Original Research

A CLINICOPATHOLOGICAL STUDY OF CENTRAL NERVOUS SYSTEM TUMORS WITH EMPHASIS ON HISTOLOGICAL PATTERNS AND ANATOMICAL DISTRIBUTION

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ABSTRACT

Background: Central nervous system (CNS) tumors are a diverse group of tumors of the central nervous system and have different histopathological characteristics and demographics. The clinicopathological profile of their disease is important to evaluate to understand the disease patterns and to make an accurate diagnosis.

Materials and Methods: The present prospective-cum retrospective study was done in the Department of Pathology, GMC, Jammu during the six year period from August 2018 to July 2024, involving histopathologically proven CNS tumors. Clinico-radiological and histopathological evaluation was done by age, sex, site of the tumour and the morphological sub type.

Results: A total of 100 CNS tumors both primary and secondary were evaluated. The most frequent tumors were meningioma (45%), astrocytic (28%), oligodendroglioma (11%), schwannoma (10%) and oligoastrocytoma (2%). With respect to age distribution, the mean age was 47.7 years and 41-50 age group had the largest number of tumors (26%), there were more female cases compared to males (53 vs. 47%). Intracranial tumors comprised 79% of cases and spinal tumors made upto 21%. The frontal lobe was the most frequently involved lobe in intracranial tumor (40.5%), followed by multilobar (24.1%) and parietal (15.2%). The most common location of tumors in the spine was the dorsal area (61.9%). In meningiomas, the most common variant was meningothelial variant (42.2%) followed by transitional and psammomatous variants (15.6% each).

Conclusion: CNS tumors showed a broad histopathological spectrum with distinct age, gender and anatomical distribution patterns. Meningioma was the predominant neoplasm and intracranial tumors were more frequent than spinal tumors. Histopathological examination remains the cornerstone for accurate diagnosis and classification of CNS neoplasms.

INTRODUCTION

Central nervous system (CNS) tumors comprise a heterogeneous group of neoplasms arising from the brain, spinal cord, meninges, cranial nerves, and related structures.

www.ajmrhs.com
eISSN: 2583-7761

Date of Received: 25-04-2026
Date Acceptance: 27-05-2026
Date of Publication: 11-06-2026

1 Although they account for a relatively small proportion of all human malignancies but they contribute substantially to morbidity and mortality because of their occurrence within a confined anatomical space and their potential to affect vital neurological functions.2 Clinical manifestations can be very pronounced even in histologically benign tumors because of compression of adjacent nervous structures and elevation of intracranial pressure. The spectrum of CNS tumors is extremely varied, involving lesions of neuroepithelial, meningeal,

cranial nerve sheath, sellar region, and metastatic origin. They occur at different rates depending on gender, age, and location.2,3 There are distinct demographic patterns of the different types of tumors, with meningiomas being more common in women, and several gliomas experienced a male predominance.3 Likewise, the distribution of tumours across compartments of the brain and spinal cord is different and epidemiological assessment is an important part of understanding tumour burden and presentation patterns. The diagnosis of CNS tumors has been significantly aided by progress in neuroimaging; however, definitive diagnosis is still obtained by histopathological examination.4 The correct diagnosis of the tissues is critical for tumor classification, grading, prognosis and therapy. According to the 5th edition of the World Health Organization Classification of Tumors of the Central Nervous System (2021), the classification of tumors now incorporates both molecular alterations and histological features, reflecting advances in the understanding of the biology of tumors.1,5 However, the importance of careful morphological examination remains as a basis for diagnosis of CNS tumors, especially in routine practice. Owing to the non-availability of molecular testing facilities at our institution during the study period, tumors were classified primarily on histomorphological grounds. There have been a few studies from India and other developing countries that have reported significant differences in the relative prevalence of the various types of CNS tumors.6-8 These can be due to demographic factors, referral practices, environmental factors, and better diagnostic services. Institution specific data are therefore useful for the local monitoring of disease trends and comparison with regional and international observations. The current study was conducted to assess distribution of CNS tumors based on age, gender and location coupled with histopathological pattern of neoplastic CNS mass lesions in a tertiary care hospital in Jammu and Kashmir.

MATERIALS AND METHODS

The present observational study was carried out in the Department of Pathology, Government Medical College (GMC), Jammu and its associated hospitals from August 2018 to July 2024 for a period of six years. The study design had a five-year retrospective component (August 2018 to July 2023) and a one year prospective component (August 2023 to July 2024). After obtaining the ethical clearance from Ethical Committee, cases diagnosed as CNS neoplasms on definitive histopathology were considered for inclusion during the study period. Tissues that were autolysed, samples considered to be inadequate for definitive diagnosis, histopathological results that were inconclusive and cases with incomplete clinical or pathological records were excluded from the study. On the retrospective arm, the retrieved histopathology records, hematoxylin and eosin (H&E) stained slides were retrieved and systematically re-evaluated with the corresponding paraffin embedded tissue block. If already existing sections did not provide adequate information for comprehensive evaluation, then additional sections were prepared from paraffin blocks whenever required. The histological requisition forms and medical records available were used to obtain clinical and radiological information. The specimens were collected prospectively, including surgical excision from lesions and biopsies obtained in the 12-month study period from lesions in the intracranial and spinal cavity. Each specimen was grossly examined for specimen type, dimensions and macroscopic changes such as hemorrhage, necrosis, cystic change, mucoid degeneration and calcification and were accordingly documented. Standard histopathological procedures were used for tissue processing. Representative areas were then fixed in (10%) neutral buffered formalin, processed through a graded series of alcohols, cleared in xylene, and processed through an automated tissue processor followed by paraffin wax embedding. Tissue sections (3-5 μm) were cut on a rotary microtome and stained routinely with H&E. Light microscopy was done on all sections. The microscopic evaluation was systematic and consisted of the assessment of tumour cellularity, nuclear pleomorphism and atypia, mitotic activity, necrosis, microvascular proliferation, fibrosis, gliosis, growth pattern, infiltrative margins, rosettes, pseudorosettes, inclusions or pathological deposits. The tumors were classified based on their histomorphological features according to neuropathological criteria. The radiological characteristics of the tumors were analysed with regard to their location (frontal, parietal, temporal, occipital, cerebellar, sellar and suprasellar, cerebellopontine angle, other sites), compartmental localization and to the presence of radiological evidence of calcification. All the demographic, clinical, radiological and histopathological variables were carefully documented and analysed descriptively.

RESULTS

In our study of CNS tumors (both primary and secondary), we observed meningioma was the most common histological subtype; accounting for (45%) which was followed by astrocytic tumors (28%) and oligodendroglioma (11%) as shown in table 1.

Table 1: CNS tumors with respect to age-wise Distribution of histological subtypes (n = 100)

Histology	≤10 Years	11–20 Years	21–30 Years	31–40 Years	41–50 Years	51–60 Years	61–70 Years	≥71 Years	Total
Meningioma	–	1	5	11	9	10	6	3	45
Astrocytic Tumors	–	3	–	3	11	4	3	4	28
Oligodendroglioma	–	1	2	3	4	–	1	–	11
Oligoastrocytoma	–	–	1	–	–	–	1	–	2
Schwannoma	–	1	1	1	–	4	2	1	10
Pituitary Adenoma	–	–	–	–	1	–	–	–	1
Craniopharyngioma	–	–	–	–	–	–	1	–	1
Pineocytoma	–	–	–	–	1	–	–	–	1
Metastasis’	–	–	–	–	–	1	–	–	1
Total Cases	0	6	9	18	26	19	14	8	100
Percentage (%)	0	6	9	18	26	19	14	8	100

Central nervous system tumors were most frequently evident in middle-aged adults with meningioma, being most common histological subtype, accounting for 45% of all tumors and was predominantly encountered in patients aged 31–60 years. Astrocytic tumors constituted about 28% of cases and were most frequently seen in the 41–50 years age group. Oligodendrogliomas accounted for 11% of tumors and were primarily distributed between the third and fifth decades of life. Ten percent of patients had schwannomas, most of whom were 51- to 60-year-old patients. Rare tumor types like; pituitary adenoma, craniopharyngioma, pineocytoma, and metastatic tumors, were each observed in a single case and none of the tumors were recorded in patients aged ≤10 years.

Table 2: Gender-wise Distribution of Histological Types of Central Nervous System Tumors (n = 100)

Histology	Male	Female	Total	Percentage (%)
Meningioma	10	35	45	45
Astrocytic Tumors	19	9	28	28
Oligodendroglioma	4	7	11	11
Oligoastrocytoma	2	0	2	2
Schwannoma	9	1	10	10
Pituitary Adenoma	1	0	1	1
Craniopharyngioma	1	0	1	1
Pineocytoma	1	0	1	1
Metastasis	0	1	1	1
Total	47	53	100	100

We studied 100 cases of CNS tumors and found that 53% were females and 47% were males. The most common tumor was meningioma, comprising 45% of all cases (35 of 45 cases were females; 77%). This was followed by astrocytic tumors, which accounted for 28% of cases and were more common in males (67.9%). Oligodendrogliomas constituted 11% of tumors and showed a slight female predominance (63.6%). Schwannomas accounted for 10% of cases, with most occurring in males (90%). Other tumor types, including oligoastrocytoma, pituitary adenoma, craniopharyngioma, pineocytoma, and metastasis, each accounted for 1–2% of cases.

Table 3: Distribution of Histological Types as per tumor location (n = 100)

Histology	Intracranial	Spinal	Total	Percentage (%)
Meningioma	32	13	45	45
Astrocytic Tumors	28	0	28	28
Oligodendroglioma	11	0	11	11
Oligoastrocytoma	2	0	2	2
Schwannoma	2	8	10	10
Pituitary Adenoma	1	0	1	1
Craniopharyngioma	1	0	1	1
Pineocytoma	1	0	1	1
Metastasis	1	0	1	1
Total	79	21	100	100
Percentage (%)	79	21	100	100

We found that out of 100 tumors studied, 79% were intracranial and 21% were spinal in location. Meningioma was the most common tumor type, accounting for 45% of all cases, with 71.1% occurring intracranially and 28.9% in the spinal region. All astrocytic tumors (28%), oligodendrogliomas (11%), oligoastrocytomas (2%), pituitary adenoma (1%), craniopharyngioma (1%), pineocytoma (1%), and metastatic tumors (1%) were intracranial. Schwannomas constituted 10% of cases and were predominantly spinal, with 80% occurring in the spinal region. Overall, intracranial tumors formed the majority of cases in the study and out of 79 intracranial tumors, 77 (97.47%) were in supratentorial region and 2 (2.53%) in infratentorial region.

Table 4: Distribution of intracranial tumors with respect to site-wise histological diagnosis (n = 79)

Histology	Frontal	Parietal	Temporal	Occipital	Multilobe	Sellar/ Suprasellar	CP Angle	Others	Total
Meningioma	14	7	2	0	9	0	0	0	32
Astrocytic Tumors	10	3	6	0	9	0	0	0	28
Oligodendroglioma	7	2	1	1	0	0	0	0	11
Oligoastrocytoma	1	0	0	0	1	0	0	0	2
Schwannoma	0	0	0	0	0	0	2	0	2
Pituitary Adenoma	0	0	0	0	0	1	0	0	1
Craniopharyngioma	0	0	0	0	0	1	0	0	1
Pineocytoma	0	0	0	0	0	0	0	1	1
Metastasis	0	0	0	0	0	0	0	1	1
Total	32	12	9	1	19	2	2	2	79

Evidently, among the 79 intracranial tumors, the frontal lobe was the most commonest involved site (40.5%), followed by multilobar involvement (24.1%), parietal lobe (15.2%) and temporal lobe (11.4%). Meningioma was the most frequent intracranial tumor (40.5%), occurring predominantly in the frontal and multilobar regions. Astrocytic tumors accounted for 35.4% of intracranial tumors and were mainly located in the frontal, temporal, and multilobar regions. Oligodendrogliomas comprised 13.9% of cases and were most commonly found in the frontal lobe. Schwannomas were confined to the cerebellopontine (CP) angle, while pituitary adenoma and craniopharyngioma were located in the sellar/suprasellar region. Pineocytoma and metastatic tumors were observed in the miscellaneous ("others") category.

Table 5: Distribution of Spinal Tumors According to Histology and Anatomical Location (n = 21)

Histology	Cervical	Dorsal	Lumbar	Cervicodorsal	Dorsolumbar	Lumbosacral	Total n (%)
Meningioma	1	8	1	1	1	1	13 (61.90%)
Schwannoma	0	5	1	0	1	1	8 (38.10%)
Total	1	13	2	1	2	2	21 (100%)

As shown in table 5, the dorsal region was the most common site for spinal tumors (61.9%). Meningioma was the predominant spinal tumor, accounting for 61.9% of cases, followed by schwannoma (38.1%). Both tumors were most frequently located in the dorsal spine.

Table 6: Distribution of morphological variants of meningioma (n = 45)		
Morphological Variant	Number of Cases (n)	Percentage (%)
Meningothelial	19	42.22
Fibroblastic	4	8.89
Transitional	7	15.56
Psammomatous	7	15.56
Angiomatous	2	4.44
Microcystic	1	2.22
Atypical	3	6.67
Clear Cell	1	2.22
Pigmented	1	2.22
Total	45	100

As reflected in table 6, meningothelial meningioma was the most common morphological variant, accounting for 42.2% of cases. Transitional and psammomatous variants each constituted 15.6%, followed by fibroblastic meningioma (8.9%). The remaining variants, including atypical, angiomatous, microcystic, clear cell, and pigmented meningiomas, were less frequently encountered.

DISCUSSION

Central nervous system tumors are a diverse group of neoplasms in which there is a wide range of variability in pathological behavior and prognosis from indolent and surgically curable tumors to highly aggressive cases of malignancy with poor prognosis. Despite being prevalent in only 1-2% of all malignancies, they have a disproportionately large effect because of their anatomical location, the functional consequences of even relatively small growth and the eventually large diagnostic and therapeutic problems that they pose. In the present series, we observed that meningiomas were predominant neoplasm comprising (45%)of all CNS tumors and 40.5% of intracranial neoplasms, a finding which is consistent with the observations of Das et al. (2000), who identified meningiomas as the largest subgroup (35.1%) in their institutional cohort and corroborated further by Suh et al. (2002) and Lee et al. (2010).[7-9] This preponderance is not unexpected; meningiomas are among the most frequently encountered intracranial tumors in surgical and autopsy series alike, with well-established associations with female sex, advancing age, and prior cranial irradiation. However, Ahmed et al., (2001), Ghosh et al., (2004), and Jalali and Datta (2008) reported the highest incidence of astrocytic tumors in their respective studies on CNS neoplasms.[10-12]

We assessed the age distribution of studied patients wherein it ranged from 13 to 79 years with mean age of 47.7 years and majority being (26%) were seen in the 41-50 years of age group, with the most common tumor in this age group being astrocytic tumors (11%) followed by Meningioma (9%), oligodendroglioma (4%), pituitary adenoma (1%), pineocytoma (1%). This is compatible with the findings of Mondal S et al., (2016) who reported 41-50 years as the most common age group for CNS neoplasms.[13] Thambi S et al., (2017) found the incidence of brain tumors to be highest in 40-60 years of age and Jaiswal et al., (2016) found the peak incidence of CNS neoplasms in 30-40 years age group.[14,15] Krishnatreya M et al., (2014) reported the most common age group as 20-39 years.[16] The bimodal peak of CNS tumors, one in childhood and second peak in 45-70 years age group as reported in literature was not observed in our study, which may be attributable to a smaller number of cases in this series. In the present study peak incidence (26%) was seen in age group of 41-50 years. Further, CNS neoplasms were slightly more common in females in comparison to males in this study, with a male to female ratio of 1:1.13. In concordance with the present study, Thambi et al., (2017) and Lee et al., (2005) also observed a slightly higher frequency of CNS neoplasms among females in comparison to males.[9,14] However, Mondal et al., Jaiswal t al., and Krishnatreya et al in their studies on CNS neoplasms encountered more males than females.[13,15,16]The higher number of female cases in present study may be attributed to the higher incidence of meningioma in female which constituted the predominant CNS neoplasm in this study.

In the present study, 79% CNS tumors were intracranial and 21% tumors were spinal and among intracranial tumors, the most common tumor was meningioma followed by astrocytoma, and oligodendroglioma. Among the spinal tumors too meningiomas were the commonest (13 cases, 61.9%) followed by schwannomas (8 cases, 38.1). Andrews et al., (2003) in their study reported intracranial tumors in 87% and spinal in 13% of the cases, which is comparable to the present study.[17] Schellinger et al., (2008) reported meningiomas (29%), nerve sheath tumors (24%), and ependymomas (23%) as the most common histologic types of spinal cord tumors.[18] Gelabert-Gonzalez (2007) reported ependymomas and astrocytomas to be the commonest intramedullary tumors and meningiomas and schwannomas as the commonest extra medullary tumors of the spinal

cord.[19] Frontal lobe was the commonest intracranial site (40.51%) and dorsal (thoracic) region (61.9%) was the most frequently involved site in spinal cord. Andrews et al., (2003) reported left frontal lobe to be the most common location of the intracranial tumors (54%) followed by the left temporal lobe (36%).[17] Larjavaara S et al reported that most gliomas were located in the cerebral lobes, with the frontal lobe being the most common site (40%), followed by temporal (29%), parietal (14%), and occipital (3%) lobes.[20] Jalali and Datta (2008) reported frontal lobe to be the most common part of the cerebrum involved by CNS neoplasms.[12]However, Rathod V et al., (2008) found parietal lobe to be the predominantly affected region and Gelabert-Gonzalez (2007) reported dorsal region to be the most frequently involved site among intradural spinal tumors.[21,22]

Histologically the most common variant of meningioma in the present study was meningothelial meningioma (42.22%) followed by transitional and psammomatous variant (15.56% each). Fibroblastic variant comprised of 8.89% of the cases. These observations are comparable to those of Kunimatsu A et al., (2016).[23] In their study on variants of meningioma, they observed meningothelial meningiomas (57.8%) to be the commonest variant followed by fibroblastic and transitional variants. Among all the histological patterns observed in meningiomas in the current study, calcification was found in 11 cases, necrosis in 4 cases, atypia in 3 cases, endothelial proliferation in 3 cases and mitosis was seen in 2 cases. Astrocytic tumors formed the second most common group of CNS tumors (28%) in the present study, consisting of diffuse astrocytomas (4%), anaplastic astrocytoma (7%) and glioblastoma multiforme (17%). Glioblastoma multiforme accounting for 17% of the CNS tumors was the commonest. Glioblastoma (WHO Grade IV) comprising of 17 cases (60.71%), formed the largest no. of glial tumors in our study. Vascular proliferation, atypical mitosis, and necrosis was seen in all the cases of GBM. Well-formed glomeruloid bodies were seen in 3 cases and calcification was seen in only one case. Nuclear palisading was also seen in the GBM cases. Mikkelsen VE et al., (2020), in their study on histological representativeness of glioblastoma, on 106 cases, also observed that necrosis, palisades, microvascular proliferation, atypia, mitotic count and Ki-67/MIB-1.[24] Proliferative index were significant features in glial tumors. 2 cases of gemistocytic astrocytoma were observed in our study, however no case of pilocytic astrocytoma was found. 11 cases of oligodendrogliomas were seen in present study. The histological findings in this study were endothelial proliferation in 72% cases, mitosis in 36% cases, atypia in 36% cases, necrosis in 18% cases and calcification in 9% of the cases. These observations are comparable to those of Mork SJ et al., (1986) who studied 208 cases of oligodendroglioma and documented calcification in 56% cases, vascular endothelial proliferation in 53% cases and medium cell density in 53% of cases.[25] Only a single case (1%) of pituitary adenoma was seen in the present study. This falls at the lower end of the spectrum compared to other studies. Stiller et al., (2020) reported a relatively low prevalence in their study, which contributes to the understanding of variability in pituitary adenoma occurrence.[26] In contrast, studies like those by Gittleman et al., (2020) reported high prevalence rate of pituitary adenomas, up to 12.2% in certain populations.[27] The significant difference can be attributed to various factors including demographic variations, diagnostic criteria and study methodologies. The present study comprised of only one case (1%) of craniopharyngioma which is comparable to the studies by Fan et al., (2021) and Crotty et al., (1995).[28,29] They observed 2-5% and 1-4% craniopharyngiomas in their studies respectively on CNS neoplasms. In the present study Craniopharyngioma was characterised by proliferation of mature squamous epithelium with calcification and xanthogranulomatous reaction. Tavangar SM et al., (2004) in in a study on craniopharyngioma observed almost all cases of adamantinomatous type, characterised by distinctive peripheral palisading of cells, loose knit stellate reticulum, microcystic degeneration and frequent calcification.[30] In this study one case (1%) of pineocytoma was also observed. The single pineocytoma encountered in this series is consistent with the established rarity of pineal parenchymal tumors in population-based data. The CBTRUS and NCI-CONNECT Study (2021) placed pineocytomas at approximately 1.6% of all primary CNS tumors, and a systematic review published in the European Journal of Medical Research (2021) similarly confirmed their consistently low prevalence across diverse institutional series.[3] That the present study yielded only one such case is therefore not anomalous, it is precisely what the epidemiology would predict in a cohort of this size. The solitary metastatic case, a papillary adenocarcinoma with intracranial spread, accounting for 1% of the series, warrants some interpretive caution before drawing epidemiological conclusions. Barnholtz-Sloan et al., (2004) observed metastatic tumors comprising 9.6% of CNS neoplasms, while Nussbaum et al., (1996) documented a striking 53%, a figure that reflects not an epidemiological anomaly but rather the specific clinical context of that study, which drew heavily from oncology referral populations with known systemic malignancies undergoing neurological evaluation.[31,32]The present series, by contrary represents a surgical pathology cohort with a primary tumor referral base, where patients with known metastatic disease are less likely to be

captured unless they present de novo or with diagnostically ambiguous lesions. Differences in diagnostic era, imaging availability, and the considerably larger denominators of those studies further complicate direct comparison. The low metastatic rate here should therefore be interpreted as a reflection of institutional case mix rather than a genuine underrepresentation of secondary CNS involvement in the broader population.

CONCLUSION

The present study demonstrated that most common neoplasms were meningioma, astrocytic and oligodendroglial tumors. CNS tumors were more common in middle-aged adults and revealed distinct patterns of gender and anatomical distribution with some tumor types having characteristic predilections for specific age, sex, and location of occurrence in the CNS. Intracranial tumours formed the bulk of the cases with most occurring in the supratentorial compartment and the dorsal spine the commonest site for spinal tumours. Histopathological analysis not only helped with accurate tumor diagnosis but also showed that the tumors exhibited a great deal of morphology diversity, especially in the case of meningiomas. Multicentric studies with larger numbers of cases could help to more clearly define regional differences and changing trends in the epidemiology of CNS neoplasms.

Limitations of study: Tumors were classified primarily on histological grounds because molecular testing facilities were not available in our institution during the study period.

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How to cite this article: Pratibha Shalini, Bindoo Goria, Komal Yadav, Deepti Mahajan, Haroon Salaria, Shafak Aggarwal, A CLINICOPATHOLOGICAL STUDY OF CENTRAL NERVOUS SYSTEM TUMORS WITH EMPHASIS ON HISTOLOGICAL PATTERNS AND ANATOMICAL DISTRIBUTION, Asian J. Med. Res. Health Sci., 2026; 4 (2): 828-835.
Source of Support: Nil, Conflicts of Interest: None declared.