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Classification of Intracranial Space Occupying Lesions (ICSOL) based on histopathology: A Narrative Review

[1]Fahad Somaa, [2]Asif Baliyan, [3]Faraz Bokari

[1]Ph.D, Assistant Professor, Occupational Therapy Department, Faculty of Medical Rehabilitation Sciences, King AbdulAziz University Jeddah, Saudi Arabia.

[2]MD DNB, Associate Consultant- Histopathology, Department of Pathology, Max Super Speciality Hospital, Vaishali, Max Healthcare, Delhi, NCR, India

[3]MBBS, M.Phil Associate Professor, Shaikh Zayed FPGMI, Lahore, Pakistan

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KEYWORDS

Histopathological changes, intracranial space-occupying lesions, neoplastic lesions, brain,

ABSTRACT:

Background

Intracranial space-occupying lesions (ICSOLs) can be classified as neoplastic and non-neoplastic. Non-neoplastic etiologies for ICSOLs can further be classified into granulomatous, infectious, vascular, iatrogenic, demyelinating, parasitic disease, and traumatic. Several non-neoplastic conditions can mimic a brain tumor both clinically and on radiology, so histopathology is very useful in reaching an accurate diagnosis for ICSOL.

Aim

This extensive literature review aimed to broadly describe the histopathological variations that occur in ICSOLs.

Method

This study employed electronic and manual data resources, including scientific literature repositories/databases such as PubMed/MEDLINE, ExcerptaMedica (EMBASE), Cochrane Library, and the Web of Science Core Collection, to screen all relevant published investigations throughout the last two decades (2000-2020).

Results

The initial electronic database/repository literature search identified 5,567 titles. Following pre-screening and inclusion/exclusion criteria implementation, 48 studies were shortlisted and consequently utilized for data extraction.

Conclusion

Intracranial tumors cover a broad spectrum, including both non-cancerous and cancerous growths, as well as those originating within the brain and those spreading from other body parts. To make an accurate diagnosis, it's essential to have comprehensive medical data, radiological findings, and a strong grasp of the cellular properties and immunohistochemistry associated with different types of tumors. The pathologist who conducts the surgery plays a pivotal role in recognizing and classifying these central nervous system lesions, which is vital for determining how patients will fare and what treatment approaches are most suitable.

INTRODUCTION

The identification of space-occupying lesions in the cranial cavity dates back to 1774 when Louis first reported a fungus and tumor of the dura mater. [1] Regarding etiology, intracranial space-occupying lesions (ICSOLs) can be classified as neoplastic and non-neoplastic (due to infection and/or inflammation) lesions. Accurate diagnosis of neoplastic etiology when investigating ICSOLs in the clinical setting is essential for timely neurosurgical intervention. [2] However, histopathology reveals that a variety of non-neoplastic etiologies (such as granulomatous, infectious, vascular, iatrogenic, demyelinating, and parasitic diseases, as well as trauma and stroke) can lead to highly similar symptom manifestation profiles as exhibited by neoplastic ICSOLs, following basic clinical evaluations and radiology analyses. [3]

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Cerebral tumors can develop from multiple cell types within the central nervous system (CNS). Such cell-types include neurons and glial cells (as gliomas, astrocytomas, ependymomas, oligodendrogliomas, germinomas, medulloblastomas), appendages (such as meningiomas, schwannomas, chondromas, osteomas), pituitary gland-derivatives (such as adenomas, craniopharyngiomas), togetherwith selectedvascular tumorssuch as angiomas, hemangioblastomas, papillomas of choroid plexus or secondary metastasis. [4]

Glial tumors include astrocytomas, ependymomas, glioblastomas, oligodendrogliomas, and various sub-types. Identification of the oligodendroglial component is critical for determining the most effective chemotherapeutic options against gliomas. [5] Non-glial tumors include embryonal, choroid plexus, pineal, meningeal, germ cell, seller region tumors, as well as tumors of hematopoietic cell origin. [5] Histological diagnosis should be necessary in most ICSOL cases (both neoplastic and non-neoplastic) before commencing any treatment, since differential diagnosis may result in the administration of inappropriate and potentially harmful therapeutic regimens. [3]

The most widely-used classification of human gliomas was modified by the World Health Organization (WHO) for the first time in 2000. [6] According to the recent WHO 2016 classification, from a histology perspective, gliomas can be classified based on malignancy grade. Diffuse gliomas are grouped into categories, distinguishing them as astrocytic tumors, oligodendrogliomas, and oligoastrocytomas. [7] Within this classification, oligodendrogliomas and oligoastrocytomas fall into grade II, while anaplastic gliomas and glioblastomas are allocated to grades III and IV, correspondingly. [7] The most commonly diagnosed cerebral tumors include pilocyticastrocytomas (WHO grade I) and ependymal tumors (WHO grade I, II, or III). [7] Histology has always been of great value in tumor diagnosis. The classification of cerebral tumors mainly relies on histogenesis where tumors are classified according to their presumed cell of origin.However, recent knowledge of the epidemiological distribution of CNS tumors has become vital as it can facilitate the timely detection and treatment of central nervous system (CNS) tumors. Typical symptom manifestations of CNS tumors include headache, vomiting, and/or seizures. Notwithstanding, any diagnosis that is based on atypical clinical presentation requires advanced local neuro-radiological techniques, such as computed tomography (CT) and/or magnetic resonance imaging (MRI) scans. [8]

Recent advances in CT and MRI technologies have significantly facilitated ICSOL diagnostics. Such techniques assist in the identification of small lesions even beforesymptom development. [9] Accurate ICSOL prognosis is paramount to select the appropriate treatment and avoid unnecessary therapy, particularly regarding non-neoplastic ICSOLs. [9] Consequently, there is an urgent need to develop a histopathology-based classifying system to identify the most commonly occurring ICSOLs within the clinical setting. [10] This review aims to compile the predominant histopathological changes that typically manifest within differing ICSOLs.

METHODOLOGY

The references for this review were found by conducting searches on databases such as PubMed and Medline, as well as various search engines. This search was conducted up until September 2000, using a combination of keywords like "space-occupying," "brain tumors," "ICSOL," "nervous system malignancy," "histopathology," "brain lesions," and "neoplasia." Additionally, the author also identified relevant articles by searching through physical copies of journals. The included articles were in English, French, or German, or had abstracts available in any of these languages. The focus was on articles presenting outcome data for space-occupying lesions, with preference given to studies involving a substantial number of patients rather than individual case reports or treatment recommendations..

Inclusion and exclusion criteria

The study included prospective, retrospective, quantitative research articles, case series, together with clinical trials and review articles, of cases including ICSOL diagnosis and/or histopathological changes in ICSOLs conducted globally between September 2000-2020. Exclusion criteria included case reports, technical reports, and animal/cadaver/in vitro studies Literature involving only non-neoplastic ICSOLs was also excluded.

Data extraction

Two independent reviewers extracted data from the shortlisted literature. Regarding eventual cases of incomplete/ambiguous data, the correspondingauthors werecontactedanddataforpredictivevariables was requested regarding various ICSOL(glial tumor/astrocytomas (GT/A) including pilocyticastrocytomas, diffuse astrocytomas, anaplastic astrocytomas, glioblastomas, ependymomas, and oligo-astrocytomas, oligodendrogliomas (Odg) including diffuse and anaplastic astrocytomas, meningiomas (Mg), nerve tumor (NT), metastases (Met), lymphomas (Lym),

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hemangioblastomas (Hb), benign tumors (BT) and germ cell tumors/germinomas (GCT).

Results

The initial search identified a total of 5,567 titles. Following the abstract screening, 5,351 unrelated articles were excluded, while the remaining 216 were selected for full-text evaluation. Manual-searching of reference lists for selected studies did not yield additional publications After applying inclusion and exclusion criteria, 48 studies were shortlisted and consequently employed for data extraction.The following data was obtained.

Study Characteristics

Demographic data:

Out of the 48 shortlisted studies, 33 were retrospective cohort studies, 7 were prospective cohort studies, five were reviews, two were case series, and one was a clinical trial. (Table 1). All ICSOL patients were in the age bracket between 4 days to 90 years, with a mean age of 40.69 years. In addition, 566,290 patients were evaluated, with a male to female ratio of 0.7:1. All patients included in the clinical and radiological study presented with ICSOLs in differing brain regions: right and left hemispheres, frontal, parietal, temporal, and occipital lobes.

Table 1: Study Characteristics and Demography of Selected Articles

Literature Article [Reference]	**Country**	**No. of cases**	**Type of study**	**Age/Mean age**	**M**	**F**
Rathod et al 2009 [1]	India	52	Retrospective	20-50	30	22
Hema et al 2016 [2]	India	62	Retrospective	26.72	29	33
Aryal et al 2011 [5]	Nepal	57	Retrospective Study	All age groups	28	29
Shrestha et al 2020 [8]	India	96	Retrospective Study	3-79	60	36
Yu et al 2000 [9]	China	550	Retrospective Study	35.5	340	
Chand et al 2016 [10]	India	59	Retrospective Study	41.2	38	21
Ahmed et al 2001 [11]	Pakistan	1110	Retrospective	All age groups	888	222
Kothari et al 2014 [12]	India	50	Prospective study	46.4	23	27
Meshkini et al 2013 [13]	Iran	158	Retrospective Study	41.3	114	44

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Butt et al 2005 [14]	Pakistan	100	Prospective Study	All age groups	54	46
Jalali et al 2008 [15]	India	656	Prospective Study	All age groups	395	261
Ghanghoria et al 2014 [16]	India	65	Retrospective Study	31 – 50	35	30
Mollah et al 2010 [17]	Bangladesh	50	Retrospective Study	46	33	17
Soyemi et al 2015 [18]	Nigeria	56	Retrospective Study	36	29	27
Mondal et al 2016 [19]	India	130	Retrospective Study	42.38	73	57
Chawla et al 2014 [20]	India	77	Retrospective Study	3 – 75	47	30
Ayaz et al 2011 [21]	Pakistan	100	Retrospective Study	39.7	73	27
Gubbala et al 2019 [22]	India	80	Retrospective Study	0 – 60	49	31
Bink et al 2005 [23]	Germany	10	Case series	6M-75Y	5	5
Kumarguru et al 2017 [24]	India	147	Retrospective Study	4D - 88Y	75	72
Kim et al 2003 [25]	Korea	275	Retrospective Study	41	180	120
Heper et al 2005 [26]	Turkey	130	Prospective Study	46	85	45

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Nishihara et al 2010 [27]	Japan	58	Retrospective Study	55	29	27
Husain et al 2010 [28]	India	147	Retrospective Study	20.7	103	44
Jain et al 2006 [29]	India	70	Retrospective Study	36.1	58	28
Boviatsis et al 2002 [30]	Greece	5	Case series	46.2	1	4
Bhatti et al 2005 [31]	Pakistan	15	Retrospective Study	15-54	9	6
Bhardwaj et al 2002 [32]	Canada	75	Prospective Study	56.9	35	41
Alkhani et al 2008 [33]	KSA	103	Retrospective Study	39.4	67	53
Calisanelleret al 2008 [34]	Turkey	74	Clinical trial	43.86	38	56
Ferreira et al 2005 [35]	Brazil	170	Retrospective Study	48.5	102	68
Fontaine et al 2000 [36]	France	100	Retrospective Study	52	57	43
Ulm et al 2001 [37]	US	200	Retrospective Study	53	115	85
Lu et al 2019 [38]	China	48	Retrospective Study	45.4	55	42
Satyarthee et al 2017 [39]	India	37	Retrospective Study	33	26	11
Akay et al 2019 [40]	Turkey	79	Retrospective Study	53.6	52	31

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Songul et al2017 [41]	Turkey	459	Prospective Study	50	384	116
Ostrom et al 2014 [42]	US	343,175	Review	All age groups	144,963	198,212
Natukka et al2019[43]	Finland	4730	Review	>20yrs	2542	2188
Fuentes-Raspall et al 2014[44]	Spain	679	Retrospective study	57.8	382	297
Fisher et al 2007[45]	US	27,776	Review	53	n/a	n/a
Crocetti et al 2012[46]	Europe	89,948	Review	All age groups	n/a	n/a
F.G. Davis et al 2001[47]	US	6908	Retrospective study	n/a	n/a	n/a
Visser et al 2015 [48]	Europe	83459	Review	15-44	n/a	n/a
Pouchieu et al 2018 [49]	France	3515	Prospective study	All age groups	1526	1989
Motah et al 2021[50]	Cameroon	150	Retrospective study	14-55	76	74
Andrews et al 2003 [51]	Ghana	30	Retrospective study	39	14	16
Olasode et al 2009 [52]	Nigeria	210	Retrospective study	All ages	105	105

Abbreviations: n/a Not available

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Table2: Incidence of various types of neoplastic ICSOL based on Histopathology

Authors	**Neoplastic ICSOL**										
	GT/A	**Odg**	**Mg**	**NT**	**Met**	**Lym**	**ET**	**Hb**	**BT**	**GCT**	**Oth**
Rathod et al 2009 [1]	13	2	5	1	3	/a	/a	/a	2	/a	1
Hema et al 2016 [2]	27	/a	6	7	/a	/a	/a	2	1	1	4
Aryal et al 2011[5]	23	n/a	8	5	8	1	2	n/a	3	n/a	7
Shrestha et al 2020 [8]	21	1	12	16	1	n/a	n/a	1	5	n/a	5
Yu et al 2000 [9]	178	0	21	0	86	0	0	0	35	48	73
Chand et al 2016 [10]	33	2	13	3	1	1	1	0	1	2	2
Ahmed et al 2001 [11]	457	81	234	77	3	36	65	/a	2	/a	46
Kothari et al 2014 [12]	16	4	11	3	1	1	4	3	4	/a	1
Meshkini et al 2013 [13]	124	/a	/a	/a	8	16	/a	/a	/a	/a	3
Butt et al 2005 [14]	34	2	23	11	8	1	1	1	3	1	4
Jalali et al 2007 [15]	318	19	19	n/a	78	n/a	47	n/a	55	n/a	120

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Ghanghoria et al 2014 [16]	21	n/a	27	5	n/a	n/a	4	2	1	n/a	5
Mollah et al 2011 [17]	22	1	7	0	0	0	2	0	0	0	17
Soyemi et al 2015 [18]	22	0	16	0	0	0	10	0	8	0	0
Mondal et al 2017 [19]	59	11	20	10	2	1	18	0	3	1	5
Chawla et al 2014 [20]	46	2	14	3	0	0	1	1	6	0	4
Ayaz et al 2011 [21]	56	8	18	1	7	1	4	4	0	0	1
Gubbala et al 2019 [22]	20	0	15	22	3	0	14	2	4	0	0
Bink et al 2005 [23]	6	0	0	0	0	0	0	0	0	0	0
Kumarguru et al 2017 [24]	35	3	34	20	8	2	5	0	0	1	16
Kim et al 2003 [25]	149	14	0	3	7	37	1	0	0	22	10
Heper et al 2005 [26]	77	3	0	0	15	9	0	0	0	2	13
Nishihara et al 2011 [27]	35	0	0	0	8	8	0	0	0	2	1
Husain et al 2010 [28]	33	3	1	1	1	0	20	4	1	4	29
Jain et al 2006 [29]	59	0	0	0	1	5	0	0	0	0	0

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Boviatsis et al 2002 [30]	4	0	0	0	0	0	1	0	0	0	0
Bhatti et al 2005 [31]	10	0	0	0	1	1	0	0	0	0	0
Bhardwaj et al 2002 [32]	55	0	0	0	9	4	0	0	0	0	2
Alkhani et al 2008 [33]	76	0	0	0	0	8	0	0	0	0	0
Calişaneller al 2008 [34]	58	0	0	0	8	0	0	0	0	0	0
Ferreira et al 2006 [35]	76	3	0	0	10	10	0	0	0	0	28
Fontaine et al 2000 [36]	61	11	0	0	4	7	0	0	0	0	1
Ulm et al 2001 [37]	114	5	0	1	16	14	0	0	1	7	7
Lu et al 2019 [38]	26	0	0	0	3	17	0	0	0	2	0
Satyartheeet al 2016 [39]	25	1	0	0	2	4	0	0	0	0	2
Akay et al 2019 [40]	47	0	0	0	4	12	0	0	0	0	1
Songul et al 2017 [41]	276	0	0	0	82	0	0	0	0	0	34

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Ostrom et al 2014 [42]	48164	3595	101748	3499	n/a	6028	n/a	4024	n/a	1183	12029
Natukka et al 2019 [43]	2284	350	n/a	n/a	n/a	6	n/a	n/a	n/a	n/a	631
Fuentes-Raspall et al 2014 [44]	397	n/a	n/a	n/a	n/a	n/a	22	n/a	n/a	24	235
Fisher et all 2007 [45]	27776	12943	19,190	n/a	n/a	n/a	1126	n/a	944	397	1668
Crocetti et al 2012 [46]	43129	2866	**n/a**	38653	n/a	n/a	1606	n/a	n/a	1822	1872
F.G. Davis et al 2001 [47]	1543	121	63	17	n/a	n/a	90	n/a	17	99	37
Visser et al 2015 [48]	47588	7356	n/a	n/a	n/a	n/a	1268	n/a	n/a	918	10933
Pouchieu et al 2018 [49]	1496	1426	1321	422	n/a	115	n/a	n/a	1967	n/a	161
Motah et al 2021 [50]	37	6	39	2	12	n/a	3	9	n/a	n/a	42
Andrews et al 2003 [51]	11	n/a	5	n/a	n/a	n/a	2	n/a	3	n/a	9
Olasode et al 2009 [52]	53	8	24	n/a	48	n/a	1	10	1	2	63

Abbreviations:

Intracranial space-occupying lesion (ICSOL), glial tumors/astrocytoma (GT/A), oligodendrogliomas (Odg), meningiomas (Mg), nerve tumors, or neural tumors (NT), Metastasis (Met), Lymphoma (Lym), Hemangioblastoma (Hb), Benign Tumor (BT), Germ Cell Tumor/Germinoma (GCT), Other ICSOLs include Craniopharyngioma PNET, etc. (Oth), Not available (n/a)

Individual study results:

Based on histology, neoplastic ICSOLs were classified into GT/A, Odg, Mg, NT, Met, Lym, Hb, BT, GCT,and Ot. Metastatic brain tumors were found to be the most prevalent CNS tumors, followed by neuroepithelial tumors (astrocytoma, oligodendroglioma, and ependymoma.

Out of all 566290 patients who underwent histopathological examination, neoplastic ICSOL prevalence classification

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was as follows: Mg 253703,GT/A 1,75,190 (all variations of astrocytomas, mixed astrocytic tumors, ependymoma),NT 42782, Odg 28,847, OT 28122,GCT 4538, ET 4207, Hb 4081, BT 3070, Met 449, Lym 422, (Table 2)

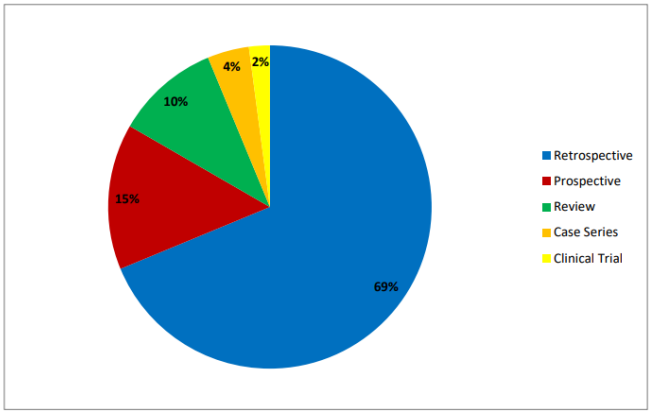

Figure1: Types of studies included in the review.

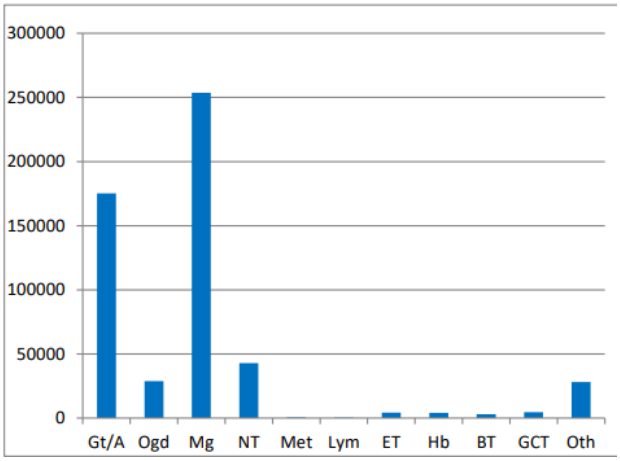

Figure2: Histopathological diagnosis/changes in neoplastic ICSOLs.

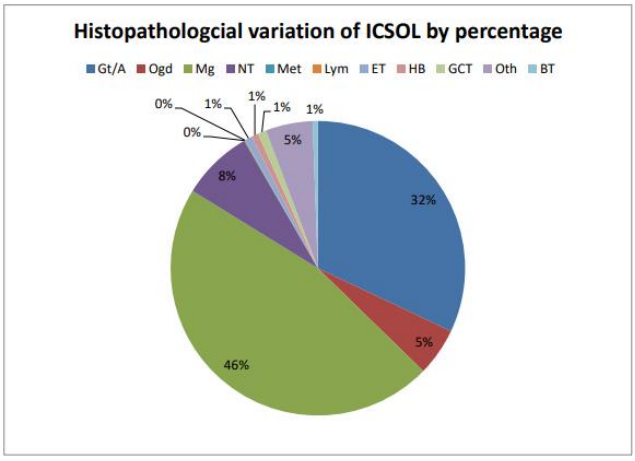

Figure3: Histopathological diagnosis ICSOLs by percentage.

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Discussion

Prevalence and socio-demographic characteristics

Brain tumors constitute 85-90% of all primary CNS tumors. [53] In 2020, the American Cancer Society recorded around 23,890 new cases of brain tumors, leading to 18,020 fatalities in the United States. Data from the Surveillance, Epidemiology, and End Results (SEER) database for the year 2011 indicated that the total occurrence rate of primary invasive brain tumors in the USA was 6.4 per 100,000 individuals annually, with an estimated death rate of 4.3 per 100,000 individuals each year. [54] On a worldwide scale, there were 256,213 newly diagnosed cases of brain and other central nervous system (CNS) tumors in 2012, resulting in 189,382 deaths. [55]

This study aimed to determine the incidence and occurrence of various histopathological types of intracranial lesions worldwide. A total of 556,290 cases were studied. Our study found an overall higher incidence of ICSOL in females. This correlates what Ostrom et al. and Pouchieu et al. found in the data from cancer registries in the US and France. [42,49] However, this differed completely from what Ahmed et al, Jalali et al., and Chawla et al. found in their studies conducted in South Asia which showed male prevalence. [11,15,20] Surprisingly the studies conducted in the African subcontinent showed an almost equal male to female ratio. [18,50-52] This points towards some regional variation along with probably associated factor/s affecting the two genders.

The incidence of primary CNS tumors is also more prevalent within the Caucasian population in comparison to the African-American population, with a higher rate of mortality in males than in females.There are only a few conclusive studies regarding occupational origins of primary CNS tumors. [53] Likely risk factors include vinyl chloride exposure (which is a risk factor for glioma), Epstein-Barr virus infection, organ transplantation, and AIDS (considerable risk factors for primary CNS lymphoma). The etiology of most childhood brain tumors is unknown, although germline mutations have been observed in approximately 8% of pediatric cancers. [45,56]

Most of the patients in our study were young adults (30-50yrs). The studies of Soyemi et al., Lu et al., and Ferreira et al. found that the incidence of brain tumors peaked around 40 years of age [18,35,38] This present study identified that almost 32.2% of pediatric brain lesions were observed in patients below the age of 20 years, which was a relatively higher percentage in comparison to the findings of studies conducted by Rathod et al. (21.3%), Kothari et al. (16%), Butt et al. (18%), and Mahmood et al. (11%), respectively [1,12,14,57]

Histopathological variations

CNS neoplasms are a distinctive and diverse group of tumors with an overall incidence of 10.82 per 100000 person/year. [2] Among all primary and secondary CNS tumors, tumors of neuroepithelial origin, were the predominant neoplastic ICSOLs, as reported by Rathod et al., Butt et al and Kothari et al. [1,12,14] Our results showed that astrocytic tumors of meningiomas were more prevalent than other primary and secondary brain tumors and benign ICSOLs. In our study, primary brain tumors in descending order of frequency consist of the following: Meningiomas 45%, Glioblastomas and astrocytomas 31%, Neural tumors 7.6%, Oligodendrogliomas 5.1%, Neural Tumors 7.6%, Ependymal tumors 0.75%, Hemangioblastoma 0.73%, Benign tumors 0.55%, Germ cell tumor 0.9%, Metastatic tumors 0.08%, Lymphomas 0.07% and others 5%. This correlates with what Ferlay et al and Fisher et al found in their studies with meningioma being the most common of all brain tumors. [45,55] Regarding the progression of CNS tumors, Baumert et al. and Reijneveld et al. have identified several genetic alterations acting as important prognostic factors for diffuse gliomas (astrocytomas, oligodendrogliomas, mixed gliomas, and glioblastomas) Specific alterations include co-deletion of chromosomes 1p and 19q, alterations in the MGMT gene promoter region and mutation of the IDH gene. Indicators of an unfavorable outlook encompass being over 40 years old, having a tumor larger than 5 cm, experiencing disease progression, having a tumor that extends across the brain's midline, displaying contrast enhancement on MRI scans, having a WHO performance status of 1 or higher, encountering neurological symptoms, and undergoing less than a complete surgical removal of the tumor [58,59]

Clinical manifestations

Although neoplasms have typical presentations, various intracranial masses show atypical features, mainly due to arterial occlusion/s, secondary to intra-tumoral hemorrhage, cerebral infarction, or the presence of asymptomatic tumors in selected cases. [5] Roughly one-fifth of individuals with brain tumors above the tentorium can develop seizures, which might appear before the formal diagnosis by several months or even years in the case of slow-growing tumors. Research indicates that around 70% of patients with tumors originating in the brain's parenchyma and 40% of those with tumors that have spread to the brain may encounter seizures at some point during their medical journey [45]

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This review explored the connection between gliomas and symptoms like seizures and visual problems. The actual occurrence of these symptoms varied depending on the specific stage of the disease. Research conducted by Jzerman-Korevaar et al. and Sizoo et al. found that patients with gliomas exhibited a similar, or in some cases, even higher frequency of neurological symptoms, including seizures, cognitive decline, and worsening neurological conditions, compared to the studies included in this comprehensive review [60,61]

Contrast-enhanced CT and MRI are commonly used for the diagnosis of CNS tumors. [53,62,63] CT is a useful tool to assess clinically unstable cases and is more useful, in comparison to MRI, for the evaluation of skull lesions, calcifications, and hyperacute hemorrhages. SPECT and PET scans are highly valuable in identifying tumor recurrence as opposed to radiation necrosis in post-treatment imaging. [62] However, biopsy remains the mainstay to confirm the diagnosis. Acting as a case in point, needle biopsy plays a vital role before/during a surgical procedure, except in those cases where clinical and radiologic findings indicate a benign tumor that can be managed with active surveillance (without biopsy or treatment). In all other cases, radiologic findings can be misleading, and consequently, a confirmatory biopsy is required to rule out other causes of ICSOLs, such as infection or metastatic cancer.

Study Limitations:

1. Systematic reviews need to be conducted, considering all intracranial tumors (i.e., primary and secondary brain tumors).
2. Only quantitative studies were evaluated in this investigation. Future reviews need to be conducted using other types of published literature as well.
3. The database search needs to be widened, using additional search engines and considering all published studies todate.

CONCLUSION

Intracranial tumors encompass a wide range of growths, some non-cancerous, others cancerous, some originating in the brain, and some spreading from elsewhere in the body. Accurate diagnosis demands precise medical information, radiological findings, and knowledge of the cellular makeup and immunohistochemistry of various tumor types. While distinguishing between primary and metastatic tumors is often possible based on location and the patient's age, careful histological analysis is necessary, especially for rare and specific tumor subtypes. It's advisable to use a comprehensive diagnostic approach that considers tumor location, its appearance under the microscope, and follows the 2016 WHO guidelines for classifying CNS tumors in all cases. Such an approach becomes particularly valuable when dealing with small biopsy samples, like those from deep brain tumors, where limited tissue can sometimes lead to errors in grading. Furthermore, histological examination helps identify specific mutations associated with tumor grades.

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