



Upper Gastrointestinal Cancer in Yemen: A hospital-based study

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ABSTRACT

Background: The incidence of gastroesophageal cancer has shown a rapid change in several areas of the world.

Aim: to determine the sub site distribution of upper gastrointestinal cancer among patients underwent endoscopic clinic at AlThowrah hospital, Sana'a city, Yemen.

Methods: Descriptive, hospital based study was carry out to study the sub site distribution of upper gastrointestinal cancers in Yemen. 1006 patients referred to Al-Thawra hospital-Sana'a from several public and privet hospitals. All gastric and esophageal cancer patients diagnosed during the period from January 2008 and July 2012 were included in the study. All patients admitted to this study were studied according to clinical protocol consisting of a standard questionnaire, clinical examination and endoscopic findings. The questionnaire was included demographic characteristics and endoscopic findings. The data were analysis using statistical package for social sciences (SPSS, Version 18.0.) descriptive statistics were apply.

Results: A total of 1006 patients with upper gastrointestinal cancers were identified, 31.2% of the patients were referred from Amran, followed by 26.8% from Sana'a and 25.9% from Saada. 54.7% of the patients' had EC and 43.3% had GC. Adenocarcinoma accounts for 46%.

Conclusion: There were considerable variations in the sub site of upper gastrointestinal cancers in the Yemen. Keywords: Cancer, Upper GI cancer, Gastric cancer, esophageal cancer, Yemen.

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Introduction:

Cancer is and will become an increasingly important factor in the global burden of disease in the decades to come. According to estimates from the International Agency for Research on

Cancer (IARC), there were 14.1 million new cancer cases in 2012 worldwide, of which 8 million occurred in economically developing countries, which contain about 82% of the world's population. The corresponding

estimates for total cancer deaths in 2012 were 8.2 million (about 22,000 cancer deaths a day)-2.9 million in economically developed countries, and 5.3 million in economically developing countries. The estimated number of new cases each year is expected to rise from 10 million in 2000 to 15 million by 2020¹.

Upper gastrointestinal cancer (UGIC) is a major contributor to mortality and morbidity worldwide. 952 000 new cases of gastric cancer in 2012 (6.8% of the total number of cancer cases), making it the fourth most common malignancy in men and the fifth most common in women worldwide. More than 70% of cases occurred in developing countries, and about half of the global total occurred in East Asia. GC was the third leading cause of cancer death in both sexes worldwide in 2012 (723 000 deaths, 8.8% of the total¹. GC shows regional variations because of differences in dietary patterns, and the prevalence of *Helicobacter pylori* infection². There has been a steady decline in recent years in most developed countries and in countries with high incidence rates in Asia³. GC is a multifactorial disease. A positive family history of gastric cancer has been associated with a two to three-fold increased risk of the disease, which suggests a genetic basis⁴. Diet is considered to play an important role in the occurrence of gastric cancer. Salty food and smoked or marinated food deficient in vitamins and antioxidants significantly increases the probability of gastric cancer⁴⁻⁶. Vegetables, especially non-starchy and allium vegetables, fruits and pulses (legumes) decrease the risk of gastric cancer⁵, and green tea also reduces the risk.⁷.

In Yemen, the knowledge about the UGIC remains poor, and there is little information available on this issue in the international literature. According to GLOBOCAN 2012, the incidence of gastric cancer in Yemen was 422 new cases per 100 000 (3.7% of the total number of cancer cases), making it the seventh most common malignancy in both sexes. In men, it was the sixth most common malignancy with 279 new cases per 100 000 (5.2% of the total) but in women, it was the 11th most common malignancy with 143 new cases per 100 000 (2.4% of the total)¹.

Aim of the study:

to determine the subsite distribution of upper gastrointestinal cancer in underwent endoscopic clinic at Al-Thowrah hospital, Sana'a city, Yemen.

Subjects and Methods

The study was conducted at Al-Thowrah Modern General

Hospital (AMGH), Sana'a city, Yemen, endoscopic clinic. Al-Thowrah hospital is public and it is a referred hospital in Yemen AMGH provides primary, secondary and tertiary health care for the patients. A descriptive, hospitalbased study was conducted to study the subsite distribution of upper gastrointestinal cancers among Yemenis patients. In this study, we investigated 1006 patients underwent upper gastrointestinal endoscopy clinic from a different part of Yemen. All patients admitted to this study were studied according to clinical protocol consisting of a standard questionnaire, clinical examination, and endoscopic findings. The questionnaire was included the following: demographic and behavioral characteristics (age, sex, and provinces) and endoscopic findings. All patients with GC and esophageal cancer (EC) diagnosed during the period from January 2008 and December 2012, were included in the study. An essential inclusion criterion was that the patients were residing there for at least the last 10 years.

Endoscopic and pathologic tests were performed by the specialist team, according to the study protocol performed. Uniform endoscopic, criteria were used to define the tumor sub site. The subsite of esophageal tumors were recorded as upper, middle, or lower based on the endoscopy. If the location of the main tumor bulk was not obvious, the cancer was recorded as "esophageal". Noncardia gastric cancer was defined as those where the center of the tumor was located over 2 cm distal to the gastroesophageal junction. The gastroesophageal junction was defined as the most proximal site of the gastric folds. Noncardia gastric cancers were further divided into antrum, body, and fundus, according to the location of

the main bulk of tumor⁹. If the main bulk was not obvious, the cancer was recorded as “gastric”. Adenocarcinomas of the gastro-esophageal junction area were classified according to the WHO/IARC guidelines as a tumor which crosses the gastro-esophageal junction regardless of the main site of the tumor bulk. Adenocarcinoma of the esophagus was located entirely above the gastro-esophageal junction, and adenocarcinoma of gastric cardia was located below the gastro-esophageal junction and was centered within 2 cm from the junction.

The data were loaded into a personal computer and statistical analysis was conducted using SPSS, Version 18.0. Copyright SPSS Inc., Descriptive statistics (frequencies, percent, and Mean±SD) was applied. Differences between variable measurements related to demographic characteristic were analyzed using ANOVA and Chi-square tests. P-Value<0.05 was taken as the level of significant.

Results

A total of 1006 patients' aged ranged from 18-96 years with a confirmed diagnosis of gastric and esophageal cancer were identified and the mean age was 63 ±12 years. There was no statistical difference with respect to the age of the patients and provinces (ANOVA= 2.7, P = 0.64).

Male represented 667 (66.3%) of the total patients while female 339 (33.7%) (Ratio 2:1). There was no statistical differences in the sex between the provinces ($\chi^2 = 9.16$, P =0.10).

Distribution of UGIC by Provinces

As regards, the distribution of upper gastrointestinal cancer among patients by provinces 314(31.2%) of the patients were referred from Amran, 270 (26.8%) from

Sana'a and 261(25.9%) from Saada. More details present in table 1.

Distribution of provinces by site of UGIC

Regarding to the distribution of provinces by sites of upper gastrointestinal cancer among patients, the data showed that there were 203(20.2%) with esophageal and 111 (11.0%) with gastric from Amran, followed by 102 (10.1%) with esophageal and 168 (16.7%) with gastric from Sana,a and 144 (14.3%) with

esophageal and 117 (11.6%) with gastric from Saada. More details present in table 2.

Distribution of provinces by type of UGIC

The results of the study regarding the distribution of provinces by type of upper gastrointestinal cancer showed that, 88 (8.7%) with Squamous cell carcinoma, 111(11.0%) with Adenocarcinoma and 115 (11.4%) with A-S (Cardia of the stomach) from Amran followed by 58 (5.8%) with Squamous cell carcinoma, 176 (17.5%) with

Adenocarcinoma and 36 (3.6%) with A-S (Cardia of the stomach) from Sana'a, and 47(4.7%) with Squamous cell carcinoma, 117 (11.6%) with Adenocarcinoma and 97 (9.6%) with A-S (Cardia of the stomach) from Saada.

More details present in table 3.

Table 1: Distribution of upper gastrointestinal cancer by provinces

Provinces	Upper Gastrointestinal Cancer	
	F	%
Amran	314	31.2
Sana'a	270	26.8
Saada	261	25.9
Hajja	80	7.9
Taiz	35	3.5
Hadramout	3	0.3
Abian	10	0.9
Aden	12	1.2
Al-bida	10	0.9
Mareeb	6	0.6
Al-Guf	5	0.5
Total	1006	100

Table 2: Distribution of provinces by site of upper gastrointestinal cancer

Provinces	Site				Total	
	Esophageal		Gastric		F	%
	F	%	F	%		
Amran	203	20.2	111	11.0	314	31.2
Sana'a	102	10.1	168	16.7	270	26.8

Saada	144	14.3	117	11.6	261	25.9
Hajja	49	4.9	31	3.1	80	8.0
Taiz	22	2.2	13	1.3	35	3.5
Hadramout	2	0.2	1	0.1	3	0.3
Abian	7	0.7	3	0.3	10	1.0
Aden	7	0.7	5	0.5	12	1.2
Al-bida	6	0.6	4	0.4	10	1.0
Mareeb	5	0.5	1	0.1	6	0.6
Al-Guf	3	0.3	2	0.2	5	0.5
Total	550	54.7	456	45.3	1006	100

Table 3: Distribution of provinces by types of upper gastrointestinal cancer

Provinces	type of cancer						T	
	Squamous cell carcinoma		Adenocarcinoma		A-S (Cardia of the stomach)		Total	
	F	%	F	%	F	%	F	%
Amran	88	8.7	111	11.0	115	11.4	314	31.2
Sana'a	58	5.8	176	17.5	36	3.6	270	26.8
Saada	47	4.7	117	11.6	97	9.6	261	25.9
Hajja	38	3.8	30	3.0	12	1.2	80	8.0
Taiz	16	1.6	13	1.3	6	0.6	35	3.5
Hadramout	2	0.2	1	0.1	0	0.0	3	0.3
Abian	2	.2	3	.3	5	0.5	10	1.0
Aden	4	0.4	5	.5	3	.3	12	1.2
Al-bida	6	0.6	4	0.4	0	0.0	10	1.0
Mareeb	5	0.5	1	0.1	0	0.0	6	0.6
Al-Guf	3	0.3	2	0.2	0	0.0	5	0.5
Total	269	26.7	463	46.0	274	27.2	1006	100

Distribution of sex by site of UGIC

Out of 1006 patient, 523 (52.0%) were male had esophageal cancer and 144 (14.3%) had gastric cancer while 27 (2.7%) were female had esophageal cancer and 312 (31%) had gastric cancer. Table 4. Distribution of sex by type of UGIC

Out of 1006 patient, 259 (25.7%) were male had squamous cell carcinoma, 329 (32.7%) had adenocarcinoma and 79 (7.9%) had A-S (Cardia of the stomach) while 10 (1.0%) were female had squamous cell carcinoma, 134 (13.3%) had adenocarcinoma and 195 (19.4%) had A-S (Cardia of the stomach). Table 5.

Distribution of type of UGI C by Site

Out of 1006 patient had upper gastrointestinal cancer, 268 (26.6%) were esophageal cancer and had squamous cell carcinoma, 276 (27.4%) had adenocarcinoma and 6 (0.6%) had A-S (Cardia of the stomach) while 1 (0.1%) were gastric cancer and had squamous cell carcinoma, 187 (18.6%) had adenocarcinoma and 268 (26.6%) had A-S (Cardia of the stomach). Table 5.

Table 4: Distribution of sex by site of upper gastrointestinal cancer.

Sex	Site of Upper GI Cancer				Total	
	Esophageal		Gastric		Total	
	F	%	F	%		
Male	523	52.0	144	14.3	667	66.3
Female	27	2.7	312	31.0	339	33.7
Total	550	54.7	456	45.3	1006	100

Table 5: Distribution of sex by type of upper gastrointestinal cancer

Type	Sex				Total	
	Male		Female		Total	
	F	%	F	%		
Squamous cell carcinoma	259	25.7	10	1.0	269	26.7
Adenocarcinoma	329	32.7	134	13.3	463	46.0
A-S (Cardia of the stomach)	79	7.9	195	19.4	274	27.2
Total	667	66.3	339	33.7	1006	100

Table 6: Distribution of type of upper gastrointestinal cancer by site

Type of upper GI cancer	Site of Upper GI Cancer				Total	
	Esophageal		Gastric			
	F	%	F	%	F	%
Squamous cell carcinoma	268	26.6	1	0.1	269	26.7
Adenocarcinoma	276	27.4	187	18.6	463	46.0
A-S (Cardia of the stomach)	6	0.6	268	26.6	274	27.2
Total	550	54.7	456	45.3	1006	100

Discussion

To the best of our knowledge, this was the first study which reported the distribution of UGI cancer among different provinces in Yemen. Mortality rates for gastric and oesophageal cancers have been changing dramatically over recent years. Incidence and mortality rates for GC have been declining for more than half a century. By contrast, EC is becoming more common. Tumours at the junction between the stomach and the oesophagus are increasing particularly rapidly. All these cancers are more common among men than women 8.

GC is the third most common malignancy in the world. Defining the exact origin of GC is sometimes difficult especially when the gastro-oesophageal junction is involved. This difficulty often leads to misclassification of cancers, especially those arising from the gastric cardia and the lower esophagus. The incidence of cancer of the gastric cardia and the lower esophagus has shown a rapid change in several areas of the world. This rapid change offers a unique opportunity to study the etiology of these cancers. Many scientists are working on the epidemiologic characteristics of these changes in order to identify the etiologic factors. Thus, the exact determination of the sub site of origin of cancers and their epidemiology is very important.

In total, 550 cases of esophageal cancer (EC) and 456 cases of GC were referred to the endoscopic clinic at AlThowrah hospital, Sana, a City. Assuming that the proportion of UGI

cancer cases referred to the endoscopic clinic was independent of tumour site, we can conclude that EC is approximately slightly higher as common as GC in our study. In addition, almost half of the GC cases occurred in the cardia of the stomach. A predominance of EC cases over GC cases and a large number of GC cases originating in the cardia are common findings in populations at high risk for EC, but are unusual findings for other areas of the world. For example, in Linxian, China, another area with very high rates of EC, the EC: GC ratio is also greater than one but in most areas of the world, the opposite proportions are found 9.

Relative to UGI cancer, EC was significantly more common in Amran, Saada and Sana,a provinces than other. Interestingly these areas are those where shamma and water pipe smoking are known to be widely prevalent.

While gastric cancer was more in Sana,a, Saada and Amran. No data on substance use habits were available, future research could conduct whether these habits are associated more with UGI cancer. The disparity in the relative frequencies of upper GI cancers in different regions could be explained by variations in the environmental and geographical factors.

There are several reports that dietary, behavioral, life style and environmental factors may play a causative role in high-risk populations^{10,11}.

In our study the majority of the patients had upper GI cancers was male 66.7%. The reasons for such differences are not clear. Environmental or occupational exposures may play a role. For example, men have been historically more likely to smoke tobacco products, although elevated rates in men appear to persist even in countries where men and women have similar smoking patterns¹².

Alternatively, sex differences may reflect physiological differences. Estrogens may protect against the development of GC. In women, delayed menopause and increased fertility may lower the risk of GC, whereas antiestrogen drugs, e.g., tamoxifen may increase the rates of GC^{13,14}. These hormones may provide protection against GC during the fertile years of

women but their effect is diminished after menopause, such that females develop GC in a manner similar to males, albeit with a 10-to-15-year lag after their male counterparts 15,16.

In our study EC was significantly more common in male 52% than female 2.7% while GC was significantly more common in female 31% than male 14.3%. However, the male preponderance seen in our result is not consistent with the fact that GC is more common in males as reported repeatedly in the literatures 17,18,19. In the neighboring gulf countries, the incidence of gastric cancer in males was approximately twice that of females. In Oman in 2006, GC was the most common cancer in men and the fourth most common cancer in women 21, and the incidence has shown no apparent decline over the last decade. With improved longevity in Oman [20], the absolute burden of GC may become even greater in the future.

GC is the fourth most common cancer worldwide 22. Its poor prognosis makes it the second most frequent cause of cancer deaths. Incidence data show wide variation between nations 23. High incidence rates are recorded in Eastern Asia, Eastern Europe and South America. Conversely, Australia, North America, Western Europe and the Arab world have lower incidence rates. Oman, in contrast to the neighbouring Gulf Cooperation Council (GCC) countries, is estimated to have higher incidence rates. In Oman, stomach cancer is the most frequent neoplasm among males 21. This problem, although known about, has not been explored.

A study done in Hadramout, Yemen, in 2006, showed that gastric cancer was the second most common type of gastrointestinal cancer after colorectal cancer. It was the sixth most common type of all cancers among men and the ninth among women 8. In Yemeni society, the habit of chewing khat (*Catha edulis*) is highly prevalent among adults of both sexes and most of them start chewing in childhood 24.

Several studies reported that GC incidence rates vary wildly between men and women and across different countries. Rates are 2- to 3-folds higher in men than women 25. Comparing nations, the highest incidence rates are observed in East Asia, East Europe, and South America,

while the lowest rates are observed in North America and most parts of Africa 26. Ecological and nutritional studies conducted by IARC and IPHR to establish the epidemiologic features and to investigate the aetiology of EC throughout the Caspian Littoral including Golestan Province 27 found geographical associations of incidence with a number of variables. A subsequent case-control study investigated these associations further and established some risk factors, especially poverty and a restricted diet very low in fresh fruit and vegetables 28, factors that have since been shown to be associated with an elevated risk for oesophageal cancer in almost all countries where diet has been studied 29, but it found no clear evidence for other potential risk factors such as hot tea or nass consumption. However, the studies in Iran were discontinued due to the sociopolitical changes there in 1979, before the complete patterns of incidence and the full complement of risk factor results could be established.

Adenocarcinoma accounts (32.7%) for the highest number of GC with male preponderance. The large majority approximately (90%) of gastric cancers are adenocarcinomas, which arise from the glands of the most superficial layer, or the mucosa, of the stomach. Therefore, if not specified otherwise, our discussion of gastric cancer (GC) mainly pertains to adenocarcinomas. There are, however, other types of cancer arising from the stomach, including mucosa-associated lymphoid tissue (MALT) lymphomas, which originate from the lymphoid tissue of the stomach, and leiomyosarcomas, which arise from the muscles surrounding the mucosa 30. Similar results was reported by Al-Samawi & Allawi 31. Adenocarcinoma accounts, for the highest number of GC with male preponderance. This study is however, useful in highlighting the distribution of the histological types of GC in Yemen. The cause of the high incidence of GC and EC in our country is unknown. We strongly feel that supported research is needed as well as further environmental and immunohistochemical studies to find out the influence of genetic predisposition and local risk

factors especially insecticides used in Khat agriculture.

Conclusion

We conclude that the largest report from Yemen identifying subsite involvement of upper GI cancers. The present analysis contradicts hospital-based study which reported higher relative frequencies of UGI cancer in all regions of Yemen. 31.2% of the patients were referred from Amran, followed by 26.8% from Sana'a and 25.9% from Saada. 54.7% of the patients' had EC and 43.3% had GC. Adenocarcinoma accounts for 46%. We observed different patterns of sub site involvement in different parts of Yemen. This difference could indicate different etiologies.

Recommendations

The importance of health education and increased awareness about risk factors. Further epidemiologic studies aimed at identifying the probable risk factors are required.

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