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Original Article

Annual Trends of Gastrointestinal Cancers Mortality in Iran During 1990-2015; NASBOD Study

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Abstract

Background: Gastrointestinal (GI) neoplasms are among the most common cancers in Iran. This study aimed to measure annual trends in mortality rates from GI cancers in Iran between 1990 and 2015.

Methods: This study was part of an ongoing study termed the 'National and Subnational Burden of Diseases' study in Iran. Data used in this study was obtained from the Iranian Death Registration System (1995 to 2010) and from 2 major cemeteries in Tehran (1995 to 2010) and Isfahan (2007 to 2010). All-cause mortality rates were estimated using the spatio-temporal model and the Gaussian process regression model. Age-standardized mortality rates (ASMR) per 100 000 person-years was calculated using data from Iran and the standard world population for comparison.

Results: Among GI cancers, gastric cancer represented the leading cause of mortality followed by cancers of the esophagus, liver, and colorectal cancers with the ASMR of 20.5, 5.8, 4.4, and 4.0 per 100 000 persons-years, respectively, between 1990 and 2015. While a decreasing trend occurred in mortality of esophageal, gastric, and colorectal cancers, particularly in the recent decade, we recorded an upward pattern and steady rise in mortality rates from liver, pancreatic, and gallbladder cancers during the study period. The ASMR of all studied causes were enhanced by advancing age and were found to be more prominent in adults aged 50 or older. Among all age-groups, higher death rates were detected in males versus females for all studied cancers except for gallbladder and biliary tract cancers.

Conclusion: Gastric cancer mortality is still high and death rates from several other GI cancers are increasing in the nation. Interventions for cancer prevention, early detection, and access to high quality cancer treatment services are needed to reduce GI cancer burden and death rates in Iran and in the region.

Keywords: Epidemiology, Gastrointestinal neoplasms, Mortality rates, Trend

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Introduction

Gastrointestinal (GI) neoplasms are known as the most common group of cancers at the global level.[1] Overall, cancers of the liver, stomach, colon and rectum, esophagus, pancreas, and gallbladder were, respectively, the most common GI neoplasms and contributed to 37.0% all cancer deaths worldwide in 2012.[2-4] GI cancers are also common in Iran, accounting for 20 719 deaths and 38.8% of all cancer mortality in the country in 2012 with gastric cancer as the leading GI cause for cancer mortality followed by esophageal and colorectal neoplasms.[2]

To date, the overall or gender specific trends of mortality rates of GI cancers have not been studied in a systematic way in Iran. Although studies are available in the literature on the annual mortality rates of common GI cancers.[5-7] To the best of our knowledge, the annual linear trends of GI cancers by gender or age groups has not been comprehensively assessed yet. Therefore, as

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part of the National and Subnational Burden of Diseases (NASBOD) study, we aimed to study and illustrate trends in e Iranian mortality rates from common GI cancers and to compare rates by gender and age-groups at the national level over the last 25 years (1990–2015) in Iran. These data will help health policy makers to better formulate national priorities for interventions that focus resources on the prevention and early detection of GI cancers.

Materials and Methods

This study was part of the NASBOD study which was designed to estimate the burden of diseases in Iran from 1990 to 2015.[8] We estimated cause specific mortality rates and trends at the national level for liver and GI cancers between 1990 and 2015. For this purpose, we used data from the Iranian Death Registration System (DRS) which was established by Ministry of Health and Medical Education since 1995. Indeed, the main data source was the DRS data from 1995 to 2010. However, we added data from two major cemeteries in Iran (i.e., Behesht-e Zahra in Tehran from 1995 to 2010 and Bagh Rezvan in Isfahan from 2007 to 2010) to achieve full coverage as DRS data did not cover all locations. Although, cancer registry and hospital data were available for some periods of time, these data sources were excluded due to large number of data collection issues in their registration systems.

In this study, we corrected DRS data and estimated all-cause mortality rates using the spatio-temporal model and the Gaussian process regression model. Also, age-standardized mortality rates (ASMR) per 100 000 person-years were calculated using Iran's death registration system data and the standard world population for comparison.[9] Iran's national population in 2015 was applied for adjustments as the standard population. In the next step, all-cause mortality rates were divided into cause-specific rates using the respective cause fractions which were calculated for all age-sex groups in each year.[10] Finally, predicted values of the statistical model were presented as mortality rates for all years. With this approach, we adjusted mortality rates for all issues and biases in the death registration system. Similar measures have been taken and recommended by the Global Burden of Disease study team.[11] The International Classification of Diseases (ICD-10) code was used to identify cause of mortality in death certificates.[12] Subgroups for malignant neoplasms of the studied organs were as follows: esophagus (C15), stomach (C16), colon and rectum (C18–21), liver (C22), gallbladder and biliary tract cancer (C23), and pancreas (C25). We estimated liver cancer mortality rates due to hepatitis B, hepatitis C, alcohol use, and other causes separately. The study profile and analysis method has been described in details in previous articles.[10,13,14]

An annual percent change (APC) based on ASMR was applied to show the mortality trend for each cancer site. The APC was calculated by considering the ASMR of initial year (y1) and second year (y2) using this formula: ((y2-y1)/y1)*100. For those cancer sites with an increasing or decreasing mortality rate (i.e., cancers of stomach, liver, pancreas, and gallbladder), we calculated the mean APC for the entire study period (1990-2015). Nevertheless, if the mortality trends had an increase followed by a plateau or a decrease, the mean APC was estimated from the time when the rates started a continuous rise or decline. All analyses were done by the software STATA/MP, v.13.0 and graphs were illustrated by R statistical software, v.3.1.3.[15]

Results

There was a total of 615 602 deaths at the national level associated with malignant GI neoplasms in the period 1990–2015. Overall, 334 160 gastric, 93 809 esophageal, 83 953 liver, 64 485 colorectal, 28 088 pancreatic cancer, and 11 107 gallbladder-related deaths were reported during the study period in Iran (Table 1). The ASMR of all studied causes were significantly enhanced by advancing age and were more prominent in adults aged 50 or older in the period 1990-2015 (Table 1). Among all age-groups, higher rates of deaths were detected in males as compared with females for all studied GI cancers except for gallbladder and biliary tract cancers. In young males and females (<50 years), we recorded greater ASMR for cancers of the stomach, esophagus, colon and the rectum versus other GI cancers in the same age group (Table 2).

The annual mortality trend between 1990 and 2015 for the leading GI cancers are presented in Figure 1. A decreasing trend was observed in ASMR of esophageal cancer, gastric cancer, and colorectal cancer, respectively since 1995, 2000, and 2003 (Figure 1). On the other hand, our data revealed an upward pattern in mortality rates of liver cancer, pancreatic cancer, and gallbladder cancer in both genders during the study period (Figure 1). The overall and gender-specific APC of mortality attributed to each cancer site were illustrated in Figures 2-4.

Gastric Cancer and Esophageal Cancer

Gastric cancer represented the leading cause of mortality with an ASMR of 20.5 per 100 000 persons-years between 1990 and 2015 (Table 1). The overall ASMR of gastric cancer after a steady increase between 1990 and 1996 remained relatively constant until a peak was recorded in 1999 and then a continuous decline was observed reaching an ASMR of 10.3 per 100 000 persons in the year 2015 (Figure 1). A similar pattern was almost seen for gender specific ASMR of gastric cancer although

Table 1. Death Number and Age-Standardized Mortality Rates* by Cancer Site and Age Groups in Iran during 1990–2015

	Stomach (n = 334160)	Esophagus (n = 93809)	Liver (n = 83953)	Colorectal (n = 64485)	Pancreas (n = 28088)	Gallbladder (n = 11107)
<40 y	1.4 (1.0–2.0)	0.5 (0.3–0.8)	0.9 (0.7–1.2)	0.7 (0.5–1.0)	0.1 (0.03–0.2)	0.1 (0.03–0.1)
40-49 y	6.6 (4.7–9.2)	2.3 (1.5–3.7)	2.7 (2.0–3.6)	2.3 (1.6–3.3)	0.9 (0.5–1.7)	0.3 (0.2–0.4)
50-59 y	20.8 (15.0–28.7)	6.4 (4.1–10.2)	6.4 (4.8–8.5)	5.3 (3.8–7.5)	2.9 (1.6–5.2)	0.7 (0.6–1.2)
60-69 y	64.4 (46.7–88.6)	18.1 (11.6–28.7)	15.2 (11.5–20.1)	11.6 (8.3–6.3)	6.1 (3.5–10.7)	2.3 (1.7–3.2)
70-79 y	185.0 (134.9–254.6)	48.7 (31.2–76.9)	36.3 (27.7–47.6)	28.3 (20.5–39.1)	13.0 (7.7–21.9)	5.3 (3.9–7.3)
≥80 y	324.0 (235.4–445.2)	85.6 (54.9–135.0)	60.3 (46.0–79.2)	46.6 (33.9–64.4)	20.0 (12.0–33.3)	9.6 (7.0–13.1)
All ages	20.5 (14.9–28.2)	5.8 (3.7–9.1)	4.4 (3.3–5.8)	4.0 (2.8–5.6)	1.7 (1.0–3.0)	0.7 (0.5–0.9)

*Age-standardized mortality rates per 100 000 persons-years with 95% CI.

males have had significantly higher mortality rates than females throughout the study period (Table 2, Figure 1). The annual decline in gastric cancer mortality was 1.8% (95% CI: 1.7–1.9%) from 1990 to 2015 (Figure 2), with greater annual decline among females versus males (Figures 3 and 4).

Esophageal cancer, with an overall ASMR of 5.8 per 100 000 persons-years (Table 1), had the highest increase in mortality between 1990 and 1995 from 5.6 to 7.9 per 100 000 persons and then slowly started a steady decrease staying at the lowest rate (2.3 per 100 000 persons) in 2015 (Figure 1). A similar pattern was monitored in both genders, yet males had relatively higher mortality rates within the study timeframe (Table 2, Figure 1). For the entire study period, we recorded 3.3% (95% CI: 3.1–3.5%) decrease in mortality of esophageal cancer every year. However, mortality of esophageal cancer had marked declines (5.6%; 95% CI: 5.5–5.8%) annually from 1995 to 2015 (Figures 2-4). Despite the observed declining pattern for cancers of the stomach and esophagus in the nation, we detected significantly higher mortality rates for these cancers in the North and Northwestern Iran, compared to South of Iran, during 1990-2015 (Data not shown).

Colorectal Cancer

As shown in Table 1, colorectal cancer had an ASMR of 4.0 per 100 000 persons-years between 1990 and 2015 (Table 1). An increasing linear trend in the overall mortality of colorectal cancer was recorded between 1990 and 1995 which was followed by a relatively stable pattern until 1999. There was a significant rise in the ASMR of colorectal cancers in 2000 with a break point in 2003, and then a downward trend occurred reaching

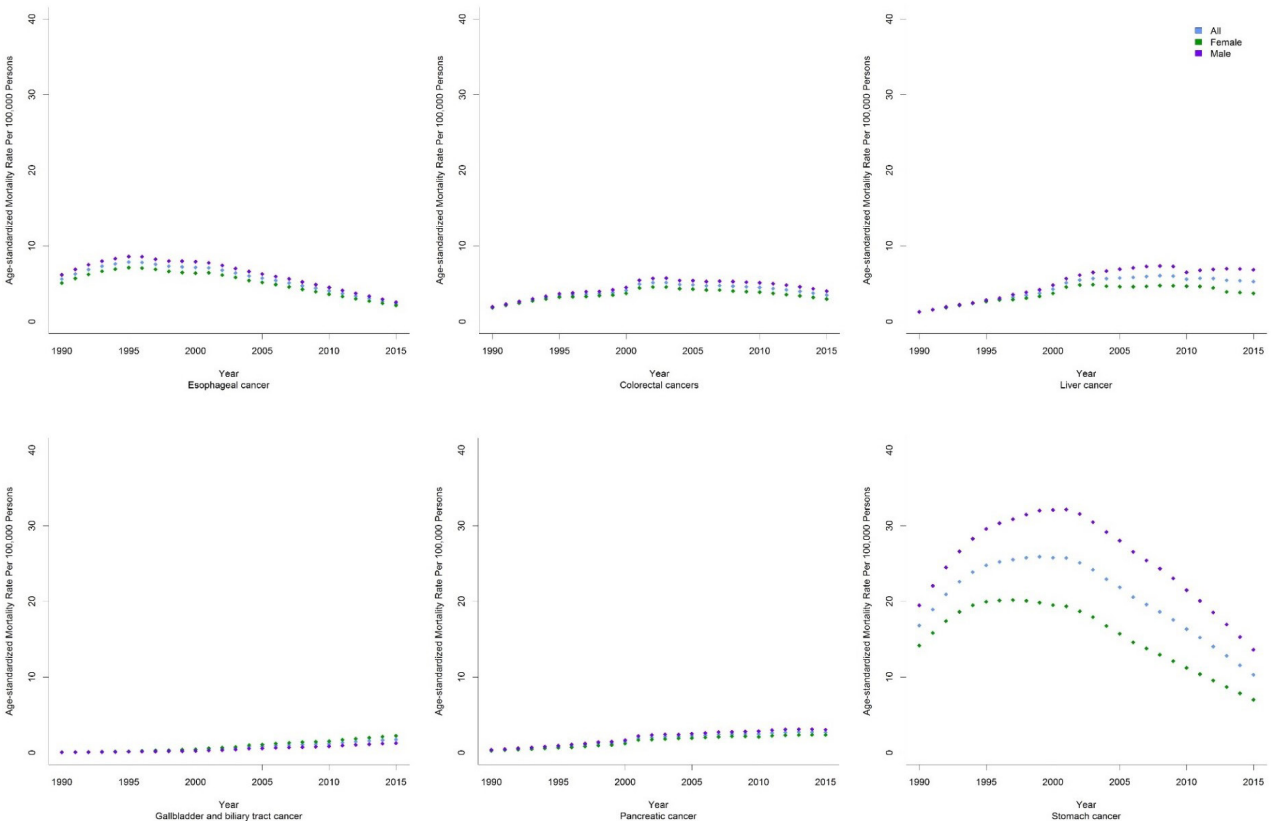

Figure 1. Age-Standardized Mortality Rates of Gastrointestinal Cancers, Overall and by Gender in Iran During 1990–2015.

Table 2. Death Number and Age-Standardized Mortality Rates* by Gender and Age Group in Iran During 1990-2015

	Stomach		Esophagus		Liver		Colorectal		Pancreas		Gallbladder	
	M (n = 207921)	F (n = 126239)	M (n = 51384)	F (n = 42425)	M (n = 49085)	F (n = 34868)	M (n = 35673)	F (n = 28812)	M (n = 16054)	F (n = 12034)	M (n = 3893)	F (n = 7214)
<40 y	1.8 (1.3–2.5)	0.1 (0.7–1.4)	0.6 (0.4–1.0)	0.4 (0.2–0.6)	1.1 (0.8–1.4)	0.7 (0.5–0.9)	0.8 (0.6–1.2)	0.6 (0.4–0.8)	0.1 (0.04–0.2)	0.1 (0.02–0.1)	0.1 (0.03–0.1)	0.1 (0.04–0.1)
40–49 y	8.7 (6.2–12.2)	4.5 (3.3–6.1)	2.7 (1.7–4.4)	1.9 (1.2–2.9)	3.24 (2.4–4.3)	2.1 (1.6–2.8)	2.7 (1.9–3.8)	1.9 (1.3–2.8)	1.2 (0.7–2.1)	0.6 (0.3–1.3)	0.3 (0.2–0.4)	0.4 (0.3–0.5)
50–59 y	27.3 (19.5–38.1)	14.3 (10.6-19.4)	7.2 (4.5–11.8)	5.6 (3.7–8.6)	7.6 (5.7–10.2)	5.07 (3.8–6.8)	5.8 (4.1–8.3)	4.8 (3.4–6.8)	3.3 (1.9–5.6)	2.5 (1.3–4.9)	0.6 (0.4–0.9)	1.1 (0.8–1.5)
60–69 y	86.0 (61.7–119.5)	46.7 (34.4–63.3)	19.9 (12.3–32.6)	16.6 (10.9–25.4)	18.8 (14.2–24.8)	12.3 (9.3–16.3)	13.2 (9.4–18.6)	10.3 (7.4–14.3)	7.0 (4.2–11.8)	5.4 (3.0–9.7)	1.6 (1.1–2.3)	2.9 (2.1–4.0)
70–79 y	240.0 (173.2–332.4)	133.0 (98.4-180.0)	54.9 (34.2–89.1)	42.9 (28.4–65.3)	44.4 (33.9–58.2)	28.6 (21.7–37.5)	32.9 (23.8–45.7)	23.9 (17.4–32.9)	15.8 (9.6–26.2)	10.3 (56.0-17.7)	4.2 (3.0–5.9)	6.3 (4.7–8.6)
≥80 y	400.0 (288.2–554.4)	253.0 (186.2–343.4)	98.1 (61.3–158.6)	74.0 (48.9–113.0)	70.1 (53.5–92.1)	51.2 (39.0–67.2)	51.4 (37.2–71.3)	42.1 (30.7–58.0)	23.3 (13.3–38.3)	16.9 (10.0–28.8)	5.7 (4.0–7.9)	13.2 (9.7–17.9)
All ages	25.5 (18.4–35.5)	15.5 (11.4–21.0)	6.3 (3.9–10.3)	5.2 (3.4–7.9)	5.1 (3.9–6.8)	3.7 (2.8–4.8)	4.4 (3.1–6.2)	3.5 (2.5–5.0)	2.0 (1.2–3.3)	1.5 (0.8–2.7)	0.5 (0.3–0.7)	0.9 (0.6–1.2)

* Age-standardized mortality rates per 100 000 persons-years with 95% CI; M, male; F, female.

an ASMR of 3.5 per 100 000 persons in 2015 (Figure 1). The mortality rates in males and females followed the same trend, however, males had higher rates in the entire study period compared to females and these differences became more prominent in particular after the year 1996 (Table 2, Figure 1). The mean APC of colorectal cancer death showed that the mortality rate was rising at 2.8% (95% CI: 2.7–2.9%) per year from 1990-2015. However, the trend was declining at a constant APC (2.8%, 95% CI: 2.7–23.0%) per year since 2004 (Figure 2). The annual decline in the cancer death rates was higher among females than in males (Figures 3 and 4).

Pancreatic Cancer and Gallbladder Cancer

The overall ASMR of pancreatic cancer was 1.7 per 100 000 persons-years, between 1990 and 2015 (Table 1). The ASMR have been trending upward from 0.3 per 100 000 persons in 1990 to 2.7 per 100 000 persons in

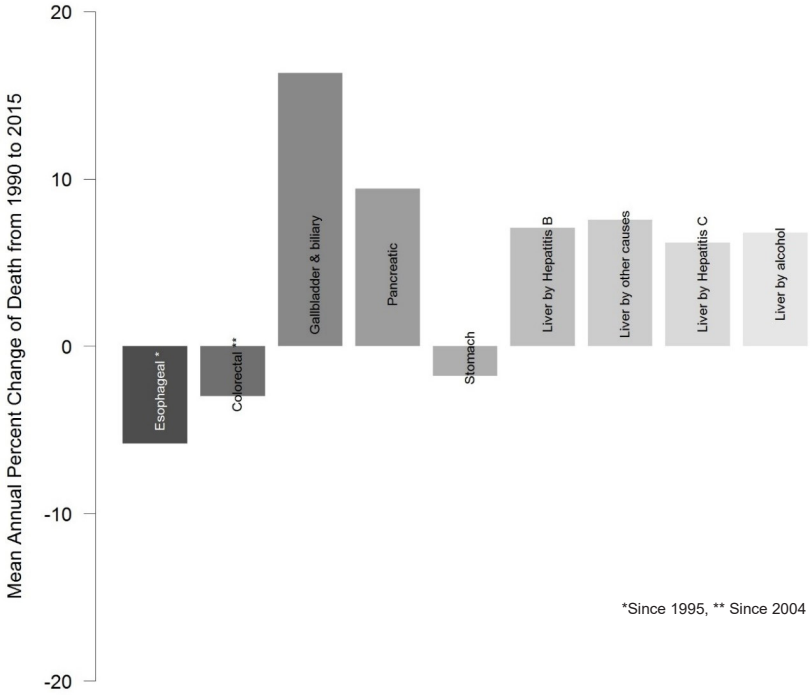

Figure 2. Mean Annual Percent Change of Gastrointestinal Cancers Mortality in Iran From 1990 to 2015.

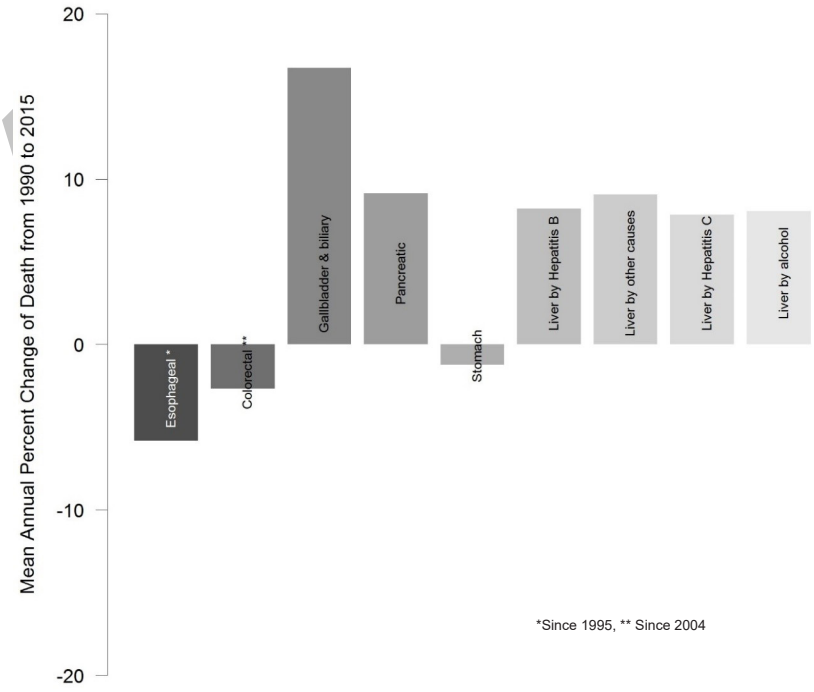

Figure 3. Mean Annual Percent Change of Gastrointestinal Cancers Mortality in Iranian Males From 1990 to 2015.

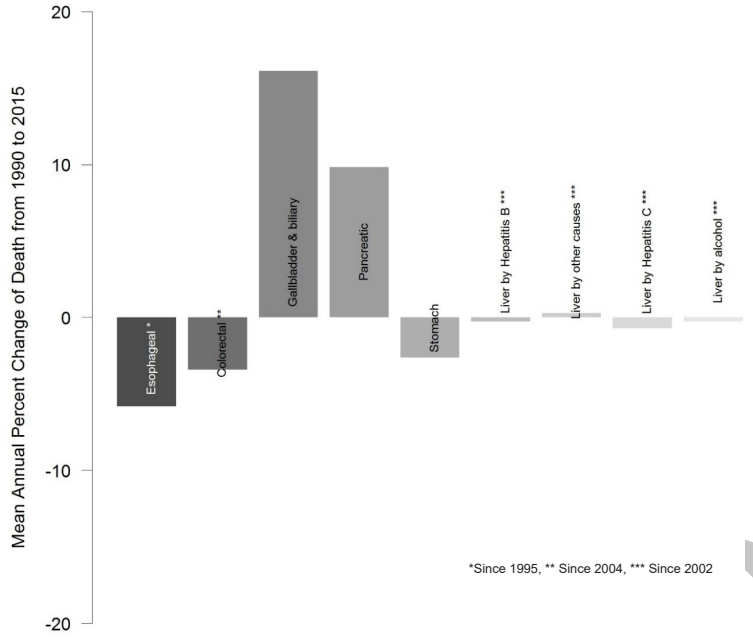

Figure 4. Mean Annual Percent Change of Gastrointestinal Cancers in Iranian Females From 1990 to 2015.

2013, a 9-fold absolute rise although a very slight decline was seen in 2010. However, the mortality rates remained relatively stable or slightly declined during the past few years, since 2013. The same trend was true for gender specific rates, with higher mortality in males compared to females (Table 2, Figure 1). As such, pancreatic cancer mortality increased at a mean annual rate of 9.4% (95% CI: 9.0–9.8%) per year from 1990 to 2015 (Figure 2). Throughout the period 1990-2015, the overall ASMR of gallbladder and biliary tract cancer has been increasing annually indicating a steep slope since the year 2000. Very similar pattern was recorded for gender-specific trends with higher rates in females than in males (Figure 1). Likewise, the mean APC of gallbladder and biliary tract cancer was 16.3% (95% CI: 15.9–16.7%) from 1990 to 2015 (Figure 2).

Liver Cancer

The overall ASMR of liver cancer was 4.4 per 100 000 persons-years during 1990 and 2015 (Table 1). The ASMR showed a constant annual increase until the year 1999 and then steeply increased until 2002 which almost leveled off thereafter until the year 2009. The ASMR attributable to liver cancer in 2010 declined and then slightly increased until the year 2012 which started slowly declining thereafter until 2015 (Figure 1). Gender specific time trend for liver cancer mortality was almost the same as the overall trend of the disease. As expected, males have had greater mortality rate during the study period particularly since 1997 which kept its upward trend until a peak in 2008 and then started declining to reach 6.9 per 100 000 persons in the year 2015. Of note, the declining pattern in females started more earlier in 2003 which was followed by a stable or downward pattern until 2015 (Figure 1). Indeed, the overall mortality showed remarkable rise per year (7.6%, 95% CI: 7.4–7.7%) from 1990 to 2015 (Figure 2).

Discussion

During the past decades, the overall mortality for gastric cancer has steadily dropped in many countries of the world and in Asia.[16,17] The same declining pattern was detected in our series which was in line with previous data from the nation.[7] The declines in the annual mortality of GI cancers, in general, can be explained by access to care or preventive services or changes in the exposure to the known risk factors.[16] Gastric cancer is associated with several risk factors such as *Helicobacter pylori* infection[17,18] and consumption of salt[19-21] or salt-preserved or nitrous containing foods.[17] Previous data have shown that about 80% of general population in Iran is infected by *Helicobacter,*[22] whereas in some Asian countries, such as Korea, the prevalence of *H. pylori* has had a decreasing trend in particular among younger birth cohorts.[23,24] However, changes in *Helicobacter* infection patterns among younger people due to the favorable hygienic conditions along with possible improvements in the nutrition[17,25] may have contributed to the downward trends in the mortality rates in Iran since 2000. Despite the desirable declines in the mortality rates, gastric cancer still represents the second leading cause of overall cancer death after breast cancer in Iran.[26] Moreover, we found that the mortality of gastric cancer was greater in males and older ages, comparable to other data.[27,28] Despite reductions in gastric cancer mortality among screened individuals, the method of screening, target

group, and start age for screening remain controversial.[16] We therefore suggest risk stratification approaches to target high-risk individuals in order to offer appropriate screening methods and control the burden of the disease in the nation.

In line with the global pattern,[16,29,30] we recorded a steeply decreasing slope for mortality from esophageal cancer in Iran since 1995. The declining trends might be attributed to changes in the environment and life style of Iranians and new advances in treatments in the recent decades.[6] However, we detected marked disparities in the mortality rates of cancer in the North (i.e., Golestan) and Northwest (i.e., Ardebil) versus South of Iran throughout the study period, which was in line with the previously published data.[31,32] Possible factors involving in these variations which have been suggested through other studies included drinking unpiped water, food preparation methods,[33] drinking hot tea, smoking, and opium use[34,35] in the North of Iran. Long term studies, however, are needed to identify the reasons behind the disparities in the mortality of esophageal cancer in the nation.

Colorectal cancer accounts for more than half of all GI cancer diagnoses and a third of GI cancer-related deaths.[16,36] Asian countries like Iran are witnessing an increase in the incidence of colorectal cancer during the last decades possibly due to aging population, urbanization, and increased prevalence of westernized lifestyle risk factors such as alcohol consumption, obesity, smoking, and unhealthy diet.[6,37,38] Despite increase in the mortality rates of colorectal cancer during the period 1990–2004, we recorded significant steady declines in the cancer mortality rates in males and females during the recent decade. Similar declining pattern in colorectal cancer death has happened in the globe and even in Asian countries.[39-42] According to data from the United States, several factors have contributed in the decrease in colorectal cancer mortality in the period 1975-2000 such as change in colorectal cancer risk factors, screening for colorectal cancer, and advanced treatments which respectively explained 35%, 53%, and 12% of the decline in the disease death.[43] As such, studies from Spain[44] and six European countries[40] suggested decreasing trends in colorectal cancer mortality possibly due to enhanced access to screening colonoscopy and early stage detection, new advances in treatments, and decrease of the modifiable risk factors.[42,45] In Iran there is no national screening program for colorectal cancer and the opportunistic screening is available with very low utilization.[46,47] This implies that reasons other than screening may contribute to the reduction in colorectal cancer death such as increased colonic polyp removal,[48] newer therapeutic and surgical methods,[49] regular use of aspirin,[50] or hormone replacement therapy,[51] or possibly healthy dietary patterns.[52] Nevertheless, the current increasing trends on the prevalence of smoking,[53] sedentary life style, and obesity[54] in Iran claim against sustained healthy lifestyle changes. Further studies therefore are needed to explore factors associated with the decrease in mortality from colorectal cancer in the recent decades despite the increasing incidence of the cancer in Iran.

The highest incidence and mortality rates of pancreatic cancer were reported from developed countries.[55] Over the past few decades, there have been no substantial advances in the treatment of pancreatic cancer, which is usually diagnosed in the advanced stages due to the natural history and the lack of screening tests.[55,56] Pancreatic cancer is less common in Iran in both males and females with mortality rates equaling incidence.[57] Our study revealed significant increases in the mortality of this neoplasm during the last two decades, which fits well with the patterns reported from Southern Europe and North East Asia.[56,58,59] Indeed, different parts of the world are witnessing rise and fall trends in the pancreatic cancer-related mortality, possibly due to use of various diagnostic methods, e.g., CT-guided or EUS-guided biopsy. Moreover, tobacco smoking as an important risk factor for pancreatic cancer is likely to explain some of the international and gender specific differences.[55,56] The age-standardized prevalence of cigarette smoking among Iranian adult males was 22.4% in 2013.[53] This probably gives some insights indicating that smoking along with other risk factors such as advancing age might account for the increasing mortality rates due to pancreatic cancer in Iranian males. However, the reason for increasing mortality due to pancreatic cancer among Iranian females are not well understood. The very low prevalence (0.9%) of smoking in Iranian females[53] suggests that causes other than tobacco may be involved. Indeed, the incidence of pancreatic cancer and cholangiocarcinoma is increasing in Iran similar to many other developing countries, and this might be the major reason for increasing mortality from these 2 cancers. Further in-depth investigations would be required to see whether the results we have observed are true.

The mortality of gallbladder cancer had an upward slope during the period 1990–2015 with significantly higher rates in females than in males. Gallbladder cancer is relatively rare and differs from other GI tract cancers as being significantly more common in females than in males.[60] Due to non-specific symptoms or signs of this neoplasm, the prognosis is poor and often is diagnosed late at advanced stages.[61] However, preventive interventions, e.g., obesity and diabetes control along with laparoscopic cholecystectomy and current advancements

in noninvasive diagnostic techniques for better detection of gallstones (e.g., endoscopic ultrasonography) contributed to substantial reductions in the incidence and mortality of gallbladder cancer, worldwide.[62,63] Hence, the increasing mortality rates of gallbladder cancer in Iran may be due to higher prevalence of diabetes or obesity, improved diagnosis and reporting of the disease, or inadequate access to cholecystectomy procedures in the country. These findings and risk factors regarding gallbladder cancer in particular among Iranian females need to be studied in-depth.

Worldwide, liver cancer represents a major cause of cancer death[16] with almost similar incidence and mortality rates due to its poor prognosis.[64,65] Our data showed that the disease, though highly fatal, is less common and contributed to a relatively smaller mortality rates compared to the other GI cancers. In contrast to upper GI cancers and colorectal cancer, during the study period the mortality rates of liver cancer have been increasing between 1990 and 2008 and then started to decline. This is comparable with the previously published data[7] which confirmed a significant rise in the mortality of liver cancer in Iranians males (88%) and females (103%). However, our rates still remain significantly lower than those reported from the East Mediterranean region in 2012.[66] These international differences can be largely explained by the widespread distribution of vaccination against hepatitis B virus and hepatitis C virus which respectively accounted for 53% and 25% of the total mortality from liver cancer globally.[64,65] Indeed, prevention and control of chronic hepatitis B and C would combat the current trends in the incidence and mortality of liver cancer,[67] which is possible through increasing the coverage of hepatitis B immunization in infants, harm reduction, injection and blood safety, and by enhancing treatment rate for hepatitis B and C.[16,68-70] In Iran, hepatitis B and hepatitis C are the main etiology of liver cancer while alcohol consumption and metabolic disorders are less common.[71] This is possibly due to the fact that the majority of Iranian adults were born before the implementation of national hepatitis B vaccination for neonates in 1994.[68] However, in coming decades we expect more reduction in liver cancer mortality as an impact of widespread hepatitis B vaccination which has reached a coverage of over 98% in infants in 2015.[72,73] On the other hand, non-alcoholic fatty liver disease as a major cause of cirrhosis and liver cancer is the most common liver disease in Iran,[74,75] which might partly explain the increasing death rates for liver cancer in Iran and calls for public health strategies and serious actions at population level.[72]

This study has covered a large scale using very comprehensive information. However, it suffers from few shortcomings given possible inconsistencies in cancer diagnosis and under-reporting or incompleteness in our death registry system. On the other hand, the proportion of known diagnosis versus unidentified causes of death has been increased overtime. These might have contributed, in part, to the observed increases in some GI cancer death rates. Therefore, the current results, particularly data of liver cancer mortality, should be interpreted with caution. Indeed, most of liver cancers are metastatic and the site of origin is mainly GI tract, but in clinical practice may be considered as primary hepatocellular caner when liver biopsies is not attempted or not possible and this is not usually specified in the death certifications. More details about the NASBOD study's limitations and strengths have been mentioned elsewhere.[10]

In conclusion, the current data indicated that overall mortality rate from GI cancers was particularly high although mortality due to cancers of the esophagus, stomach, colon, and rectum has been declining in the recent decade. We also detected annual increases in mortality rate from cancers of liver, pancreas, and gallbladder and biliary tract throughout the period 1990–2015. Therefore, we suggest preventive interventions and early stage detection of these malignancies which eventually would decline mortality. Indeed, effective health strategies should consider lifestyle modification (e.g., obesity, physical activity, smoking, alcohol consumption, etc.) and better access to high quality cancer screening and treatment services in the Iranian population.

Authors' Contribution

General design of study: HS, AD, FK, NR, MM, RS, MC, HZ, FF, RM; Analysis of data and designing of graphs: FD, NeR, AS, KG, NaR; Interpretation of data: HS, CS; Writing primary draft: HS; Manuscript critical revision: CS, AD, FF, RM.

Conflict of Interest Disclosures

The authors have no conflicts of interest.

Ethical Statement

The ethical committee of Tehran University of Medical Sciences declared ethical approval for the current study..

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