

## RESEARCH ARTICLE

# Trend Analysis of Gastric Cancer Incidence in Iran and Its Six Geographical Areas During 2000-2005

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### Abstract

**Objective:** gastric cancer is the fourth most common cancer worldwide. While it is one of the most common cancers in Iran, there are only limited data regarding incidence trends in the country. This study is the first of its type to investigate trends across six geographical areas during 2000-2005 using cancer registry data. **Materials and methods:** The registered data for gastric cancer cases in National Cancer Registry System were extracted from the Ministry of Health and Medical Education, Center for Disease Control & Management, code C16. First, according to WHO population, the sex-standardized incidence rate in both sexes and then the trends of incidence rate during 2000-2005 were investigated separately for different geographical areas of the country. **Results:** the incidence rates of gastric cancer in Iran and its six geographical areas during 2000-2005 were increasing albeit with differences in their slopes. The overall incidence rate increased from 2.8 in 2000 to 9.1 per 100,000 persons per year in 2005, rising from 4.1 to 13.2 in men. The average six-year incidence of gastric cancer in the central and northwestern border of Caspian Sea was 7.8 per 100,000 persons per year, while it was 0.9 per 100,000 persons per year in the border of the Persian Gulf. Generally the incidence rate in men was higher than in women. **Conclusion:** Iran is one of the high-risk areas for gastric cancer. Increase in incidence might continue in the future partly because of improvement in cancer registry systems as well as increase in risk of this cancer.

**Keywords:** Gastric cancer - incidence - trend - geographical regions - Iran

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### Introduction

Gastric cancer is one of the most important gastrointestinal tract cancers. According to the latest global report on cancers in 2008, gastric cancer is ranked as the fourth most common cancer worldwide, accounting for 934000 cases per year. The 5-year survival rate is less than 24 percent (Parkin et al., 1999) and after lung cancer, it is the second leading cause of mortality from cancer worldwide (Pisani et al., 1999; Boyle et al., 2004). Geographically, there are many variations in gastric cancer incidence among various areas, as North America and Canada with the incidence rate of less than 5.5 per 100,000 persons per year, and Japan, China and Eastern Europe with the incidence rate of 60 per 100,000 persons per year are the most risky geographical areas (Lambert et al., 2002).

The most important determining causes of gastric cancer are chronic *Helicobacter pylori* infection and a salty diet lacking fresh vegetables and fruits (Boyle et al., 2004; Marmot et al., 2007). *Helicobacter pylori* is one of the most common human infections; its prevalence is 50 percent in the world, and 90 percent in developing countries (Boyle et al., 2004). There is abundant evidence supporting the strong association between this bacterium

with gastric cancer (Al-Marhoon et al., 2004; Pirzadeh et al., 2011). In Japan with the highest risk of gastric cancer incidence, decrease in the prevalence of this bacterium has been followed by a decrease in gastric cancer incidence (Haruma, 2000). In addition, changes in the lifestyle and nutrition have important contribution to the recent observed decline in incidence of gastric cancer (Kaneko & Yoshimura, 2001).

There are many studies investigating trends in incidence of gastric cancer. Sharp decline reported in incidence of gastric cancer in countries such as the Kazakhstan (Igissinov et al., 2011) and United States during recent decades (American Cancer Society, 2009). However, decrease in incidence of gastric cancer in Eastern Asian countries like Korea, Japan, Latin America such as Colombia, Central Europe (Fuchs, 1995) and Asian developing countries (Moore et al., 2010) is very slow. In spite of the global decline in gastric cancer in recent decades, it is still remained as a major public health problem in 21 countries in the world (Pourfarzi et al., 2009) and in some countries such as; Denmark in Northern Europe (Botterweck et al., 2000), Italy (Brunetti et al., 2009), Oman (Nooyi and Lawati, 2011) and China (He et al., 2008), where there is an increase in the incidence of this cancer.

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In Iran cancers are the third cause of mortality (Yavari et al., 2008; Kolahdoozan et al., 2010) and gastric cancer is the first and second cause of mortality from cancer in men and in women respectively (Mohagheghi et al., 2009). Mean and median survival time of patients in Iran are 41.7 and 27 months respectively (Roshanaei et al., 2011). There have been few provincial studies on cancers which, in general, reveal the high incidence rate of gastric cancer. In some studies, gastric cancer has been reported as the most common cancer in males and females and even its incidence rate has exceeded the global value (Sadjadi et al., 2006). In Semnan province, central Iran, during 1998-2002, gastric cancer with the standard incidence rate of 27.5 per 100,000 persons per year has been the most prevalent cancer with the highest incidence in Iran (Babaei et al., 2005). Mousavi et al. (2009) by studying reports of incidence and mortality from 2003 to 2008, demonstrated that gastric cancer is the most prevalent cancer in men and they anticipated a sharp increase in incidence rate in future, considering the registry system evolution and change in lifestyle toward a western culture (Mousavi et al., 2009). Similar to most other cancers, the incidence in men is by far higher than in women (Eskandar et al., 2006; Ghadimi et al., 2007). and due to late diagnosis, it is mostly diagnosed in the advanced stages of the disease (Eskandar et al., 2006). Gastric cancer incidence has had a slow increase during three past decades in Iran and in 2002 has increased twice in comparison with the three past decades (Malekzadeh et al., 2004; Sadjadi et al., 2006). The incidence trend of gastric and esophagus cancer has decreased dramatically in the Iranian residents of Canada (Sadjadi et al., 2009) which could be an indication for the high impact of lifestyle and environmental factors in the incidence of stomach cancer. The prevalence of this cancer, particularly in north and northwest of Iran reported in high rate (Rafsanjani et al., 2004; Malekzadeh et al., 2009).

Studies on trends in epidemiology of cancers in Iran are in their early stages and in fact the changes in incidence of cancers with reliance upon the valid data has not been reported yet. Cancer registry system has had an evolutionary trend with improvement in the public knowledge and diagnosis techniques (Brunetti et al., 2009). In Iran, similar to other countries in the world, the registry of cancers has improved over recent years (Etemadi et al., 2008) although there are still serious problems that need to be taken into account (Mousavi et al., 2009). The present study aimed to investigate trends in incidence of gastric cancer during 2000-2005 in both males and females in six geographical areas separately for the first time in Iran, using national cancer registry system.

## Materials and Methods

A cross-sectional population-based study designed and the registered data for gastric cancer cases in National Cancer Registry System were obtained from Ministry of Health and Medical Education, Center for Disease Control (CDC). The data had been collected at the end of each year from pathology centers all over the country and after

receiving the data, CDC controlled the data in terms of proper coding, missing in demographic information, and deleting the repeated cases. Meanwhile, cancers were coded based on International Classification of Diseases ICD-10 (second edition) (Constance & Valerie, 2000). In this study, code C16 was extracted for gastric cancer. Then we divided the country into six geographical areas: Guilan and Mazandaran provinces as the Central and Western border of Caspian Sea; Golestan province alone as the eastern border of the Caspian Sea; Tehran, Qom, Qazvin, Zanjan, East Azerbaijan, West Azerbaijan and Ardabil provinces as flat areas; Kermanshah, Kurdistan, Hamedan, Ilam, Chahar Mahal Bakhtiari, Kohkiluyeh Boyer Ahmad and Fars provinces as mountainous areas; Kerman, Sistan Baluchistan, Yazd, Semnan, Khorasan, Birjand and Isfahan provinces as desert areas; and finally Khozestan, boushehr, and Hormozgan provinces as border of Persian Gulf areas. Meanwhile, residential provinces of a high proportion of registered cancer cases were unidentifiable that were accounted for in the calculation of total incidence rate in the country but they were not considered in the computation of different geographical areas.

The results of national census data in 2006 were used to calculate the crude and age-specific incidence. By computing the annual growth rate of 1.01% and based on the population rate in 2006, the population of different geographical areas for the years 2000, 2001, 2002, 2003, 2004, and 2005 were estimated. Also, WHO standard population was used as standard population. (35) Using direct method and Stata11 software, age- and sex-standardized incidence rates with 95% confidence intervals (CI) were computed for the whole country and its six different geographical areas separately and were shown for various age and sex groups separately. Stata11 software and Poisson regression model were used to assess the significance of incidence trends and  $p < 0.05$  was considered significant.

## Results

During the 6-year period, 21348 cases of gastric cancer were registered in Iran which had increased from 1666 cases in 2000 to 5836 cases in 2005 with the sex proportion of 2.5 male to female. The average age for all subjects, women and men were  $57.0 \pm 16.8$ ,  $53.3 \pm 16.0$  and  $60.8 \pm 16.8$  respectively. The age-standardized incidence rate in Iran was significantly increased from 2.8 in 2000 to 9.1 per 100,000 per persons per year in 2005, with different slopes was observed in each of six geographical areas (Table 1). In men it increased from 4.1 in 2000 to 13.1 per 100,000 persons and in women from 1.5 in 2000 to 5.0 (Table 1).

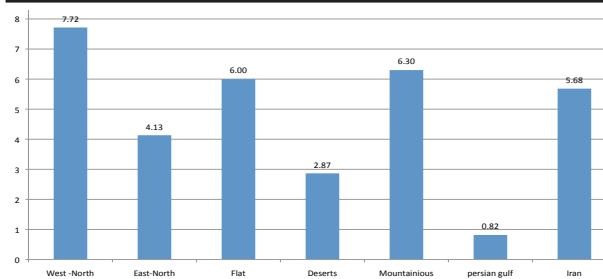
In regard to different age groups, although with different slopes, showed growing incidence over the period of study for all age groups. Meanwhile, cancer incidence rate had increased rapidly in age group 50-59 and had reached its maximum in oldest age (Figure 1).

### *Central and western border of the Caspian Sea*

If we average out the incidence rate of gastric cancer in the total 6 years and rank different geographical areas, the central and western border of Caspian Sea is ranked

**Table 1. Trend of Changes in Age-Standardizes Incidence Rate (Per 100,000 Persons) of Gastric Cancer in 6 Geographical Areas in Iran During 2000-2005**

	2000	2001	2002	2003	2004	2005	Slope/ PValue
<b>Central and Western border of Caspian</b>							
Male	7.4 (6.2-8.5)	3.5 (2.7-4.3)	6.9 (5.8-8.1)	12.8 (11.3-14.3)	19.6 (17.7-21.5)	18.4 (16.6-20.2)	0.28 (0.0001)
Female	2.9 (2.2-3.7)	1.1 (0.7-1.6)	3.1 (2.4-3.9)	4.6 (3.7-5.5)	6.5 (5.4-7.6)	6.1 (5.1-7.1)	0.24 (0.04)
Total	5.1 (4.4-5.8)	2.3 (1.8-2.8)	5.0 (4.3-5.7)	8.7 (7.8-9.5)	13.0 (11.9-14.1)	12.2 (11.2-13.2)	0.25 (0.003)
<b>Eastern border of Caspian</b>							
Male	0.9 (0.1-1.7)	6.7 (4.4-9.1)	1.9 (0.6-3.1)	4.3 (2.4-6.1)	8.1 (5.6-10.7)	14.1 (10.8-17.4)	0.37 (0.003)
Female	1.0 (0.1-1.7)	2.4 (1.0-3.8)	1.2 (0.2-2.3)	1.9 (0.6-3.1)	2.6 (1.2-4.0)	4.6 (2.8-6.5)	0.25 (0.12)
Total	0.9 (0.3-1.5)	4.5 (3.2-5.9)	1.5 (0.7-2.3)	3.1 (2.0-4.2)	5.4 (3.9-6.9)	9.4 (7.5-11.3)	0.34 (0.005)
<b>Desert area</b>							
Male	3.0 (2.6-3.5)	2.0 (1.7-2.4)	2.4 (2.0-2.8)	3.1 (2.7-3.5)	3.9 (3.5-4.4)	9.4 (8.6-10.1)	0.29 (0.01)
Female	1.3 (1.0-1.6)	1.1 (0.8-1.3)	0.7 (0.5-0.9)	1.4 (1.1-1.7)	1.6 (1.2-1.9)	4.0 (3.5-4.6)	0.27 (0.14)
Total	2.2 (1.9-2.4)	1.6 (1.3-1.8)	1.6 (1.4-1.8)	2.3 (2.0-2.5)	2.8 (2.5-3.1)	6.7 (6.3-7.2)	0.27 (0.05)
<b>Flat area</b>							
Male	4.2 (3.6-4.7)	4.3 (3.7-4.8)	4.7 (4.1-5.3)	8.1 (7.3-8.8)	11.2 (10.3-12.0)	17.4 (16.4-18.5)	0.32 (0.0001)
Female	1.4 (1.1-1.7)	2.0 (1.7-2.4)	2.0 (1.7-2.4)	3.5 (3.0-4.0)	5.4 (4.8-6.0)	6.9 (6.3-7.6)	0.33 (0.01)
Total	2.8 (2.5-3.1)	3.2 (2.9-3.5)	3.2 (2.9-3.5)	5.8 (5.4-6.2)	8.4 (7.8-8.9)	12.3 (11.7-12.9)	0.33 (0.001)
<b>Mountainous area</b>							
Male	6.0 (5.2-6.7)	6.6 (5.9-7.4)	7.1 (6.3-7.9)	8.3 (7.5-9.2)	11.6 (10.6-12.6)	13.4 (12.3-14.4)	0.17 (0.03)
Female	1.9 (1.5-2.4)	2.8 (2.3-3.3)	3.4 (2.8-3.9)	3.4 (2.8-3.9)	4.3 (3.7-4.9)	5.8 (5.0-6.5)	0.19 (0.12)
Total	4.0 (3.5-4.4)	4.8 (4.3-5.3)	5.3 (4.8-5.8)	5.9 (5.4-6.5)	8.1 (7.5-8.7)	9.7 (9.0-10.4)	0.18 (0.06)
<b>Border of Persian gulf</b>							
Male	0.1 (0.0-0.1)	0.3 (0.1-0.6)	1.2 (0.7-1.7)	1.1 (0.6-1.6)	0.9 (0.5-1.4)	1.3 (0.8-1.9)	-0.09 (0.62)
Female	0.2 (0.0-0.5)	0.2 (0.0-0.6)	0.6 (0.2-1.0)	0.6 (0.2-0.9)	0.9 (0.5-1.3)	2.4 (1.7-3.2)	0.46 (0.12)
Total	0.1 (0.0-0.3)	0.3 (0.1-0.5)	0.9 (0.6-1.2)	0.8 (0.5-1.2)	0.9 (0.6-1.2)	1.9 (1.4-2.3)	0.41 (0.14)
<b>Iran</b>							
Male	4.1 (3.9-4.4)	3.6 (3.4-3.8)	6.4 (6.2-6.7)	10.3 (9.9-10.7)	11.3 (11.0-11.7)	13.1 (12.6-13.5)	0.26 (0.002)
Female	1.5 (1.3-1.6)	1.6 (1.4-1.7)	2.7 (2.5-2.8)	3.9 (3.7-4.2)	4.4 (4.1-4.6)	5.0 (4.8-5.3)	0.25 (0.06)
Total	2.8 (2.7-2.9)	2.6 (2.5-2.7)	4.6 (4.4-4.7)	7.1 (6.9-7.4)	7.9 (7.7-8.1)	9.1 (8.8-9.3)	0.26 (0.01)

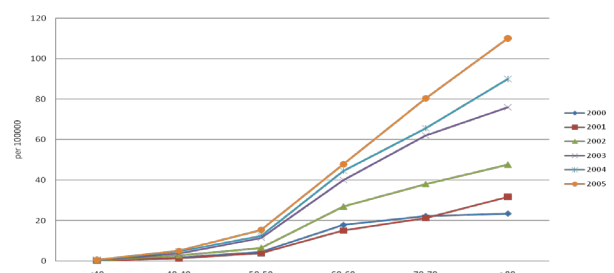
**Figure 1. Average of Age-Standardized Rate of Gastric Cancer in 6 Geographical Areas in Iran, 2000-2005.**

first and its average incidence rate was higher than that of the whole country (Figure 2). Incidence of gastric cancer declined over the period of study two times: first in 2001 and second in 2005. Similar changes were observed in the incidence rate in both sexes.

In the whole country, during 6 years the incidence rate in men was higher than in women. The age-standardized incidence rate in this region had increased from 5.1 in 2000 to 12.2 per 100,000 per persons per year in 2005. The age-standardized incidence rate of gastric cancer in men had increased from 7.4 in 2000 to 18.4 per 100,000 per persons per year in 2005, whereas the corresponding values in women had increased from 2.9 in 2000 to 6.1 per 100,000 per persons per year in 2005.

#### Eastern border of Caspian Sea

In the eastern border of Caspian Sea, the 6-year average of gastric cancer incidence rate was lower than the country average and higher than the border of Persian Gulf and desert areas (Figure 1). It was ranked fourth among the

**Figure 2. Age-Standardized Rate of Gastric Cancer in Iran by Age Group and Year.**

six geographical areas. The age-standardized incidence rate in this region had increased from 0.9 in 2000 to 9.4 per 100,000 per persons per year in 2005. Except for 2002 which there was a decrease in incidence of gastric cancer, for rest of the years there was a consistent increase. The age-standardized incidence rate of gastric cancer in men had increased from 0.9 in 2000 to 14.1 per 100,000 per persons per year in 2005, whereas the corresponding values in women had increased from 1.0 in 2000 to 4.6 per 100,000 per persons per year in 2005. The change in incidence of gastric cancer for both sexes was similar although not significant in women (Table 1). For the whole period of study except 2000, gastric cancer incidence rate in men was higher than in women and this difference reached its maximum in 2005.

#### Mountainous area

After central and western border of Caspian Sea as the most risky geographical area of Iran, mountainous area was ranked second (Table 1 and Figure 1). After a

moderate increase in gastric cancer till 2004, the incidence increase sharply. Although both sexes were similar in terms of trends over the period of study, the increase in men was statistically significant. The age-standardized incidence rate in this region had increased from 4 in 2000 to 9.7 per 100,000 per persons per year in 2005. The age-standardized incidence rate of gastric cancer in men had increased from 6 in 2000 to 13.4 per 100,000 per persons per year in 2005, whereas the corresponding values in women had increased from 1.9 in 2000 to 5.8 per 100,000 per persons per year in 2005.

#### Desert area

In terms of the comparison of the 6-year average of incidence rate, desert area was ranked fifth among other geographical areas of the country and after the border of Persian Gulf area; it was one of the least risky geographical areas of Iran in terms of gastric cancer incidence (Figure 1). As other areas of the country, the general trend of age-standardized incidence rate of gastric cancer in this area was increasing. It had increased from 2.2 in 2000 to 6.7 per 100,000 per persons per year in 2005. The incidence rate of gastric cancer in this area in 2001 had declined half the incidence rate of previous year and then in 2002 had increased again so that after 2002 the trend of changes had sloped up. If we separate the incidence rate in both sexes we can observe that the trend of changes in incidence rate in women and men has a similar status. The age-standardized incidence rate of gastric cancer in men had increased from 3 in 2000 to 9.4 per 100,000 per persons per year in 2005, whereas this amount in women had increased from 1.3 in 2000 to 4.0 per 100,000 per persons per year in 2005.

#### Flat area

This geographical area, after central and western border of Caspian Sea and mountainous area, was the third most risky area in terms of gastric cancer (Figure 1). The age-standardized incidence rate of gastric cancer had increased from 2.8 per 100,000 in 2000 to 12.3 per 100,000 per persons per year in 2005; a four fold increase during 6 years. There was a slight decline in the incidence rate of gastric cancer in this area in 2002 and after that the incidence rate had increased noticeably. The trend of changes in the age-standardized incidence rate in both sexes was similar and there was a slight decline in both of them in 2002. The incidence rate in the total 6 years was higher in men than in women and while the incidence rate had increased from 4.2 in 2000 to 17.4 in 2005 in men, and from 1.4 in 2000 to 6.9 per 100,000 per persons per year in 2005 in women.

#### Border of Persian Gulf area

This area was the least risky geographical area in terms of gastric cancer incidence (Figure 1). Compared to mountainous area as the most risky geographical area of Iran for gastric cancer, the 6-year average of incidence rate in this area was approximately 10 fold less than that in mountainous area. Although the incidence rate during the total 6 years had also increased in this area, the slope of these changes was more moderate than other areas of

Iran and the age-standardized incidence rate had increased from 0.1 in 2000 to 1.9 per 100,000 per persons per year in 2005. Like mountainous area and unlike some other geographical areas, the incidence rate had increased during 6 years in this area without any decline. In the analysis of the trend of incidence in both genders, unlike other areas of Iran, there was a partial difference in the incidence of gastric cancer in men and women and even in 2000 there was a higher incidence in women. While the age-standardized incidence rate of gastric cancer in men had increased from 0.1 per 100,000 in 2000 to 1.3 per 100,000 per persons per year in 2005, among women it had increased from 0.2 in 2000 to 2.4 per 100,000 per persons per year in 2005. The only difference lay in the fact that unlike the consistent growing trend in men, there was a slight decline in the incidence rate in women in 2004.

## Discussion

The present study revealed that despite differences among various geographical areas, gastric cancer has a growing trend in Iran, a result that does not seem to be in line with some provincial studies in Iran (Najafi, 2011). However, there are two main explanations for such increase: 1) an increase in exposure to the risk factors of this cancer which generally related to the prevalence of chronic *Helicobacter pylori* infection and a change in the dietary pattern toward salty foods poor in fresh vegetables and fruits, 2) an improvement in cancer diagnosis techniques in the country, increase in public knowledge and doctor's sensitivity in the early diagnosis of cancer, and most importantly, improvement in the quality of cancer registry system.

The evidence indicate that one of the leading causes of gastric cancer is helicobacter pylori and decline in its prevalence trend in developed countries is in line with the significant decrease in gastric cancer incidence in such countries. This bacterium is so important that the International Agency for Research on Cancer (IARC) has announced that it is the leading cause of gastric cancer (Forman & Coleman, 1993). Generally, the prevalence of helicobacter pylori in developing countries including Iran is more than 80 percent compare to less than 30 percent in developed countries (Atherton, 2006). Based on bulk of evidence showing the association between helicobacter pylori and gastric cancer (Forman & Coleman, 1993; Atherton, 2006), one may suggest that the causes of increase in gastric cancer incidence in Iran is an increase in the chronic infection with *Helicobacter pylori* that along with other increasing factors of this cancer has resulted in an increase in the incidence trend in the country. However, the growing use of antibiotics for treatment also of other infectious diseases in the country could have also decreased its prevalence (Tomatis et al., 1990).

Apart from helicobacter pylori, changes in life style and dietary pattern are two important factors that should be investigated to determine their association with the growing trend in gastric cancer incidence. The bulk of evidence suggests the association between use of salt and salty foods (Marmot et al., 2005) with increase in gastric cancer. Besides, using fresh fruit especially citrus

and vegetables (containing alliums and anti oxidant) (Matsuzaka et al., 2007; Bafandeh & Farhang, 2009), and fresh fish (Terry et al., 2001; Kim et al., 2004) have been mentioned by various studies as preventive factors of gastric cancer. Although the diet of Mediterranean and Middle Eastern countries include safe food like fresh vegetables and fish (Hosseini, 2010), they have also turned to western foods and lifestyle in recent decades. In Iran, we can notice such a change in the dietary pattern of population too, and studies indicate the increasing trend of facing the risk of this cancer as well as change in the food consumption in Iran (Alikhani et al., 2005). Of course, in the analysis of the lifestyle and nutrition of Iranians we should notice that the change in food preservation (keeping foods in refrigerator instead of making smoked and smoked salt foods) could also have caused, to some extent, a decline in the incidence of gastric cancer, though in some areas of Iran, the proper use of refrigerator is not customary and there are still some improper methods of traditional food preservation among people. While Iran is facing with an increase in incidence of gastric cancer other research suggest a decreasing trend in gastric cancer incidence in some countries such as Israel (Katz & Steinitz, 1979), Cyprus, Jordan, Egypt, South America (Parkin et al., 1980) and European countries like Spain (Cabanes, 2010) and Amberia State in Italy (Fabrizio & Antonio, 2007). It is worth mentioning that there is an increase in the incidence of gastric cancer in most developing countries such as Korea (Jung & Won, 2005) and Portugal (Pinheiro & Teyczinski, 2003). The decline in incidence of gastric cancer in the United States and West Europe may resulted from helicobacter pylori infection control, high quality of food, and the impact of long term programs of controlling cancers. Japan is a good example of the impact of abovementioned programs in the control of gastric cancer. While this country is one of the most risky countries in the world in terms of gastric cancer, it has been able to decrease the incidence trend of gastric cancer by the proper administration of cancer control programs, changing the dietary pattern, and use of healthy eating (Haruma, 2000; Kaneko & Yoshimi, 2003).

Smoking has also been an influential factor in the incidence of most of the cancers. In a cohort study in 2007 it was revealed that gastric cancer risk in smokers was twice more than non-smokers (Sjodahl et al., 2007) and in some other studies there was a strong association between smoking and gastric cancer (Pisani et al., 1997; Sasazuki et al., 2002; Derakhshan et al., 2007). The general trend of gastric cancer is rather similar to that of smoking where there is a decline in smoking in the developed countries and an increase in developing countries. Although we don't have exact information about smoking prevalence in the population of the country, but considering the extensive media pressure against smoking side effects, smokers population expected to decline in recent decades and not to have much impact on the status of gastric cancer incidence in Iran.

Gender is an important factor in all studies of medical sciences, mainly cancer studies. As it was observed, gastric cancer incidence during the total 6 years was much higher in men than in women. Some researchers have attributed

the cause of such difference to the protective role of female hormones (Chandanos & Lagergren, 2008). In addition, the sensitivity of individual health care in women is much higher than in men and this may lead to better and earlier diagnosis of gastric cancer among women.

As this study showed, the western border of Caspian Sea and then mountainous area are the most risky areas and the border of the Persian Gulf and desert areas the least risky geographical areas in terms of gastric cancer incidence. The northwestern border of Caspian Sea is a coastal area with a high consumption of smoked fish which seem to be the major factors in the high incidence rate of gastric cancer in this area. The residents of mountainous area are mostly belonging to Kurdish and Lors ethnic background. Low social-economical and welfare of the people and poor food health in the villages along with genetic sensitivity may be the major causes of high incidence of gastric cancer in these areas. In contrast, the people in the border of Persian Gulf and desert areas belong to Persian and Arabic ethnic background with better social-economical and welfare as well as environmental factors may be the major contributing factors for low incidence of gastric cancer in these areas. Also familial aggregation may be one of the related factors for high rate of incidence in this areas (Moghimi-Dehkordi et al., 2011).

A proportion of observed changes in incidence of gastric cancer may be related to improvement in diagnosis techniques, increase in the public sensitivity to their health, and advancement in cancer registry system. Similar study in Italy indicated that a high proportion of increase in the incidence rate of gastric cancer pertained to the improvement in diagnosis techniques and cancer registry system (Brunetti et al., 2009) that is also true for the registry system and diagnosis in Iran (Mousavi et al., 2009). Etemadi et al have clearly discussed the improvement in cancer registry in Iran in their reports (Etemadi et al., 2008) and based on the report from Iranian Ministry of Health, cancer registry has dramatically improved from 1999 to 2005 (NDCO, 2007). Therefore, a proportion of the increase in gastric cancer incidence in Iran and its different geographical areas may have resulted from improvement in cancer registry system. For instance, there was a sudden increase in gastric cancer incidence in northeastern border of Caspian Sea in 2001 and then a decline again. In contrast, in the northwestern border, there was a sudden decline in the incidence rate in 2001. Considering the nature of chronic conditions such as cancers, such changes in the incidence rate cannot be real and are mostly the result of the change in the quality and method of data collection for cancer. However, it is worth mentioning that such problems will not diminish the trend studies which are based on a registry system even in a country such as Iran. In addition, to present the direction of changes and predicting the future patterns, they will provide the evidence and desirable circumstances for the future analyses of cancer registry system. Based on the above-mentioned reasons, the problems and the evolutionary trend of cancer registry system should be taken into account in the interpretation of the results of all cancer studies. But how much of this increase in the incidence trend is related to the improvement in cancer

registry system, is what researchers have to put an effort into, in the future studies.

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