Incidence Trends of Gastric Cancer in Southern Iran: Adenocarcinoma and Non-Cardia Gastric Cancer Are More Rising Among Younger Ages

Mahanaz Hosseini-Bensenjan
Shiraz University of Medical Sciences
Hossein Molavi Vardanjani
Shiraz University of Medical Sciences
Zahra Khosravizadegan
Shiraz University of Medical Sciences
Kamran Bagheri-Lankarani (m.hosseyni42@gmail.com)
Shiraz University of Medical Sciences Medical School

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Abstract

Background

Gastric cancer (GC) is still one of the major causes of cancer mortality. Due to health-related transitions, the epidemiology of GC subtypesmaybe changed. These changes may have profound effects on the clinical approaches, and public health management of GC. Iran, as a developing country, has experienced huge demographic and epidemiological transitions during recent decades. We aimed to investigate subtype-specific population-based incidence trends of GC in southern Iran.

Methods

We used data on GC incidence in southern Iran for 2001–2015. Data preparation and subtype grouping were done based on the ICD-O-3. Trends of age-standardized incidence rate (ASR), truncated ASRs, the incidence rate of early-onset, adenocarcinoma, and cardia GC, and age-gender specific rates were analyzed applying joinpoint regression modeling. Annual percentage change (APC) and its 95%confidence intervals (CI) were estimated.

Results

Overall APC was estimated at 7.2 for males and 8.7 for females. Estimated APCs for trends of overall GC, and gastric adenocarcinoma were stable for both genders during 2009 to 2015, while the trends of cardia GC were increasing for both genders. Estimated APCs for trends of non-cardia GC wasalso stable.

Conclusion

Overall trends of incidence of GC in southern Iran have been stable for the last decade. However, significant and different changes in the pattern of GC have occurred.Etiological and prognostic studies are needed in Iran for improvement of the GC management.

Introduction

Gastric cancer (GC) is still one of the major causes of cancer mortality while its incidence trend has been decreasing over the past decades.(1, 2)Despite the decreasing trend of the incidence of GC, decomposing this trend has provided valuable information.(3) As it has been shown that the trends of incidence of cardia and non-cardia GC have different patterns across the globe.(4, 5)There is also evidence regarding a morphological transition in GC. The trend of incidence of gastric adenocarcinoma in some developed countries has been increasing in the recent decade. (6)

Based on the available evidence, trends of incidence of GC subtypes have been changed in different ways for men and women. (7) On the other hand, in some areas, incidence rates in younger age groups have increased more than in other age groups.(8)These trends also varied across different geographic regions and different socio-demographic development.(2, 9) These geographic and demographic differences may have been due to differences in the population distributions of risk factors of GC, the completeness of cancer incidence data, differences in the quality of diagnostic services, or treatment-seeking behavior of these populations.

Therefore, decomposing the GC incidence trend may provide evidence on its risk factors and subtype transitions, and consequently providing updated evidence for developing more effective preventive programs, diagnostic approaches, and clinical management of GC.

Iran, as a developing country, has experienced a remarkable health transition during the recent four decades. (10)Significant increase in popularity of westernized lifestyle, and population aging as well as improvements in sanitation, diagnostic methods, medical care, and quality of cancer registration led to an epidemiological transition.(10)Now, Iran is experiencing a huge burden of non-communicable diseases including GC.(11)

Studies show that the prevalence of correlates of GC, including obesity, smoking, alcohol consumption, and Helicobacter pylori have undergone major age and gender-specific transitions in Iran. (12, 13) Accordingly, we hypothesized that the trend of incidence of GC has not been similar across different subtypes and also across age-gender subgroups.

We aim to investigate stratum-specific incidence trends of GC in southern Iran considering age, gender, topological (cardiac/non-cardia), and morphological (adenocarcinoma/ non-adenocarcinoma) subtypes.

Methods

We used data on GC incidence in the catchment area of Shiraz Population-Based Cancer Registry (SPBCR) for 2001–2015.

Shiraz Population-Based Cancer Registry (SPBCR) is affiliated with Shiraz University of Medical Sciences. This registry was initiated in 2001 as a pathology-based registry and then improved in 2007 to a population-based system. As in Shiraz, the capital city of the Fars province, the quality, and accessibility of cancer diagnosis and treatment services is much better than the other cities throughout southern Iran, Shiraz is the most known referral center for cancer care in southern Iran. On the other hand, The Shiraz Population-Based Cancer Registry (SPBCR) collects the data on new cancer reports from almost all of the diagnostic and therapeutic centers as well as death registries in the Fars province. SPBCR is the most qualified cancer registry in southern Iran regarding the completeness of case ascertainment, comparability, data quality, and timeliness. (14)

Based on the most recent census, the population of the SPBCR catchment area, i.e. Fars province, is more than 4851000 with a female: male ratio of 1: 1.03. Fars (80%), Turk (10%), and Lor (7.7%) are the most common ethnicities in Fars province. Most (≈ 68%) of its inhabitants are living in urban/suburban areas. (15)

Patient data including age, gender, place of birth and living, date of birth, date of current cancer diagnosis, and date of death are collected, abstracted, and computerized by well-experienced cancer registrars. In addition, topographic and morphological data of the malignancies are abstracted and registered to apply the third edition of the International Classification of Diseases for Oncology (ICD-O-3).

Duplicated cases are identified and removed applying software-based techniques.(16) Multiple primaries are registered as new cases. An adapted version of CanReg5 software is used by SPBCR.

Data Preparation And Analysis

New cancer cases with ICD-O-3 codes of C16.0 to C16.9 were retrieved and prepared. New annual cases were counted for categories defied based on age group (under 25, 25–34, 35–44, 45–54, 55–64, 65–74 and 75 and older), gender (male, female), topography (cardia [ICD-O-3 code: C16.0], non-cardia[ICD-O-3 code: C16.1- C16.5], overlapping lesions [ICD-O-3 code: C16.8], and others), and morphology (adenocarcinoma [ICD-O-3 behavior code: 8140–8574], and others). Patients were also categorized into two additional age groups including younger than 45 and older than 45 years. Cases with missing data were redistributed if applicable.

Crude incidence rates and their 95% confidence intervals (CI) were calculated by dividing the number of new cases by stratum-specific mid-year population. Annual age-standardized incidence rates (ASR) and their 95% CI were also estimated based on the 2000 world population. Incidence data were truncated at 25 (considering a very low number of new cases with an age of younger than 25, and assuming that younger populations are less at risk of GC), and then truncated incidence rates were estimated.

Temporal trends of estimated stratum-specific ASRs were analyzed using joinpoint regression program (release 4.7.0), and annual percentage change (APC) and its 95% CI were estimated for each trend. As the quality of data was stable for years after 2009, we also estimated APCs for trend lines from 2009 to 2015 and considered these estimates as the most plausible APCs to show the current situation of the trend of incidence of GC in southern Iran. A p-value of less than 0.05 was considered statistically significant. Data were prepared and analyzed by using MS office excel, Stata software (release 11, College Station, TX: StataCorp LLC).

Results

Descriptive

A total number of 3413 (2312 male; 1101 female) new GC were registered by SPBCR from 2001 to 2015. Estimated mean of age at diagnosis was 66.0 (95 % CI: 65.4, 66.5) for males and 62.0(95% CI: 61.0, 62.0) for females.Majority (87.7%; 95% CI: 86.5, 88.8) of cases were gastric adenocarcinoma. 21.2% (95% CI: 23.0, 29.8) were cardia GC and 65.8% (95% CI: 68.6, 79.0) were non-cardia GC. Overall proportion of female cases was 32.2% (95% CI: 30.38, 34.2, it was 32.0% (95% CI: 30.0, 34.1) among adenocarcinomas, and also 33.3% (95% CI: 29.0, 38.2) among non-cardia GCs.

Recent Gastric cancer incidence rate

The estimated annual ASR of GC was 14.39 (95% CI: 14.37, 14.40) per 100000 population for males and 7.17 (95% CI: 7.14, 7.20) per 100000 population for females by 2015. The age-specific incidence rate in males was more than females across age groups except for 35–44 years age groups (Fig. 1).

Trends of overall and age-specific incidence of GC

Overall APC was estimated at 7.2(95% CI: 5.3, 9.1) for males and 8.7(95 CI: 5.3, 12.1) for females. Estimated APCs for trends of ASRs from 2009 to 2015 was not statistically significant for males ($APC_{2009\text{-}2015}$: 3.0%, 95% CI: -2.0, 8.3) and females ($APC_{2009\text{-}2015}$: 3.4%, 95% CI: -6.5, 14.4)(Fig. 2).

Estimated $APC_{2009-2015}$ for trends of age-specific incidence rates were not statistically significant for all age groups in both genders, except for 25–34 years old males with an APC of78.2(95% CI: 56.7, 102.7; Table 1).

Adenocarcinoma

Despite of increasing trends of gastric adenocarcinoma in males ($APC_{2001-2015}$: 5.0%, 95% CI: 1.5, 8.5)and females ($APC_{2001-2015}$: 8.0%, 95% CI: 1.8, 14.6)over the study period, estimated APCs for these trends were not statistically significant for both of males ($APC_{2009-2015}$: 1.5%, 95% CI: -5.4, 8.9)and females ($APC_{2009-2015}$: 3.7%, 95% CI: -5.7, 14.2)for the period of 2009 to 2015 (Table 1)

Cardia and non-cardia

Trends of ASRs of cardia GC were increasing for males ($APC_{2009\text{-}2015}$: 31.9%, 95% CI: 23.8, 40.5) and females ($APC_{2009\text{-}2015}$: 15.5%, 95% CI: 5.9, 25.9)from 2009 to 2015. But estimated APCs of trends of ASRs of non-cardia GC were not statistically significant for males ($APC_{2009\text{-}2015}$: 9.1%, 95% CI: -2.6, 22.3) and females ($APC_{2009\text{-}2015}$: 1.9%; 95% CI: -29.1, 46.5; Table 2).

Discussion

We reported rates and trends of incidence of GC in southern Iran. We showed that trends of overall and age-specific incidence of GC have been stable from 2009 to 2015 for both genders, after a rising trend from 2001 to 2008. An increasing trend was observed in 25–34 years old males. Similar trends were

observed for gastric adenocarcinoma and non-cardia GC. An increasing trend was observed for cardia GC in males. The trend of incidence of cardia GC was decreasing for younger females.

ASR of GC was 14.3 among males and 7.2 among females in 2015.These rates are lower than most of the available estimates from Iran. Hajizadeh and Pourhoseingholi showed that Fars province has the lowest risk of GC in Iran.(17, 18) It may be due to higher socio-development, lower prevalence of Helicobacter pylori, and higher healthcare coverage in this region compared with other regions. (19–21)

Our results showed that the overall trend of ASRs of GC has been stable from 2009 to 2015. According to the joinpoint regression, the last observed trends had been started in 2009. It may be partially due to more stability of procedures, data sources, and competency of registrars, and standards used by the Shiraz cancer registry since 2007.(14) It also maybe because of very low and stable population exposure to H. pylori in this region.(20) This finding is inconsistent with previous reports from developed countries, which showed a decreasing trend for the incidence of GC. (22, 23)However, this could be considered as a starting point for the significant decrease in the incidence of GC in this region.

The trend of gastric adenocarcinoma was only increasing in younger men. It is inconsistent with reports from developed countries.(6)It may be due to more alcohol consumption among this age group and very low and ignorable alcohol consumption among older age groups in Iran. An increasing trend of prevalence of alcohol consumption has been reported among Iranian younger men by several reports. (24, 25) On the other hand, lower exposure to H. pylori among younger Iranians has been reported. (26)Although the overall trend of ASRs of cardia GC was increasing for years after 2009 for both genders more rising among males. This finding is consistent with reports from western countries and also countries with a westernized lifestyle.(4, 5)Although our knowledge is less about the etiology of cardia GC, we know that its prognosis is poor compared with non-cardia GC. (9)The higher prevalence of cigarette smoking and increasing prevalence of obesity among Iranian men may be underlying factors for this rising trend.(27–29)

We observed decreasing trends of incidence of cardia GC among women for the most of age groups. Lower rates of cigarette smoking among Iranian women except for older women may be an explanation of these trends. (28) However, further studies are needed to explore the causes of GC in each age-gender subgroup, separately.

The trend of incidence of Non-cardia GC was increasing for younger men (age group 25–34 years). As the prevalence of exposure to H. pylori has an increasing trend in Iran, we think that the rising trend of non-cardia GC may be more likely to be a result of the change in health-seeking behaviors among the Iranian younger population including younger men. (30) This trend was stable for other age groups, which we think may be a result of the decrease in the prevalence of H. pylori exposure in Iran.

This study has some limitations. As a proportion of new cases were registered with an unspecified topography, we have to redistribute those applying a proportional to size approach and then categorized them into broad categories including cardia, non-cardia, and others GC. Therefore, although our findings

are rubout in the case of topography there is a need for a significant improvement in pathology reporting or abstracting.

As the pattern of lifestyle transition and trends of the prevalence of most of the risk factors of different subtypes of GC in Fars province is similar to other regions located in southern and central Iran, our study results are generalizable to most of Iran's population.

Conclusion

The incidence of GC in southern Iran is low. Gastric adenocarcinoma is the most common morphology. Cardia GC accounts for one-fifth of new cases. The trend of incidence of GC in southern Iran has been stable for the last decade. Significant and different changes in the pattern of GC have occurred in each age-gender subpopulation. These changes are in some cases different from those in developed countries. Early GCs show very different patterns of change among both males and females. Further etiologic and prognostic studies in each population subgroup in Iran can be very helpful.

Declarations

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Conflict of interests: ZK is affiliated withthe Shiraz Population-Based Cancer Registry. Others declare no conflict of interests.

Ethics approval: The study was approved by the Ethics Committee of Shiraz University of Medical Sciences.

Consent to participate: not applicable

Consent for publication: not applicable

Availability of data and material: : The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Authors' contribution: KBL, proposed the idea and supervised the study; HMV, conceptualized and designed the study, analyzed the data, and revised the manuscript; MHB, conducted data cleaning and data preparation, participated in conceptual frame-working and data analysis, and drafting the manuscript; ZKh, were responsible for data collection and its quality. All authors read the final version of the manuscript.

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Tables

Table 1. Trends of age-specific, age standardized, and Age truncated incidence rate of gastric adenocarcinoma in southern Iran

	Overall		Adenocarcinoma	
AAPC (95% CI)				
Age group/ gender	2001-2015	2009-2015	2001-2015	2009-2015
Female				
under 25	51.8(-28.6,222.7)	-40.5(-95.6, 697.8)	123.7(-51.8, 937.7)	66.9(-53.6, 500.1)
25-34	57.1(-14.4, 188.1)	16.2(-55.2, 201.0)	88.6(-56.1, 710.3)	20.8(-52.5,207.7)
35-44	4.2(-1.3, 10.1)	17.4(-5.6, 46.1)	3.8(-8.4, 17.7)	25.1(-2.8, 60.8)
45-54	11.3(5.9, 16.9) *	-3(-10.3, 5.0)	11.4(6.1, 16.9)*	-3.8(-11.0, 4.0)
55-64	4.7(-8.4, 19.5)	-0.1(-24.6, 32.3)	8.3(-4.3, 22.7)	11.0(-14.6, 44.3)
65-74	6.1(-3.7, 16.8)	3.4(-8.8, 17.2)	4.7(-5.2, 15.6)	2.4(-12.7, 20.0)
75+	15.1(7.3, 23.4) *	4.7(-9.0, 20.5)	13.9(3.4, 25.4)*	7.8(-12.1,32.2)
overall	8.7(2.1, 15.7) *	3.4(-6.5, 14.4)	8.0(1.8,14.6)*	3.7(-5.7,14.2)
Truncated	8.7(2.0, 15.9) *	3.2(-6.9, 14.3)	7.6(1.3, 14.4)*	2.6(-9.2, 15.9)
Male				
under 25	-	-	-	-
25-34	7.6(-7.8, 25.5)	78.2(56.7, 102.7)*	7.0(-66.8, 244.8)	139.3(13.0, 406.7)*
35-44	-3.3(-14.2, 9.0)	-8.9(-27.2, 14.2)	-4.1(-17.7, 11.7)	-9.4(-33.3,23.0)
45-54	9.9(5.9, 14.1)*	3.5(-0.5, 7.6)	7.9(3.2, 12.9)*	1.6(-3.1, 6.5)
55-64	7.2(-0.6, 15.6)	1.8(-9.9, 14.9)	5.6(-2.1, 13.9)	2.4(-7.2, 13.0)
65-74	4.0(-1.1, 9.4)	-0.9(-9.9, 9.0)	2.5(-2.8, 8.2)	-1.8(-11.9, 9.3)
75+	10.0(4.6, 15.6)*	5.8(-4.8, 17.6)	9.5(5.1, 14.0)*	1.9(-5.6, 10.0)
Overall	7.2(3.9, 10.6)*	3.0(-2.0, 8.3)	5.0(1.5, 8.5)*	1.5(-5.4, 8.9)
Truncated	7.1(3.7, 10.5)*	3.0(-2.1, 8.4)	4.9(1.4, 8.6)*	1.5(-5.6, 9.2)

Table 2. Trends of age- specific age standardized and truncated incidence rate of gastric cancer in southern Iran by cardia/non-cardia

	Cardia		Non-cardia	
APC(95% CI)				
Age group/ gender	2001-2015	2009-2015	2001-2015	2009-2015
Female				
under 25	-	-	50.9(-7.0, 144.7)	27.6(-60.0, 119.4)
25-34	19(-20.9, 79.2)	-37.9(-37.9, -37.9) *	106(-2.2, 334.0)	40.6(-58.5, 375.9)
35-44	-61.2(-79.7, -25.9) *	-90.8(-97.5, -66.5) *	122.5(27.5, 288.3)*	45.6(-33.0, 216.1)
45-54	-9.8(-40.8, 37.5)	-28.1(-89.9, 411.5)	150.4(43.8, 335.9)*	13.5(-61.8, 237.3)
55-64	-63.9(-79.7, -35.5) *	-92.8(-97.9, -75.5) *	208.5(60.7, 492.2)*	-2.8(-36.0, 47.7)
65-74	-13.5(-47.7, 43.0)	-34.7(-93.7, 578.6)	202.4(54.4, 492.1)*	76.7(-27.8, 332.4)
75+	22.7(21.5, 23.8)*	48.0(37.5, 59.3)*	302.1(76.6, 815.3)*	7.8(-45.7, 114.1)
Overall	7.2(-4.6, 20.5)	15.5(5.9, 25.9) *	195.8(68.0, 420.9)*	1.9(-29.1, 46.5)
Truncated	7.4(-5.8, 22.6)	16.0(5.8, 27.1) *	208.4(71.3, 455.0)*	2.7(-29.5, 49.7)
Male				
under 25	-	-	-	-
25-34	19.0(-20.9, 79.2)	-37.9(-37.9, -37.9)	65.7(-21.3, 248.9)	157.7(12.0, 258.9) *
35-44	-2.6(-36.0, 48.4)	87.3(46.3, 139.7) *	20.7(-41.5, 149.1)	-41.3(-97.8, 149.1)
45-54	14.7(8.8, 20.8)*	24.8(9.8, 41.7) *	107.7(16.8, 269.2)*	-2.6(-32.6, 40.9)
55-64	17.9(11.5, 24.7)*	33.2(23.8, 43.3)*	53.3(-4.1, 145.1)	8.2(-57.2, 173.1)
65-74	20.1(11.9, 28.9)*	38.1(26.0, 51.5)*	246.9(71.9, 600.3)*	-3.4(-38.4, 51.6)
75+	10.2(1.5, 19.7)*	24.2(10.1, 40.0) *	64.1(-0.8, 171.6)	23.5(-47.6, 191.3)
Overall	15.4(11.9, 19.0)*	31.9(23.8, 40.5) *	195.8(68.0, 420.9)*	9.1(-2.6, 22.3)

	Cardia		Non-cardia	
APC(95% CI)				
Age group/ gender	2001-2015	2009-2015	2001-2015	2009-2015
Truncated	15.9(13.2, 18.7)*	32.6(24.3, 41.4) *	208.4(71.3, 455.0)*	9.4(-5.0, 25.9)

Figures

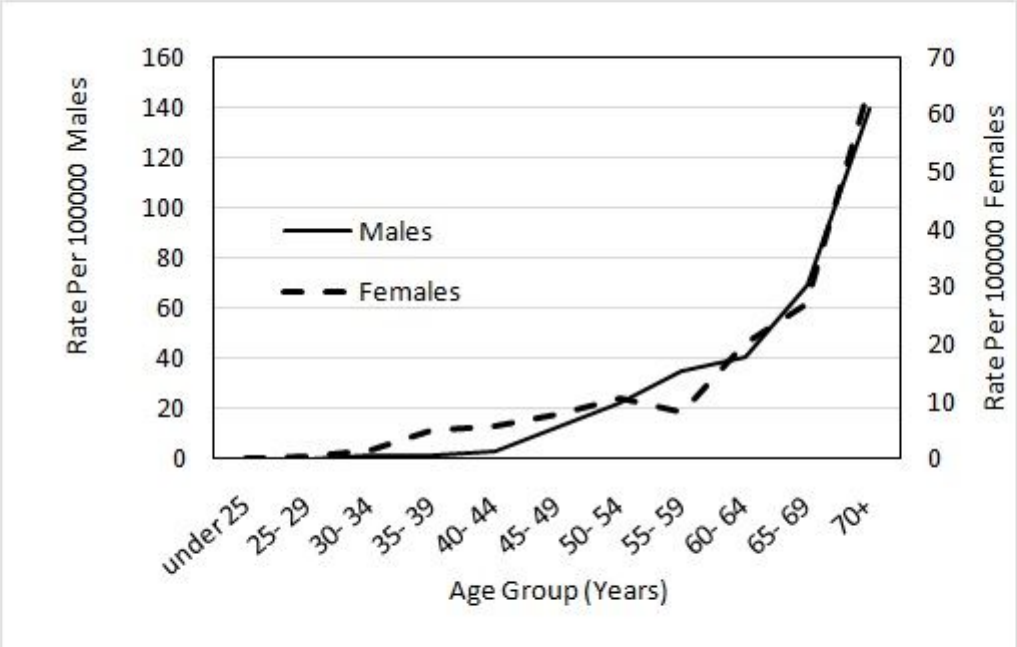

Fig1.

Figure 1

Incidence of gastric cancer across age groups in males and females in Southern Iran, 2015

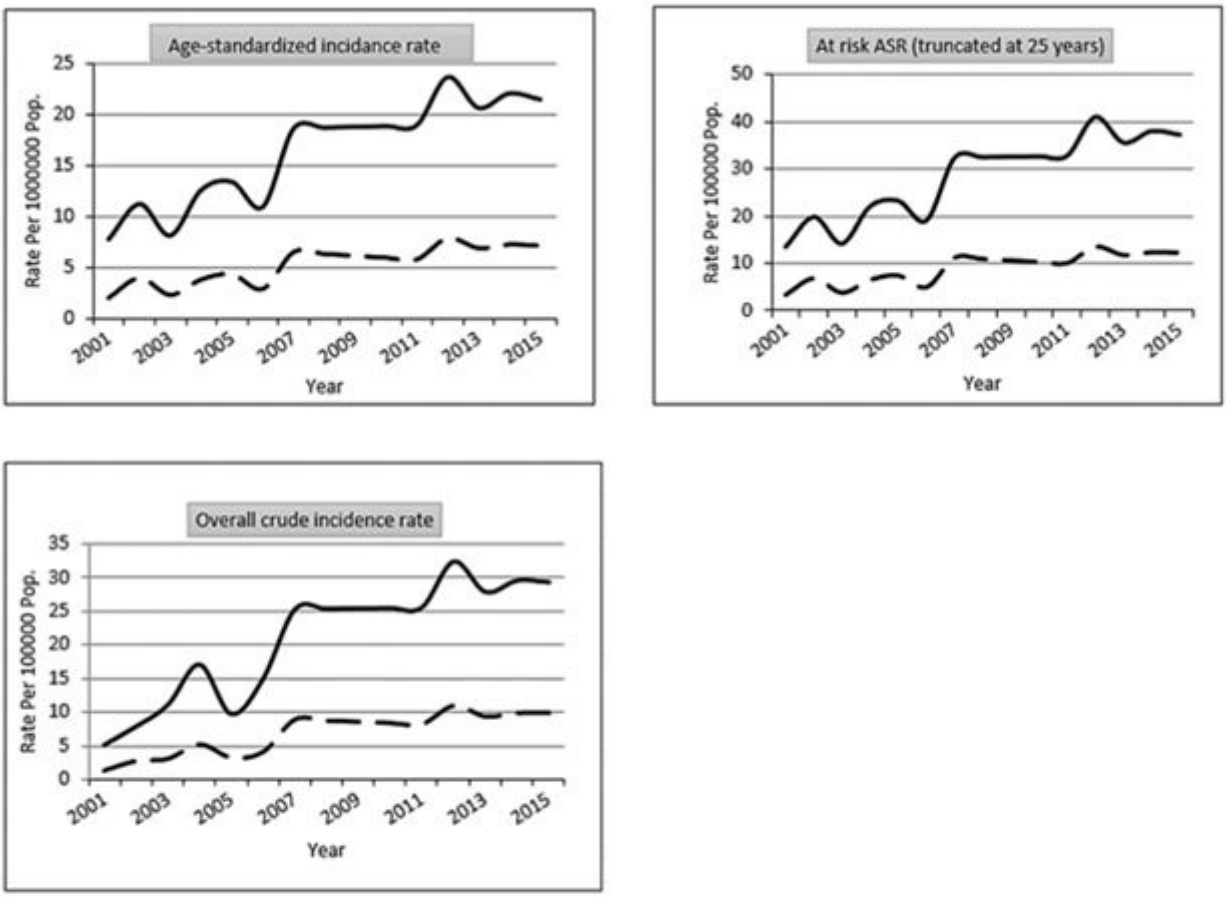

Fig2.

Figure 2

Trends of age standardized, truncated and crude rates of gastric cancer in southern Iran, 2001-2015, by gender