

RESEARCH COMMUNICATION

Time Trends in the Occurrence of Major GI Cancers in Iran

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Abstract

Objective: The aim of this study was to study the changes in occurrence of esophageal, stomach and colon cancers (cancers of interest) over the last 30 years in Iran.

Material and Methods: Cancer cases referred to two main cancer centers in the country (the Shiraz cancer center and the Tehran cancer center) during last 30 years and published by the two centers were utilized. Morbidity odds ratios (MOR) were used to study trend in the occurrence of each cancer site in each center. For this purpose the cancers of interest were considered as cases; childhood cancers as controls; and calendar year as exposure. A regression line was fitted to morbidity odds ratios over years and the slope of the regression line was considered to indicate the overall trend. MORs and 95% CIs comparing the last five and first five years were computed to measure the magnitude of the change over time.

Result: The overall trend for esophageal cancer was decrease (slopes = -0.02 for Shiraz and -0.03 for Tehran); for stomach was increase (slopes = 0.04 for Shiraz and 0.08 for Tehran), and for colon cancer was sharp increase (slopes = 0.02 for Shiraz and 0.10 for Tehran). The magnitude of changes showed stomach cancer to increase by 35% in Shiraz (MOR = 1.35 with 95% CI 1.1, 1.65) and 13% in Tehran (MOR = 1.13 with 95% CI 0.96, 1.38), esophageal cancer to decrease by 20% in Shiraz (MOR = 0.82 with 95% CI 0.62, 1.11) and 50% in Tehran (MOR = 0.52 with 95% CI 0.45, 0.60), and colon cancer to increase by 65% in Shiraz (MOR = 1.65 with 95% CI 1.26, 2.16) and 82% in Tehran (MOR = 1.82 with 95% CI 1.52, 2.25).

Conclusion: During the last thirty years the occurrence of major GI cancers has changed in Iran with sharp increase in colon cancer, slight to moderate increase in stomach cancer and sharp decrease in esophageal cancer.

Key Words: Cancer - time trends - esophagus - stomach - colon - Iran

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Introduction

Cancers of upper gastrointestinal tract, mainly esophagus and stomach are the most frequent cancers in Iran (Mosavi-Jarrahi et al., 2001). The existence of geographic variation in the frequency of GI cancer in the country has been noted since the first report on high rate of esophageal cancer in north-eastern part of Iran was published (Kemet and Mahboubi, 1972). The variations seen in the incidence of different cancers in the country have been subject of interest among epidemiologist, both locally and internationally. There is consensus among Iranian epidemiologists to divide the country into two regions for cancer incidence, the Caspian littoral for high rates of upper GI cancer mainly esophagus and gastric cancers, and other parts of the country with low rates of esophageal cancers and high rate of skin

cancers and malignancy of lymphoproliferative and hemopoietic systems (Mosavi-Jarrahi et al., 2001). However, certain changes in patterns of cancer occurrence are anticipated, especially since the country has transformed from a static-agricultural society to a dynamic-urban society during the last 50 years.

Epidemiologic investigations of major GI cancers in the countries where reliable cancer registry is available have generated data demonstrated certain trends in incidences, mainly lowering cancers of esophagus and stomach and increase in the incidence of colon and lower GI cancers (Muir and Nectoux, 1996). Although, there are recent population data regarding the incidence of GI cancers in Iran, due to lack of population based cancer registries, monitoring the changes in cancer morbidity and mortality over years is not as straight-forward as comparing rates at different times and

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Table 1. The Frequency of Cancers of Interest as well as Childhood Cancers in the Two Sources of Data

The data Source	All Cancers	Stomach No. (%)	Esophagus No. (%)	Colon No. (%)	Childhood No. (%)
Tehran	16383	656 (4%)	1697(10)	573 (4)	1718(10)
Shiraz	19276	860(4%)	765(4)	662(4)	1740(9)

other methodologies need to be employed. The aim of this study was to study the changes of GI cancer occurrence over the last 30 years in Iran by utilizing large case series reported by two major cancer centers.

Materials and Methods

The Data

Two large cancer case series compiled in two main referral centers in the country were utilized. The centers are located in the city of Shiraz (located in the central part of Iran) and Tehran. The two have been referral centers providing comprehensive cancer treatment and diagnosis to the population residing in their geographically adjacent areas. The data of the Shiraz center (Salabian, 1972-1995) included 19276 cases of cancer referred to the center from 1976 till 1995. The Shiraz data were abstracted from yearly-published reports of the center. The Tehran data was available in electronic format and it included 16383 cases referred to the center from 1972 till 1995 (Mortazavi et al., 1995).

The Analyses

Analyses were done for the cancers of esophagus, stomach, and colon. Morbidity odds ratio was used to analyze the data. For this purpose, cancers of interest (esophagus, stomach, and colon) were considered as cases. The childhood cancers (all cancers of age less than 15 years) were considered as controls. Calendar years were considered as exposure and the reference for exposure were the first-three-years. Each consecutive year was compared to the first three years and morbidity odds ratios were calculated for each year. The yearly odds ratios were plotted against calendar years and a linear regression line was fitted to the odds ratios over years. The slope of the line was considered as an "overall trend" in the occurrence of cancers of interest during the period studied. In order to quantify the magnitude of the changes in occurrence of each cancer, morbidity odds ratios comparing the first five years with the last five years were calculated for each site in each center. 95% confidence intervals were calculated for the odds ratios. Analysis was done using Excel Microsoft software.

Results

During the years of study, a total of 5213 cases of esophageal, stomach and colon cancers referred to the two centers comprising 18% of Tehran referred cases and 12% of Shiraz referred cases. Table 1 shows the frequency of cancers of interest with the corresponding frequency of childhood cancers in each center. The result of analytical

analysis for each cancer is as follow:

Esophageal Cancer

During the years of study, total of 2462 cases of esophageal cancers were referred to the two centers comprising 10% of cancers in the Tehran center and 4% of cancers in the Shiraz centre. In both centers, the overall occurrence of esophageal cancer sharply decreased (Figure 2). The decrease was more in Tehran compared to Shiraz. (The slope of regression was - 0.11 for Tehran, and - 0.03 for Shiraz). The magnitude of this reduction as measured by comparing the last five years to the first five years was; 48% for Tehran and 18% for Shiraz (Table 2).

Stomach Cancer

During the years of study, total of 1516 cases of stomach cancers were referred to the two centers comprising 4% of cancers in the Tehran and 9% of cancers in the Shiraz centre (Table 1). In both centers, the overall occurrence of stomach cancer slightly increased (Figure 2). The increase was almost the same for the two centers (the slope of regression was + 0.08 for Tehran, and +0.03 for Shiraz). The magnitude of this increase as measured by comparing the last five years to the first five years was; 13% for Tehran and 35% for Shiraz (Table 2).

Colon Cancer

During the years of study, total of 1232 cases of colorectal cancers were referred to the two centers comprising 3% of cancers in the Tehran and 4% of cancers in the Shiraz centre (Table 1). In both centers, the overall occurrence of colorectal cancer increased (Figure 3). The increase was more in Tehran compared to Shiraz (the slope of regression was + 0.12 for Tehran, and +0.02 for Shiraz). The magnitude of this increase as measured by comparing the last five years to the first five years was; 82% for Tehran, and 65% for Shiraz (Table 2). The magnitude of increase was statistically significant (odds ratio =1.82 with 95%CI of 1.52, 2.25 for Tehran and odds ratio = 1.65 with 95% CI of 1.26, 2.16 for Shiraz).

Table 2. The Odds Ratios Comparing the First Five with the Last Five Years for the Cancers of Interest in the Two Centers

Cancer Site	Shiraz center OR (95%CI)	Tehran center OR (95%CI)
Stomach	1.35 (1.1 , 1.65)	1.13 (0.93 , 1.38)
Esophagus	0.82 (0.62 , 1.11)	0.52 (0.45 , 0.60)
Colorectal	1.65 (1.26 , 2.16)	1.82 (1.52 , 2.25)

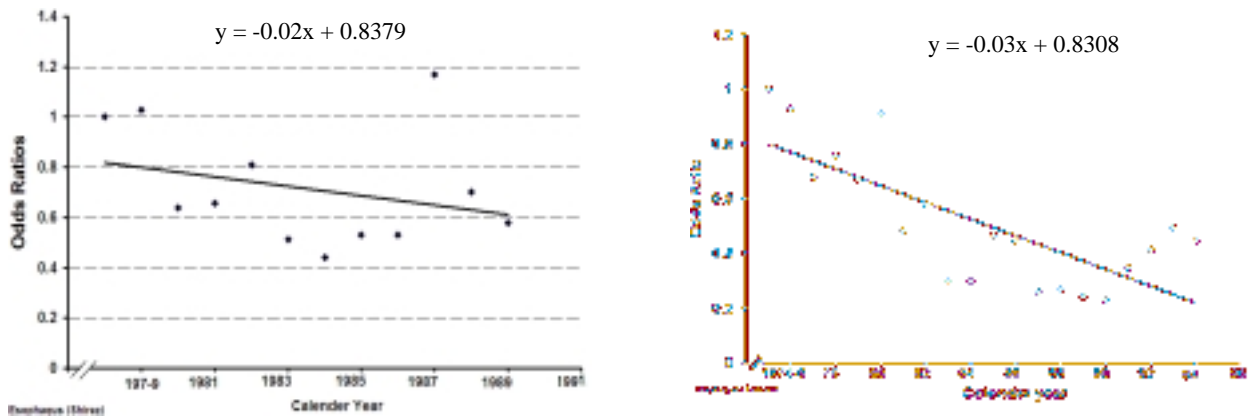


Figure 1. The distribution of MORs comparing each successive year with the first three years, the fitted regression line* showing overall trend of occurrence for esophageal cancer in Tehran and Shiraz.

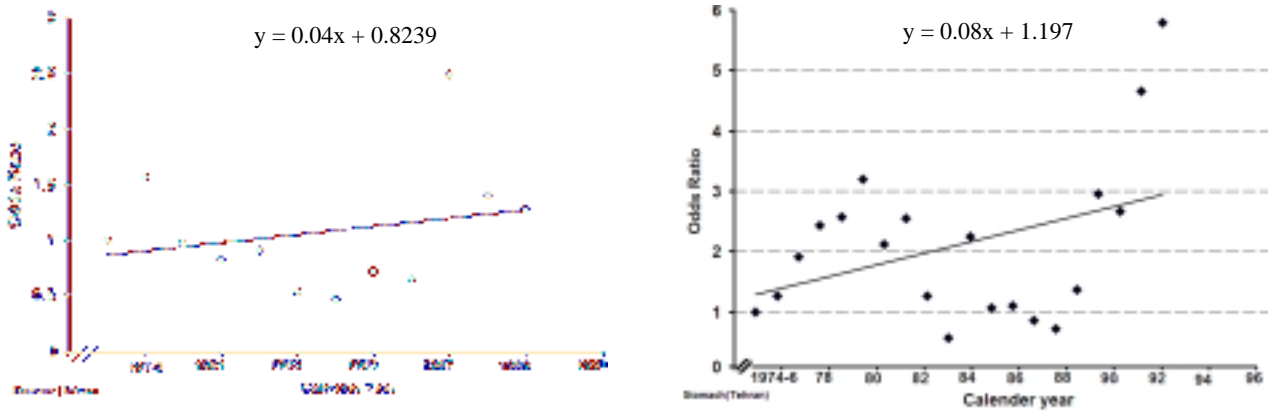


Figure 2. The distribution of MORs comparing each successive year with the first three years, the fitted regression line* showing overall trend of occurrence for stomach cancer in Tehran and Shiraz.

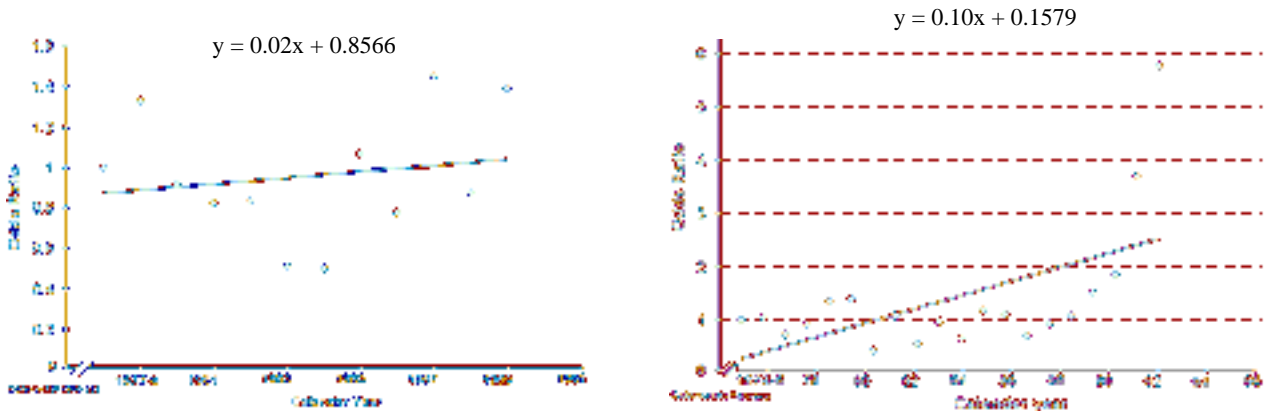


Figure 3. The distribution of MORs comparing each successive year with the first three years, the fitted regression line* showing over all trend of occurrence for colorectal cancer in Tehran and Shiraz.

Discussion

Our study demonstrated changes in occurrence of major GI cancers over last thirty years in Iran. After skin and breast, the cancers of upper GI are most frequent cancer in Iran; the incidence of esophageal cancer has been estimated 6.4 per 100,000 in Tehran population and 15.4 per 100,000 in Ardabil (a city located in north western part of Caspian

littoral) based on recent cancer registry reports (Alireza et al., 2003; Mohagheghi and Mosavi-Jarrahi, 1998). Time trend using incidence data has shown that since 1955, the incidence of esophageal cancer has decreased in Singapore, has been stable in Japan and increased in Male population of New Zealand (Coleman et al., 1993). In countries located in the “Asian esophageal cancer belt”, the incidence of esophageal cancer has decreased; the decrease has been

substantial in Central Asian republic of Karakalpakstan (Zaridze et al., 1992) and up to 50% in Shanghi (Zheng et al., 1993) and few percents in the Linxin China (Lu et al., 1985). Our study demonstrated decrease in the incidence of esophageal cancer consistent with the changes seen in the countries of esophageal belt. The reason behind these changes in incidence of esophageal cancer has been attributed to changes in environmental and life styles (Lee and Day, 1998). The same reason could have contributed to the decrease seen in Iran as major changes in social and behavioral life of Iranian has been happening in the last fifty years.

The Stomach Cancer currently is the most frequent cancer among males and second to breast cancer among females in Iran. Recent data (Alireza et al., 2003; Mohagheghi and Mosavi-Jarrahi, 1998) indicates moderate incidence (14.4 for males and 5.6 for female in 100,000 population) and more homogenous incidence through out the country with the exception of Ardabil province, where an high incidence (47 per 100000) has been reported (Alireza et al., 2003). The incidence of stomach cancer varies among different countries and ethnicities (as high as 85.4 cases per 100,000 population in Miagi Japan to 4 cases per 100,000 population in the Filipinos migrating to Los Angles, USA (Parkin et al., 1992). Studies on the time trend of stomach cancer in other countries have shown decrease in incidence over time, mainly, in developed countries (Muir and Nectoux, 1996). In countries of Japan, Chile, Netherlands, Canada, England, and USA, the mortality due to stomach cancer has decreased with varying degrees (Kurihara, 1979). Our study demonstrated a slight increase in the occurrence of stomach cancer. The increase in incidence of cardia gastric cancer has recently been reported in Iran (Yazdanbod et al., 2001). A high rate of stomach cancer has been attributed to high prevalence of helicobacter pylori as well as consumption of salted foods and food containing nitrous compound in the countries where the incidence of stomach cancer is high. Studies on the prevalence of *H. pylori* in Iran have shown 70-80% of general population is infected by *H. pylori* (Mikaeli et al., 2000). Our result of slight increase in the occurrence of stomach cancer over years is not consistent with the time trend seen in the incidence of stomach cancers in other countries of Asia where a decrease in incidence has been reported for most of the countries except Hiroshima district in Japan (Le Tran and Takesumi, 2002).

Colon cancer is one of the most frequent cancers of GI tract in several part of the world. Information on the incidence of colon cancer in Iran is coming from recently establish cancer registries; the Tehran cancer registry has estimated an incidence of 9.2 for male and 6.6 for female in 100,000 population (Mohagheghi and Mosavi-Jarrahi, 1998), and the Ardabil registry has estimated an incidence of 7.9 for male and 5.9 for female in 100,000 population (Alireza et al., 2003). Information on the time trend of colon cancer in several countries has shown an increase in incidence of colon cancer during last 40 years (Schottenfeild and Winawer, 1996). Our study demonstrated that colon

cancer in Iran has increased during last thirty years. The increase in incidence of colon cancer has been attributed to westernized lifestyle demonstrated by the observation of increase in the incidence of colon cancer among the immigrant to western countries (Muir and Nectoux, 1996). The behavioral and lifestyle changes may have contributed to the increase in occurrence of colon cancer in Iran as Iranian society has undergone major changes toward urbanization and western lifestyle in the last fifty years (Jalal-Shavazi et al., 2003).

To assess time trend in incidence of any disease, one needs to have the incidence in different time period to conclude about the magnitude and direction of changes occurring in the incidence. Accurate incidence information in cancer needs well funded registries to handle both case ascertainment and keep up with the rapid changes in their defined population. We used a novel method to address the needs of assessing trend in the absence of incidence rates. The use of mortality (or morbidity) odds ratio (MOR) as an alternative to proportional mortality (or morbidity) ratios (PMR) was recommended by Miettinen, 1981, to assess cancer risk in the absence of denominators (Miettinen and Wang, 1981). The MOR is less subject to "Borrowing factor bias" especially if an appropriate choice of control is chosen. In this study, the choice of control was childhood cancer. In fact, the increase or decrease in the occurrence of cancer of interest was examined in the assumption that no major changes in the occurrence of childhood cancer has occurred in the population and during the time period studied. There is no data to examine the validity of this assumption for our population. However, trend in the incidence of childhood cancer in the countries with reliable data on childhood cancer has shown little or no variation in the incidence of childhood cancer over time. The SEER data (Schottenfeild and Winawer, 1996) on the changes in the incidence of leukemia in five different geographic area of the United States from 1969 to 1989 has shown no major changes in incidence over time (42.3 cases per million in 1969 versus 43.5 cases in 1989). The same pattern has been observed for childhood lymphomas (12.2 cases per million in 1971 versus 16.4 cases per million in 1989), and Neuroblastoma (11.0 cases per million in 1971 versus 11.0 cases per million in 1989). A slight increase in the incidence of brain and CNS cancer has been observed in USA (25.6 cases per million in 1971 versus 32.8 cases per million in 1989) but the increase has been attributed to improvement in imaging technology available to the population in recent years (de Nully et al., 1989; Lantering et al., 1990). In the light of the fact that no major changes in the incidence of childhood cancer have been reported, the choice of control in our study further strengthen the validity of the methods used. Another possible explanation for our finding is that overtime, the advance of technology and better availability of treatment and diagnosis facilities may discriminately affect childhood and GI cancers causing a bias analog to the "barrowing effect bias" in PMR studies. The possibility for such a bias diminishes due to the consistency in result seen among different cancer sites and

centers.

In conclusion, our study demonstrated that during last thirty years the incidence of esophageal cancer has decreased, the rate of stomach cancer slightly increased and colon cancer incidence sharply increased in Iran.

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