

## Original Research Article

# Correlation between histopathological variant and anatomical site of meningiomas: a single centre study

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### ABSTRACT

**Background:** Meningiomas are among the most common primary tumors of the central nervous system, arising from arachnoidal cap cells. They show diverse histopathological variants and occur at various sites within the craniospinal axis. Studying the correlation between histological subtype and tumor location may help in predicting tumor behavior, guiding surgical management and assessing prognosis.

**Methods:** A retrospective study was conducted over one year for a sample size of 51 histopathologically confirmed cases of meningioma. Clinical details, anatomical location, histopathological subtype and WHO grade were reviewed. Tumors were classified according to WHO 2021 criteria and the association between histological variants and anatomical sites was analysed.

**Results:** Of all the cases studied, 58.8% were females and 41.2% males, with the highest incidence in the 51–60 years age group (33.3%). The most common site was the parasagittal region (41.1%), followed by free convexity (19.6%) and spinal region (11.7%). Histologically, meningothelial meningioma was the most frequent subtype (60.7%), followed by fibroblastic (13.7%), transitional (5.88%) and psammomatous (5.88%) variants. WHO Grade I tumors accounted for 86.2% of cases, Grade II for 9.88% and Grade III for 3.92%. Higher-grade tumors demonstrated increased mitotic activity, hypercellularity, necrosis and brain infiltration. A significant correlation was observed between certain histological variants and anatomical sites, particularly meningothelial meningioma in the parasagittal region.

**Conclusions:** Meningiomas commonly occur in middle-aged females and are most frequently located in the parasagittal region. The meningothelial subtype and WHO Grade I tumors predominate. Correlation between histological subtype and tumor location provides useful insights for clinical management and prognosis.

**Keywords:** Anatomical site, Central nervous system tumors, Histopathology, Meningioma, WHO grading

### INTRODUCTION

Meningiomas are common primary tumours of the central nervous system and are generally believed to arise from arachnoid cap cells within the meningeal coverings of the brain and spinal cord.<sup>1</sup> They account for a substantial proportion of primary CNS tumours and an even larger share of benign intracranial neoplasms. Their incidence increases with age, with a peak in later adulthood and they show a clear female predominance. In children,

meningiomas are less common but are more likely to present as higher-grade tumours with a greater tendency for recurrence.<sup>2</sup> Meningothelial cells form an important cellular component of the meninges and contribute to the protective barrier separating neural tissue from cerebrospinal fluid.

These cells help maintain the local microenvironment of the optic nerve and are involved in the clearance of metabolic waste from cerebrospinal fluid. They may also participate in central nervous system immune responses by

producing pro-inflammatory cytokines under stress or pathological conditions.<sup>3</sup> Although most intracranial meningiomas are dural-based, some occur in locations without a clear dural attachment, such as the ventricles. Tumours arising in sites including the posterior fossa, skull base, intraventricular region and parasagittal or falx areas may show more frequent histopathological atypia. Since the World Health Organization classifies meningiomas into benign, atypical and malignant categories, preoperative estimation of tumour grade based on site of origin may be useful for planning the extent of resection and the possible need for adjuvant therapy.<sup>4,5</sup>

**METHODS**

This retrospective descriptive study was conducted in Karnataka Medical College and Research Institute, in Department of Pathology over a period of one year, from January 2024 to January 2025. Sample size for this study is total of 51. All meningioma specimens received in the histopathology section during this period were included in the study.

Patient demographic details, clinical information and histopathological findings were obtained from departmental records. Hematoxylin and eosin (H&E) stained slides were reviewed and where necessary, slides were re-evaluated to confirm the diagnosis and histological subtype. Cases with incomplete clinical data or inadequate tissue for evaluation were excluded. The collected data were compiled and analyzed using descriptive statistical methods.

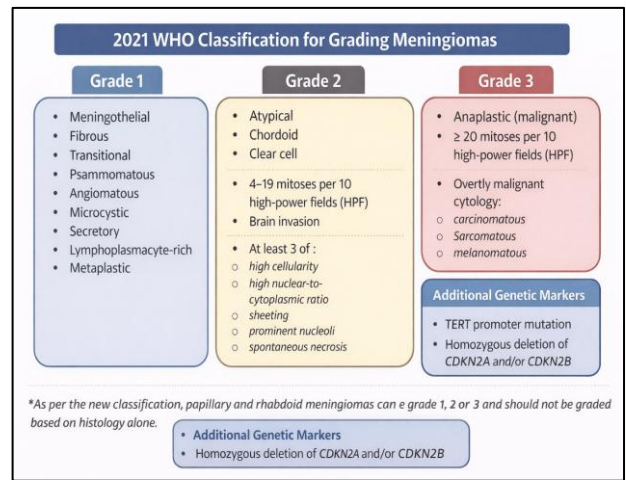
**RESULTS**

Amongst the cases studied, 58.8% were females and 41.2% were males. (Table 1) The most common age group involved was 51-60 years which was (17 cases) 33.3%. Childhood meningioma (<18 years) accounted for 1.96% of total cases which are rare and was found to be of high-grade variant which was grade- II clear cell carcinoma in this study. The highest incidence was observed in the 41–50 and 51–60 age groups, comprising 12 (23.5%) and 17 (33.3%) cases, respectively. Even in these age group, females were more affected than males. In most of the cases, the site of origin was Parasagittal region which was 41.1% followed by free convexities (19.6%), Spinal (11.7%), Sella (7.8%), Cerebello-pontine angle (5.8%), Sphenoid ridge (3.9%) and the rest showed tentorial region, Intraventricular region, cerebellum, posterior fossa and parafalcine (1.9% each) (Table 2).

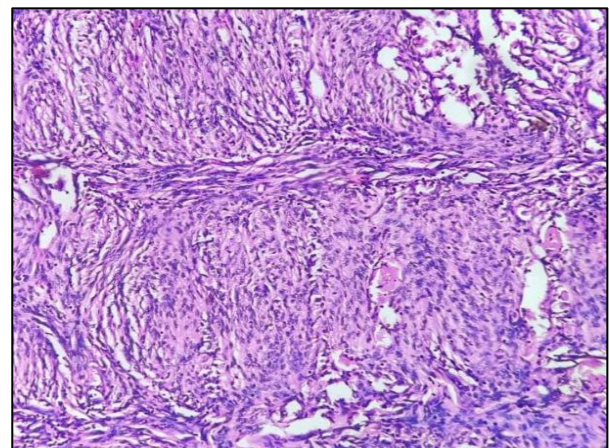
The less common histopathological types of meningiomas had common locations of origin in the parasagittal, free convexity, parafalcine and intraventricular regions. Meningiomas of 58.8% were found in females, while 41.2% were found in males. Amongst them, highest incidence was in the age group of 51-60 years which is 33.3% in total. Meningioma in childhood is rare which accounted for 1.96% in our studies. The most common

type of histopathological variant of meningioma was Meningothelial meningioma which is 60.7%. The most common location involved is parasagittal which is 41.1%.

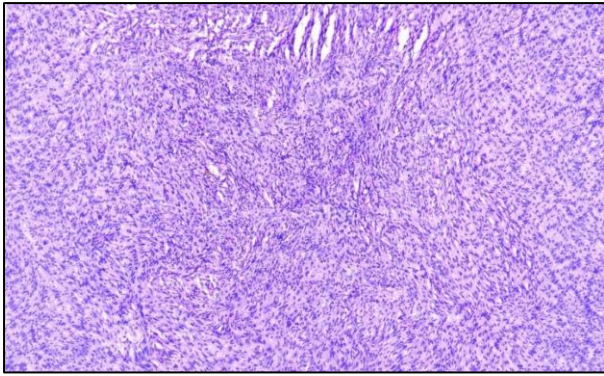
The uncommon meningioma variants (Grade-II and III) were 9.88% and 3.92% respectively. Histopathologically, the common types of meningiomas were the meningothelial (60.7%=31/51), fibroblastic (13.7%=7/51), transitional (5.88%=3/51) and psammomatous (5.88%=3/51) of comprising 86.2% (44/51). Whereas the uncommon types of meningiomas, such as, atypical (3.92%=2/51), clear cell (3.92%=2/51), chordoid (1.96%=1/51); anaplastic (3.92%= 2/51) comprising of 13.8%% (7/51) of all meningiomas.



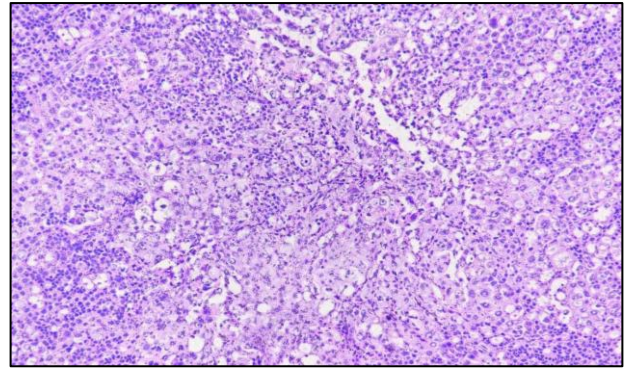
**Figure 1: Grading of meningiomas according to the WHO 2016 classification and the modifications introduced in the WHO 2021 CNS5 classification, including the addition of molecular criteria for grading and the removal of certain histological subtypes previously designated as grade 3.<sup>21</sup>**



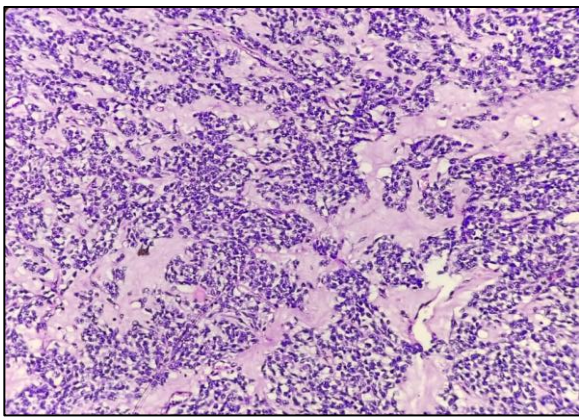
**Figure 2: Meningothelial meningioma showing meningothelial cells arranged in sheets and nests with a characteristic syncytial growth pattern due to indistinct cell borders. The stroma is scant. Mitotic activity is low and necrosis is absent, WHO Grade I. (H&E,100X).**



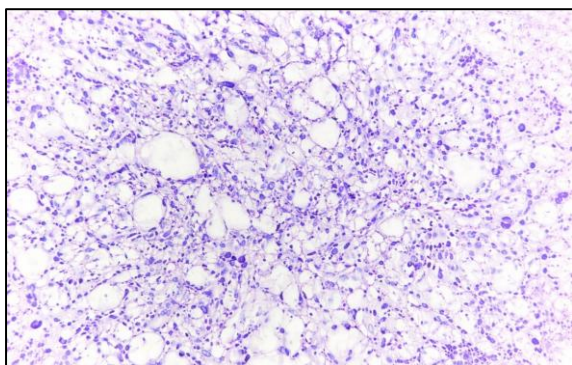
**Figure 3: Fibrous meningioma of cells arranged in interlacing fascicles or bundles composed predominantly of elongated spindle-shaped cells. Cells have elongated nuclei with inconspicuous nucleoli and indistinct cytoplasmic borders. Whorl formation is less prominent WHO grade I (H&E, 100X).**



**Figure 6: Anaplastic meningioma shows highly cellular tumor composed of sheets of markedly atypical cells with prominent nuclear pleomorphism, hyperchromatic nuclei and prominent nucleoli. Mitotic activity (4/ high power field) noted. WHO Grade III (H&E, 100x).**



**Figure 4: Chordoid meningioma showing cords, trabeculae or clusters of epithelioid tumor cells embedded in an abundant myxoid or mucinous stroma, resembling chordoma. WHO grade II (100X).**



**Figure 5: Clear cell meningioma characterized by sheets or nests of polygonal tumor cells in a patternless or sheet-like architecture. Abundant clear cytoplasm seen due to intracytoplasmic glycogen accumulation. The nuclei are round to oval with fine chromatin and inconspicuous nucleoli. WHO grade II (H&E, 100X).**

#### *Co-relation between site of tumour and type*

The most common histological type of meningioma was meningotheelial type and 35.4% (11/31) of these arose from the parasagittal region; 19.35% (6/31) from the free convexity; 12.9% (4/31) from the spinal region, 9.67% (3/31) from the CP angle, 6.45% (2/31) each from the sellae and sphenoid wing followed by 3.22% (1/31) each from cerebellum, tentorium and posterior fossa.

Similarly, the other common histological types, such as, the fibroblastic, transitional and psammomatous, originated from the most common sites of origin such as, the parasagittal, anterior parafalcine, sphenoid ridge convexity and tentorial regions.

While the less common atypical meningioma (2/2) and chordoid meningioma (1/1) arise from parasagittal region; clear cell meningioma from cerebral convexity 50% (1/2) and from parafalcine 50% (1/2); were areas anaplastic meningioma from convexity and posterior fossa, 50% each.

The observation from shows the distribution of cases and their percentage according to the WHO grading. WHO grade I consisting of 44 cases (86.2%), WHO grade II consisting of 5 cases (9.88%) and WHO grade III consisting of 2 cases (3.92%) (Table 3). Tumours were classified into subtypes according to their dominant microscopic patterns and grades of WHO.

Various microscopic features have been considered such as-hypercellularity, pleomorphism/high nucleocytoplasmic ratio, prominent nucleoli, sheeting, defined as lack of typical meningioma growth pattern, necrosis, increased mitosis, brain infiltration. The above-mentioned features were found to be more in grade- II and grade- III.

**Table 1: Age and gender distribution of meningioma cases.**

Age span (in years)	Female	Male	Total
0-10	--	--	--
11-20	1	--	1
21-30	1	4	5
31-40	4	3	7
41-50	8	4	12
51-60	10	7	17
61-70	5	2	7
>71	1	1	2
<b>Total</b>	<b>30 (58.8%)</b>	<b>21 (41.2%)</b>	<b>51</b>

**Table 2: Anatomical location related to histological variants of meningiomas.**

Anatomical location	MEN	FIB	TRA	PSAM	CHOR	CLE	ATY	ANA	Total
Parasagittal	11	4	3	0	1	0	2	0	21 (41.1%)
Convexity	6	2	0	0	0	1	0	1	10 (19.6%)
Spinal	4	0	0	2	0	0	0	0	6 (11.7%)
Sellae	2	1	0	1	0	0	0	0	4 (7.8%)
CP angle	3	0	0	0	0	0	0	0	3 (5.8%)
Sphenoid wing	2	0	0	0	0	0	0	0	2 (3.9%)
Tentorial	1	0	0	0	0	0	0	0	1 (1.9%)
Intraventricular	0	0	0	0	0	0	0	1	1 (1.9%)
Cerebellum	1	0	0	0	0	0	0	0	1 (1.9%)
Posterior fossa	1	0	0	0	0	0	0	0	1 (1.9%)
Parafalcine	0	0	0	0	0	1	0	0	1 (1.9%)
<b>Total</b>	<b>31</b>	<b>7</b>	<b>3</b>	<b>3</b>	<b>1</b>	<b>2</b>	<b>2</b>	<b>2</b>	<b>51</b>

**Table 3: Distribution of cases and their percentage according to the WHO grading.**

S.NO	WHO grade-I	WHO- grade-II	WHO grade-III
Number of cases	44	5	2
%	86.2	9.88	3.92

**Table 4: Comparative analysis of meningioma studies.**

Study	No. of cases	Female: male ratio/female %	Common age group	Common site	Common histological variant	WHO grade I	WHO grade II	WHO grade III
<b>Present study (2024–2025)</b>	51	58.8%Female	51–60 years	Parasagittal (41.1%)	Meningothelial (60.7%)	86.2%	9.88%	3.92%
<b>Backer-Grøndahl et al<sup>1</sup>, 2012</b>	196	Female predominance	Middle age	Intracranial	Multiple grade I variants	68.9%	30%	1%
<b>Bhat et al<sup>4</sup>, 2014</b>	729	64.6% Female	41–50 years	Parasagittal /Falx	Multiple grade I variants	89.3%	5.9%	4.8%
<b>Gadgil et al<sup>9</sup>, 2016</b>	324	F:M=2.2:1	41–60 years	Intracranial	Transitional	85.6%	—	—
<b>Shenoy et al<sup>19</sup>, 2019</b>	63	F:M=2.3:1	4th–6th decade	Cerebral hemisphere	Meningothelial/Transitional	88.89%	11.11%	0%
<b>Pant et al<sup>20</sup>, 2021</b>	302	Female predominance	5th decade	Cerebral convexity	Transitional	93.05%	5.3%	1.65%

## DISCUSSION

Meningiomas are primary central nervous system tumors that arise from arachnoid cap cells located within the meningeal coverings of the brain and spinal cord. These tumors typically exhibit slow growth and are frequently discovered incidentally during neuroimaging. Clinical manifestations primarily result from compression of adjacent neural tissues and surrounding structures. The neurological deficits depend on the tumor location and may be overt or subtle. Headache and seizures often herald the presence of meningioma.

Most meningiomas are intracranial in location. Anywhere along the neuroaxis from the dura, most commonly within the skull and at dural reflection sites such as the falx cerebri, tentorium cerebelli and venous sinuses it can be seen arising. Within the cranial cavity, many tumors arise along the cerebral convexities and are often located near the falx cerebri and superior sagittal sinus. Other sites include the olfactory grooves, sphenoid ridges, parasellar regions, optic nerve sheath, petrous ridges, tentorium cerebelli, posterior fossa and ventricles. Extracranial meningiomas are rare and may occur in the orbit, skin, subcutaneous tissue, paranasal sinuses, nasal cavities and bone.<sup>5,6</sup>

Meningiomas are usually benign and occur more frequently in females than males. The female predominance may be attributed to hormonal influences, particularly progesterone and estrogen receptor activation, which has been linked to the development of meningiomas in women. Hormone replacement therapy (HRT) has also been associated with an increased incidence of meningiomas in women between the ages of 26 and 55 years. This observation suggests that hormones may play a role in the development of meningiomas.<sup>7</sup>

Apart from hormonal influences, radiation exposure is another important etiological factor. Meningiomas are known to be induced by low, moderate and high-dose radiation. Most patients with radiation-induced meningiomas have a history of low-dose irradiation to the scalp for tinea capitis. The second largest group of patients with radiation-induced meningioma received high-dose irradiation for primary brain tumors. Radiation-induced meningiomas are more commonly atypical or aggressive, multifocal, highly proliferative and generally occur in younger age groups.<sup>8</sup>

The order of involvement of sites of meningiomas is as follows: parasagittal region and free convexity (50%), sphenoid ridge, tuberculum sellae, olfactory groove, foramen magnum, optic nerve, tentorium cerebelli and choroid plexus. In rare intraventricular meningiomas, the left ventricle is most involved.<sup>8</sup> Spinal meningiomas are less common compared to intracranial meningiomas and most frequently occur in the thoracic region. Meningiomas are classified based on histological features and biological behavior according to the World Health Organization

classification. In the histologic grading defined by the 2021 WHO classification, intracranial meningiomas are categorized into WHO grade I, grade II and grade III (Figure 1).

The observations from the present study show that WHO grade I constituted 44 cases (86.2%), WHO Grade II constituted 5 cases (9.88%) and WHO Grade III constituted 2 cases (3.92%). Similarly, Gadgil et al, observed that 85.6% of meningiomas were Grade I tumors, emphasizing the predominance of benign variants in most series.<sup>9</sup>

### *Histological classification of meningiomas*

WHO grade I meningiomas with low risk of recurrence and aggressive growth meningotheial meningioma, fibrous (fibroblastic) meningioma, transitional (mixed) meningioma, psammomatous meningioma, angiomatous meningioma, microcystic meningioma, secretory meningioma, lymphoplasmacytic-rich meningioma, metaplastic meningioma, meningotheial meningioma.

This is a classic and common variant. The tumor cells are arranged in lobules surrounded by thin collagenous septae and show a syncytial pattern. The cells are largely uniform with oval nuclei and delicate chromatin. Occasional cells may show central clearing due to glycogen formation. Well-formed whorls and psammoma bodies are uncommon and mitotic activity is low or absent (Figure 2).

### *Fibrous meningioma*

This is also a common variant. The tumor cells are predominantly spindle-shaped and arranged in parallel, storiform and interlacing bundles within a collagen-rich matrix. The nuclei retain the features of meningotheial cells. Whorl formation and psammoma bodies may be seen focally (Figure 3).

### *Transitional meningioma*

These tumors display features intermediate between meningotheial and fibrous meningiomas. Meningotheial cells arranged in lobules alternate with spindle-shaped cells forming fascicles. Prominent whorls with psammoma bodies and clusters of syncytial cells are frequently seen.

### *Psammomatous meningioma*

These tumors contain abundant psammoma bodies that may coalesce into irregular calcified masses. The tumor cells typically have a transitional appearance with whorl formation and are commonly found in the spinal region.

### *Angiomatous meningioma*

This variant is characterized by numerous blood vessels within the tumor. The vascular channels may be small or medium-sized and may have thin or thick hyalinized walls.

### ***Microcystic meningioma***

These tumors consist of stellate cells with elongated cytoplasmic processes in a loose mucinous stroma, producing a microcystic appearance. The cystic spaces may contain pale eosinophilic material and pleomorphic cells may occasionally be seen.<sup>12</sup>

### ***Secretory meningioma***

This variant demonstrates focal epithelial differentiation characterized by intracellular lumina containing eosinophilic hyaline material known as pseudopsammoma bodies. These are PAS and carcinoembryonic antigen (CEA) positive and are surrounded by cell membranes with microvilli on ultrastructural examination. Marked vascular pericyte proliferation and peritumoral edema are usually seen.<sup>13,14</sup>

### ***Lymphoplasmacytic-rich meningioma***

These tumors exhibit extensive inflammatory infiltrates composed of lymphocytes and plasma cells, often obscuring the tumor cells. The basic architecture may resemble meningothelial, fibrous or transitional variants.

### ***Metaplastic meningioma***

These tumors demonstrate mesenchymal differentiation such as osseous, cartilaginous, lipomatous, myxoid or xanthomatous changes. Areas showing these changes may alternate with the usual meningioma pattern.

### ***Who grade II meningiomas***

These tumors have a greater likelihood of recurrence and aggressive behavior chordoid meningioma, clear cell meningioma, atypical meningioma, chordoid meningioma. This variant contains areas resembling chordoma, with trabeculae of eosinophilic vacuolated cells in a myxoid background. These areas are interspersed with typical meningioma regions and chronic inflammatory infiltrates may be present (Figure 4).

### ***Clear cell meningioma***

These tumors are composed of sheets of polygonal cells with clear glycogen-rich cytoplasm. Typical meningioma features may be minimal and whorl formation and psammoma bodies are rare. These tumors are associated with aggressive behavior (Figure 5).

### ***Atypical meningioma***

These tumors show increased mitotic activity or at least three of the following features: increased cellularity, small cells with high nuclear-cytoplasmic ratio, prominent nucleoli, sheet-like growth pattern and foci of spontaneous necrosis. Increased mitotic activity is defined as  $\geq 4$  mitoses per 10 high-power fields.<sup>15</sup>

Brain invasion is considered an unfavourable prognostic feature and may upgrade the tumor to WHO grade II.

### ***WHO grade III meningiomas***

Rhabdoid meningioma and papillary meningioma according to old classification (WHO 2016), anaplastic (malignant) meningioma.

### ***Papillary meningioma***

These rare tumors occur predominantly in younger patients and show a perivascular papillary or pseudopapillary pattern. They are associated with aggressive behavior, frequent recurrence and potential metastasis.<sup>16</sup>

### ***Rhabdoid meningioma***

These tumors contain sheets of rhabdoid cells with eccentric nuclei, prominent nucleoli and abundant eosinophilic cytoplasm containing paranuclear inclusions composed of intermediate filaments. These tumors demonstrate aggressive clinical behavior.<sup>17,18</sup>

### ***Anaplastic (malignant) meningioma***

These tumors exhibit frank malignant cytology with a high mitotic index of 20 or more mitoses per 10 high-power fields. Histologically, they may resemble sarcoma, carcinoma or melanoma. Brain invasion alone is not sufficient for diagnosing anaplastic meningioma.

However, papillary and rhabdoid meningioma types are no longer grade III tumors as it was in WHO 2016 classification. They can be grade 1, 2 or 3 and should not be graded based on histology alone (Figure 6).<sup>21</sup>

### ***Molecular and genetic characteristics of meningioma***

Recent advances have shown that molecular alterations play an important role in tumor behavior, recurrence risk and classification. The 2021 WHO CNS classification integrates molecular markers with histology for grading.

### ***Key molecular alterations***

#### ***NF2 mutation and chromosome 22 deletion***

Most common genetic alteration, seen in 40–60% of sporadic meningiomas, frequently associated with fibroblastic and transitional meningiomas common in convexity meningiomas.

#### ***TERT promoter mutation***

Leads to increased telomerase activity and is associated with aggressive behavior and poor survival, considered a molecular criterion for WHO grade III meningioma now.

#### *CDKN2A/B deletion*

Tumor suppressor gene deletion, associated with highly aggressive tumors, also used as a molecular marker for WHO grade III classification.

#### *TRAF7 mutation*

Second most common mutation, frequently seen in skull base meningiomas, often associated with secretory meningioma subtype.

#### *AKT1 mutation*

Common in meningothelial meningiomas, often seen in skull base tumors.

#### *SMO mutation*

Associated with olfactory groove meningiomas and is linked with higher recurrence risk in anterior skull base tumors.

#### *KLF4 mutation*

Often occurs with TRAF7 mutation, characteristic of secretory meningiomas and is associated with prominent peritumoral edema.

#### *PIK3CA mutation*

Seen in some skull base meningiomas and is associated with low chromosomal instability.

#### *POLR2A mutation*

Found almost exclusively in WHO Grade I meningothelial meningiomas, often located in the tuberculum sellae region.

#### *BAP1 mutation*

Seen in rhabdoid meningiomas, associated with aggressive clinical behavior.

#### *SMARCE1 mutation*

Associated with clear cell meningioma, may occur in familial multiple spinal meningiomas.

#### **Epigenetic and genomic changes**

Recent studies highlight the importance of DNA methylation profiling in predicting recurrence risk and tumor behavior. Loss of H3K27me3 trimethylation has been associated with higher tumor grade and poor prognosis, particularly in grade III meningiomas. High-grade meningiomas frequently show chromosomal losses,

including: 1p, 6q, 14q. Loss of chromosome 1p is strongly associated with tumour recurrence and progression.<sup>21</sup>

#### **Histological spectrum and prognostic significance**

The histological spectrum observed in the present study corresponds with previously published literature, where meningothelial and transitional meningiomas are the most common variants, followed by fibroblastic and psammomatous types (Table 5). Although grade II and grade III meningiomas occur less frequently, they are of significant clinical importance because they demonstrate higher proliferative activity, aggressive behavior and increased recurrence rates. Recurrence rates range from 7–25% in grade I tumors to as high as 50–94% in grade III tumors. Histopathological features such as increased cellularity, mitotic activity, brain invasion, necrosis and prominent nucleoli are key criteria in WHO grading and play a vital role in differentiating benign from atypical and malignant meningiomas.

Overall, the findings of the present study reinforce the importance of detailed histopathological examination and WHO grading, as these factors remain the cornerstone in the diagnosis, prognostication and management of meningiomas.

#### **CONCLUSION**

Meningiomas predominantly affect middle-aged adults with a female preponderance and most commonly arise in the parasagittal region. In the present study, meningothelial meningioma was the most frequent histological subtype and the majority of tumors belonged to WHO grade I, indicating their generally benign nature. Higher-grade meningiomas were relatively uncommon but demonstrated characteristic features such as increased mitotic activity, hypercellularity, necrosis and brain infiltration. A notable correlation was observed between certain histopathological variants and specific anatomical locations, particularly the predominance of meningothelial meningiomas in the parasagittal region. These findings emphasize the importance of detailed histopathological evaluation and WHO grading in the diagnosis, prognostication and management of meningiomas, while highlighting the value of correlating tumor subtype with anatomical site to better understand tumor behavior and guide clinical decision-making.

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