

Short communication

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Mortality trends of brain and central nervous system cancers in Babol, northern Iran (2013-2021)

Abstract

Background: Cancers of the brain and central nervous system, with more than 250,000 deaths in 2020 and an age-adjusted mortality rate of 3.05 per 100,000, rank twelfth in mortality among various cancers. Our study aimed to investigate the crude rate, age-standardized mortality rate (ASMR) and the trends of brain and CNS malignancies over nine years in northern Iran.

Methods: This cross-sectional study conducted a thorough analysis of mortality caused by brain and CNS cancers in Babol between the years 2013 and 2021. Death registration and classification systems at Babol University of Medical Sciences were used to collect the cause-of-death data. A census sampling method was used to determine the number of brain and CNS cancers deaths. All analyses were done using SPSS Version 22 and STATA Version 14. The significance level was set at ($p < 0.05$). The crude and age-standardized mortality rate was calculated. The Cochran-Armitage Trend Test was utilized to determine the mortality trend.

Results: The crude rates and ASMRs for brain and CNS cancers increased, from 3.3 and 3.2 per 100,000 people in 2013 to 7.0 and 6.3 per 100,000 in 2021, respectively ($p < 0.001$). Additionally, over the nine years, an increasing trend was explicitly observed for brain cancer ($p < 0.001$), while the trends for other cancers remained stable.

Conclusion: The ASMR and the trend of brain and CNS cancers are on the rise. This study's findings could be beneficial for designing monitoring programs and investigating cancer risk factors.

Keywords: Brain neoplasms, Central nervous system, Mortality, Meningeal neoplasms.

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Brain and central nervous system (CNS) cancers are among the most significant concerns for health systems globally, with an estimated over 308,000 new cases and more than 250,000 deaths in 2020 (1). These diseases rank tenth in terms of Disability-Adjusted Life Years (DALYs) and twelfth in mortality among various cancers worldwide (1, 2). Brain and CNS cancers exhibit highly heterogeneous characteristics (3, 4). These malignancies present with symptoms such as seizures, cognitive problems and psychiatric disorders (4). Despite various potential risk factors, the only currently confirmed factor is exposure to moderate to high doses of ionizing radiation (5). Using GLOBOCAN 2020 data, a recent study has estimated the ASMR of 2.6 for CNS cancers in Asia, which is lower than the Global ASMR of 3.05 for brain and CNS cancers in 2019; however, these values were highest in Iran, Armenia, and Turkey at 6.20, 6.20, and 5.10 per 100,000, respectively (6, 7). In addition, according to a study by Liu et al. CNS cancer mortality in Asia has slightly decreased from 2.76 per 100,000 in 1990 to 2.75 per 100,000 in 2019 (8). CNS cancers are among the most prevalent cancers in Iran, and are projected to see a 40% rise in occurrence by the year 2025 compared to 2016, reaching approximately 6,266 new cases (9). With 5,744 deaths recorded as a result of these cancers in Iran, according to GLOBOCAN statistics, these cancers ranked fourth on the list of the leading causes of cancer death (10).



With 5,744 deaths recorded as a result of these cancers in Iran, according to GLOBOCAN statistics, these cancers ranked fourth on the list of the leading causes of cancer death (10). The ASMR of brain and CNS cancers in Iran is higher compared to other Asian countries. However, the ASMR of these cancers decreased from 4.63 per 100,000 in 1990 to 4.57 per 100,000 in 2019, consistent with the general trend observed for CNS cancer mortality in Asia (8). Analyzing data and trends in cancer mortality is valuable for assessing diagnostic and therapeutic approaches, identifying healthcare priorities, and planning economic and health policies (11). In Iran, the Civil Registration and Vital Statistics (CRVS) system records cancer mortality data, making it a resource for examining these statistics (12). In this study, we aimed to examine the crude rates, age-standardized mortality rates (ASMRs) and trends of brain and CNS cancers in Babol, northern Iran with a population exceeding 500,000 individuals, during a span of nine years.

Methods

This study is a cross-sectional analysis conducted over the years 2013-2021 on all deaths registered and classified by the Vice Chancellor for Health at Babol University of Medical Sciences due to brain and central nervous system (CNS) cancers in Babol City. Based on valid death certificates, the Health Vice-Chancellor registers cause of death data covering the entire Babol, which has over 500,000 people from reliable sources (cemeteries, forensic medicine, hospitals, and trained physicians who register causes of death). All these entries are rechecked by the relevant expert and entered online into the Ministry of Health's death registration system. International Classification of Diseases (ICD-10) tenth edition was used to code the causes of death (4). Therefore, the cancer codes under study are as follows: malignant neoplasm of spinal cord, cranial nerves, and other parts of the CNS (C72), malignant neoplasm of brain (C71), and malignant neoplasm of meninges (C70). This study used a census sampling method to determine the number of deaths attributed to brain cancers and CNS cancers over the study period. To determine and compare brain and CNS cancer mortality rates, population estimates from 2013 to 2021 were derived using population growth rates from census data provided by the Iranian Statistics Center (13). Qualitative data were presented as frequency and percentage, while quantitative data were expressed as mean and standard deviation. The crude mortality rate was calculated based on census data categorized by age group.

Additionally, the ASMRs per 100,000 population was calculated using the direct method, based on the world standard population from the International Agency for Research on Cancer (IARC) and the standard population provided by GLOBOCAN. Subsequently, the crude rate and ASR with 95% confidence intervals were reported. The Cochran-Armitage Trend Test was utilized to determine the mortality trend over the study years. We used SPSS software Version 22 and STATA software Version 14 for all analyses, and Excel 2013 for all graphing. The significance level was set at ($p < 0.05$).

Results

Out of 3,294 cancer-related deaths registered in Babol during the years 2013-2021, 228 (6.9%) deaths were due to brain and CNS cancers. Among these, 118 (51.8%) were men, and 110 (48.2%) were urban residents. The frequency of the cancers under study included: brain cancer with 203 (89.0%) deaths, which was the most common cancer-causing death, followed by meningeal cancer with 14 (6.1%) deaths, and spinal cord, cranial nerves, and other parts of the CNS cancer with 11 (4.8%) deaths. The average age of patients who died from brain and CNS cancers was 57.4 ± 17.5 years (range 1-88 years), with 61 (26.8%) patients being under 50 years old. Highest and lowest average age of patients in 2018 and 2013 was 62.6 ± 14.2 years and 52.3 ± 22.6 years, respectively (figure 1).

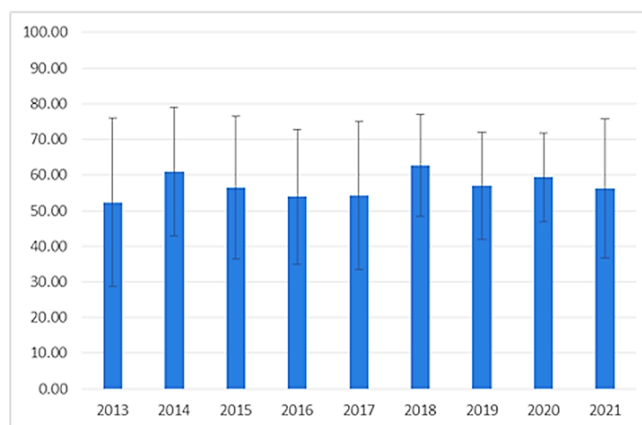


Figure 1. Mean (standard deviation) age of brain and CNS cancers between 2013-2021 in Babol

In the analysis of deaths by age group and sex, the highest frequency of deaths in men (35 deaths) and women (30 deaths) was in the 60-69 years age group, and the lowest frequency of deaths in men (10 deaths) and women (7 deaths) was in the over 80 years age group. It is noteworthy that crude death rates in the 0-29 year's age group were one

per 100,000 for both sexes. Women and men over 80 years of age had rates of 21 and 18 per 100,000, respectively, showing a significant increase ($p < 0.001$) (figure 2). The highest crude mortality rate (7.0 per 100,000) and age-standardized mortality rate (ASMR) (6.3 per 100,000) were in 2021. Additionally, the lowest crude mortality rate (2.8 per 100,000) and ASMR (2.6 per 100,000) were in 2017. The crude rates and ASMRs of brain and CNS cancers in 2013 were 3.3 and 3.2 per 100,000, respectively, which increased significantly to 7.0 and 6.3 per 100,000 in 2021 ($p < 0.001$) (figure 3). In the analysis of brain and CNS cancer mortality rates by gender and year, the year 2019 had the highest crude rates and ASMRs among men, 7.9 and 7.5 per 100,000 respectively, while the year 2021 had the highest crude rates and ASMRs among women, 7.8 and 6.9

per 100,000 respectively. In the analysis of the mortality trend by gender, crude rates and ASMRs among men increased significantly from 3.1 and 2.9 per 100,000 in 2013 to 6.3 and 5.7 per 100,000 in 2021 ($P=0.015$). This significant increase was also observed in the mortality trend in women, where the crude and age-standardized mortality rates increased from 3.6 and 3.5 per 100,000 in 2013 to 7.8 and 6.9 per 100,000 in 2021 ($P=0.001$) (table 1). In examining the trend of brain and CNS cancer mortality, brain cancer with crude and age-standardized rates of 2.9 and 2.8 per 100,000 in 2013 showed a significant increasing trend, reaching 6.7 and 6.0 per 100,000 in 2021 ($p < 0.001$). However, a stable trend was observed for meningeal cancer, and spinal cord, cranial nerves, and other parts of CNS cancers (table 2).

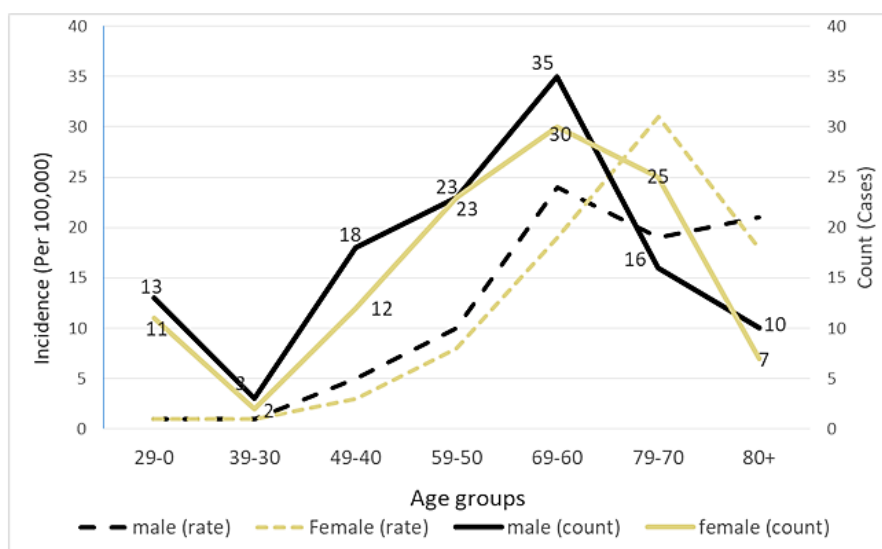


Figure 2. Trend analysis of the number and incidence rate of deaths per 100,000 population due to brain and CNS cancers by age group and gender in Babol, Iran (2013-2021) (p -value trend < 0.001 for men and p -value trend < 0.001 for women).

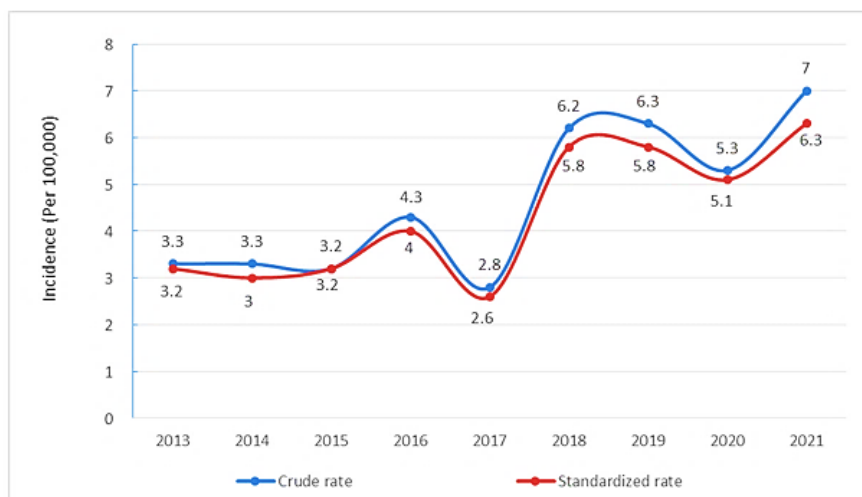


Figure 3. Trend of crude rates and ASMRs of brain and CNS cancers per 100,000 population in Babol (Iran) during 2013-2021

Table 1. Crude rates and ASMRs of brain and CNS cancers by study years and gender per 100,000 population in Babol (Iran) 2013-2021

Years	Male			Female		
	Crude death rate	Age- Standardized mortality rate rate 95% Confidence Interval		Crude death rate	Age- Standardized mortality rate rate 95% Confidence Interval	
2013	3.1	2.9	0.8 – 5.0	3.6	3.5	1.1 – 5.8
2014	3.8	3.7	1.3 – 6.0	2.7	2.4	0.6 – 4.3
2015	3.8	3.6	1.3 – 6.0	2.7	2.6	0.7 – 4.5
2016	5.2	5.0	2.3 – 7.7	3.4	3.2	1.0 – 5.3
2017	2.6	2.4	0.6 – 4.2	3.0	2.9	0.8 – 5.0
2018	5.1	4.7	2.2 – 7.3	7.4	6.7	3.7 – 9.6
2019	7.9	7.5	4.3 – 10.7	4.7	4.2	1.9 – 6.5
2020	5.3	5.3	2.6 – 8.0	5.4	4.9	2.4 – 7.4
2021	6.3	5.7	3.0 – 8.4	7.8	6.9	3.9 – 9.9

* P-value trend for males = 0.015 and females = 0.001

Table 2. Trend of crude rates and ASMRs by study years for each type of brain and CNS cancer per 100,000 population in Babol (Iran) 2013-2021

Years	Rate	Meninges	Brain	Spinal cord, cranial nerves and other parts of central nervous system
2013	Crude	0.4	2.9	0
	Standardized (95%CI)	0.3 (0 – 0.8)	2.8 (1.4 – 4.3)	0
2014	Crude	0	3.1	0.2
	Standardized (95%CI)	0	2.9 (1.5 – 4.4)	0.1 (0 – 0.3)
2015	Crude	0.4	2.9	0
	Standardized (95%CI)	0.5 (0 – 1.1)	2.7 (1.3 – 4.1)	0
2016	Crude	0	4.1	0.2
	Standardized (95%CI)	0	3.9 (2.2 – 5.6)	0.1 (0 – 0.4)
2017	Crude	0.4	2.4	0
	Standardized (95%CI)	0.3 (0 – 0.8)	2.3 (1.0 – 3.5)	0
2018	Crude	0.4	5.1	0.7
	Standardized (95%CI)	0.3 (0 – 0.6)	4.7 (2.9 – 6.5)	0.8 (0 – 1.5)
2019	Crude	0.4	5.4	0.5
	Standardized (95%CI)	0.3 (0 – 0.7)	5.0 (3.2 – 6.8)	0.6 (0 – 1.2)
2020	Crude	0.5	4.6	0.2
	Standardized (95%CI)	0.5 (0 – 1.1)	4.4 (2.7 – 6.1)	0.2 (0 – 0.6)
2021	Crude	0.2	6.7	0.2
	Standardized (95%CI)	0.1 (0 – 0.3)	6.0 (4.0 – 7.9)	0.2 (0 – 0.7)
P-trend		0.555	<0.001	0.162

CI: Confidence Interval

Discussion

Our research has shown a significant increase in the crude rates and ASMRs due to brain and CNS cancers in Babol over the years 2013-2021. During this nine-year period, only brain cancer deaths increased significantly among CNS cancers, while other types of CNS cancers remained stable. A total of 7% of all cancer-related deaths in this city were caused by brain and CNS cancers. These deaths were mainly due to brain cancers, followed by meningial cancers and cancers of the spinal cord and cranial nerves. The trend of changes in mortality rates from brain and CNS cancers in our study showed a significant increase. In contrast, the results of Yang et al.'s study indicated that despite the increase in crude mortality rates from CNS cancers globally, the global ASMR for these cancers significantly decreased from 2000 to 2019, reaching 3.05 (2.29–3.36) per 100,000 population (7). On the other hand, a recent study investigating the burden of brain and CNS cancers in Iran between 1990 and 2019 has indicated an increase in the ASMRs of these cancers over the past 15 years (14). Previous studies reported the age-standardized mortality rate of CNS cancers in Iran in 2012 as 2.7 in men and 2.5 in women (15). Additionally, according to GLOBOCAN data, the ASR of mortality from these cancers in Iran in 2022 was 6.9 in men and 5.7 in women (10).

Comparing these data reveals not only a difference between the global mortality trend of these cancers and the observed trend in Iran and Babol City, but also shows that the mortality data of this city are higher than the national data. Although multiple studies have highlighted the potential role of factors such as ionizing radiation, genetic factors, and immune hyper-reactivity in the development of brain cancers, however, no risk factor has been identified that can cause this malignancy on a large scale in the population (5). Among the cancers examined in our study, all except brain cancers had stable trends. Therefore, the increase in crude rates and ASMRs for CNS cancers can be attributed solely to the rise in brain cancer cases. The global ASMRs for brain cancers in 2019 were 3.9 per 100,000 for men and 2.6 per 100,000 for women. Additionally, Palestine recorded the highest brain cancer mortality rate in 2019, with 7.2 deaths per 100,000 (both sexes combined) (16). The Eastern Mediterranean region had an annual percent change (APPC) of +0.4 for men and +0.9 for women in ASR, bringing the 2019 rates to 3.7 and 2.6 per 100,000 population for men and women, respectively (16).

Our study also showed that with each decade increase in patient age, the mortality rate significantly increased. Additionally, the highest mortality frequency in this study was found in the 60-69 age group. This finding is supported

by some similar studies. A study by Chen J. et al. in Wuhan, China, indicated that the age distribution of mortality from brain and CNS cancers peaked at ages 65 to 69 in middle-aged and elderly groups (17). Despite these similar results, the global trend in age distribution of these deaths differs. A recent study examining the burden of these cancers from 1990 to 2019 in different levels has reported that the highest ASMR globally was in men aged 80 to 89 years and women aged 85 to 95 years. In contrast, our study found the lowest frequency of deaths in those over 80 (7). This difference might be due to a shorter average natural lifespan in the country, leading to natural deaths before the onset of this cancer at older ages, or possibly the underdiagnosis and lack of follow-up for these conditions in older patients.

One of the limitations of this study is the potential underreporting or overreporting of mortality from brain and CNS cancers due to the lack of diagnosis and registration of cancer in elderly patients with underlying conditions, or the classification of metastatic cancers as primary brain and CNS cancers. Additionally, due to the lack of available variables, our analysis was limited to gender and age. The strength of our study was that it is a population-based cross-sectional study conducted during a period of nine years in northern Iran. Future studies could investigate the role of underlying factors such as a history of hypersensitivity diseases, exposure to ionizing radiation, and occupational and economic status, and provide a more comprehensive analysis of our results. The crude and age-adjusted mortality rates of brain cancers are increasing. Considering the higher mortality rate of CNS cancers in northern Iran than national and international data, there is a need for a precise follow-up program for each type of cancer and an investigation of factors affecting the mortality of these patients.

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Ethics approval: This study was conducted in accordance with the Declaration of Helsinki. The study protocol was reviewed and approved by the Ethics Committee of Babol University of Medical Sciences with the code: (IR.MUBABOL.HRI.REC.1401.153).

Conflicts of interest: There are no competing interests to declare.

Authors' contribution: M.K., H.N., and S.H.B. designed the study; P.E. performed the statistical analysis; A.L. and

M.G. drafted the initial manuscript; all authors (M.K., A.L., P.E., S.H.-B., M.G., H.N.) revised the manuscript and approved the final version.

Availability of data and materials: The datasets can be obtained from the corresponding author.

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