Trend of Geographical Distribution of Stomach Cancer in Iran From 2004-2014

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Abstract

Background: Among different common types of cancer, Gastric cancer (GC) is a worldwide health priority in both developing and developed countries. The aim of this study was to map the distribution of incident cases of GC in Iran to provide a geographical presentation of the incidence of the disease.

Methods: This study used the Iranian National Cancer Registry (INCR) data from 2004 to 2014. Excel was used to do the primary analysis including calculation of GC incidence for each province and also to provide a frequency table of the type and location of GC by the provinces. ArcGIS 10.5 (Redlands, CA, USA) mapping software was used to map the provincial age-standardized incidence rates by sex. The type and location of the GC cases were obtained from the NCR dataset.

Results: According to the results of the present study, the patients were predominantly male 49,907 (70.0%). During the study period, the highest and lowest age-standardized incidence rates of GC in Iran in 2014 were reported from Ardebil (IR=30.19) and Ghom (IR=1.00) respectively. A significant difference was observed when the distribution of the location of GC tumors was compared between males and females ($P<0.001$).

Conclusions: The results of the current study suggested a lower rate of GC incidence rate was reported in Iran when compared to the global figure in both females and males. The findings suggest involving different factors with different effects in GC among Iranian populations. Further studies are needed to better understand the epidemiology and etiology of the disease.

Background

Cancer is the second leading cause of death worldwide (1). Along with the changes in the social and demographic statuses of the world's population, cancer is becoming a more serious health issue (1). In 2020, 18.1 and 9.5 million new cases and deaths of cancer were Globally reported respectively (2). It is estimated that in 2030, cancer will be responsible for approximately 21.7 million new cases worldwide (2). In this regard, during the last decades, the incidence of cancer has raised 46% in Eastern Mediterranean Region (EMRO) from 495000 cases in 2005 to 723000 cases in 2015 (3). Cancer is responsible for approximately 2.6 million disability-adjusted life years among both men and women in the EMRO region (3). Among different common types of cancer, Gastric cancer (GC) is a worldwide health priority in both developing and developed countries because of its fatal and nonfatal consequences that are rising continually (5, 6). The disease is the fourth most common type of cancer and the second leading cause of death due to cancer in the world. Gastric cancer causes about 10.4% of deaths globally (2). It is estimated that 930,000 new cases of stomach cancer occur in the world and about 700,000 deaths due to GC are reported each year (2). The incidence of the disease is especially high in East Asia, Eastern Europe, and some parts of Central and South America (6). In Iran, possibly due to the recent demographic and epidemiological transitions, the number of incident cases of cancer is rising constantly (4). In Iran, the incidence of stomach cancer is the first cause of death due to cancer (7). Among regions, the north and northeast regions have the highest rates of GC nationally (8). For example, Ardebil (in the northeast of Iran) has the highest incidence rate of GC compared to not only the other counties of Iran but also many parts of the world (2).

With regard to the pathology and clinical aspects of GC, the anatomic appearance of cancer (cardia and non-cardia) and histological type of the disease (enteric and non-enteric) are two important characteristics of GC. These features may come with different etiology, symptoms, and prognosis (9). According to a study, in different parts of Iran (i.e. Khorasan, Lorestan, Tehran, East-Azarbajjan, Sistan&Baluchestan, Kurdistan, Mazandaran, and Khoozestan) distal Gastric tumors are more common than proximal gastric tumors (10). Also, based on a study in Golestan province (a province with endemic incidence of GC) stomach and Esophageal cancers are the first and second most common types of malignancies (11). With regard to the differences between genders in GC with being more common among men, a team of researchers reported that *Helicobacter pylori* infection is also more common in men than women (15). However, Hae Won Kim suggested that Signet ring cell carcinoma (SRC) in GC was more prevalent among younger females than males (12). In addition, the incidence of GC is highly variable in different parts of the world. This phenomenon may represent the potential differences in the etiology of GC around the world. Numerous studies are conducted to identify factors contributing to stomach cancer in different parts of the world and the results came out in favor of a wide range of factors including *H. Pylori* infection, dietary nitrite, physical inactivity, smoking, alcohol, obesity, radiation, and family history (6). As a result, mapping incident cases of GC is a very informative step in better understanding the etiology of the disease. Due to the higher occurrence and seriousness of stomach cancer in Iran, the issue has become of great national health concerns. The aim of this study was to map the distribution of incident cases of GC in Iran to provide a geographical presentation of the incidence of the disease. The study also aimed to identify regions with an unusual higher rate of GC in the country.

Methods

During the last 3 decades, the Iranian National Cancer Registry (INCR) is founded and improved rapidly as a part of the National Health Care System. More information about NCR program in Iran is provided before (8). In summary, all cancer cases are to be confirmed by pathologic diagnosis and then to be registered with the NCR. As with other types of cancers, cases of GC are also pathologically confirmed and registered to the NCR database. This study used the NCR data from 2004 to the latest available data in 2014. The primary aim of the current study was to investigate the geographical distribution of the incidence of stomach cancer during the study period. The study was also conducted to measure the change in the incidence of GC by province ($n = 31$) to see if there is any substantial difference between the provinces in the risk of SC. Also, by studying the geographical distribution of the anatomic locations and morphology of GC, we investigated the potential differences between the provinces in these two important indexes.

Case definition

Diagnosis of the GC cases was confirmed by a positive pathology report issued by a pathologist using a microscopic verification method in each province.

Data source and preparation

The Iranian NCR is under the ministry of health and covers all provinces and all pathology centers in each province. Due to the large number of centers reporting cancer cases in each province, there is a high possibility of errors during data entry. As a result, data is to go under a long and rigorous checking, correction, and cleaning procedures. The procedures take about 5–6 years to make data ready for being published. In the current study, in addition to the routine checking of the NCR data, the dataset was again quality controlled and rechecked for any duplicate cases or errors before being used for analysis. The size of populations of the provinces was obtained from a national census conducted in 2012.

Spatial and statistical data analysis

Excel (2015) was used to do the primary analysis including calculation of GC incidence for each province and also to provide a frequency table of the type and location of GC by the provinces. ArcGIS 10.5 (Redlands, CA, USA) mapping software was used to map the provincial age-standardized incidence rates by sex. The type and location of the GC cases were obtained from the NCR dataset. All plots, GIS maps and figures were designed in GIS center, Department of Epidemiology, Shiraz University of Medical Sciences.

Results

According to the results of the present study, the patients were predominantly male 49,907 (70.0%) and were between 0 to 116 years of age (mean = 65.9, SD = 14.7). The 10-year incidence of stomach cancer by age and sex are presented in Table 1 and supplementary figure S1 & S2. The incidence of GC in Iran is less than the corresponding global and regional rates (15.4×10^5 and 14.1×10^5 respectively) in both men and women (21.7×10^5 and 9.9×10^5 respectively). In addition, although the age-specific incidence rate of GC is rising by age in both genders, GC starts earlier and raises faster in men compared to women.

Table 1
The 10-year incidence of stomach cancer by age, sex

men				women			Total
Age Group	Cases	Population	incidence/ 100,000	cases	Population 2014	incidence/ 100,000	incidence/ 100,000
[0–5)	7	3459169	0.0	0	3274638	0.0	0.0
[5–10)	2	3123814	0.0	1	2971835	0.0	0.0
[10–15)	3	2895688	0.0	0	2773242	0.0	0.0
[15–20)	5	3004634	0.0	8	2902202	0.0	0.0
[20–25)	25	3616279	0.1	19	3571851	0.0	0.1
[25–30)	55	4218536	0.1	35	4151876	0.1	0.1
[30–35)	80	3999442	0.2	69	3927181	0.2	0.2
[35–40)	111	3273844	0.3	110	3158103	0.3	0.3
[40–45)	205	2675355	0.7	134	2583994	0.5	0.6
[45–50)	304	2277422	1.2	171	2222709	0.7	1.0
[50–55)	519	1886531	2.5	223	1870494	1.1	1.8
[55–69)	718	1528642	4.3	304	1546018	1.8	3.0
[60–65)	797	1101117	6.6	404	1164036	3.2	4.9
[65–70)	882	740984	10.8	409	819830	4.5	7.7
[70–75)	919	565960	14.8	394	586293	6.1	10.4
[75–80)	1050	461003	20.7	432	434622	9.0	14.9
[80–85)	842	317822	24.1	339	293916	10.5	17.3
85+	536	220979	22.1	265	209044	11.5	16.8
Total	7060	39367223.6	17.9	3317	38461884.2	8.6	13.3

During the study period, the highest and lowest age-standardized incidence rates of GC in Iran in 2014 were reported from Ardebil (IR = 30.19) and Ghom (IR = 1.00) respectively (Fig. 1). With regard to the rate of change of the GC, in general, the rate of stomach cancer was rising during the study period (5.63 in 2004 to 13.33 in 2014, 136.65% increase). The highest rates of change (from 2004–2014) were also observed from Ardebil (1100% increase) and Ghom (%30 decrease) respectively (Fig. 2).

With regard to the type of tumour, the most prevalent type of tumour was A1 (almost 96.4%) and C3(2.0%). Also, a significant difference was observed between males and females in the distribution of the types of tumour ($P < 0.001$). In addition, a comparison of the distribution of the types of GC in Iran suggested that a significant difference exists between the provinces (Fig. 3, $P < 0.001$). Accordingly, the highest rate of A1 type of cancer was observed in Zanjan, ($n = 1279$, 98.5%) (Fig. 4). Whereas, the highest rate of C3, (the second most common type of cancer among Iranian population) was observed in

Hormozgan (30(6.6%)) (Supplementary Figure S3). With regard to the location of tumor, significant difference was observed between the two genders and location of tumor ($P < 0.001$). Accordingly, in males, cardia and fundus were the most common location of GC tumor whereas in female pylorus was the most common location of tumor in the study population (Supplementary Figure S4).

Again, a significant difference was observed when the distribution of the location of GC tumors was compared between males and females ($P < 0.001$). According to Fig. 4, pylori and cardia are the most common location of cancer among the study population (28.1% and 31.3% respectively). Comparing the location of GC in provinces, Azarbaejan Sharghi and Bushehr had the highest and lowest rates of fundus based GC (Fig. 4 & Supplementary Figure S3). With regard to the tumours located in pylori, Hoemozgan and Azarbaejan Sharghi were the provinces with the highest and lowest figures (Fig. 4 & Supplementary Figure S5).

Discussion

Sex-age-specific incidence rate of GC suggested a clear difference between males and females as GC starts much earlier in men (even during childhood) when compared to women. A traditional explanation for such difference between the two genders is the higher rate of smoking and alcohol use in men compared to women. However, according to the results of the present study, GC in men is more common even in the young ages, a fact that raises a serious concern on the above justification as in late childhood and early adulthood the above risk factors are either not existed yet or have no sufficient time to start the causal chain of actions to cause GC. However, the GC incidence rate started raising sharply in men (compared to women) at about 40 years of age, an expected time for seeing the causal actions of smoking and alcohol and drug use in men. As a result, it seems GC among Iranian population is driven by factors affecting the disease in both childhood and adulthood period of life but with largely different scales.

Since GC is a serious health issue in Iran, determining high risk regions is necessary. According to the results of the geographical analysis, Ardebil had the highest rate of GC incidence and the highest rate in GC. The province also comes with the highest age-standardized incidence rates in both men and women. Previous studies suggested that the high incidence of Esophageal cancer in these provinces (Ardebil and Golestan) could be due to a presumed belt for upper gastrointestinal tract cancers, including stomach and esophagus, which has originated in the Far East or East Asia and crosses the Central Asian countries and the Near East (Iran)(16). It is worth noticing that distribution of Esophageal cancer in Iran is also highly various. The results of the present study also showed that Ghom had the lowest incidence rate of stomach cancer during the study period. Measuring the rate of change during the study period suggest that all provinces in the northern part of the country were among the provinces with the higher rates of incidence of GC but with lower rates of increase in the GC incidence in Iran. The only exception was observed for Ardabil (the province with the highest rate of incidence). The higher incidence rates observed in the northern provinces is in accordance with what was reported by Almasi and Moradzadeh's study (9, 13). However, the observed patterns of change in the incidence rates of GC during the study period (10 years) suggested that (except for Ardabil), the lowest rates of change (raise) in the provinces were observed from the northern and southern parts of the country (the rate of change was even negative for Hormozgan, Kordestan, Zanjan Azarbaijan gharbi, Alborz, Gilan, and Kohkilooei and Boirahmad) suggesting the persistence or gradual improvements in the affecting factors in these regions. Interestingly, except for Ardabil which has the highest rate of increase in GC (followed by Bushehr with the second highest rate of increase) all other provinces in the northern part shown a slide and gradual increase in the incidence of GC. On the other hand, the results suggested that the incidence of GC is rising alarmingly in the central parts of the country, suggesting a steady change in the factors affecting GC in Iran. based on the Pourhoseingholi's study, the highest risk of GC in Iran was reported in the north and south of the country (14).

With regard to the geographical distribution of the type of GC, the results of the present study showed that in Iran, different types of gastric cancer are observed with a wide intra-country variation. For example, the results of the present study showed that the highest and lowest percentage of A1 type of GC was reported from Zanjan and Hormozgan respectively when compared to the other Iranian provinces ($P < 0.001$). This discrepancy is possibly due to differences in the differences in the environment, ethnicity, and living styles in Iran (16).

With regard to the location of GC tumor, the results of our study suggested that cardia is the most common location of GC in Iran. This observation was also reported globally as according to WHO, gastric cardia cancer was responsible for 49.5% (17). The results of the present study also suggested that pylori was the most common location of GC tumor in Iranian men whereas, in females, fundi was more common. The results of a Sought Korean study conducted by Hae Won Kim reported that signet ring cell carcinoma (SRC) in GC was more prevalent in younger females than males (12). Also, our study suggested that the location of GC is more common in cardiac than the other parts of stomach in the northern provinces, whereas pylorus is the more common location of GC in the southern parts of the country. The distribution of the location of GC in men and women is almost similar suggesting the similarity of factors determining the location of cancer in the stomach between the two genders. These findings may suggest differences in the etiology of GC between the two genders in different countries. In that regard, Abdulrazak reported that *Helicobacter pylori* infection is more frequent among men than women (18). The difference between the two genders may also indicate not only hormonal differences but also factors like behavior (e.g. smoking, alcohol, and drug use), environmental, and occupational factors (19). For example, a history of smoking, drug use, and alcohol are more common among men than women. It is reported that a risky lifestyle, especially physical inactivity and obesity, plays an important role in the risk of cardiac gastric cancer (but not non-cardiac) (19). It is also suggested that sturgeon in women may protect them against the progression of gastric cancer (19). Accordingly, delayed menopause and increased fertility may decrease the risk of gastric cancer among females (19). The differences in the regional distribution of some risk factors may explain the observed geographical differences and trends of many types of cancer (16). Norouzinia reported that in different parts of Iran (Khorasan, Lorestan, Tehran, East-Azarbahijan, Sistan&Balochestan, Kurdistan, Mazandaran, and Khozestan) the majority of tumors were distal gastric. They also suggested that many factors such as environmental, lifestyle, and ethnicity in different geographical locations may contribute to the overall incidence and the anatomical location of GC (10). For example, variation in diet and certain cooking methods including broiling of meats, roasting, grilling, baking, sun drying, and curing that increase the risk of GC, highly vary in different regions of Iran (17, 20). Accordingly, the upward change in GC in Ardebil and Nuorten part of Iran could be due to more consumption of smoked fish and meat (21). Low fiber intake is also suggested to be another important factor contributing to GC (22). It is suggested that 50 gr/day intake of allium vegetables would reduce the risk of GC by 23% (22).

Limitations

Cancer registry in Iran is fast improving. However, several important concerns regarding the validity and reliability of the Iranian NCR exist (23). The expected flaws may affect our understanding of the epidemiology of cancer in Iran.

Conclusion

The results of the current study suggested a lower rate of GC incidence rate was reported in Iran when compared to the global figure in both females and males. However, despite the downward trend of stomach cancer globally, our study suggested a significant rise in the incidence of the disease in Iran. The results also suggested significant discrepancies between provinces in incidence rate and also type and location of the tumors. The findings suggest involving different factors with different effects in GC among Iranian populations. Further studies are needed to better understand the epidemiology and etiology of the disease.

Abbreviations

EMRO: Eastern Mediterranean Region; GC: Gastric cancer; INCR: Iranian National Cancer Registry; SRC: Signet ring cell carcinoma.

Declarations

Acknowledgments

Not applicable.

Authors' contributions

All authors contributed to the study conception and design. FM performed data collection and wrote the manuscript. MK wrote the manuscript. MF revised the manuscript. MGG and ZG helped with statistical analysis and prepared the illustrations. ZN edited the manuscript, AA and MA conceived the study and reviewed the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

All relevant data are within the paper and its supporting information files.

There is no separate data set to share.

Ethics approval and consent to participate

Not applicable.

Consent for publication

All the authors agreed this article be published.

Competing interests

The authors declare that they have no competing interests.

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Figures

Figure 1

distribution of ASR of stomach cancer by the province in Iran in 2014 (both genders) (GIS map were designed in GIS center, Department of Epidemiology, Shiraz University of Medical Sciences) Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

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Figure 2

Rate of change in GC incidence from 2004- 2014 by the province in Iran (GIS map were designed in GIS center, Department of Epidemiology, Shiraz University of Medical Sciences) Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

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A1

C3:

Figure 3

M code of gastric cancer by provinces. A) Malignant Epithelial Neoplasm; A1-Adenocarcinoma, A2-Squamous Cell Carcinoma, A3-Others. B) Neuroendocrine Tumors; B1) Well Differentiated Neuroendocrine Tumors, B2) Neuroendocrine Carcinomas. C) Non Epithelial Tumors; C1) GIST, C2) Sarcoma, C3) Lymphoma. D) Metastasis.

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Figure 4

Location of Gastric cancer by province

Figure 4

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Figure 4

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