ORIGINAL ARTICLE

Clinicopathological study of gastric cancer in a Malaysian tertiary public health care centre

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ABSTRACT

Introduction: Gastric cancer (GC) is one of the leading causes of all new cancer cases globally. Although it is no longer reported in the top 10th most common cancer in Malaysia, geographical distribution and ethnic influences still obviously exist.

Materials and Methods: This is a retrospective analysis of histopathological records in a public tertiary health care centre in Malaysia. The computerised laboratory information system from the histopathology department of the hospital was retrieved for the period of 2005–2018. Descriptive analysis was done using Microsoft Excel.

Results: There was a total of 233 histologically confirmed GC cases. The burden of GC was observed to be an increasing trend from 2016 onwards. Among them, 64% were male and 36% were female. The youngest age of diagnosis was 19, while the oldest one was 93. Malaysian Chinese were found to have the highest incidences (41.63%), followed by Malays (32.19%) and Malaysian Indians (23.61%). All cases were of adenocarcinoma cell types and were found to have poorly differentiated in majority at the time of diagnosis.

Conclusion: Although this report only represents one tertiary health care centre in Malaysia, the Indian Enigma was still observed, as stated in other literatures. Over time, the incidence of GC in Malays has increased. Consideration of lifestyle modifications, health education and *Helicobacter pylori* eradication in various nations' National Health Insurance plans, are encouraged as prevention is always better than treatment or cure, including the cost load.

KEYWORDS:
Stomach neoplasms, Malaysia, Ethnic, Geographical, Enigma

INTRODUCTION

Gastric cancer (GC) is the fifth leading cause of all newly diagnosed cancer globally and the fourth leading cause of cancer-related death in 2020.[1] The incidence rate, mortality rate and the 5-year prevelance rate of GC were the highest in Asia compared to other regions.[1] In addition, around 1 in 12 cancer-related deaths were attributable to GC in 2018.[2] Although nearly a million new GC cases are diagnosed globally every year, GC is one of the most preventable cancer due to its highly behaviourally influenced nature.[2] However, the incidence, the age-standardized incidence and mortality of GC also declined globally.[3] Although GC was reported as the second-highest incidence and mortality worldwide according to the Global Cancer Observatory (GLOBOCAN) 1998, GC was reported as the fifth most common neoplasm of all new cancer cases in GLOBOCAN 2018.[3] New GC cases are still detected, especially in the Eastern Asian countries and these countries still have a high risk of GC.[3] GC was ranked as the 10th most common cancer in Malaysia in 2007–2011 (Malaysia National Cancer Registry) MNCR report but it was not reported in the top 10 list in the 2012–2016 MNCR report.[4,5]

Incidence and mortality of GC are highly variable by geography as well as are greatly influenced by diet, environmental factors, and *Helicobacter pylori (H. pylori)* infection in the community. GC was common in the United States in previous centuries, but now it is no longer prevalent.[2] This decreasing trend was most obvious in countries such as Japan and South Korea.[2] More than 50% of new incident cases were reported from developing countries. This downward trend in some regions could be due to the earlier detection of GC using screening procedures such as upper gastrointestinal endoscopy or radiography and might be due to the reduced *H. pylori* infection in some countries.[2]

The age-standardized 5-year net survival rate for GC is still between 20% and 40%, where 33.1% for the USA and 20.7% for the UK.[2] In these countries, although being the well-developed countries, GC tends to be diagnosed at an advanced stage.[2] In contrast, the age-standardized 5-year net survival rate for Eastern Asian countries such as South Korea and Japan also has higher rates. The 5-year survival rate for GC in 2010–2014 was reported as 68.9% for South Korea and 60.3% for Japan. It was strongly believed that the early detection of GC had contributed to these favourable health outcomes. However, the median survival rate of GC is less than 12 months in the advanced stage of GC.[6]

The survival rate of GC has improved globally over the decades due to improved case detection, early diagnosis, and better treatment strategies.[2] However, there is still room for improvement to achieve a favourable survival rate worldwide.[2] Early diagnosis of GC plays an important role in achieving a better survival outcome of GC and an understanding of its epidemiology, variation in ethnicity, age, gender and genetic predispositions are crucial. The

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Table I: Number of GC cases reported annually at the HTJ, Seremban, Negeri Sembilan, Malaysia from 2005–2018

Year reported	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Number of GC cases	13	11	13	5	17	23	23	12	12	17	15	22	21	29

Note: GC = gastric cancer

Table II. Age, gender, and ethnic incidences of GC cases reported annually at the HTJ, Seremban, Negeri Sembilan, Malaysia from 2005 to 2018

Gender	Ethnicity	Number of cases n (%)	Mean age of GC cases a at the time of diagnosis Age in years ± SD	Age in years (range)
Female	Chinese	31 (37.35)	68.41 ± 12.77	45–92
	Indian	26 (31.33)	59.38 ± 14.04	23–80
	Malay	24 (28.92)	57.76 ± 14.06	34–83
	others	2 (2.41)	60 ± 20	40–80
	Female (Total)	83 (100)	61.99 ± 14.64	23–92
Male	Chinese	66 (44)	66.67 ± 10.84	42–93
	Indian	29 (19.33)	54.63 ± 12.74	30–83.2
	Malay	51 (34)	63.42 ± 13.33	28–91
	others	4 (2.67)	43.25 ± 10.96	31–61
	Male (Total)	150 (100)	62.38 ± 13.7	19–93
Total	Chinese	97 (41.63)	67.23 ± 12	42–93
	Indian	55 (23.61)	55.74 ± 14.29	19–83.2
	Malay	75 (32.19)	61.61 ± 13.83	28–91
	others	6 (2.58)	48.83 ± 16.61	31–80
	Total	233 (100)	62.24 ± 14.04	19–93

Note: SD = standard deviation

objective of this study is to investigate the incidence and trend of GC in Malaysia at one of the tertiary health care centres, i.e., Hospital Tuanku Ja'afar (HTJ), Seremban, Negeri Sembilan state, Malaysia from 2005 to 2018.

MATERIALS AND METHODS

This is a retrospective cross-sectional study of the histologically confirmed GC data from 2008 to 2018. All patient records of histologically confirmed GC cases during the study period at the Hospital Tuanku Ja'afer (HTJ), Seremban, Negeri Sembilan, Malaysia were reviewed. Data collected were clinicopathological parameters which included histopathological diagnosis, age, gender, identification card number, patient registration number, ethnic group, date of biopsy and histological diagnosis. Inclusion criteria included that the patients must have attended HTJ between 2005 and 2018 and paraffin-embedded gastric biopsy must be available. The patients diagnosed with GC before 1 January 2005 or after 31 December 2018, patients who were diagnosed with oesophageal cancer alone were excluded from the study. The index date was defined as the date of the first outpatient or inpatient visit with a diagnosis of GC. Records of the patients who were first diagnosed with GC before 1st January 2005 were excluded from the study. Data were analysed using Microsoft Excel. Confidentiality of the collected information was maintained by strict measures. The names, ethnic groups and ages of the patients were kept private and confidential apart from the research team. The identities of patients were not revealed in this report.

RESULTS

There was a total of 233 cases reported as histologically confirmed GC cases in HTJ, Seremban from 2005 to 2018. The number of annual reported cases of GC from 2005 to 2018 was found to be varied. The number of reported GC cases in HTJ was observed as an increasing trend starting from 2016 onwards (Table I).

The youngest reported case was a 19-year-old Malaysian Indian man, and the oldest reported case was a 93-year-old Malaysian Chinese woman. The mean age of diagnosis is 62.24 ± 14.04 years. However, there were 38 cases whose ages were not included in the report, and the estimated age was calculated from the identification card (IC) number of the patient (which usually starts with the birth year of the person in Malaysia) and the year of the biopsy report. The number of reported and confirmed GC cases was found to be highest among the age group of 61–70, 51–60 and 71–80, respectively (Table II).

Among 233 cases, 64% (n = 150) cases were males and 36% (n = 83) were females. The youngest age of reported GC cases for females was 23, and the oldest one was 92. The youngest age of reported GC case for men was 19 and the oldest was 93. Malaysian Chinese ethnic group has the highest incidence of GC with 41.63% (n = 97), followed by Malays with 32.2% (n = 75) and Malaysian Indians with 23.61% (n = 55). There were a few cases reported from ethnic minorities 1 case each (0.43%) from Orang Asli, Singh and others (Table II).

All reported cases were adenocarcinoma 100% (n = 233). In terms of histopathological grading, 45% (n = 104) were

poorly differentiated type, 21% (n = 21) were moderately differentiated type, 3% (n = 7) were well-differentiated type, while there were 1 moderate to poorly differentiated type and 1 moderate to well-differentiated type, 30% (n = 70) were not reported. According to Lauren's classification, 13% (n = 31) were intestinal type, 15% (n = 34) were diffuse type and 1% (n = 2) were mixed type, while 74% (n = 172) did not find a report for pathological subtype. Seven reported cases with signet ring cell types which were considered as diffused type.

DISCUSSION

Comparison with Previous Findings

The shifting pattern of ethnic incidence of GC in Malaysia is the most noticeable characteristic of this study. Among the 233 laboratory-confirmed GC cases from the HTJ, Seremban from 2005 to 2018, 41.6% of diagnostically confirmed GC cases were Malaysian Chinese population, 31.8% were Malay population and 23.6% were Malaysian Indian population. An earlier study which was done at the HTJ in 2013 showed 55.0% Malaysian Chinese, 27.8% Malaysian Indian and 16.6% Malay population.[7] The second study which was carried out at the Hospital Ipoh, Perak state, Malaysia also showed 53.6% Malaysian Chinese, 36% Malaysian Indian and 26% Malay population. The study represented data from 1988 to 1998.[8] It indicates the increasing incidence of GC in Malay population.

The age-standardized rate for GC was 4–5 times lower in Malay than in the Malaysian Chinese and Malaysian Indian populations. This gap seemed to be narrower due to the increased number of GC cases in the Malay population and decreased the number of cases in the other two populations.[9] The findings from this study agrees with the fact of the increased number of GC cases in the Malay population. However, the incidence rate in the Malaysian Chinese and Malaysian Indian populations does not seem to decline significantly. This partly agrees with the MNCR report (2012–2016), which stated as the Malaysian Chinese have the highest incidence rate in both genders.[4] According to MNCR 2012–2016, the rate of GC was declined in Malaysia and was no longer listed as the 10th most common cancer. However, the incidence of GC in Seremban, Negeri Sembilan state does not seem to be declining until 2018. Globally, the highest number of cases was observed in Asia, specifically in China.[10]

The mean age of diagnosis for GC was 62.75 ± 13.95 years and only 9.8% of them (n = 23) are diagnosed under the age of 45 in this study. This agrees with the previous reports 60.8 ± 14.744 years (19–91) and 65 years (male 65.3 years and female 63.2 years, $p > 0.05$).[7,8] In our study, 9.8% of the reported cases were early-onset GC (45 years or younger) and the remaining 91.2% were conventional GC (older than 45). This finding agrees with the data from Machlowska et al (6), which stated that GC is not prevalent in younger age groups who are <45 years of age.[6] Early-onset GC was rare and not more than 10% of patients underwent disease development.[6] However, the youngest reported case in this study was a 19-year-old Malaysian Indian male patient, and such cases could have a genetic influence as a big role in the development of GC.

There were 56.3% male patients in the study by Tata et al (7) whereas our current study indicates that 63% male, indicating male predominance in GC.[7] Both studies were done in HTJ, Seremban, Negeri Sembilan state, Malaysia. In another study done at the Hospital Ipoh, 68.4% (171 out of 250 GC patients) were male patients.[8] This clearly demonstrates the male predominance in the incidence of GC. In our study, among different populations, men had a higher incidence than women (68%, 68% and 52.7%) in all Malaysian populations: Malaysian Chinese, Malay and Malaysian Indian, respectively. The findings of our study agree with the previous reports, that there is a male preponderance in all main ethnic groups of Malaysia.[4,6] Globally, men have higher incidence than women, and double the number of cases were reported.[9]

Around the 1980s, only 3% of GC patients are diagnosed with early GC but this was increased to 27% as stages 1 and 2 in the twenty-first century, indicating an earlier diagnosis trend.[9] The mortality to an incidence rate (MIR) for GC in South East Asia (SEA) was reported as 0.88 and a similar rate was observed for Malaysia.[10] Incidence of GC in Malaysia was declined by 48% among males and 31% among females in their last reported period of 13 years.[10]

All 233 cases in our review reported as adenocarcinoma type, and this agrees with the previous study.[7] Most of the reported cases 45% were diagnosed as poorly differentiated, 21% were reported as moderately differentiated and only 3% were reported as well-differentiated. The site of the tumour was not consistently informed. In the previous study, 45.6% were diagnosed with stage 4B; 36% with stage 4A; and only 3.6% with stage 1.[8] This implied the late diagnosis nature of the disease. Survival rate of the studied cases in this report was not traced. The survival rate of GC has improved globally over the decades due to improved case detection, early diagnosis, and better treatment strategies.[2] However, there is still room for improvement to achieve a favourable survival rate worldwide.[2]

In addition, GC can be classified into intestinal type and diffuse type depending on the histopathology.[2,4] There was a decline in the sporadic intestinal-type GC, but in contrast, the incidence of diffuse-type GC has reportedly increased.[6] This study does not have any prior data to explore further.

Geographic Diversity of GC

The incidence of GC displays immense geographical diversity.[6,9] This study only represents the data from the Negeri Sembilan state, Malaysia. Geographically, Kelantan state, which is northeast of the Peninsular Malaysia, was observed as having the lowest incidence of GC and Kelantan Malays were probably having the lowest rates of GC globally.[9] Thailand Enigma was reported where the Southern part of Thailand, was also observed as a lower incidence of *H. pylori* infection compared to North, Northeast and Central Thailand.[11] Geographically, Kelantan state and the Southern part of Thailand are neighbouring states and share a significant pattern of similarity in diet and the abundance of sea foods, vegetables and deep-sea water.[12]

The Indian enigma had reported by Misra in 2014.[13] The geographical distribution of GC differs widely in the different regions of India.[13] Southern and Eastern India had shown a high incidence of GC frequency approximately four times compared to North India.[13] Non-vegetarian foods, particularly, spicy and salty meat, fish, pickled food, high rice intake, excess chilli consumption, high-temperature foods, smoked dried salted meat, use of soda and consumption of dried salted fish were observed as significant risk factors for GC compared to North India, where diet is mainly wheat-based, a greater proportion of vegetarians and a higher intake of fruits and spices such as turmeric, garlic etc. These dietary habits were proposed as one of the explanations for the Indian enigma.[13]

Globally, the age-adjusted incidence rate was observed as a downward trend in Japan which was probably due to improved early diagnosis efforts and improved treatment outcomes in Japan.[2,10] However, due to the increased number of elderly populations, the crude incidence rate of GC continued to increase, and GC was more frequently detected in Japan. After the two peaks in 2030–2034 (in men) and 2025–2029 (in women), the decreasing trend of GC could be observed as the younger generation in Japan was more aware of health, and they tend to adopt a healthy lifestyle compared to the older generation.[2] In February 2013, Japan became the first country in the world to cover *H. pylori* eradication for chronic gastritis under its National Health Insurance (NHI) system.[10] *H. pylori* eradication reduces the risk of second GC to approximately one-third that of patients who do not undergo eradication therapy (JAPANGAST study). This indicates the benefit of *H. pylori* eradication in preventing GC.[14,15]

Risk Factors of GC

As known, *H. pylori* is classified as a type I carcinogen and is reported as a major risk factor for GC, especially for non-cardia GC. The reduction of the *H. pylori* infection rate in the population has contributed to the decline in the incidence of non-cardia GC. In addition, this trend could be explained by the increased standard of hygiene, better food conservation and a high intake of fruits and vegetables.[2,4] For cardia GC, it is more related to risk factors such as body fat. It was expected that cardia GC might be more frequent in future.[2] Most of the cases are non-cardia GC in Malaysia, except in Kelantan, where the main site of involvement is cardia.[9] The site of the tumour of GC, either cardia or non-cardia did not report consistently and hence, we do not have a precise data regarding the cardia and non-cardia types in this study.

Five-Year Survival Rate of GC

The 5-year survival rate for GC in 2010–2014 was reported as 68.9% for South Korea and 60.3% for Japan. However, the 5-year survival rate of GC globally is still around 20%.[10] It was strongly believed that the early detection of GC had contributed to these favourable health outcomes. However, the median survival rate of GC is less than 12 months in the advanced stage of GC.[6] Due to its high aggressiveness and heterogeneous in nature, even with early diagnosis, GC will still constitute as a global health issue.[6]

Accessing the trend of GC from one hospital data is not sufficient despite the data obtained are more than a decade. Some data, such as the age of the patients from certain reports, were not included. Confounding factors such as family history, occupation, comorbidities (e.g., diabetes mellitus, history of gastritis), social history (alcohol drinking, smoking etc), dietary history, body mass index (BMI), status of H. pylori infection and physical activity were unable to include in this analysis.

The epidemiology of GC in different geographical locations can be sought out in future. The trend and the changes in the incidence of GC in previous low-incidence areas such as Kelantan should also be studied along with the dietary and lifestyle changes. The prevalence of H. pylori infections and the incidence of GC in different geographic locations could be studied for Malaysia as well as for Asia and globally.

CONCLUSION

In this retrospective study, we studied the clinicopathological data of GC, although the data we reported represented only one hospital. The incidence of GC cases in Malay population was observed to be increased. Late-onset GC cases were found to be more common than early-onset cases, while all reported cases were adenocarcinoma types. Globally, it was estimated that there could be 1.8 million new cases and 1.3 million deaths related to GC by 2040.[16] And a higher incidence will be found in medium and low HDI (Human Development Index) countries compared to high HDI countries, hence, the SEA countries should be observant on the burden of GC.[16] Although GC showed a downward trend in Malaysia, it could again lead to an increasing trend of GC. Because of the nature of high aggressiveness, late diagnosis, association with lifestyle and non-communicable diseases such as diabetes mellitus, the prevalence of *H. pylori* infection, variation in responsiveness and awareness of the eradication regimens, GC could still constitute a local and global health issue. Consideration of lifestyle changes, health education, detection and eradication of *H. pylori* infection and early diagnosis of GC by health check-ups should be encouraged by the authorities. Hence, the authorities should consider adapting the *H. pylori* eradication regimen as a part of the insurance scheme; detection of *H. pylori* as a part of routine health check-ups; early referral and an exploration of upper GI endoscopy of middle-aged people who are above 50 with dyspeptic symptoms should be considered. Since certain countries and regions are estimated to have more burden of GC, health authorities should plan cancer control initiatives without delay.

DISCLOSURE

The authors have no other relevant affiliations or financial involvement with any organisation or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed. No writing assistance was utilised in the production of this manuscript.

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