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Original Article

The Trend of Years of Life Lost due to Gastrointestinal Cancers in Fars (Iran) 2004-2019

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Abstract

Background: Gastrointestinal cancers can cause major health problems globally since their burden is increasing in many countries. We aimed to investigate the trend of years of life lost due to gastrointestinal cancers in Fars Province, southern Iran during the 2004-2019.

Methods: In this cross-sectional survey study, we obtained the information regarding all deaths due to gastrointestinal cancers in Fars Province from the electronic population-based death registration system (EDRS). Years of Life Lost **(**YLL) was calculated using the YLL template of 2015 by the WHO. To examine the trend for different years, join point regression based on the log-linear model was used. Joinpoint regression analysis describes changing trends over successive periods of time and the increasing or decreasing rate within each period.

Results: During the years of 2004-2019, 9742 deaths due to gastrointestinal cancers occurred in Fars Province. 6013 (61.72%) cases were male and 3729 (38.28%) cases were female (Male / Female Sex Ratio: 1.61). Overall, 4152 cases (42.63%) were due to gastric cancer and 2112 cases (21.68%) were due to liver cancer. Total years of life lost due to premature death from gastrointestinal cancers during the 16-year study period was 73565 yr (2.33 per 1000 persons) in men, 52766 yr (1.71 per 1000 persons) in women, and 126331 yr (2.02 per 1000 persons) in both sexes.

Conclusion: Among all cancers, the highest mortality rates in both sexes belong to gastric cancer. This study showed the trend of YLL rate of malignant neoplasms of liver and intrahepatic bile ducts, esophagus, oral cavity, and colon cancer were increasing in both sexes, however, the trend of YLL rate for malignant neoplasms of the small intestine was decreasing in both sexes. Variation of GI cancers patterns and trends around the Fars Province indicated that a more comprehensive control plan is needed to control these variations.

Keywords: Gastrointestinal; Cancer; Years of life lost; Iran; Joinpoint regression

Introduction

Cancer is one of the leading causes of death and disability in the world. Gastrointestinal cancers can cause major health problems globally since their burden is increasing in many countries (1). Gastric, esophageal, and colorectal cancers are the most common gastrointestinal tract cancers and some of the leading causes of cancer-related deaths in the world (2). Gastrointestinal cancers are estimated to be responsible for one-third of all cases of dementia in developing countries (3).
Gastrointestinal cancers have poor prognoses due to being asymptomatic in the early stages and being diagnosed in the advanced stages of the disease(4). According to Iranian Ministry of Health, cancer is the third leading cause of death in Iran (5). Gastrointestinal cancers are some of the most important cancers in Iran because they cause more than 60% of cancer deaths. Along with the sedentary lifestyle and rapid economic development, many developing countries, such as Iran, will experience an increased incidence of gastrointestinal cancers (6). They have important socio-economic effects on the population.
Premature death is one of the indicators used to evaluate screening programs, early detection, and prognostic factors. It also plays an important role in making decisions related to community health (7). During the past years, very good information was provided about the epidemiology and burden of cancer in different regions of Iran, the purpose of which was to study the trend of cancer in different regions of Iran and design strategic plans for the healthcare system(8). The Years of Life Lost is an essential criterion for ranking society's health status and evaluating its challenges. Based on the WHO report, the value of one year of life is three times more than the gross domestic product of each country (9).
Due to the lack of research on the trend of premature death due to gastrointestinal cancers in Fars Province, this study was conducted to investigate the trend of years of life lost due to gastrointestinal cancers in Fars Province during the past 16 years.

Material and Methods

In this cross-sectional survey study, we obtained the information (2004-2019) regarding all deaths due to gastrointestinal cancers in Fars Province from the electronic population-based death registration system (EDRS) from the Statistics Unit of Health Vice-Chancellor of Shiraz University of Medical Sciences. Fars Province is located in the southwest of Iran and has an area of 122,400 square kilometers with more than 4 million population (10). The extracted data in this study included various types of gastrointestinal cancers, including cancers of the stomach, esophagus, liver, pancreas, mouth, rectum, colon, and small intestine. Causes of death were coded using the 10th edition of the International Classification of Diseases (ICD-10). Relevant codes for causes of death in this study included lip, mouth, and throat cancer (COO-C14), esophageal cancer (C15), stomach cancer (C16), liver and biliary tract cancer (C22-C24), pancreatic cancer (C25), small bowel cancer (C17), colon cancer (C18), and rectal and recto sigmoid cancer (C19-C21).
To assess the rate of mortality due to gastrointestinal cancers, we used the information of national census of the population from 1996 to 2016 and estimated the population of each year based on annual growth for the rest of the years. We used the 2013 standard population for low- and middle-income countries to calculate the Age-Standardized Mortality Rate (ASMR) of the gastrointestinal cancers.
To calculate the YLL, the life expectancy of different age and sex groups were used using the standard life tables. Moreover, the number of deaths due to gastrointestinal cancers in each age and sex group were extracted. Finally, YLL was calculated using the following formula (11).

$$YLL = N\,Ce^{(ra)} / (\beta+r)^2\,[e^{-(\beta+r)(L+a)}[-(\beta+r)(L+a)-1] - e^{-(\beta+r)a}[-(\beta+r)a-1]]$$

Where N is the number of deaths at a certain age and sex, L is the standard life expectancy of the age and sex group of the deceased, r is discount-

ing rate, which is equal to 0.03, β is a constant value used in calculating the age value, which is equal to 0.04, C is a modified constant value equal to 0.1658 and the value of different ages is estimated with these two numbers, and also a is the age at which death occurred and e is fixed and equal to 2.71.

The analysis of the number of years of life lost due to premature death caused by gastrointestinal cancers was performed using the YLL template of 2015 by the WHO in Excel version page spreader software 2016. To examine the trend for different years, join point regression based on the log-linear model was used. Joinpoint regression analysis describes changing trends over successive periods of time and the increasing or decreasing rate within each period. The resulting line segment between join points is described by the annual percent change (APC) that is based on the slope of the line segment and the average annual percent change (AAPC). The analysis for the trend was carried out by Joinpoint Regression Program 4.9.0.0. A *P*-value of <0.05 was considered statistically significant.

Results

During the years of 2004-2019, 9742 deaths due to gastrointestinal cancers occurred in Fars Province. 6013 (61.72%) cases were male and 3729 (38.28%) cases were female (Male / Female Sex Ratio: 1.61). 4152 cases (42.63%) were due to gastric cancer and 2112 cases (21.68%) were due to liver cancer. The highest mortality rates in both sexes were caused by gastric cancer (8.67 and 4.62 per 100,000 population in men and women, respectively). The lowest death rate in both sexes was related to rectal cancer (Table 1).

Table 1: crude and Age-standardized mortality rates (per 100,000 population) stratified by sex and gastrointestinal cancers in Fars (Iran) during 2004-2019

Cancer	*Number of death*			*Crude mortality rate (per 1000 00persons)*			*Age –standardized mortality rate (95% CI)*		
	Male	Female	Total	Male	Female	Total	Male	Female	Total
Gastric cancer	2730	1422	4152	8.67	4.62	6.67	9.83 (9.51-10.16)	5.16 (4.92-5.40)	7.51 (7.31-7.72)
Liver cancer	1178	934	2112	3.74	3.03	3.39	4.26 (4.05-4.48)	3.43 (3.23-3.62)	3.85 (3.70-3.99)
Colon cancer	838	586	1424	2.66	1.90	2.28	2.98 (2.80-3.16)	2.08 (1.93-2.24)	2.53 (2.42-2.65)
Pancreatic cancer	577	361	938	1.83	1.17	1.50	2.10 (1.95-2.25)	1.35 (1.23-1.47)	1.73 (1.63-1.83)
Esophageal cancer	308	160	468	0.97	0.51	0.75	1.11 (1.00-1.22)	0.59 (0.51-0.67)	0.85 (0.78-0.92)
Small bowl cancer	186	129	315	0.59	0.41	0.50	0.62 (0.54-0.71)	0.46 (0.38-0.53)	0.54 (0.48-0.60)
Cancer of the lips, mouth and throat	103	86	189	0.32	0.26	0.29	0.36 (0.29-0.42)	0.29 (0.23-0.35)	0.32 (0.28-0.37)
Rectal cancer	93	51	144	0.29	0.16	0.23	0.32 (0.26-0.38)	0.18 (0.13-0.22)	0.25 (0.21-0.29)
Total	6013	3729	9742	19.10	12.10	15.64	21.62 (21.13-22.10)	13.57 (13.18-13.96)	17.62 (17.31-17.93)

Total years of life lost due to premature death from gastrointestinal cancers during the 16-year study period was 73565 yr (2.33 per 1000 persons) in men, 52766 yr (1.71 per 1000 persons) in women, and 126331 yr (2.02 per 1000 persons) in both sexes. Among gastrointestinal cancers, the most yr of life lost due to premature death were due to gastric cancer (52426 yr, 0.84 per 1000) (Tables 2 and 3). The highest years of life lost due to premature death occurred the age groups of 50-64 yr and 79-65 yr; moreover, the lowest rate was seen in the under-20 age group (Fig. 1).

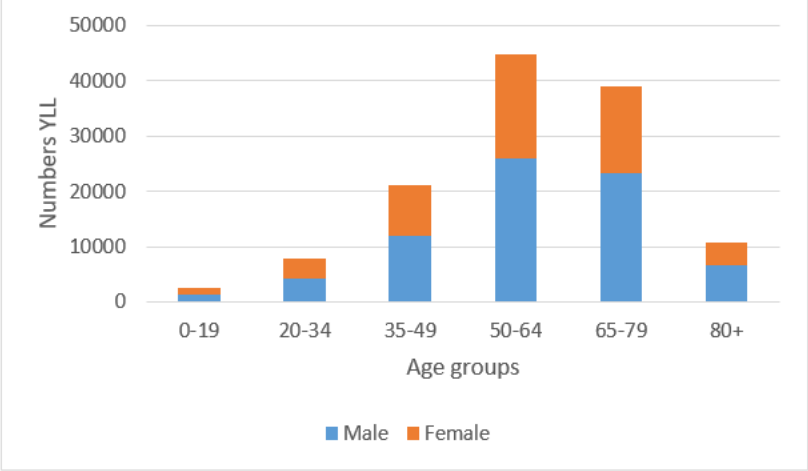

Fig. 1: Years of life lost due to premature mortality, stratified by gender and age groups.

According to the join point regression analysis, the 16-year trend of YLL rate due to premature mortality was increasing: the APC was 3.1% (95% CI 2.2-4.0, *P*<0.001) for males, 4.3% (95% CI 2.9-5.7, *P*<0.001) for females, and 3.6% (95% CI 2.7-4.5, *P*<0.001) for both sexes. The model did not show any join point; hence, the AAPC is the same as APC (Figs. 2-3).

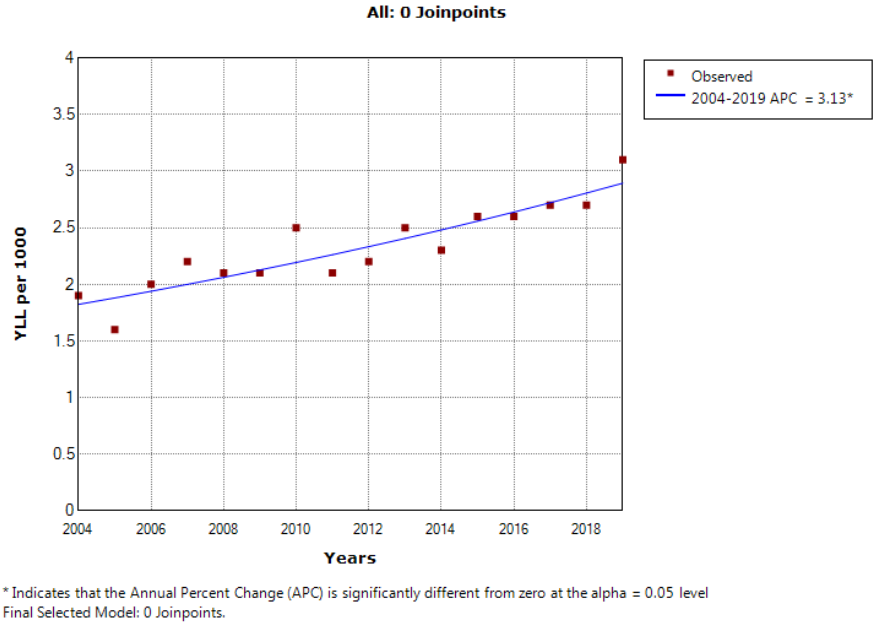

Fig. 2: The trend of years of life lost due to gastrointestinal cancers in men during 2004-2019

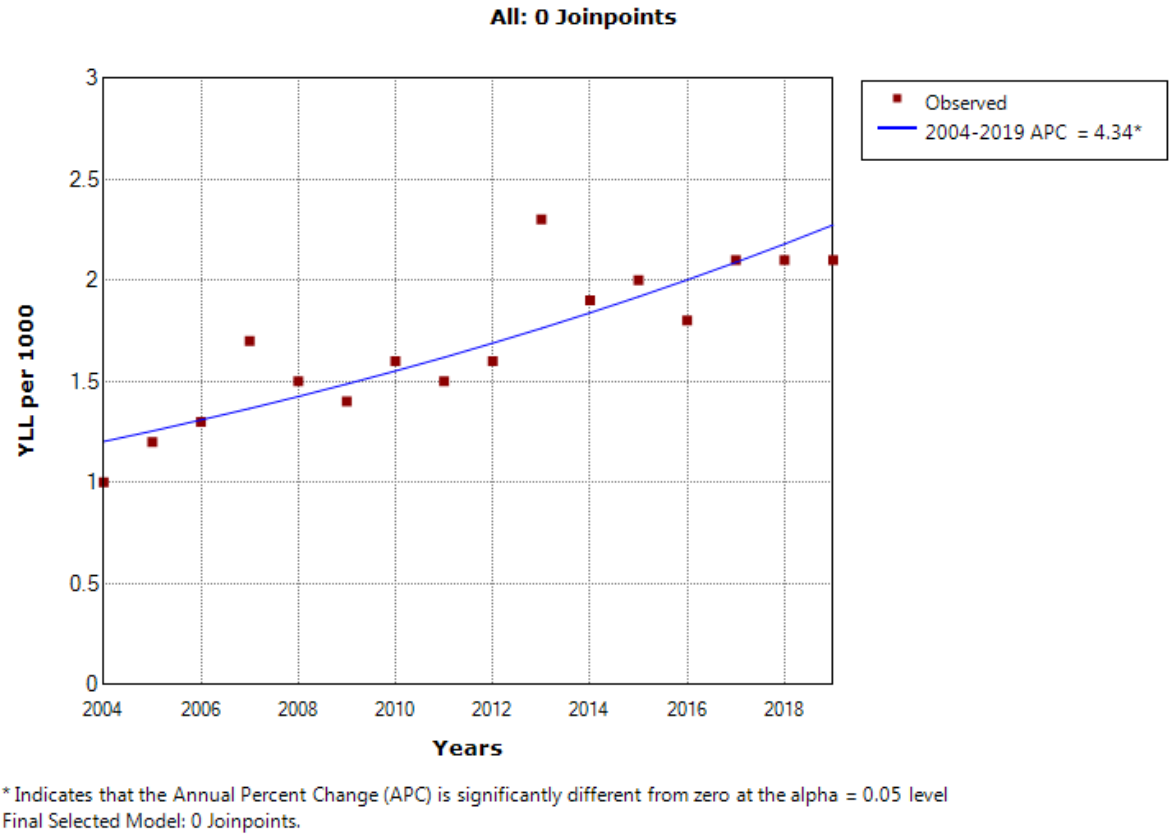

Fig. 3: The trend of years of life lost due to gastrointestinal cancers in women during 2004-2019

Moreover, the trend of YLL rate due to premature mortality in stomach cancer showed an increasing pattern: the APC was 0.9% (95% CI -0.3 to 2.1, *P*>0.05) for males, 1.2% (95% CI -0.1 to 2.6, *P*>0.05) for females, and 1% (95% CI 0.01-2, *P*<0.05) for both sexes. The trend of YLL rate for Malignant neoplasms of liver and intrahepatic bile ducts was increasing in nature: the APC was 1.1% (95% -1.3 to 3.5, *P*>0.05) for males, 3.3% (-3 to 9, *P*>0.05) for females, and 1.4% (95% CI -1.4 to 4.3, *P*>0.05) for both sexes. The trend of YLL rate for Malignant neoplasms of the esophagus was also increasing: the APC was 2.3% (95% CI -1.1 to 5.9, *P*>0.05) for males, 3.7% (95% CI -0.4 to 8.1, *P*>0.05) for females, and 2.7% (95% CI -0.4 to 5.8, *P*>0.05) for both sexes. However, the trend of YLL rate for Malignant neoplasms of the small intestine was decreasing: the APC was -9.4% (95% CI -13.1 to -5.5, *P*<0.001) for males, -5.7% (95% CI -10 to -1.3, *P*<0.05) for females, and -7.7% (95% CI -9.9 to -5.3, *P*<0.001) for both sexes. Furthermore, the trend of YLL rate for Malignant neoplasms of oral cavity was increasing: the annual percent change (APC) was 13.3% (95% CI 4.4 to 23, *P*<0.0.05) for males, 14.4% (95% CI 6.8-22.4, *P*<0.001) for females, and 13.4% (95% CI 6-21.3, *P*<0.001) for both sexes. Moreover, the trend of YLL rate for Malignant neoplasms of the recto sigmoid was increasing for males with an APC of 1.3% (95% CI- 12.8 to 17.7, *P*>0.05) and decreasing for females with an APC of -5.4% (95% CI -16.5 to 7.2, *P*>0.05). The trend was also decreasing when assessing the both sexes with an APC of -2.9% (95% CI -11.6 to 6.7, *P*>0.05).

For stomach, liver, esophageal, small intestine, oral, and recto sigmoid cancers, the models did not show any join point, and hence, the AAPCs

(average annual percent change) were the same as APCs.

The trend of YLL rate due to premature mortality for colon cancer was increasing: the annual percent change (APC) was 13.1% (95% CI 10.3 to 15.9, $P<0.001$) for males, 24.5% (95% CI 10.8 to 39.9, $P<0.001$) for females, and 14.7% (95% CI 11.7 to 17.7, $P<0.001$) for both sexes.

The model shows one join point in 2006 for females when the APC was 138.1% (95% CI -6 to 502.6, $P>0.05$).

The trend of YLL rate due to premature mortality for pancreatic cancer was increasing: the APC was 14% (95% CI 9.2 to 19, $P<0.001$) for males, 19.3% (95% CI 11.9 to 27.2, $P<0.001$) for females, and 14.7% (95% CI 10.7 to 18.8, $P<0.001$) for both sexes.

The model shows one join point in 2007 for females when the APC was 54.5% (95% CI 11.5 to 11.4.2, $P<0.05$) (Table 3).

Table 2: Years of life lost due to premature mortality, stratified by gender and gastrointestinal cancers in Fars (Iran) 2004-2019.

Variables		*2004*	*2005*	*2006*	*2007*	*2008*	*2009*	*2010*	*2011*	*2012*	*2013*	*2014*	*2015*	*2016*	*2017*	*2018*	*2019*	*Total*
		No. YLL	No. YLL	No. YLL	No. YLL	No. YLL	No. YLL	No. YLL	No. YLL	No. YLL	No. YLL	No. YLL	No. YLL	No. YLL	No. YLL	No. YLL	No. YLL	No. YLL
Gastric cancer	Women	1082	1084	1035	1338	1011	1128	1073	1018	1402	1487	1412	1300	1201	1462	1322	1600	19955
	Men	1804	1696	1763	2256	2020	1976	1907	1664	1660	2034	2005	2402	2322	2398	2135	2429	32471
Liver cancer	Women	407	681	697	940	992	646	1008	881	849	1177	798	1019	758	957	769	878	13457
	Men	871	597	864	542	904	929	1146	1062	1002	1107	743	829	1045	858	898	1197	14594
Colon cancer	Women	40	79	276	331	249	290	244	318	325	960	731	714	1008	938	1126	881	8510
	Men	206	198	232	481	333	334	335	542	906	605	910	849	1021	1122	1192	1415	10681
Pancreatic cancer	Women	46	50	125	203	156	223	176	229	233	451	437	431	353	577	697	672	5059
	Men	166	51	167	311	254	229	373	301	282	690	503	447	686	708	993	845	7006
Esophageal cancer	Women	92	39	120	78	151	90	190	106	142	104	222	101	150	143	154	138	2020
	Men	135	124	249	288	136	258	313	177	259	166	247	204	241	265	205	378	3645
Small bowl cancer	Women	86	186	107	150	129	59	232	194	118	94	96	66	79	69	48	89	1802
	Men	290	214	304	205	156	167	182	156	110	145	112	165	40	127	136	47	2556
Cancer of the lips, mouth and throat	Women	12	49	18	20	21	33	27	40	46	184	53	279	96	73	154	75	1180
	Men	35	50	29	10	30	18	105	29	42	224	89	302	90	76	134	149	1412
Rectal cancer	Women	38	36	31	4	118	108	130	65	0	12	54	62	69	20	32	4	783
	Men	23	16	77	19	124	94	356	64	109	66	0	71	42	74	46	19	1200
Total	Women	1803	2204	2409	3064	2827	2577	3080	2851	3115	4469	3803	3972	3714	4239	4302	4337	52766
	Men	3530	2946	3685	4112	3957	4005	4717	3995	4370	5037	4609	5269	5487	5628	5739	6479	73565

Table 3: Years of life lost (YLL) rate per 1000 persons and YLL trend by gender and gastrointestinal cancers in Fars (Iran) 2004-2019

Type of cancer	*YLL (years)*			*YLL rate (per 1000 persons)*			*AAPC for YLL trend*			*P for YLL trend*		
	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total
Gastric cancer	32471	19955	52426	1.03	0.64	0.84	0.9 (-0.3-2.1)	1.2 (-0.1-2.6)	1.0 (0.01-2.0)	0.145	0.062	0.045
Liver cancer	14594	13457	28051	0.46	0.43	0.45	1.1 (-1.3-3.5)	3.3 (-2.0,-9.0)	1.4 (-1.4-4.3)	0.345	0.326	0.230
Colon cancer	10681	8510	19191	0.33	0.27	0.30	13.1 (10.3-15.9)	24.5 (10.8-39.9)	14.7 (11.7-17.7)	0.001	0.001	<0.001
Pancreatic cancer	7006	5059	12065	0.22	0.16	0.19	14 (9.2-19)	19.3 (11.9-27.2)	14.7 (10.7-18.8)	0.001	0.001	<0.001
Esophageal cancer	3645	2020	5665	0.11	0.06	0.09	2.3 (-1.1-5.9)	3.7 (-0.4-8.1)	2.7 (-0.4-5.8)	0.176	0.074	0.080
small bowl cancer	2556	1802	4358	0.08	0.05	0.07	-9.4 (-13.1,-5.5)	-5.7 (-10.0,-1.3)	-7.7 (-9.9,-5.3)	0.001	0.016	<0.001
Cancer of the lips, mouth and throat	1412	1180	2592	0.04	0.03	0.04	13.3 (4.4-23.0)	14.4 (6.8-22.4)	13.4 (6.0-21.3)	0.005	0.001	0.001
Rectal cancer	1200	783	1983	0.03	0.02	0.03	1.3 (-12.8-17.7)	-5.4 (-16.5-7.2)	-2.9 (-11.6-6.7)	0.712	0.357	0.514
Total	73565	52766	126331	2.33	1.71	2.02	3.2 (2.3-4.1)	4.3 (2.9-5.6)	3.6 (2.7-4.5)	<0.001	<0.001	<0.001

Discussion

In this study, we aimed to calculate the YLL of gastrointestinal cancers in Iran and evaluate its temporal trend in a 16-year period in Fars Province, Southwest of Iran. Stomach cancer had the highest death rate and DALY among gastrointestinal diseases in Iran. Esophageal and Liver cancers are also highly ranked in death rates in Iran. Moreover, although the death rate of such neoplasms has declined from 1990 to 2010, the number of deaths attributed to these pathologies have increased. Consequently, a deep understanding of the extent of this problem seems to be of utmost importance (12).

In a study on rural and urban Chinese population, the YLL rates for liver and gastric cancer were 572.03 and 504.43 in 1990 and 389.00 and 229.44 in 2017 respectively with an APC of -1.33% and -2.52%. Our study depicted a lower YLL rate for these cancers; however, unlike China, we had positive APCs (13).

In Poland, the highest YLL rate due to malignant digestive system neoplasms in 2000 belonged to gastric cancer (32.5 yr per 10,000) followed by colon cancer (26.7 yr per 10,000); however, in 2014, colon cancer ranked first (33.3 yr per 10,000) while gastric cancer placed second in that ranking (26.4 yr per 10,000) followed closely by pancreatic cancer (25.3 yr per 10,000) (14). In our study on the other hand the YLL rate for liver cancer has always been higher than the YLL for

colon cancer. And gastric cancer has always ranked first in YLL rate of gastrointestinal cancers. This finding might be due to the fact that Iranian population usually do not abide by the screening rules for colorectal cancers.

An analysis was performed on the deaths due to gastrointestinal malignancies in Peru during 2005 to 2014. In that period of time gastric cancer, hepatic and biliary cancer, and colorectal cancers had the highest rate of YLL. The mortality rates for gastric cancer, gall bladder cancer, hepatic and biliary cancer, as well as esophageal cancer showed a declining trend in that period (15). In our study, the highest mortality rate belonged to gastric cancer, although the temporal trend of mortality rates was not assessed.

The average YLL for various cancers in Yazd Province of Iran were calculated. Gastric cancer in male patients of Yazd accounted for an average loss of 8.3 yr in male patients and 10.0 yr in female patients, while these numbers for our study were 11.89 and 14.03 respectively. Liver cancer was accounted for 8.60- and 8.20-yr prematurity in death in male and female patients of Yazd, where the AYLL in the patients of Fars was 12.39 and 14.41 yr for males and females respectively. Colorectal cancers took 10.0 and 10.2 yr of Yazdi patients' lives while the same index was 12.76 and 14.59 yr for Farsi patients. The indices for pancreatic cancer was 8.9 and 7.8 in Yazd and 12.1 and 14.0 in Fars (16).

The highest number of years of life lost due to cancer in Iran in 2016 was related to stomach cancer, which supports the findings of our study (17). *Helicobacter pylori* is the most important risk factor for gastric cancer, about 75% of all stomach cancers are due to H. pylori infection. Diet and lifestyle (smoking, coffee, and alcohol) are responsible for 33% to 50% of stomach cancers. The rate of stomach cancers was significantly lower in women than in men. Possible explanations for this could be those differences in diet, the protective effect of estrogen in women, and occupational exposure in men (18, 19).

A limitation of the present study was that YLL was not evaluated throughout the whole of Iran due to the unavailability of the necessary data. This study was of high quality and with a strong study design, large sample size, and extensive time-period of data analyzed.

Conclusion

The highest mortality rates in both sexes belong to gastric cancer. This study showed the trend of YLL rate of malignant neoplasms of liver and intrahepatic bile ducts, esophagus, oral cavity, and colon cancer were increasing in both sexes, however, the trend of YLL rate for malignant neoplasms of the small intestine was decreasing in both sexes. Variation of GI cancers patterns and trends around the Fars Province indicated that a more comprehensive control plan is needed to control these variations. For example: The access of screening for CRC (Colorectal Cancer), developing a gastric cancer early detection program and conducting a program to increase general awareness of known and probable risk factors of EC (Esophageal Cancer).

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

The authors declare that there is no conflict of interests.

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