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# Clinicopathological Features of Gastric Cancer in a Cohort of Gulf Council Countries' Patients: A Cross Sectional Study of 96 Cases

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## ABSTRACT

**Objective:** This retrospective work aims to report the epidemiologic and clinicopathological features of Gulf Cooperation Council (GCC) patients with Gastric Cancer (GC).

**Patients and Methods:** This retrospective study evaluated patients from GCC countries presenting with GC, treated at the MD Anderson cancer, University of Texas , Houston , Texas from 1981 to 2015. after obtaining an Institutional Review Board approval to conduct this retrospective study the data were collected from the charts of 96 consecutive GCC patients diagnosed with GC electronic and paper medical records (for cases prior to the implementation of the electronic medical records): The charts were reviewed for demographic data, clinical data, diagnostic tools, endoscopic location of the tumour and clinicopathological features of the GC. Statistical analyses were performed by using SPSS version 20. Numerical data were presented as mean +/- standard deviation (SD) (For normally distributed data); median and range (For not normally distributed data). Nominal data were expressed by percentages.

**Results:** 96 patients identified with histologically confirmed gastric carcinoma from the, from KSA (40%) , UAE (26%) , Qatar (16%) Kuwait (10%), Oman (3%) and Bahrain (2%) of cases. They have a median age of 54.5 years and 40 patients (42%) were aged less than 50 years and a sex-ratio of 1.7(male 61%, female 39%). Intestinal type was the most common histological type in 61% of cases, 30% had signet cell histology and 20.1% (6 out of 28 cases tested) had *HER-2* amplification. 76% of the patients presented with stage IV metastatic.

**Conclusion:** GC in patients from GCC countries is diagnosed at a 10 years earlier age than in Western population. Intestinal-type histology is the most common similar to the western population and *HER-2* amplification rate is similar to Western populations. Most of the cases are metastatic.

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## Introduction

GC(GC) is the fifth most common cancer worldwide, and the third leading cause of death from cancer making up 7% of cases and 9% of deaths. GC have a poor prognosis due to the predominance of locally advanced and/or metastatic stages at presentation [1]. GC incidence affect more males than females. It has a geographic variation, with the highest incidences in East Asia (Korea with 65/9) and South America and the lowest in North America like US at 7.8.10000 [2,3]. For Arab countries and specially the Gulf Cooperation Council (GCC) countries, we have few retrospective or registry-based series suggesting an increase of GC cases during the last decade [4,5]. GC cancer is a multifactorial cancer, and demonstrating the important role of Helicobacter pylori infection [6,7]. There is a lack of studies evaluating the clinicopathological features from the GCC countries and the aim of this study is to evaluate the clinicopathological features of patients from this understudied population.

## Patients and methods

This retrospective study evaluated patients from GCC countries presenting a gastric carcinoma, treated at the MD Anderson cancer, University of Texas, Houston, Texas from 1981 to 2015. after obtaining an Institutional Review Board approval to conduct this retrospective study the data were collected from the charts of

96 consecutive GCC patients diagnosed with GCelectronic and paper medical records (for cases prior to the implementation of the electronic medical records): The charts were reviewed for demographic data, clinical data, diagnostic tools, endoscopic location of the tumour and clinicopathological features of the GC of note the electronic records were manually searched to identify patients from Arab countries; whose primary language was Arabic (using demographic data in the electronic medical records) or those who were self-identified as Arabs. These were considered as surrogate proofs of the patients' Arab origin. Statistical analyses were performed by using SPSS version 20. Numerical data were presented as mean +/- standard deviation (SD) (For normally distributed data); median and range (For not normally distributed data). Nominal data were expressed by percentages.

## Results

After excluding 9 cases of lymphoma's, Gastrointestinal stromal tumor or others subtypes of gastric sarcoma, we identified 96 patients with GC , presenting an histologically confirmed gastric adenocarcinoma, They came from KSA (41.6%) , UAE (27%), Qatar (14.6%), Kuwait (9.5%),Oman (4.2%) and Bahrain (3.1%) of cases. Initial symptoms are represented by epigastric pain in 52%, dyspepsia in 67.7 %, weight loss in 72.9%, and melena in 7.3% and the median time from first symptoms to diagnosis was 9.3 months ( 2 to 18 months ). The median age of diagnosis was 54.5 years (26 to 80), 40 patients (42%) were younger than 50 years of age and the sex-ratio was at 1.7 (61% male and 39% female). Diagnosis was performed before the departure to MD Anderson in 90% (86) of cases and in US in 10.4 % (10) of the GC cases. Histology showed the predominance of intestinal type in 61% of cases and 30% had a "signet cell " histology , with 9% indeterminate type, Interestingly the predominance of signet ring type in younger patients 71.4% (30 out of the 40 cases under the age of 50 years ) was observed. On the 28 tested samples, 6 (20.1%) had *HER-2* amplification. 76%(73) were diagnosed with metastatic disease at time of diagnosis (Table 1).

**Table 1. Patients' characteristics**

| | Total number | % |
|---|---|---|
| Mean Age in years | 96 | 100 |
| Sex | | |
| Males | 60 | 61% |
| Females | 36 | 39% |
| Sex-ratio | 1.7 | |
| Geographic origin | | |
| KSA | 40 | 41.6% |
| Emirates | 26 | 27% |
| Qatar | 14 | 14.6% |
| Kuwait | 9 | 9.5% |
| Oman | 4 | 4.2% |
| Bahrain | 3 | 3.1% |
| Histology | | |
| Intestinal type | 59 | 61.5% |
| Signet Ring | 29 | 30.2% |
| Indetermined | 8 | 8.3% |
| Anatomical site of the GC | | |
| Antral | 51 | 53% |
| Body | 24 | 25% |
| Fundus | 9 | 10% |
| Cardia | 12 | 12% |
| Stages | | |
| I-III | 23 | 24% |
| IV | 73 | 76% |

## Discussion

This is the first study reporting the clinicopathological features of GC in patients from the GCC. Previous reports evaluated GC patients in each GCC country separately [5,8,9]. Our retrospective study evaluated 96 patients from GCC origin, treated outside their country, at the MD Anderson cancer center for a gastric carcinoma over a period of 34 years from 1981 to 2015, coming mostly from Saudi Arabia, UAE and Qatar. 57%(55 patients) were treated before the year of 2000, likely due to the lack of adequate structured cancer centers in the GCC region. The clinicopathological features are summarized in (Figure.1).

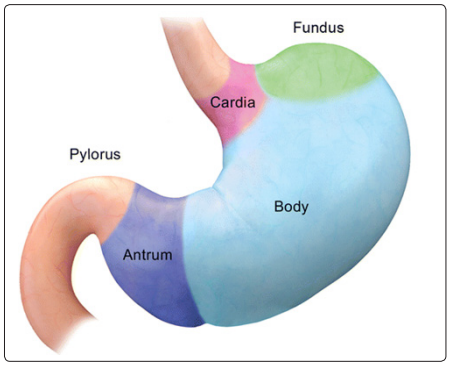


**Figure 1:** The anatomical location of GC in different populations/ studies

The mean age of this cohort of GCC patients was 54.5 years (20 to 80) and 40 patients (42%) were younger than 50 years. This is similar to the KSA study with median age of diagnosis of GC was 57% , but this is in contrast to median age in the US which is 67.4 years as per SEER data from 1973-2014 period [10]. Our cohort is 12.9 years younger than US GC population. This is also in keeping with data from other Arab countries for example a study from Tunisia evaluated 860 GC cases having a median age 59 years and 27% younger than 50 years [6]. The sex ratio was at 1.7 affecting more males, This is similar to the study from Oman with similar ratio of 1.7 and lower than the reported study from KSA of male to female ratio of 2.3 [8,9].

The most common classification of gastric carcinoma is the Lauren's classification, which was established in 1965. It differentiates intestinal and diffuse types of GC, which show distinguishing features like morphology, genetics, clinical characteristics, progression pattern, and epidemiology [11]. In our cohort, the histology classification showed the predominance of intestinal type in 61.5% of cases and 30.2% had a "signet cell " histology, with 8.3% indeterminate GC type. This is in contrast with the KSA study reporting 91.5% of the GC cases with intestinal type [9]. Interestingly the predominance of signet ring type in younger patients 71.4% (30 out of the 40 cases under the age of 50 years ) was observed, This is in keeping with previous reports were the diffuse type is more common in younger population, worst prognosis and the highest recurrence frequency (63%) of the four subtypes Molecular GC subtypes [12].

There are limited data on the *HER-2* rate in the GC patients from the GCC. The only study reported the *HER-2* was the

study mentioned earlier from the KSA and was only done in 9 patients and it was negative in all 9 patients. In our cohort 28 patients were tested and 6 (20.1%) had *HER-2* amplification. This is the first report of *HER-2* amplification rate in GCC patients and this is in keeping with the reported incidence of *HER-2* amplification in advanced GC. Where between 7 and 38 percent of gastroesophageal adenocarcinomas have amplification and/or overexpression of *HER-2*. The frequency of overexpression is slightly greater for cancers of the EGJ as compared with those of the stomach (32 versus 21 percent). Overexpression in the stomach varies according to histologic type (intestinal-type more than diffuse-type gastric cancers; 3 to 23 versus 0 to 6 percent, respectively) and with differentiation (well and moderately differentiated more than poorly differentiated) [13].

The anatomical location of the GC were as follow: Antral 51(53%) Body 24(25%) Fundus 9(10%) Cardia 12(12%), comparison with studies from KSA and Oman are illustrated. Initial symptoms are represented by epigastric pain in 52%, dyspepsia in 67.7 %, weight loss in 72.9%, and melena in 7.3% and the median time from first symptoms to diagnosis was 9.3 months (2 to 18 months). The rate of these symptoms are similar to the previously reported GC symptoms [14]. The duration from symptom initiation to disease diagnosis was similar to previously data were 6–12 months from symptoms to diagnosis in 80% of cases [15]. 76%(73 patients) were diagnosed with metastatic disease at the time of diagnosis. This is higher than the Oman study finding of 56% and the KSA study with 60% presenting with stage IV [8,9].

Of note *H.Pylori* status, *MSI* and *PDL-1* status data were not performed /available in this cohort. As the cohort represent a cohort from 1981 to 2015 were the clinical implication and use of these modalities were not implemented at the time of the study period. The current study has an importance of evaluating the clinicopathological features from the GCC countries which is an understudied population. It highlights important findings with higher younger population with GC in our region, albeit a referral bias could be potential a reason for this finding, were younger patients are more likely to be referred to a tertiary referral center for more aggressive treatment. Of note this finding is in keeping with the increasing incidence of early-onset GC in the United States, comprising >30% of new GC cases today [16].

## Limitations

We acknowledge the limitations of this study being a single-institutional retrospective study. Furthermore, our study is the relatively small sample size, which could potentially limit the generalizability of our findings. There is also a potential selection bias, although all consecutive GCC patients identified as being diagnosed with GC were included in this study.

## Conclusion

GC in the GCC countries is presenting at an earlier age than US population (12.9 years earlier) where 42% were under the age of 50 years old. Intestinal-type histology is the most common and *HER-2* amplification is similar to the US population. This GC continues to present in advanced stages in GCC population. This is the first study to report these findings in GCC population with gastric cancer. Further collaboration and research is needed a cross the GCC countries to better characterise GC in this region and to understand the early onset pattern of GC observed in this report. The relative frequencies are approximately 54% for intestinal type, 32% for the diffuse type, and 15% for the indeterminate type (19) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3418539/pdf/jgo-03-03-251.pdf

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