Published in final edited form as:

Childs Nerv Syst. 2017 September ; 33(9): 1481–1490. doi:10.1007/s00381-017-3468-0.

Comprehensive analysis of Iranian reports of pediatric central nervous system tumors

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Abstract

Purpose—Iran lacks a national registry reporting the data of central nervous system (CNS) tumors in children. Consequently, treatment success and failure rates are unknown, and a centralized system for disease-management recommendations does not exist.

Methods—To critically evaluate the current state of pediatric CNS tumor studies and reporting in Iran, we performed an extensive retrospective analysis of all known reports identified with multiple search engines.

Results—Of 409 initially retrieved articles, we evaluated 123 matching our inclusion criteria. We further narrowed these reports to 74 by excluding studies pertaining to adult patients only, non-CNS tumors, or brain metastases. We also excluded studies that were performed outside of Iran or that did not contain relevant data from our analysis. We divided the remaining studies into those describing exclusively pediatric patients (3,484 patients) and those describing mixed populations of adults and children (18,641 patients). In total, our analysis included 22,125 patients.

Conclusions—We identified many limitations in the reporting of studies describing the treatment or prevalence of CNS tumors in children in Iran. Our results may guide future efforts in Iran to improve the care for children with CNS tumors and may provide a valuable template for other comprehensive country- and disease-specific retrospective analyses.

Keywords

CNS tumors; Iran; Pediatric Oncology; Retrospective studies

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Conflict of interest

The authors declare no conflict of interest.

Introduction

The prevalence of central nervous system (CNS) tumors is estimated to be lower in Iran (especially in Iranian women) than in western countries [1]. However, it is unclear whether this difference is the result of a lower level of reporting due to a reduced availability of health care services. Most reports of brain tumor studies in Iran describe results from single center-based clinical trials and, therefore, do not adequately address the difference in the overall prevalence of CNS tumors [2–5]. In addition, specific population-based estimates and a national cancer registry reporting system for pediatric CNS tumors are lacking in Iran [6].

The aim of our retrospective analysis was to comprehensively evaluate all studies regarding pediatric patients with CNS tumors in Iran. In doing so, we easily identified the limitations in the reporting of such studies. Because most developing countries, including Iran, do not have a central registry dedicated to the reporting of specific patient populations with CNS tumors, the novel and systematic approach we describe here may be useful for the guiding of future reports in Iran and other developing countries. We have compiled the results of our analysis in a single database that can also serve as a practical point of reference for the treatment of children with CNS tumors in Iran. This can be used as a template for reporting analyses from other countries that lack a central registry describing CNS tumor studies, potentially improving the quality of reporting and clinical research design in the developing world.

Materials and methods

We performed electronic searches of articles published in English or Persian from 1980 through April 2016 with the Scopus, Web of Science, PubMed, Google Advanced Web Search, and Google Scholar search engines. The following Medical Subject Headings terms were used: “central nervous system tumors” OR “brain” OR “spine” OR “spinal” OR “CNS” AND “tumor” OR “tumors” OR “neoplasm*” OR “medulloblastoma*” OR “glioma*” OR “astrocytoma*” OR “germ cell” OR “germinoma*” OR “embryonal brain tumors*” OR “peripheral neuroectodermal*” OR “PNET*” OR “atypical rhabdoid teratoid*” OR “ATRT*” OR “choroid plexus tumors*” OR “ependymoma*” AND “child” OR “children” OR “childhood” OR “pediatric” OR “adolescent”. Asterisks on search terms allow investigators to specifically search terms that are the major topics of the article and are usually included in the title or statement of purpose. The search terms were combined (i.e., AND) with the word “Iran” to limit the searches to studies conducted in Iran.

A screen of the initial search results based on the title and abstract of each research article was performed, limiting the results to studies of brain tumors in Iran. These articles were subsequently acquired as full-text documents; however, four reports were available only as abstracts. Full-text research articles and abstracts were then subjected to the following exclusion criteria: (i) studies pertaining to only adult patients (in Iran, adults are persons > 15 years); (ii) studies describing CNS and non-CNS cancers; (iii) studies pertaining primarily to brain metastases; (iv) studies conducted by Iranian researchers outside Iran; (v) studies lacking specific patient age ranges; (vi) and studies lacking any relevant data. After

applying the exclusion criteria, we divided the remaining articles into two categories: those describing pediatric studies (i.e., studies including patients exclusively < 15 years) or those describing mixed-population studies (i.e., studies including both pediatric and adult populations). Because the Iranian health care system defines pediatric patients as children younger than 15 years [6], we considered reports of studies that specifically described patients who were less than 15 years as pediatric articles. We extracted the following data, if available, from the research articles: patient age at diagnosis (range, median, or mean), patient sex, CNS tumor type, 5-year overall survival, 5-year event-free survival, patient outcome (alive, dead, or lost to follow-up), total number of patients enrolled, study design, study objective, status of ethics committee approval, province where the study was conducted, written language of the article, and other notable points or findings.

Results

Search results

Initial searches with specific Medical Subject Headings yielded 409 potential research articles for analysis. After screening article titles and abstracts for irrelevant studies, we subjected the remaining 123 articles to further exclusion criteria (described in Methods). On the basis of these criteria, we excluded 49 additional articles. We categorized the remaining 74 articles as those reporting pediatric studies (n = 35 articles, Table 1) or mixed-population studies (n = 39 articles, Table 2).

Reports of pediatric studies

From 35 articles published from 1980 through 2015, we analyzed the characteristics and outcomes of 3,484 pediatric patients in Iran with CNS tumors (Table 1) [2–4, 7–37]. The majority (57.7%) of the patients studied were boys. Approximately 84% of the patients in our analysis were described in 13 articles [2–5, 7–15] that were published from 1980 to 2008. Two articles were written in Persian [8, 12], whereas the remaining 33 were written in English. Most studies (n = 27) took place in Tehran province [4–5, 8, 11–13, 15–23, 25–29, 31–37] in hospitals and centers affiliated with the three main medical universities in Tehran: Tehran University of Medical Sciences (n = 16) [4–5, 11, 13, 16–17, 19–22, 26, 28–29, 31–32, 37], Shahid Beheshti University of Medical Sciences (n = 6) [12, 15, 18, 25, 27, 34,], Iran University of Medical Sciences (n = 4) [8, 23, 35, 36], and Army University of Medical Science (n = 1) [33]. Only four articles [18, 23, 26, 34] stated that approval by an ethics committee had been obtained.

The study objectives were categorized as clinical (n = 18 articles, 173 patients), epidemiologic (n = 9 articles [5, 8, 12–13, 16, 26, 28, 33–34], 1,881 patients), pathologic (n = 4 articles [11, 14, 15, 18], 1,160 patients), genetic (n = 2 articles [7, 30], 75 patients), surgical (n = 1 article [21], 172 patients), or radiologic (n = 1 article [29], 23 patients). Study designs were primarily single case reports (n = 16 articles [2–4, 9, 16–17, 19–22, 24, 29, 31–32, 36–37], 19 patients) and cross-sectional studies (n = 15 articles [7–8, 10–14, 15, 18, 25–26, 28, 30, 33–34], 3,271 patients). Other study designs included cohort (n = 2 articles [23, 35], 131 patients), case series (n = 1 article [5], 7 patients), and case control (n = 1 article [27], 56 patients) (Table 1).

Of the 18 articles categorized as clinical, 13 were case reports (19 patients) [2–4, 9, 17, 19–20, 22, 24, 31–32, 36–37]; two were cross-sectional studies (98 patients); two were cohort studies (98 patients); and one was a case-control study (56 patients). Clinical case reports described the disease presentation and management for each patient. Of the 35 total pediatric study articles, six (published from 2006 to 2014) described the prediagnostic symptomatic interval (PSI) in children with CNS tumors [2, 5, 12, 19, 24, 33]. The follow-up of patients, 5-year overall survival, and event-free survival rates were reported in nine articles [8, 23, 25–28, 30, 33, 35].

Reports of mixed-population studies

From 1997 to 2016, 39 published articles described the treatment and characteristics of 18,642 pediatric and adult patients in Iran with CNS tumors (Table 2) [39–76]. One article was written in Persian [69], and the remaining articles were written in English. Eight reports described whether approval from an ethics committee was obtained [59–60, 64, 66, 69–71, 75]. The majority (58.3%) of patients described in the articles was male [38, 41–50, 52, 56–57, 60–61, 63–64, 67–68, 72–75]. We were unable to determine the number of patients who were children, as most of the reports did not include this information. From 1997 to 2008, 16 articles reported studies describing 4,302 pediatric and adult patients [38–53]. In contrast, 14,340 patients were described in 23 publications from 2009 through 2015 [54–76].

Of the 39 mixed-population studies, 21 were conducted in Tehran province [39–41, 43, 45–46, 48–49, 51–54, 59–61, 64–66, 72–73, 75], specifically at Tehran University of Medical Sciences (n = 16) [39–41, 43, 45–46, 48–49, 51, 59–61, 65–66, 73, 75] or Shahid Beheshti University of Medical Sciences (n = 5) [52–54, 64, 72]. The study objectives were categorized as genetic (n = 9 articles [38, 44, 50, 56, 62, 65–66, 70–71], 449 patients), epidemiologic (n = 7 articles [47, 49, 60–61, 63, 69, 74], 13,193 patients), pathologic (n = 7 articles [46, 48, 52, 55, 67–68, 72], 4,365 patients), clinical (n = 6 articles [39, 41, 43, 45, 57, 76], 393 patients), radiologic (n = 4 articles [, 86 patients), radiotherapy (n = 3 articles [54, 58–59, 73], 54 patients), surgical (n = 2 articles [42, 51], 44 patients), or virologic [75] (n = 1, 58 patients).

The most prevalent study design was cross sectional (n = 25 articles, 5,323 patients). Three studies were case series (47 patients) [39, 44, 54], two were case reports (7 patients) [40, 76], two were cohorts (12,750 patients) [60–61], two were case controls (150 patients) [69–70], and two were descriptive (178 patients) [50, 55]. One study was retrospective (141 patients) [43], and two articles [59, 66] did not report the type of study design (46 patients). The single retrospective study reviewed the clinical presentation, radiographic evaluation, treatment, and follow-up of 141 patients with craniopharyngiomas. PSI was evaluated in only one study [41], which was reported in 2004. Seven articles described the follow-up of patients [41, 51, 53, 57, 64–65, 75].

Reports of excluded studies

Forty-nine articles were excluded from the study. The excluded articles included 34 that pertained only to adult patients and were categorized as clinical (n = 16), epidemiologic (n = 5), genetic (n = 5), surgical (n = 4), radiologic (n = 3), or pathologic (n = 1). Six studies

were conducted by Iranian researchers outside of Iran. The study objectives in those articles were clinical (n = 3), epidemiologic (n = 1), or surgical (n = 1), and one article was a letter to the editor. We excluded four articles because the age of enrolled patients was not reported. These articles were categorized as epidemiologic (n = 1), clinical (n = 1), or genetic (n = 2). We excluded two epidemiologic articles because they reported studies of CNS and non-CNS tumors. We excluded two articles that were clinical and epidemiologic because they reported studies of only brain metastases. Finally, we excluded one clinical article because it did not report any data.

Discussion

Our analysis of the data extracted from the pediatric studies revealed some limitations in these reports. A large majority (77%) of the pediatric studies were conducted in Tehran province. The remaining eight studies were conducted in eight other provinces [2, 3, 7, 9, 10, 14, 24, 30]. Because the city of Tehran contains three major pediatric cancer referral centers and pediatric patients in Iran are frequently referred to these centers, it is not surprising that most of the studies were conducted there. Four articles did not report the median or mean age of the patients in their studies [7, 10, 12, 14]. The study objectives of those four studies were genetic, pathologic, or epidemiologic. Of the 20 pediatric studies with clinical study objectives, 16 (80%) presented unique cases, three described patient survival rates, and one evaluated the PSIs of the patients. All case reports focused on disease presentation. From our analysis of these studies, it is apparent that adequate reporting of treatment protocols used for CNS tumor therapy in children is lacking in Iran.

Only two articles described pediatric studies with a genetic objective. The lack of genetic studies of pediatric patients in Iran is most likely due to a limited number of facilities employing genetic researches and an inability of pediatric oncologists to conduct genetic studies. Iranian pediatric hematologists-oncologists are more likely to present case reports (fostering consultations) and design epidemiologic studies. A lack of collaboration among referral centers most likely contributed to the limited number of cohort and cross-sectional studies. In addition, very few studies (17%) measured survival or followed up their pediatric patients with CNS tumors. Only four articles reported approval of their study by an ethics committee, although all studies in Iran with human subjects are required to obtain approval from an institutional review board or equivalent ethics committee. It is difficult to discern whether this discrepancy is due to a lack of reporting by the authors or a lack of ethics committee approval.

Unlike the pediatric studies in our analysis, the mixed-population studies were conducted in many additional provinces throughout Iran. Although a majority of these studies were conducted in Tehran province (54%), many were conducted in Isfahan (18%) and Fars (15%) provinces. In addition, five studies were conducted in five other provinces [47, 69–76]. Our findings demonstrate that studies with mixed populations of adults and children are less likely to be conducted at the three major cancer referral centers located in Tehran.

The most frequently reported study objectives in the mixed-population studies were genetic, epidemiologic, pathologic, and clinical. Other study objectives were radiologic,

radiotherapy, surgical, and virologic. The most commonly reported type of study design was cross sectional. Six cross-sectional studies evaluated the survival and follow-up of patients, and only one determined the PSIs of patients [41]. Of the 38 reports of mixed-population studies, eight indicated whether ethics committee approval was obtained. One report of a cross-sectional pathologic study stated that ethics committee approval was not required [72].

In conclusion, our analysis of the reporting of CNS tumors in pediatric patients in Iran revealed many limitations. The most frequently published articles are case reports, and articles that report data obtained from the treatment, outcome, and follow-up of patients are rare. Nevertheless, identification of the limitations of the reporting of disease-specific clinical studies in Iran may provide insight for future research studies and their publication. In addition, our comprehensive analysis may provide a valuable guideline for future initiatives in Iran or other developing countries, encouraging investigators to avoid the limitations we have described. To our knowledge, this study is the first systematic analysis of every report describing pediatric brain tumor studies from a single developing country. The strategy we have employed will be useful for future analyses of the reporting efficiencies and limitations in other developing countries, especially those that do not have a central registry describing CNS tumor studies.

Acknowledgments

This work was supported by a grant (CA21765) from the National Institutes of Health and by ALSAC. We thank Vanessa Hays, librarian specialist at St. Jude Children's Research Hospital, for her help performing reference searches. We also thank Nisha Badders for editing the manuscript.

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Table 1

Summary of reports describing pediatric patients with CNS tumors

Patient characteristics							Study characteristics										
Age at diagnosis																	
Range (Yrs)	Median (Yrs)	Sex (M/F)	OS (%)	EFS (%)	FU (Yrs)	Dead/alive	Pathology (n)	Type	Objective	Language	Province	Ethics approval	Ref				
NA	15	1/0	NA	NA	NA	Alive	EP (1)	CR	Clinical	English	Fars	NA	2				
4–8	NA	15/4	NA	NA	NA	NA	MB (19)	CS	Genetic	English	Fars	NA	7				
0.5–15	NA	53/4	15	NA	NA	22 dead/11 alive/40 loss/27 patients had < 5 yr treat	MB (47), EP (18), AST (18), PNET (3), GBM (3), GL (3), other (8)	CS	Epidemiol	Persia n	Tehran	NA	8				
11–14	NA	1/2	NA	NA	NA	NA	GL (3)	CR	Clinical	English	Khorasan Razavi	NA	9 ^a				
NA	6	0/1	NA	NA	NA	NA	GGL (1)	CR	Clinical	English	West Azarbaijan	NA	3				
NA	10	1/0	NA	NA	NA	NA	CPP (1)	CR	Clinical	English	Tehran	NA	4				
0–15	NA	217/181	NA	NA	NA	NA	AST (142), MB (89), EP (43), CP (38)	CS	Clinical	English	Isfahan	NA	10				
0–15	NA	369/264	NA	NA	NA	NA	AST (250), MB (114), EP (65), CP (55), MG (36)	CS	Pathol	English	Tehran	NA	11 ^b				
0–14	NA	72/4	NA	NA	NA	NA	AST (50), MB (24), EP (16), CP (6), GL (2), MG (2)	CS	Epidemiol	Persia n	Tehran	NA	12				
0–15	9	361/258	NA	NA	NA	NA	AST (250), MB (114), EP (65), CP (54), MG (26)	CS	Epidemiol	English	Tehran	NA	13				
0–14	NA	213/136	NA	NA	NA	NA	CP (112), AST (96), EP (87), MB (66), other (27)	CS	Pathol	English	West Azarbaijan	NA	14				
0–0.2	NA	2/5	NA	NA	NA	6 dead/one alive	Congenital (7)	Case series	Epidemiol	English	Tehran	NA	5 ^b				
0–15	NA	84/5	NA	NA	NA	NA	NA	CS	Pathol	English	Tehran	NA	15				

Patient characteristics					Study characteristics													
Age at diagnosis					Range (Yrs)	Median (Yrs)	Sex (M/F)	OS (%)	EFS (%)	FU (Yrs)	Dead/alive	Pathology (n)	Type	Objective	Language	Province	Ethics approval	Ref
NA	12	1/0	NA	NA	NA	NA	NA	NA	NA	NA	NA	PMAST (1)	CR	Epidemiol	English	Tehran	NA	16
NA	2.5	1/0	NA	NA	NA	NA	NA	NA	NA	NA	NA	EP (1)	CR	Clinical	English	Tehran	NA	17
0–15	NA	103/69	NA	NA	NA	NA	NA	NA	NA	NA	NA	AST (55.2), PAST (7), GBM (3)	CS	Pathol	English	Tehran	Yes	18
NA	12	1/0	NA	NA	NA	NA	NA	NA	NA	NA	Death	MG & AST (1)	CR	Clinical	English	Tehran	NA	19 ^b
7–12	NA	0/2	NA	NA	NA	NA	NA	NA	NA	NA	NA	GBM (2)	CR	Clinical	English	Tehran	NA	20
NA	14	0/1	NA	NA	NA	NA	NA	NA	NA	NA	NA	MG (1)	CR	Surgical	English	Tehran	NA	21
NA	4	0/1	NA	NA	NA	NA	NA	NA	NA	NA	NA	Congenital spinal tumor (1)	CR	Clinical	English	Tehran	NA	22
0.5–14.9	NA	47/3	68.5	35.2	Median: 1.7	NA	NA	NA	NA	NA	NA	MB (49), AST (20), LGG (9), HGG (11), EP (12)	CH	Clinical	English	Tehran	Yes	23
NA	13	0/1	NA	NA	NA	NA	NA	NA	NA	NA	Alive	PXAST (1)	CR	Clinical	English	Yazd	NA	24 ^b
0–14	NA	52/3	NA	NA	Mean: 6.5	NA	NA	NA	NA	NA	NA	MB (36), AST (24), EP (12), BS (6), other (6)	CS	Clinical	English	Tehran	NA	25 ^b
4–9.3	NA	11/1	NA	NA	2	NA	NA	NA	NA	NA	NA	OPG (23)	CS	Epidemiol	English	Tehran	Yes	26
0–15	NA	30/2	16–18	NA	NA	NA	NA	NA	NA	NA	NA	AST (34), MB (20), EP (28), other (18)	CC	Clinical	English	Tehran	NA	27
0.9–7	NA	9/2	NA	NA	Mean: 3.6	2 dead	NA	NA	NA	NA	NA	EXGL (11)	CS	Epidemiol	English	Tehran	NA	28
NA	15	1/0	NA	NA	NA	NA	NA	NA	NA	NA	NA	EP	CR	Radiol	English	Tehran Khoras	NA	29
2–15	10	43/4	58–92	NA	Median: 1.3 and 3.2	NA	NA	NA	NA	NA	NA	AST (87)	CS	Genetic	English	an Razavi	NA	30
NA	7	0/1	NA	NA	NA	Alive	NA	NA	NA	NA	NA	GBM (1)	CR	Clinical	English	Tehran	NA	31
NA	8	0/1	NA	NA	NA	NA	NA	NA	NA	NA	NA	GBM (1)	CR	Clinical	English	Tehran	NA	32
0–15	6.1	124/74	51.7	NA	Mean: 1.8	11 loss, 82 dead, 105 alive	NA	NA	NA	NA	NA	MB (66), LGG (53), HGG (40), EP	CS	Epidemiol	English	Tehran	NA	33 ^b

Patient characteristics					Study characteristics								
Age at diagnosis													
Range (Yrs)	Median (Yrs)	Sex (M/F)	OS (%)	EFS (%)	FU (Yrs)	Dead/alive	Pathology (n)	Type	Objective	Language	Province	Ethics approval	Ref
0–15	NA	168/147	NA	NA	NA	NA	(22), PNET (9), other (8)	CS	Epidemiol	English	Tehran	Yes	34
0.5–14	NA	29/2	69.5	37.4	NA	NA	AST (66), EP (39), GBM (11), other (25)	CH	Clinical	English	Tehran	NA	35 ^a
NA	5	1/0	NA	NA	NA	NA	CP	CR	Clinical	English	Tehran	NA	36
NA	7	1/0	NA	NA	NA	NA	PAST	CR	Clinical	English	Tehran	NA	37

AST astrocytoma, BS brain stem, CC case-control, CH cohort, CP craniopharyngioma, CPP choroid plexus papilloma, CR case report, CS cross-sectional, EFS 5-year event-free survival, EPependymoma, Epidemiol, epidemiologic, EXGL exophytic glioma, Ffemale, FU follow-up period, GB glioblastoma, GBM glioblastoma multiforme, GL glioma, HGG high-grade glioma, LGG low-grade glioma, loss lost to follow-up, M male, MB medulloblastoma, MG meningioma, NA not available, OPG optic glioma, OS 5-year overall survival, PAST pilocytic astrocytoma, Pathol pathologic, PMAST pilomyxoid astrocytoma, PXAST pleomorphic xanthoastrocytoma, Radiol, radiologic, Ref reference, Yrs years

^aReferences were available as abstracts only.

^bPredictive symptom interval data was included in report.

Table 2
Summary of reports describing mixed populations of adult and pediatric patients with CNS tumors

Patient characteristics					Study characteristics													
Age at diagnosis					Range (Yrs)	Median (Yrs)	Sex (M/F)	OS (%)	EFS (%)	FU (Yrs)	Dead/a live	Pathology (n)	Type	Objective	Language	Province	Ethics approval	Ref
7–61	NA	NA	15/6	NA	NA	NA	NA	NA	NA	NA	NA	EP (21)	CS	Genetic	English	Fars	NA	38
2–17	NA	NA	10/13	NA	NA	NA	NA	NA	NA	NA	Alive	MG (24)	Case series	Clinical	English	Tehran	NA	39
2.3–18	NA	NA	1/2	NA	NA	NA	NA	NA	NA	NA	NA	MG (1), CA (1), Ch (1)	CR	Radiother	English	Tehran	NA	40
4–48	NA	NA	58/35	NA	NA	Mea n: 4.7	12 dead	CP (93)	CS	Clinical	English	Tehran	NA	41 ^a				
1.2–65	NA	NA	14/9	NA	NA	NA	NA	GCT (6), GL (5), ED (4), MG (3), other (5)	CS	Surgical	English	Fars	NA	42				
2–58	NA	NA	101/40	NA	NA	NA	NA	CP (141)	Retrospec	Clinical	English	Tehran	NA	43				
7–43	NA	NA	9/3	NA	NA	NA	NA	CP (12)	Case series	Genetic	English	Fars	NA	44				
0.3–18	NA	NA	65/43	NA	NA	NA	NA	AST (48), MB (29), BS (14), EP (12), other (5)	CS	Clinical	English	Tehran	NA	45				
13–76	NA	NA	42/39	NA	NA	NA	NA	MG (81)	CS	Pathol	English	Tehran	NA	46				
3–80	NA	NA	82/38	NA	NA	NA	NA	GBM (120)	CS	Epidemiol	English	Kerman	NA	47				
1–95	34	NA	1,904/1	NA	NA	NA	NA	MG (26), AST (23.4), PA (14.2), GB (5.1), EP (4.8)	CS	Pathol	English	Tehran	NA	48				
6–80	NA	NA	57/41	NA	NA	NA	NA	MG (31), PA (19), Sch (9), AST (7), GBM (4), MB (3), other (28)	CS	Epidemiol	English	Tehran	NA	49				
4–71	NA	NA	46/56	NA	NA	NA	NA	PAST (38), AST (22), AAST and GBM (29), GL (25)	Descriptive	Genetic	English	Isfahan	NA	50				
9–18	NA	NA	9/12	NA	NA	Mea n: 13.4	2 dead/19 alive	PA (21)	CS	Surgical	English	Tehran	NA	51				

Patient characteristics					Study characteristics											
Age at diagnosis					Sex (M/F)	OS (%)	EFS (%)	FU (Yrs)	Dead/a live	Pathology (n)	Type	Objective	Language	Province	Ethics approval	Ref
Range (Yrs)	Median (Yrs)															
6-78	50	140/23	NA	NA	NA	NA	NA	NA	NA	MG (378)	CS	Pathol	English	Tehran	NA	52
6-35	NA	10/12	25.4	NA	Median: 0.9	2 dead/20 alive	CP (22)	CS	Radiother	English	Tehran	NA	NA	NA	NA	53
5-23	NA	5/6	NA	NA	NA	NA	CP (10)	Case series	Radiol	English	Tehran	NA	NA	NA	NA	54
4-48	33	36/28	NA	NA	NA	NA	AST (64)	Descriptive	Pathol	English	Isfahan	NA	NA	NA	NA	55
0->20	NA	NA	NA	NA	NA	NA	GBM (60)	CS	Genetic	English	Isfahan	NA	NA	NA	NA	56
10-20	16	14/9	8.7	8.7	NA	NA	GBM (23)	CS	Clinical	English	Fars	NA	NA	NA	NA	57
12-54	NA	12/14	NA	NA	NA	NA	AST (11), MB (3), OGL (3),	CS	Radiol	English	Fars	NA	NA	NA	NA	58
1-75	NA	12/4	NA	NA	NA	NA	GBM (10), PAST (1), OGL (1), AAST (2), other (2)	NA	Radiol	English	Tehran	Yes	Yes	Yes	Yes	59
0-20	NA	1,108/8	NA	NA	NA	NA	AST (826), GB (204) MB (425), other (493)	CH	Epidemiol	English	Tehran	Yes	Yes	Yes	Yes	60
0-80	NA	6,489/4	NA	NA	NA	NA	AST (1642), GB (1491), OGL (324), MB (270), EP (194), other	CH	Epidemiol	English	Tehran	NA	NA	NA	NA	61
7-70	NA	18/32	NA	NA	NA	NA	MG (26), AST (24)	CS	Genetic	English	Isfahan	NA	NA	NA	NA	62
0-65	NA	59/43	NA	NA	NA	NA	NSh (34), EP (23), AST (16), MG (15), other (14)	CS	Epidemiol	English	Isfahan	NA	NA	NA	NA	63
2.5-64	29	16/13	81	56	NA	15 dead/11 alive/3 loss	LGG (29)	CS	Radiother	English	Tehran	Yes	Yes	Yes	Yes	64
2-80	48	30/31	NA	NA	Median: 11.3	NA	MG (61)	CS	Genetic	English	Tehran	NA	NA	NA	NA	65
7-82	NA	30 ^c	NA	NA	NA	NA	MG (14), AST (6), GBM (7), other (3)	NA	Genetic	English	Tehran	Yes	Yes	Yes	Yes	66

Patient characteristics				Study characteristics																		
Age at diagnosis				Range (Yrs)	Median (Yrs)	Sex (M/F)	OS (%)	EFS (%)	FU (Yrs)	Dead/a live	Pathology (n)						Type	Objective	Language	Province	Ethics approval	Ref
4–75	39	138/82	NA	NA	NA	NA	NA	NA	NA	NA	AST (75), GB (68), OGL (21), MG (16), BS (11), MB (4), EP (6), PA (8)	CS	Pathol	English	Hamadan	NA	67					
1.5–83	NA	161/14	38	NA	NA	200 dead	NA	NA	NA	NA	AST (113), GBM (76), MG (50), OGL (18), EP (16), MB (14)	CS	Pathol	English	Yazd	NA	68					
1.5–19	NA	50/50	NA	NA	NA	NA	NA	NA	NA	NA	GL (80), PNET (12), Oth (8)	CC	Epidemiol	Persia n	Markazy	Yes	69					
0–50	NA	25/25	NA	NA	NA	NA	NA	NA	NA	NA	MG (25), AST (25)	CC	Genetic	English	Isfahan	Yes	70					
5–82	NA	26/25	NA	NA	NA	NA	NA	NA	NA	NA	AST (26), MG (25)	CS	Genetic	English	Isfahan	Yes	71					
3–77	NA	167/10	NA	NA	NA	NA	NA	NA	NA	NA	AST (97), MG (25), Oth (151)	CS	Pathol	English	Tehran	Waived	72					
6–68	NA	20/13	NA	NA	NA	NA	NA	NA	NA	NA	GB (13), AST (11), OGL (2), MB (2), other (5)	CS	Radiol	English	Tehran	NA	73					
0–20	NA	14/9	NA	NA	NA	Mea n: 1.3	NA	NA	NA	NA	GBM (23)	CS	Epidemiol	English	Fars	NA	74 ^b					
5–83	NA	58 ^c	NA	NA	NA	NA	NA	NA	NA	NA	Sch (NA), MG (NA), GBM (NA)	CS	Virologic	English	Tehran	Yes	75					
7–27	NA	0/4	NA	NA	NA	NA	NA	NA	NA	NA	MB (4)	CR	Clinical	English	West Azarbaijan	NA	76					

AAST anaplastic astrocytoma, *AST* astrocytoma, *BS* brain stem, *CA* cavernous angioma, *CC* case-control, *Ch* chondrosarcoma, *CH* cohort, *CP* craniopharyngioma, *CPP* choroid plexus papilloma, *CR* case report, *CS* cross-sectional, *ED* epidural, *EFS* 5-year event-free survival, *EP*ependymoma, *Epidemiol* epidemiologic, *EXGL* exophytic glioma, *F* female, *FU* follow-up period, *GB* glioblastoma, *GBM* glioblastoma multiforme, *GGL* ganglioglioma, *GCT* germ cell tumor, *GL* glioma, *HGG* high-grade glioma, *LGG* low-grade glioma, *loss* lost to follow-up, *M* male, *MB* medulloblastoma, *MG* meningioma, *NA* not available, *NSH* nerve sheath, *OGL* oligodendroglioma, *OPG* optic glioma, *OS* 5-year overall survival, *PA* pituitary adenoma, *PAST* pilocytic astrocytoma, *Pathol* pathologic, *PMAST* pilomyxoid astrocytoma, *PXAST* pleomorphic xanthoastrocytoma, *Radiol* radiologic, *Radiother* radiotherapy, *Ref* reference, *Retrospec* retrospective, *Sch* schwannoma, *Yrs* years

^a Prediagnostic symptom interval data was included in report.

^b Reference was available as an abstract only.

Male and female patient data was not available. Number represents total patient population in study.

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