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An Analytical Study on the Clinicopathological Features of 209 Cases of Meningiomas Operated At A Tertiary Care Institute.

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Abstract: *Meningiomas are one of the most important and common tumours of the central nervous system. They comprises of about 25 to 30% of the primary tumours of CNS. They occur more commonly in females with increased occurrence in the middle age. They may be of intracranial or intraspinal location. World health organization classifies meningiomas in to numerous variants under three grades (grade I,II and III). Though close to 80% of meningiomas are benign, some of the grade I and all of the grade II and III meningiomas exhibits aggressive behaviour. It is very important to analyse the various clinical parameters and histological types that causes aggressive nature of meningiomas which is what this study is all about. Here with analyzing 209 cases of meningiomas on its various clinicopathological characteristics and their effect on grading of tumours since they form one of the most common tumours of the CNS.*

Keywords: *Atypical meningioma, Anaplastic meningioma, Meningioma grading.*

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I. Introduction

Meningiomas are second most common primary central nervous system neoplasm [1] originating from the arachnoidal cells. It accounts for about for 24–30% of all primary intracranial neoplasms [2]. They are characterized by attachment to the inner surface of dura mater. The prevalence of Meningiomas were approximately found to be 97.5/100,000 according to CBTRUS(Central Brain Tumor Registry of the United States) [3]. Various studies were undertaken to study the role of histological parameters in grading meningiomas.

The aim of this study is

1) To analyse the various clinical attributes and histological types of meningiomas and to look for their association with regard to the behaviour and grading of the tumour.

2) To statistically study and compare the clinical parameters and frequency of occurrence of various histological types of meningiomas with various studies.

II. Materias And Methods

This is a retrospective & prospective study done at a tertiary care hospital in the department of Pathology for a period of 3 years from 2013 – 2016. Out of the total 877 CNS tumour specimens received at the department of pathology for a period of three years, Meningiomas constituted of about 209 cases (23.83%). This study included all the three WHO grades of intracranial and intraspinal Meningiomas and it excludes all other tumours of meningeal origin such as hemangiopericytoma and solitary fibrous tumours. All the clinical data of the meningioma cases were obtained from the patient files in the pathology registers. The hematoxylin and eosin stained slides were retrieved, reviewed and graded according to the WHO classification of Meningiomas (2007) guidelines without the knowledge of previous grading [4]. Statistical analysis was carried out using SPSS software version 17. Various tests used in the study were the chi square test for discrete variables .and the T test for continuous variables. A significant association between various factors analyzed in the study was found with a level of significance 95% confidence interval and a P cut off value of less than 0.05.

III. Results

The incidence of meningiomas among the other central nervous system tumours was found to be 23.83%. In this study about Meningiomas, 209 cases operated during a period of three years were included among which 198 (94.7%) and 11(5.3%) cases were intracranial and intraspinal Meningiomas respectively. The total number of male and female cases in the study were 78 (37.3%) and 131(62.7%) cases respectively. Among intracranial Meningiomas, male patients accounted for 77 cases and female patients accounted for about 121 cases with a male: female ratio of about 1: 1.6 . Among intraspinal Meningiomas, only one case belonged to male and female patients accounted for about 10 cases with a male: female ratio of about 1:10. The mean age of occurrence of Meningiomas were found to be 48.12 and it did not vary significantly among male (49.24) and

female (47.46). Maximum number cases were seen in fifth (29.2%) and sixth(29.2%) decade of life. Meningiomas were least prevalent in less than 30 years of age accounting for about 8.1 % of cases. The age distribution of Meningiomas are given below in table 1.

Table 1:- Age Distribution Of Meningiomas:-

Age (in years)	Frequency	Percentage
UPTO 30	17	8.1
31-40	42	20.1
41-50	61	29.2
51-60	61	29.2
61 & ABOVE	28	13.4
Total	209	100

Among the radiological features, peritumoural odema and indistinct brain- tumour interface (important radiological features to assess aggressive nature of meningiomas) was seen in 30 cases. Though most of these cases belonged to grade II and III, it also included cases of microcystic and angiomatous variants of meningiomas. The mean size of Meningiomas were 4.4cm.The average maximum diameter of grade I, II and III Meningiomas were 3.4cm, 5.06cm, and 5cm respectively. High grade Meningiomas were slightly large in size when compared to the grade I Meningiomas. The frequency of occurrence of different types of Meningiomas in various sites is compared in table 2. The convexity Meningiomas (57.4%) that includes those on the convexity, falx and parasagittal regions together constitutes the most common site of occurrence of Meningiomas in this study.

Table 2:- Site Distribution Of Meningiomas:-

SITE	Frequency	Percentage
Convexity Meningioma	120	57.4
CP angle	10	4.8
Intra ventricular	3	1.4
Multiple meningioma	1	0.5
Olfactory groove	18	8.6
Optic nerve sheath	1	0.5
Para/Supra sellar	6	2.9
Posterior fossa	5	2.4
Sphenoid wing	27	12.9
Tentorial sol	4	1.9
Tubeculum sella	3	1.4
TOTAL	209	100

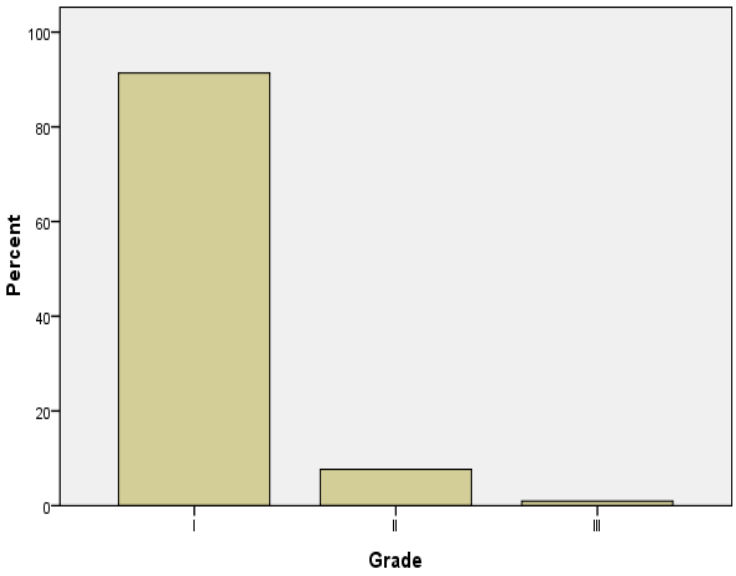
The various histopathological types of Meningiomas are given below in table 3. The most common types encountered in this study were meningothelial meningioma (40.7%) and transitional Meningiomas(25.4%).

Table 3:- Frequency Of Occurrence Of Different Histopathological Types Of Meningiomas:-

GRADE	HPE TYPES	FREQUENCY	PERCENTAGE
GRADE I	Meningothelial Meningioma	85	40.7
	Transitional Meningioma	53	25.4
	Fibrous Meningioma	15	7.2
	Lympho plasmacytic Meningioma	1	0.5
	Microcystic Meningioma	6	2.9
	Angiomatous Meningioma	15	7.2
	Psammomatous Meningioma	16	7.7
GRADE II	Atypical Meningioma	13	6.2
	Chordoid Meningioma	1	0.5
	clear cell Meningioma	2	1.0
GRADE III	Anaplastic Meningioma	1	0.5
	Papillary Meningioma	1	0.5
Total		209	100

The number of cases in grade I, II & III were 191(91.4%), 16(7.6%) & 2(1%) respectively and is illustrated in chart 1. Grade 1 or benign Meningiomas were found to be in higher numbers compared to grade II or III Meningiomas.

Chart 1:- Frequency Of Occurence Of Various Grades Of Meningiomas:-

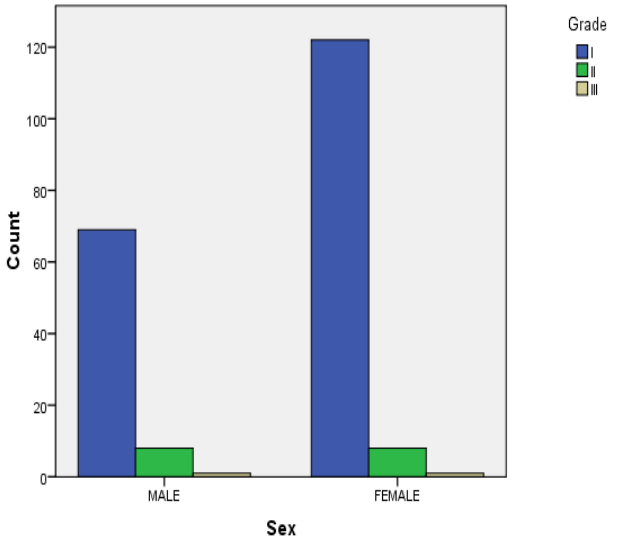


The male:female ratio for grade I, II and III Meningiomas were 1:1.76, 1:1 and 1:1 respectively. This showed that grade I Meningiomas were predominant in females and the male female ratio gets equalized as grade increases. However when subjected to statistical analysis the association between sex distribution among various grades of Meningiomas were not significant (P value= 0.508). Comparison of sex distribution among different grades of meningiomas is given below in table 4 and chart 2:-

Table 4:- Comparison Of Sex Distribution Among Different Grades Of Meningiomas:-

	Grade I Meningiomas (number of cases & %)	Grade II Meningiomas (number of cases & %)	Grade III Meningiomas (number of cases & %)	TOTAL (number of cases & %)
MALE	69(36.1%)	8(50.0%)	1(50.0%)	78 (37.3%)
FEMALE	122 (63.9%)	8(50.0%)	1(50.0%)	131(62.7%)
TOTAL	191(100.0%)	16(100.0%)	2(100.0%)	209(100.0%)

Chart 7:- Comparison Of Sex Distribution Among Different Grades Of Meningiomas:-



The mean age of occurrence of grade I, II and III Meningiomas were 48.07, 49.44 and 43 respectively. The age distribution among various grades of Meningiomas are given below in table 5. The association between the age of occurrence of Meningiomas and it's various grades were not significant (P value= 0.345).

Table 5:- Comparison Of Age Distribution Among Different Grades Of Meningiomas:-

Age In Years	**Grade I Meningiomas (Number Of Cases & %)**	**Grade II Meningiomas (Number Of Cases & %)**	**Grade III Meningiomas (Number Of Cases & %)**	**Total (Number Of Cases & %)**
UPTO 30	16(8.4%)	1(6.3%)	0(.0%)	17(8.1%)
31-40	37(19.4%)	5(31.3%)	0(.0%)	42(20.1%)
41-50	56(29.3%)	3(18.8%)	2(100.0%)	61(29.2%)
51-60	58(30.4%)	3(18.8%)	0(.0%)	61(29.2%)
61	24(12.6%)	4(25.0%)	0(.0%)	28(13.4%)
Total	191(100.0%)	16(100.0%)	2(100.0%)	209(100.0%)

Among intracranial and intraspinal Meningiomas, all intraspinal Meningiomas were of grade I type and all grade II and III Meningiomas were intracranial in distribution. There was no significant association (with a P value of 0.579) between different grades of Meningiomas and their distribution among intracranial and intraspinal location. The intracranial and intraspinal distribution of grade I,II and III Meningiomas are given below in table 6.

Table 6:- Comparison Of Intracranial And Intraspinal Location Of Meningiomas And Their Different Grades :-

	Grade I Meningiomas (Number Of Cases & %)	**Grade II Meningiomas (Number Of Cases & %)**	**Grade III Meningiomas (Number Of Cases & %)**	**Total (Number Of Cases & %)**
INTRACRANIAL	180(86)	16(7.7)	2(1)	198(94.7)
INTRASPINAL	11 (5.3)	0 (0)	0 (0)	11 (5.3)
	191 (91.4)	16 (7.7)	2 (1)	209 (100)

There is also no association between the three grades of Meningiomas and their various intracranial location (statistically insignificant, P value= 0.995). The various intracranial location of Meningiomas with regard to different grades are given in table 7.

Table 7:- Comparison Of Various Sites Of Location Of Meningiomas And Their Different Grades :-

Site	**Grade I Meningiomas (Number Of Cases & %)**	**Grade II Meningiomas (Number Of Cases & %)**	**Grade III Meningiomas (Number Of Cases & %)**	**Total**
Convexity Meningiomas	107 (54)	12 (6)	1 (0.5)	120 (60.6)
CP angle	9 (4.5)	1 (0.5)	0 (0)	10 (5)
Intra ventricular	3 (1.5)	0 (0)	0 (0)	3 (1.5)
Multiple Meningiomas	1 (0.5)	0 (0)	0 (0)	1 (0.5)
Olfactory groove	16 (8)	1 (0.5)	1 (0.5)	18 (9)
Optic nerve sheath	1 (0.5)	0 (0)	0 (0)	1 (0.5)
Para/Supra sellar	6 (3)	0 (0)	0 (0)	6 (3)
Posterior fossa	5 (2.5)	0 (0)	0 (0)	5 (2.5)
Sphenoid wing	25 (12.6)	2 (1)	0 (0)	27 (13.6)
Tentorial sol	4 (2)	0 (0)	0 (0)	4 (2)
Tubeculum sella	3 (1.5)	0 (0)	0 (0)	3 (1.5)
Intraspinal	11(5.3)	0 (0)	0 (0)	11(5.3)
TOTAL	191 (90.9)	16 (8)	2 (1)	209 (100)

Hence it was derived that clinical parameters such as age, sex, size and site of the tumour has no role to play with the grading or the behaviour of the tumour. Histopathological classification and proper grading helps in the better prediction of the rates of reccurence and prognosis of the tumour.

IV. Discussion

Meningiomas are the most common benign CNS neoplasms with a higher prevalence in women having a female:male ratio of 3.5:1 [5]. Spinal Meningiomas exhibits a even more striking female preponderance. Atypical and malignant Meningiomas (grade II and III) shows a slightly higher male predominance [6] . Meningiomas occurs commonly in elderly and middle-aged patients. They produce focal neurological deficit's due to compression of adjacent structures. Some of the meningiomas are asymptomatic slow growing tumours that the diagnosis is made incidentally or at autopsy autopsy [7].

Among the various risk factors that have been enumerated for the development of meningiomas, the most significant ones are as follow: exposure to ionizing radiation increases the risk of development of Meningiomas by 6 to 10 folds [8] . Various epidemiological features suggests the role of female sex hormones in

the development of meningiomas. For example, females show an increased growth rate of Meningiomas following hormonal therapy and during pregnancy [6] .

The world health organisation categorises meningiomas in to three grades- grade I,II and III. Though majority of the meningiomas are benign (80 to 90 %)[4] with a slow growth rate, many of them with atypical and anaplastic features show extensive invasion of brain and vessels making it inoperable. The incidence of grade II and III meningiomas includes 4.7% to 7.2% and 1.0% to 2.8% respectively[9].

The diagnostic criteria based on mitotic figures for grade I, II and III meningiomas includes <4, 4 to 19 and > 20 /10 high power field (hpf) respectively[4]. Grade II meningiomas in addition shows the presence of 3 or more out of the following five features: 1. increased cellularity 2. foci of 'spontaneous' or 'geographic' necrosis 3.pattern less or sheet-like growth, 4. small cells having a high nuclear/cytoplasmic ratio and 5. prominent nucleoli . Grade III meningiomas exhibits loss of differentiated features resulting in melanoma , carcinoma, or sarcoma like appearances. [4]

The most common types among the meningiomas are meningothelial, transitional and fibrous Meningiomas. They exhibit a relatively low rates of recurrence and are less aggressive in behaviour . Certain site of the tumour has a major impact on the prognosis of Meningiomas. For illustration :- convexity Meningiomas are completely surgically resectable where as those found at base of skull have a slow invasive and destructive growth leading to the erosion of bony structures. These tumours may remain histologically benign for long time or transform to higher grades over years[4]. Though these tumours have benign cytological features they have tendency to invade brain, dura and it's sinuses, skull, and rarely orbit, skin and soft tissues [10] . Histomorphology of Meningiomas are so diverse that it required a revision in the WHO 2000 to WHO 2007 classification [11] . This study is undertaken not only to analyse the various clinical and histological types of meningiomas but also to look for their association with regard to the behaviour and grading of the tumour.

The incidence of meningiomas (23.83%) among the other central nervous system tumours in this study matched well with the study done by Cordera S et al (25-30%)[2]. One of the important radiological characteristics of Meningiomas are presence of dural tail surrounding the perimeter of dura around the mass. According to study done by New et al in 1982, imaging features such as central areas of tumour necrosis,peritumoral odema, bony destruction, indistinct brain and tumour interface (interdigitation of tumour with brain)and mushrooming(prominent tumour or pannus, extending away from the globoid tumour mass with extensive perifocal oedema) have been described to be associated with aggressive nature of tumour pointing to their malignant behaviour [12].

The mean age at surgery or the diagnosis of benign, atypical and malignant Meningiomas were correlated well with other studies done by M taghipour et al, Thomas backer- grondahl et al, Arlete hilbig et al and Ramesh babu telungu et al[11,13,14,15] except for a slightly lower age of occurrence of grade III meninigomas in this study. Comparison of age distribution of Meningiomas among various studies as given below in table 8.

Table 8:- Comparison Of Age Distribution Of Meningiomas Between The Present Study And Other Studies:-

	Age In Years		
	Benign	**Atypical**	**Malignant**
Present study	48	49	43
M taghipour et al [13]	47	49	58
Thomas Backer-Grondahl et al [11]	58	59	61
Arlete hilbig et al [14]	48	44	44
Ramesh babu telungu et al [15]	45	44.2	50.6

As in other studies, there was a greater prevalence of Meningiomas among female patients in this study also, that explains the hormonal dependant growth of these tumours [11,13] .Comparison of sex distribution of Meningiomas among various studies as given below in table 9.

Table 9:- Comparison Of Sex Distribution Of Meningiomas Between The Present Study And Other Studies:-

	Male	**Female**	**Male : Female Ratio**
Present study	37.3%	62.7%	1 :1.6
Arlete hilbig et al [14]	32.1%	67.9%	1:2.5
Thomas Backer-Grondahl et al [11]	25%	75%	1 : 3
Nasrin shayanfar et al [16]	32%	68%	1:2.5
Ramesh babu telungu et al [15]	34.82%	65.18%	1:1.9

Convexity Meningiomas were the ones that were most commonly encountered in various studies as like this study of interest. Few studies states about the predilection of atypical meninigiomas for non skull base locations as encountered in this study [17,18]. Comparison of site distribution of Meningiomas among various studies as given below in table 10.

Table 10:- Comparison Of Location Of Meningiomas Between The Present Study And Other Studies:-

Site	Present Study (%)	Thomas Backer-Grondahl Et Al [11] (%)
Falcine and Convexity Meningiomas	60.6	59
Posterior fossa & Tentorial sol	7.5	10.8
Intra ventricular	1.5	0.7
Basal	30.4	29.5

According to Nasrin shayanfar et al and Thomas Backer-Grondahl[11,16] et al the first 3 most common types of ,Meningiomas were meningothelial, transitional and fibrous types and this correlates well with this study also. The distribution of various types of Meningiomas in this study parallels the finding in other studies also such as done by Thomas backer at al, Willis J et al and Uzum N et al[8,19]. Comparison of the frequency of occurrence of the different histopathological types of Meningiomas among various studies as given below in table 11. The minor differences in the proportion of cases in each type of Meningiomas between the current study and study done by ramesh babu telungu et al may be due to subjective error in the grading of the tumour.

Table 11:- Frequency Of Occurrence Of Different Histopathological Types Of Meningiomas Between The Present Study And A Study By Ramesh Babu Telungu Et Al:-

Various Types Of Meningiomas	Present Study(%)	Ramesh Babu Telungu Et Al [15] (%)
Meningothelial	40.7	23.6
Transitional	25.4	17.85
Fibrous	7.2	12.5
Lympho plasmacyte- rich	0.5	-
Microcystic	2.9	2.67
Angiomatous	7.2	4.91
Psammomatous	7.7	14.28
Secretory	-	0.44
Atypical	6.2	1.33
Clear cell	0.5	1.33
Chordoid	0.5	-
Anaplastic	0.5	0.52
Papillary	0.5	2.23

The grade I or benign Meningiomas were most frequently encountered in all the studies. Except for a slight degree of variation in the proportion of cases among various grades, this study goes well with most other studies done by Thomas backer- grondahl et al, Arlete hilbig et al, Nasrin shayanfar et al, Norden et al and Ramesh babu telungu et al[11,14,15,16,20] with regard to the three grades of Meningiomas. Comparison of the frequency of occurrence of the different grades of Meningiomas among various studies as given below in table 12.

Table 12:- Frequency Of Occurrence Of Various Grades Of Meningiomas In The Present Study And Other Studies:-

	Grade I	Grade II	Grade III
Present study	91.4%	7.7%	1%
Thomas Backer-Grondahl et al [11]	68.9%	30.1%	1%
Arlete hilbig et al [14]	75.2%	19.9%	5.68%
Nasrin shayanfar et al [16]	80.7%	12.8%	6.4%
Norden AD et al [20]	90%	5-7%	1-3%
Ramesh babu telungu et al [15]	86%	10.7%	3.1%

The age of occurrence of grade III meningiomas were slightly lower in the present study than that depicted in the other studies. Some studies suggested that the prevalence of atypical and malignant Meningiomas were high among males [11,20, 21] .But the current study did not correlate with these findings and there was a higher female prevalence among benign meninigiomas where as the prevalence was equal among male and female cases among high grade Meningiomas as given below in table 13. There were no association between the grade or behaviour of the tumour and the site or the age of occurrence of meningiomas as described in the above said studies.

Table 13:- Frequency Of Occurrence Of Various Grades Of Meningiomas Among Males And Females In The Present Study And A Study Done By Ramesh Babu Telungu Et Al:-

Sex		Grade I	Grade II	Grade III
Male	Present study	36.1%	50.0%	50.0%
	Ramesh babu telungu et al [15]	34.7%	35.2%	28.6%
Female	Present study	63.9%	50.0%	50.0%
	Ramesh babu telungu et al [15]	65.28%	62.5%	71.43%

V. Conclusion

After an extensive analytical work up it is concluded that the various parameters such as age, sex, site of occurrence (intracranial versus intraspinal and also among the various intracranial locations),size of the tumour, the various histopatholgical types and their grading matched up well with other studies. Clinical parameters did not guide one to assess the behaviour of the meningiomas. Hence histological subtyping plays a very important role in the grading of the tumour than the clinical parameters and also helps predict the likelihood of recurrence of the tumour.

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