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Review Article

The Incidence of Brain Tumours in Iran: A Systematic Review and Meta-Analysis

Soheil Hassanipour[1,2], Gholamreza Namvar[3], Mohammad Fathalipour[4], Mohammad Ghorbani[5], Elham Abdzadeh[6], Saber Zafarshamspour[7], Shirin Riahi[8], Abdollah Mohammadian-Hafshejani[9], Hamid Salehiniya[10,11]

[1]Gastrointestinal and Liver Diseases Research Center, Guilan University of Medical Sciences, [6]Department of Biology, Faculty of Science, University of Guilan, Rasht, Departments of [2]Student Research Committee and [7]Neurosurgery, Shiraz University of Medical Sciences, Shiraz, [3]Department of Physiology, Tabriz University of Medical Sciences, Tabriz, [4]Department of Pharmacology, Faculty of Pharmacy, Hormozgan University of Medical Sciences, Bandar Abbas, [5]Department of Public Health, School of Health, Torbat Heydariyeh University of Medical Sciences, Torbat Heydariyeh, [8]Non-Communicable Diseases Research Center, Alborz University of Medical Sciences, Karaj, [9]Department of Epidemiology and Biostatistics, School of Public Health, Shahrekord University of Medical Sciences, Shahrekord, [10]Department of Public Health, Zabol University of Medical Sciences, Zabol, [11]Department of Epidemiology and Biostatistics, Tehran University of Medical Sciences, Tehran, Iran

Abstract

Background: Brain tumours (BTs) constitute approximately 88% of all central nervous system tumours. The present study aimed to determine the age-standardised rate (ASR) of BTs in Iran. **Methods:** A comprehensive search was conducted on all studies of BTs incidence using Medline/PubMed, Scopus, Embase, Google Scholar and Web of Sciences as international databases and Scientific Information Database, MagIran, IranMedex and IranDoc as Iranian databases until April 2018. This systematic review was done based on the preferred reporting items for systematic reviews and meta-analyses. **Results:** The primary search yielded 312 relevant studies. A total of 17 studies were included after more detailed retrieval. The results of the random-effect model were demonstrated the ASR of BTs was 4.16 (95% confidence interval [CI], 3.20–5.12) for males and 3.40 (95% CI, 2.67–4.13) for females**. Conclusion**: The incidence of BTs is lower in Iran compared to other parts of the world. The incidence of nervous system cancers is increasing base on region, geographical, and economic conditions in Iran. Hence, training programmes can be considered to reduce the risk factors, complications of nervous system cancers and early diagnosis of nervous tumors.

Keywords: Brain tumours, incidence, Iran, systematic review

Introduction

Brain tumours (BTs) constitute approximately 88% of all central nervous system (CNS) tumours.[1] However, the International Classification of Disease for Oncology defines meningeal, pituitary gland, pineal gland and nervous tumours (NTs) as CNS tumours.[2]

The malignant and benign BTs consist of a group of diverse and uncommon diseases with various presentations according to location, morphology, molecular biology and clinical behaviour.[3] Due to the different location of these tumours, the clinical outcome of malignant or benign tumours is different and often life-threatening.[3] The current prevalence of BTs is not critical; however, their incidence is rapidly rising worldwide.[4] These tumours may present with mental changes and neurological deficits, and the social burden of these types of tumours is as high as other tumours. Thus, it is essential to improve the knowledge of the BTs epidemiology to facilitate the diagnosis, prevention and even initial treatment of the diseases.[5]

Previous reports demonstrated that the incidence of BTs is different among countries worldwide. In general, the incidence of BTs is higher in the West than the East and higher in developed countries than developing countries.[6] In 2012, the CNS tumours accounted for approximately 255,000 new cases, <30% of all new cancers worldwide.[7] The age-adjusted

Address for correspondence: Dr. Hamid Salehiniya, Department of Public Health, Zabol University of Medical Sciences, Zabol, Iran. Department of Epidemiology and Biostatistics, Tehran University of Medical Sciences, Tehran, Iran.
E-mail: alesaleh70@yahoo.com

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distribution of these diseases is also different worldwide, with the highest incidence in Australia, North America and North Europe and the lowest incidence in Africa. The incidence is far more among the Caucasians than African Americans.[8]

Epidemiologic studies in different regions of the world indicate that men are more likely at higher risk for BTs than women.[9] In addition, an age distribution model also indicates that the highest incidence of these cancers occurs in adults over 60 years old, adolescents and also children aged 0–4 years.[10,11]

In Iran, there are a few epidemiological studies about the CNS tumours,[12,13] and there is no report of estimate about the incidence of these cancers. Since prevention, diagnosis and treatment planning need to know about the incidence and trend of BTs. No systematic review of the epidemiology of CNS cancers carried out in Iran and the present study aimed to determine the age-standardised rate (ASR) of brain and CNS cancers in Iran.

Methods

The systematic review and meta-analysis were designed and conducted based on the preferred reporting items for systematic reviews and meta-analyses checklist in 2018.[14]

Search strategy of systematic reviews

A comprehensive search was conducted on all published studies of BTs incidence using Medline/PubMed, Scopus, Embase, Google Scholar and Web of Sciences as international databases and Scientific Information Database (www.sid.ir), MagIran (www.magiran.com), IranMedex (vwww.barakatkns.com) and IranDoc (www.irandoc.ac.ir), as Iranian national databases until April 2018.

The medical subject headings keywords included 'brain tumors', 'brain cancers', 'brain neoplasms', 'central nervous system tumours', 'nervous system tumours', 'epidemiology', 'incidence' and 'Iran'. All obtained papers from primary searches were imported into an EndNote X7 (Thomson Reuters, Carlsbad, CA, USA) library and the duplicates were then removed. No time or language limitations were applied.

Inclusion and exclusion criteria

All studies with reports about ASR of BTs among Iranian populations were included in the present study. In addition, studies with results of prevalence rate, studies with inadequate and unreliable sample size and research articles (abstracts, poster, letters, comments and editorial papers) were excluded from the study.

Quality assessment

The quality of the studies was assessed using the Joanna Briggs Institute appraisal.[15] The main objective of this checklist is to evaluate the methodological quality and the possibility of bias in the design, conduct and analysis of studies. The quality assessment results were presented in Table 1.

Risk of bias across studies

Random-effect model was used to minimise the risk of bias.[16,17]

Statistical analysis

All analyses were performed using STATA version 12.0 software (Stata Corp LP, College Station, TX, USA). Cochran's Q-test (significance level, $P \leq 0.1$) complemented with I^2 statistic (significance, >50%) was used to evaluated heterogeneity of results of included studies. The meta-analysis was conducted with a random-effect model (with inverse variance method) in the studies with significant heterogeneity ($P \leq 0.1$ and $I^2 \geq 50\%$).

Table 1: Joanna Briggs Institute critical appraisal checklist applied for included studies in the systematic review

Author name, years	Q. 1	Q. 2	Q. 3	Q. 4	Q. 5	Q. 6	Q. 7	Q. 8	Q. 9
Sadjadi, 2003	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
Babaei, 2005	No	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	No
Esmaeilnasab, 2007	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Unclear
Sadjadi, 2007	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
Mehrabani, 2008	Yes	No	No	Unclear	Yes	Yes	No	Yes	Yes
Somi, 2008	Yes	Yes	Yes	Unclear	Yes	Yes	No	No	Yes
Babaei, 2009	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes
Mohagheghi, 2009	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Mousavi, 2009	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No
Somi, 2009	Yes	Yes	Yes	Yes	Unclear	Yes	No	No	No
Masoompour, 2011	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Roshandel, 2012	No	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes
Fateh, 2013	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Roshandel, 2014	No	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes
Almasi, 2016	Yes	Yes	Yes	Unclear	Yes	Yes	No	No	Yes
Amori, 2016	No	Yes	Yes	Yes	Yes	Yes	No	No	Unclear
Masoompour, 2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes

Q. 1: Samples were representative?, Q. 2: Participants were appropriately recruited?, Q. 3: Sample size was adequate?, Q. 4: Study subjects and the setting were described?, Q. 5: Data analysis was conducted?, Q. 6: Objective, standard criteria and reliably were used?, Q. 7: Appropriate statistical analyses were used?, Q. 8: Confounding factors, subgroups and differences were identified and accounted?, Q. 9: Subpopulations were identified using objective criteria?

Results

Description of literature search

The primary searches of databases and also references searching of obtained studies yielded 312 potentially eligible studies. In total, 95 studies were selected to evaluate more accurately, and the review finally included 17 unique studies. Duplicate (n = 7) and irrelevant studies (n = 182), studies with incorrect study population (n = 11) and inadequate data (n = 8) were excluded from the study. The flowchart of the studies retrieval and selection in this review has been shown in Figure 1.

Description of the included studies

The included studies were published from 2003 to 2016. Based on geographical locations, four studies were conducted in all states of Iran,[18-21] three in Fars province,[22-24] two in Ardabil province,[25,26] two in East Azerbaijan province,[27,28] one in Kerman province,[29] one in Kurdistan province,[30] one in Golestan province,[31] one in Semnan province,[32] one in Tehran metropolis[33] and one in Shahroud city.[34] All the studies have reported ASR of BTs. The main characteristics of the selected studies have been represented in Table 2.

The results of individual studies

The highest ASR was reported from East Azerbaijan province between 2006 and 2007 (9.39 for men and 8.06 for women/100,000).[28] On the other hand, the lowest ASR was reported from Kurdistan Province in 2003 (0.5 for men and 0.8 for women/100,000).[30]

The results of meta-analysis

The results of the random-effect model were demonstrated the ASR of BTs was 4.16 (95% confidence interval [CI], 3.20–5.12) among men and 3.40 (95% CI, 2.67–4.13) among women. Furthermore, the heterogeneity of the studies was confirmed by the results of Cochran's Q-test (Q = 2879.8, df = 18, I^2 = 98.4%, P < 0.001) for men and (Q = 1864.2, df = 18, I^2 = 99%, P < 0.001) for women. The forest plots of the random-effect meta-analysis for ASR of BTs among Iranian population have been represented in Figures 2 and 3 for men and women, respectively.

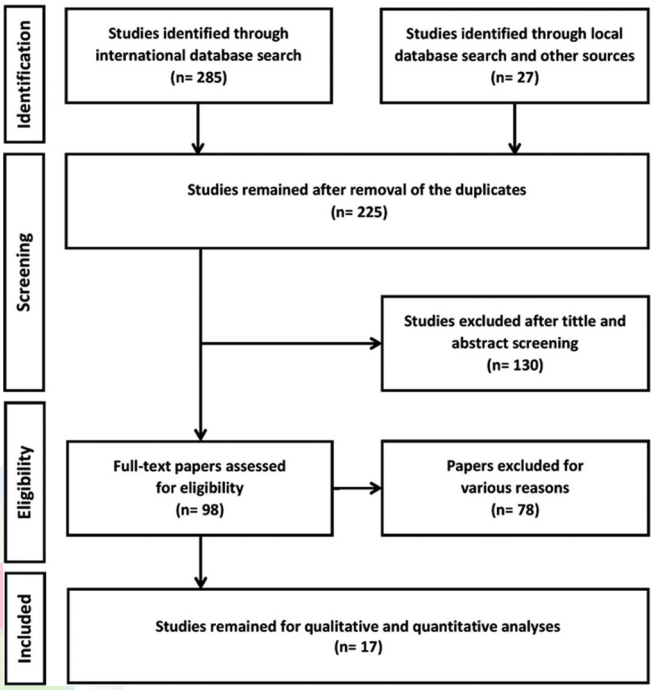

Figure 1: Flowchart of the included studies in the systematic review.

Table 2: Basic characteristics of included studies in the systematic review

Order	Author, years	Time period	Location	Sample size	ASR (males)	ASR (females)
1	Sadjadi, 2003	1996-1999	Ardabil	3455	4.4	3.2
2	Babaei, 2005	1996-2000	Semnan	1732	7	6.26
3	Esmaeilnasab, 2007	2002	Kurdistan	1294	1.3	2.5
		2003			0.5	0.8
4	Sadjadi, 2007	1996-2000	Kerman	5884	3.6	3.3
5	Mehrabani, 2008	1990-2005	Fars	2993	2.8	1.46
6	Somi, 2008	2006-2007	East Azerbaijan	4922	4.98	3.68
7	Babaei, 2009	2004-2006	Ardabil	4300	7	6.9
8	Mohagheghi, 2009	1998-2001	Tehran	34,318	6	4.5
9	Mousavi, 2009	2003-2004	Iran	43,014	1.88	1.26
		2004-2005	Iran	51,518	2.37	1.64
		2005-2006	Iran	61,031	2.51	1.71
10	Somi, 2009	2006-2007	East Azerbaijan	4922	9.39	8.06
11	Masoompour, 2011	1998-2002	Fars	8359	3	2.2
12	Roshandel, 2012	2004-2008	Golestan	9724	7.2	5.3
13	Fateh, 2013	2000-2010	Shahroud	2240	3.65	2.79
14	Roshsndel, 2014	2012	Iran	-	4.6	3.8
15	Almasi, 2016	2012	Iran	84,829	-	-
16	Amori, 2016	2004-2008	Iran	301,055	2.71	2.32
17	Masoompour, 2016	2007-2010	Fars	-	4.44	3.26

ASR: Age-standardised rate

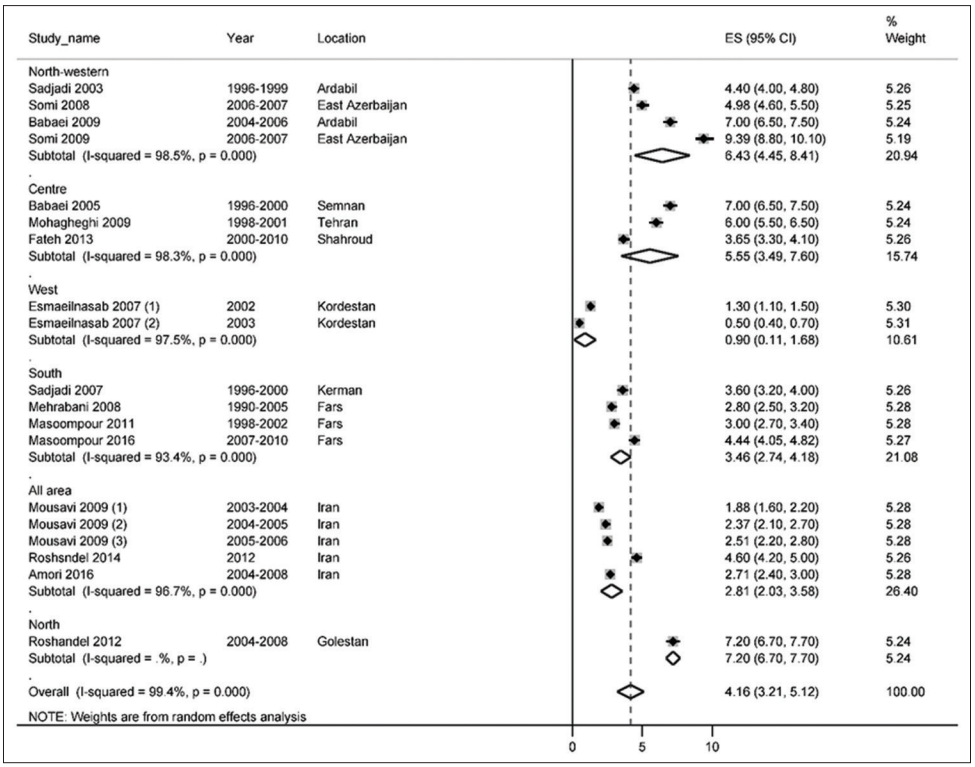

Figure 2: Forest plot of the random-effect meta-analysis for age-standardised rates of brain tumours among Iranian men.

Publication bias

Egger's test[35] used to evaluated publication bias. Results of Egger's test showed lack of publication bias ($P = 0.185$ for men and $P = 0.227$ for women).

Discussion

Cancer is the third leading cause of death in Iran.[36] There are a few studies on the epidemiology of cancer among population of developing countries including Iran.[37-42]

Results of the present study indicated that the ASR of BTs was lower in Iranian men and women than those of other countries (4.16 and 3.4/100,000 men and women, respectively). Based on the previous reports, the incidence of these cancers is higher in developed countries such as the United States, Canada, England and Australia, than in developing countries.[43] Jazayeri *et al*. have demonstrated in a similar study that the standardised incidence of primary CNS tumours in Iran is 5.69/100,000. This study was limited to obtained data from the cancer registry during 2001–2008 and did not cover other newer studies.[12] The possible causes of BTs among the Iranian population may be associated with the socioeconomic level, present risk factors and absence of advanced diagnostic methods for BTs in Iran.

There is a huge difference in the incidence of BTs worldwide.[44] European countries and Eastern European region including Albania, Macedonia, Serbia and Croatia had a high incidence, while other countries such as Cyprus, Belarus, Russia and Moldova had a low incidence of BTs.[45]

According to the results of conducted studies on refugees, the incidence of BTs among migrants to more advanced areas was higher than that of native people, indicating the effects of environmental factors on CNS malignancy.[46] Global studies show an increasing trend for these cancers probably due to the aging of those communities.[47,48] The reasons of this increasing trend have not been completely determined yet, but one of the possible assumptions is the advancement of technology and more modern diagnostic methods and tools of these types of cancer.

The present study showed that the highest ASR of BTs among people belonged to East Azerbaijan Province and Tabriz city (9.39/100,000 for men and 8.68/100,000 for women). The high incidence of BTs in this region may be attributed to the specific cultural and economic factors, occupational, nutritional and environmental exposure, genetic factors and access to better diagnostic facilities such as the computed tomography scan, magnetic resonance imaging and neurosurgical technologies.[49] In other global studies, the ASR was also slightly higher in men than women. Regarding race, the incidence of nervous system cancers is the highest among American white men and the lowest among American black women.[50,51]

Results of the present study indicated that the lowest ASR of BTs among Iranian people belonged to Kurdistan province (0.5/100,000 for men and 0.8/100,000 for women). It is probably due to the incidence of other diseases, cultural issues, low levels of risk factors and the lack of advanced diagnostic systems in Kurdistan compared to other regions of Iran.[30] Environmental factors, including exposure to radiation, special dietary factors such as consumption of fruits

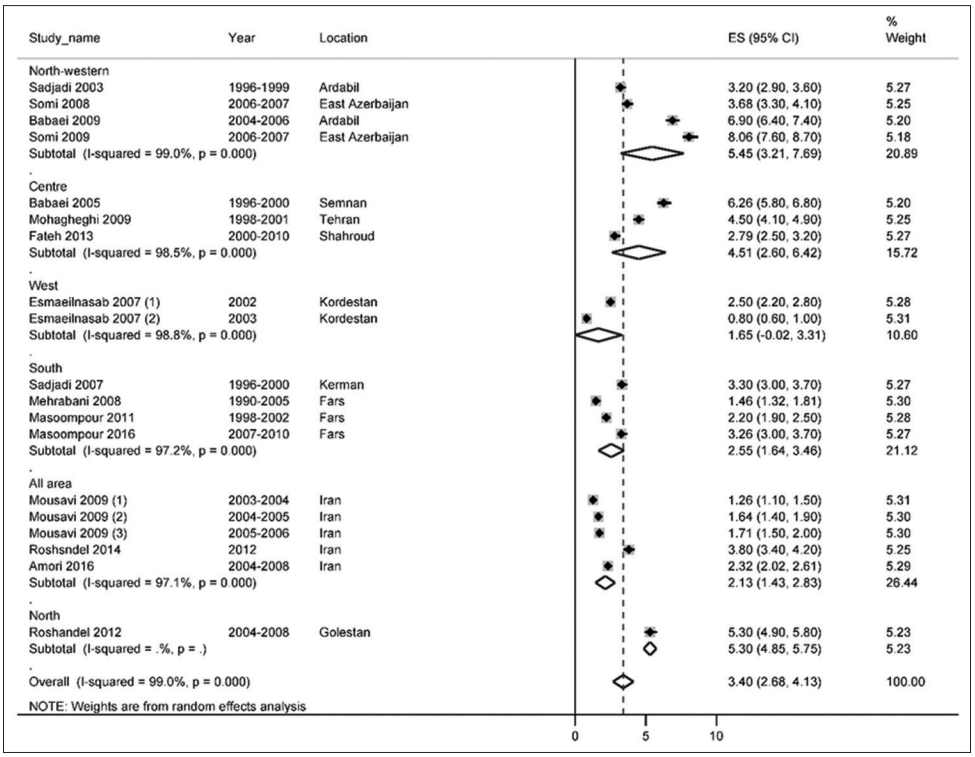

Figure 3: Forest plot of the random-effect meta-analysis for age-standardised rates of brain tumours among Iranian women.

and vegetables and occupational exposure, play important roles in the incidence of these types of cancer.[52,53] According to studies in the region, stomach, skin, oesophagus and bladder cancers among men and skin, oesophagus, stomach and breast cancers among women are more prevalent than CNS cancers.[30]

Conclusion

In comparison to other geographical locations, the incidence of BTs is lower in Iran. The incidence of nervous system cancers is increasing based on region, geographical and economic conditions in Iran. Changes in the public lifestyle and increasing risk factors are the main causes of increasing incidence of BTs in Iran. Hence, training programmes can be considered to reduce the risk factors, complications of nervous system cancers and early diagnosis of NTs.

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Conflicts of interest

There are no conflicts of interest.

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