

TREND OF THE INCIDENCE OF BRAIN CANCER IN IRAN AND IT'S 6 GEOGRAPHICAL REGIONS DURING 2000-2005

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ABSTRACT

Background: Brain cancer is an illness with serious symptoms and poor prognosis. Tumors of the central nervous system is about 2% of all cancers with mortality rate about 4.2-5.4 per 100,000 persons per year worldwide. This study evaluates the incidence during 2000 to 2005 in 6 geographical areas in Iran using national cancer registry data.

Materials and Methods:

Data from the cancer registry system in Iran during 2000 to 2005 was extracted. Incidence rates were standardized directly using WHO population and also 95% confidence intervals were calculated in STATA. The significant incidence of changes over the years under study were tested by Poisson regression models.

Results:

The age-standardized incidence rate of brain cancer, in 2000 in men and women respectively reached from 0.6 and 0.4 per 100000 to 2.4 and 1.6 per 100000 in 2005. The highest incidence rate of brain cancer seen in the provinces of mountains areas and the lowest rate seen in the province settled in Central and Western area of the Caspian Sea. Trends incidence in all geographic areas of the country is rising despite the difference in slope. Ratios of male to female was 1.54 and the mean age of patients was 39.2 with a standard deviation of 19.6. **Conclusion:**

In general, along with other cancers, the incidence of brain cancer is growing in all geographic regions in Iran.

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Introduction

Tumors of the central nervous system (CNS) is estimated to be about 2% of all cancers worldwide. Incidence (mortality) is about 4.2 to 5.4 cases per 100,000 populations per year [1]. Despite the low incidence of brain tumors compared with other malignancies, it has a very severe symptoms and poor prognosis [2].

Due to rapid growth and a desire to expand throughout the brain and spinal cord, brain tumors are difficult to treat, from 18,000 Americans that each year are diagnosed with primary malignant brain tumors, only 1.3 survive more than 5 years [3]. This cancer is now the second cause of cancer death in children and it's the third leading cause of death in young people from

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20 to 39 years [4,5]. Based on the Tumor Association of America (ABTA) in 2010, 62,930 new cases of primary brain tumors diagnosed which among them 23720 were malignant and 39210 were benign tumors [6] in the UK every day 11 patients are diagnosed with brain cancer and 9 cases of brain cancer will die [7]. In Iran it is estimated each year about 50800 new cases of cancer occurs which 3.67 % belongs to the brain and almost 4% of all cancer mortality [8].

In recent years, advances are obtained in therapies including surgical incisions promotion and radiation therapy procedure. New systemic factors for these tumors and also dramatic improvements in molecular biology diagnosis of these tumors were helpful in discovering several new therapies [9]. Despite aforementioned issues, incidence of brain tumors over the past 20 years in all age groups, particularly adults has increased more than 40% [2]. This rate in England has increased in men 23% and women 25% during 1970-2012 [10]. The prevalence of primary tumors of the central nervous system in the United States reached from 11.5 in 1994, to 20.1 in 2008 [11,12]. The prevalence of this trend is more obvious in the elderly. Improvement in diagnostic methods and also increasing life expectancy could be the reason for this increase [13, 14].

Incidence of the brain and central nervous system's tumors in men for all types of neoplasms except meningioma that affects women more than men (80% prevalence of meningioma in women and 20% in men) is slightly more common in the women [15]. Global incidence of malignant brain tumors in 2008 was 3.7 in men and 6.2 in women per 100000 which in developed countries was 5.8 for men and 4.1 in women per 100,000 and in underdeveloped countries it was 3 in men and 2.1 in women per 100,000 [12]. In United States between years 1998-2002, there were 6.4 cases per 100,000 populations and in men it was more than women (7.6 versus 5.3 per 100,000) [16]. In our country, cancer is one of the most important health problems and after road accidents and cardiovascular diseases, cancers are the most important cause of death [17] each year more than 30,000 people die in Iran because of cancers [18] Due to the growing percentage of elderly population, improvements in life expectancy, advances in technology, changes in peoples lifestyle and other cancer risk factors, it is predicted that the number of deaths from cancer in Iran for 2020 reaches to 62,000 [18]. Brain cancer is the eleventh most common cancer among all cancers and its annual incidence in men is about 550 cases and approximately 800 in women [19]. In general, it seems that the population prevalence of brain tumors, in specifically meningioma is relatively high among the population of the Middle East as well as Iranian population [20 and 21].

Worldwide prevalence of central nervous system and the primary malignant brain's tumors is 3.6 cases per 100,000 in men and 2.5 in women. The prevalence in more developed countries is 5.9 cases in men and 4.1 cases per 100,000 in women, compared to less developed countries 2.8 per 100,000 cases in men and 2 cases in women. This difference in the prevalence mainly reflects the lower equipment for diagnostics and reporting [22].

Our knowledge about the etiology of the brain tumors and other cancers of the central nervous system is low [23-25]. Only known risk factor for cancers of the brain and central nervous system is contact with therapeutic ionizing radiation, other risk factors include contact with synthetic rubber manufacturing, vinyl chloride, Petroleum refining and consumption of cured foods [26]. Contact with filtered cigarettes, diagnostic ionizing radiation, and residential electromagnetic fields, formaldehyde, using of cellphone and active or passive maternal tobacco smoking are not proven risk factors [26].

Due to the limited number of good national studies dealing with incidence trend of this cancer, in present study we review the incidence of brain cancer during the years 2000-2005 in two sex and six separate geographic regions of the country. The results of this study will be important for policy makers in the health system to identify the risk of brain cancer incidence in the future.

Materials and methods

In the present study, which is a population-based cross sectional study, data obtained from the Center for Disease Control (CDC) of the Ministry of Health. This data is collected at the end of each year from pathology centers across the country which CDC after receiving this data review them in terms of correct coding, deficiencies in the identification, demographic information and removal of the duplicates report. Cancers have been coded based on the International Classification of Diseases ICD_O (second edition) [27].

The code C33 and C34 were for lung cancer. According to classification of comprehensive general health by H. Hatami we divided the country into six climatic zones. Thus, the provinces of Gilan and Mazandaran provinces as the center and the West of the Caspian Sea, Golestan province alone as the East of Caspian region, the provinces of Tehran, Qom, Qazvin, Zanjan, East Azarbaijan, West Azarbaijan and Ardebil provinces as the region foothills, Kermanshah, Kordestan, Hamedan, Ilam, Chahar Mahal and Bakhtiari, Kohgiluyeh and Boyer Ahmad and Fars as mountainous region, province of Kerman, Sistan and Baluchestan, Yazd, Semnan, Khorasan, Birjand and Isfahan as the desert area and the province of Khuzestan, Bushehr and Hormozgan provinces were selected as the Persian Gulf coastal region. In addition, a high proportion of registered cancer cases has unknown place of residence that were considered in the overall incidence of country, but has not been considered in the calculation of different geographical areas. In order to standardize of the incidence, the population census results in 2006 were used that which estimated by considering the country in annual population growth rate of 1.01 percent and the population in 2006 based on different geographical areas population for years 2000, 2001, 2002, 2003, 2004 and 2005 respectively. Also standard population of WHO was used as the standard population. Incidence rates age - sex and 95 percent of them for the whole country and according to different geographical areas with a direct method was calculated by using the software Stata11 and showed by sex and age groups. A significant incidence trends was testing by using software Stata11 and a Poisson regression model. Alpha error of less than 0.05 was assumed significant. Excel2007 software was used for drawing the graphs.

Results

The total number of registered cases of brain cancer in Iran during this study was 4409 case which from 282 cases in 2000 reached to 1257 cases in 2005 and the sex ratio of male to female is 1.54. The average age was 39.2 years with a standard deviation of 19.6 years which in women was 38.4 years with a standard deviation of 19.7 years and in men it was 39.7 years with a standard deviation of 19.4 years. The 6-year average of brain cancer incidence in Iran was 1.2 cases per 100,000 people. The age standardized incidence rate of brain cancer has increased in Iran, and from 0.47 cases per 100,000 in 2000 increased to 1.99 in 2005 cases per 100,000 people. Age-standardized incidence rate for males' population in all years of the study was higher than women, so that in men the rate from 0.56 cases per 100,000 people in 2000 increased to 2.41 cases per 100,000 people in 2005 and in females from 0.38 cases per 100,000 people in 2000 reached to 1.56 in 2005 cases per 100,000 people.

Table 1. Geographical regions and cases per 100,000 people from 2000 to 2005.

		2000	2001	2002	2003	2004	2005	Slope/ PValue
Center and Western border of Caspian area	Male	0.2(0-0.4)	0.1(0-0.3)	0.2(0-0.4)	0.6(0.3-0.9)	1(0.6-1.4)	1.3(0.8-1.7)	0.49(0.20)
	Female	0(0-0.1)	0(0-0.1)	0.2(0-0.3)	0.4(0.2-0.6)	0.9(0.6-1.3)	0.6(0.3-0.9)	0.57(0.27)
	Total	0.1(0-0.2)	0.1(0-0.2)	0.2(0-0.3)	0.5(0.3-0.5)	1(0.7-1.2)	0.9(0.7-1.2)	0.48(0.25)
Eastern border of Caspian area	Male	0(0)	0.5(0-1.1)	0(0)	0.2(0-0.5)	1.6(0.6-2.6)	2.3(1.2-3.5)	0.71(0.07)
	Female	0(0)	0.5(0-1.1)	0.3(0-0.8)	0.6(0-1.2)	0.6(0-1.1)	0.5(0-1.1)	0.21(0.57)
	Total	0(0)	0.5(0.1-0.9)	0.1(0-0.4)	0.4(0.1-0.7)	1.1(0.5-1.7)	1.4(0.7-2.1)	0.51(0.18)
Desert area	Male	0.7(0.5-0.9)	0.3(0.2-0.5)	0.2(0.1-0.3)	0.4(0.2-0.5)	0.5(0.3-0.6)	1.9(1.6-2.3)	0.3(0.33)
	Female	0.5(0.3-0.7)	0.3(0.2-0.5)	0.3(0.1-0.4)	0.3(0.2-0.4)	0.5(0.3-0.6)	1.6(1.2-1.9)	0.31(0.35)
	Total	0.6(0.5-0.8)	0.3(0.2-0.4)	0.2(0.1-0.3)	0.3(0.2-0.4)	0.5(0.3-0.6)	1.7(1.5-1.9)	0.31(0.35)
Flat area	Male	0.2(0.0-0.3)	0.2(0.1-0.4)	0.2(0.1-0.3)	0.4(0.3-0.6)	1.3(1-1.5)	2.7(2.3-3.1)	0.69(0.06)
	Female	0.1(0-0.2)	0.2(0.1-0.3)	0.3(0.1-0.4)	0.4(0.2-0.5)	1.2(0.9-1.5)	1.9(1.6-2.3)	0.61(0.11)
	Total	0.2(0.1-0.2)	0.2(0.1-0.3)	0.2(0.1-0.3)	0.4(0.3-0.5)	1.2(1-1.4)	2.3(2.1-2.6)	0.64(0.09)
Mountainous area	Male	0.5(0.3-0.7)	0.7(0.5-1)	0.9(0.6-1.1)	0.9(0.7-1.2)	1.7(1.4-2.1)	1.7(1.4-2.1)	0.25(0.30)
	Female	0.2(0.1-0.4)	0.4(0.2-0.6)	0.6(0.4-0.8)	0.6(0.4-0.9)	0.8(0.6-1.1)	1.2(0.9-1.5)	0.29(0.36)
	Total	0.4(0.2-0.5)	0.6(0.4-0.7)	0.7(0.6-0.9)	0.8(0.6-1)	1.3(1.1-1.5)	1.4(1.2-1.7)	0.24(0.36)
The border of Persian gulf area	Male	0(0-0.1)	0.2(0-0.4)	0.5(0.2-0.8)	0.6(0.3-0.9)	1.2(0.8-1.6)	2(1.4-2.6)	0.6(0.10)
	Female	0.1(0-0.2)	0.1(0-0.2)	0.3(0.1-0.5)	0.3(0.1-0.5)	0.7(0.3-1)	1.2(0.7-1.6)	0.54(0.23)
	Total	0.1(0-0.1)	0.1(0-0.3)	0.4(0.2-0.6)	0.4(0.2-0.6)	0.9(0.7-1.2)	1.6(1.2-2)	0.57(0.15)
Iran	Male	0.6(0.5-0.7)	0.5(0.4-0.6)	0.9(0.8-1)	1.8(1.6-1.9)	2.1(2-2.3)	2.4(2.2-2.6)	0.32(0.14)
	Female	0.4(0.3-0.5)	0.3(0.2-0.4)	0.7(0.6-0.8)	1.2(1.1-1.3)	1.4(1.3-1.6)	1.6(1.4-1.7)	0.31(0.23)
	Total	0.5(0.4-0.5)	0.4(0.3-0.4)	0.8(0.7-0.9)	1.5(1.4-1.6)	1.8(1.7-1.9)	2(1.9-2.1)	0.32(0.18)

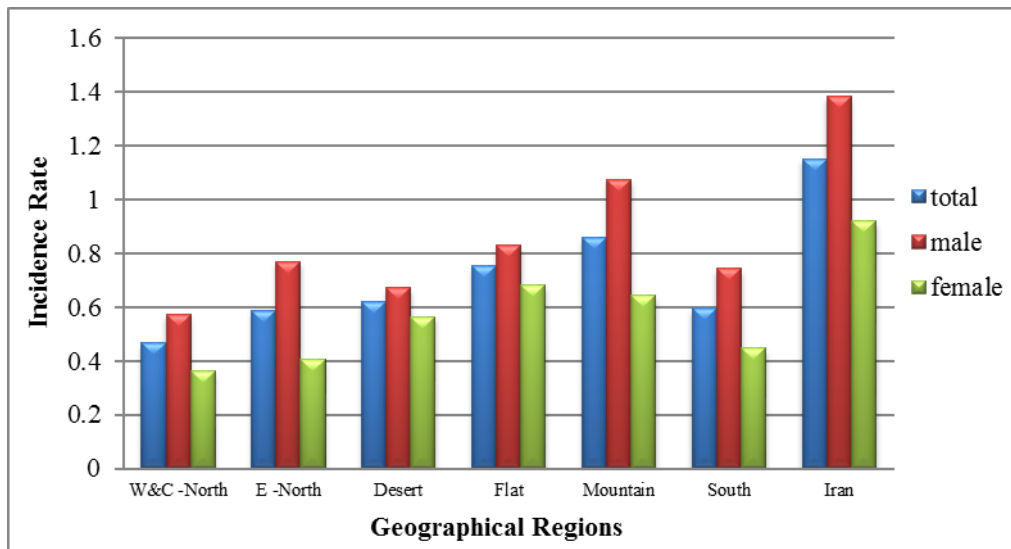


Figure 1. Average of Age-standardized incidence rate of brain cancer for different areas during 2000-2005 by sex

Central and Western Caspian Sea region:

During the years of study, this region had the lowest incidence of brain cancer, and lower than the national average and allocated ranks sixth in six studied districts (Figure 1). In the study of brain cancer in this area had an increasing trend with a slight slope from 0.1 in 2000 reached to 0.9 per 100,000 of the population in 2005 which in years 2000 and 2001 had a fixed value and from the year 2001 to 2004, every year nearly got doubled and in 2005 had decreased. In terms of gender segregation, it's observed that the incidence in both sexes has different variations. In men, age standardized incidence rate from years 2000 to 2005 from 0.2 in 2000 reached 1.3 cases per 100,000 of the population and in women from 0 reached to 0.6 per 100,000 people and in all studied year incidence trend for men was nearly more than women (Table 1). The incidence rate increased in older ages (Figure 2).

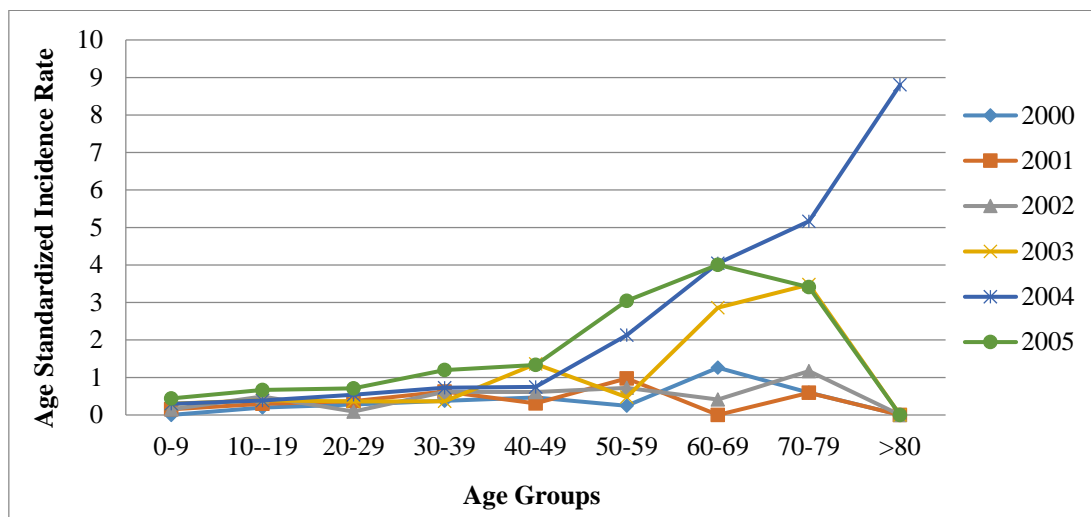


Figure 2. Age standardized incidence rate of brain cancer in Center and Western border of Caspian during 2000-2005 by age groups and years

The Eastern coast of the Caspian Sea region:

This geographical area after mountainous and foothill areas is the third area of high risk of brain cancer in Iran (Figure 1). In this region, like other regions we can see a significant increase in brain cancer rates so that the standard age from 0 cases in 2000 reached to 1.4 cases per 100,000 of the population in 2005. Age-standardized incidence rate from 2000 to 2002 each year almost got doubled than the previous year and in 2003 it reduced and from this year onwards we saw an increase in the slope of brain cancer trends in later studied years. The incidence of this cancer in terms of gender segregation has different changes, this rates in men from zero in 2000 reached to 2.4 cases per 100,000 of the population and among women from zero cases, 2000 reached to 0.5 cases per 100,000 of the population in 2005 (Table 1). The incidence rate increased in older ages with some variation in different years (Figure 3).

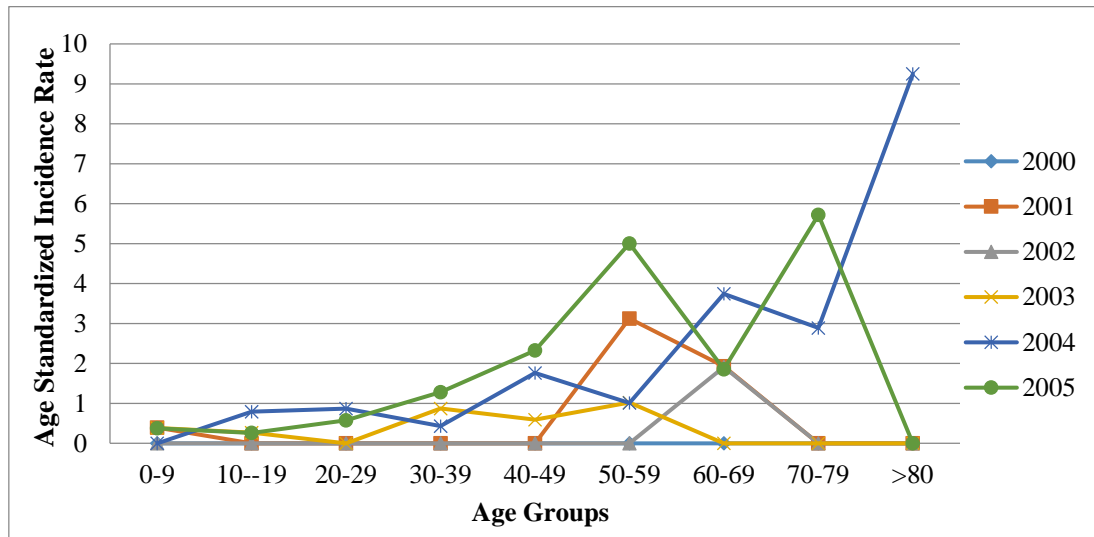


Figure 3. Age standardized incidence rate of brain cancer in Eastern border of Caspian during 2000-2005 by age groups and years

Desert area:

Among the 6 districts geographical regions, the desert region ranks fifth in terms of brain cancer risk, and the incidence of brain cancer in this area is less than the national average. The incidence rate increased in older ages (Figure 1).

In this area, the age-standardized incidence rate from 0.6 cases in 2000 reached to 1.7 cases per 100,000 of the population in 2005, in this area we witnessed a decrease and increase in the change slope of cancer in studied years which since 2000 to 2002 the slope of cancer decreased and then we are seeing steadily an increasing in incidence trend. The incidence of this cancer has a different slope in terms of gender segregation and is generally more common in men, this rate in men from 0.7 in 2000 reached to 1.9 cases and in women from 0.5 to 1.6 cases per 100,000 of population and it should be noted that in the review process of this cancer in the studied years, in 2001 and 2004 had the same slope and in 2002 the incidence rate among

women was higher than men (Table 1). Same as other areas the incidence rate increased in older ages (Figure 4).

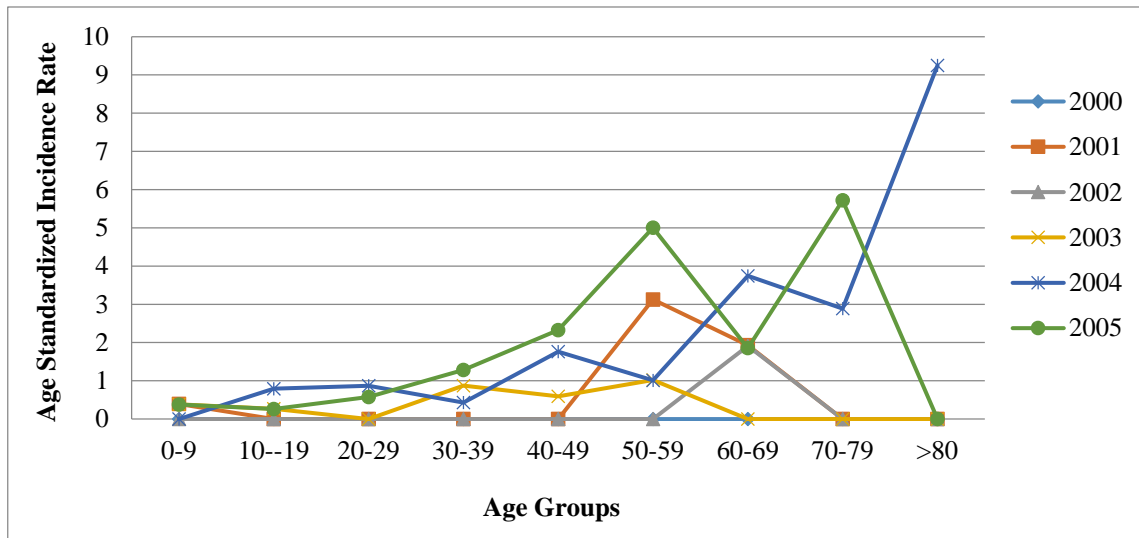


Figure 4. Age-standardized incidence rate of brain cancer in Desert area during 2000-2005 by age groups and years

Foothills area:

After mountainous area, foothills area as the riskiest geographic regions of Iran, ranked second in terms of the incidence of brain cancer (Figure 1). During 6 years of studying, we witnessed increasing trends in brain cancer incidence in this geographical area. In the study of the brain cancer incidence in this area, between 2000 to 2005, incidence trends of brain cancer has been increasing and among men since 2000 to 2002 with 0.2 had a constant slope, while the rate between mentioned year was increasing in women and since 2000 to 2001, from 0.1 reached to 0.2 and this amount reached to 0.3 cases per 100,000 people in 2002. In continuing since 2002 to 2005 has increased for both sexes and in 2005 reached to 2.7 cases in men and 1.9 cases in women per 100,000 of the population. Age-standardized incidence rate of brain cancer in men from 0.2 cases per 100,000 people in 2000 reached to 0.6 cases per 100000 people per year in 2005 while among women this rate from 6.5 cases per 100,000 people per year in 2000 reached to 18.2 cases per 100,000 people in 2005 (Table 1). The incidence rate increased in older ages (Figure 5)

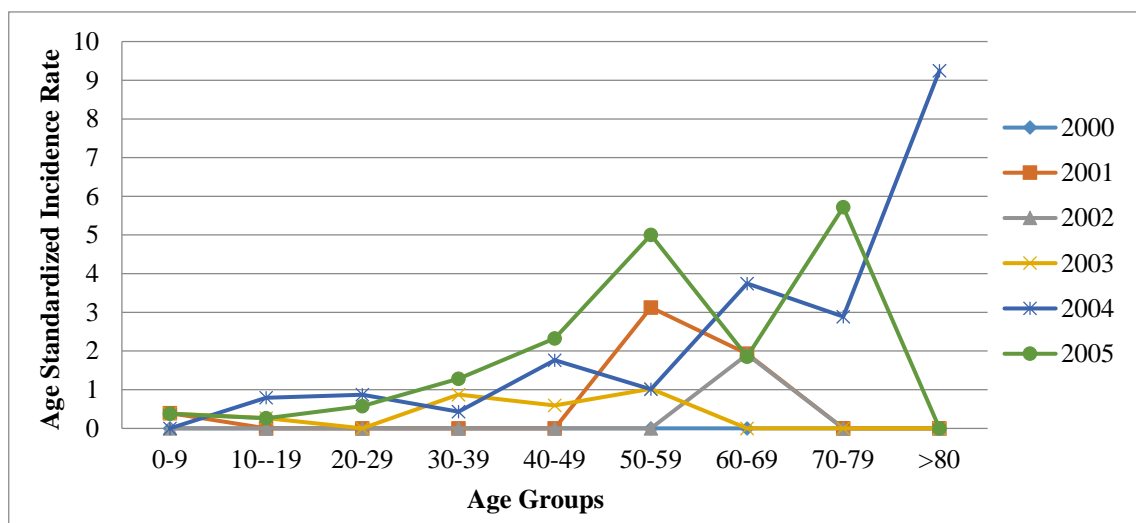


Figure 5. Age-standardized incidence rate of brain cancer in Foothills area during 2000-2005 by age groups and years

Mountainous area:

If we get the average of the brain cancer incidence in 6 years of studying and classify different geographical areas in terms of it, brain cancer incidence rates are lower than the national average and 6 under study districts have the largest amount of incidence (Figure 1). In the study of the brain cancer incidence in mountainous regions of Iran, trend incidence increased in both sexes from 2000 to 2005 and among men from 0.5 cases in 2000 reached to 1.7 cases per year in 2005 and among women in 2000 from 0.2 cases reached to 1.2 cases per 100,000 of the population in 2005. In the continuing of the incidence trend of brain cancer in mountainous areas, from 2002 to 2003 this rate among both sexes with 0.9 in men and 0.6 in women has been with a constant slope and from year 2003 onwards in men with a corresponding increase reached to 1.7 cases per 100,000 populations while among women with 0.8 cases in 2004 and 1.2 cases per 100,000 of the population in 2005 shown an increasing trend and generally in men it is more than women. In the analysis of trend incidence of brain cancer in age groups in this area was observed that in all age groups increases with age and in the age group of 60 to 69 years reached to maximum and after age 60 to 69 it will decrease (Table 1). The incidence rate increased in older ages (Figure 6)

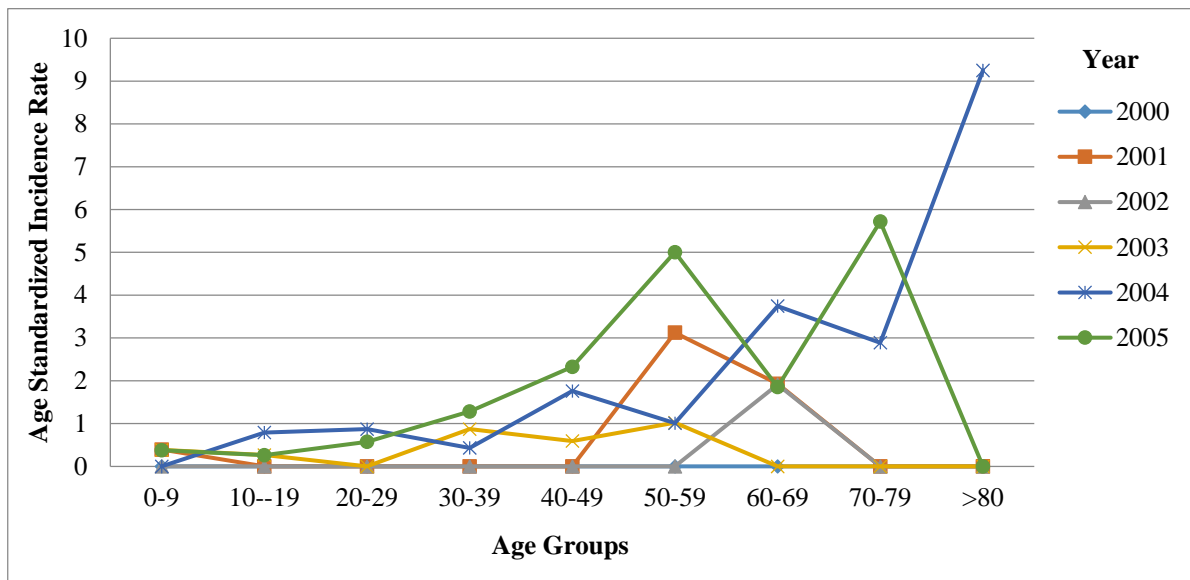


Figure 6. Age-standardized incidence rate of brain cancer in Mountainous area during 2000-2005 by age groups and years

The margin of the Persian Gulf region:

The incidence of brain cancer in this area is higher than the national average and ranks second in 6 under study district. In the review of incidence trend of brain cancer in the margins of the Persian Gulf among men in 2000 no cases of brain cancer were a report which in 2001 has increased to about 0.2 and among women between 2000 and 2001 with 0.1 cases per 100,000 populations has been a stable trend. Between 2002 and 2003 the incidence of brain cancer has been increased from 0.5 to 0.6 in 2003 while trend incidence of cancer among women between these years, with about 0.3 cases had an increasing stable trend. Between 2004 and 2005 had an increasing incidence trend of brain cancer in both sexes and in men in 2004 from 1.2 cases reached 2 and in women from 0.7 cases in 2004 reached to 1.2 cases in 2005 per 100,000 populations.

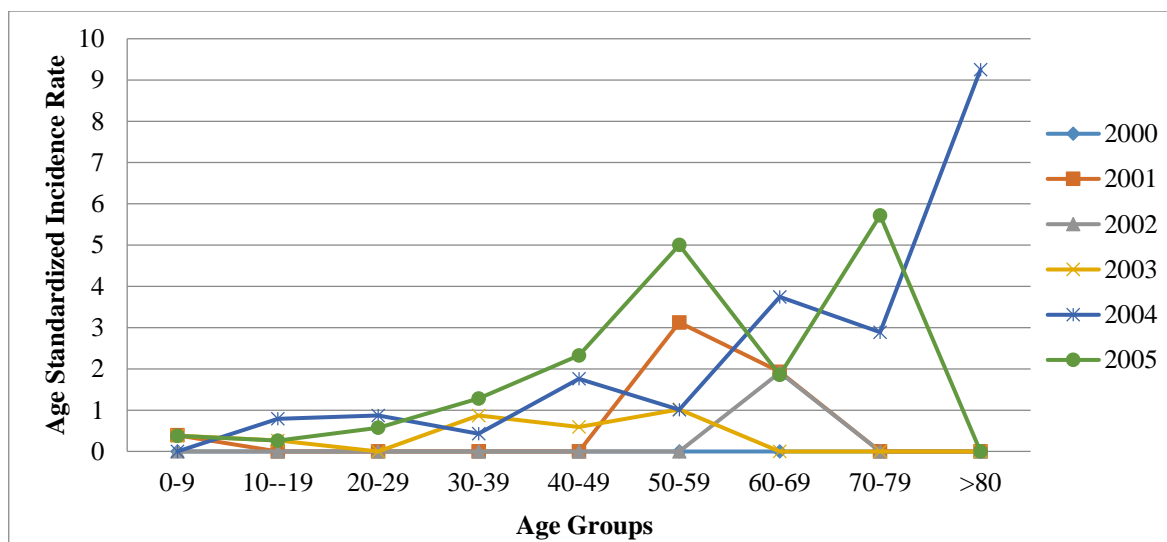


Figure 7. Age-standardized incidence rate of brain cancer in the border of Fars gulf area during 2000-2005 by age groups and years

Conclusion:

Based on the study results, generally, there is an increase in the incidence of brain cancer in males more than females. According to recorded data from the National Cancer Center between 2000 and 2009, brain cancer incidence is more common in males, which is consistent with our result [28]. It seems that the men are more exposed to the risk factors. Study conducted in Kerman has showed that incidence of brain tumors were more common in women [29]. Other studies found that increase in central nervous system tumors in women is higher than men and the reported probable cause of this increase are use of oral contraceptives, hormone replacement therapy and treatment of infertility which also increases the hormones in women [30]. We can conclude that the proportion of these differences in various regions may be due to geographical differences or low level of health services available for women in developing countries. Based on the results of this study, the highest rates of central nervous system's cancer was seen in the mountainous area and the lowest rate in the central and western area of the Caspian Sea region. Overall, the incidence cases of cancer in Ardabil province have been reported 132 in men and 96 in women per 100,000 populations [31]. This amount generally in 2005 in Semnan, was 156 men and 136 in women per 100,000 [32]. The reason for differences in the incidence of cancers among different regions could be due to lack of access to programs of screening and medical care or possibly prevalence of different risk factors.

Other possible causes of increase in brain cancer in Iran could be the beams of ionizing radiation. The only known factor associated with the occurrence of benign and malignant brain tumors is high or moderate doses of ionizing radiation, such as those caused by head radiation, which is only a small portion of brain tumors [33 and 34]. The main source of contact with Applied Radiation therapy is that commonly used to treat Kapitis Taenia (a fungal infection) and tuberculosis adenitis in children in the middle of the last century. This therapy is considered as a safe and simple treatment and it is performed in different regions of the United States [35] and also widely used in the Middle East. However, there is no direct evidence, its widespread use noticed by those researchers that have been studied the long-term effects in Iran and Turkey [36-38]. In Iran, according to a Mortazavi et al. study, most meningiomas incidence are probably caused by radiation for fungal infection (tinea capitis) in children [39]. Based on these

studies, we can consider that a portion of brain tumors in Iran was caused by the increased use of ultraviolet radiation.

Age is the main risk factor for developing cancer. Although cancer can be increased at any age but the chances of developing cancer increases with age [40]. Studies on brain cancer patients in America shows that the incidence of this disease increases with age [41]. Mehrazin and his colleagues in 2006 showed that the average age of diagnosis was 33.9 [42], which is almost parallel with the study. Currently, 6% of the total population of Iran constituted of the elderly above 60 years which is equivalent to four million and 562 thousand people and it is predicted that these figures until 2050 reach to 26 million and 393 thousand, equivalent to 26% of the population of the country [43]. It is expected that in the future we will see further increase of this cancer in Iran.

Other reasons for interpretation of the increase in the rate of brain cancer in Iran could be the development of diagnostic and treatment services. In the recent years, the health-care system had a growing trend and care services and diagnosis has improved [44] which it would be one of the most important factors of increasing of the brain cancer incidence in Iran. Along with these advances in diagnosis and consequently increasing of this equipment can cause an increase in brain cancer in Iran.

In interpreting the results of this study and justify the increasing trend of brain cancer, the most important issue is the accuracy of cancer registry system in Iran. Cancer registry system in Iran has an increasing trend during recent years [45] according to the Ministry of Health, the completeness of cancer registry in the country from 18 percent in 1999 has increased to 80% in 2005 [46]. Lack of the quality is the problem of some international cancer reports. For example, there is a gap between the result of the global burden of disease cancer collaboration (GBD-CC) and available data in Iran [47]. Therefore, it is essential for interpreting the results of all cancer studies in Iran consider this promotion of registration system. But how much of this increase and more in what geographic areas related to the issue is a subject that should be addressed in the future research.

Another part of the causes of brain tumors can be caused by genetic factors. Farwell and his colleague shown a higher incidence of brain tumors in relatives of children with brain tumors [48] According to recent studies conducted by Taghipoor and colleagues in 2010 an increase in the risk of meningioma in the Jewish population of Shiraz and the authors suspect that some genetic factors may be involved [49].

Other possible causes of brain cancer in Iran can be attributed to the low awareness of public about the early symptoms and treatment of this cancer. In Iran, studies have shown that the percentage of those with moderate and low knowledge is 85%, 76% and 94%, respectively [50-52] and can be deduced that by teaching risk factors and training cancer symptoms to the community, the cancer is somewhat controlled. Limited knowledge about cancer can cause late consultation for diagnosis and treatment and subsequently cancer development and metastasis which increases the costs, reduces the chance of treatment and increase in deaths from cancers.

In addition to the awareness of people's can note the economic situation. According to Mckean-Cowdin studies, parents of patients with brain tumors had lower educational levels than the control group and belonging to the lower socio-economic classes of society [53], which can prove the above results. Therefore, it is necessary to saw the evolving trend of the cancer records system as had been mentioned in other cancer studies in Iran [54-60]. Considering the change of mortality rates also could help the interpretation of the trends which evidence had shown the increase of prevalent cancers in Iran [61].

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