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Original Article

Trends in the Incidence of Stomach Cancer in Golestan Province, a High-risk Area in Northern Iran, 2004–2016

Fatemeh Ghasemi-Kebria, MSc[1]; Taghi Amiriani, MD[1]; Abdolreza Fazel, MD[2,3]; Mohammad Naimi-Tabiei, MD[2]; Alireza Norouzi, MD[1]; Masoud Khoshnia, MD[1]; Mohammadreza Seyyedmajidi, MD[1]; Abdollah Pooshani, MD[1]; SeyedeFatemeh Mousaviemadi, MD[1]; Houshang Poorkhani, MD[4]; SeyedMehdi Sedaghat, MD[5]; Faezeh Salamat, MSc[1]; Susan Hasanpour-Heidari, MSc[1]; Nastaran Jafari-Delouie, MSc[1]; Masoomeh Gholami, MSc[6]; Shahryar Semnani, MD[3,1]; Gholamreza Roshandel, PhD[1*]; Elisabete Weiderpass, PhD[7†]; Reza Malekzadeh, MD[8*]

[1]Golestan Research Center of Gastroenterology and Hepatology, Golestan University of Medical Sciences, Gorgan, Iran
[2]Cancer Research center, Golestan University of Medical Sciences, Gorgan, Iran
[3]Omid Cancer Research Center, Omid Preventive and Health Promotion Center, Golestan University of Medical Sciences, Gorgan, Iran
[4]Department of Hematology/oncology, Golestan University of Medical Sciences, Gorgan, Iran
[5]Deputy of Public Health, Golestan University of Medical Sciences, Gorgan, Iran
[6]Death registry unit, Deputy of Public Health, Golestan University of Medical Sciences, Gorgan, Iran
[7]International Agency for Research on Cancer, World Health Organization, Lyon, France
[8]Digestive Oncology Research Center, Digestive Diseases Research Institute, Tehran University of Medical Sciences, Tehran, Iran

Abstract

Background: We aimed to present the temporal and geographical trends in the incidence of stomach cancer in the Golestan province, a high-risk area in Northern Iran.

Methods: This study was conducted on stomach cancer cases registered in the Golestan Population-based Cancer Registry (GPCR) during 2004-2016. Age-standardized incidence rates (ASRs) per 100 000 person-years were calculated. The Joinpoint regression analysis was used to calculate the average annual percent changes (AAPC). We also calculated the contribution of population aging, population size and risk to the overall changes in incidence rates.

Results: Overall, 2964 stomach cancer patients were registered. The ASR of stomach cancer was significantly higher in men (26.9) than women (12.2) ($P<0.01$). There was a significant decreasing trend in incidence of stomach cancer in men (AAPC = -1.80, 95% CI: -3.30 to-0.28; $P=0.02$). We found a higher ASR of stomach cancer in the rural (21.4) than urban (18.1) ($P=0.04$) population, as well as a significant decreasing trend in its rates (AAPC = -2.14, 95% CI: -3.10to-1.17; $P<0.01$). The number of new cases of stomach cancer increased by 22.33% (from 215 in 2004 to 263 in 2016), of which 18.1%, 25.1% and -20.9% were due to population size, population aging and risk, respectively. Our findings suggest a higher rate for stomach cancer in eastern areas.

Conclusion: We found high incidence rates as well as temporal and geographical diversities in ASR of stomach cancer in Golestan, Iran. Our results showed an increase in the number of new cases, mainly due to population size and aging. Further studies are warranted to determine the risk factors of this cancer in this high-risk population.

Keywords: Epidemiology, Iran, Stomach cancer

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Introduction

Stomach cancer was the most common cancer in the world less than a century ago.[1] More recent reports have suggested decreasing trends in incidence and mortality rates of this cancer worldwide.[2] Stomach cancer is now the fifth most common malignancy worldwide, after cancers of the lung, breast, colorectum and prostate, with 1 033 701 new cases (5.7% of the total) estimated in 2018.[3] It is the third most common cause of cancer-related death with 782 685 deaths (8.2% of the total) in 2018.[3] There are large differences in the incidence of stomach cancer by country. The highest estimated age standardized incidence rates (ASRs) as well as the highest mortality rates are reported from East Asia.[3] *H. pylori* infection may play an important role in this geographical variation, while other environmental factors should also be mentioned in this context.[4] The ASRs of stomach cancer in the West Asian population are 19.6 and 9.2 in men and women, respectively.[5] The results of cancer registry studies in Iran have shown that stomach cancer is one of the most incident cancer types, in particular

† Where authors are identified as personnel of the International Agency for Research on Cancer / World Health Organization, the authors alone are responsible for the views expressed in this article and they do not necessarily represent the decisions, policy or views of the International Agency for Research on Cancer / World Health Organization.

***Corresponding Author:** Reza Malekzadeh, MD; Professor of Medicine, Digestive Disease Research Institute, Tehran University of Medical Sciences, Tehran, Iran. Tel: +98 21 82415300; Fax: +98 21 82415400; Email: malek@tums.ac.ir. Gholamreza Roshandel, PhD; Golestan Research Center of Gastroenterology and Hepatology, Golestan University of Medical Sciences, Gorgan, Iran. Tel: +98 911 375 7327; Fax: +98 17 32451657; Email: roshandel_md@yahoo.com; roshandel@gums.ac.ir

in northwestern and northern regions of the country.[6] Epidemiological studies have indicated increasing trends in the incidence rates of stomach cancer in Iran.[5-8] The Golestan province, located in northeastern Iran, has been known as a high-risk area for upper GI cancers since the 1970s.[9] Previous reports from the Golestan province suggested that stomach cancer was the most common cancer in men and the third malignancy in women from 2004 to 2008.[10] The aim of this study is to describe the incidence rates as well as the temporal and geographical variations of stomach cancer in the Golestan province during the 13-year period (2004–2016).

Methods

The Golestan province is located in the northeast of Iran, encompassing14 counties, 33 cities and 1051 villages. According to the 2016 National Population and Housing Census by the Center of Statistics of Iran, the Golestan province has a population of about 1 900 000, of whom 50% are men and about 50% live in urban areas.[11] The Golestan Population-based Cancer Registry (GPCR), a voting member of the International Association of Cancer Registries (IACR) since 2007, is a high-quality cancer registry collecting data on cancer patients throughout the province. The protocol and standards of data collection in the GPCR were described previously.[12] Briefly, the GPCR collects data on new incident primary cancers. The sources of GPCR data include health care centers and all public and private diagnostic and therapeutic centers throughout the province.

Data on cancer mortality were also obtained from the Golestan Death Registry unit in the deputy of health of the Golestan University of Medical Sciences. Cancer mortality data were linked to the incidence data to define cases with death certificate only.

The GPCR observes the third edition of the International Classification of Diseases for Oncology (ICD-O-3) for coding tumor characteristics, including topography, morphology, behavior and grade.[13]

For the present study, data on newly diagnosed primary stomach cancers in the Golestan province during 2004-2016 were obtained from the GPCR. CanReg-5, a free software created and published by the International Agency for Research on Cancer (IARC) was used for data entry and analysis.[12,14] ASRs were calculated using the world standard population. We used the 18-group Segi's World standard population to calculate the ASR. Data on the Golestan population (2004-2016) was obtained from the statistics office of the deputy of health of the Golestan University of Medical Sciences (Figure S1). To assess the geographical distribution of stomach cancer in the study population, we calculated the ASR of stomach cancer by major subdivisions (cities) of the Golestan province and presented the results on the map of Golestan. The joinpoint regression analysis was used to assess the temporal trends in incidence rate of stomach cancer. We used the Joinpoint software version 4.6.0.0 for this analysis. Average annual percent change (AAPC) and corresponding 95% confidence intervals (CI) were calculated. We also calculated the contribution of population aging, population size and risk to the changes in the incidence of stomach cancer using a previously described method.[15] *P* values less than 0.05 were considered statistically significant.

Results

Overall, 2,964 new cases of stomach cancer were registered in the GPCR during the study period. Among these, 2,041 (68.9%) were men and 923 (31.1%) were women with a mean (standard deviation) age of 65.3 (13.5) and 62.6 (13.5) years in men and women, respectively. Also, 1418 (47.8%) of patients lived in urban areas (cities) and 1546 (52.2%) lived in rural areas (villages). Table 1 shows the numbers, crude rate, and ASR of stomach cancer by gender, residence area, and calendar years. The age specific rate (per 100 000 person-years) of stomach cancer indicated increasing rates after 40 years of age in both genders and residence areas (Figure 1).

The ASR of stomach cancer was significantly higher in men (26.9) than women (12.2) ($P<<0.01$). The ASR of stomach cancer was estimated at 18.1 and 21.4 in urban and rural areas, respectively ($P=0.04$). Our results suggested significantly decreasing trends in the incidence of stomach cancer in men (AAPC= -1.80, 95% CI: -3.30 to -0.28) ($P=0.02$) during the study period (2004–2016), while the trends were not significant in women (AAPC=-0.18, 95%CI: -1.70 to 1.37) ($P=0.80$).

As shown in Figure 2, there was a significant decreasing trend between 2004 and 2010 (AAPC = -4.36; $P<0.01$), and a plateau during 2010–2016 (AAPC=0.83; *P* value =0.48) in the incidence of stomach cancer in the population of men in Golestan.

Our results suggested a significant decreasing trend in the ASR of stomach cancer in the rural population (AAPC= -2.14; $P<0.01$), while there were no significant time trends in stomach cancer rates in urban areas (AAPC= 0.36; $P=0.46$) (Figure 3).

The results of partitioning analysis are shown in Table 2. It presents the number of incident cases of stomach cancer in 2004 and 2016, overall change (2004–2016) and contributions of population size, population aging and risk by gender and residence area in Golestan, Iran. Overall, our results suggested a 22.33% increase (from 215 in 2004 to 263 in 2016) in the number of new cases of stomach cancer in the Golestan population. Table 2 shows that changes in population structure, including population aging and population size, resulted in a 43.26% increase in the number of new cases of stomach cancer during 2004–2016. The results also suggested that changes in risk factors could result in a 20.93% decrease in the number of stomach cancer cases during the study period.

Table 1. Numbers, Crude and Age Standardized Incidence Rates (ASRs) and 95% Confidence Intervals (CI) of ASRs of Stomach Cancer in Golestan, Iran by Gender, Place of Residence and Year (2004–2016)

		Male				Female			
		Number	Crude Rate	ASR	95% CI of ASR	Number	Crude Rate	ASR	95% CI of ASR
Residence	Total	2041	18.1	26.9	25.7 - 28.2	923	8.2	12.2	11.3– 13.0
	Urban	972	17.0	24.6	23.0 - 26.3	446	7.8	11.5	10.4 –12.6
	Rural	1069	19.3	29.9	28.1 - 31.8	477	8.6	12.9	11.7 –14.1
Year	2004	158	19.8	32.0	26.8 - 37.2	57	7.1	11.4	8.4 – 14.4
	2005	159	19.8	31.4	26.2 - 36.5	69	8.5	13.7	10.4 – 17.1
	2006	158	19.5	30.4	25.4 - 35.3	57	7.0	11.1	8.1 –14.0
	2007	152	18.2	28.8	24.0 - 33.6	71	8.5	13.4	10.2 –16.7
	2008	149	17.7	26.7	22.3 - 31.2	64	7.6	12.1	9.0 –15.2
	2009	151	17.8	26.7	22.2 - 31.1	68	8.0	11.7	8.7 –14.6
	2010	133	15.5	23.5	17.5 - 25.8	73	8.4	12.9	9.8 –16.0
	2011	145	16.4	24.1	20.0 - 28.2	72	8.2	12.2	9.3 –15.1
	2012	161	18.0	27.4	23.0 - 31.9	74	8.3	12.5	9.5 –15.4
	2013	170	18.8	27.4	23.0 - 31.7	63	7.0	9.8	7.2 – 12.3
	2014	171	18.7	25.8	21.8 - 29.8	78	8.5	12.0	9.2 – 14.7
	2015	159	17.2	24.3	20.3 - 28.2	89	9.6	13.2	10.3 –16.0
	2016	175	18.7	26.3	22.2 - 30.3	88	9.4	12.2	9.5 –14.9

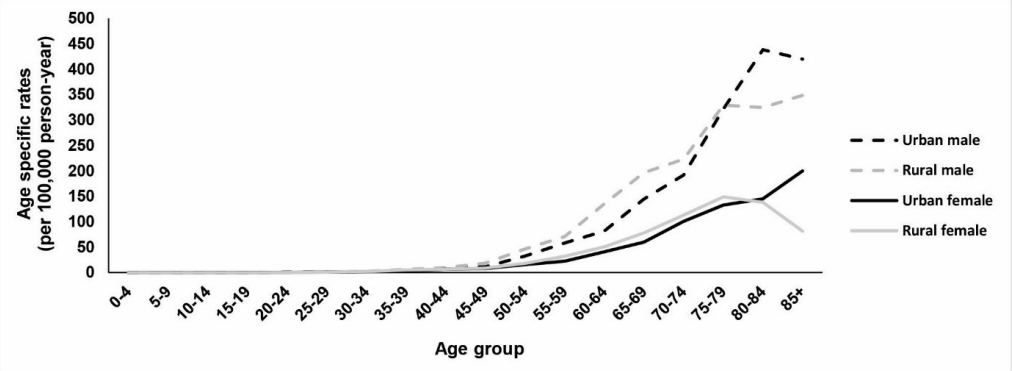

Figure 1. Age Specific Incidence Rates (Per 100 000 Person-Year) of Stomach Cancer in Golestan, Iran by Sex and Residence Area, (2004–2016).

As shown in Figure 4, there were geographical diversities in the ASR of stomach cancer in the subdivisions of the Golestan province. We found higher rates for stomach cancer in eastern parts of the province, especially in Kalaleh city (ASR = 38.9 in men and 15.8 in women) (Figure 4).

Discussion

We presented the 13-year trends in incidence of stomach cancer in high-risk area in the Golestan province, northern Iran. The ASRs of stomach cancer were 26.9 and 12.2 in men and women, respectively. According to the Globocan 2018 estimates, the worldwide ASRs of stomach cancer were 15.7 and 7.0 for men and women, respectively[3]. The Globocan 2018 report also suggested lower ASRs of stomach cancer in West Asian countries (11.3 and 6.0 in men and women, respectively).[3] The results of the IARC Cancer in Five Continents project suggested relatively low rates of stomach cancer in some neighboring countries of Iran including Saudi Arabia (3.5 and 2.1 in men and women, respectively), Kuwait (2.6 and 2.2 in men and women, respectively), and Qatar (6.6 and 4.9 in men and women, respectively) as well as some high rates of this cancer in parts of Turkey including Erzurum and Trabzon.[16] According to the most recent report form the Iranian National Cancer Registry, the ASRs of stomach cancer in Iran were reported at 21.2 and 9.4 in men and women, respectively.[17] There were diversities in incidence rates of stomach in different parts of Iran with lower rates in central and eastern parts Iran and higher rates in northern and northwestern areas including the Golestan province.[17,18] Previous reports from the Golestan province also suggested high rates of stomach cancer in this area.[9,10,19] Therefore, these findings confirm that the Golestan province is a high-risk area for stomach cancer.

The high prevalence of *Helicobacter pylori* infection in the Golestan province,[20,21] a class I risk factor for gastric

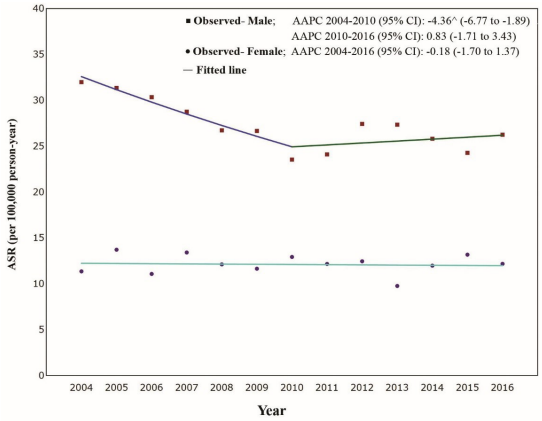

Figure 2. Temporal Variations in Age Standardized Incidence Rates (ASRs) of Stomach Cancer in Golestan, Iran, by Gender (2004–2016). AAPC, Average annual percent change; CI, confidence interval. ^indicates that AAPC is significantly different from zero at alpha = 0.05 level.

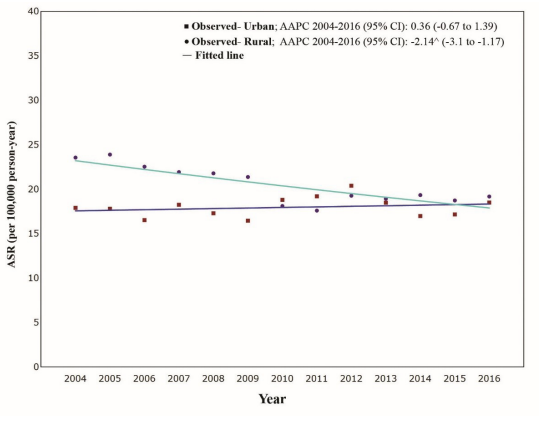

Figure 3. Temporal Variations in Age Standardized Incidence Rates (ASRs) of Stomach Cancer in Golestan, Iran, by Residence Area (2004–2016). AAPC, Average annual percent change; CI, confidence interval. ^indicates that AAPC is significantly different from zero at alpha = 0.05 level.

cancer,[22] may be considered as a potential explanation for the high rates of stomach cancer in this area. In populations where the rates of *H. pylori* infection remain high, stomach cancer remains a major health problem even with implementation of other interventions.[2,23] Low consumption of fruit and vegetable,[24,25] tobacco smoking,[4,26] high consumption of salt[27-29] and opium consumption[30-32] were proposed as other risk factors for stomach cancer. The results from a large-scale cohort study[33] suggested the high prevalence of these risk factors and their relationship with esophageal cancer in Golestan, Iran.[34,35] Therefore, these risk factors may partly explain the high incidence of stomach cancer in this high-risk population. Further studies are warranted to clarify the issue in this area.

In the present study, stomach cancer was significantly higher in men and there was a peak in age-specific rates after the age of 40 years, which may be partly explained by the higher prevalence of known risk factors in men in the Golestan province, including alcohol consumption and cigarette smoking.[35] These finding are in line with previous reports, suggesting gender and age as risk factors for stomach cancer.[36,37] These factors should be considered in designing cancer control programs for stomach cancer.

Our findings also suggested higher rates of stomach cancer in rural areas (mostly villages). Similar disparities were reported in incidence rates of esophageal cancer in this population.[38] A number of known risk factors of esophageal cancer in Golestan, including low socioeconomic, opium and tobacco consumption, poor oral health, drinking un-piped water and exposure to polycyclic aromatic hydrocarbons[39-44] are likely more prevalent in the rural (village) population, although studies are scarce.[45] Most of these risk factors are common risk factors for both esophageal and gastric cancers. Further studies are needed to clarify this point and it should be mentioned by health policy makers.

Table 2 shows that changes in risk factors contributed to a 20.93% decrease in the number of new cases of stomach cancer in 2016 compared to 2004. The results of joinpoint regression analysis also suggested significant decreasing trends in the incidence rates of stomach cancer in men and the rural population. These changes may be partly explained by the reduction in the prevalence of some risk factors (e.g. low socioeconomic status). This risk lowering due to improved socioeconomic status may reflect reduced *H. pylori* infection rates,[46] especially in areas with high rates of *H. pylori* infection such as the Golestan province.[20,21] This point should be further investigated in future studies.

Our findings also showed a plateau of decreasing trend in incidence of stomach cancer in men of the province after the year 2010. Similar findings have been previously

Table 2. Contribution of Population Aging and Population Size and Risk to Observed Changes in the Incidence of Stomach Cancer in Golestan, Iran, 2004–2016, by Place of Residence and Gender

Subgroups		Number of Cases in 2004	Number of Cases in 2016	Overall Change, 2004-2016 (%)	Change Due to		
					Population Size (%)	Population Aging (%)	Risk (%)
Total population		215	263	22.33	18.14	25.12	-20.93
Sex	Male	158	175	10.76	16.46	23.42	-29.11
	Female	57	88	54.39	22.81	26.32	5.26
Residence	Urban	88	137	55.68	37.50	29.55	-11.36
	Rural	127	126	-0.79	4.72	16.54	-22.05

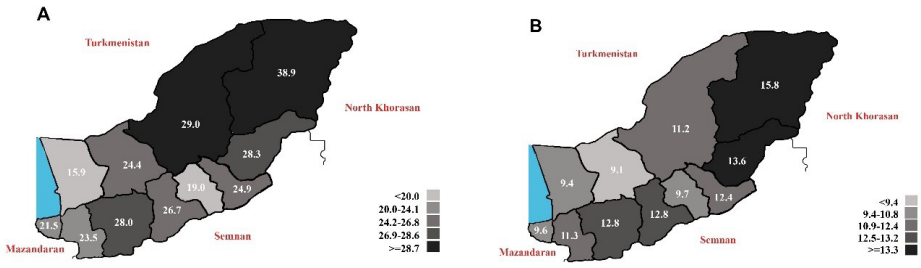

Figure 4. Geographical Distribution of Age Standardized Incidence Rates (ASRs) (Per 100 000 Person-Year) of stomach cancer in Golestan, Iran, 2004–2016. A, Male; B, Female.

reported.[47,48] Our results also suggested a slight increasing trend in the rates in the urban population. Life style changes toward Westernized habits (e.g. fast food consumption, low physical activities) may be proposed to partly explain these trends.

Other factors, such as interventions, or changes in the data quality from the GPCR, may have also affected these trends. There were, however, no marked changes in GPCR protocols (sources, methods of data collection, definitions, and rules) since its start in 2004,[49] while no population-level cancer screening programs have been implemented in our population. Change in access to diagnostic and therapeutic services may, however, be in part responsible for the trends in the incidence rates of stomach cancer. Although there was no considerable change in the number of main sources used by the GPCR (pathology centers and hospitals) during the study period, the availability of other diagnostic services (e.g. imaging centers) as well as physicians (specialists and subspecialists), especially in the private sector, increased from 2004 to 2016.

Despite the decreasing trends in the ASR, there was a 22.33% increase in the number of new cases of stomach cancer during the study period, mainly due to changes in the population structure (population aging and population size). These findings may suggest an increasing trend in the burden of stomach cancer in the Golestan population. This point should be taken into account in future studies and should be considered as top priority and appropriate interventions should be designed and implemented for this cancer in this high-risk area.

We found geographical diversities in the incidence rates of stomach cancer with the highest rates in eastern parts of the Golestan province, especially Kalaleh city. These geographical patterns almost match those of esophageal cancer, suggesting (at least some) common risk factors for these two cancers in the Golestan province. Further investigations are needed to clarify this matter.

As in other population-based cancer registries, lack of data on risk factors was the major limitation of this study. Therefore, we could not provide appropriate interpretations for differences and trends in the incidence rates of stomach cancer in our population. This point should be addressed in future studies (e.g. case-control or cohort studies) to identify the most important risk factors of stomach cancer in Golestan, Iran.

In conclusion, our results emphasized the high incidence rates of stomach cancer in the Golestan province. We found higher rates of stomach cancer in men and the rural population. Our findings also suggested temporal and geographical diversities in the incidence rates of stomach cancer in this high-risk population. There were significant decreasing trends in the ASRs of stomach cancer in men (during 2004 to 2010) and the rural population (during 2004 to 2016). The incidence rates of stomach cancer were considerably higher in eastern parts of Golestan, especially Kalaleh city, which had been well known as high-risk regions for esophageal cancer. Stomach cancer should be addressed by local health policy makers as top priority in our population. Further studies are warranted to determine risk factors related to these trends and diversities.

Authors' Contribution

FGK: collaborated in data processing; collaborated in analysis; wrote the manuscript; AF, MNT, SS: initiated, conceptualized and designed the study; edited and critically reviewed manuscript; AN, FME, HP: collaborated in collection of data; critically reviewed manuscript; SMS, MG: interpreted results; critically reviewed manuscript; NJD, FS: edited and critically reviewed manuscript; collaborated in quality control; EW: edited and critically reviewed manuscript; collaborated in quality control; GR: performed statistical analysis; wrote the manuscript; All authors read and approved the final manuscript.

Conflict of Interest Disclosures

Authors have no conflict of interest to declare.

Ethical Statement

This study was approved by ethics commiittee of Golestan University of Medical Sciences.

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Supplementary Materials

Supplementary file 1 contains Figure S1.

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