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CLINICOPATHOLOGICAL EVALUATION OF MENINGIOMA VARIANTS IN BASRAH CITY (2020-2024)

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ABSTRACT

Introduction: Meningiomas are among the most common central nervous system (CNS) tumors. Multiple predisposing factors have been associated with increased meningioma risk. In adults, there is a distinct female predominance, with a female-to-male ratio of 3:1. It has multiple variants listed under the World Health Organization (WHO) grading system for meningiomas based on histopathological criteria into three grades. Age and sex were significant determinant in certain subtypes. **Aim:** The study aims to ascertain the prediction of sex and age toward a specific variant of meningioma which guide the diagnosis and prognosis prediction. **Methodology:** A total 216 Cases of meningioma were collected from governmental and private laboratories reports were collected; the study period was conducted from January 2020 to December 2024. Data analyzed according to age, sex, grade, and histological subtype. **Results:** Over a period of 5 years, meningioma cases were 216, on which we found a female predominance in this study (73.1%) with a male-to-female ratio of 1:2.7. An age-related trend was evident, with the 46–65 years group (59.7%). meningothelial meningioma was found to be the most common subtype. **Conclusion:** The majority of cases occurred in individuals within the fourth to sixth decades of life. A notable female predominance was observed, particularly among grade 1 meningiomas. Conversely, grade 3 (malignant) meningiomas were more frequently encountered in male patients, particularly those in the older age category.

INTRODUCTION

Meningiomas are among the most common central nervous system (CNS) tumors, comprising approximately 36% of all CNS neoplasms in adults and 53% of non-malignant

CNS tumors.[1] In contrast, they are infrequent in children and adolescents of both sexes, with an incidence ranging from 0.4% to 4.6%. In adults, there is a distinct female predominance, with a female-to-male ratio of 3:1, which rises to 9:1 in spinal meningiomas.[2]

These tumors typically arise along the external surfaces of the brain and spinal cord. Less commonly, they may originate within the ventricular system or occur ectopically outside the CNS as ectopic meningiomas.[3]

Multiple predisposing factors have been associated with increased meningioma risk. These include genetic conditions such as neurofibromatosis type 2, prior radiation exposure, hormonal therapies, and a positive family history.[4][5][6] Meningiomas express hormone receptor namely, progesterone, estrogen, and androgen receptor on their cell membranes.[5] The higher incidence in females is thought to be linked to hormonal influences. Familial predisposition is also notable, particularly in individuals with first-degree relatives affected by meningioma. Furthermore, various hereditary syndromes are associated with increased risk, including neurofibromatosis type 2, von Hippel-Lindau disease, multiple endocrine neoplasia type 1, Li-Fraumeni syndrome, Cowden disease, and Gorlin syndrome.[4][5]

The World Health Organization (WHO) grading system for meningiomas is based on histopathological criteria.[8]

- **Grade 1** meningiomas account for over 80% of cases and are characterized by the absence of anaplastic features. This grade includes nine histologic subtypes: meningothelial, fibroblastic, transitional (mixed), psammomatous, angiomatous, microcystic, secretory, lymphoplasmacyte-rich, and metaplastic variants.[5]

- **Grade 2** meningiomas, classified as atypical tumors, are defined by the presence of at least three of the following features: necrosis, sheet-like growth pattern, prominent nucleoli, increased cellularity, or a small cell with high nuclear-to-cytoplasmic ratio.

Mitotic activity ranging from 4 to 19 mitoses per 10 high-power fields also supports this diagnosis. Histological subtypes within this grade include atypical, clear cell, and chordoid variants. Additionally, meningiomas exhibiting brain invasion are now classified as grade 2 lesions.[9][10]

- **Grade 3** meningiomas are anaplastic malignant lesions and may resemble high-grade sarcomas, carcinomas, or melanomas. These tumors demonstrate aggressive behavior and a high propensity for distant metastasis. A mitotic index of 20 or more mitoses per 10 high-power fields is indicative of grade 3 tumors. Anaplastic, papillary and rhabdoid subtypes fall within this category.[9]

Tumor recurrence correlates strongly with histological grade. Grade 1 meningiomas have a recurrence rate of approximately 4.9%, grade 2 tumors recur in 18.4% of cases, and grade 3 lesions show a recurrence rate of 27.3%.[11]

Despite their aggressive nature, the 10-year survival rate for malignant meningiomas has improved in recent years due to advancements in therapeutic strategies.[12][13] Notably, tumor grade is a crucial prognostic factor for patients receiving postoperative radiation therapy.[14]

METHODOLOGY

In Basrah, Iraq, from January 2020 to December 2024, a retrospective study was conducted. All the clinicopathological informations of Meningioma are released by histopathology departments of all major governmental hospitals and from pathological private laboratories were collected in the governorate and analyzed, totaling (216) cases. The data collected included information on age, sex, grade, and histopathological variants.

Only already diagnosed cases were discussed in this study.

Recurrent cases with incomplete information were not included.

Spinal meningiomas were excluded due to their distinct clinical and anatomical characteristics.

Cases of meningiomatosis and tumors associated with syndromes (like Neurofibromatosis type 2 and other associated syndromes) were excluded to avoid bias from syndromic or multifocal pathology.

RESULTS

Over a period of 5 years, 216 meningioma cases were detected, on which we found a female predominance in this study, 158 out of 216 (73.1%) were females while a 58 were males (26.9%) as shown in (table1).

An age-related trend was evident, with the 46–65 years age group comprising the largest share of cases (59.7%, n = 129), highlighting a predominance of this age group (table 1).

Table 1: Demographic characteristics of the study sample.

Variable	Frequency	Percent
Sex:		
Male	58	26.9
Female	158	73.1
Age group (Year):		
25-45	49	22.7
46-65	129	59.7
66-85	38	17.6
Total	216	100.0

- Histologically, **meningothelial meningioma** was found to be the most common subtype (146 cases)

Occupied mostly by females (121 cases, 82.9%)

and the rest were males (25 cases, 17.1%) (table 2).

-**Atypical meningiomas** were mostly found in males (10 cases 76.9%), the rest are females (3 cases 23.1%) (table 2).

-**Anaplastic meningiomas** were 100% males (4 cases) (table 2).

Table 2: The association between meningioma variants and sex.

		Sex			P-value*
		Male	Female	Total	
Variant	Meningiothelial	25 17.1%	121 82.9%	146 100.0%	<0.0001
	Angiomatous	5 29.4%	12 70.6%	17 100.0%	
	Atypical	10 76.9%	3 23.1%	13 100.0%	
	Fibroblastic	9 52.9%	8 47.1%	17 100.0%	
	Psammomatous	5 31.3%	11 68.8%	16 100.0%	
	Anaplastic	4 100.0%	0 0.0%	4 100.0%	
	Microcystic	0 0.0%	2 100.0%	2 100.0%	
	Secretory	0 0.0%	1 100.0%	1 100.0%	
Total		58 26.9%	158 73.1%	216 100.0%	

The meningiomas were graded according to WHO grading system (2021). 199 cases were **grade1** (77.9% females, 22.1%males) (figure1)

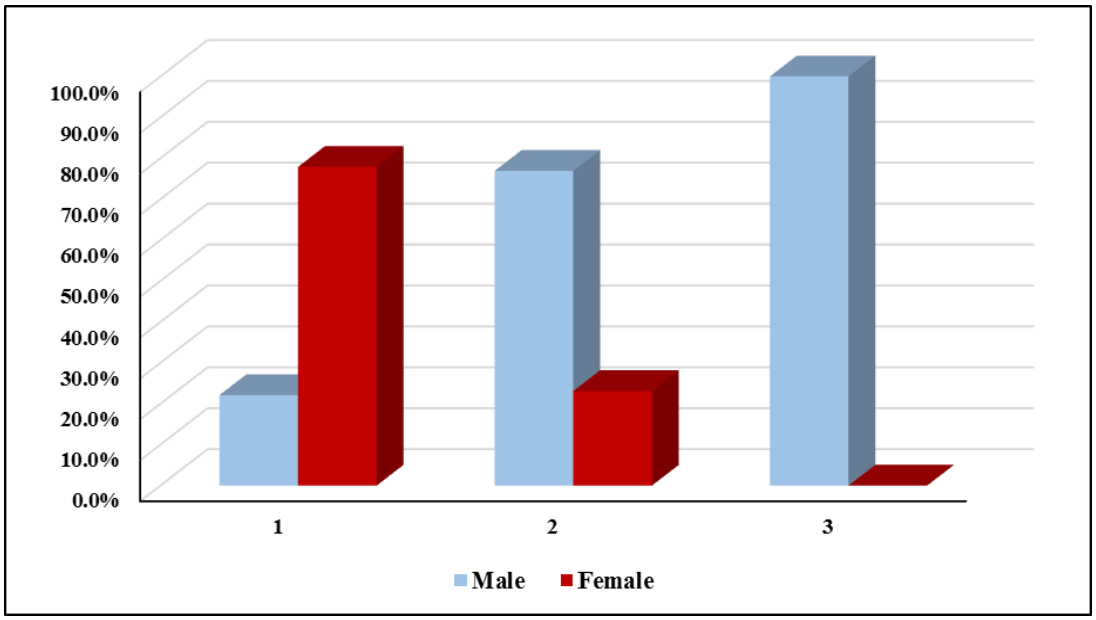

Figure 1: the association between meningioma grades and sex.

The most targeted age group by meningiomas were **46-65** year (129 cases, 59.7%), histologically speaking were mostly **meningothelial meningiomas** (86 cases, 58.9%) as shown in table 3.

Table 3: The association between meningioma variants and age.

		Age group (Year)			Total	P-value*
		25-45	46-65	66-85		
Variant	Meningiothelial	38 26.0%	86 58.9%	22 15.1%	146 100.0%	0.012
	Angiomatous	2 11.8%	13 76.5%	2 11.8%	17 100.0%	
	Atypical	1 7.7%	7 53.8%	5 38.5%	13 100.0%	
	Fibroblastic	4 23.5%	10 58.8%	3 17.6%	17 100.0%	
	Psammomatous	3 18.8%	12 75.0%	1 6.3%	16 100.0%	
	Anaplastic	0 0.0%	0 0.0%	4 100.0%	4 100.0%	
	Microcystic	1 50.0%	1 50.0%	0 0.0%	2 100.0%	
	Secretory	0 0.0%	0 0.0%	1 100.0%	1 100.0%	
Total		49 22.7%	129 59.7%	38 17.6%	216 100.0%	

Grade 1 meningiomas were labeled mostly at the **46-65** years (61.3%), while **grade 3** were exclusively at age **66-85** (figure 2).

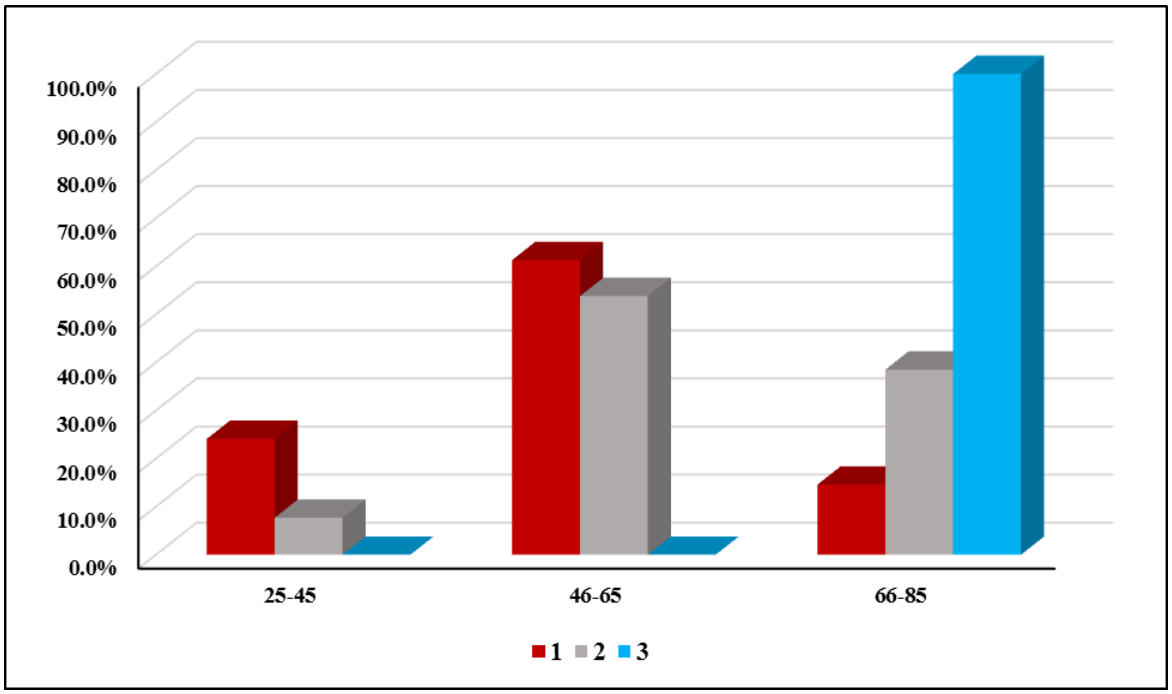

Figure 2: The association between meningioma grades and age.

DISCUSSION

Meningiomas are the most prevalent non-glial tumors of the central nervous system and represent the most frequent type of extra-axial neoplasm. According to the World Health Organization (WHO) classification of central nervous system tumors, meningiomas are defined as "meningothelial (arachnoid) cell neoplasms typically attached to the inner surface of the dura mater"[10] Clinically, the presentation of meningiomas varies, with most patients exhibiting neurological symptoms resulting from the mass effect exerted by the tumor on surrounding neural structures. In some cases, meningiomas remain asymptomatic and are discovered incidentally during autopsy. Histologically, meningiomas display considerable heterogeneity and are categorized into three grades under the WHO classification system. While the majority are benign, a subset demonstrates atypical or malignant characteristics. Tumors of higher grade are correlated with a greater likelihood of recurrence and exhibit more aggressive biological behavior.

In the current study, the majority of meningioma cases (129 cases, 59.7%) occurred in individuals between the **fourth and sixth** decades of life. The youngest patient was a 25-year-old female, while the oldest was a 77-year-old male. The calculated mean age was 54.17

years. These findings are consistent with those reported by Backer et al.[9] who observed the highest incidence of meningioma in the fourth and fifth decades.

Among the 216 total cases analyzed, 158 were female and 58 were male, resulting in a male-to-female ratio of approximately **1:2.7**. This female predominance is in agreement with existing literature, including a study by Perry et al.[15] which reported a male-to-female ratio of 1:3. The higher frequency among females may be attributed to hormone-related mechanisms, particularly the role of progesterone in tumor growth, as supported by various studies.[16]

Regarding tumor grading, **199 cases (92.13%)** were classified as WHO **grade1**, **13 cases (6.02%)** as **grade 2**, and **4 cases (1.85%)** as **grade 3**. These proportions are consistent with the findings of Gadgil et al.[17] who reported 85.6% grade 1, 11.5% grade 2, and 2.9% grade 3 cases, and also with Desai et al.[18] whose study revealed 90% grade 1, 8% grade 2, and 2% grade3 meningiomas. Collectively, these results reaffirm that grade 1 (benign) meningiomas constitute the most common subtype.

In this cohort of 216 cases, 199 were classified as **grade 1**. Among these, 44 patients (22.1%) were male and 155 (77.9%) were female, yielding a male-to-female ratio of 1:3.5. Similarly, in the study by Backer et al.[9] among 135 grade I meningioma cases, 107 (79.3%) were female and 28 (20.7%) were male, resulting in a ratio of 1:3.8.

The most frequently observed subtype of WHO grade 1 meningioma in this study was **meningothelial meningioma**, comprising **146** out of the total 216 cases **(67.59%).** This predominance is consistent with previous findings. For example, Moradi et al.[19] Jindal et al.[20] and Patil et al.[21] reported meningothelial variants as the most common, accounting for 33.7%, 50%, and 43.67% of cases, respectively. However, Backer et al.[9] identified the transitional variant as the most prevalent in their series.

In this cohort, angiomatous and fibroblastic meningiomas each accounted for 17 cases/216 total cases (7.87%). Although angiomatous meningiomas are generally rare, representing around 2.1% of all meningiomas[22], Desai et al.[18] found them in 8% of their sample which is of a close comparable result with the one of this study. The incidence of fibroblastic meningiomas varies in the literature, typically ranging between 4.8% and 16%.[23][24]

Psammomatous meningiomas were identified in 16 /216 cases (7.41%), and all were intracranial.

Microcystic and secretory meningiomas were less frequent, observed in 2 cases (0.93%) and 1 case (0.46%), respectively. Microcystic meningiomas are considered rare; our findings align with those of Gadgil et al.[17] and Lakshmi et al.[25] who reported incidences of 0.6% and 0.78%, respectively. Secretory meningiomas, although infrequent, have been reported with a prevalence ranging from 1.2% to 9.3% in the literature,[26] and accounted for 1.35% in the study by Wang et al.[27]

No cases of lymphoplasmacyte-rich, transitional, or metaplastic meningioma variants were identified during the course of this study.

Grade 2 meningiomas were identified in **13** / **216** total cases included, accounting for **6.02%** of the cohort. This percentage is comparable to the findings reported by Gadgil et al.[17] and Shah et al.[23] who documented incidences of 11.5% and 8%, respectively. Notably, recent data revealed a male predominance, with **10 cases** (4.63%) observed in males compared to **3 cases** (1.39%) in females. Similarly, Samadi et al.[24] reported a higher occurrence of grade2 meningiomas among males, suggesting a potential gender-related risk factor. All of the grade 2 tumors in our series were atypical meningiomas, with no cases of chordoid or clear cell subtypes identified.

Grade 3 meningiomas were exclusively observed in **male** patients, comprising **4 cases (1.85%)**, all of which were classified as **anaplastic meningiomas** and occurred in the **older age group**. This observation may indicate a potential correlation between advancing age and increased risk of high-grade meningioma in males. However, this finding contrasts with the study by Achey et al.[28] which reported no significant sex-based difference in the incidence of malignant meningiomas across various age groups.

No cases of **rhabdoid** or **papillary** variants were encountered during the study period. The absence of these rare subtypes, as well as others not recorded in our data, may be attributed to the **limited sample size**, or possibly to **genetic and environmental influences**.[24]

While it is well-documented that **meningiomas are generally more common in females**, several studies have highlighted a **higher risk of atypical and anaplastic meningiomas in males**.[29] This disparity may be influenced by differences in **hormonal levels and receptor**

status, as research indicates that **progesterone receptor expression** is more prominent in benign meningiomas compared to higher-grade ones.[30] Moreover, an **inverse relationship** has been observed between progesterone receptor expression and WHO tumor grade. Collectively, these factors may support the hypothesis that **male sex represents a risk factor** for the development of **grade 2 and 3 meningiomas**.

CONCLUSION

Throughout the duration of this study, various **meningioma subtypes** were identified, with **survival and recurrence rates deteriorating progressively** as tumor grade increased.

-The **meningothelial subtype** emerged as the most prevalent variant among the cases analyzed.

-The majority of cases occurred in individuals within the **fourth to sixth decades of life**, indicating this age group as the most commonly affected.

-A **notable female predominance** was observed, particularly among **grade 1 meningiomas**, warranting emphasis.

-Conversely, **grade 3 (malignant) meningiomas** were more frequently encountered in **male patients**, particularly those in the **older age category**.

RECOMMENDATIONS

-Further studies with larger sample sizes are recommended to validate the observed variant-specific patterns.

- Integration of molecular profiling in routine diagnostics may improve subclassification and prognostication of meningioma.

- Long-term follow-up is essential to better understand the recurrence rates and clinical outcomes associated with different meningioma subtypes.

- Pathologists should maintain awareness of rare variants, as they may mimic higher-grade or metastatic tumors.

- Collaboration between clinicians and pathologists is necessary to correlate radiologic, surgical, and histopathologic findings for optimal patient management.

- Further research into the correlation between histologic subtype and treatment response may help guide individualized therapy.

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