Clinicopathological Features of Gastric Cancer; Single Center Experience

Amrallah A. Mohammed, MBBCh, MSc, MD[1, 2]; Abdullah S. Al-Zahrani, MD, ABIM,FRCPC[1]; Amr T. El-Kashif, MBBCh, MSc, MD[1, 3]

(1) Oncology Center, King Abdullah Medical City-Holy Capital, Saudi Arabia.
(2) Department of Medical Oncology, Faculty of Medicine, Zagazig University, Egypt.
(3) Department of Clinical Oncology, Faculty of Medicine, Cairo University, Egypt.

Corresponding Author: Dr. Amrallah A. Mohammed, MD
Oncology Center
King Abdullah Medical City-Holy Capital, Saudi Arabia
Email: amrallaabdelmoneem@yahoo.com

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Abstract

Gastric carcinoma remains a common disease worldwide with a dismal prognosis. This investigation was undertaken to define the demographic, clinicopathological and treatment modalities in patients with gastric adenocarcinoma.

Methods: We did a retrospective study of 56 patients with primary gastric cancer who had been at King Abdullah Medical city In Holly capital; a tertiary care hospital in KSA from January 2011 to December 2012, and follow up till December 2013.

Results: The mean patient age at diagnosis was 60.3 years (range= 26-94 years), and 62.2% were male. The male to-female ratio of patients was 1.6/1. 88.8%of the patients were Saudis and 11.2% were non Saudi (3 Yamani and 1 Pakistani). No family history of gastric cancer. 82.2% presented with stages III and IV disease. Histological types of adenocarcinoma lesions were present as intestinal, diffuse, and mixed with percent; 46.7%, 33.3% ,and 20% respectively. The H. pylori infection was documented in 20% of patients. Common chief complaint was abdominal pain (88.9%). 71.1% of our patients died within the first year and only 11% of them lived more than 2 years.

Conclusion: Gastric cancer is the second most common GI malignancies after colorectal cancer in King Abdullah Medical city. Most of our patients presented with advanced cancer stage which reflect its poor prognosis. This fact will need to be confirmed by a longer period of observation and enough sample size.

Introduction

Gastric cancer (GC) is a major contributor to the global burden of cancer morbidity and mortality. It is the fourth most commonly occurring worldwide (1). Moreover, because of its poor prognosis, it is the second most common cause of cancer death after the lung cancer. There are substantial variations in the incidence of GC by region and nation, with highest rates being observed in East Asia, Eastern Europe, and parts of Central and South America. Changes in the histology and location of upper GI tumors in some parts in Europe (2).In Western countries, the most common sites of GC are the proximal lesser curvature, cardia, and EGJ (3).It is possible that in the coming decades these changing tends to will also occur in South America and Asia. In 2013, an estimated 21,600 people were expected to be diagnosed and 10,990 would be eventually died of their disease in the United States (4).

GC, like other cancers, is the end result of the interplay of many risk factors as well as protective factors. Environmental and genetic factors are also likely to play a role in the etiology of the disease (5).Various epidemiological and pathological studies have suggested that gastric carcinogenesis develops with the following sequential steps, chronic gastritis, gastric atrophy, intestinal metaplasia and gastric dysplasia (6). Genetic factors play an important role in gastric carcinogenesis. The most common genetic abnormalities in gastric cancer tend to be the loss of the heterozygosity of tumor suppressor genes, particularly of p53 or "Adenomatous Polyposis Coli" gene (7).

GC is difficult to cure as it is often either asymptomatic or it may cause only nonspecific symptoms in its early stages. By the time symptoms occur, the cancer has often reached an advanced stage and may have also metastasized, which is one of the main reasons for its relatively poor prognosis. The modest efficacy and considerable toxicities associated with chemotherapy in advanced gastric cancer has prompted the pursuit of novel systemic treatment strategies (8).The difficulties encountered in the development of targeted therapy in advanced gastric carcinoma are caused by the lack of biomarkers to guide patient management. In the clinic to date, except for HER2, there are no established biomarkers predictive of tumor response to targeted agents. Few potential biomarkers are pending clinical validation, including amplification of MET (9), and fibroblast growth factor receptor 2 (FGFR2) (10) while others are more controversial. Moreover, the process of gastric carcinogenesis is complex.

Several reports from the Kingdom of Saudi Arabia have studied general patterns of cancer (11), and patterns of gastrointestinal tract malignancies (12, 13). Only a few reports have been devoted to the study of the pattern of gastric cancer (14). The aim of this study was to describe the clinicopathological features and our experience in management of these patients in our local setting and suggesting ways to improve treatment outcome. Which might gives us a clue about whether or not screening programs are needed in our regions.

Methods

The current retrospective study included 45 patients with histological diagnosis of gastric carcinoma treated at oncology center in King Abdullah Medical City between (KAMC) January 2011 and December 2012. The details of patients were retrieved from patients' files kept in the medical record department and histopathology laboratory. Information retrieved included socio-demographic data, clinical presentation, anatomical site, TNM stage, histopathological type, grade, presence of metastasis and treatment modalities. The clinical stage of the disease was assigned to each patient by using TNM; this is a staging system which is an expression of the anatomical extent of the disease based on the extent of the primary tumor (T), absence or presence of and extent of regional lymph node metastasis (N) and absence or presence of distant metastasis (20). The histological classification was based on Laurens (1965) classification as follows: (1) Intestinal type, (2) Diffuse type and (3) Mixed type (15). Treatment modalities included surgery, chemotherapy, radiotherapy and palliative. Patients were followed up for one year or death.

Statistical analysis: Descriptive statistics included frequencies, means, medians, ranges, and percentages. Analytic statistics included chi-square tests and unpaired Student t test .P value of <.05 was considered statistically significant.

Ethical consideration: Ethical approval to conduct the study was sought from the IRB review committee before the commencement of the study.

Results

Demographic data

Out of 1471 patients who were registered with malignancies at our center during the study period, 56 patients were cases of gastric cancer representing 3.8% of cases. Of these, 4 patients were excluded from the study due to incomplete data. Seven patients were non carcinoma, (one NHL, one liomyosarcoma, one neuoendocrinal, and 4 GISTs; one low risk, tow intermediate and one high risk). There were 28 (62.2%) males and 17 (37.8%) females giving a male to female ratio of 1.6:1. The ages ranged from 26 to 94 years with a mean age of 60.3 years. The peak incidence was in the age group of > 60 years (53.3%), followed by the age group of 40- 60 years(33.3%), and ages less than 40 years (13.3%) . 88.7% of patients were Saudi and 11.3% were non Saudi (3 Yamani and 1 Pakistani) ; table 1.

Table 1: Demographic features.

	Number (45)	Percentage (%)
Age in years		
Mean	60.3	
Median	61.00	
Range	26-94	
Age peaks		
> 60	24	53.4%
40- 60	15	33.3%
< 40	6	13.3%
Sex		
Male	28	62.2
Female	17	37.8
Ratio (M/F)	1.6/1	
Nationality		
Saudi	41	88.7
Non Saudi	4	11.3

Clinical presentation

Most patients presented with features of advanced disease such as, abdominal pain in 40 patients (88.9%), nausea and vomiting in 32 patients (71.1%), epigastric mass in 19 patients (42.2%), jaundice in 17 patients (37.8%), hematemesis in 12 patients (26.7%) and ascites in 7 patients (15.6%); table 2.

Table 2: Clinical presentation.

Main complain	Number (n=45) adenocarcinoma	Percentage (%)
Abdominal pain	40	88.9
Epigastric mass	19	42.2
Nausea and vomiting	32	71.1
Jaundice	17	37.8
Hematemesis	12	26.7
Ascites	7	15.6

Anatomical site, TNM staging and histopathologically type

The noncardiac region was the most frequent anatomical site involved in (64.4%) of cases. The gastric adenocarcinoma was the most common histopathologically type, occurring in 86.5% of cases, and most of the tumors had a poorly differentiated grade in 66.7% of cases. According to Lauren classification of gastric adenocarcinoma, 21 patients (46.7%) were intestinal, 15 patients (33.3%) were diffuse and 9 patients (20%) were mixed. According to TNM staging, 82.2% of the patients were diagnosed with advanced gastric cancer (Stages III and IV); table 3.

Diagnosis of gastric cancer

The diagnosis of gastric cancer was confirmed pathologically by upper GI endoscopic biopsies in 39 (86.7%) patients and the remaining 6 (13.3%) patients were diagnosed during laparotomy for gastric obstruction or definite surgery; table 3.

Treatment modalities

Out of 45 patients, 17 (37.8%) patients underwent surgical procedures for gastric cancer and the remaining 28 (62.2%) patients were not candidate for surgery with gastro-jejunostomy was the most frequent performed procedure; accounting for 58.8% of cases. 31.1% of patients were under palliative care from the start; table 3.

Table 3: Disease features.

	Number (n=45) adenocarcinoma	Percentage (%)
Adenocarcinoma		
Poorly differentiated	30	66.7
Moderate differentiated	13	28.9
Well differentiated	2	4.4
Her-2 status		
Positive	5	11.1
Negative	7	15.6
Not done	33	73.3
Helicobacter pylori status		
Positive	9	20
Not done	36	80

Lauren classification		
Intestinal	21	46.7
Diffuse	15	33.3
Mixed	9	20
TNM staging		
III and IV	37	82.2
Diagnostic method		
Upper GI endoscopic	39	86.7
Laparotomy	6	13.3
Anatomical sites		
Noncardiac	29	64.4
Cardiac	16	35.6
Treatment modalities		
Curative surgery	4	8.9
Palliative surgery	13	28.9
Palliative chemotherapy	14	31.1
Palliative radiotherapy	0	0
Best supportive care from the start	14	31.1

Discussion

GC is one of the most frequent cancers in the world; in terms of geographic distribution, almost two-thirds of gastric cancer cases and deaths occur in less developed regions. High rates apply to Japan, China, Korea, Central and South America, Eastern Europe, and parts of the Middle East, and low rates to North America, Australia and New Zealand, Northern Europe, and India (16). It is usually easier to treat if it is diagnosed early with a highly favorable prognosis and avoid extended surgery, which may produce complications, especially in the elderly people. However, many of the symptoms are similar to less serious conditions, which mean it can be difficult to recognize GC in the early stages and when symptomatic patients experience epigastric pain, discomfort and definitive symptoms such as weight loss or obstructive symptoms and metastases that often impede curative radical resection.

Although there are improved surgical techniques and adjuvant treatments, still the results of GC treatment do not differ markedly from the past results. Five-year relative survivals of around 20% or less are frequently reported (17).

In this review, gastric cancer accounted for 3.8% of all histopathologically-diagnosed malignancies seen during the studied period in our setting. These data are comparable with other studies which reported the incidence of gastric cancer up to 6.0% of all cancers (18, 19).

Our figure for GC in this study may actually be underestimated by the retrospective nature of the study. A better picture of its incidence in this region requires a prospective comprehensive data collection.

According to the Saudi Cancer Registry (SCR) between January and December 2004, 3158 gastric cancer male patients were diagnosed and analyzed with gastric cancer percentage 4.4% which represent the second common GIT cancers post colorectal (20). The cause of the high incidence of gastric cancer in our country is unclear and may be due to rapid change in Saudi life style including the increase in the prevalence of smoking among all age groups in comparison to other countries (21, 22) and dietary habits as Canned food, hot spices, salt and animal proteins which constitute a good media for foods fermentation and nitrosamine production. Both nitrosamine production and salt have been implicated as a risk factor for GC in many studies (23, 24). However, to further investigate this association we need more comprehensive and detailed data. In most developed countries, there has been a persistent and progressive decline in both the incidence and the mortality of gastric cancer in the past 50 years. This is principally related to changes in diet and food preparation and preservation (25). In agreement with other studies (26), the peak age incidence of gastric cancer in this study was found to be in the sixth decade of life.

The male predominance demonstrated in this study was in keeping with previous observations reported in studies done elsewhere (27). The exact reason for this male preponderance is not known; although the higher prevalence of smoking among men with the possible protective effect of estrogen may explain this predominance (28).

Many studies confirm the importance of lifestyle and environmental factors including H. pylori-induced inflammation, atrophy of the gastric mucosa and a diet rich in salt and nitrites and poor in fruit and vegetables (29).

Retrospective studies of the risk of GC in relation to H. pylori infection underestimate the true risk, due to loss of infection with onset of cancer. H. pylori does not colonise areas of cancer, intestinal metaplasia, or atrophy, and there is evidence that with the development of advanced gastric disease the organism can be lost from the stomach (30), which partially explain the lower percentage of documented H. pylori in our results (only 20%) . One estimate attributed more than 70% of distal gastric cancers to H. pylori, and the presence of cytotoxin CagA-positive H. pylori increases the risk of gastric cancer 20-fold compared with CagA-negative (31). H. pylori eradication treatment can reduce risk of gastric cancer (32).Determination of H. pylori seroprevalence was not performed in this retrospective study, because tests for H. pylori status were not routinely performed in patients with gastric cancer during the study period and, therefore, it was difficult to establish the association between H. pylori infection and gastric cancer.

A meta-analysis published in 1997 and in 2008 suggested a risk of stomach cancer among smokers of the order of 1.5-1.6 compared to non-smokers and the risk seen among current smokers was significant higher than that seen among ex- smokers (33). In this study, we could not determine the association among gastric cancer and smoking due to insufficient data in the files about the smoking history and type.

The most important method that is likely to improve the survival rates is early detection of GC. In the present study, the majority of patients presented late with an advanced stage of cancer (stage III and IV), which is in keeping with other studies in developing countries (34).Although there are sufficient endoscopic services. Which can be can be explained by many factors; firstly, the frequent visits to non-specialist physicians who prescribe medications to treatment the symptoms without treating or investigating the underlying cause. Subsequently, these patients will be diagnosed either with late stage GC or one of its complications. Secondly, elderly people usually fail to make use of available medical services. Lastly, still there is no public screening system for gastric cancer detection in our area. So to improve chances of early detection, we need a long term plan including patients and physicians as general practitioners should be more liberal in referring patients for endoscopy especially in high risk people, open- access endoscopy, greater efforts in education of patients and the improvement of diagnostic technical skills.

This study showed a wide spectrum in the histopathological features. The common anatomical site for gastric cancer in this study was distal gastric (non cardiac) 64.4% which is similar to studies done in developing countries (35, 36). The most common histopathological type of gastric cancer in this study was adenocarcinoma, accounting for 86.5% of cases, which is consistent with what is reported in the literature (37-39). Her-2 was not routinely done in our center during the study period. It is requested in 12 patients with 5 patients were positive.

The treatment of gastric cancer requires a multidisciplinary approach. Treatment modalities of GC include surgery combined with chemotherapy and radiotherapy given either as neo- or adjuvant therapy (40). Surgery is and, most probably, will remain the cornerstone of curative management of resectable disease; however, this benefit is limited to patients who present with early and, perhaps, localized disease. However, most of the patients we see in our environment present late with advanced disease at the time of diagnosis, for which only palliative surgery is possible (41). In this study, only 4 patients had gastric resection with curative intent. 32 patients (71.1%) died during the first year and only 5 patients extended more than 2 years. The prognosis of GC has remained poor in most developing countries where most patients are already in an advanced stage of the disease at the time of diagnosis, which has been proven both in the present study and in most studies (42-44). However, when it is diagnosed and treated early, gastric cancer is curable as a five-year survival rate of over 90% has been achieved in Japan (45).

Limitations

The potential limitations of this study included the following: first, the fact that information about some patients was incomplete in view of the retrospective nature of the study might have introduced some bias in our findings. Second, we did not determine the association of H. pylori with gastric cancer because of lack of necessary facilities at the study center. Third, this study included small sample size patients who were evaluated and treated at a single institution, which may not reflect the whole population in this region.

Conclusion

Gastric cancer is the second most common gastro intestinal malignancy after colon cancer in our center. The majority of gastric cancer when become symptomatic, usually become beyond the cure. In absence of screening program, the only way to improve the prognosis is to change unhealthy dietary habits. Although this study has highlighted the general epidemiological and clinicopathological features of gastric malignancy in our center, further prospective studies with enough sample size are needed studies are needed to evaluate the environmental risk factors, treatment outcomes and survival rate.

Conflict of interest

The authors certify that is no potential or actual conflict of interest related to this research.

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