

Geographic distribution of important cancers in Iran

Nayereh Esmailzadeh ¹ Abdolreza Salahi-Moghaddam ² Alireza Khoshdel ³

MSc of Epidemiology ¹, Mashhad University of Medical Sciences, Mashhad, Iran. Associate Professor Department of Parasitology ², Hormozgan University of Medical Sciences, Bandar Abbas, Iran. Associate Professor Department of Epidemiology ³, Health Geomatics Research Center, AJA University of Medical Sciences, Tehran, Iran.

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Original Article

Abstract

Introduction: Each year, 10 million people are faced with cancer and about 6 million of them die throughout the world. This study aimed at investigating the geographical distribution of cancer and its environmental risk factors in Iran.

Methods: The present study was mapping the available data collected from the reports of Iranian Center for Disease Control (Cancer Bureau) regarding the frequency of 10 common cancers (stomach, esophageal, colorectal, bladder, lung, CNS, lymphoma, prostate, ovarian, and breast) as their age-standardized incidence rate (ASR) for each province in between 2005 and 2006 using ArcGIS 9.3. The published information about environmental risk factors was also gathered based on reviewing available public sources of digital databases including Scopus, Pubmed and Persian sources of IranMedex, Iran DOC, SID, and magiran, as well as through hand searching of books and manuals using keywords.

Results: Geographically, the incidence of certain cancers varied in different regions of Iran. Between 2005 and 2006, the estimated ASR of cancers was 102.4 and 117.3 per 100,000 among females and males, respectively. The ASR of cancer was higher in the north than in the south of Iran. This difference is possibly due to the methods of registry and difference in the site. Lifestyle, infectious agents, environmental exposures, and constitutional factors are risk factors that have been attributed to certain types of cancer.

Conclusion: Development, establishment, and implementation of Comprehensive National Cancer Control Program should be the first priority for health policy-makers. Given its nationwide distribution, Iranian Army can provide substantial assistance in collection and analysis of data on cancer in case of access to a record and control system of cancer.

Key words: Cancer – Mapping - Risk Factors - Iran

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Introduction:

Each year, 10 million people are faced with cancer and about 6 million of them die throughout

the world. Cancer is one of the most common causes of death in the world, and its incidence and prevalence is increasing. It is estimated that the

incidence of cancer will increase about 45% in developed countries by 2025 (1,2). Cancer epidemiology is gradually changing in Iran as a result of demographic and epidemiological transition (3). While cancer was the fifth leading cause of death between 1979 and 1981, it became the fourth during 1982 to 1986, and the third in recent years during which a significant growth in population and changes in socioeconomic status has been occurred (4). Several reasons have been proposed for this growing trend including factors related to changes in lifestyle, environmental factors, occupational and industrial risk factors, nutrition, smoking, drugs and hormone therapy, alcohol, lack of exercise, stress, pollution in urban areas, toxins, and infections (5).

This growth will turn cancers into a challenge for the current decade and the future in Iran. As a result, establishment of prevention and monitoring centers beside development and tooling of registration databases and informational databases are the most important strategies for prevention, diagnosis, treatment, and care of cancer in Iran. In this regard, mapping the distribution of cancers will allow comparison of distribution pattern of pathogens and elucidate the relationships between them. According to the type of data collection, the plotted maps can be displayed based on age and sex groups, different time periods, different administrative divisions of Iran (province, city, ethnic, geographical, climatic, etc.), as well as based on any relevant and focused factors regarding a specific disease. Methods such as mapping can transfer large amounts of information in a short time so that valid conclusions can be achieved based on the findings, and appropriate actions can be taken as a result. Relevant experts can propose hypotheses about the disease distribution and its relationship with risk factors and protective factors using these maps and can make suggestions for further studies in different regions. On the other hand, they can help policy-making and strategic management for addressing this growing epidemic.

In the present study, the most prevalent cancers of Iran, including stomach, esophageal, colorectal, bladder, lung (men), central nervous system, lymph nodes, prostate, ovarian, and breast (women) cancers, were mapped based on the age-standardized incidence (ASR) for the provinces in

order to identify their frequency distribution during the time period of 2005 to 2006. Since the data belong to a time period, digital information resources were reviewed and available resources were manually searched in order to determine environmental risk factors.

Methods:

The present research is a combination of available information and review study. The available information was used to determine the distribution frequency of cancer incidence from ASR data visualized by the Iranian Center for Disease Control (Cancer Bureau) for each province on the map of Iran using ArcGIS 9.3 during 2005 to 2006.

ASR of ten common cancers including carcinomas of stomach, esophagus, colorectal, bladder, lung, central nervous system, lymph nodes, prostate, ovarian, and breast (women) was used for mapping.

The division of provinces and the meaning of the colors used were as follows: to divide the provinces by software, the Quantile method was used. In this method, the provinces are sorted from the lowest to the highest ASR; then the series of numbers obtained are divided into five equal parts. Since ASR was obtained from 30 provinces, there are 5 or 6 provinces in each part.

Thus, if we assume that all the information is 100%, each part contains 20% of the information; and 20% of the provinces with the highest ASR have the darkest and 20% with the lowest frequency have the lightest spectrum.

In addition, in order to determine the environmental risk factors, available digital information resources were reviewed including public resources of Scopus and Pubmed using keywords such as cancer, tumor, epidemiology, Iran, incidence, gastric cancer, stomach cancer, esophageal cancer, colorectal cancer, ovarian cancer, breast cancer, lung cancer, urinary bladder cancer, prostate cancer, brain cancer, CNS cancer, non-Hodgkin lymphoma, lymphoma, medical geography, risk factor, Geographic Information System (GIS), mapping, as well as Persian sources including IranMedex, IranDOC, SID, and Magiran using the same keywords in Persian as well as

cancer registration, industry, and war separately and in combination. Manual search of books and manuals was also performed.

Data has been adopted from the Cancer Bureau of the Center for Disease Control. Cancer registry of the data has been actively performed based on population, so that the data have been collected by experts active in cancer registry from cancer pathology centers, hospitals, radiotherapy centers, and cemeteries and recorded and mapped in the GIS at the Health Geomatics Center of the Military Medical Sciences University using ArcGIS 9.3. In order to maintain the confidentiality of information regarding the distribution of diseases, the data are made public after 5 years.

Ranking of the provinces using color maps based on ASR can well demonstrate the geographic areas with high and low incidence of disease. Since information in the maps shows only the provincial distribution of cancer, and other geographical and environmental factors, cultural factors, lifestyle, and ethnicity are not depicted and belong to a period of time; therefore, in this case, the environmental risk factors were determined using the findings of other studies in available public and Persian digital information resources, and manually searching books and manuals.

Results:

Stomach Cancer

Figure 1 shows the geographical distribution map of stomach cancer ASR in 2005. This cancer is of high prevalence in the north and northwest Iran, especially in Azeri-speaking provinces, of average prevalence in the central and western regions, and of low-prevalence in the southern regions. Ardabil and Kerman provinces had the highest (25.4 men and 49.1 women in 100,000) and the lowest (1.5 men and 10.2 women in 100,000) incidence, respectively. Etiology of gastric cancer is different according to classification by anatomic location (cardi/non-cardia) and Lauren's histology (intestinal-type/diffuse-type) (6).

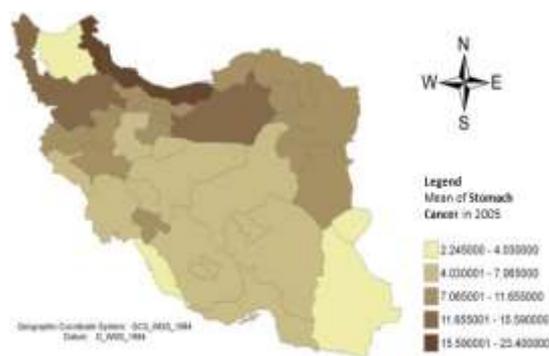


Figure 1. Geographical distribution map of Stomach Cancer ASR, 2005

In high-prevalent regions of Iran, stomach cancer is more seen in the cardia areas; this is in contrast with the prevalence pattern in high-prevalent countries of the world such as Japan in which non-cardia areas are mainly involved (7). The high incidence of gastrointestinal cancers in the north and northwest of Iran can be justified with respect to a supposed belt of upper GI tract cancers (including stomach and esophagus) which originates from the Far East, i.e. East Asia (Japan, Korea, and China) and crosses the Central Asian countries (Uzbekistan and Turkmenistan) and the Near East (Iran and Caucasus and Eastern Anatolia region of Turkey). West Azerbaijan and Kurdistan provinces of Iran are located on the belt.

Esophageal Carcinoma

Figure 2 shows the geographical distribution map of esophageal cancer ASR in 2005. The highest incidence is seen in provinces at the north and northeast of Iran, especially in Golestan, Mazandaran, Khorasan, and Ardebil. Esophageal cancer (EC) includes two primary groups of squamous cell carcinoma (SCC) and adenocarcinoma (ADC), both of which are among the most lethal cancers (8).

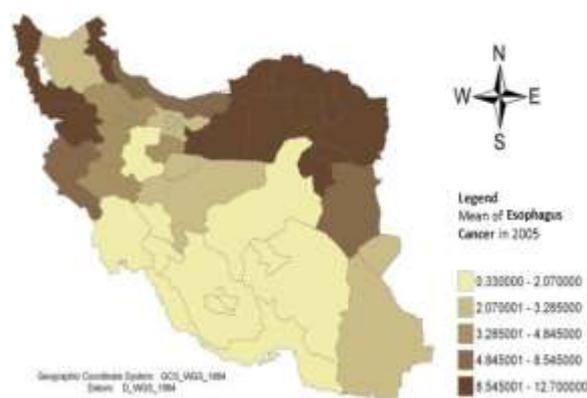


Figure 2. Geographical distribution map of Esophageal Cancer ASR, 2005

From a total of 35,000 annual deaths from cancer, 5800 cases are due to esophageal cancer, and Iran is statistically the second among countries with the highest mortality rate of cancer in the Middle East region of the World Health Organization (9). The incidence of EC is highly variable in different regions of the world and in different provinces of Iran. SCC is the most common esophageal cancer in Iran and the third in the world and comprises of about 90% of esophageal cancers (10). Over the last twenty years, SCC has been declining and ADC had a growing trend (11).

Colorectal Cancer

Figure 3 shows the geographical distribution map of colorectal cancer ASR in 2005. The geographical distribution of this cancer is higher in the central and western regions of the Caspian Sea and the central region of Iran. In the first published report in Iran, colorectal cancer was the third most common cancer among men (ASR=8.19-8.3) and the fourth among women (ASR=6.5-7.56) (12). But in recent reports, it was the third among men and women according to Kolahdoozan, and the fourth among men and the second among women according to Mousavi et al. (13). This difference is due to statistical methods and distribution of registration centers as well as sampling methods. According to the National Cancer Registration, the ASR of colorectal cancer at that year was 9.9 per 100,000 in men and 13.9 per 100,000 in women, and 5,000 people (7 per 100,000) per year develop colorectal cancer in Iran (14).

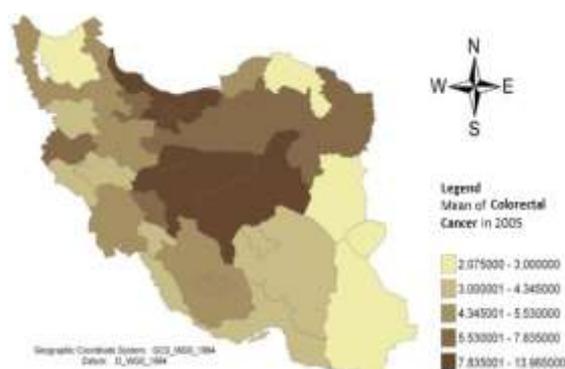


Figure 3. Geographical distribution map of Colorectal Cancer ASR, 2005

Prostate Cancer

In Iran, prostate cancer was at thirteenth rank in 1986 and reached the fourth in 2005. A part of this increase is related to the increase in early detection of prostate cancer (PSA test) and a part to the real increase in its prevalence due to lifestyle-related risk factors (15). Review of the first reported incidence of prostate cancer in Tehran shows that with an ASR of 15.6, it is the second most common cancer among men in Tehran (16). Also, according to data obtained from cancer registry reported in five provinces (Gilan, Mazandaran, Golestan, Ardabil, and Tehran) over five years (1996-2000), the ASR of prostate cancer was calculated 5.1. With aging over 65 years, the incidence rises significantly; this can be due to the effects of aging and the accumulation of risk factors over time. In Iran, the disease is in the age group of 65 to 75 years (12). According to Figure 4 showing the geographical distribution map of prostate cancer ASR in 2005, the highest prevalence is in Tehran, and then in Isfahan, Mazandaran, and Fars, and the lowest in Ilam provinces.

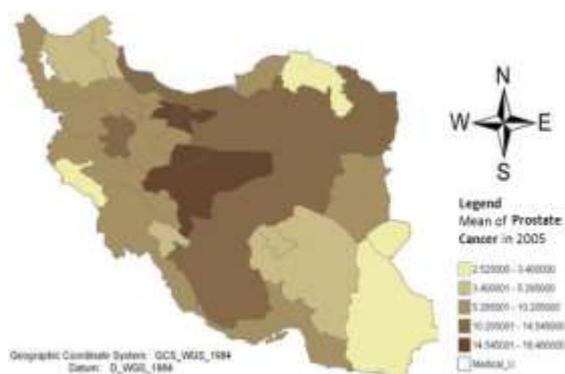


Figure 4. Geographical distribution map of Prostate Cancer ASR, 2005

Breast Cancer

Breast cancer is the most common type of cancer in women and the third most common cancer in Iran. According to the national data from 2001 to 2006, the average incidence of this cancer has increased from 13.02 per 100,000 in 2001 to 17.88 per 100,000 in 2006. The maximum incidence of breast cancer (463 per 100,000) is in the age group of 45 to 54 years, while it occurs at ages 75 to 79 years in 483 per 100,000 in the western countries, which indicates that breast cancer occurs at a younger age in Iranian women unlike the western countries (17). Regarding the frequency distribution in Iran, according to Figure 5 showing the geographical distribution map of women's breast cancer ASR in 2005, the highest and the lowest rates have been reported in Tehran and Chaharmahal and Bakhtiari provinces, respectively. In the first reported incidence and age distribution of breast cancer in Iran, ASR was calculated 17.1 based on population-based data from five provinces subject to cancer registry (Gilan, Mazandaran, Golestan, Ardabil, and Kerman) (11). According to the annual incidence rate of breast cancer in 2003, the provinces Yazd, Khorasan, Fars, Qom, and Khuzestan are next to Tehran province, respectively. By increasing women's social role in urban areas, social effects of exposure to cancer risk factors can be effective in development of cancer, so that it is more prevalent in large cities like Tehran and Yazd in comparison with provinces away from Tehran such as Kurdistan and Hormozgan with lower population densities and different lifestyle (17). A positive relationship exists between cancers including breast cancer with socioeconomic development (18). Iran

is a developing country and is faced with an increase in breast cancer.

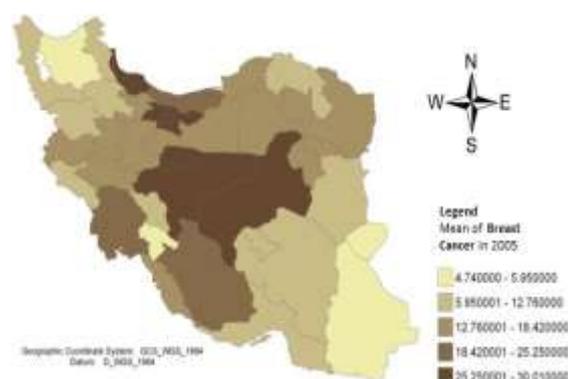


Figure 5. Geographical distribution map of Women's Breast Cancer ASR, 2005

Bladder and Ureter Cancers

In terms of origin, these tumors include transitional cell carcinoma (urothelial carcinoma), which is the most common type of cancer in Iran and in the industrialized countries, and tissue types including squamous cell carcinoma and adenocarcinoma. Association of the squamous type with schistosoma infection has been proven and the human papillomavirus is involved in creation of bladder uretral type cancer (19). In Iran, the male to female ratio is 4/7, and the age of occurrence is 67 years for men and 77 years for women. This cancer is the third most common cancer in Iranian men (17).

According to Figure 6 depicting the geographical distribution map of bladder cancer ASR in 2005, Gilan, Fars, Yazd, and Kurdistan have the highest and Hamedan, Hormozgan, and Sistan-Baluchestan provinces have the lowest incidence. Smoking has been known as the most important risk factor for bladder cancer. Opium use is common in Iran and since it is mostly associated with smoking, proving its hazard is difficult, but it is considered as a risk factor (20).

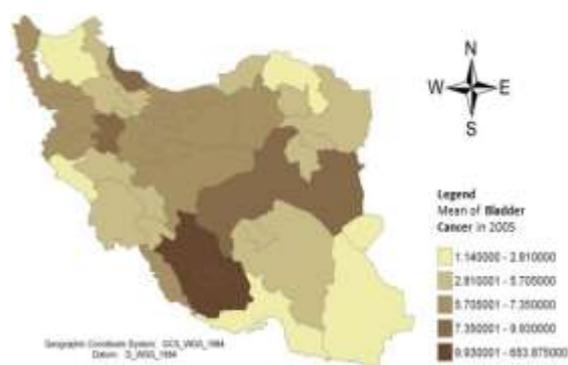


Figure 6. Geographical distribution map of Bladder Cancer ASR, 2005

Lung Cancer

Figure 7 demonstrates the geographical distribution map of men's lung cancer ASR in 2005. Accordingly, the highest frequency is in Kurdistan and West Azerbaijan provinces. Smoking is the strongest risk factor for lung cancer, and smokers are almost 20 times more at risk for lung cancer than non-smokers, which increases based on increased duration, inhalation, and number (21).

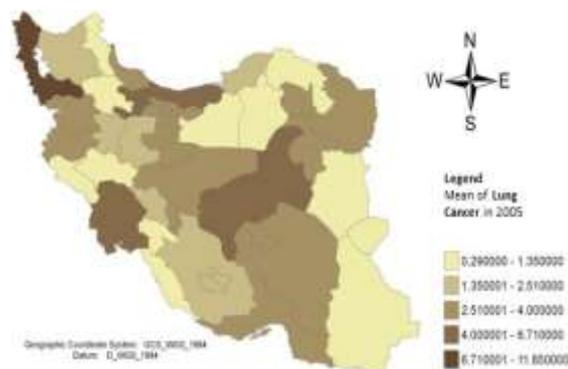


Figure 7. Geographical distribution map of Men's Lung Cancer ASR, 2005

Lung cancer is among the most common occupational cancers. Occupational risk factors include exposure to tar, smoke, coke, arsenic, chromium, nickel, asbestos in silica mine, and radiation. Asbestos is a well-known occupational carcinogen which acts synergistically with smoking, resulting in an exponential increase in the risk for lung cancer. Increased lung cancer has been seen in miners of uranium and other underground mines, and due to air pollution caused by fossil fuels and formation of carcinogens such as cyclic

hydrocarbons, arsenic, nickel, and chromium (22); urbanization and lung cancer confirm this association (23). A relationship has been observed between lung cancers and acquired airflow-blocking diseases such chronic obstructive pulmonary disease (COPD) or fibrotic disorders such as pneumoconiosis. Lower socioeconomic status is associated with late diagnosis of the disease, interaction with a collection of risk factors for lung cancer including smoking, poor diet, and occupational and whole environment exposure to carcinogens. Understanding these complex relationships between socioeconomic components and the risk of lung cancer is essential for effective recognition of this social inequality and reducing the rate of lung cancer in the poorer segments of society (15).

Dust and its increased distribution range is another problem that has been exacerbated in recent years in Iran, and may account for higher prevalence of lung cancer in the western areas of the country. According to various studies, it is claimed that the main sources of dust in Iran are the deserts and dry swamps of Iraq. Dust arises from June to September at the northwest territories of the Middle East and flows to the Persian Gulf through Iraq and Syria. Normal texture of these areas, particularly the Hour-al-Azim Lagoon, as well as measures taken to stabilize the soil in recent years, such as mulching and gravelling, have prevented dust emission. But the dust scope and volume has increased during the last 5 years due to drying of wetlands, inattention to soil stabilization in Iraq and Syria, drought, and loss of vegetation so that it crossed the mountains of Zagros and Alborz in the summer of 2009 and reached to the coastal areas of Gilan, and almost entirely covered Iran in 2010. Despite the role of dust in increasing lung cancer, claims about the presence of depleted uranium in weapons used in the war zones of Iraq and Syria, and studies which described the 180-day mission of US troops in Iraq dangerous due to repeated exposure to the dust and wanted to shorten the mission's duration, there is no strong scientific evidence on the efficacy of the dust on the health of those exposed in the mentioned areas, including Iran.

Ovarian tumors

Figure 8 shows the geographical distribution map of ovarian cancer ASR in 2006. Gilan, Tehran, Isfahan, and Yazd provinces have the highest frequency. In terms of the origin, about 90-95% of ovarian cancers are epithelial (24).

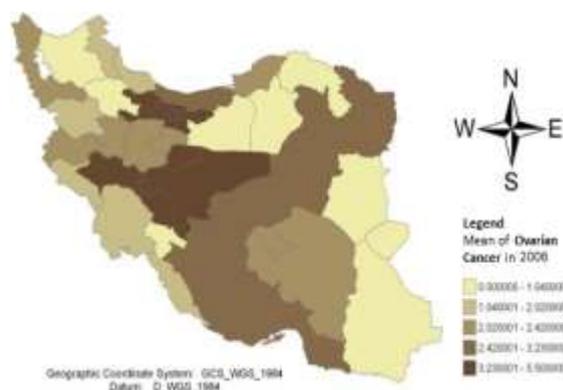


Figure 8. Geographical distribution map of Ovarian Cancer ASR, 2006

Tumors of the Central Nervous System

Figure 9 shows the geographical distribution map of CNS cancer ASR in 2006. The highest frequency is reported from Lorestan, Khorasan, Tehran, Isfahan, Fars, and Kerman provinces. The distribution pattern can be affected by accessibility to specialized groups and diagnostic methods. The tumors of CNS include the cancers of brain and other parts of CNS including those that occur in the brain (more than 90% of cancers), meninges (3%), and cranial or spinal nerves (about 3%). Brain and CNS cancer is mainly a disease of young people. Work in petrochemical, rubber, and nuclear industries or living near these industries increase the risk due to exposure to compounds such as vinyl chloride, acrylonitrile, and aromatic hydrocarbons. The risk of brain cancer increases due to exposure to high levels of electron magnetron frequency (EMF) in jobs that are in contact with the fields and living in proximity of high-voltage lines (25).

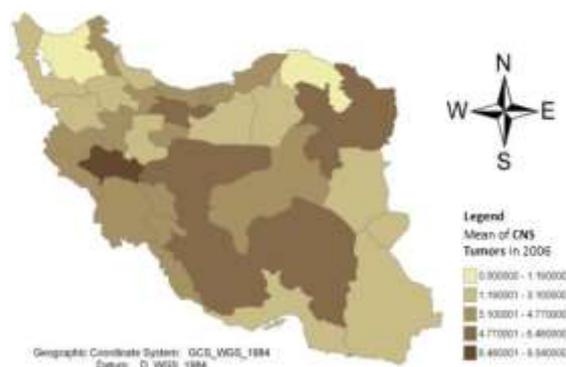


Figure 9. Geographical distribution map of CNS tumors ASR, 2006

Tumors of the Lymphatic System

These tumors have 2 age-related prevalence peaks in developed countries. The first peak is in the third decade of life (20-24 years) and the second after age 50 (80-84 years) (26). Its cause is unknown in most cases, although risk factors include exposure to chemicals such as benzene, pesticides, and insecticides, chemotherapy, exposure to radiation, weakened immune system, and some specific infections including HTLV-1. Almost all cases of non-Hodgkin's lymphoma occur in adults, and the average age at diagnosis is the 60s. Adult T-cell leukemia/lymphoma (ATLL) is a rare type of non-Hodgkin's lymphoma which is associated with HTLV-1 infection. It is believed that the virus is transmitted through sexual contact and exposure to infected blood through contaminated needles and syringes, and mother-fetus blood circulation (27).

Figure 10 shows the geographical distribution map of lymph nodes cancer ASR in 2006. Khorasan, especially Mashhad and Nishapur, are proposed as new endemic areas for HTLV-1 in Iran so that about 2-3% of these areas and 0.7% of blood donors have been reported infected with HTLV-1 (28).

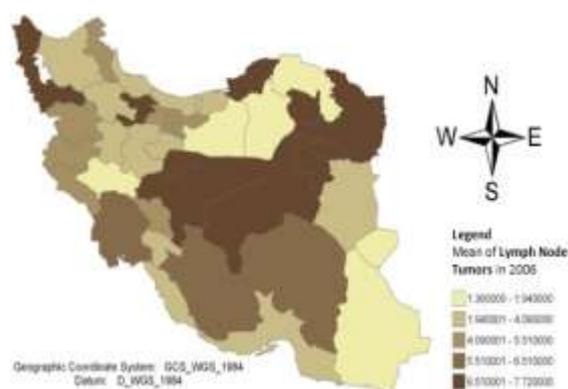


Figure 10. Geographical distribution map of Lymph Node Cancer ASR, 2005

Conclusion:

Statistical comparison of disease in different geographical areas help recognizing the causes and the methods of control; this depends on the accuracy of data collection and comparability of populations. The pattern of cancer types in Iran has significant difference compared to that of the developed countries. For example, gastric and esophageal cancers which are the most common cancer in Iran are much lower in other countries; *i.e.* it is not among the ten most common cancers in the United States. This clearly represents the importance of access to accurate and reliable local information. According to the reports in 2006, the incidence of all cancers in Iran was 117.3 in men and 102.4 in women per 100,000 people. This figure is based on pathology data and has not been collected from other sources. Therefore, the amount provided is much less than the actual amount. The first step in planning to fight cancer is to determine its amount and the way it disseminates, through officially recording the various types of cancer, and to allocate special budgets and necessary human resources. There is sporadic information in Iran about the incidence, prevalence, and mortality of cancer which cannot help national planning and subsequent evaluation, mainly due to being local (5).

So that some centers and research groups independently and actively collect cancer data from pathology centers, medical records, radiotherapy settings, and cemeteries and publish them as the population cancer registries. They include cancer registries in Tehran, Ardebil, Golestan, Semnan,

and Kerman Provinces. Even in these cases, no proper structure exists for cancer registry and the quality of data is affected by various problems and issues, except for cancer registry in Golestan Province which had a regular performance and has published three annual reports in 2004, 2005, and 2006. In other cases, only data of a period of 3 to 4 years has been collected retrospectively and reported. For this reason, they are not qualified for publication in the International Cancer Institute book. Data elements currently collected not only do not meet the national needs, but also are not consistent with the recommendations of the International Agency for Research on Cancer (29).

Different climatic conditions in Iran (seven climates including the coastal areas at the west, center, and east of the Caspian Sea, the coastal areas of Persian Gulf and Oman Sea, high mountains, and desert) have limited some of the diseases to certain areas. On the other hand, economic and cultural conditions may lead to injustice in the distribution of resources, planning, and policy-making in different regions, which *per se* leads to concentration of industries, facilities, and expertise in these areas. This concentration, on the one hand, has helped better identification of problems including cancer, resulting in false registration of cancer in the industrial provinces due to lack of recording population statistics in previous years. Uncontrolled immigration from other regions to these areas, on the other hand, has led to marginalization, health problems, *etc.* and hence increased the cancer-associated risk factors. The presence of industry and its risk factors increase the problem burden. Based on the combination index, Isfahan, Yazd, Markazi (Tehran, Qom, and Markazi), Khuzestan, Semnan, and Kermanshah are relatively industrialized provinces, West Azerbaijan and Zanjan are semi-industrial provinces, and other provinces has lower industrial levels (30), and most cancers occur in industrial regions or areas which have favorable climatic and economic conditions. One possibly important issue in the unequal distribution of cancer may be the effects of the Iran-Iraq War which had ended more than twenty years ago, while its long-lasting results are emerging. In that war, Iran was seriously invaded for 5 years (1983 to 1988) by the Iraqi chemical bombs such as mustard gas, sarin, tabun,

and more than one hundred thousand chemical bullets and weapons. Sulfur mustard gas has been reported to affect respiratory system, blood, ear, skin, and eyes and to induce genetic changes and carcinogenesis. Other effects which were unknown until recent decades include effect on the endocrine system. The effects of mustard gas during the war and sulfur mustard-containing chambers disembarked in the sea years ago were also reported, the latter recently was seen particularly in contact with fishermen (31). Perhaps many unknown factors of cancer are related to the events of this period. Immigration was also performed at this time, and an accurate cancer registry system may assist solving many of the unknowns. The effect of air pollution on the incidence of cancers requires weather data mining along with information on the disease dissemination. In general, help obtained from the maps in this regard and points that should be considered are as follows: maps do not show cancer cause, but show in which region of Iran we can test a hypothesis; high incidence in some regions can be quite accidental; researchers can focus on areas where several neighboring provinces have a high incidence, these areas may be exposed to risk factors or have a certain life style; areas with low incidence may reflect low risk factors or high protective factors.

The above issues will be achievable when accurate and reliable information with a more detailed location and with an acceptable length of time is available; and fortunately this has attracted more attention in recent years.

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بررسی پراکندگی جغرافیایی سرطان‌های مهم ایران

نیره اسماعیل‌زاده^۱ عبدالرضا صلاحی مقدم^۲ علیرضا خوشدل^۳

^۱ کارشناس ارشد، اپیدمیولوژی، دانشگاه علوم پزشکی مشهد، مشهد، ایران. ^۲ دانشیار، گروه انگل‌شناسی، دانشگاه علوم پزشکی هرمزگان، بندرعباس، ایران. ^۳ دانشیار، گروه اپیدمیولوژی، مرکز تحقیقات ژنوماتیک سلامت، دانشگاه علوم پزشکی آجا، تهران، ایران.

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چکیده

مقدمه: سالانه در جهان ۱۰ میلیون نفر با تشخیص سرطان روبرو می‌شوند و حدود ۶ میلیون نفر از آنها فوت می‌کنند. این مطالعه با هدف بررسی توزیع جغرافیایی (کشوری) سرطان و عوامل محیطی مؤثر بر توزیع آنها در ایران انجام شده است.

روش کار: مطالعه حاضر بر مبنای اطلاعات موجود است که به منظور تعیین توزیع فراوانی بروز ده سرطان شایع کشور (کارسینوم‌های معده، مری، کلورکتال، مثانه، ریه، سیستم اعصاب مرکزی، غدد لنفاوی، پروستات، تخمدان و پستان) از نقشه‌سازی داده‌های بروز تعدیل شده سنی (ASR) مربوط به هر استان، بر روی نقشه کشور با نرم‌افزار ArcGIS 9.3 در سال‌های ۱۳۸۴ تا ۱۳۸۵ توسط مرکز مدیریت بیماری‌ها (اداره سرطان) انجام شده است، می‌باشد و همچنین به منظور تعیین عوامل خطر محیطی، مطالعه مروری از منابع اطلاعاتی دیجیتال در دسترس شامل منابع عمومی و منابع انگلیسی و فارسی از جمله: *magiran* و *SID IranDOC IranMedex Pubmed Scopus* و جستجوی دستی از کتاب‌ها و دستورالعمل‌ها با کلید واژه‌های مورد نظر انجام شد.

نتایج: از نظر جغرافیایی بروز برخی سرطان‌ها در نواحی مختلف کشور متفاوت است. در سال‌های ۱۳۸۴ تا ۱۳۸۵ ASR سرطان ۱۰۲/۴ و ۱۱۷/۳ در میان زنان و مردان است که این میزان سرطان در شمال بیش از جنوب ایران و بین پایگاه‌های داده متفاوت است که ممکن است به دلیل روش ثبت و تفاوت سایت باشد. فاکتورهای سبک زندگی، عوامل عفونی، مواجهه‌های محیطی و عوامل داخلی بدن، با انواع خاصی از سرطان‌ها این اختلافات را تا حدی توجیه می‌کند.

نتیجه‌گیری: توسعه، استقرار و اجرای برنامه جامع ملی کنترل سرطان باید اولین اولویت برای سیاست‌گذاران سلامت و درمان باشد و به نظر می‌رسد ارتش با توجه به پراکندگی کشوری در صورت دارا بودن سامانه ثبت و کنترل موارد سرطان می‌تواند کمک بزرگی به گردآوری و تحلیل اطلاعات کند.

کلیدواژه‌ها: سرطان - نقشه‌سازی - عوامل خطر - ایران

نویسنده مسئول:
دکتر علیرضا خوشدل
مرکز تحقیقات ژنوماتیک سلامت
دانشگاه علوم پزشکی آجا
تهران - ایران
تلفن: +۹۸ ۲۱ ۸۸۳۳۷۹۰۹
پست الکترونیکی:
dr_khoshdeld@armyums.ac.ir

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