

Original Article

Cancer Incidence in Golestan Province: Report of an Ongoing Population-based Cancer Registry in Iran between 2004 and 2008

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Abstract

Background: Golestan Province, at the western end of the Asian esophageal cancer (EC) belt in northeastern Iran, was reported to have one of the highest worldwide rates of EC in the 1970s. We have previously shown a declining incidence of EC in Golestan during the last decades. This study reports additional new results from the Golestan Population-based Cancer Registry (GPCR).

Methods: The GPCR collected data from newly diagnosed (incident) cancer cases from all 68 public and private diagnostic and therapeutic centers in Golestan Province. CanReg-4 software was used for data entry and analysis based on the guidelines of the International Agency for Research on Cancer (IARC). Age-standardized incidence rates (ASR) of cancers were calculated using the 2000 world standard population.

Results: From 2004 through 2008, 9007 new cancer cases were reported to the GPCR. The mean (SD) age was 55.5 (18.6) years, and 54% were diagnosed in men. The ASRs of all cancers were 175.3 and 141.1 per 100,000 person-years for males and females, respectively. Cancers of the stomach (ASR:30.7), esophagus (24.3), and lung (15.4) were the most common cancers in males. In females, breast cancer (ASR:26.9) was followed by malignancies of the esophagus (19.1) and stomach (12.4). The diagnosis of cancer was based on histopathological reports in 71% and on death certificate only in 9% of cases.

Conclusions: The EC incidence rate continues to decline in Golestan, while the incidence rates of stomach, colorectal, and breast cancers continue to increase.

Keywords: Cancer registry, esophageal cancer, Golestan, Iran

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Introduction

In Iran it is mandatory to report all confirmed or suspicious cancer diagnoses to the Iranian Ministry of Health (IMOH).¹

Iranian health authorities have maintained a pathology-based cancer registry since 1986.² The first report of this registry, which includes at maximum 80% of the new cancer cases, was published recently.³ The Digestive Diseases Research Center (DDRC) of Tehran University of Medical Sciences (TUMS) has established population-based cancer registries in two northern provinces of Iran, Ardabil, and Golestan, in collaboration with the International Agency for Research on Cancer (IARC), the Center for Disease Control at IMOH and local medical universities.⁴ Golestan Province is located at the southeastern corner of the Caspian Sea (northeast Iran), at the western end of the Asian esophageal cancer (EC) belt.⁵ It is located in the steppe grasslands of the

Turkmen plain and neighboring hills⁶ and includes Turkmen (35%) and Fars (65%) ethnic groups. Historically, the incidence of EC was found to be very high in this region.⁷ Mahboubi et al. in 1973 reported exceptionally high age-adjusted incidence rates (up to 165.5/100,000 in men and 195.3/100,000 in women) for EC in this region.⁶

The Golestan Population-based Cancer Registry (GPCR) began in 2001. The first report from this registry was a retrospective cancer surveillance for 1996 to 2000, published in 2006. This study showed a declining incidence of EC and an increasing incidence of gastric, colorectal, and breast cancers in this region compared to the data published from this area in the 1970s.⁸ GPCR is now run by the Golestan Research Center of Gastroenterology and Hepatology (GRCGH) of Golestan University of Medical Sciences (GOUMS), under the supervision of DDRC/TUMS. Since January 2006, all data in the GPCR was collected prospectively, and the GPCR has been a member of the International Association of Cancer Registries (IACR) since 2007. In this report, we present cancer incidence data collected by the GPCR over the 5-year period from 2004 through 2008.

Materials and Methods

GPCR collected information on newly diagnosed (incident) cancer cases from all public and private diagnostic and therapeutic centers in Golestan Province, including hospitals, pathology/labo-

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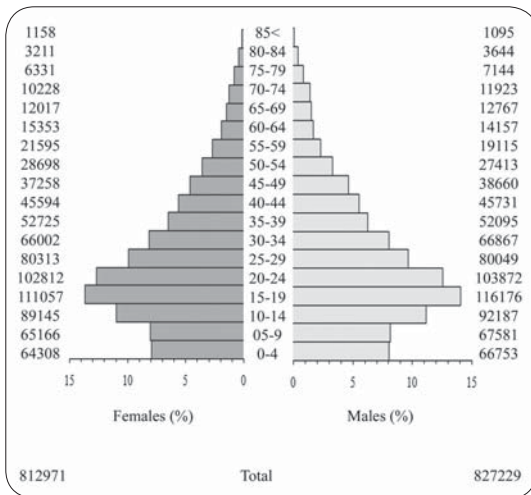


Figure 1. Population pyramid of Golestan Province, 2006. (Source: Health Department of Golestan University of Medical Sciences)

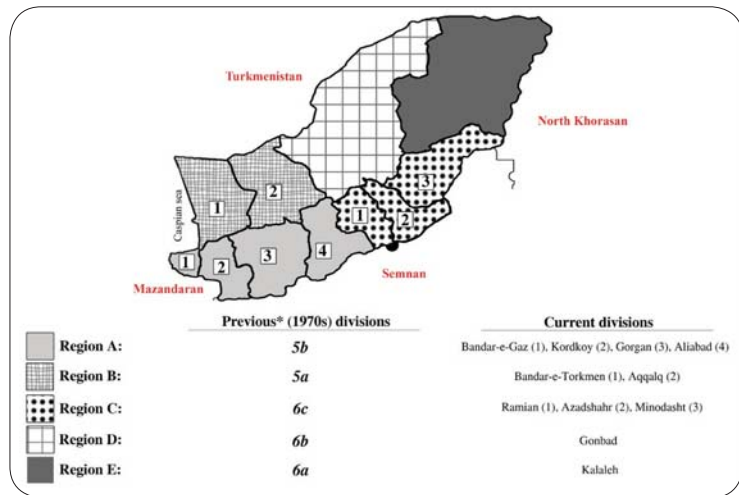


Figure 2. Previous* (1970s) and current divisions of Golestan Province, Iran (*Reference 6).

ratory centers, imaging centers and some specialist physicians' private offices from 2004 through 2008. We also obtained information from medical centers and regional registries in the neighboring provinces, particularly Khorasan Razavi, Mazandaran, and Tehran, to minimize loss of data for Golestan residents who were diagnosed in other provinces. Data was collected both actively and passively by well-trained registry staff that regularly visited all centers and collected information on cancer cases. GPCR also regularly received information on cancer-related deaths from the death registry at the health department of GOUMS and matched this data against the file of registered cancer patients to identify additional unreported cases, which were classified as death certificate only (DCO) cases.

GPCR registered only primary cancers; secondary tumors resulting from the invasion or metastasis of primary cancers were excluded from this report. Malignant tumors of all organs were registered based on IARC standards.⁹

10% of data collection forms were checked and compared with the original documents in the source centers to verify the accuracy and completeness of the abstraction process. The results of this checking process were acceptable in the majority of centers. The third edition of the International Classification of Diseases for Oncology (ICD-O-III) was used to code the anatomical site and histology of the tumors.¹⁰ IARC multiple primary rules¹¹ were used for patients with malignant tumors of more than one site.

Cases reported to GPCR were initially checked for duplications before entry into the database.¹² This duplication check included comparisons of the reported last name, first name, age, father's name, topography of tumor, place of residence, and year of diagnosis. The Persian version of CanReg4 software was used for data entry, and the data was checked with the IARC check program.¹²

Incidence rates were age-adjusted to the 2000 world standard population in 18 age categories of 5 years each (0-4, 5-9..., 85+), and expressed per 100,000 population. Information about the Golestan population in 2006 was obtained from the provincial census done by the Health Department of GOUMS. Figure 1 shows the population pyramid of Golestan in 2006. We used Segi's method to calculate the age-standardized incidence rates (ASRs) per 100,000 person-years for all cancers as well as the

truncated (34-65 years) ASR (TASR) of EC.¹³ *P*-values of less than 0.05 were considered statistically significant.

The protocol was approved by the Ethics Committee of GOUMS and the DDRC Institutional Review Board. Confidentiality measures were used to ensure the preservation of anonymity of the cancer cases, the best quality of registry data, and the best possible usage of the data.^{9,14}

Results

During the 5-year period from 2004 through 2008, 9007 new cancer cases were reported to GPCR from 68 healthcare centers across the province, the provincial death registry, and medical centers and cancer registries in neighboring provinces. More than half, 4862 (54%), of the cases were male (male to female ratio = 1.2; *P* = 0.001). Of all 9007 cases, 69% were confirmed by histopathological and 2% were confirmed by cytological examinations. The other methods of diagnosis were DCO in 9%, clinical in 10%, and para-clinical (e.g., imaging studies or surgical reports) in 10% of cases. The overall ASRs for all cancers were 175.3 (95% CI: 166.5-184.5) and 141.1 (95% CI: 133.2-149.5) per 100,000 person-years in males and females, respectively. Male patients were generally older than female patients, with median (inter-quartile range) ages of 62 (48-73) and 53 (41-66) years, respectively (*P* = 0.001).

Microscopic verification (MV) was done in 71% of all cancer cases. The MV% of the five most common cancers in males and females are shown in Table 1. Table 2 shows several indices of data quality for GPCR data collected between 2004 and 2008. The MV% increased from 60% in 2004 to 75% in 2008, with a concomitant decline in the DCO% from 23% in 2004 to 5% in 2008. The proportion of cases with an unknown primary site decreased from 6% in 2004 to 2% in 2008. There were no cases with an unknown method of diagnosis or an unknown age or sex in the GPCR between 2004 and 2008.

Table 3 shows the case numbers, crude rates and ASRs of the ten most common cancers in each sex. Stomach and esophageal malignancies were the most common cancers in males, while

Table 1. Proportion of cases with microscopic verification (MV%) for the five most common cancers in males and females of Golestan Province, Iran (2004–2008).

Sex	Location	MV%
Male	Stomach	68
	Esophagus	73
	Trachea, bronchus, lung	29
	Hematopoietics	98
	Colorectal	74
Female	Breast	75
	Esophagus	73
	Stomach	64
	Hematopoietic	100
	Colorectal	73

Table 2. Trend of data quality indices in Golestan Population-based Cancer Registry (GPCR), 2004–2008.

	2004	2005	2006	2007	2008
Total population	1592989	1614376	1640200	1668561	1693165
Number of cancer cases	1513	1709	1851	1937	1997
ASR of all cancers-male	156	177	187	172	174
ASR of all cancers -female	118	130	149	151	150
Microscopic verification (%)	60	70	71	74	75
Death certificate only (%)	23	11	8	6	5
Unknown primary site (%)	6	2	1	2	2
Unknown method of diagnosis (%)	0	0	0	0	0
Unknown age (%)	0	0	0	0	0
Unknown sex (%)	0	0	0	0	0

ASR: Age standardized incidence rates (per 100000 person-years).

Table 3. Case numbers, crude incidence rates and age-standardized incidence rates (ASR) per 100,000 persons-years of the top ten cancers in Golestan Province, Iran (2004–2008).

Male				Female			
Organ	Number of cases	Crude rate	ASR	Organ	Number of cases	Crude rate	ASR
Stomach	793	19.17	30.7	Breast	886	21.80	26.9
Esophagus	622	15.04	24.3	Esophagus	478	11.76	19.1
Lung	405	9.79	15.4	Stomach	325	8.00	12.4
Colorectal	345	8.34	12.4	Colorectal	266	6.54	9.5
Leukemia	338	8.17	10.5	Leukemia	238	5.86	7.4
Skin	324	7.83	12.6	Skin	207	5.09	8.2
Prostate	267	6.46	10.1	Ovary	187	4.60	5.7
Lymphoma	263	6.36	7.6	Nervous system	165	4.06	5.3
Nervous system	242	5.85	7.2	Lymphoma	161	3.96	4.7
Bladder	222	5.37	8.7	Lung	160	3.94	5.9
Total: All sites	4862	117.55	175.3	Total: All sites	4145	101.97	141.1
All sites, except skin	4561	110.27	163.8	All sites except skin	3953	97.25	133.6

breast and esophageal cancers were the most common tumors in females.

Table 4 shows the ASRs and TASRs (34–65 years) of EC in the different regions of Golestan Province (Figure 2) reported in 1968–1971 and in the current Cancer Registry data. The incidence rate of EC was higher in Gonbad and Kalaleh districts, located in the eastern area of the province, than in the other districts at both time points, both in males and in females. Between 1968–1971 and 2004–2008, the district- and gender-specific EC ASRs declined 57%–82%.

Discussion

The Golestan Population-based Cancer Registry showed improvement in several quality measures during 2004–2008 (Table

2). The proportions of cases with microscopic verification increased from 60% to 75% and the cases diagnosed only by death certificate decreased from 23% to 5% during this time, and from 2006 on, all data has been collected prospectively. Indices of data quality are now within acceptable ranges according to IARC standards,¹¹ which suggests that the GPCR is now a qualified population-based cancer registry by these standards.

The incidence of cancers was higher in males than in females, which is in agreement with the results of most other cancer registries.^{3,11,15} The mean age for cancer cases in our study (55.5 years) was similar to other reports from Iran.^{15,16}

According to this study, the ASRs of cancer in Golestan Province were 175.3 for males and 141.1 for females, which were similar to the findings of another population-based cancer registry in Iran.¹⁷ A recent pathology-based National Cancer Registry from

Table 4. Age standardized incidence rates (ASR) and truncated (34–65 years) ASR (TASR) for esophageal cancer (EC) in different regions of Golestan Province, Iran in 1968–1971 and 2004–2008.

	Previous study [†] 1968–1971				GPCR* 2004–2008			
	Male		Female		Male		Female	
	ASR	TASR	ASR	TASR	ASR	TASR	ASR	TASR
Region A [‡]	53.8	104.1	38.7	92.7	14.9	34.4	12.7	30.9
Region B [‡]	83.7	173.7	76.9	185.4	18.1	72.1	13.6	39.4
Region C [‡]	81.3	151.6	59.6	128.1	21.5	68.5	23.3	70.9
Region D [‡]	96.6	217.7	137.7	334.9	37.5	126.4	27.3	84.8
Region E [‡]	165.5	515.6	195.3	480.7	70.7	193.7	42.6	140.4

* Golestan Population-based Cancer Registry
[†] Reference 6
[‡] Refer to Figure 2

IMOH, on the other hand, has underestimated the incidence of cancer in Golestan (reporting ASRs of cancers for Golestan as low as 61 in males and 54 in females)³ and other parts of the country. This is most likely due to the different methodologies of the two registries: the only data source for the IMOH registry is pathology reports, and all data is collected passively, which are well-known shortcomings of this type of registry. Therefore, it is highly recommended that national cancer incidence and mortality rates be estimated based on population-based cancer registries with active case ascertainment, as they were estimated in the past.¹⁸

Stomach and esophageal cancers were the most common cancers in Golestan males during this time period. These results are similar to reports from some other Asian countries.¹⁹ The most frequent female cancers in Golestan Province were breast and esophagus, similar to the findings in East Azarbaijan Province.²⁰ Babaei et al. also reported breast cancer to be the most common female cancer in Semnan Province, although this site was followed in frequency by cancers of the uterus and ovary.¹⁶ In contrast, in Yemen, another country in the region, the most frequent cancers in males were leukemia and lymphoma, and the most common malignancies in females were breast cancer and leukemia.²¹ As incidence rates and common causes of cancers show considerable variation between countries and even between different regions of the same country, cancer control programs need to be planned with population-specific priorities.

We found an increasing trend in the incidence of cancer in both males and females between 2004 and 2006 (Table 2). The most likely explanation for this trend is that the cancer cases in 2004 and 2005 were registered retrospectively, and underestimation is an important limitation of retrospective data collection. The prospective phase of the GPCR was started since 2006, and our results show no significant change in cancer incidence rates from 2006 to 2008.

We found a decreasing trend in EC rates and increasing trends in the incidence of colorectal, breast and lung cancers and leukemia when compared to previous reports from this area.^{6,8} These changing rates may be partly due to the adoption of a western type lifestyle in Golestan during the last 20 years. The decreasing trend of EC, which has been reported previously,⁸ was confirmed in this study. Recent epidemiological studies in the Turkmen plain of Iran by our group have shown that alcohol and tobacco are not the main risk factors for EC in this area.²² Other risk factors, such

as socioeconomic status, drinking hot tea, opium consumption, poor oral health, and drinking non-piped water, are probably more important in the etiology of EC in Golestan.^{22–25} One major reason for declining EC rates in this area is the overall improvement in socioeconomic status, including higher incomes, availability of electricity, access to safe drinking water, natural gas for heating and cooking, television, telephone communication and public transport in 98% of the urban areas and 92% of the rural areas in today's Golestan.^{26,27}

Table 4 compares the current incidence rates of EC in the different regions of Golestan Province (Figure 2) with the rates reported during the 1970s.⁶ Despite the striking 57% - 82% drop in ASRs, the geographical distribution of EC in the present study was similar to that of the previous report.⁶ For example, the incidence rate of EC was considerably higher in Gonbad and Kalaleh (regions 6a and 6b in the previous report) in both the current and previous studies.⁶ Thus, despite its overall declining trend, EC remains a major health problem in this part of Golestan Province, which needs further investigation to determine unknown risk factors. In addition, implementation of an EC control program may be beneficial in this area.

In conclusion, GPCR is now a qualified population-based Cancer Registry based on IARC standards, and a major asset for planning cancer prevention strategies in this province. It may also be considered a good model for establishing population-based Cancer Registries in other provinces of Iran and in other Middle Eastern countries. Similar to our previous report,⁸ we have found that the EC incidence rate continues to decline in Golestan, while the rates of stomach, colorectal, and breast cancers continue to increase.

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References

- Islamic Parliament of Iran. *Mandatory Registration of Cancer*; 2010. Available from: URL: http://lawoffice.mohme.gov.ir/laws/dedicated_law/laws_all.jsp?from=s&id=1&id2=148 (Accessed 7.12.2010)
- Cancer Office of the Iranian Ministry of Health. *National Cancer Registry Report 2000–2001*. Tehran: Iranian Ministry of Health; 2002.
- Mousavi SM, Gouya MM, Ramazani R, Davanlou M, Hajsadeghi N, Seddighi Z. Cancer incidence and mortality in Iran. *Ann Oncol*. 2009; **20**: 556 – 563.
- Etemadi A, Sadjadi A, Semnani S, Nouraie SM, Khademi H, Bahadori M. Cancer registry in Iran: a brief overview. *Arch Iran Med*. 2008; **11**: 577 – 580.
- Kamangar F, Malekzadeh R, Dawsey SM, Saidi F. Esophageal cancer in Northeastern Iran: a review. *Arch Iran Med*. 2007; **10**: 70 – 82.
- Mahboubi E, Kmet J, Cook PJ, Day NE, Ghadirian P, Salmasizadeh S. Oesophageal cancer studies in the Caspian Littoral of Iran: The Caspian Cancer Registry. *Br J Cancer*. 1973; **28**: 197 – 214.
- Kmet J, Mahboubi E. Esophageal cancer in the Caspian littoral of Iran: initial studies. *Science*. 1972; **175**: 846 – 853.
- Semnani S, Sadjadi A, Fahimi S, Nouraie M, Naeimi M, Kabir J, et al. Declining incidence of esophageal cancer in the Turkmen Plain, eastern part of the Caspian Littoral of Iran: a retrospective cancer surveillance. *Cancer Detect Prev*. 2006; **30**: 14 – 19.
- Jensen OM. *Cancer Registration: Principles and Methods*. Lyon: International Agency for Research on Cancer; 1991.
- Fritz A, Percy C, Jack A, Shanmugaratnam K, Sobin L, Parkin DM, et al. *International Classification of Diseases for Oncology*. 3rd ed. Geneva: World Health Organization; 2000: 240.
- Curado MP, Edwards B, Shin HR, Storm H, Ferlay J, Heanue M, et al. *Cancer Incidence in Five Continents*. Vol 9. Lyon: International Agency for Research on Cancer; 2007.
- Cooke AP, Parkin DM, Ferlay J. *CanReg: Computer Software for Cancer Registries*. 4th ed. Lyon: International Agency for Research on Cancer; 2001.
- Segi M. *Cancer Mortality for Selected Sites in 24 Countries (1950–57)*. Sendai: Department of Public Health, Tohoku University of Medicine; 1960.
- Storm H, Brewster DH, Coleman MP, Deapen D, Oshima A, Threlfall T, et al. Guidelines for confidentiality and cancer registration. *Br J Cancer*. 2005; **92**: 2095 – 2096.
- Sadjadi A, Malekzadeh R, Derakhshan MH, Sepehr A, Nouraie M, Sotoudeh M, et al. Cancer occurrence in Ardabil: results of a population-based Cancer Registry from Iran. *Int J Cancer*. 2003; **107**: 113 – 118.
- Babaei M, Mousavi S, Malek M, Tosi G, Masoumeh Z, Danaei N, et al. Cancer occurrence in Semnan Province, Iran: results of a population-based cancer registry. *Asian Pac J Cancer Prev*. 2005; **6**: 159 – 164.
- Babaei M, Jaafarzadeh H, Sadjadi AR, Samadi F, Yazdanbod A, Fallah M, et al. Cancer incidence and mortality in Ardabil: report of an ongoing Population-Based Cancer Registry in Iran, 2004–2006. *Iran J Public Health*. 2009; **38**: 35 – 45.
- Sadjadi A, Nouraie M, Mohagheghi MA, Mousavi-Jarrahi A, Malekzadeh R, Parkin DM. Cancer occurrence in Iran in 2002, an international perspective. *Asian Pac J Cancer Prev*. 2005; **6**: 359 – 363.
- Moore MA, Eser S, Iginov N, Iginov S, Mohagheghi MA, Mousavi-Jarrahi A, et al. Cancer epidemiology and control in North-Western and Central Asia-past, present and future. *Asian Pac J Cancer Prev*. 2010; **11**: 17 – 32.
- Somi MH, Farhang S, Mirinezhad SK, Naghashi S, Seif-Farshad M, Golzari M. Cancer in East Azerbaijan, Iran: results of a population-based cancer registry. *Asian Pac J Cancer Prev*. 2008; **9**: 327 – 330.
- Saleem HOB, Bawazir AA, Moore M, Abdulla K. Five years cancer incidence in Aden Cancer Registry, Yemen. *Asian Pac J Cancer Prev*. 2010; **11**: 507 – 511.
- Nasrollahzadeh D, Kamangar F, Aghcheli K, Sotoudeh M, Islami F, Abnet CC, et al. Opium, tobacco, and alcohol use in relation to oesophageal squamous cell carcinoma in a high-risk area of Iran. *Br J Cancer*. 2008; **98**: 1857 – 1863.
- Abnet CC, Kamangar F, Islami F, Nasrollahzadeh D, Brennan P, Aghcheli K, et al. Tooth loss and lack of regular oral hygiene are associated with higher risk of esophageal squamous cell carcinoma. *Cancer Epidemiol Biomarkers Prev*. 2008; **17**: 3062 – 3068.
- Islami F, Kamangar F, Nasrollahzadeh D, Aghcheli K, Sotoudeh M, Abedi-Ardekani B, et al. Socio-economic status and oesophageal cancer: results from a population-based case-control study in a high-risk area. *Int J Epidemiol*. 2009; **38**: 978 – 988.
- Islami F, Pourshams A, Nasrollahzadeh D, Kamangar F, Fahimi S, Shakeri R, et al. Tea drinking habits and oesophageal cancer in a high-risk area in northern Iran: population based case-control study. *BMJ*. 2009; **338**: b929.
- Pourshams A, Khademi H, Malekshah AF, Islami F, Nouraei M, Sadjadi AR, et al. Cohort profile: The Golestan Cohort Study—a prospective study of oesophageal cancer in northern Iran. *Int J Epidemiol*. 2010; **39**: 52 – 59.
- Pourshams A, Saadatian-Elahi M, Nouraie M, Malekshah AF, Rakhshani N, Salah R, et al. Golestan cohort study of oesophageal cancer: feasibility and first results. *Br J Cancer*. 2004; **92**: 176 – 181.