ORIGINAL ARTICLE

A clinical audit on the diagnosis and management of infective endocarditis in a tertiary heart centre in Malaysia

Yik Hon Ho, MRCP[1], Caryn Tsujean Lim, MRCP[1], Chelfi Zhi Fei Chua, BPharm[1], Hock Hin Chua, FRCP[2], Tiong Kiam Ong, FRCP[1]

[1]Department of Cardiology, Sarawak Heart Centre, Ministry of Health, Malaysia, [2]Infectious Disease Unit, Department of Medicine, Sarawak General Hospital, Ministry of Health, Malaysia

ABSTRACT

Introduction: Infective endocarditis (IE) has a high mortality rate in developing countries including Malaysia. This clinical audit aims to identify the shortcomings in the diagnosis and management of IE patients in a local tertiary centre to implement changes for improvement.

Materials and Methods: This retrospective audit had two cycles – the first includes all IE patients in Sarawak Heart Centre, Malaysia from January 2020 to December 2022 with different parameters (blood culture, echocardiogram, the appropriateness of antibiotics and surgery) assessed against Malaysian Clinical Practice Guideline (CPG); and re-audit from July 2023 to December 2023. Interventions before re-audit include presentation at different hospital levels and continuing medical education.

Results: Fifty patients were recruited (37 in the first cycle, 13 in the second cycle). The median age was 48.5 years with male predominance. Valve prosthesis (12.0%) and rheumatic heart disease (10.0%) were the commonest predisposing factors. Native mitral (44.0%) and aortic valves (28.0%) were most commonly involved. Twenty-eight (56.0%) patients were culture-positive. In the first cycle, most parameters (culture technique 0.0%, vegetation measured 54.1%, empirical 5.4%, culture-guided 29.7% antibiotics therapy, indicated surgery 0.0%) did not achieve the expected standard except timeliness of echocardiograms and blood culture incubation period. After initial interventions, all parameters showed statistically significant improvement (culture technique p<0.001, echocardiography p<0.001, empirical p<0.001, culture-guided p=0.021, surgery p<0.001) during the re-audit.

Conclusion: Compliance with clinical practice guidelines (CPG) on IE management was suboptimal during the first audit but improved after interventions. Hence, regular continuing medical education (CME) is essential, and a written hospital protocol may be useful. Regular audits alongside multidisciplinary teamwork are crucial efforts.

KEYWORDS:
Clinical audit, infective endocarditis, blood culture technique, echocardiogram, antibiotic therapy, surgery

INTRODUCTION

Infective endocarditis (IE) is an uncommon yet deadly disease.[1] In developing countries, the IE mortality ranges from 7-46% as shown in a systematic review involving 19 studies.[2] This is also resonated by two studies in Peninsular and East Malaysia which reported mortality rates of 35.7% and 44.4% respectively.[3-4]

IE is most commonly caused by *Staphylococcus aureus* and oral *Streptococci*.[5] These organisms can be easily identified with appropriate blood culture techniques. However, in cases of culture-negative IE, echocardiographic detection of vegetation has gained a more important position in the diagnosis of IE. This is reflected through the serial revisions of Duke's criteria since its introduction in 1992.[6-7] Many countries including Malaysia have since adopted the modified Duke's criteria in the diagnosis and management of IE.[8-10]

Although pyrexia of unknown origin and a new heart murmur are the cardinal clinical features of IE, microbiological diagnosis and clinical management of IE are often challenging, especially for clinicians unfamiliar with the condition, resonated by various studies.[5,11-13] Furthermore, timely diagnosis and management have been proven to improve mortality outcomes, especially valve surgeries.[14-17] Hence, this clinical audit was performed to identify the shortcomings in the diagnosis and management of IE patients in a local tertiary centre and to implement changes for improvement.

MATERIALS AND METHODS

Study Design and Setting

This is a retrospective audit of two cycles adopting the Plan, Do, Study, Act (PDSA) model.[18] The audit team was led by two medical officers and a clinical pharmacist, supported by a senior consultant cardiologist and a senior consultant infectious disease physician. The first cycle includes all patients who were hospitalised and treated for IE in Sarawak Heart Centre in Sarawak, Malaysia from January 2020 to December 2022. The cases were identified from the hospital patients' records with a diagnosis of infective endocarditis. The admission medical notes of all IE patients were traced and reviewed.

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Corresponding Author: Caryn Tsujean Lim
Email: carynlim1992@gmail.com

Participants
All patients with discharge diagnoses of IE were shortlisted from the medical record department and recruited by tracing their case notes (n=59). Patient without their case notes were excluded (n=9).

Data Collection
Each case was audited independently by two auditors with the data keyed into a database. Any discrepancies between the findings of the two auditors were examined and resolved by a third auditor.

The data collected were the objectives including the appropriateness of blood culture technique, the timeliness of transthoracic echocardiogram (TTE) or transoesophageal echocardiogram (TOE), the appropriateness of the empirical and culture-guided antibiotic therapy and surgery. The standards for the objectives were specific, measurable, agreed, relevant and theoretically sound (SMART).[19]

The appropriateness of the blood culture technique was assessed based on four criteria including at least three sets of cultures taken, at least 30 minutes apart, in peripheral veins and paired aerobic and anaerobic blood culture bottles. The standards of echocardiography include whether it was performed within 24 hours, vegetation size being measured based on the longest diameter and the window for which the measurement was done. The appropriateness of antibiotic therapy was assessed based on five parameters which were the choice, dose, duration, administration route and administration frequency of antibiotics.[20] Antibiotic therapy was considered appropriate if all the five parameters were fulfilled for both empirical and culture-guided antibiotic therapy. If the choice of antibiotics was wrong, the remaining four criteria would not be assessed.

Data Analysis and Presentation
The data collected were then analysed against standards to determine which standards were being met and which were not. Statistical analysis was performed with IBM SPSS version 27. Categorical data with quantitative variables were presented in frequency (percentage). Pearson's chi-square test or Fisher's exact test was used to compare independent categorical variables pre- (first audit cycle) and post-intervention (second audit cycle). Statistical significance was set at $p<0.05$. The findings of the first audit cycle were presented at the departmental and hospital levels in March 2023.

Changes Implementation and Re-audit
Regular continuing medical education (CME) was held for all healthcare professionals involved in the management of IE patients, including cardiologists, cardiothoracic surgeons, internal medicine physicians, medical officers, house officers, echocardiography technicians and nurses from April 2023 to June 2023. This was followed by a re-audit which includes all IE patients from July 2023 to December 2023.

Ethics
This study was approved by the Medical Review and Ethics Committee (MREC), Ministry of Health (MOH) in 2023 (Approval code: NMRR ID-23-01673-6JT).

RESULTS
Baseline Characteristics
A total of 50 patients were recruited from two audit cycles (37 in the first audit cycle and 13 in the second audit cycle). The median age was 48.5 (32.8 – 62.3) years. Thirty-six (72.0%) patients were male. The most common ethnic was non-Malay indigenous (40.0%). Predisposing factors of IE include chronic rheumatic heart disease (10.0%), valve prosthesis (12.0%), cardiac implantable electronic device (2.0%), history of IE (6.0%), recreational drug use (6.1%) and invasive procedure (6.0%). Sixteen (32.0%) had definite IE. Native valve IE was most common (90.0%) with the mitral valve (44.0%) and aortic valve (28.0%) being the most common valves involved. Twenty-eight (56.0%) were culture-positive with α-Streptococci (37.0%) and methicillin-sensitive *Staphylococcus aureus* (29.6%) being the most common organisms.

First Audit
In the first audit cycle, a total of 37 patients were recruited. None of the blood culture techniques fulfilled all four criteria. The compliance with each criterion is shown in Table I. All the blood cultures were incubated for at least 5 days. All the echocardiograms were performed within 24 hours of the suspected IE. TOE was performed for all patients with prosthetic valves and cardiac implantable electronic devices. TOE was also done for all patients with initially negative or inadequate TTE but with persistent suspicion of IE. Half of the echocardiogram reports had measured vegetation size and none reported the window for which the vegetations were measured. Only two had appropriate empirical antibiotic therapy whereas about one-third had appropriate culture-guided antibiotic therapy. The most common cause of inappropriate antibiotic therapy was the wrong antibiotic choice at 91.2%. Only one received the wrong dose of antibiotics. Surgical management was indicated according to recommendations for 35 (94.6%) of the patients but none of the patients underwent surgery.

Re-audit
In the re-audit, a total of 13 patients were recruited. There have been statistically significant improvements in blood culture technique, echocardiogram, appropriateness of empirical and culture-guided antibiotics therapy and surgery (Tables I and II). For those who underwent surgery, all the pathological specimens obtained were sent for histopathological examination. The in-hospital mortality rate reduced from 44.4 to 30.8%, with all the patients who underwent surgeries surviving their admissions.

DISCUSSION
Improvement seen in many areas of diagnosis and management of IE after the intervention from this clinical audit further reinstated the importance of clinical audit, especially in this condition whereby the clinical research studies on IE are scarce, with even fewer clinical audits in the region of Southeast Asia. Many countries struggle with the lack of research funding and infrastructure in this uncommon but important disease to provide stronger clinical evidence to guide clinical practice.[12] Hence, the information from this clinical audit is vital in contributing to the

Table I: Objectives assessed during the first audit and re-audit

Objectives	First audit n=37 n (%)	Re-audit n=13 n (%)
Blood culture technique	0 (0.0)	10 (76.9)
At least three sets	24 (64.9)	10 (76.9)
At least 30 minutes apart	1 (3.0)	10 (76.9)
Different peripheral veins	19 (51.4)	12 (92.3)
Paired aerobic and anaerobic blood culture bottles	16 (43.2)	12 (92.3)
Echocardiography		
Performed within 24 hours	37 (100.0)	13 (100.0)
Vegetation size was measured based on the longest diameter	20 (54.1)	11 (91.7)
Window for which the vegetation was measured	0 (0.0)	11 (91.7)
Empirical antibiotics therapy	2 (5.4)	9 (69.2)
Culture-guided antibiotics therapy	11 (29.7)	11 (91.7)
Surgery if indicated	0 (0.0)	5 (62.5)

Table II: Comparison of appropriateness pre- and post-intervention using Pearson's Chi-square test.

Appropriateness	Intervention		χ2 (df)	P-value
	Pre n (%)	Post n (%)		
Blood culture technique				
Yes	0 (0.0)	37 (100.0)	35.577	<0.001
No	10 (76.9)	3 (23.1)		
Echocardiography				
Vegetation size was measured and was based on the longest diameter				
Yes	20 (64.5)	11 (35.5)	3.814	0.051
No	17 (89.5)	2 (10.5)		
Window for which the vegetation was measured				
Yes	0 (0.0)	11 (100.0)	40.138	<0.001
No	37 (94.9)	2 (5.1)		
Empirical antibiotics therapy				
Yes	2 (18.2)	9 (81.8)	21.052	<0.001
No	32 (88.9)	4 (11.1)		
Culture-guided antibiotics therapy				
Yes	11 (50.0)	11 (50.0)	5.304	0.021
No	10 (90.9)	1 (9.1)		
Surgery if indicated				
Yes	0 (0.0)	5 (100.0)	21.937	<0.001
No	35 (89.7)	4 (10.3)		

improvement of local and global practice in the management of IE.

Blood culture Technique

Blood culture is the primary tool for microbiological diagnosis of IE. Hence, the correct blood culture technique is vital in identifying the causative organisms. We identified several factors contributing to the poor scoring of blood culture techniques in the first audit cycle. The major weaknesses were due to poor documentation of the time and site of the blood cultures taken. Some were due to the unavailability of anaerobic blood culture bottles. Others had only one set of blood cultures taken because of low suspicion of IE in sepsis of unknown origin. This is unsurprising as many clinicians were unfamiliar with this uncommon disease. The lack of specificity in the initial presentation of IE further poses challenges in the clinical diagnosis with a high index of clinical suspicion required. Hence, the CME focused on the awareness of having high suspicion for IE and the importance of taking three sets of blood cultures and good documentation. Feedback was also given to ensure the availability of anaerobic culture bottles all times. The effectiveness of these interventions was translated into the clinical outcome of an improvement in the blood culture technique.

Echocardiography Assessment

Echocardiography assessment has been an important tool in the diagnosis and management of IE among many other radiological adjuncts.[13,21-23] In this clinical audit, all echocardiograms were performed within 24 hours of suspected IE. However, many echocardiography technicians did not measure the size of the vegetation and failed to document the window for which the measurement was taken. This has important clinical implications in the decision for surgery and the subsequent follow-up echocardiogram for comparison of vegetation size after antibiotic therapy.[22] Hence, the targeted CME for the echocardiography

technicians after the first audit stressed on these important aspects of echocardiographic assessment resulting in improvements in the subsequent re-audit results.

Antibiotic Therapy

Our first audit cycle demonstrated a low appropriateness of empirical (5.4%) and culture-guided (29.7%) antibiotic therapies which is comparable with a study in France with an overall appropriateness of 14%.[11] The reason for the wrong antibiotic choice in our first audit was due to clinicians' preference for ceftriaxone as monotherapy in the local setting. Ceftriaxone was preferred as the empirical antibiotic therapy and continued for 4-6 weeks if the cultures were negative. Due to its single daily dosing frequency with a better adverse effect profile, it is not recommended by the older guidelines.[8,9] However, it is included in the recently published ESC guideline as the alternative empirical therapy in combination with ampicillin.[10] CME on the adherence to guideline-directed antibiotics therapy and regular antibiotics review by the ward pharmacists had resulted in significant improvement in appropriateness to 69.2% for empirical therapy and 91.7% for culture-guided therapy in the re-audit.

Prior antibiotic therapy has been found to be the main contributor of culture-negative IE.[24] Hence, a meticulous history taking in recent antibiotic use can affect the management of culture-negative IE. This also highlights the importance of blood culture taking prior to administration of antibiotics to increase the accuracy of culture results in discriminating a true negative IE by fastidious organisms from false negative IE.

Surgery

There is a strong consensus on surgical treatment for patients with IE complications such as heart failure, uncontrolled infection and high risk of embolism or established embolism,[10,23,24] supported by evidence showing an improvement in clinical outcomes for indicated patients who received timely surgical intervention.[25] In the first cycle of this audit, none of the patients underwent valve surgery despite being indicated for surgery, as compared to a 30-48% surgery rate in other studies.[17,26] After the results were presented at the hospital level, a multidisciplinary team approach was adopted for all IE patients. This resulted in 62.5% of the patients undergoing surgeries in the re-audit.

Implications

The clinical audit highlighted the non-adherence to recommendations in most of the audit criteria in a tertiary cardiac centre in Malaysia. However, after interventions were carried out, all of the criteria showed significant improvement in the re-audit. This directly translated into an improvement in in-hospital mortality outcomes for the patients.

Recommendations

When IE is diagnosed, a multidisciplinary team including cardiologists, cardiothoracic surgeons, infectious disease physicians, clinical microbiologists and pharmacists should be involved as per the appropriateness of clinical indication to strive for the best management outcome. The multidisciplinary effort is supported by many other studies as well.[22,27] In addition, CME should be done regularly especially when new clinicians are joining the department. Further to that, a hospital protocol on IE should be written and uploaded onto the intranet for the reference of all healthcare professionals involved in treating IE patients. On top of the above measures, clinical audits should also be done yearly to ensure compliance with the guidelines.

LIMITATION

This is a single-centre study which did not capture all IE patients in the region as most uncomplicated patients and those who were not indicated for surgery were kept in the referring hospitals till discharge. The delay for surgery during the re-audit was also not explored in this audit. The interval between the intervention and re-audit was only 3 months which might be too short to see the complete adherence to all the audit criteria.

CONCLUSION

Compliance with the national guidelines on infective endocarditis (IE) management was suboptimal during the first audit but improved significantly during the re-audit after interventions were made. Regular continuing medical education is essential to ensure timely diagnosis and appropriate management for IE patients. A written hospital protocol may also be useful. Regular audits must be undertaken to ensure compliance with the guidelines, best achieved with multidisciplinary efforts.

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CONFLICTS OF INTEREST

All authors of this study have no conflicts of interest to declare.

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