



Clinical and Histopathological Characteristics of Gastric Adenocarcinoma in Yemeni Patients: A 2 Years Prospective Study

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Abstract

Objectives: To study the clinical and the histopathological characteristics of gastric cancer concentrating more on the gastric adenocarcinoma. **Design:** Prospective study of one hundred thirty Yemeni patients confirmed with gastric malignancies during the period from July 2016 to July 2018. **Setting:** Specialized center of gastrointestinal and liver diseases in Ibb city, Yemen. **Subjects:** All patients with histopathologically proved gastric cancer. **Results:** We collect 130 patients with gastric cancer during the study period, they were 93 males and 37 females with age ranged between 25 years and 100 years and the mean age was 64.98 ± 15.15 years. The most frequent clinical presentations of our patients were epigastric pain (81.5%), weight loss (74.6%), dysphagia (46.9%), vomiting (49.2%), palpable epigastric mass (19.2%) and hematemesis/melena (20%). Proximally located gastric cancer represented 46.1%; 48.9% of males patients and 38.9% of females patients. Adenocarcinoma constituted 92.4%, of which the intestinal type was 82.5% and the diffuse type was 17.5%. Squamous cancer accounted in 1.5%, and the non-epithelial tumor was in 6.1%, of which 4.6% were lymphoma and 1.5% were GIST. **Conclusion:** Adenocarcinomas are the major histological type of gastric cancer and represent 92.4% of all gastric malignancies in which intestinal type represented 82.5% and diffuse type represented 17.5%, and proximally located gastric cancer within stomach was the commonest in both sexes.

Subject Areas

Gastroenterology & Hepatology

Keywords

Gastric Adenocarcinoma, Histopathology, Lauren Classification, Yemen

1. Introduction

Globally, the incidence and mortality of gastric cancer have fallen dramatically over the past 70 years [1] [2]. However, gastric cancer is currently the fourth most common cancer and the second leading cause of cancer-related death worldwide [3] [4]. In 2012, the World Health Organization estimated about one million new cases of gastric cancer, more than 70% of the cases (677,000 cases) occurred in developed countries with 2:1 male to female ratio and half of those cases were on the Asian continent mainly China [5] [6]. There are two main histologic variants of gastric adenocarcinoma: “intestinal-type” (which resembles intestinal cancers in forming glandular structures) and “diffuse” (which is poorly differentiated, has signet-ring cells, and lacks glandular formation) according to Lauren’s classification [7] [8]. The intestinal type is more common in males, blacks, and older age groups, whereas the diffuse type does not show gender predominance, and is more frequent in younger individuals [1] [9] [10]. Intestinal type tumors predominate in high-risk nations of gastric cancer, such as East Asia, Eastern Europe, Central and South America [9]. Moreover diffuse type adenocarcinomas have a more uniform geographic distribution [11]. The recent decrease in the incidence of gastric cancer worldwide caused by decline in the incidence of the intestinal type tumors [9] [12]. However; the incidence of diffuse type gastric carcinoma, particularly the signet ring type, has been increasing [13]. The two main tumor sites of gastric cancer are proximal (cardia) and distal (non-cardia) and despite a dramatic decline in distal gastric cancers, proximal tumors have been increasing in incidence especially in the Western countries [1] [7] [14] [15]. They may differ in genetic susceptibility, pathologic profile, clinical presentation, and prognosis [16]. The observed differences between gastric cancers by anatomic site suggest that they are distinct diseases with different etiologies [17] [18]. Although the etiology of gastric cancer is complex, the most important and well-studied risk factors are *Helicobacter pylori* (*H. pylori*) infections, environmental factors, nutritional factors and host genetic factors, such as a positive family history for gastric cancer and/or a genetic pro-inflammatory profile [1] [3] [17] [19]. Several environmental exposures have already been identified as risk factors for gastric cancer including diet, smoking, bacterial infections and a variety of occupational exposures [1] [3] [17] [20]. The effects of *H. pylori* on gastric tumor development may vary by anatomical site in which there is a strong link between *H. pylori* infection and distal gastric cancer and not the proximal one [3] [21]. Gastric cancer is generally

asymptomatic until the disease is quite advanced [3] [17]. Symptoms of gastric cancer are nonspecific and may include anorexia, weight loss, abdominal pain or discomfort, nausea, vomiting, early satiety and gastrointestinal bleeding [3] [7] [17]. There are only a few studies regarding the epidemiologic distribution of gastric cancer in developing countries and the Middle East [22] [23] [24]. According to the WHO, the reported incidence of gastric cancer in the neighboring countries such as Saudi Arabia in 2012 was 3.14% [25]. It is not known whether the incidence has changed in the Middle East, and the actual epidemiologic distribution of gastric cancer according to age, sex, location within the stomach, and tumor histologic types are not fully established in this part of the world [26].

2. Materials and Methods

This study was carried out in Ibb city-Yemen during the period from July 2016 and July 2018 at gastrointestinal and liver diseases center. We enrolled in this study consecutive patients with histologically confirmed gastric cancer. Patients with endoscopic gastric tumor without histological confirmation were excluded. To all patients included in the study sociodemographic data, presenting symptoms, clinical findings, risk factors, ultrasonographic, endoscopic and histopathologic findings were collected. Verbal consent was also obtained from patients or their relatives. CBC, LFT, RBS, RFT, *H. pylori* serology and fecal Ag test were done to all patients. One experienced endoscopist performed an upper GI endoscopy using (PENTAX-EPK-5000 Unit) to all studied patients. Location, size and endoscopic appearance of the lesion were described and six biopsy specimens were minimally taken for histopathologic examination. In all cases 10% formalin was used as fixative. Histopathological examination which carried out by two independent expert pathologists. Histological classification of gastric cancer was based on Lauren's criteria [8]. Statistical analyses were performed by using SPSS version 20 sciences. Results were presented as mean \pm standard deviation (SD). Nominal data were expressed by percentages. P-values < 0.05 were considered to be statistically significant.

3. Results

We collected 130 patients with confirmed gastric cancer during the study period. Their demographic data and risk factors were shown in **Table 1**. The most frequent clinical manifestations were shown in **Table 2**. The anatomical site of the tumor within the stomach, the macroscopic and microscopic types were all shown in **Table 3**. The correlation of gastric adenocarcinoma histopathologic types with age, sex, *H. pylori* infection and location were shown in (**Table 4, Table 5**).

4. Discussion

Gastric cancer is a major health issue worldwide [17]. Adenocarcinomas represent about 90% of all gastric cancers [18]. It is subdivided into two main

Table 1. Demographic characteristics and risk factors of our patients (n = 130).

Characters	Male		Female		Total		P value
	n	(%)	n	(%)	n	(%)	
	93	71.5	37	28.5	130	100	
Age							0.29
Less than 40	4	4.3	4	10.8	8	6.2	
40 - 49	8	8.7	4	10.8	12	9.3	
50 - 59	8	8.7	4	10.8	12	9.3	
60 - 69	21	22.8	12	32.4	33	25.6	
>70	51	55.4	13	35.1	64	49.6	
Residence							0.21
Rural	83	89.2	30	81.1	113	86.9	
Urban	10	10.8	7	18.9	17	13.1	
Risk factors							
<i>H. pylori</i>	60	64.5	23	62.2	83	63.8	0.80
Smoking	52	55.9	4	10.8	56	43.1	0.00
Khat chewing	73	78.5	22	59.5	95	73.1	0.03
History of gastric cancer in 1 st or 2 nd degree relatives	3	3.2	1	2.7	4	3.1	0.87
Previous gastric surgery	1	1	0	0	1	0.8	0.52

Table 2. Clinical presentations of the studied patients (n = 130).

Clinical manifestations	Male		Female		Total	
	n	(%)	n	(%)	n	(%)
Epigastric pain	74	79.6	32	86.5	106	81.5
Weight loss	73	78.5	24	64.9	97	74.6
dyspepsia	59	63.4	26	70.3	85	65.4
Vomiting	44	47.3	20	54.1	64	49.2
Dysphagia	43	46.2	18	48.6	61	46.9
Postprandial fullness	19	20.4	13	35.1	32	24.6
Upper GIT bleeding	19	20.4	7	18.9	26	20
Palpable epigastric mass	22	23.7	3	8.1	25	19.2

histologic types; intestinal and diffuse type [7] [8] [18]. The incidence of intestinal-type adenocarcinoma has declined significantly, but it is still the most common type (70% - 80%) [7]. There are little studies in Yemen that classify and study adenocarcinoma by subtypes. In our study 130 cases of confirmed gastric cancer were identified between July 2016 to July 2018 which may denote an increasing incidence of gastric cancer in our country as compared to the reported data from neighboring countries [27] [28]. The mean age of our studied patients was of 64.98 ± 15.15 years with a range between 25 - 100 years. The mean age for males was of 67.31 ± 14.39 and was of 58.84 ± 15.65 for females. Over 70% of

Table 3. Anatomical site, macroscopic appearance and histopathological types (n = 130).

Variables	Response	Male		Female		Total		
		n	(%)	n	(%)	n	(%)	
Anatomical site	Non-proximal	Body	21	22.8	6	16.7	27	21.2
		Antrum	14	15.2	8	22.2	22	17.2
		PM	7	7.6	4	11.1	11	8.6
	Proximal	MD	2	2.2	1	2.8	3	2.3
		Diffuse	3	3.3	3	8.3	6	4.7
		Cardia & Fundus	45	48.9	14	38.9	59	46.1
Macroscopic appearance	Ulcerative, infiltrative	69	75	24	64.9	93	72.1	
	Polypoidal	13	14.1	8	21.6	21	16.3	
	Diffuse	10	10.9	5	13.5	15	11.6	
	Adenocarcinoma							
Histopathologic type	Intestinal type	73	78.5	26	70.2	99	76.2	
	Diffuse type	14	15.1	7	18.9	21	16.2	
	Others							
	Squamous	1	1.1	1	2.7	2	1.5	
	GIST	1	1.1	1	2.7	2	1.5	
	Lymphomas	4	4.3	2	5.4	6	4.6	

PM = Proximal and middle part of the stomach. MD = middle and distal part of the stomach.

Table 4. Histopathological classification of gastric adenocarcinoma in correlation with sex (no = 120).

Histopathological type	Male		Female		Total		
	n	(%)	n	(%)	n	(%)	
Intestinal type	Well differentiated	27	31.0	11	33.3	38	31.7
	Moderate differentiated	10	11.5	4	12.1	14	11.7
	poorly differentiated	28	32.2	8	24.2	36	30
	Mucinous	7	8	1	3	8	6.7
Diffuse type	Papillary	1	1.1	2	6.1	3	2.5
	Undifferentiated	6	6.9	2	6.1	8	6.7
	Signet cell ca	8	9.2	5	15.2	13	10.8
Total	87	100	33	100	120	100	

male patients and over 60% of female patients were over 60 years of age and this is in consistent with those reported for patients from high risk countries and medical literatures [17] [18] [26] [27] [28]. Male to female ratio in our study was 2.5:1 which is similar to what is known in the medical literatures and previous studies from our country and neighboring counties [3] [17] [18] [29] [30] [31] [32]. The risk factors studied in our research were *H. pylori* infection, khat

Table 5. Correlation of gastric adenocarcinoma (n = 120) with age, sex, H pylori infection & tumor location.

Histological types	Age (years)		Sex				H pylori nfection		Location			
	Mean		Male		Female		no	%	Proximal		Distal	
			No	%	no	%			no	%	no	%
Intestinal	65.12 ± 15.1	73	84.9	26	81.3	65	65.7	50	50.5	49	49.5	
Diffuse	67.6 ± 13.2	13	15.1	6	18.8	13	68.4	8	42.1	11	57.9	
Total	65.5 ± 14.8	86	100	32	100	78	66.1	58	49.2	60	50.8	
P value	0.83			0.51			0.92				0.81	

chewing, smoking and others (**Table 1**). *H. pylori* infection prevalence in developing countries including Yemen ranges between 70% and 90% in adult population [33] [34], compared to a much lower prevalence in developed countries such as USA where the prevalence is <20% at the age of 20 years and 50% at 50 years [35]. It has been reported in Yemen that the prevalence of *H. pylori* infection among patients underwent upper GIT endoscopy in Sana'a major hospitals was very high (99.6%) [36]; however prevalence data for the general population are lacking. In our studied patients the *H. pylori* seropositivity was seen in 63.8%. This high prevalence of *H. pylori* infection in addition to other risk factors could explain the increasing incidence of gastric cancer in our country. Smoking is a risk factor for many cancers [37]. A significant relationship between smoking and gastric cancer was reported in many studies [38] [39] [40] [41]. In a large population-based study in Europe (EPIC), 17.6% of gastric cancer cases were attributed to smoking [39]. In our study smoking was encountered in 43.1% more in males (55.9%) than in females (10.8%). Khat chewing habit became very common in Yemen where approximately 60% - 90% of males and 35% of females chew Khat daily [42]. Chemically khat leaves contains cathinone (S-(-)-a-aminopropiophenone) and cathine (S, S-(-)-norpseudoephedrine [41]. Farmers used many kinds of pesticides mostly in illegal way for most of the cultivated plants including Khat. Khat chewing was reported in many studies to be a risk factor in many disorders including cancers [43]. In our study 73.1% (78.5% of males and 59.5% of females) were chewed Khat. There is statistically significant differences regarding smoking and Khat chewing with sex (P value = 0.00 and 0.03 respectively) in which smoking and Khat chewing were more in males (**Table 1**). The proximal gastric cancer was found to be the most common in our community in both males and females, accounting for 48.9% of male patients and 39.9% of female patients, this is similar to the reported studies from western countries and our previous study and medical literatures [3] [15] [44] [45], but not in agreement with many studies from developing countries [28] [46] [47]. In developed countries, increasing cardia gastric cancer was believed to be due to reduction in the incidence of *H. pylori* infection and subsequently reduction in the distally located gastric cancer at the expense of the proximal one

[3]. In our country *H. pylori* infection incidence still high and despite of this, the proximal location in our studied patients was the commonest (Table 3). This may reflect emerging of new risk factors in our community such as chewing khat habit and/or the pesticides used in it and in mostly all kinds of vegetables and fruits cultured in our country, as it is already reported in some studies [48]. The most frequent symptoms reported by stomach cancer patients in the present study were abdominal pain (81.5%), weight loss (74.6%), dyspepsia (65.4%), vomiting (49.2%) and dysphagia (46.9%) Table 2. The proportions of presenting symptoms in the present study are much higher than those reported by Selcukbiricik *et al.* [49]. Because of active screening programs in Eastern Asia, and developed world many patients are now detected while asymptomatic [50]. However, most patients with gastric cancer in our country are presented in advanced stages as indicated by the high percentage (46.9%) of patients presented with dysphagia in this study and other studies from Yemen [32] [44]. This could be attributed to the poverty and a little accessibility to the available specialized health care centers in one hand, and lack of active screening programs and policies in the country on the other hand.

Analyzing the histologic subtypes of gastric cancer in our patients, gastric adenocarcinoma was found in 120 (92.3%); where the intestinal type seen in 99 cases (82.5%) and diffuse type seen in 21 cases (17.5%) and the other types of gastric cancer were lymphoma in 4.6%, GIST in 1.5% and squamous type in 1.5% (Table 3) and this is similar to some degree with studies from our country and neighboring area [32] [44] [51], and in discordance with M.G. Martínez-Galindo *et al* in which diffuse-type adenocarcinoma was reported in 55.2%, intestinal-type in 28.2% [52]. This difference between our study results and the results of M.G. Martínez-Galindo *et al* could be explained by using different classification system. In our study tubular adenocarcinoma was the predominant type seen in 88 (73.4%) patients in which well differentiated grade seen in 38 (31.7%), moderately differentiated in 14 (11.7%) and poorly differentiated in 36 (30%). This was followed by signet ring cell, mucinous, undifferentiated and papillary adenocarcinoma in 13 (10.8%), 8 (6.7%), 8 (6.7%) and 3 (2.5%) respectively. This is consistent with other studies in Yemen [44] [51]. We compared between intestinal and diffuse type adenocarcinoma regarding the mean age, sex, *H. pylori* infection and location of the tumor and we found no significant statistical differences between intestinal and diffuse type regarding all studied variables as P value was >0.05 (Table 5), and this is in agreement with a study from KSA done by Hamdi *et al.* regarding the mean age and sex [53], but not in agreement with what is known in the global literatures and other studies [3] [7] [53]. This difference should be further investigated considering various geographical and demographical features of our country.

5. Conclusions

Clinical and pathological characteristics of gastric adenocarcinoma among Ye-

meni patients are somewhat similar to those in other parts of the world.

Histopathologically, intestinal-type adenocarcinoma with their different sub-types was the most common types of stomach cancers among Yemeni patients.

Proximally located gastric cancer is more frequent in our patients in both sexes.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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