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Original Article

Predictors of Recurrence and Long–Term Outcomes of Intracranial Meningiomas: A Retrospective Multicenter Study from Saudi Arabia

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Abstract

Introduction: Meningioma is the second most prevalent primary tumor of the central nervous system. The World Health Organization (WHO) categorizes meningiomas into three grades, with the less frequent higher grades (2 and 3) demonstrating a high local recurrence rate even after complete resection. This study aims to elucidate the tumor recurrence predictors and treatment outcomes associated with various histopathological types of intracranial meningiomas.

Methods: A retrospective study was conducted to analyze the electronic medical records of histopathologically confirmed meningioma patients at two tertiary centers in Jeddah, Saudi Arabia, from 2005 to 2015. The primary objective was to delineate the clinical and radiological characteristics associated with various histopathological types of meningioma, as well as to ascertain the long–term outcomes and risk factors for tumor recurrence.

Results: A comprehensive review of 255 patients demonstrated a predominance of females (72.9%) and a mean age at presentation of 51.8 years. The follow–up period had a minimum duration of five years. The most prevalent clinical manifestation was headache, occurring in 41.6% of cases. Notably, 90.6% of cases did not exhibit apparent preoperative sensory–motor neurological deficits, while 5.5% presented with marked hemiparesis. The histopathologic pattern predominantly consisted of meningothelial meningioma (47.1%). The overall tumor recurrence rate during follow–up was observed in 26 patients (10.2%). This rate varied depending on the WHO grade: 13 patients (5.1%) with grade 1, 9 patients (3.5%) with grade 2, and 5 patients (1.6%) with grade 3 meningiomas. The recurrence rate exhibited a statistically significant correlation with the extent of resection. Notably, there was a higher recurrence rate associated with Simpson's grade 3 and 4 resections ($p<0.008$ and <0.003, respectively). The radiological findings, including peritumoral edema (56.2%), midline shift (17.9%), calcification (14.3%), and central necrosis (6.3%), exhibited no significant correlation with recurrence. Notably, there was a substantial correlation between tumor size and the probability of recurrence, with a likelihood ratio of 1.75 ($p<0.04$).

Conclusion: Our study presents comparable findings to international data pertaining to clinical behaviors, radiological, and histopathological characteristics. Its significance lies in underscoring the statistically significant coefficients for recurrence, encompassing WHO grading, extent of resection, and tumor size.

Key words: Intracranial meningioma; Epidemiology; Prognostic factors; Recurrence; Surgery; Outcome; Saudi Arabia.

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Introduction:

Meningioma is a benign, slow–growing extra–axial brain tumor that is believed to originate from arachnoid cap cells. It is the most prevalent primary neoplasm, accounting for approximately 26–37% of all primary intracranial tumors. Its annual incidence ranges from 1.31 to 7.8 per 100,000 individuals. [1,2] Epidemiological and clinical studies have demonstrated that over 80% of meningiomas are classified as grade 1 tumors according to the revised 2021 World Health Organization (WHO) Classification. Approximately 18% are classified as WHO grade 2, while 2% are categorized as WHO grade 3 tumors. [3]

Patients diagnosed with grade 1 meningiomas generally exhibit a favorable prognosis. In contrast, individuals with tumors classified as grades 2 and 3 demonstrate disease progression and extensive invasion of brain and cranial tissue. [4] Notably, atypical meningiomas (WHO grade 2), characterized by a Ki 67 or MIB–1 proliferation index exceeding 4%, exhibit a heightened risk of recurrence. Conversely, anaplastic meningiomas (WHO grade 3), characterized by a Ki 67 index surpassing 20%, are associated with a significantly higher recurrence and mortality rates. [5,6]

As previously reported, the survival rates in patients diagnosed with grade 1 meningioma are highly favorable following gross total resection, demonstrating a 5–year survival rate of approximately 90%. [7] The indication of radiation treatment following surgical resection of grade 3 meningiomas is definite. However, there is currently no consensus regarding the optimal standard of care for radiating grade 2 meningioma after surgical resection. [8,9] Nevertheless, there are recent reports that suggest radiation improved local control and associated with a longer survival. [10,11]

The prevalence of meningiomas has been extensively studied across various nations, as it exhibits distinct patterns, such as gender predominance. Female gender, likely due to sex hormones, is considered a non–modifiable risk factor for developing low–grade meningioma. [12] However, male gender is considered a risk factor for high–grade meningioma. [13] Other risk factors, such as exposure to ionizing radiation, are significant risk factors for the development of meningioma. [14] A historical account of head trauma has been postulated as a potential risk factor for the development of meningioma. This hypothesis was investigated in a population–based case–control study conducted by Phillips LE, et al., to elucidate the correlation between head trauma and meningioma. The study revealed a significant association between head trauma and an elevated risk of meningioma, particularly head traumas occurring within the age range of 10 to 19. However, whether the associations observed in this study are causal remains uncertain. [15] Recently, Chao H, et al., investigated the risk of cigarette smoking as hypothesized to be a risk factor for meningioma. They found that cigarette smoking is not associated with a significantly increased risk of meningioma in the general population, but there is a positive association in men but not in women. [16] Another risk factor was reported by Alqurashi A, et al. as the initial potential association or proposed causal link between previous scalp traditional cautery and the development of meningioma in two patients after two decades, which requires further verification. [17]

A study conducted by Fonkem et al. aimed to ascertain the prevalence of meningiomas across diverse racial populations. The study's findings indicated that meningiomas were most prevalent among white individuals, comprising 76.9% of the cases. Conversely, black individuals exhibited a prevalence of 11.8%, while Hispanic individuals had a prevalence of 6.2%. The remaining 5.1% of meningioma cases were distributed among the other racial groups included in the study. [18] Previous studies have indicated that racial characteristics and low socioeconomic status are risk factors for patients undergoing intracranial meningioma resection, which are associated with poorer outcomes and higher mortality rates. A systematic review and meta–analysis conducted by Lei H, et al., revealed the existence of disparities in outcomes for patients undergoing meningioma surgery, with Black and low socioeconomic status patients experiencing worse outcomes. However, the conclusions were somewhat limited and contained confounding relationships that were not adequately accounted for. [19]

The epidemiology of meningioma in the Gulf and Middle East regions is relatively understudied. Tamimi et al. reported a 26.2% incidence of meningioma among all primary CNS tumors, based on a prospective study conducted over one year in 16 hospitals across Jordan. [20] Another study conducted in Lebanon analyzed 195 patients to identify the characteristics, risk factors and outcomes. [21]

In Saudi Arabia, one of the earliest studies conducted in 1990 by Jamjoom Z, et al., over a two–year period analyzed 53 cases of meningioma and observed a prevalence of 22.7%. Following total resection, the recurrence rate was 5.6%, while after partial resection, the recurrence rate was 30%. [22] Recently, AlKhoshi AM, et al., conducted a retrospective study involving 53 patients who underwent surgical resection for intracranial meningioma. The study aimed to identify prognostic factors and their correlation with patient outcomes. The findings revealed that a short duration of hospitalization and a superficial location of the tumor are associated with optimal outcomes. [23]

In this study, we intend to assess the clinical and radiological characteristics of various histopathological patterns of meningiomas treated in two tertiary care centers. Our objective is to identify prognostic factors for surgical resection of meningiomas and their correlation with patient outcomes. Additionally, we will identify risk factors associated with meningioma recurrence and survival.

Material and Method:

Study Design

The study employed a retrospective cohort design to obtain a substantial sample size and represent a diverse population. Two referral tertiary care centers in Jeddah, which encompass the western province of Saudi Arabia, were selected as representative institutions: King Abdulaziz University Hospital (KAUH) and King Faisal Specialist Hospital and Research Centers (KFSH&RC). The study was approved by the Biomedical Ethics Research Committee at KAUH (reference number 329–15) and by the institutional review board (IRB) at KFSH&RC (IRB number 2017–44).

The sample included 255 confirmed cases of primary intracranial meningioma with histopathologic tissue diagnoses from January 2005 to December 2015. Patients with unclear tissue diagnoses, previously resected or recurrent tumors, or incomplete follow–up were excluded. Data collection was conducted through the hospital's electronic searching engine, utilizing patient medical records. Patient confidentiality was maintained through data anonymization, with a single access provider responsible for data collection on the XL datasheet.

Data Description

Demographic data, encompassing age, gender, and nationality, was meticulously documented. Clinical manifestations and signs, including incidental findings observed during routine MRI imaging unrelated to the current presentation, non–specific symptoms such as headaches, visual disturbances, dizziness, diminished level of consciousness, seizures, nausea, and vomiting, and localizing signs such as visual, speech, or hearing abnormalities, motor or sensory deficits, cranial nerve palsies, brainstem or cerebellar syndromes, were comprehensively recorded. Past medical, surgical, and familial history, as well as the preoperative Glasgow Coma Scale (GCS) status at the time of presentation, are of paramount importance in comprehending the patient's overall condition.

Radiological characteristics that were evaluated to assess the risk of recurrence included cranial and brain invasion, peritumoral edema, midline shift and mass effect, tumor size, calcification, and hemorrhage. Furthermore, the tumor's location and the extent of surgical resection, as determined using the Simpson grading system, were also considered.[24]

Postoperative neurological complications, including surgical site infection, cerebrospinal fluid leak, neurological deficit, seizure, were also addressed. Furthermore, non–neurological complications, such as chest infection, deep vein thrombosis (DVT), pulmonary embolism (PE), and urinary tract infection (UTI), were also considered.

Histopathologic patterns documented in the cases included grade 1 Meningothelial, psammomatous, fibroblastic, transitional, angiomatous, microcystic, secretory, lymphoplasma–rich, and metaplastic; WHO grade 2 Chordoid, clear cell, and atypical; and WHO grade 3 Papillary, rhabdoid, and anaplastic. Additionally, we followed the WHO 2016 guidelines to classify these tumors. Grade 1 meningiomas are considered benign and exhibit a low mitotic rate (<4/10 high–power field [HPF]) and lack brain invasion. Grade 2 or atypical meningiomas exhibit a mitotic rate of 4–19/10 HPF, brain invasion, or meet at least three of five specific histologic features (spontaneous or geographic necrosis; prominent nucleoli; high cellularity; small cells with a high nucleus–to–cytoplasm ratio; and pattern–less sheet–like growth). Grade 3 meningiomas exhibit a mitotic rate >20/10 HPF or an overtly malignant appearance. Molecular studies were not available at the time of diagnosis.

Statistical Analysis

The statistical analysis of the data was conducted using SPSS version 26.0 (IBM Corporation, Armonk, NY). Descriptive statistics were presented, including means, standard deviations, ranges, and percentages. Complications were categorized, quantified, and presented using frequencies and percentages. The chi–square test was utilized to evaluate the disparities between variables. Statistical significance was established based on a p–value less than 0.05.

Results

A comprehensive review of 255 patients revealed a mean age of 51.8 years (range: 13–91 years). Approximately 72.9% of the patients were female, while the majority were of Saudi nationality (80.8%). The duration of symptoms from onset to initial diagnosis ranged from 0.23 to 21.9 months (mean: 34.5 months). Notably, up to 94.9% of the cases were admitted through outpatient departments (Table 1).

The most prevalent presenting symptoms were headache (41.6%), followed by seizures (16.9%), visual

Variables	Frequency	Percent
Gender		
Women	186	72.9%
Men	69	27.1%
Nationality		
Saudi	206	80.8%
Non–Saudi	49	19.2%
Admission route		
OPD	242	94.9%
ER	13	5.1%

Table 1. Socio–demographic and admission characteristics of the patients

Abbreviations: ER, emergency room; OPD, outpatient department.

disturbances (12.9%), and incidental symptoms (8.2%). As indicated in Table 2, the least common presenting symptoms were diplopia, diminished hearing, ocular pain, limb weakness, slurred speech, menorrhagia, and facial pain (trigeminal neuralgia). At the initial examination, the majority of patients did not exhibit apparent focal motor or sensory deficit (90.6%). Hemiparesis and cranial nerve palsy were present in 5.5% and 2.0% of the patients, respectively. Eighty–three and a half percent of the patient population did not have any medical comorbidities.

Radiological assessments indicated hydrocephalus in five patients (2.0%). The most common locations were the convexity (34.1%), sphenoid wing (14.9%), and parafalcine (12.5%) areas, while the least common were the pineal (0.8%), tuberculum sellae (0.8%), and petroclival (0.8%), foramen magnum (0.8%), and Meckel's cave region (0.4%) (Figure 1).

The grading systems employed by the Simpson and WHO were comprehensively described for all patients in the study, as summarized in Table 3. Notably, Simpson grade I and II resections were successfully achieved in 92% of the cases based on intraoperative assessment. Nevertheless, a preliminary postoperative MRI scan indicated the presence of residual tumor in approximately 4.7%.

Postoperative neurologic complications documented include intracranial hemorrhage (2.4%), new onset hemiparesis (1.6%), hydrocephalus (1.2%), epidural hematoma (0.8%), subdural hematoma (0.8%), cranial nerve palsy (0.8%), seizures (0.8%), wound infections (0.8%), cerebrospinal fluid leaks (0.4%), and minor stroke (0.4%). Systemic complications were infrequent and included chest infections, pulmonary embolisms, urinary tract infections, and hoarseness, which were documented

Variables	Frequency	Percent
Presenting symptoms		
Headache	106	41.6%
Seizures	43	16.9%
Visual disturbance	33	12.9%
Incidental	21	8.2%
Dizziness	11	4.3%
Nausea/vomiting	6	2.4%
Numbness	5	2.0%
Decreased LOC	4	1.6%
Walking difficulties/ gait disturbance	4	1.6%
Personality changes / altered behavior	4	1.6%
Pain at the back/ neck	3	1.2%
Diplopia	2	0.8%
Reduced hearing	2	0.8%
Eye pain	2	0.8%
Limb weakness	2	0.8%
Slurred speech	1	0.4%
Menorrhagia	1	0.4%
Facial pain (trigeminal neuralgia)	1	0.4%
Signs on clinical examination		
No focal motor or sensory deficit	231	90.6%
Weakness	14	5.5%
Cranial nerve palsy	5	2.0%
Cerebellar signs	2	0.8%
Numbness	2	0.8%
Loss of sphincter control	1	0.4%

Table 2. Clinical characteristics of the patients

Abbreviations: LOC, level of consciousness.

in one patient each (total 4 patients). The 30–day postoperative mortality rate was 1.2%.

Histopathological examination revealed that the most prevalent histological subtypes were meningothelial (47.1%). Metaplastic, chordoid, and papillary meningiomas were also detected (Figure 2). The meningiomas were predominantly WHO grade 1 (87.8%), followed by grade 2 and 3, 7.5% and 4.7% respectively (Figure 3 and Table 3).

The overall tumor recurrence rate during follow–up was observed in 26 patients (10.2%). This rate varied depending on the WHO grade: 13 patients (5.1%) with

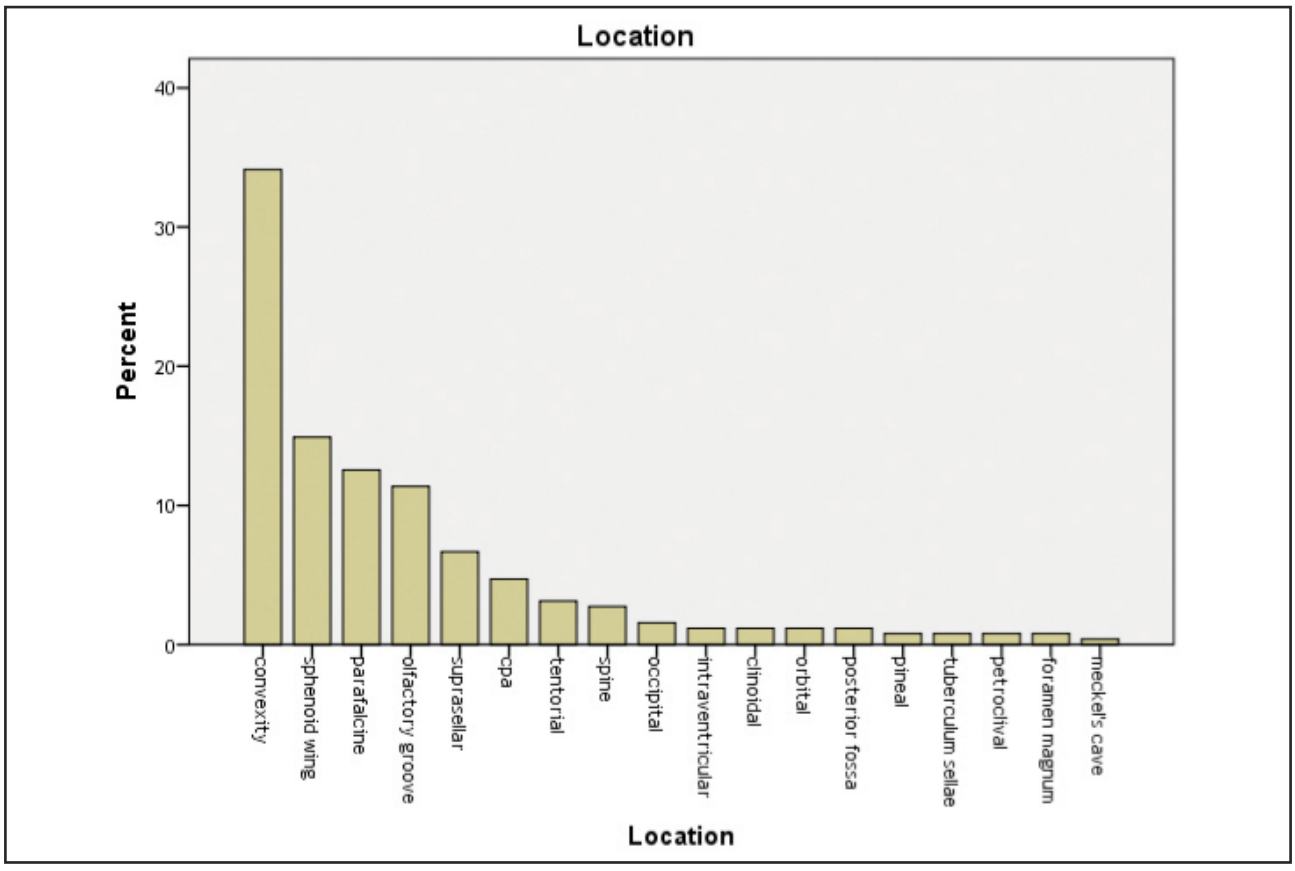


Figure 1: Locations of meningiomas in the cranium, shown by percentages.

Grading System	Frequency	Percent
Simpson grading		
Grade I	143	56.1%
Grade II	91	35.7%
Grade III	18	7.1%
Grade IV	3	1.2%
Grade V	0	0
World Health Organization Grading		
Grade 1	224	87.8%
Grade 2	19	7.5%
Grade 3	12	4.7%

Table 3. Distribution of meningiomas by the World Health Organization and Simpson grading:

grade 1, 9 patients (3.5%) with grade 2, and 5 patients (1.6%) with grade 3 meningiomas. Adjuvant radiotherapy was administered to all 12 patients with WHO grade 3 meningiomas (4.7%). Patients with grade 2 tumors that underwent gross total resection were also monitored, as were those with documented early radiological residual. In such cases, radiation therapy was administered after the second resection of the 9 patients (3.5%).

Further analysis revealed a significantly increased recurrence rate in patients undergoing grade IV Simpson resection ($p = 0.008$), cases diagnosed with WHO grade III, and those necessitating adjuvant radiotherapy ($p = 0.002$). Furthermore, patients with medium sized tumors with dimensions exceeding 3.5 cm and less than 6 cm exhibited a significantly higher recurrence rate in comparison to smaller tumors ($p = 0.048$) (Table 5). Patients with large tumors > 6 cm demonstrated significantly shorter recurrence–free time in comparison to those with small tumors ($p < 0.05$). Although Kaplan–Meier plots are frequently utilized for comparing survival rates across diverse treatment modalities, in this specific context, we employed Cox regression to elucidate the correlation between various factors and survival outcomes. (Table 5, Figure 4). In contrast, no significant correlation was observed between the recurrence rate and gender, admission route, or residual disease (Table 5). Additionally, clinical examination findings did not reveal any significant differences among the patients ($p = 0.148$). The presence of preoperative hydrocephalus ($p = 0.419$), surrounding edema ($p = 1.000$), MRI features of central necrosis ($p = 0.387$), calcification ($p = 0.390$), midline shift ($p = 0.277$), or herniation ($p = 0.261$), as well as tumor location ($p = 0.673$), were also not indicative of any differences.

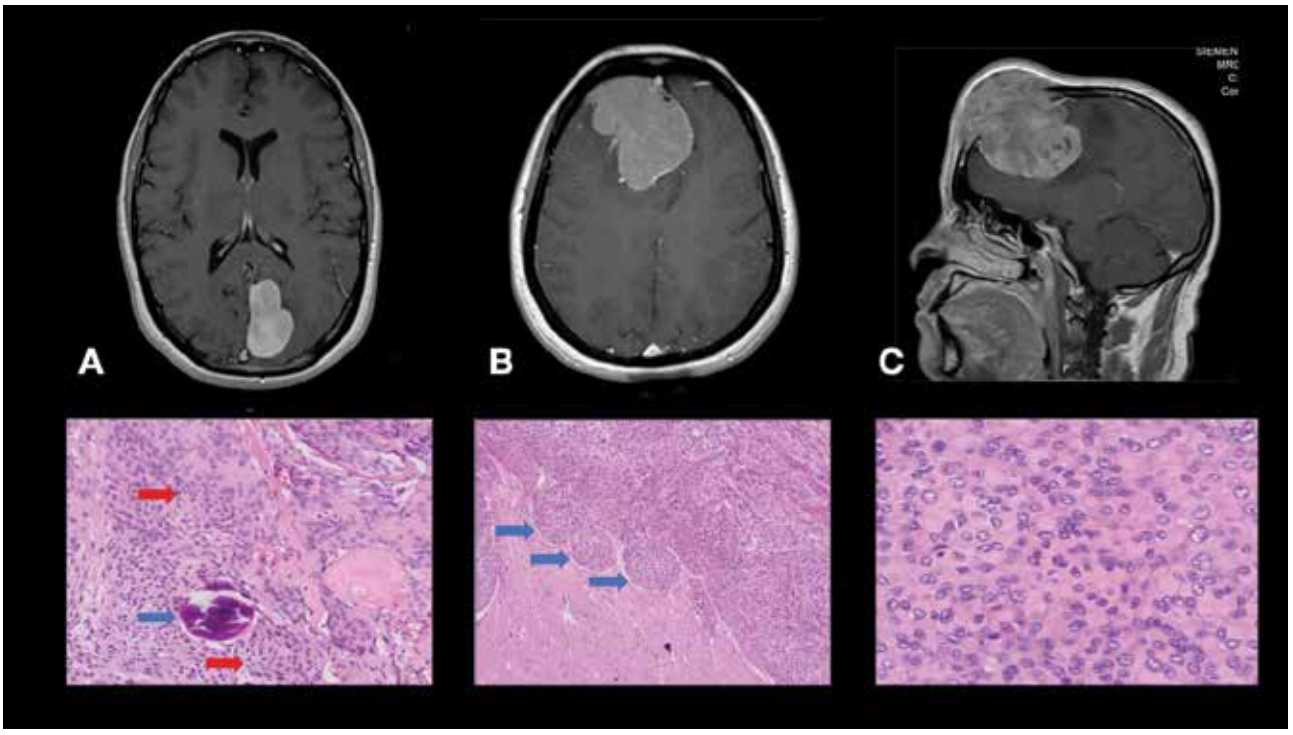


Figure 2: Illustrations of MRI and histopathological patterns of meningiomas.

A. WHO grade 1 meningioma: left occipital falx meningothelial variant (most common pattern) with psammoma body (blue arrow): epithelioid cells arranged in whorls (red arrows) (Hematoxylin and eosin stain, original power x200)

B. WHO grade 2 (Atypical meningioma): right frontal falx meningioma with histological brain invasion (blue arrows). (Hematoxylin and eosin stain, original power x100)

C. WHO grade 3 (Rhabdoid meningioma): Bifrontal parasagittal meningioma with brain and skull invasion. Histological findings include sheets of rhabdoid cells with eccentric nuclei and eosinophilic cytoplasm (Hematoxylin and eosin stain, original magnification x200)

Discussion

Meningioma constitutes one–third and the second most prevalent type of primary central nervous system (CNS) tumors globally, following glioma. Incidence rates (sex– and age–standardized, usually based on United State or World standard populations) reported by population–based registries range from 1.3 to 7.8 per 100,000 individuals.[1] A comparable prevalence has been documented in various local and regional Arab countries, with the exception of Jordan, where Tamimi et al. reported it as the most prevalent primary CNS tumor. [20–25]

Over the past several decades, there has been a notable rise in the incidence of primary brain tumors, particularly meningiomas, in various countries. However, it is essential to consider that this observed trend may be an artifact and could be attributed to several factors. Firstly, the aging population is a contributing factor, as older individuals tend to have a higher risk of developing brain tumors. Secondly, improvements in healthcare access and diagnostic procedures have enhanced the identification and detection of these tumors. Additionally, changes in the coding classification of tumors recorded in registries and the increased rate of histological confirmation, even in elderly patients, could also contribute to this observed increase.

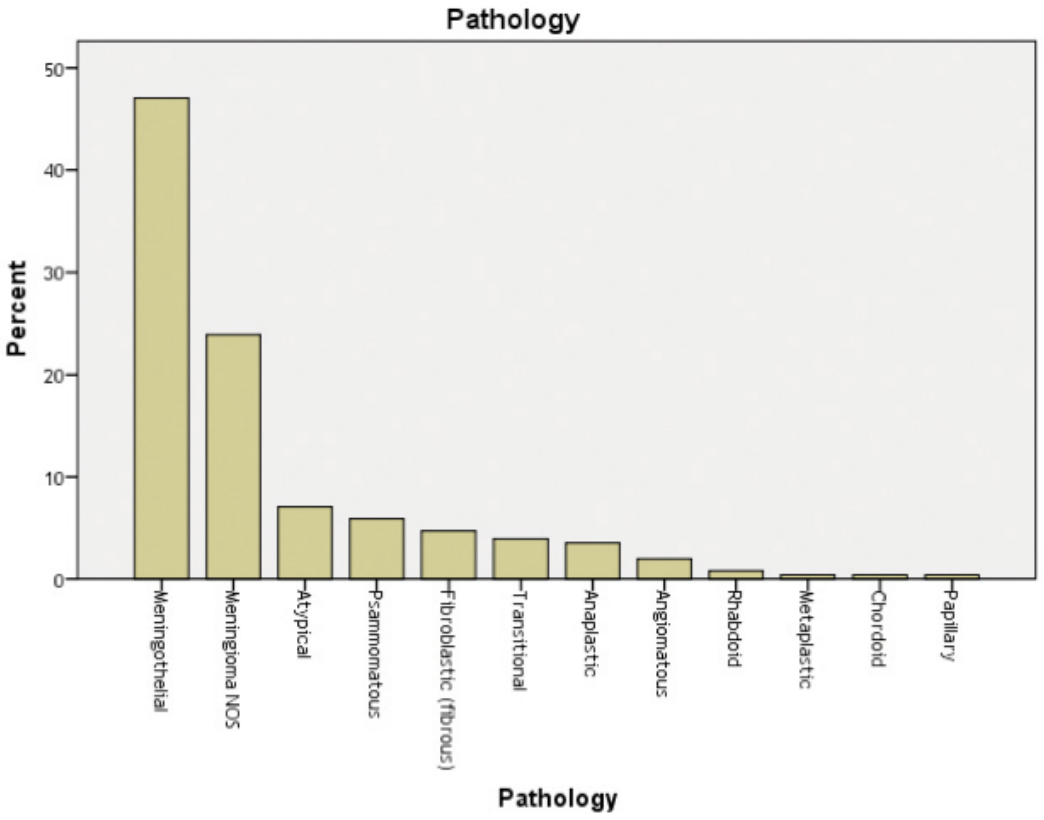
Our study revealed that the majority of (186) patients diagnosed with intracranial meningioma at our institutions were female (72.9%) while 69 male patients constituted 27.1%. This data supports international figures, albeit with a slightly higher ratio compared to the commonly cited ratio of 2:1. [26, 27]. This could be related to the hormonal effect. [28] Despite this, when comparing our data with the regional and local literature, the higher proportion of meningiomas in female patients in this study is consistent with that reported by other authors investigating the incidence of meningiomas. [22–23]. Although the mean age at presentation of our patients is approximately 47.7 years, the tumor location in our patients exhibited significant variability compared to the location reported by the investigators.

The majority of the diagnosed patients were Saudi nationals (80.8%). This percentage is attributed to the location of the centers; KFSHRC is a governmental institution. Consequently, the non–Saudi patients primarily came from KAUH, which is also a governmental institution but primarily a teaching hospital.

Variables	Recurrence		P–value
	Yes	No	
Gender			
Men	8 (3.1%)	61 (23.9%)	0.816
Women	18 (7.1%)	168 (65.9%)	
Histological subtype			
Meningioma NOS	7 (2.7%)	54 (21.2%)	0.000
Meningothelial	6 (2.4%)	114 (44.7%)	
Psammomatous	0 (0.0%)	15 (5.9%)	
Fibroblastic (fibrous)	0 (0.0%)	12 (4.7%)	
Transitional	0 (0.0%0)	10 (3.9%)	
Angiomatous	0 (0.0%)	5 (2.0%)	
Metaplastic	0 (0.0%)	1 (0.4%)	
Chordoid	1 (0.4%)	0 (0.0%)	
Atypical	8 (3.1%)	10 (3.9%)	
Papillary	1 (0.4%)	0 (0.0%)	
Rhabdoid	1 (0.4%)	1 (0.4%)	
Anaplastic	2 (0.8%)	7 (2.7%)	
Tumor size (cm)			
< 3	3 (1.3%)	63 (26.4%)	0.048
3.5–6	12 (5.0%)	120 (50.2%)	
> 6	8 (3.3%)	33 (13.8%)	
Simpson grade of meningioma resection			
Grade I	9 (3.5%)	134 (52.5%)	0.008
Grade II	12 (4.7%)	79 (31.0%)	
Grade III	3 (1.2%)	15 (5.9%)	
Grade IV	2 (0.8%)	1 (0.4%)	
WHO grading system			
Grade 1	13 (5.1%)	211 (82.7%)	0.000
Grade 2	9 (3.5%)	10 (3.9%)	
Grade 3	4 (1.6%)	8 (3.1%)	
Residual disease			
Yes	1 (0.4%)	11 (4.3%)	1.000
No	25 (9.8%)	218 (85.5%)	
Adjuvant Radiotherapy			
Yes	4 (1.6%)	3 (1.2%)	0.002
No	22 (8.6%)	226 (88.6%)	

Table 4. Association between recurrence rate and different clinical variables

Abbreviations: NOS, not otherwise specified.



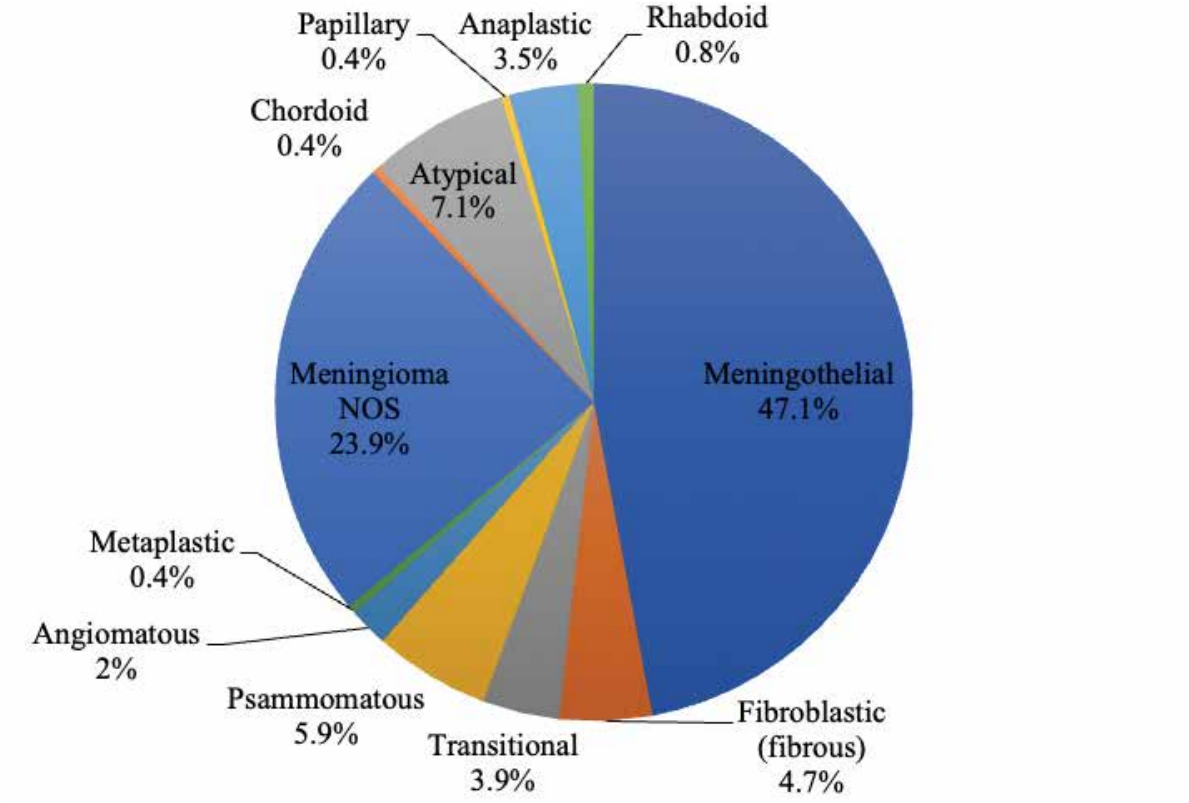


Figure 3: Histopathological pattern of meningiomas, shown in percentages.

	B	SE	Wald	df	Sig.	Exp (B)
Tumor Size	–.032	.119	.072	1	.788	.968
Simpson resection			14.753	3	.002	
Grade I	–3.136	.827	14.392	1	.000	.043
Grade II	–2.841	.823	11.925	1	.001	.058
Grade III & IV	–2.696	1.015	7.049	1	.008	.068
Location	–.034	.070	.239	1	.625	.966

Table 5: Effect of different factors on the survival using cox–regression.
Note: Exp(B) is the hazard ratio.

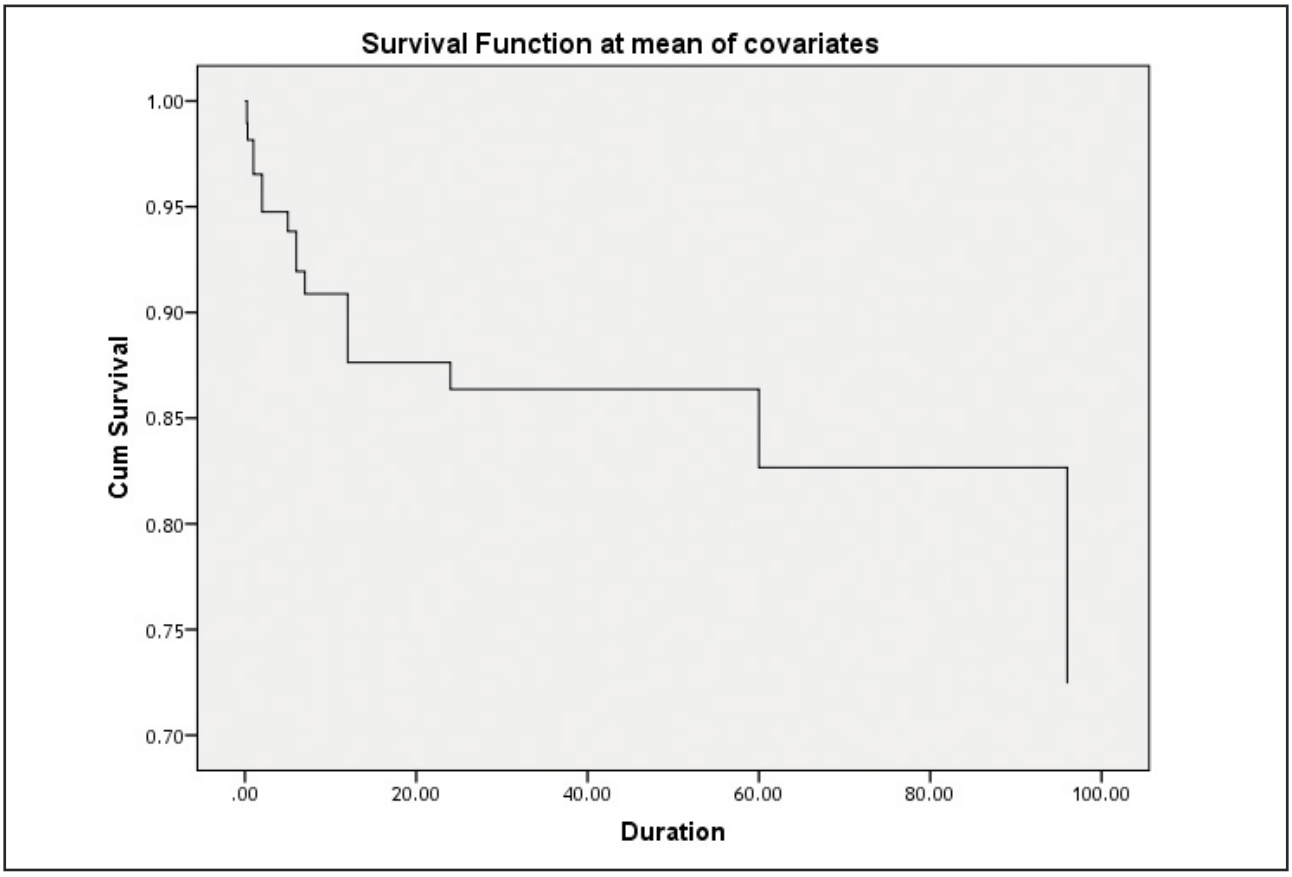


Figure 4: Survival curve using the Cox–regression to determine the association of different factors in the survival (months).

In our cohort, the most prevalent clinical presentation was characterized by headaches, followed by seizures and visual disturbances. During an initial clinical evaluation, the majority of our patients did not manifest apparent focal motor or sensory impairments. However, a small subset of patients exhibited signs such as weakness and cranial nerve palsy. We cannot draw definitive conclusions from these findings because the signs and symptoms of the disease are dependent on the location of the tumor within the brain. This result may be biased because we are reporting from two referral centers in the western region, which tend to accept serious and operable cases rather than simple, silent, or remotely calcified lesions. It is noteworthy that these presentations are not uncommonly reported in the literature. [29]

Meningiomas predominantly develop in the convexity, parasagittal, and falx regions. Conversely, locations such as the olfactory groove, sphenoid wing, and posterior fossa are reported to be less common sites of meningioma development. [1] Nevertheless, certain reports indicated a significant variation in the location of intracranial meningiomas across different studies. [30] In our study, the most frequent anatomical locations were the cerebral convexity, followed by the sphenoid wing, and the

parafalcine area. Our findings are consistent with those of investigators who reported that the cerebral convexity was the most common location in adult patients. [31]

Previous studies have suggested that the overall recurrence rate of intracranial meningiomas is between 10.5% and 35.0%. [32–34] Numerous radiological predictors of recurrence have been reported in the literature, including peritumoral edema, tumor necrosis, and skull base location. Furthermore, pathologic predictors associated with a high probability of recurrence encompass a mitotic rate exceeding 7/10 high–power field (HPF), a Ki67 value greater than 15%, WHO grade 2 and 3 tumors, and subtotal resection. [32–39] In our cohort of meningioma patients, the recurrence rate was 10.2%, and 4.7% exhibited residual tumors. The recurrence rate was not correlated with the radiological presence of edema or tumor location but was positively correlated with the extent of resection, tumor volume, and the WHO high grade. Pathological reports in our study exhibited inconsistent reporting of Ki67 values, which rendered the analyses and conclusions challenging.

There is strong evidence in the literature, similar to our observation, demonstrated that the extent of the initial tumor resection was important significant factor influencing recurrence rates. Furthermore, investigators discovered that recurrence rates were significantly increased in patients who did not undergo complete tumor resection, with a reported range of up to 37–52%. [39, 40]

Molecular profiling is emerging as a crucial field, with specific areas of focus including gene panel sequencing and genomic methylation profiling. A recent extensive review by Dwianingsih EK, et al, reported that mutations in TNF receptor–associated factor 7, Krüppel–like factor 4 (KLF4), v–Akt murine thymoma viral oncogene homolog (AKT1), Smoothened frizzled–class receptor (SMO), Phosphatidylinositol–4,5–bisphosphate 3–kinase catalytic subunit alpha (PIK3CA), and RNA polymerase II subunit A (POLR2A) were associated with a good prognosis and a low recurrence rate. By contrast, mutations in NF2, TERT promoter, SMARCB1, SMARCE1, CDKN2A/B and BAP1 are associated with poor prognosis and higher recurrence rates. They also reported in their review that DNA methylation status plays a role in diagnosis, predicting tumor recurrence and prognosis. [41] This combination of World Health Organization grading and molecular biomarkers has the potential to yield improved diagnostic outcomes, prognoses, and targeted therapies for meningioma. Our ongoing research in the Gulf and Middle East regions necessitates the study of molecular profiles for meningiomas. However, there is one report studying the landscape of meningiomas, and another studying stem cells–like biomarkers in meningiomas. [42–44]

Recently, the European Association of Neuro–Oncology (EANO) published its guidelines for the diagnosis and treatment of meningioma. [45] They recommended a gross total surgical resection that included the involved dura, which is typically curative. In cases of inoperable or recurrent tumors that necessitate treatment, radiosurgery may be considered if the tumor's size or the proximity of critical structures permits it. Alternatively, fractionated radiotherapy can be employed as a treatment option. A growing trend is emerging that combines surgery with radiosurgery or fractionated radiation therapy for WHO grade 2 meningiomas. However, there are ongoing controversies regarding the optimal timing, type, and dosing of these various radiotherapy approaches. Systemic chemotherapy is currently in the experimental phase, with trials underway to evaluate the efficacy of radionuclide therapy targeting somatostatin receptors and bevacizumab or multikinase inhibitors targeting vascular endothelial growth factor receptor. However, no standard of care systemic treatment has yet been established. [45]

Study limitations

The strength of our study lies in our large number of cases that were eligible for analyses from two tertiary care centers, each receiving a substantial number of cases. These centers, which are free of charges and are located Jeddah city, represent the western province of Saudi Arabia, which encompasses a diverse range of ethnic backgrounds and an understudied population. This study provides valuable insights into the necessity of conducting further genetic investigations, as these may hold significant importance in studying the population of Saudi Arabia risk factors for meningiomas.

In contrast, we have encountered certain limitations in documenting our records, aside from being a retrospective study. This is because we are referring to the period from early 2005 onwards, as this is a transition period to electronic records. Consequently, our follow–up study was meticulously designed to span a five–year interval, commencing from the date of the last patient's examination in 2015. Another complicating factor in treatment is the interval between the initial mild symptoms and the disease's progression into a severe form. For instance, the delayed presentation of the condition, characterized by the progression of visual deterioration from mild to severe loss, as observed in the gradual growth of suprasellar meningiomas, presents a challenge in managing the condition effectively. Additionally, as previously mentioned, there is a growing emphasis on conducting more comprehensive pathological assessments and detailed reporting of Ki67 values. Molecular profiling of patients with meningiomas is also being increasingly utilized as a diagnostic tool.

Conclusion

In our cohort study, predictors of meningioma recurrence were associated with WHO grade, Simpson grading of surgical resection, and tumor size. Notably, these factors associated with a high risk of recurrence were consistent with those reported in international literature.

We underscore the paramount significance of national collaboration in establishing a National Saudi Brain Tumors Registry. This registry would serve as a comprehensive platform for conducting in–depth research on meningioma epidemiology and molecular cytogenetic analysis within Saudi Arabia. The establishment of such a registry would be instrumental in elucidating the risk factors associated with meningioma development and potentially identifying discrepancies between regional and international reports.

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