



RESEARCH ARTICLE

PREVALENCE OF CNS TUMORS AND HISTOLOGICAL RECOGNITION IN THE OPERATED PATIENTS: 10 YEARS EXPERIENCE IN YEMEN

Monya Abdullah Yahya El-Zine¹ , Maged Ali Amer Ali² , Hassan Abdulwahab Al-Shamahy³ 

¹Departement of Histopathology, Faculty of Medicine and Health Sciences, Sana'a University, Republic of Yemen.

²Department of Neurosurgery, Faculty of Medicine and Health Sciences, Sana'a University, Republic of Yemen.

³Department of Basic Sciences, Faculty of Dentistry, Sana'a University, Republic of Yemen.

Article Info:



Article History:

Received: 1 February 2021

Reviewed: 2 March 2021

Accepted: 9 April 2021

Published: 15 May 2021

Cite this article:

El-Zine MAY, Ali MAA, Al-Shamahy HA. Prevalence of CNS tumors and histological recognition in the operated patients: 10 years experience in Yemen. Universal Journal of Pharmaceutical Research 2021; 6(2):20-27. <https://doi.org/10.22270/ujpr.v6i2.563>

*Address for Correspondence:

Dr. Hassan A. Al-Shamahy, Faculty of Dentistry, Sana'a University, P.O. Box 775 Sana'a, Yemen, Tel- +967-770299847. E-mail: shmahe@yemen.net.ye

Abstract

Background: Tumors of the central nervous system consist of a heterogeneous grouping of neoplasms of enormous histological variety. In spite of the increasing prevalence of CNS tumors in developing countries, certain places like Yemen do not have representative studies showing the true impact of these tumors on the population.

Aims: Description of the distinctiveness of primary and secondary tumors of the CNS in the past ten years in one Yemeni institute.

Materials and methods: A descriptive-observational study was performed on patients with tumors of the CNS who were selectively treated by surgical excision with subsequent diagnosis through a study of pathological tissues at the Saudi German Hospital SGH- Sana'a, over a period of 10 years from January 1, 2009 to December 31, 2019. The variables of the study were qualitative (histological type, gender, affected anatomical position) and quantitative (age). Both group and histopathological diagnoses were formed in line with the 2006 WHO classification of CNS tumors.

Results: There were a total of 359 central nervous system tumors. Of these, 200 were females and 159 were males, with a ratio of 1.3: 1 and a mean age of 49.3 years. The most common tumors were the neuroepithelium (28.4%), meningiomas (26.55%), followed by mesenchymal tumors (13.4%), sellar region tumors (11.14%) and the nerve sheath tumors (11.14%). Meningiomas had the highest prevalence in female patients (20.33%), while it was in male neuroepithelial tumors (15.32%). Single entity repeat point form, Grade I meningioma was the most common (18.11%) followed by pituitary adenomas (9.2%), Glioblastoma multiform (8.6%), Class II meningiomas (7.24%) and Schwannoma (6.7%).

Conclusion: This is the firstly study of a sequence of cases in Yemen to be conducted on both benign and malignant tumors of the CNS, with all age groups patients with a extent of 10 years. Whilst this work represents no more than a retrospective analysis of a single institute, it can be a strong indicator of the epidemiology of the CNS tumors in Yemen.

Keywords: Central nervous system tumors, histology, pathology, prevalence, Yemen.

INTRODUCTION

The tumors of central nervous system are a heterogeneous grouping of tumors of enormous histological variety and are restricted to the spinal cord, brain, meninges; and paraspinal and cranial nerves¹⁻³. A large series was conducted by diverse groups all-around the world in order to verify the epidemiological and clinical features. It can be noticed in these studies that there has been a significant rise in latest decades, particularly in non-industrialized countries such as Yemen¹⁻⁵.

In some study series, these tumors are the leading cause of cancer-related death in children and draw attention to that more than 50% of children survivors of brain tumors have impaired cognitive function linked to the tumor or its treatment⁵. For that reason it is important to determine the recent features of these tumors in the environment. Nevertheless, in Yemen as in the majority of Arab countries, there are few specialized epidemiological records dedicated to this field, and for that reason it is important to encourage, update, build up and continue to offer studies on the manners of CNS tumors with the purpose of achieve a

greater extent and influence on public health, with early diagnosis and suitable treatment with the purpose of enhance survival and reduce possible subsequent consequences.

The 6-year-old Saudi-Emirati aggression on Yemen has transformed this already weak country into the largest man-made humanitarian crisis in the world, taking away what its people need most, including basic needs, such as health care⁶. The United Nations report stated that in the year 2020-2021, more than 19.7 million people need health care services in Yemen, while only less than half of health facilities are still functioning. There are also about 1.5 million IDPs currently suffering from existing vulnerabilities including increased exposure to carcinogens⁶. According to the Limited Yemen Cancer Studies, the most common cancer among Yemeni children and adults were leukemia (33.1%), lymphoma (31.5%), central nervous system tumors (7.2%) and bone tumors (5.2%)⁶⁻⁸. This study was performed to give base line description of histopathological pattern of CNS tumors recorded in regional hospital SGH-Sana'a. These registers are not population-based cancer registration but is the only available source. Current study served to prove the basic demographic and histological data which can be competed with available studies on literatures. On other hand to provide primary base line tool to work-up for future population studies on CNS tumors.

PATIENTS AND METHOD

A descriptive observational study was performed in patients with CNS tumors that were treated selectively by surgical excision with succeeding diagnosis by studying pathological tissues at the Saudi German Hospital SGH - Sana'a, in excess of an interval of 10 years from first of January, 2009 to December 31, 2019. The study variables were qualitative (histological group, gender, affected anatomical site) and quantitative (age). Both group and histopathological diagnoses were formed in line with the 2007 WHO classification of nervous system tumors⁹. According to WHO classification, the patients were divided into 7 groups: neuroepithelial neoplasms, cranial nerve tumors, paraspinal tumors, tumors arising in the meninges, lymphomas, hematopoietic tumors, germinal cell tumors, sellar region, and metastatic tumors. We then classified subgroups according to morphological diversity.

Inclusion criteria: Inclusion criteria included the histopathological diagnosis of primary brain tumor of any age and gender, availability of clinical data, and histological slides to confirm the diagnosis.

Exclusion criteria: Exclusion criteria included no histopathological slides and insufficient clinical data.

Statistical analysis

Data were reported using appropriate descriptive statistics (including frequency, mean, standard deviation, and P-value). All statistical analyzes of the data were performed using the Statistical Package for Social Sciences (SPSS) version 24 and Excel 2007.

Ethical approval

The ethical approval was obtained from the Medical Research and Ethics Committee at the Faculty of Medicine and Health Sciences at Sana'a University with a reference number (202) dated 12-01-2021. Also, all data, including patient identification, have been kept confidential.

RESULTS

For age and gender distribution: This study included 359 CNS tumors patients, 200 (55.7%) females with a mean age of 36.7 years, while 159 (44.3%) were male patients with a mean age of 39.5 years (Figure 1).

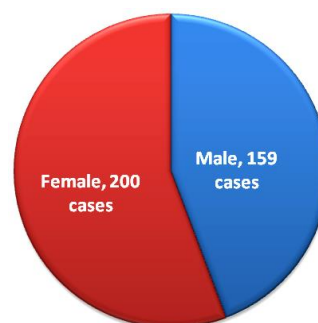


Figure 1: Sex distribution of CNS tumors.

Total 295 (82.2%) were adult patients aged 19-70 years with a mean age of 44 years (Figure 2).

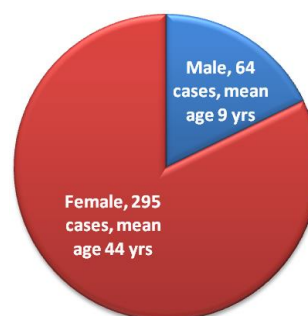


Figure 2: Age distribution of CNS tumors.

Total 164 patients (55.6%) were female with a mean age of 42.5 years, and 131 patients (44.4%) were male with a mean age of 45.9 years (Figure 4). 64 (17.8%) were paediatric patients aged 1-18 years, with a mean age of 9.8 years. 36 patients (56.25%) were female with a mean age of 10 years, and 28 patients (43.8%) were male with a mean age of 9.4 years (Figure 3).

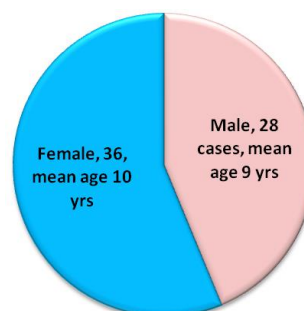


Figure 3: Paediatric age distribution in relation to sex, n= 64 patients.

Frequency of CNS tumors: Of all CNS tumors 359 cases, neuroepithelial neoplasms showed the most common tumor (28.4%) followed by meningiomas (26.5%) then mesenchymal tumors (13.4%) and equal presence of NST with sellar tumors (11.4%) for each (Figure 5). In single entity repeat point form, grade I meningioma was the most common 65 cases (18.11%) followed by pituitary adenomas 33 cases (9.2%), GBM 31 cases (8.6%), grade II meningiomas 26 cases (7.24%) and schwannoma 24 cases (6.7%).

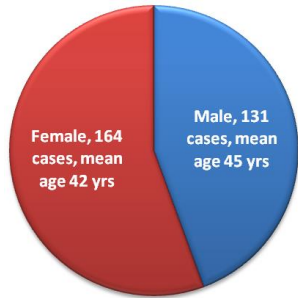


Figure 4: Adult age distribution in relation to sex, n= 295 patients.

Frequency of CNS tumors with respect to gender: Male patients showed a predominance in

neuroepithelial tumors (15.3%) and sellar tumors (7.2%) while females showed a predominance over males in the other tumors except for NSTs were evenly distributed in both sexes (0.56%) (Figure 6).

Frequency of CNS tumours in relation adult age: Meningiomas were the first common adult group tumours (31.5%) with predominance of grade-I meningioma 64cases (68.8% of all meningiomas), grade-II 26 cases (28%) and grade-III 3 cases (3.2%). Gliomas were the second common tumours (25.4%) with predominance of astrocytomas 55 cases (73.3% of all Gliomas). GBM was the commonest type of astrocytoma 29 cases (52.7% of all astrocytomas). The third tumours category was NSTs (12.9%), equally in both male and female. Schwannoma was commonest type 24 cases (63.2% of all NSTs) affected more male patients (70%). Mesenchymal tumours (MTs) category were (12.2%), lymphoma was the commonest single entity 8 cases (22.2% of al MTs) followed by hamangioblastoma 6 cases (16.7% of all MTs) both showed male predominance (31.8%) (18.2%) respectively. Sellar tumours category were (11.9%) with male predominance (16.4%), pituitary adenomas were 32 cases (91.4% of all sellar tumours) (Figure 7, Table 1).

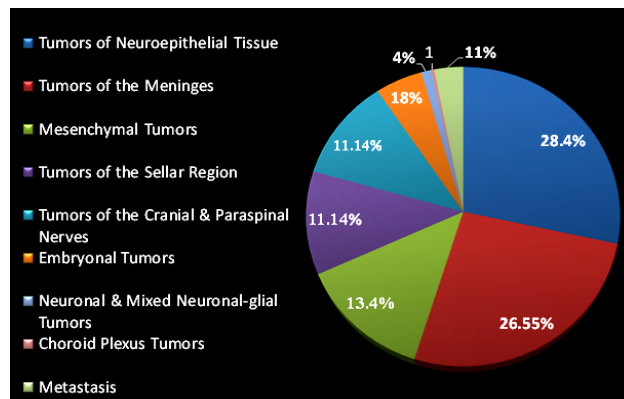


Figure 5: Frequency of CNS tumors in 359 cases.

Table 1: The frequency of CNS tumors in relation to WHO grading in total, adult, and pediatric cases.

Tumors	Total cases	Adults cases	Pediatric cases
Grade 1	53.3	55	46.2
Gliomas	8.1	3.6	26.9
Mesen TO	2.2	2.7	0.0
Sellar	2.6	1.4	7.7
NST	14	16.4	3.8
Meninges	24.6	29.5	3.8
Mixed	1.1	0.9	1.9
Ch plexus	0.4	0.0	1.9
Emberyo TO	0.4	0.5	0.0
Grade 2	23.2	24	19.2
Gliomas	13.2	12.3	17.3
Meninges	9.6	11.8	0.0
Mesent TO	0.4	0.0	1.9
Grade 3	17.6	5.9	5.8
Gliomas	13.2	5	3.8
Meninges	9.6	0.9	1.9
Mixed	0.4	0.0	28.8
Grade 4	5.9	15	25
Emberyo TO	6.3	1.8	0.0
Gliomas	11.4	13.2	3.8
Total	100	82.2	17.8

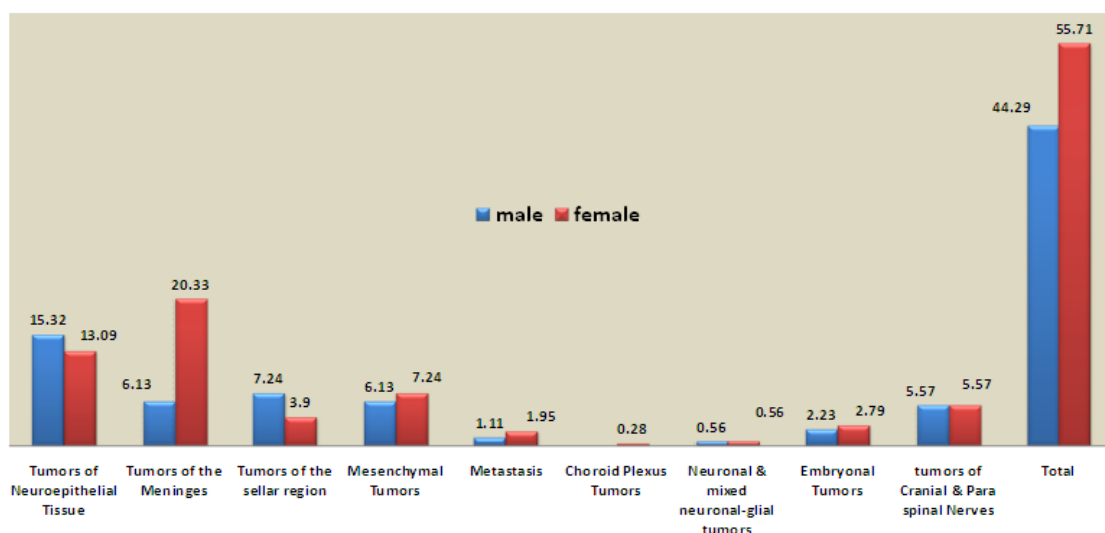


Figure 6: Sex distribution of CNS tumors in percentage.

Frequency of CNS tumours in relation pediatric age (Figure 8, Table 3): Gliomas were the first common tumours (42.2%) with predominance of astrocytomas 20 cases (74.1% of all Gliomas). Pilocytic astrocytoma was the commonest type of astrocytoma 14 cases (70% of all astrocytomas). More common in male (34.6%). Embryonal tumours were the second common tumours

(20.31%) with predominance of medulloblastoma 10 cases (76.9% of all ETs). The third tumours category was Mesenchymal tumours (MTs) (18.75%), lymphoma was the commonest single entity 5 cases (41.67% of all MTs) followed by cavernous angioma and chondroma 2 cases (16.67% of all MTs) for each.

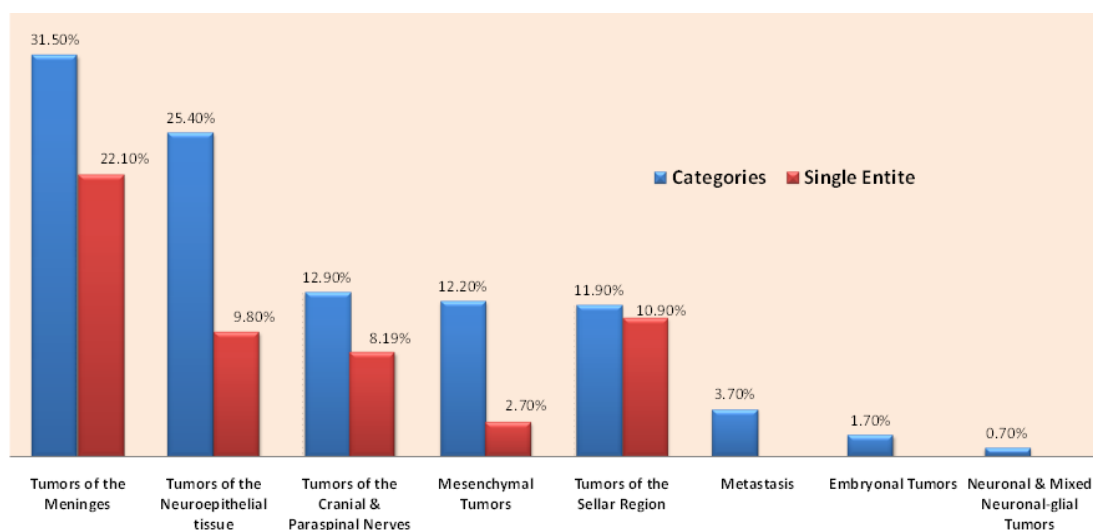


Figure 7: The frequency of different types of CNS tumors in adult.

Prevalence rate of CNS tumours with site (Figure 8): 81.64% of all tumours located intracranial while (18.36%) were intraspinal which was the main site for metastasis 6/11 cases and NSTs 28/40 cases.

Distribution of CNS tumours by grading in adult (Table 1): 79.1% were non malignant tumours (WHO grade I/II), included meningiomas (41.3%), NSTs (16.4%), Gliomas (15.9%). 20.5% were malignant included gliomas (18.2%), embryonal tumours 1.8% and MPNST 0.5% (Figure 9, and Figure 10).

Distribution of CNS tumours by grading in pediatric (Figure 9, Table 1): 65.4% were non malignant tumours (WHO grade I/II), included gliomas (44.2%) sellar tumours (7.7%), meningiomas, NSTs (3.8%) for each. 34.6% were malignant included

embryonal tumours 25%, gliomas 7.6% and MPNST 0.5%.

DISCUSSION

Tumors of the CNS are one of the primary tumors in children and one of the most common causes for consulting neurosurgery services for adults. The endurance rate can be as deprived as 26% at 5 years for posterior fossa tumors and 7% when the brainstem is affected¹⁰⁻¹². Neurocognitive sequelae are another major concern, primarily because of the managing of neurosurgery and the neurotoxicity of chemotherapy and radiation^{13,14}. The tumor series reported in Yemen either specifically focus on cancer in general, with no publications on CNS cancers^{4,7,8}.

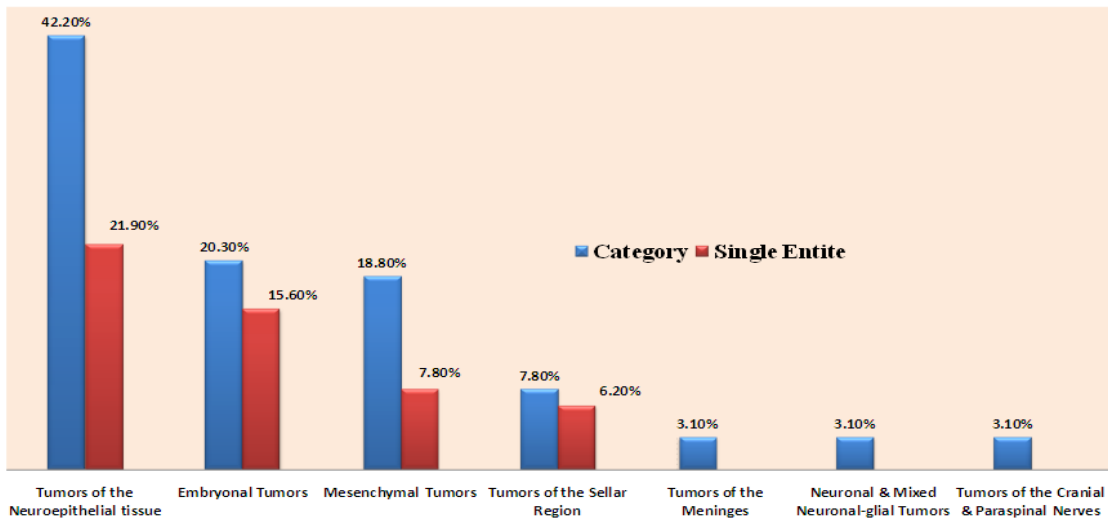


Figure 8: Frequency of different types of CNS tumors in pediatric patients.

Studies of different groups containing large numbers of adults indicate that there are differences in terms of histological group and the most prevalent tumors; in the neighboring and world series, meningiomas are more common, at about 35%^{3,15,16}. In the current study, Gliomas were the most common central nervous system tumors with 28.4% (Figure 5). In the European series, neuroepithelial tumours are more prevalent with 33.3% in Greece and 53.9% in France. In the series from China, neuroepithelial neoplasms reported for 38% and meningiomas 36.5%. In Japan, Nakamura, *et al.*,¹⁷ reported a comprehensible prevalence of meningiomas of 38.2%¹⁷⁻²⁰. From Latin America the only report was the study by Ramos Clason *et al.*,²¹. This study performed in Colombia, and reviewed a total of 390 cases, meningiomas were the most

common 50%. The difference in proportions in CNS tumors may be caused by that there are dissimilarities in the methodology employed in each of the different reports, that a few series reported primary and secondary tumors and that the study period is an additional important variable, as the number of centers contributing in each study and the sample size of the patients in each study. In the current study, in the adult group, meningiomas were the most common tumor with a rate of 25.9% with a Grade I-I of 17.8%, and these results are consistent with many studies in both developing and developed countries; for example, in Saudi Arabia about 26%²²⁻²⁴, Jordan 26.2%²⁵, Iran 27.1%²⁶. However, the results are lower than those recorded in the United States (36.1%)²⁷.

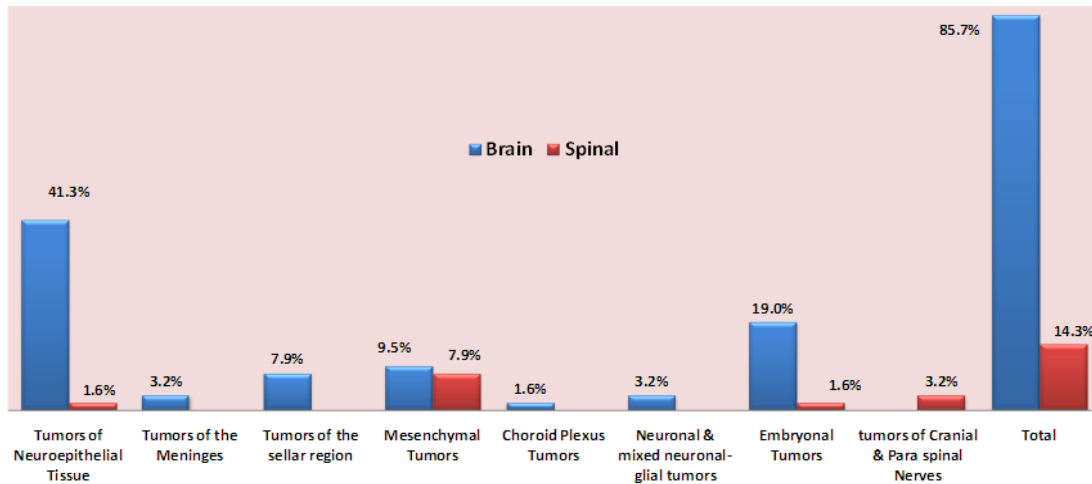


Figure 9: Frequency of CNS Tumors among children by site.

In the current study, meningioma is predominantly a female cancer (20.33%) (Figure 6). This is similar to studies conducted in Saudi Arabia²²⁻²⁴ as well as the study reported by Adalberto Miranda-filo *et al.*,²⁸ and it may be related to the high incidence of breast cancer among Yemeni patients⁴, confirming the hormonal effects that make females more susceptible to meningioma²⁹. Astrocytomas was the second entity of individual neoplasms in adults after meningiomas in

the current study, which represented 18.43% of all adult central nervous system tumors and 72.9% of glioma subtype tumor roughly close to the findings from Zalata *et al.*,³⁰ who reported that astrocytomas was the common one with predominant of glioma subtype (79.4%), but our results were lower than Mohammad *et al.*,³¹ (29%) of all CNS tumors; and are higher than Suh *et al.*, in Korea³². Although GBM was the most common glial tumor (39.2%) in this study,

this is roughly close to Zalata *et al.*,³⁰ (38.3%), and higher than the Jordanian study of 18.9%²⁵ but still lower than other studies by Mohammad *et al.*,³¹ (65.2%) and Cibtrus 2006³³ 50.7%. It has been noticed that a third of the current study GBM cases appeared after the war on Yemen, and many of these cases came from areas that were subjected to the air attacks. Pituitary adenoma was frequent in this study 31 cases (10.9%) of adult CNS tumors with male dominant and was the second adenoma after a grade I meningioma which is similar to Bary *et al.*,³⁴ (10%) but slightly lower than Zalata *et al.*,³⁰ (11.6%) but higher

than Mohammed *et al.*,³¹ (6.2%) and Cibtrus³³ (6.3%). In the pediatric group in this study, pilocytic astrocytoma was the first single entity tumor of 22.7% followed by medulloblastoma at 15.15%, and these results are consistent with Gaidi *et al.*,³⁵ and Cibtrus 2015³³ who stated that pilocytic astrocytoma is the leading histological type in infants and children. Contrary to the current study findings, previous studies conducted in Yemen and Saudi Arabia showed that medulloblastoma was the most common childhood tumor followed by astrocytomas^{7,8,23,24}.

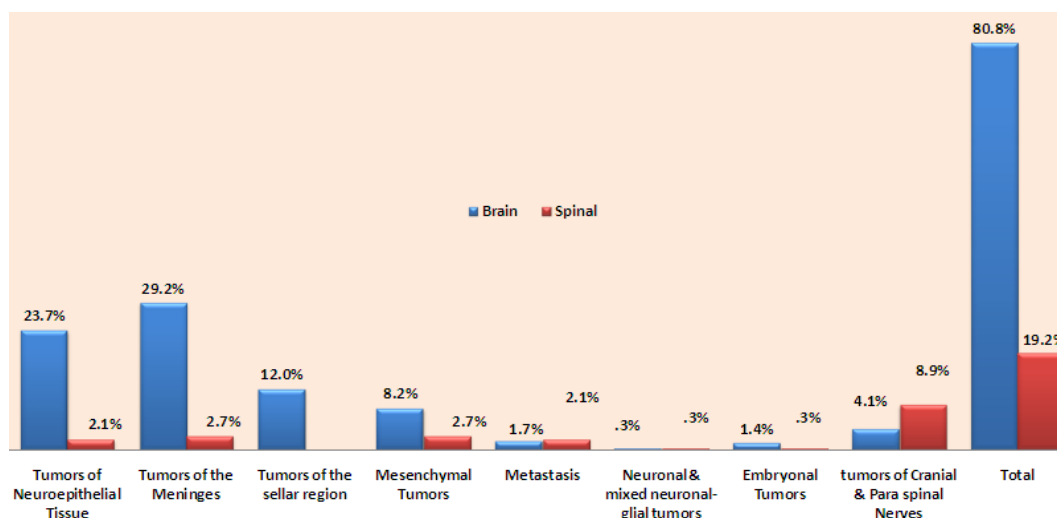


Figure 10: Frequency of CNS Tumors among adult by site.

Also, this study found that the rate of medulloblastoma was 15.15% which is still lower than that reported in several studies such as Govindan *et al.*, (30.9%)³⁶ and Catch *et al.*, (25.7%)³⁷. The Yemen Cancer Center stated^{7,8} that lymphoma is one of the most common tumors among Yemeni children, which may be in line with our conclusion that lymphoma is the third most common type of tumor in the children's group (7.75%). Primary intracranial tumors accounted for 82.8%, which is less than that reported by Suh *et al.*, (93.4%)³² and Cibtrus (2006) (94.3%)³³, but close to Zalata *et al.*, (86.7%)³⁰. Almost all astrocytomas and all gliomas and embryonal were intracranial as is the case with Komot and Mills³⁸. In the current study, primary spinal tumors accounted for 17.2% which is higher than that reported by Zalata *et al.*,³⁰ (10.9%) and Schillinger *et al.*, (4.8%)³⁹. In this study, 47% of intraspinal tumors were nerve sheath tumors followed by mesenchymal tumors which differed from those reported by Jalali *et al.*, who reported that nerve sheath is more common followed by meningioma⁴⁰. In the current study, ependymoma accounted for 71.4% of all spinal gliomas and are higher than those reported by Razi *et al.*,⁴¹ (30-60%) and Zalata *et al.*,³⁰ (54%). Metastasis were also recorded at 3.1% in this study, which appeared to be lower than many studies conducted by Zalata *et al.*,³⁰ (5.8%) and Suh *et al.*,³² (6%). In the current study, most of the metastatic lesions were in females (63.63%) with intraspinal perdition (54.54%).

CONCLUSIONS

This is the firstly study of a sequence in Yemen looking at CNS tumors, which includes patients of all age groups over a period of 10 years. Even though this study is no more than a retrospective analysis of a single institution, it can be a strong indicator of the epidemiology of CNS tumors in Yemen. In addition, the current study recorded data matches with those in the global literature and neighboring country studies, with some differences.

ACKNOWLEDGEMENTS

The authors would like to acknowledge the Saudi German Hospital (SGH)- Sana'a, Yemen which supported this work.

AUTHOR'S CONTRIBUTION

El-Zine MAY: writing original draft, clinical work. **Ali MAA:** methodology, formal analysis, conceptualization. **Al-Shamahy HA:** data curation, investigation. All authors revised the article and approved the final version.

DATA AVAILABILITY

The data supporting the findings of this study are not currently available in a public repository but can be

made available upon request to the corresponding author.

CONFLICT OF INTEREST

None to declare.

REFERENCES

- Stranjalis G, Kalamatianos T, Stavrinou LC, Mathios D, Koutsarnakis C, Tzavara C, et al. The evangelismos hospital center nervous system tumor registry: analysis of 1414 cases (1998–2009). *Surg Neurol* 2013; 4 (2013):23. <http://dx.doi.org/10.4103/2152-7806.107893>
- Lönn S, Klæboe L, Hall P, Mathiesen T, Auvinen A, Christensen HC, et al. Incidence trends of adult primary intracerebral tumors in 4 Nordic countries. *Int J Cancer* 2004; 108:450-455. <http://dx.doi.org/10.1002/ijc.11578>
- Taha MS, Almsned FM, Hassen MA, et al. Demographic and histopathological patterns of neuro-epithelial brain tumors in eastern province of Saudi Arabia. *Neurosciences* 2018; 23 (1):18–22. <https://doi.org/10.17712/nsj.2018.1.20160543>
- Alsabani JA, Gilan W, Saadi AA. Incidence data for breast cancer among Yemeni female patients with palpable breast lumps. *Asian Pac J Cancer Prev* 2015; 16(1):191-4. <https://doi.org/10.7314/apjcp.2015.16.1.191>
- Kurt BA, Nolan VG, Ness KK, J.P. Neglia JP, et al. Hospitalization rates among survivors of childhood cancer in the childhood cancer survivor study cohort. *Pediatr Blood Cancer* 2012; 59:126-132. <https://doi.org/10.1002/pbc.24017>
- WHO. Cancer patients in Yemen face the - WHO EMRO.
- Ba-Saddik IA. Childhood cancer in Aden, Yemen. *Cancer Epidemiol* 2013; 37(6):803-806. <https://doi.org/10.1016/j.canep.2013.10.001>
- Bawazir AA. Cancer incidence in Yemen from 1997 to 2011: a report from the Aden cancer registry. *BMC Cancer* 2018; 18:540. <https://doi.org/10.1186/s12885-018-4411-9>
- Louis DN, Perry A, Reifenger G, et al. The 2016 World Health Organization classification of tumors of the central nervous system: A summary. *Acta Neuropath* 2016; 131:803–20. <https://doi.org/10.1007/s00401-016-1545-1>
- Murray G, Jimenez L, Baez F, Colon-Castillo LE, Brau RH. Descriptive profile of surgically-confirmed adult central nervous system tumors in Puerto Rico. *P R Health Sci J* 2009; 28:317-28. *PMID: 19999240*
- Fleming AJ, Chi SN. Brain tumors in children. *Curr Probl Pediatr Health Care* 2012; 42:80-103. <https://doi.org/10.1016/j.cppeds.2011.12.002>
- International Agency for Research on Cancer and World Health Organization. The Global Cancer Observatory. GLOBOCAN 2018, 2019.
- Ullrich NJ, Embry L. Neurocognitive dysfunction in survivors of childhood brain tumors. *Semin Pediatr Neurol* 2012; 19: 35-42. <https://doi.org/10.1016/j.spen.2012.02.014>
- Mulhern RK, Merchant TE, Gajjar A, Reddick WE, Kun LE. Late neurocognitive sequelae in survivors of brain tumours in childhood. *Lancet Oncol* 2004; 5:399-408. [http://dx.doi.org/10.1016/S1470-2045\(04\)01507-4](http://dx.doi.org/10.1016/S1470-2045(04)01507-4)
- Dolecek TA, Propp JM, Stroup NE, Kruchko C. CBTRUS statistical report: primary brain and central nervous system tumors diagnosed in the United States in 2005–2009. *Neuro Oncol* 2012; 14:v1-v49. <http://dx.doi.org/10.1093/neuonc/nos218>
- Porter KR, McCarthy BJ, Freels S, Kim Y, Davis FG. Prevalence estimates for primary brain tumors in the United States by age, gender, behavior, and histology. *Neuro Oncol* 2010; 12:520-527. <http://dx.doi.org/10.1093/neuonc/nop066>
- Nakamura H, Makino K, Yano S, Kuratsu J. Kumamoto Brain Tumor Research Group. Epidemiological study of primary intracranial tumors: a regional survey in Kumamoto prefecture in southern Japan 20 year study. *J Clin Oncol* 2011; 16:314-321. <https://doi.org/10.1007/s10147-010-0178-y>
- Rigau V, Zouaoui S, Mathieu-Daudé H, et al. French brain tumor data base: 5-year histological results on 25756 cases. *Brain Pathol* 2011; 21:633-644. <http://dx.doi.org/10.1111/j.1750-3639.2011.00491.x>
- Crocetti E, Trama A, Stiller CC, et al. Epidemiology of glial and non-glial brain tumours in Europe. *Eur J Cancer* 2012; 48:1532-1542. <http://dx.doi.org/10.1016/j.ejca.2011.12.013>
- Chen L, Zou X, Wang Y, Mao Y, Zhou L. Central nervous system tumors: a single center pathology review of 34,140 cases over 60 years. *BMC Clin Pathol* 2013; 13:14. <http://dx.doi.org/10.1186/1472-6890-13-14>
- Khan M, Bangash S, Baeesa, et al. Epidemiological trends of histopathologically WHO classified CNS tumors in developing countries: systematic review. *Asian Pacific J Cancer Prev* 2015; 16(1): 205–216. <https://doi.org/10.7314/apjcp.2015.16.1.205>
- Almutrafi A, Bashawry Y, AlShakweer W, Al-Harbi M, Altwairgi A, Al-Dandan S. The epidemiology of primary central nervous system tumors at the national neurologic institute in Saudi Arabia: A Ten-Year Single-Institution Study. *J Cancer Epidemiol* 2020; 2020: 1429615. <https://doi.org/10.1155/2020/1429615>
- Taha MS, Almsned FM, Hassen MA, et al. Demographic and histopathological patterns of neuro-epithelial brain tumors in Eastern province of Saudi Arabia. *Neurosciences (Riyadh)* 2018; 23:18–22. <https://doi.org/10.17712/nsj.2018.1.20160543>
- Almutrafi A, Bashawry Y, AlShakweer W, et al. The epidemiology of primary central nervous system tumors at the National Neurologic Institute in Saudi Arabia: a ten-year single-institution study. *J Cancer Epidemiol* 2020; 1429615: 9. <https://doi.org/10.1155/2020/1429615>
- WHO. International Agency for Research on Cancer and World Health Organization, The Global Cancer Observatory, GLOBOCAN 2018, 2019.
- Jazayeri SB, Rahimi-Movaghgar V, Shokrane F, Saadat S, Ramezani R. Epidemiology of primary CNS tumors in Iran: a systematic review. *Asian Pac J Cancer Prev* 2013; 14(6):3979-85. <https://doi.org/10.7314/apjcp.2013.14.6.3979>
- Ostrom QT, Gittleman H, Fulop J, Liu M, Blanda R, Kromer C, et al. CBTRUS statistical report: Primary brain and central nervous system tumors diagnosed in the United States in 2008-2012. *Neuro Oncol* 2015; 17 (Suppl 4):iv1–62. <https://doi.org/10.1093/neuonc/nov189>
- Miranda-Filho A, Piñeros M, Soerjomataram I, Deltour I, Bray F. Cancers of the brain and CNS: global patterns and trends in incidence, *Neuro Oncol* 2017; 19 (2): 270-280. <https://doi.org/10.1093/neuonc/now166>
- Pouchieu C, Gruber A, Berteaud E, et al. Increasing incidence of central nervous system (CNS) tumors (2000-2012): findings from a population based registry in Gironde (France). *BMC Cancer* 2018 Jun 14; 18(1):653. <https://doi.org/10.1186/s12885-018-4545-9>
- Zalata KR, El-Tantawy DA, Abdel-Aziz A, et al. Frequency of central nervous system tumors in delta region, Egypt. *Indian J Pathol Microbiol* 2011; 54:299-306. <https://doi.org/10.4103/0377-4929.81607>
- Mohammed AA, Hamdan AN, Homoud AS. Histopathological profile of brain tumors: a 12-year retrospective study from Madinah, Saudi Arabia. *Asian J Neurosurg* 2019; 14(4):1106-1111. https://doi.org/10.4103/ajns.AJNS_185_19
- Suh YL, Koo H, Kim TS, Chi JG, Park SH, Khang SK. Tumors of the central nervous system in Korea: A multicenter study of 3221 cases. *J Neurooncol* 2002; 56:251-9. <https://doi.org/10.1023/a:1015092501279>
- CBTRUS, Central Brain Tumor Registry of the United States. Primary brain tumors in the United States: Statistical report, 1998-2002.

34. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries, CA: A Cancer J Clin 2018; 68(6): 394–424. <https://doi.org/10.3322/caac.21492>
35. El-Gaidi MA. Descriptive epidemiology of pediatric intracranial neoplasms in Egypt. *Ped Neurosurg* 2012; 47(6):385–395. <https://doi.org/10.1159/000337872>
36. Govindan A, Parambil RM, Alapatt JP. Pediatric intracranial tumors over a 5-year period in a tertiary care center of North Kerala, India: A retrospective analysis. *Asian J Neurosurg* 2018; 13:1112-7. https://doi.org/10.4103/ajns.AJNS_251_17
37. Kaatsch P, Rickert CH, Kühl J, Schüz J, Michaelis J. Population-based epidemiologic data on brain tumors in German children. *Cancer* 2001 Dec 15; 92(12):3155-64. [https://doi.org/10.1002/1097-0142\(20011215\)92:12<3155::aid-cncr10158>3.0.co;2-c](https://doi.org/10.1002/1097-0142(20011215)92:12<3155::aid-cncr10158>3.0.co;2-c)
38. Mills CN, Newsheen S, Bonner JA, Yang ES. Emerging roles of glycogen synthase kinase 3 in the treatment of brain tumors. *Front Mol Neurosci*. 2011; 4:47. <https://doi.org/10.3389/fnmol.2011.00047>
39. Schellinger PD, Meinck HM, Thron A. Diagnostic accuracy of MRI compared to CCT in patients with brain metastases. *J Neurooncol* 1999; 44:275–281. <https://doi.org/10.1023/A:1006308808769>
40. Jalali R, Datta D. Prospective analysis of incidence of central nervous tumors presenting in a tertiary cancer hospital from India. *J Neurooncol* 2008; 87:111–114. <https://doi.org/10.1007/s11060-007-9487-z>
41. Rezai AR, Woo HH, Lee M, Cohen H, Zagzag D, Epstein FJ. Disseminated ependymomas of the central nervous system. *J Neurosurg* 1996; 85(4):618-24. <https://doi.org/10.3171/jns.1996.85.4.0618>