ORIGINAL ARTICLE

Trend of gastric cancer in a province in Western Iran: A population-based study during 2001–2014

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Background: There are no studies on the trend of gastric cancer (GC) incidence in Kurdistan, a province in the west of Iran. We aimed to estimate the trend, age-standardized incidence rate (ASR), and annual percentage change (APC) of GC in this province during 2001–2014. **Materials and Methods:** The data of newly diagnosed GC patients were obtained from the regional Cancer Registering Database. The ASRs were calculated per 100,000 population during 2001–2014. Direct standardization and 95% confidence intervals (CI) were calculated by an efficient method. The temporary changes in ASRs were determined based on the APC by the joinpoint regression model. **Results:** Overall, 2225 newly diagnosed GC patients were identified. The ASRs ranged from 13.5 (95% CI: 10.4–17.3) to 29.0 (95% CI: 24.5–34.0). The highest ASRs were related to the men and women lived in Divandareh as 32.26 and 13.66, respectively. The respective APC value of GC incidence in women demonstrated a nonsignificant increase during 2001–2008 and a nonsignificant decrease during 2008–2014 (P = 0.1). Accordingly, the incidence of GC in men increased during 2001–2004 (P = 0.1) and decreased during 2004–2014 (P = 0.001). **Conclusion:** The incidence of GC showed nonsignificant and significant decreasing trends in women and men in Kurdistan province, respectively. Despite such decreasing trends, the Kurdistan province is still considered as one of the regions with high incidence of GC in Iran. Therefore, it is necessary to implement screening programs in the province to early diagnose GC.

Key words: Incidence, Iran, joinpoint, Kurdistan, stomach neoplasms, trends

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INTRODUCTION

Gastric cancer (GC) is a multifactorial neoplasm; its development is affected by both environmental and genetic determinants.[1] GC constitutes the fifth common neoplasm following lung, breast, colorectal, and prostate cancers and the third most common cause of cancer-related mortality worldwide.[2,3] In Southeast Asia, GC constitutes the most common etiology of cancer.[1] In 2015, around 1.3 million new GC cases had been diagnosed worldwide leaving behind 819,000 deaths.[4] GC has also caused 17.4 million disabilities as 98% of them contributed as the lost years of life, delivering the highest ratio among all cancers.[4]

More than 70% of GC new cases are diagnosed in developing countries.[2] The incidence of GC in Iran has been higher than other countries in the west of Asia. This higher rate has been attributed to factors such as obesity, genetic determinants, nutritional habits, and lifestyle.[5-8] A relationship has also been suggested between air pollution and GC development in men.[9] Nevertheless, the disability-adjusted life years trend of GC in Iran showed a 38% decrease from 1990 to 2010.[10]

There are some studies on the trend of GC incidence in Iran and the world. However, to establish preventive measures and policies, there is a need for performing the trend analyses in local level. This is important as the risk factors of GC may vary in different regions of a country.

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According to the annual reporting of Ministry of Health of Iran, the incidence of GC was high in this province, and this province was identified as one of the high-risk provinces of Iran. In addition, lifestyle factors of Iranian population were changed during decades, including nutrition factors related to the GC. Therefore, there was a need to know the pattern of change of GC in parallel with the mentioned changes. On the other hand, in other regions of Iran, the traditional methods were applied to investigate the trend of cancer, but in this study, we were applied a new approach to estimate the trend of GC.

As there were no studies on the incidence rate and trend of GC in Kurdistan, a western province of Iran, here, we aimed to estimate the trend, age-standardized incidence rate (ASR), and annual percentage change (APC) of GC incidence using the archives of the regional Cancer Registering Database from 2001 to 2014. For this purpose, we applied joinpoint regression statistical software which is used to develop simple joinpoint models for cancer incidence trend.

MATERIALS AND METHODS

Study population

Kurdistan is a province located in the western region of Iran and constitutes eight counties. The majority of the residents of this province are farmers and ranchers. In the national census in 2016, the overall population of this province was estimated as 1,600,000 with 71% of them lived in urban areas.

In this study, all the patients newly diagnosed with GC (the International Classification of Diseases 10 code of 16) during 2001–2014 were included. In our province, local pathology clinics, laboratories, and hospitals regularly report that all the new cases of cancer are to a regional cancer registry center affiliated with the Health Deputy of Kurdistan University of Medical Sciences.[11] In the case of migration of patients to other regions for diagnosis, follow–up, and treatment, these cases are still monitored by or regional cancer registry center.

After gathering the intended information, the duplicates were identified (based on comparing information such as national code, first and last names, sex, age, and address) and removed by independently reviewing the records by two of the authors (RM and AN). Finally, 2229 unique cases of GC were identified from whom four patients with unknown age were excluded from the final analysis.

The characteristics of local population that used for calculating of intended incidence rates were interpolated from the population data provided by the Iranian Health Ministry.[12] These indices included the annual birth and death rates by individual gender and age groups.

We also recorded the age, year of diagnosis, as well as patient's gender. The age spectrum of 30–80-year-old was divided into 10-year intervals including <30, 30–39, 40–49, 50–59, 60–69, 70–79, and >80-year-old categories.

Statistical analysis

The ASRs were calculated per 100,000 population from 2001 to 2014. The impact of age on the incidence rate was adjusted using the direct standardization method. In this method, 95% confidence intervals (CIs) are calculated applying the efficient method introduced by Consonni *et al*.[13] The impact of age was further adjusted based on the standard world's population.[14] The ASR is a weighted average of the age-specific incidence rates per 100,000 population, where the weights are the proportions of persons in the corresponding age groups of the standard world's population.[13] ASR with direct standardization method is obtained as weighted averages of the stratum-specific rates r_j for the k groups, taking the weights (person-years Y_j) from standard world's population:[13]

$$\text{ASR} = \frac{\sum_{jk} Y_j r_{jk}}{\sum_{j} Y_j}$$

The results were separately presented for women and men among studied years. The estimated annual population size of each gender and age group was estimated based on the birth and death reports[12] and used to calculate the annual incidence rates.

To detect significant trends in GC incidence, the ASRs were determined based on the respective APCs and 95% CI applying the joinpoint regression model. The software takes trend of GC data and fits the simplest joinpoint model that the data allow. The user supplies the minimum and maximum number of joinpoints. The program starts with the minimum number of joinpoint (e.g., 0 joinpoint, which is a straight line) and tests whether more joinpoints are statistically significant and must be added to the model (up to that maximum number). This enables the user to test that an apparent change in trend is statistically significant by the use of Monte Carlo Permutation method. The models incorporate estimated variation for each point or use a Poisson model of variation. In addition, the software allows viewing one graph for each joinpoint model.[15,16] The Bayesian information criterion approach was recruited to determine the optimal number of joinpoints. The "joinpoint" concept refers to the point in which multiple regression lines are met.[15,17] The analyses were performed in STATA 12.0 (StataCorp., 2011, Stata Statistical Software: Release 12, College Station, TX, USA: StataCorp LP.) and joinpoint regression 4.7.0.0 (Joinpoint Regression Program, version 4.7.0.0, February 2019; Statistical Methodology and Applications

Branch, Surveillance Research Program, National Cancer Institute) software.

RESULTS

Descriptive analysis

Overall, 2225 newly diagnosed GC cases were identified within 2001–2014 in Kurdistan province. From these, 580 (26%) and 1645 (74%) were women and men, respectively. The highest incident cases were observed in 2008, in which 72 women and 160 men were diagnosed with GC. The highest frequency of GC was related to the women (31%) and men (33%) of 70–79 years old.

Age-standardized incidence rate estimation based on the world's standard population

The highest ASRs per 100,000 population were observed in men (32.26, 95% CI: 27.03–38.16) and women (13.66, 95% CI: 10.14–17.95) who lived in Divandareh, a county located in the north of the province. On the other hand, the lowest ASRs were observed in women (2.75, 95% CI: 1.63–4.34) who lived in Bijar and men (9.71, 95% CI: 7.06–12.92) resided in Baneh.

The range of ASRs per 100,000 population of women was 5.4 (95% CI: 3.4–8.2) in 2002 and 14.3 (95% CI: 11.1–18.0) in 2008. On the other hand, the ASR ranged from 13.5 (95% CI: 10.4–17.3) in 2002 to 29.0 (95% CI: 24.5–34.0) in 2008 per 100,000 population of men. The pooled ASRs per 100,000 general population also ranged from 9.7 (95% CI: 7.8–12.0) in 2002 to 21.8 (95% CI: 19.0–24.9) in 2008.

From 2001 to 2014, the annual ASRs per 100,000 women, men, and general population were 8.18 (95% CI: 7.51–8.89), 21.59 (95% CI: 20.52–22.71), and 15.09 (95% CI: 14.44–15.74), respectively [Table 1].

The age-standardized incidence rate trends

The joinpoint regression analysis [Table 2 and Figure 1] demonstrated that ASR in women established two trends, first insignificantly increased 8.2% (95% CI: −1.1–18.4, P = 0.1) from 2001 to 2008 and second insignificantly decreased 8.3% (95% CI: −16.3–0.6) from 2008 to 2014.

Similar changes were also observed in the ASRs in men diagnosed with GC during 2001–2014. In this regard, two trends also established for ASRs in men that they are nonsignificantly increased 30.0 (95% CI: −2.8–73.7, P = 0.1) during 2001–2004 and significantly decreased 3.7% (95% CI: −0.3–2.4, P = 0.001) during 2004–2014. The pooled ASRs in general population insignificantly increased 19.0% (95% CI: −1.6–43.9, P = 0.1) from 2001 to 2005 and significantly decreased 5.0% (95% CI: −9.3,–0.5) from 2005 to 2014.

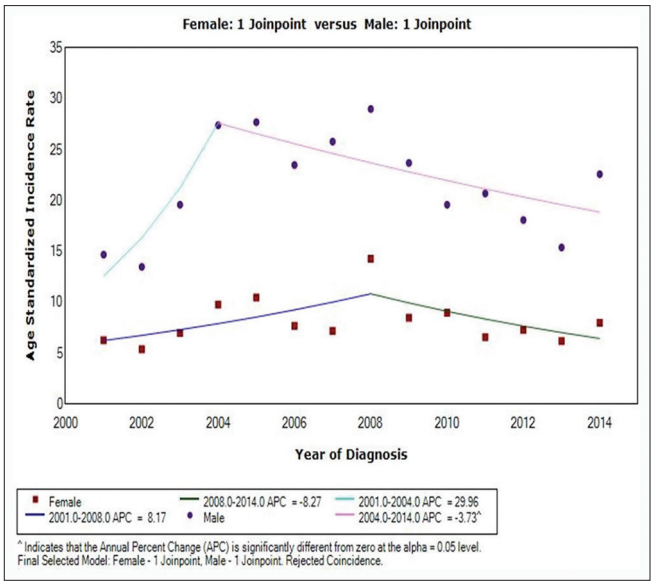

Figure 1: Trends of gastric cancer according to age-standardized rates per 100,000 population in women, men, and general population in Kurdistan, Iran, from 2001 to 2014. APC: Annual percentage change

DISCUSSION

The results of the present study indicated that the ASR of GC was markedly higher in men than women resided in Kurdistan province. The Divandareh country represented the highest ASR compared with other regions of the province.

Despite the increases in ASRs of GC in men (2001–2004) and women (2001–2008), these changes were not statistically significant. Furthermore, the decreasing trend of ASR observed in women during 2008–2014 was not statistically significant. Nevertheless, a statistically significant decrease was observed in ASR of GC in men from 2004 to 2014. Despite the overall decreasing trends of ASRs during 2001–2014, the incidence rate of GC in Kurdistan province remained notably higher in comparison with studies conducted in other regions of Iran. In a study in Yazd province in the center of Iran during 2005–2009, the ASRs of GC per 100,000 population were reported 4.8 and 9.4 in women and men, respectively,[18] which were considerably lower than the rates obtained in our study. In another study on the incidence and mortality rates of cancers in Western Asian countries in 2012, the ASRs of GC per 100,000 population were reported as 16.5 and 9.2 in Iranian men and women, respectively. Among three Iranian provinces with local cancer registries (i.e., Golestan, Ardbil, and Kerman provinces), the pooled ASRs of GC per 100,000 population have been recorded as 20.6 and 9.7 in men and women, respectively. In comparison with the above-mentioned rates,[19] our results rendered higher ASR in men and lower ASR in women.

Table 1: Age-standardized annual incidence rates of gastric cancer per 100,000 population by gender in Kurdistan Province, Iran, during 2001-2014

Year	Total			Women			Men		
	Incid[a]	*n*[b]	ASIR (95% CI)	Incid[a]	*n*[b]	ASIRc (95% CI)	Incid[a]	*n*[b]	ASIR (95% CI)
2001	95	1,393,260	10.7 (8.6-13.0)	27	685,827	6.3 (4.1-9.2)	68	707,433	14.7 (11.4-18.6)
2002	87	1,393,260	9.7 (7.8-12.0)	23	685,827	5.4 (3.4-8.2)	64	707,433	13.5 (10.4-17.3)
2003	124	1,393,260	13.7 (11.3-16.3)	29	685,827	7.0 (4.7-10.0)	95	707,433	19.6 (15.8-24.0)
2004	170	1,393,260	19.2 (16.4-22.3)	41	685,827	9.8 (7.0-13.3)	129	707,433	27.4 (22.8-32.6)
2005	176	1,393,260	19.6 (16.8-22.8)	43	685,827	10.5 (7.5-14.1)	133	707,433	27.7 (23.1-32.9)
2006	172	1,440,149	16.0 (13.6-18.6)	38	710,442	7.7 (5.4-10.6)	134	729,707	23.5 (19.5-27.9)
2007	181	1,449,308	16.9 (14.4-19.6)	38	716,384	7.2 (5.1-9.9)	143	732,924	25.8 (21.6-30.6)
2008	232	1,459,589	21.8 (19.0-24.9)	72	722,826	14.3 (11.1-18.0)	160	736,763	29.0 (24.5-34.0)
2009	178	1,470,912	16.3 (13.9-18.9)	46	729,738	8.5 (6.2-11.4)	132	741,174	23.7 (19.7-28.3)
2010	161	1,483,194	14.5 (12.3-17.0)	48	737,085	9.0 (6.6-12.0)	113	746,109	19.6 (16.1-23.7)
2011	147	1,496,357	13.6 (11.5-16.0)	37	744,825	6.6 (4.7-9.2)	110	751,532	20.7 (16.9-25.1)
2012	166	1,503,000	12.8 (10.9-14.9)	45	749,000	7.3 (5.3-9.7)	121	754,000	18.1 (14.9-21.7)
2013	138	1,514,000	10.8 (9.1-12.8)	39	754,000	6.2 (4.4-8.5)	99	760,000	15.4 (12.5-18.9)
2014	198	1,523,000	15.2 (13.1-17.5)	54	762,000	8.0 (6.0-10.5)	144	761,000	22.6 (19.0-26.7)
All of year	2225	1,454,449	15.1 (14.4-15.7)	580	719,605	8.18 (7.51-8.89)	1645	734,844	21.59 (20.52-22.71)

[a]Incidence number, [b]Total number of population, ASIR=Age-standardized annual incidence rate per 100,000 population; CI=Confidence interval

Table 2: Annual percentage changes based on the joinpoint regression model

Sex	Trend 1		*P*	Trend 2		*P*
	Years	APC (95% CI)		Years	APC (95% CI)	
Women	2001-2008	8.2 (−1.1-18.4)	0.1	2008-2014	−8.3 (−16.3-0.6)	0.1
Men	2001-2004	30.0 (−2.8-73.7)	0.1	2004-2014	−3.7 (−7.1-−0.3)	0.001
Women and men	2001-2005	19.0 (−1.6-43.9)	0.1	2005-2014	−5.0 (−9.3-−0.5)	0.001

Two trends were found for changes of ASRs gastric cancer in Kurdistan province, Iran, from 2001 to 2014. ASRs=Age-standardized incidence rates; CI=Confidence interval; APC=Annual percentage change

In a report on the data of 25 years from 1990 to 2015 in developing countries, the age-standardized mortality rate of GC has been reported as 20.5/100,000 of Iranian population,[20] rendering a relatively low incidence to mortality ratio that emphasized on a high incidence rate of GC.[21] In another study in Guilan province of Iran from 2003 to 2011, the highest ASR of GC was reported as 15.38 in 2011,[22] which was lower compared with the value obtained in the present study. The ASRs of GC have been reported as 7.69 and 23.07 in women and men, respectively, in East Azarbaijan province in north-west of Iran during 2007–2011,[23] which were slightly higher in men and lower in women in comparison with the values reported in our study. In Khuzestan, a province in the southwest of Iran, the ASR of GC in men was reported as 13.8 from 2004 to 2008,[24] which was considerably lower respective to the value reported in the present study. In another study in Iran, the ASRs of GC per 100,000 population were described as 17.96 (in men) and 8.73 (in women) in Shahrud, a city in the north-east of Iran, from 2001 to 2010,[25] which were again lower than our values. In the central province of Qom, the reported APC of 8.08 for all cancers in women showed a significantly increasing trend from 2004 to 2008.[26] In Kermanshah, the southern neighbor province to Kurdistan, ASR of GC per 100,000 population was recorded as 9.2 during 1993–2007, showing a notably lower value than the one observed in the present study.[27] The estimations revealed an annual decrease of 0.28 in the incidence of GC in Kermanshah province.[27] In addition, the trend of noncardial GC rendered an annual decrease of 3.5% in a study performed in the Netherlands during 1973–2011.[17]

ASIRs of GC in men and women were the highest in 2008. Probable reason for this issue may be more accurate registration of cancer cases by the local registry center or due to true increasing incidence in GC.

There have been no studies divulging the risk factors of GC in Kurdistan province. Nevertheless, and based on the studies performed in other regions of Iran, the possible GC risk factors include excessive salt consumption,[28] consuming red-meat rich diets,[28] smoking,[29] obesity,[4] H*elicobacter pylori*-contaminated water,[30] tooth implanting at younger ages,[31] excessive use of nonsteroidal anti-inflammatory drugs,[1] and alcohol abuse.[28,32] In a study in Sanandaj city, the capital of Kurdistan province, the prevalence of *H. pylori* infection was reported as 64.2% in children aged 4 months–15 years old.[33] In a study by Yazdanpanah *et al*. in 2006, the prevalence of *H. pylori* in Kurdistan general population was estimated as 36.5%, rendering a considerably lower ratio than other regions of Iran.[34] Regarding the high incidence of GC and relatively low

prevalence of *H. pylori* in our province, the possible roles of other important contributing factors should be considered in the elevated risk of GC in Kurdistan. Furthermore, the relatively high exposition to the above-mentioned risk factors may in part explain the higher occurrence of GC in men respective to women. From reasons underlying the decreasing trend observed in the incidence of GC in Kurdistan province, which was in parallel to the decreasing trend reported in the other regions of Iran and other countries, may be improved general health status as well as more accessibility to healthy foods during recent years.[5,7] In a study by Balakrishnan *et al*., improvements in food production and preservation methods, as well as decline in *H. pylori* infection, have been noted to participate in the lower incidence of GC. On the other hand, smoking is still a preventable risk factor of GC.[35]

There are some limitations in the present study. First, the quality assessment of cancer registration centers has not been validated in Iran and Kurdistan province as well.[5,36] This fact escalates the risk of misclassification bias due to errors in recording patients' data in the registry databases.[6-8,37,38] Furthermore, a number of patients in our province might have referred to the neighbor provinces such as Hamedan and Zanjan or to Tehran, the capital, which benefit from more sophisticated diagnostic and therapeutic modalities. These patients might not be reported to the cancer registry center of Kurdiastan province, leading to underreporting of GC cases.[6,7,36]

It is advisable to conduct case–control studies addressing the etiological factors contributing to the risk of GC in Kurdistan province.[7] Furthermore, it is recommended to assess the quality of patient registration and data recording processes in local cancer registries across Iran. It is also suggested to reevaluate the data provided here, considering the cohort and age effects.

CONCLUSION

The incidence of GC showed nonsignificant and significant decreasing trends in women and men in Kurdistan province, respectively. Despite such decreasing trends, the Kurdistan province is still considered as one of the regions with high incidence of GC in Iran. Therefore, it is necessary to implement screening programs in the province to early diagnose GC.

Acknowledgments

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Conflicts of interest

There are no conflicts of interest.

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