

## RESEARCH COMMUNICATION

**Cancer Occurrence in Iran in 2002, an International Perspective**

**Sadjadi Alireza<sup>1</sup>, Nourai Mehdi<sup>1</sup>, Mohagheghi Mohammad Ali<sup>2</sup>, Mousavi-Jarrahi Alireza<sup>2</sup>, Malekezadeh Reza<sup>1</sup>, Donald Maxwell Parkin<sup>3</sup>**

**Abstract**

For almost 30 years no population-based cancer statistics have been available with which to estimate the cancer burden in Iran. In 2002 and 2003 two separate reports of population based cancer registries were published from Iran and the cancer incidence rates from these sources have permitted informed estimates of cancer incidence and mortality to be prepared. They suggest that more than 51,000 cases of cancer are diagnosed and 35,000 deaths due to cancer occur each year. The 5 most common cancers in males (by ASR) are stomach (26.1 per 10<sup>5</sup>), esophagus (17.6), colon-rectum (8.3), bladder (8.0) and leukemia (4.8), and in females are breast (17.1), esophagus (14.4), stomach (11.1), colon-rectum (6.5) and cervix uteri (4.5). The incidence rates of esophageal and stomach cancer in Iran are high, well above the world average, while the incidence of lung cancer is very low. Breast cancer, although the most common cancer of females in Iran, has rates that are low by world standards, especially those observed in Europe and USA. Similarly, the incidence of cervix cancer in Iran is very low, even lower than such low risk countries as China, Kuwait and Spain. Comparing these rates with the data of 30 years ago, the incidence of esophageal cancer has decreased dramatically, but gastric cancer has increased about two fold.

**Key Words:** Cancer incidence - population based cancer registries - GLOBOCAN - Iran

*Asian Pacific J Cancer Prev*, 6, 359-363

**Introduction**

The global burden of diseases has changed during the last century. The decreasing importance of infectious diseases is not limited to developed countries - developing countries have experienced such changes too. (Lopez and Murray, 1998) Iran, for example, has experienced rapid development in socioeconomic status during the past three decades; almost all economic indices show that, since the 1979 revolution, living standards have improved dramatically across the entire country (Statistical center of Iran, 1997). A recent report from Ministry of Health shows that more than 70% of deaths are caused by cardiovascular diseases, injuries and cancers, while fewer than 3 % of deaths are the consequence of infectious or parasitic diseases. Therefore understanding and quantifying the burden of cancer as one of the three major causes of death in the country is essential (Naghavi, 2000).

In 2002 and 2003 two separate reports of population based cancer registries published from Iran (Sadjadi et al, 2003)(Mohagheghi et al,2002). The current article is going to report the first cancer incidence and mortality rates

estimated from population based data after 30 years, which was published in GLOBOCAN, an official publication from IARC (Ferlay et al, 2004).

**Material and Method***Source of Data*

Two separate sources of information providing population-based cancer incidence rates were used (Fig 1). The first source is the population-based study of new cancer cases during 1996-2000 in 3 provinces (Golestan, Mazandaran, Kerman), and in Ardabil province during 1996-1999. The population covered is 6.4 million, around 10.7% of the population of Iran. These registries were run by provincial medical sciences universities and supervised by the Digestive Disease Research Centre (DDRC), Tehran University of Medical Sciences. In these studies, information on newly diagnosed cancer cases was collected from all available sources. Survey teams were trained to go to hospitals, pathology laboratories, diagnostic radiology departments, outpatient public and private clinics to check all records for cases of cancer. All collected data were then sent to the provincial registry office and later to the registry

<sup>1</sup> Digestive Disease Research Center, Tehran University of Medical Sciences <sup>2</sup> Cancer Research Center, Tehran University of Medical Sciences <sup>3</sup> Clinical Trials Service Unit and Epidemiological Studies Unit, Oxford, UK

Address for correspondence: Professor Reza Malekzadeh, Digestive Disease Research Center, Shariati Hospital - Kargar St. Tehran 14114 - Iran Email: malek@ams.ac.ir



**Figure 1. Map of Cancer Surveillance and Population Based Registry Area**

unit in DDRC Tehran where a final data check was performed by a team of epidemiologists.

The documents then were checked for any duplication. To increase the completeness of data, all new cancer cases from the neighboring provinces were also collected, to identify cases resident in the study provinces, but receiving treatment elsewhere (Sadjadi et al, 2003).

The second data source was the population-based cancer registry covering metropolitan (Mohagheghi et al , 2002) Tehran with a population of about 6,758,845, which was established and operated by the Cancer Research Institute of Tehran University of Medical Sciences. The data on new cancer cases were collected from multiple different sources within the city, including pathologists, hospital, and cancer treatment services. The most recent data available are for the year 1997.

**Statistical Methods**

*Incidence*

The total population of these five registries is 13,194 424 representing about 22% of the total population of Iran. The estimates were derived from the data of the five mentioned cancer registries described above (Table 1).

**Table 1. Population under Coverage of 5 Cancer registry Areas during 1996.**

| Province               | Age group |          |         |         |         | Total     |
|------------------------|-----------|----------|---------|---------|---------|-----------|
|                        | 0 – 14    | 15 – 44  | 45 – 54 | 55 – 64 | > 65    |           |
| Kerman                 | 846654    | 882563   | 104276  | 84791   | 85825   | 2004328   |
| Golestan               | 515479    | 783514   | 102200  | 59512   | 61763   | 1522468   |
| Mazandaran             | 634688    | 807796   | 116072  | 92942   | 88709   | 1740772   |
| Ardabil                | 492837    | 507332   | 64284   | 53193   | 50292   | 1168011   |
| Tehran                 | 2635949   | 3109069  | 405531  | 337942  | 270354  | 6,758,845 |
| Total (registry areas) | 5125607   | 6090274  | 792363  | 628380  | 556943  | 13194424  |
| (% Iranian Population) | 21.6%     | 22.2%    | 22.4%   | 22.9%   | 21.5%   | 22.0%     |
| Iran                   | 23725545  | 27410614 | 3542118 | 2749674 | 2595181 | 60055488  |

A simple mean of the age (0-14, 15-44, 45-54, 55-64, 65+), sex, and site (25 sites) specific incidence rates calculated. The numbers of cases of cancer in the year 2002 (by site, sex, and age group) was calculated using this estimated “national” rate, and the population of Iran, by sex and age, estimated for 2002 (United Nations, 2003).

*Mortality*

Mortality was estimated from the numbers of new cases (by site, sex, and age-group) and estimated cancer survival. For a given cancer site and age group, mortality (M) is the product of incidence (I) and the probability of dying from the disease:  $M = I[k-S_j]$  where  $S_j$  is the relative survival at year j of follow-up and k is a constant depending on j.

When 5-year relative survival probabilities are used, the constant k tends to be very close to 1 (Pisani et al., 1999). The survival estimates were based on both sexes combined, as sex has been shown to have relatively little effect on cancer survival if other risks factors and competing causes of death are adequately controlled for (Pisani et al., 2002).

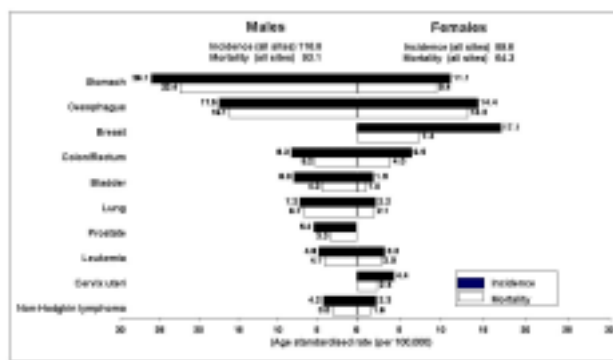
There are no data on survival from cancer (for population-based samples of cases) in Iran. We therefore used a pooled estimate of survival in developing countries, based upon data from Cancer Survival in Developing Countries (Sankaranarayanan et al., 1999) and including data from populations in The Philippines, Thailand and India, for all of the sites considered.

**Results**

It is estimated that about 50800 new cancer cases occur in Iran each year (Table2). Among them more than 53% belong to male with age standardized incidence rate (ASR) of 116.8 per 100000 for males and 93.1 per 100000 in females. The most common organ system involved by cancer is the gastrointestinal tract in both sexes, where more than more than 38% of all cancers occur. The 5 most common cancers in males (by ASR) are stomach (26.1 per 10<sup>5</sup>), esophagus (17.6 per 10<sup>5</sup>), colon and rectum (8.3 per 10<sup>5</sup>), bladder (8.0 per 10<sup>5</sup>) and leukemia (4.8 per 10<sup>5</sup>), and in females the five most common cancers are breast (17.1 per 10<sup>5</sup>), esophagus (14.4 per 10<sup>5</sup>), stomach (11.1 per 10<sup>5</sup>), colon and rectum (6.5 per 10<sup>5</sup>), and cervix uteri (4.5 per 10<sup>5</sup>) (Fig 2).

**Table 2. Islamic Republic of Iran. Estimates Numbers of Cases, Deaths, and Prevalent Cancer Cases (5 year) in 2002**

| SITE                    | MALES |        |            | FEMALES |        |            | BOTH SEXES |        |            |
|-------------------------|-------|--------|------------|---------|--------|------------|------------|--------|------------|
|                         | Cases | Deaths | 5-yr prev. | Cases   | Deaths | 5-yr prev. | Cases      | Deaths | 5-yr prev. |
| 1 Stomach               | 5393  | 4575   | 7199       | 2450    | 2063   | 3339       | 7843       | 6638   | 10538      |
| 2 Oesophagus            | 3683  | 3349   | 3256       | 3163    | 2870   | 2828       | 6846       | 6219   | 6084       |
| 3 Breast                |       |        |            | 4742    | 2039   | 16626      | 4742       | 2039   | 16626      |
| 4 Colon and rectum      | 2046  | 1276   | 5225       | 1595    | 986    | 3986       | 3641       | 2262   | 9211       |
| 5 Leukaemia             | 1540  | 1300   | 1628       | 1002    | 854    | 1058       | 2542       | 2154   | 2686       |
| 6 Bladder               | 1677  | 855    | 4807       | 406     | 204    | 1163       | 2083       | 1059   | 5970       |
| 7 Lung                  | 1502  | 1386   | 1207       | 506     | 466    | 419        | 2008       | 1852   | 1626       |
| 8 Brain, nervous system | 1091  | 878    | 1569       | 776     | 623    | 1134       | 1867       | 1501   | 2703       |
| 9 Non-Hodgkin lymphoma  | 1228  | 837    | 2460       | 633     | 433    | 1274       | 1861       | 1270   | 3734       |
| 10 Cervix uteri         |       |        |            | 1118    | 581    | 3502       | 1118       | 581    | 3502       |
| 11 Thyroid              | 364   | 78     | 1401       | 721     | 128    | 2834       | 1085       | 206    | 4235       |
| 12 Prostate             | 1066  | 649    | 2851       |         |        |            | 1066       | 649    | 2851       |
| All sites but skin      | 27263 | 20088  | 48174      | 23557   | 15466  | 51791      | 50820      | 35554  | 99965      |



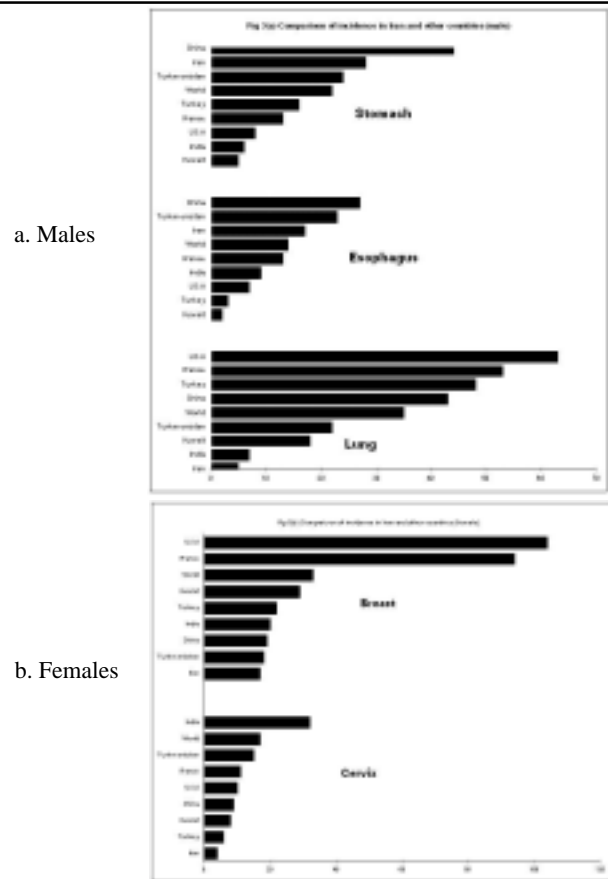
**Figure 2. The Most Important Causes of Death from Cancer**

The yearly number of cancer deaths is estimated as more than 35000, with mortality to incidence ratio equal to 70%, ranging from 19% for thyroid cancer to 94% for liver cancer. The most important causes of death from cancer in males are Stomach, Esophagus, Lung and in females, Esophagus, Stomach, and Breast (Table 2 and Fig 2).

Figs 3a and b show comparisons of incidence rates of the major cancers in Iran, with those in selected other countries. For stomach cancer, incidence rates in Iran are high, above the world average figure (22.0 per 100,000) in men, but rather lower than the incidence in China. Similarly, the incidence of esophageal cancer is high by world standards, while the incidence of lung cancer is very low (Fig 3a). Although breast cancer is the most common cancer of women in Iran, with an ASR of 17.1 per 100,000, the rates are low by world standards, and way below those observed in the USA and France, for example. Similarly, the incidence of cervix cancer in Iran is low, even lower than in such low risk countries as China, Kuwait and Turkey (Fig 3b).

**Discussion**

The cancer registry has a crucial role in cancer control. The information it provides is the primary source not only for epidemiological research on cancer determinants but also for planning and evaluating cancer control programs (Jensen



**Figure 3 (a,b). Comparison of Incidence Data for Iran and Other Countries**

et al, 1991).

Cancer has become the second most common non-traumatic cause of death in Iran (Naghavi, 2000). This undoubtedly relates to the marked changes in lifestyle and distribution of risk factors in the population in the last 30 years (Pourshams et al, 2005) For example, a recent study of rural and urban areas in Gonbad District in Northeastern Iran revealed that 60 % of the inhabitants were overweight, with a body mass index (BMI) greater than 25 kg per m<sup>2</sup>, and 25% of them were obese (BMI>30). Refrigerator ownership in rural areas has increased from less than 5% in

1970 to more than 90% at present time (Pourshams et al, 2005). Improvements in overall socioeconomic status, including higher income, availability of electricity, healthy drinking water, natural gas for heating and cooking, telephone communication and transport involves 98% of urban and 90% of rural areas in present day Iran (Pourshams et al, 2005).

We estimate that more than 35000 cancer deaths are occurring in Iran each year, the second highest number of cancer death in Eastern Mediterranean Region of WHO (Ferlay et al, 2002). The cancer problem is best approached through the establishment of a comprehensive national cancer control programme (NCCP) integrating prevention, early detection, treatment, and palliation/rehabilitation services (WHO,2002). But, a NCCP requires an effective surveillance and monitoring system, providing accurate data on cancer incidence and outcome from population based cancer registries. Cancer registration in Iran began in 1965, when the Public Health Research Institute (PHRI) of Tehran University and the International Agency for Research on Cancer (IARC) jointly established a cancer registry in the city of Babol in Mazandaran Province in the Caspian Littoral (Habibi et al, 1965) (Mahboubi et al,1973). The registry mainly covered the two provinces of Gilan and Mazandaran and the nearby city of Ardabil. Information gathered by this cancer registry soon showed an unusually high incidence of esophageal cancer in the Caspian littoral, with, interestingly, a very uneven geographic distribution. There were very high rates in the eastern Turkoman plain (ASR: 165.5 and 195.3 per 100000 for men and women, respectively, the highest ever recorded in the world (Habibi et al, 1965) (Mahboubi et al,1973). This cancer registry relied on clinical and simple radiological means for recording the final diagnoses, as endoscopy, surgery and histological diagnosis was not readily available at the time. Despite this shortcoming, the project drew the attention of interested national and international investigators who launched studies to unravel the possible risk factors for esophageal cancer in the region. These efforts came to a halt during the revolution of 1979, and no report of cancer incidence in Iran has been published during the last 2 decades. In its worldwide "GLOBOCAN" estimates, IARC estimated Iranian cancer incidence and mortality from rates in other Middle Eastern countries and relative frequencies of different cancers in hospital and pathology series from Iran (Ferlay et al, 2001).

Now population-based cancer registries are present in four provinces (Ardabil, Golestan, Mazandaran and Kerman) established in 2002 by Digestive Disease Research Center of Tehran University of Medical Sciences in collaboration with Ardabil ,Mazanderan, Golestan and Kerman university of Medical sciences, and in Tehran, where the Cancer Research Institute of Tehran University of Medical Sciences has established a registry. These sources have been used to estimate national incidence and mortality in this paper. We have no idea how representative of the other provinces, where there are no available data, are the incidence rates recorded in these registries. Therefore, we used simple means

of the site-age-sex specific rates to estimate the national figure, rather than trying to weight their individual contributions by population size, or geographic region. The resulting overall estimated age-standardized incidence of 116.8 in males and 93.1 in females is amongst lowest in the world. The high incidence of gastrointestinal cancer (especially Upper GI cancer) is another important finding. While more than 38% of all cancers are located in the gastrointestinal system in Iran, in the USA the proportion is less than 20% (Jemal et al, 2003). Compared with the data of 30 years ago, the incidence of esophageal cancer is much lower, but gastric cancer has increased about two fold (from 10 per 10<sup>5</sup> in 1972 to 26.1 in 2002 (Mahboubi et al,1973)(Sadjadi et al,2003). The decline of the esophageal cancer rate is similar to reports from developed countries, which show a decline in the incidence rates of esophageal squamous carcinoma (Parkin et al,2001), which is the main histological type of esophageal cancer in Iran (Sadjadi et al,2003) (Islami et al,2004). This decrease can be attributed to better economic status, and personal health, better nutrition, and changing in high-risk behavior (Malekzadeh et al, 2005) (Pourshams et al, 2005). The increase in the rate of gastric cancer is a challenging area of cancer epidemiology in Iran. A recent study from Ardabil, one of the provinces with the highest incidence of gastric cancer in Iran (ASR close to 50 per 10<sup>5</sup> in males) (Sadjadi et al, 2003) has clearly showed that the most common type of gastric cancer is located at the cardia (Derakhshan et al, 2004) (Malekzadeh et al ,2004), although in Tehran non-cardia gastric cancer is still the predominant type (Mohagheghi et al,2002). The possibility of misclassification of cardia cancer as esophageal cancer 30 years ago, when diagnostic facilities (notably upper GI endoscopy) were poor, may be another reason for this apparent rise in gastric cancer incidence (Ekstrom et al, 1999). A high prevalence of infection with *Helicobacter pylori* has been reported in the Iranian adult population; for example, in Ardabil, nearly 90% of the adult population more than 40 years of age has *H. pylori* infection by histopathology (Malekzadeh et al, 2004), and the seroprevalence of *H. pylori* infection in the central and southern part of the country in the population aged more than 35 years is 90% (Massarat et al, 1995). Although this high rate of infection is consistent with the high rate of gastric cancer throughout the country, it does not explain the high rate of cardia cancer in Ardabil and other parts of the Azerbaijan region of the country. Environmental exposures other than *H. pylori* infection must be involved. Several epidemiological and molecular studies are presently going on to address these questions (Kamangar et al, 2005) (Yazdanbod et al, 2004) (Farhadi et al, 2005) (Sepehr et al, 2004) (Nouarie et al, 2004).

The low incidences of lung and prostate cancer in Iranian men are very different from developed countries, where these two cancers are the most common cancers of men (Parkin et al, 2001 ). The low incidence of lung cancer is surprising, since the prevalence of smoking in Iranian males over the age of 15 is 12.9% (Noorbala and Mohammad, 1999). Under reporting and difficulty in tissue diagnosis may explain some

part of this low incidence.

There is a very low incidence of cancer of the cervix uteri in Iran (Sadjadi et al, 2003), even by the standards of other countries in western Asia. It is highly likely that religious beliefs and rules have had a great effect on the risk of this disease. On the other hand, breast cancer, already the most common cancer of women, can be expected to increase, with changes in diet, body weight, and fertility of the population. With improving prognosis, this cancer will have the highest number of survivors, and the development of special programmes to support these victims will be very important.

## Acknowledgements

This study was funded by a grant from Digestive Disease Research Center Tehran University of Medical Sciences. We also would to Thank Iranian society of gastroenterology and Hepatology for their support.

## References

- Brown LM, Devesa SS (2002). Epidemiologic trends in esophageal and gastric cancer in the United States. *Surg Oncol Clin N Am*, **11**, 235-56.
- Derakhshan MH, Yazdanbod A, Sadjadi AR, et al (2004). High incidence of adenocarcinoma arising from the right side of the gastric cardia in NW Iran. *GUT*, **53**, 1262-6.
- Farhadi M, Tahmasebi Z, Merat S, et al (2005). Human papillomavirus in squamous cell carcinoma of esophagus in a high-risk population. *World J Gastroenterol*, **11**, 1200-3.
- Ferlay J, Bray F, Pisani P, Parkin DM (2004). GLOBOCAN 2002: Cancer Incidence, Mortality and Prevalence Worldwide Version 2.0. IARC CancerBase No.5. Lyon, IARC Press.
- Ferlay J, Bray F, Pisani P, Parkin DM (2001). GLOBOCAN 2000: Cancer Incidence, Mortality and Prevalence Worldwide, Version 1.0. IARC CancerBase No. 5. Lyon, IARC Press.
- Habibi A (1965). Cancer in Iran. A Survey of the most common cases. *J Natl Cancer Inst*, **34**, 553-69.
- Haghighi P, Nabizadeh I, Asvadi S, Mohallatee EA (1971). Cancer in southern Iran. *Cancer*, **27**, 965-77.
- Islami F, Kamangar F, Aghcheli K, et al (2004). Epidemiologic features of upper gastrointestinal tract cancers in Northeastern Iran. *Br J Cancer*, **90**, 1402-6.
- Jensen OM, Parkin DM, Maclennan R, Muir CS, Skeet RG (1991). Cancer registration principle and methods, International Agency for Research on Cancer, Lyon.
- Jemal A, Murray T, Samuels A, et al (2003). Cancer statistics. *CA Cancer J Clin*, **53**, 5-26.
- Kamangar F, Strickland PT, Pourshams A, et al (2005). High exposure to polycyclic aromatic hydrocarbons may contribute to high risk of esophageal cancer in northeastern Iran. *Anticancer Res*, **5**, 425-8.
- Lopez AD, Murray CC (1998). The global burden of disease, 1990-2020. *Nat Med*, **4**, 1241-3.
- Mahboubi E, Kmet J, Cook PJ, et al (1973). Oesophageal cancer studies in the Caspian Littoral of Iran: the Caspian cancer registry. *Br J Cancer*, **28**, 197-214.
- Mikaeli J, Malekzadeh R, Ziad-Alizadeh B, et al (2000). Prevalence of Helicobacter pylori in two Iranian provinces with high and low incidence of gastric carcinoma. *Arch Iranian Med*, **3**, 6-9.
- Mohagheghi MA, Mosavi-Jarrahi A (2002). The 3rd annual report of Tehran Metropolitan Area Cancer Registry. Tehran, Cancer Institute Research Center. The Cancer Institute Research Center Publication.
- Malekzadeh R, Sotoudeh M, Derakhshan MH, et al (2004). Prevalence of gastric precancerous lesions in Ardabil, a high incidence province for gastric adenocarcinoma in the northwest of Iran. *Journal of clinical pathology*, **57**, 37-42.
- Noorbala A, Mohammad K (1999). Iran National Health Survey. Tehran, Ministry of Health.
- Nouarie M, Pourshams A, Kamangar F, et al (2004). Ecologic study of serum selenium and upper gastrointestinal cancers in Iran. *World J Gastroenterol*, **10**, 2544-6.
- Naghavi M (2000). Death report from 10 provinces in Iran. Tehran, Ministry of Health.
- Pourshams A, Saadatian-Elahi M, Nourae M, et al (2005). Golestan cohort study of oesophageal cancer: feasibility and first results. *Br J Cancer*, **92**, 176-81.
- Pisani P, Parkin DM, Bray F, Ferlay J (1999). Estimates of the worldwide mortality from twenty-five cancers in 1990. *Int J Cancer*, **83**, 18-29.
- Sankaranarayanan R, Black RJ, Parkin DM (eds) (1999). Cancer Survival in Developing Countries, IARC Scientific Publications No 145, IARC, Lyon.
- Sepehr A, Kamangar F, Abnet CC, et al (2004). Genetic polymorphisms in three Iranian populations with different risks of esophageal cancer, an ecologic comparison. *Cancer Lett*, **213**, 195-202.
- Parkin DM, Bray FI, Devesa SS (2001). Cancer burden in the year 2000. The global picture. *Eur J Cancer*, **37 Suppl**, S4-66.
- Pisani P, Bray F, Parkin DM (2002). Estimates of the worldwide prevalence of cancer for twenty-five sites in the adult population. *Int J Cancer*, **97**, 72-81.
- Statistical Center of Iran (1977). Iran National Census, Tehran, Statistical Center of Iran.
- Sadjadi A, Malekzadeh R, Derakhshan MH, et al (2003). Cancer occurrence in Ardabil: results of a population-based cancer registry from Iran. *Int J Cancer*, **107**, 113-8.
- United Nations (2003). World population prospects. The 2002 Revision. Population database. <http://esa.un.org/unpp/>.
- Verdecchia A, Micheli A, Colonna M, et al (2002). A comparative analysis of cancer prevalence in cancer registry areas of France, Italy and Spain. *Ann Oncol*, **13**, 1128-39.
- Yazdanbod A, Nasseri-Moghaddam S, Malekzadeh R (2004). Upper gastrointestinal cancer in Ardabil, North-West of Iran. a review. *Arch Iranian Med*, **7**, 173-7.