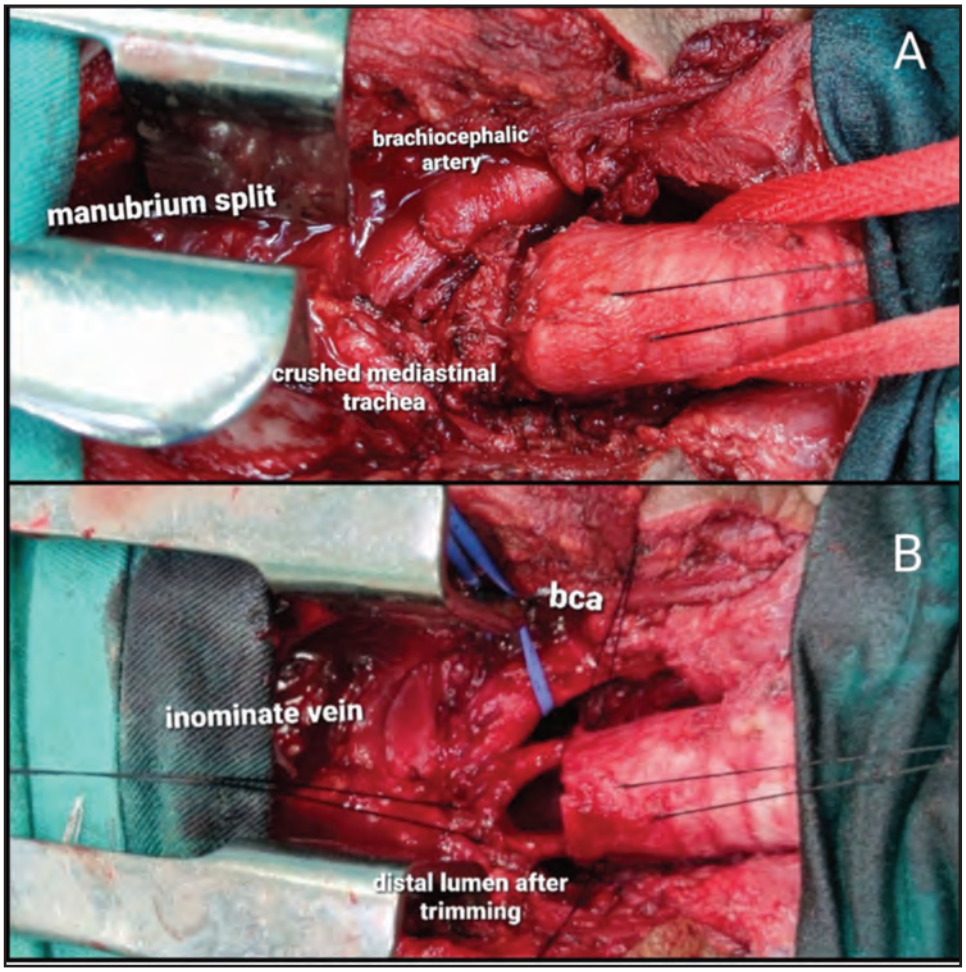

Fig. 1: (A) Case of traumatic injury to the mediastinal trachea where a manubrial split was performed to safely dissect the densely adhered brachiocephalic artery to the crushed trachea. (B) Right before anastomosis of the mediastinal trachea after resecting the crushed segment.

intervention as well as bias due to the low number of patients in our series.

CONCLUSION

Tracheal resection and anastomosis can be performed safely in complex stenosis and malignant tumours in experienced centres. Pre-operative planning with a multidisplinary approach is vital to ensure a good outcome. Capability of performing both intubated and non-intubated tracheal surgeries safely provide an option to manage the airway effectively without the need to use bypass procedures. Adequate release manoeuvres both in the larynx and mediastinum ensures tension-free anastomosis with minimal post-operative complications.

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SHORT COMMUNICATION

Efficacy of high-dose intravenous iron in middle-aged to elderly iron-deficient patients

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ABSTRACT

Iron deficiency (ID) impacts about fifty percent of elderly patients with many symptoms present before iron deficiency anaemia . If left untreated, ID may increase morbidity and mortality. Oral iron is often not tolerated or the absorption is suboptimal. We describe our initial experiences of using high-dose intravenous ferric derisomaltose (Monofer®) infusions of 500 and 1000mg for iron deficiency and iron deficiency anaemia respectively in the outpatient setting. Rapid correction of laboratory parameters and improvement in common symptoms (such as fatigue) were observed. Intravenous iron may be an option for symptomatic iron deficient patients unsuitable for oral iron.

INTRODUCTION

Iron deficiency (ID) may result when there is a negative imbalance between iron intake and loss.[1] ID impacts 58% of women and 20% of men (mean age 56.9 years) in Singapore.[2] Common signs and symptoms of ID include hair loss, fatigue, and brain fog (Figure 1)[1,5,10]. Middle aged and the elderly are at increased risk for ID due to poor diet, reduced intestinal absorption, concomitant medications such as proton-pump inhibitors, blood loss secondary to chronic disease, and increased incidence of surgeries with associated blood loss.

Data from the English Longitudinal Study of Ageing assessing 4451 patients demonstrated a mortality hazard ratio (HR) in ID patients of 1.58 (95% confidence interval (CI) 1.29–1.93) over a 14-year period.[3] The key drivers of mortality were increased respiratory deaths (HR 2.14, 95% CI 1.30–3.50) and cancer (HR 1.58, 95% CI 1.14–2.20).

In Taiwan, a longitudinal study of 32,390 patients (median observational period 5.43 years) suggested iron deficiency anaemia (IDA) increased the risk of developing cancer (Standardised Incidence Ratio of 2.15 (95% CI 2.06–2.25))[4]. The authors hypothesised that cancer development was due, among other reasons, to ID impairing the molecular and metabolic functions of cells. They also highlighted that IDA alters immune activities and may create a microenvironment permissive for carcinogenesis.

Ironically, treating ID is considered simple yet the high ID prevalence suggests otherwise. In elderly, oral iron may be ineffective (if tolerated) due to upregulated hepcidin or interference with concomitant medications. Whilst many misconceptions remain, there have been strong advancements in the safety and usability of parenteral iron.[5] Parenteral iron complexes have an iron core with a carbohydrate shell. Whilst administering similar cumulative doses results in similar efficacy, the ability of newer formulations to reduce the number of infusions with higher doses may improve patient compliance and hospital resources.[6]

Ferric derisomaltose (Monofer®; FDI), previously iron isomaltoside, and ferric carboxymaltose (Ferinject®; FCM) permit administration of doses of 500, 1000, or 1500–2000mg iron (for FDI) as a single infusion over 15–30 minutes. Despite having similar effectiveness, symptomatic and severe hypophosphataemia have been ascribed to FCM.[7-9] In a randomized controlled study, 11.3% of FCM patients (versus 0% for FDI) developed severe hypophosphataemia (serum phosphate level ≤1.0mg/dL).[7] A pharmacokinetic study demonstrated that FCM reduces serum phosphate in a dose-dependent manner.[8] The phosphate nadir appears at approximately day 14 and whilst initially believed to be benign and short acting, increasing cases with significant clinical symptoms (and studies demonstrating long lasting hypophosphataemia) have resulted in revision of this understanding and subsequent updates to global labels (i.e. USA, Australia, and Europe).[9] Patients are at increased risk for developing hypophosphataemia with age.

MATERIALS AND METHODS

We performed a retrospective review on 11 middle-aged to elderly patients treated with FDI at either Pantai Hospital Ayer Keroh, Malaysia or the Integrative Medical Centre, Singapore. We described our first experiences from a practical, effectiveness, and outcomes perspective. Whilst significant data has been published with FDI, there is little or no publications of use in the local population.

Dosing of FDI was 500mg iron (for patients with ID only) or 1000mg (for patients with IDA). ID was diagnosed with serum ferritin <30ng/mL or, when anaemic (haemoglobin (Hb)<12g/dL), with ferritin <100ng/mL and/or transferrin saturation (TSAT)<20%. FDI was administered after careful setting of a cannula (first pass technique to minimise risk for extravasation) and iron then infused over 15–30 minutes (in 10–100mL normal saline) followed by a 30-minute observation.

RESULTS

The average age of patients was 67.3 (51–89) years old. All were of Asian descent and complained of commonly

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Table I: Summary of patient laboratory data pre/post ferric derisomaltose administration

Patient Information			Iron	Timing (days)	Hb (g/dL)		Ferritin (ng/mL)		TSAT (%)	
Age	Sex	Med History	(mg)	Post Tx labs	B/L	Post Tx	B/L	Post Tx	B/L	Post Tx
75	F	Hypertension	1000	42	8.7	13.6	9	108	4	17
55	F	Endometrial cancer; uterine fibroids	1000	38	8.7	11.9	6	247	4	26
73	F	Hypertension and osteoporosis	1000	43	9.3	12.8	106	438	7	39
68	F	CKD	1000	42	10.3	11.4	67	443	20	28
75	F	Stroke, hypertension, and CKD	1000	41	10.3	11.6	134	509	13	13
80	F	CKD	1000	43	10.4	11.1	44	297	10	28
65	F	TKR planned*	500	91	11.1	10.6	74	292	15	33
89	F	Hypertension andosteoporosis	1000	35	11.4	11.9	94	422	6	36
56	F	Nil**	500	57	12.4	12.8	10	165	22	32
53	F	HMB***	500	115	12.7	12.3	6	50	26	39
51	M	ADHD; GERD	500	64	14.5	14.7	25	178	17	22
		Average	**818**	**56**	**10.9**	**12.2**	**52**	**286**	**13**	**29**

ADHD: attention deficit hyperactivity disorder; CKD: chronic kidney disease; HMB: heavy menstrual bleeding; GERD: gastroesophageal reflux disease; TKR: total knee replacement.

* Patient underwent a total knee replacement the day following administration of IV iron with significant blood loss and suffers from anaemia of chronic disease.
** Patient was a vegetarian with sub-optimal dietary habits leading to iron deficiency.
***Patient required a second dose of 500mg iron to resolve symptoms. Post second infusion (cumulatively 1000mg iron) the serum ferritin concentration increased to 149ng/mL

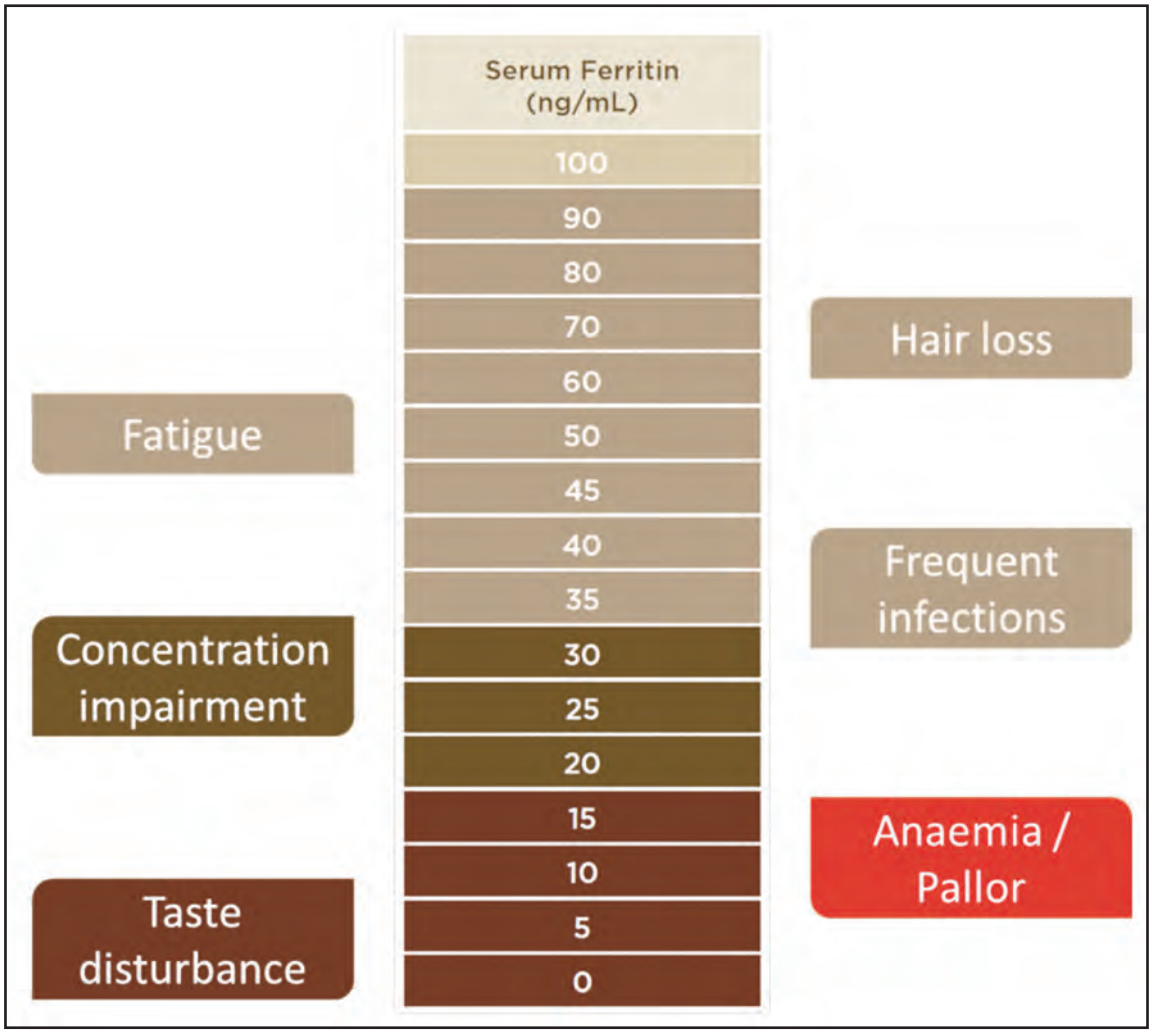

Fig. 1: Relationship of serum ferritin concentration and common symptoms of iron deficiency (in patients without underlying inflammatory conditions)

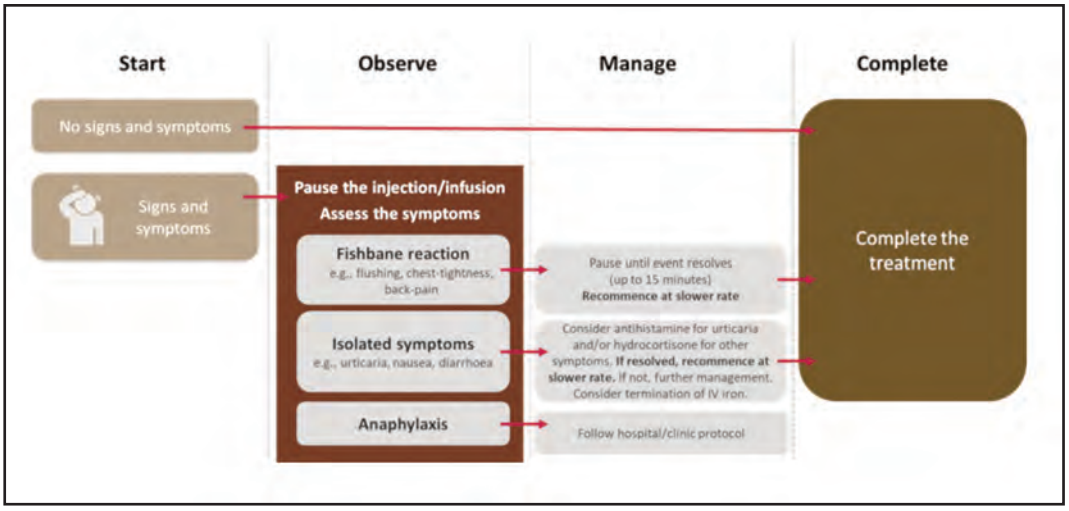

Fig. 2: Clinic protocol for the management of adverse events. *Adapted from Lim et. al., Vox Sanguinis (2019) 114*

expressed symptoms of ID (namely fatigue) with an average baseline ferritin of 52ng/mL and TSAT of 13% and for anaemic subjects, the average Hb was 10g/dL. Repeat labs were performed on average 56 (35–115) days later with clinically significant increases in all laboratory parameters post-infusion and ID(A) resolution (Table I).

Patients generally reported feeling less fatigued 1–2 weeks post-infusion and a patient undergoing surgery after receiving IV iron had an uneventful recovery with no significant decrease in Hb concentration or need for a blood transfusion.

All patients have at least 3 months of follow-up and only one patient, with recent history of heavy menses, required additional iron. Pre-infusion Hb was 12.7g/dL and she was administered 500mg iron. Several months post-infusion she complained of fatigue and the repeat ferritin was 50ng/mL. A second dose of FDI resulted in the resolution of symptoms with ferritin improving to 149ng/mL. No adverse events were recorded with reported cases.

DISCUSSION

Iron formulations can be associated with acute chest and back tightness and these reactions, potentially related to "free" or "labile" iron, normally resolve spontaneously without any medical therapy (within minutes of pausing the infusion) and rarely recur when IV administration recommences.[5] Expert reviews estimate serious adverse event rates at <1:250,000 administrations.[5] Figure 2 illustrates our protocol for managing side effects.

The promising results of this local data combined with the ease of administration and improved symptoms in patients should encourage clinicians to conduct regular iron studies in middleaged and elderly patients with and without anaemia.[2] Treatment of symptomatic ID(low ferritin) prior to anaemia with IV iron may rapidly improve quality of life whilst potentially reducing consequences of other comorbidities (e.g., development of cancer, heart failure or infections).

CONCLUSION

IV iron rapidly corrects IDA and early treatment may aid in recovery for those planned or requiring surgical intervention and reduce the chances of requiring red cell transfusions.

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Making physical examination in medicine user-friendly

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ABSTRACT

Physical examination (PE) techniques used in medical schools appear redundant in several aspects: unnecessarily regimental, lacking in efficiency, and lengthy. Many techniques are sustained solely because of the age-old tradition. This commentary suggests a simplification of PE techniques to make them acceptable to all the stakeholders, such as patients, medical students, and medical teachers. This is especially relevant in this era when imaging is widely used for diagnosis, and the confidence and reliance on PE are declining. Opinions of 10 senior consultants active in medical practice, teaching, and assessment were sought to know their concurrence with the authors' views. Seven of them provided their opinions, which showed considerable agreement with the authors' views regarding PE. All the items presented in this paper are mostly supported by the opinions of the senior consultants, textbooks, and literature. We consider sharing this work with the fraternity worthwhile.

KEYWORDS:
physical examination; physical signs; jugular venous pressure

INTRODUCTION

Prevailing anomalies in physical examination (PE) have been disturbing. Some traditional methods make PE lengthy and cumbersome. History taking and PE should not be tiringly long and uncomfortable for the patients and the doctors. It is reassuring that many doctors still believe that history taking and PE are essential, and doctor–patient rapport should be at the heart of medical care.[1-11] If the art and science of clinical medicine are not implanted in medical students from the beginning of their training, it would be impossible to attain this goal.[12] There were errors repeated by students year after year, which point to the care needed in training[12] and the existence of problems in PE methods. We see the trend of clinical acumen being eroded by algorithms and guidelines dictating clinical practice. If the technology takes over, as it appears to happen in recent times, (i) clinical teaching would wither, (ii) patient management would become less efficient, (iii) medical errors would increase,[13] healthcare would become exorbitant, and litigations surge.[4,7,9,11,14,15] The unavailability or lack of standardisation in patients has led to the use of trained actors and simulators for teaching and assessment. Actors, unlike real patients, offer uniformity and consistency. However, simulations used to teach medical students might not match the real.[4] The currently insisted PE regime and methods are constraining for medical students, patients, and teachers. Imaging might compensate for a lack of expertise in PE, but it will be problematic in emergencies.[5] Knowledge of the pathophysiology of clinical signs is vital for interpretations.[16] Moreover, investigations become more meaningful and easy to interpret when done in the light of clinical diagnosis.[15,17,18]

Medical students learn PE system by system, but as doctors, they would need to adopt a holistic approach. Sub-specialisation compartmentalises the body systems, but the approach has to be holistic in terminal stages and the elderly. All systems should be examined in order to avoid surprises. For all these to become practical, PE needs to become easier, faster, efficient, and user-friendly. Hence, we recommend some modifications in the difficult areas of PE.

Endorsement for our recommendations

To cater legitimacy to our views, the opinions of 10 consultants active in medical practice, teaching, and assessment of medical students from four institutions were sought through email using 105 statements from problematic areas of PE. Seven of them responded. All agreed to the opening statement, *"There are areas in physical examination in medicine that can be modified to make them less regimental and more efficient."* Forty-one suggestions received full and 24 majority endorsement. Forty items received partial endorsement with very little comments because they did not belong to their speciality. The most senior among them showered praises for the project and agreed with all items except two. Forty items with authors' conviction, textbook, and literature support are presented. Harrison's Principles of Internal Medicine 21st edition, which appeared after this project, was found to support many of the authors' views.

Simplifying JVP examination

Jugular venous pressure / pulse (JVP) is important for all areas except neurology. Many authors consider its assessment difficult, inaccurate, time-consuming, and tedious.[1,32,33] In practice, the clinician needs to know whether JVP is raised or not, not its exact measurement.[32,34] Except in very thin and elderly, where carotid pulsation may be visible, no pulsation is visible in the neck of a healthy individual in sitting or standing position.[1] The vertical distance from the sternal angle to the clavicle is around 6 cm, and the normal JVP is only 3 or 4 cm. So, if venous pulsation is seen above the clavicle in upright position with legs dangling, JVP is raised.[22] Hepatojugular reflux, an uncomfortable procedure, is often used to assess JVP.[3] It is much easier to inspect the neck in an upright position for this purpose. The common practice of asking the patient to turn the head to the left makes the

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Table I: Recommendations for improving physical examination

No.	Physical examination: recommendations for improvement	Status
1	Do not diagnose anaemia by inspection of palms alone. Use conjunctivae and tongue.[19]	FE Literature
2	Feel the hands. Cold and sweaty hands indicate circulatory failure.[19]	Literature
3	Examine both eyes to avoid missing abnormalities of pupils, conjunctivae, and sclera.[1]	ME
4	Use swinging light to demonstrate consensual light reflex and afferent pupillary defect. A quick swing of light would show the state of the pupil before it resumes its original size.[20]	FE Literature
5	Use a spatula to expose teeth and gums to check oral hygiene. A casual look into oral cavity will miss dental caries and gingivitis.[18,19]	Literature
6	Do not insist on the 45° incline for cardiovascular examination. Any incline which shows jugular venous pulse (JVP) should be acceptable.[21] The precordial examination is unaffected by the incline. With the patient sitting upright and legs dangling, raised CVP is ruled out, if no JVP is seen.[22]	Literature
7	Avoid the routine lifting of arm to elicit collapsing pulse. It is unnecessary and misleading. Appreciate the slapping/bounding character of pulse in conditions causing collapsing pulse. Use arm lifting to confirm this, if necessary.[19,23,24]	ME
8	Use the midline as the landmark for apex beat location, as midclavicular line (MCL) is subjective.[13,25,26] But for keeping the tradition, the use of MCL has no advantage. Use the midline as the landmark for apex beat location, as MCL is subjective.[13,25,26]	Literature
9	Separate fingers and press them into intercostal spaces to feel the apex beat. It is often missed otherwise.	AO
10	Examine the peripheral pulses also in CVS examination. Peripheral arteries reflect condition of coronary and cerebral arteries.[20]	Literature
11	Using thumb for pulse examination is more convenient in many areas, and it is no less efficient than using fingers.[24] Use right thumb to feel left carotid artery.	Literature
12	Inspection and auscultation are the most useful steps in the PE of respiratory system. These can be supplemented with chest expansion, percussion, and vocal fremitus, as required.[20,27]	Literature
13	Look for features of airway resistance like soft tissue recession, pursed-lip breathing, and tachypnoea.[3]	FE Literature
14	Chest deformities are easily missed, if the patient is not inspected in sitting or standing position.	FE
15	Use fingers to feel tactile vocal fremitus. They are sensitive and easier to apply to axillary and infra-axillary regions, compared to the ulnar border of the hand.[19,20]	Literature
16	It is unnecessary and impractical to search for intercostal spaces while percussing and auscultating the chest.[1,19]	ME
17	It is not feasible to estimate chest expansion in numbers on palpation.[1,3,4] Determine which side is expanding less, as all lung pathologies decrease lung expansion.	ME
18	Percuss for superficial cardiac dullness in the left parasternal region, not at MCL. The bare area of the heart does not extend to MCL. Resonance here indicates hyperinflated lung.	AO
19	Inspect the abdomen carefully for organomegaly. Massive organomegalies show on inspection. The umbilicus is deep in obesity, flat and transversely stretched in ascites.[3]	ME Literature
20	Starting palpation of the liver and spleen in the right iliac fossa and advancing cranially breath by breath is disturbing to the patient and unnecessary. Enlarged liver, spleen, large kidneys, and large masses can be felt on superficial palpation. Use deep breathing only to check their downward movement on inspiration.[3,20,28]	ME Literature
21	Use fingertips rather than the radial border of index finger for palpation of abdominal organs and masses, as they are more sensitive, agile, and user-friendly.[1,3,20,24] Radial border is traditionally used with no advantage and is difficult for palpating the spleen.	ME Literature
22	For ascites, demonstrate that the dullness has shifted to a previously resonant area, not just that the flank has become less dull.[1,20,26,28,29]	Literature
23	The lower border of liver, when palpable, does not need percussion for confirmation, as palpation is more sensitive than percussion.[3]	ME Literature
24	Liver pulsations can be detected by the palm firmly pressed over the right lower thorax, as the liver is positioned above the costal margin.[30] Palpating the liver border for this is unnecessary.	Literature
25	Pressing down the midline of the abdomen while eliciting fluid thrill is needed only when the thrill is present.[1,3,24] It helps to block the waves passing through the abdominal wall.	ME Literature
26	Auscultating abdomen for bowel sounds in one area is sufficient.[1,3,19,20,24]	ME Literature
27	Auscultate an inch above the umbilicus on either side for renal bruit.[19,24] Renal arteries, branches of the abdominal aorta, are near the midline.	FE Literature
28	Renal punch can be painful and annoying to the patient. Just a thumb pressure is sufficient to elicit renal angle tenderness.[19]	Literature
29	Romberg sign indicates dorsal column dysfunction.[1] Vision helps to maintain body balance when proprioception is impaired. In cerebellar lesions, patient will not be able to stand with feet close together even with eyes open.	Literature
30	Avoid using the term facial asymmetry to indicate facial palsy. Facial symmetry is rare in the population. Examine facial muscle contractions to determine.	AO SE
31	Use finger wiggle to test visual fields. Colour is not well perceived in the periphery.[20] Using a red pin for peripheral fields is meritless.	Literature
32	For eliciting ankle clonus, use eversion and dorsiflexion of the foot. Clonus could be missed, if the foot is dorsiflexed in inversion.	AO SE

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Table I: Recommendations for improving physical examination

No.	Physical examination: recommendations for improvement	Status
33	While eliciting plantar reflex, stop the stimulus as soon as a response is seen.[1,20,31] Continuing the stimulus would make it confusing.	FE Literature
34	While eliciting muscle tone, move the joint through full range, first slowly and then fast. Spasticity, being velocity dependent, can be missed otherwise.[3]	ME Literature
35	While assessing muscle power, isolate the part and allow movement only at the part being tested. Test both sides separately except the shoulder and hip abduction and adduction.	ME
36	In a cerebral stroke, trapezius muscle, innervated by cranial nerve XI, could be weak, like the lower face.[24] This fact is not well described.	ME
37	Rapid alternating movements like supination-pronation, finger tapping, and foot-tapping could be tested on both sides simultaneously and compared for speed and accuracy. It saves time and allows comparision.	SE
38	Before declaring the sensory system normal, perform discriminatory sensations (cortical sensations) like stereognosis, graphesthesia, and two-sides discrimination.[1,20] Primary sensations are appreciated at thalamus.	Literature
39	Whenever any sensory loss is detected, determine its extent and pattern.[24]	Literature
40	Sensory loss in strokes cannot be confined to face, arm, and leg. There is no anatomical basis for this distribution. It has to be hemisensory loss including the trunk.[3,12]	ME Literature

Status = endorsement from experts and literature, FE = fully endorsed by experts, ME = endorsed by majority of experts, SE = endorsed by some experts, AO = authors' opinion

sternocleidomastoid muscle (SCM) stand out and obscure the JVP.[33] Instead, extending the head relaxes SCM and makes JVP examination easier. Use simultaneous left carotid palpation and right neck inspection to differentiate JVP from carotid pulsation.[33] Hand veins can be used to judge central venous pressure (CVP), if JVP is doubtful.[29] The peripheral veins also reflect CVP, although slower.

PE need to be sustainable and efficient

Currently, we are facing two deterrents to clinical training of medical students: (i) practical difficulties in using real patients for teaching and assessment, and PE techniques being too tedious and time-consuming. While the former is hard to resolve, especially in a pandemic-like situation, the latter could be helped.[1,16,32,33] PE techniques could be made less regimental, more efficient, and easier to perform to make them sustainable for medical students and patients, just as Campbell et al. opined.[16] In medical schools, students are trained and assessed examination of each system separately. In clinical practice, PE is done area-wise in a holistic manner.[16] Although compartmentalisation is unlikely to go away, the authors felt that a holistic approach would be more beneficial, practical, and realistic, as suggested by Earl Campbell et al.[16]

CONCLUSION

Observation of medical students' ongoing struggle with physical examination techniques and interpretation of findings prompted the authors to highlight this issue and make some recommendations for making physical examination sustainable and easier rather than risk losing its importance in this era of overarching technologies and the demand for quick decisions. Some of the most useful items are included in the table.

ETHICS APPROVAL

Approval was obtained from the Ethics Committee of the Faculty of Medicine and Health Sciences of the Universiti Malaysia Sarawak (REF. NO.: FME/21/78) for this project and the use of the questionnaire. Participation in the questionnaire was voluntary, with no incentives offered. All methods were in accordance with the guidelines and regulations of the Declaration of Helsinki.

COMPETING INTERESTS

There is no competing interest.

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