Gastric Cancer in South East of Iran

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Abstract:

Introduction: Gastric cancer is the second most common GI malignancy in Zahedan. This investigation was undertaken to define the demographic, clinicopathological, and prognostic factors relevant to patients with gastric adenocarcinoma.

Methods: We did a retrospective study of 100 patients with gastric cancer who had been at Ali Ebne Abitaleb Hospital and Khatam al Anbia Hospital in 2004-2006. Data analysis was done using the Kaplan-Meier method and the Cox proportional hazard model.

Results: The mean patient age at diagnosis was 50 years (range= 28-83 years), and 68% were male. The male-to-female ratio of patients was 2.1/1. Ninety-six percent of the patients were Iranian and in the Balouch ethnic group was presented more than the Sistani ethnic group, and 4% were Afghan. Five percent of the patients reported a family history of gastric cancer. 67 patients (67 %) presented with stages III or IV disease, whereas 33 patients, with stages I or II disease. Poorly differentiated lesions were present in 71%. In 16 patients, metastasis was seen. Common chief complaint was abdominal pain in epigastria (58 %). Survival data was available in 78 cases. The median survival was 8 months.

Conclusion: Gastric cancer is the second most common GI malignancies in Zahedan. This pattern is different from other regions in Iran that gastric cancer is most common GI malignancies. This fact will need to be confirmed by a longer period of observation.

Key words: Gastric cancer,South east of iran

Received: 4, Aug., 2009
Accepted: 26, Sep., 2009

Introduction

Gastric cancer has a wide geographic variation. Countries in Asia with a high incidence include Japan, China, and South Korea; those with a low incidence include India, Pakistan, and Thailand. Until recently, gastric cancer was the second most common cancer worldwide. Now, it has moved to third place, behind breast cancer. Gastric cancer is the second most common cause of death from cancer (734,000 deaths annually).(1) Gastric carcinoma remains a common disease worldwide with a dismal prognosis.(2) The five-year survival rate for gastric carcinomas is low (10%).(3, 4, 5)

Gastric cancer is the most common malignancy in Iran and its incidence is particularly high in Ardabil Province in the northwest of the country. In this province, the age standard incidence rate is 49.1 and 25.4/100,000 persons per year in males and females, respectively. The cause of the high incidence of GC in this geographical region is unknown.(4, 5)

Gastric cancer, 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. Among the environmental factors, diet and infection with Helicobacter pylori are the most common suspects in gastric carcinogenesis. 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. The initial stages have been linked to excessive salt intake(6) and infection with the H. pylori.(7) Genetic factors play an important role in gastric carcinogenesis; this leads to either abnormal genes over expression or inappropriate expression of normal genes, whose products confer the malignant phenotype. Advances have been made in the discovery of the genetic changes, mostly of the intestinal type; its development is probably a multi-step process. 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.(8)

The epidemiology of GC has been widely studied in the Western world as well as in Japan.(6-9) However, only a few scattered reports from the developing world have been published.(10-14) There is a lack of good descriptive data on GC from Middle Eastern countries, where both cancer registration and the prevalence of risk factors are relatively unknown. Because of the decreasing trend taking place in the Western world as a result of possibly socio-economic development and its consequences, it is important to gain an insight into what is happening in other parts of the world, such as in the Middle East. This prompted us to report the epidemiological and clinicopathological features of gastric malignancy in Sistan and Balouchestan, Southeast of Iran, in comparison to other countries. This might assist in a better understanding of the important risk factors which contribute to the development of GC. This also gives us a clue about whether or not screening programs are needed in our region.

Materials and Methods

We retrospectively analyzed the clinicopathologic characteristics of 100 gastric adenocarcinoma patients who had been admitted to Zahedan Ali Ebne Abitaleb Hospital from September 1, 2003 to October 1, 2006. Age, sex, method of operation, size of lesion, location of cancer in the stomach and stage were analyzed in those patients, retrospectively. Histologically confirmed gastric malignancy was found in 100 patients, including 86 patients with adenocarcinoma, and 14 patients with malignant gastric metastasis. All available endoscopy reports were reviewed. Initially, clinical symptoms, demographic data and medical history were recorded. Gastroscopy was performed to establish the endoscopic diagnosis and status of H pylori infection.

Patients and/or family members were contacted. Gastric adenocarcinoma was classified into intestinal type (IT), diffuse type (DT) or mixed type according to the histological criteria of Lauren.(15) Tumor staging in each patient was based on clinical information, preoperative radiological investigations, operative findings and pathological examination. The staging was made in accordance with the TNM system.(16)

Clinicopathologic data were compared using the χ^2 and Fisher's exact tests. $P < 0.05$ was considered statistically significant.

Results

During the study period, 100 patients with GC were identified, 68 (68.0%) patients were males with a male to female ratio of 2.1:1. the peak incidence was in the age group of >60 years (42%), followed by the age group of 50-60 years (21%) ,and ages 40 -50 years (16%). Approximately 16% of the patients were younger than 40 years and 5% of the patients were younger than 30 years (Table-2). The mean age for the whole group was 59 years (range 19-80 years). Table- 3 shows the age distribution in the patient groups.

According to IARC study, the annual incidence of cancer in men is as follows: prostate cancer: 451/100,000; lung cancer: 449/100,000; colon cancer: 176/100,000; and in women aged 65 years or older: breast cancer: 548/ 100,000; colon cancer: 133/100,000; and lung cancer: 118/ 100,000; makes up 48% of all tumors of the elderly.

According to IARC study the annual incidence of gastric cancer is 64/100,000.

Patients characteristics have been summarized in Table 1.

Carcinomas were located most frequently in the lower third of the stomach, accounting for 84% (84/100) of all patients.

Ninety-six percent of the patients were Iranian. The Balouchs ethnic group was represented more than Sistani ethnic group. Four percent of the patients were Afghan. Five percent of the patients reported a family history of gastric cancer.

In our study, the 80% of the patients had a history

Table- 1. Characteristics of the studied patients

Signs and symptoms	Ptients (%)	Prevalence (%)
Abdominal pain	90	90
Weight loss	15	15
Dyspepsia	70	70
Nausea ; vomiting	55	55
Abdominal mass	15	15
Anorexia	55	55
Dysphagia	15	15
Gastrointestinal bleeding	5	5
Ascites	8	8
Constipation	15	15

Table- 2: Age distribution

Age (years)	Percent %
>60	42%
50-60	21%
40-50	16%
<40	16%
< or = 30	5%

Table- 3. TNM staging

Stage (TNM) and methods of operation patients	Patients(n)	%
I	7	7%
II	22	22%
III	45	45%
IV	26	26%

xof smoking and tobacco use such as tobacco, cigarrete, Paan and Naas (chewable tobacco).

The H. pylori infection was documented in more than 85% of the patients.

Discussion

Gastric cancer is the most prevalent malignancy in Iran. If GC is diagnosed at an early stage, patients can have a highly favorable prognosis and avoid extended surgery, which may produce complications, especially in the elderly people. However, the symptoms of GC are non-specific and vague, when symptomatic patients experience epigastric pain and discomfort and definitive symptoms such as weight loss or obstructive symptoms and metastases that often impede curative radical resection. Additionally, the results of GC treatment do not differ markedly from the past results though there are improved surgical techniques and adjuvant treatments. Researchers have shown that the prognosis of GC has not changed in the past 20 years.(17, 18) The only method that is likely to improve the survival rates is early detection of GC. Our patients tended to be diagnosed late, as evidenced by the fact that there was a long interval between the onset of symptoms and diagnosis. This is not due to insufficient current endoscopic services, but is due to the fact that many people in our area who have dyspeptic symptoms visit with non-specialist physicians who either prescribe medications for long term treatment or use drugs in order to ameliorate the pain. Subsequently, some of these patients whose cause of dyspepsia is cancer are diagnosed with late stage GC or one of its complications. In addition, elderly people usually fail to make use of available medical services. However, general practitioners should be more liberal in referring patients for endoscopy and resist the temptation to treat dyspeptic patients with anti-ulcer therapy without endoscopy, especially in elderly people and in patients with evident signs. Open- access endoscopy, greater efforts in education of patients and the improvement of diagnostic technical skills may improve chances of early detection.

The etiology of gastric cancer is multifactorial. In a case–control study from Chennai, smokers had a twofold increased risk of gastric cancer compared with nonsmokers, and the risk seen among current smokers was significantly higher than that seen among ex-smokers. The risk among those who smoke “bidi” (a type of local cigarette made from suncured tobacco that is rolled in a rectangular piece of dried leaf of diospyros melanoxylon) was three times that of cigarette smokers.(7) According to TNM staging, more than two-thirds of the patients were diagnosed with advanced GC.

These results re-emphasize that GC symptoms are non-specific and need an early screening examination. A public screening system for gastric cancer has not yet been introduced in Iran and in our area.

Gastric cancer is the most common malignancy in Iran. Its incidence is particularly high in Ardabil Province in the northwest of the country.(19-21) In this province, the age standard incidence rate is 49.1 and 25.4/100 000 persons per year in males and females, respectively.

The cause of the high incidence of gastric cancer in our country is unknown.

In Southeast of Iran (Sistan & Balouchestan), gastric cancer is the second most common gastroenterointistinal malignancy. The first most common malignancy of GI cancer is esophageal cancer.

The following two factors may play a role. First, the rapid change in Iranian dietary habits constitutes a risk factor. Vitamin C-rich fresh vegetables and fruits, starch and natural unprocessed wheat products are the major constituents of traditional Iranian food. However, canned food, hot spices, pickles and animal proteins are now dominant in the Iranian diet.

The fermentation of foods involves the production of nitrosamine. This compound has been implicated as a risk factor for GC in many studies and consumption of fermented food may be a risk factor for GC in our region because people frequently use such compounds.

However, to further investigate the association between fermentation and GC, more comprehensive and detailed data are required. Salt has been indicated as a risk factor for GC in many previous studies. Since the use of salt and fermentation in our

regional food preparations is strongly inter-related, we are unable to clearly separate the independent effects of the two variables.

It is known that the environmental risk factors for GC are dietary in origin.(22, 23) 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 because of changes in diet and in the preparation and preservation of food (and an increase in the use of refrigeration).

Patterns of GC in our area are similar to those reported from high-risk regions worldwide.(25) In our study, the gastric cancer is the second most common malignancy, (the most common malignancy was esophageal cancer), the male to female ratio was 2.1:1 and the peak incidence was in the age group of >60 years (42%), followed by the age group of 50-60 years (21%), and age 40-50 years (16%). Approximately 16% of the patients were younger than 40 years and 5% of the patients were younger than 30 years of age. The mean age of the entire group was 67 years (range= 19-86 years). Histologically confirmed gastric malignancy was found in 100 patients, including 86 patients with adenocarcinoma, and 14 patients with malignant gastric metastasis.

In Western countries, PGL and metastasis are represented only in 2%-5% of gastric malignancies.(26) It was 14% in our series, which was higher than 9% from neighboring Iraq,(27) and lower than 14%-22% from Saudi Arabia.(28, 29) During the past three decades, the site of PGL in the Middle East has changed. Small intestinal involvement has become less common and gastric involvement more frequent. This varying pattern seems to be environmental in origin.

Conclusion: In Southeast Iran (Sistan and Balouchestan), gastric cancer is the second most common gastroenterointistinal malignancy. The first most common malignancy of GI cancer is esophageal cancer.

Several symptoms of GC are non-specific. The majority of identified gastric adenocarcinoma in patients is symptomatic, and has a lesser chance of being cured through operation and a lower survival rate. The patients with dyspeptic symptoms and evident signs should be referred for earlier diagnostic endoscopy. Improvements in diet and food storage and control of H pylori infection, by indirect means such as generally improving sanitary conditions or by direct interventions such as eradication, are likely to offer great potential for the prevention of GC in this area. Reducing tobacco usage, improving dietary habits and public health education would be a more affordable approach in reducing the occurrence of this cancer.

Although this study has highlighted the pertinent epidemiological and clinicopathological features of gastric malignancy in Sistan and Balouchestan Province in Iran, further studies are needed to evaluate the environmental risk factors, incidence, treatment outcomes and survival rate.

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