**Scholars Journal of Applied Medical Sciences**
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

**Pathology**

# The Expression of Progesterone Receptor in Meningothelial Meningioma

Dr. Syeda Sadia Afrin[1*], Dr. Nazma Shaheen[2], Dr. Md. Oyes Quruni[3], Umme Kulsum Munmun[4], Dr. Mridul Kumar Saha[5], Dr. Shifayat Sultana[6]

[1]Lecturer, Dept. of Pathology, Dhaka Medical College, Dhaka, Bangladesh
[2]MBBS, MD (Pathology), Assistant Professor, Gonoshasthaya Samaj Vittik Medical College, Bangladesh
[3]MBBS, BCS, MD (Pathology), Assist Prof. Pathology, Sheikh Hasina Medical College, Tangail, Bangladesh
[4]Assistant Professor (Pathology), Chandpur Medical College, Bangladesh
[5]Assistant Professor, Colonel Maleque Medical College, Manikganj, Bangladesh
[6]Assistant Professor, Dept. of Pathology, Central Medical College, Cumilla, Bangladesh

**DOI:** 10.36347/sjams.2023.v11i07.018 | **Received:** 08.06.2023 | **Accepted:** 11.07.2023 | **Published:** 17.07.2023

***Corresponding author:** Dr. Syeda Sadia Afrin
Lecturer, Dept. of Pathology, Dhaka Medical College, Dhaka, Bangladesh

**Abstract** **Original Research Article**

***Background:*** By elucidating the role of PR expression in meningothelial meningiomas, this study may contribute to our understanding of the underlying molecular mechanisms driving tumor development and progression. Additionally, it may provide insights into the potential utility of hormonal therapies as adjuvant treatment options for PR-positive meningothelial meningiomas. Ultimately, this research has the potential to impact clinical decision-making, leading to more personalized and effective management strategies for patients with meningothelial meningioma. ***Objective:*** To assess the expression of progesterone receptor in meningothelial meningioma. ***Method:*** This descriptive cross-sectional study was carried out at the Department of Pathology, Dhaka Medical College over a period of two years from January 2018 to December 2019. A total of 60 Patient of any age group with histologically diagnosed meningiomas of the central nervous system were included as a sample population. During the collection of specimens, all relevant information were recorded systematically in a prepared proforma. All the cases were numbered chronologically and the same number was given to H&E as well as in immunohistochemically stained slides. ***Results:*** It was observed that 55% cases were meningothelial meningioma, 8 (13.3%) patients had atypical meningioma, 5 (8.3%) patients had transitional meningioma, 4 (6.7%) patients had psammomatous meningioma and 1(1.7%) cases had anaplastic meningioma. According to PR expression, It was observed that 56.7% study patients had positive PR expression and 43.3% had negative PR expression. 68.8% patients with age group 51-60 years were found positive PR expression and 50% male patients had positive PR expression and 50% male patients had negative PR expression. In female 59.5% cases showed positive and 43.3% showed negative PR expression. It was found that in meningothelial subtype 72.7% cases were PR positive and 27.3% cases were PR negative. In atypical subtype 87.5% cases were PR negative and 12.5 % cases were PR positive**.** ***Conclusion:*** In our study, a significant correlation was found between immunohistochemical expressions of PR with WHO 2016 grades of meningiomas. So as a marker, they can be used in assessing high grade meningiomas. It can help us to estimate the accurate biological behavior of meningiomas to select the appropriate treatment protocol. Appropriate patient screening for PR status may yield important insights into patient response and may guide the development of useful therapies for high risk patient.

**Keywords:** Progesterone, meningothelial meningioma, tumor.



## INTRODUCTION

Meningiomas are the most common primary intracranial tumors, accounting for approximately one-third of all adult brain tumors. These tumors arise from the meninges, the protective membranes surrounding the brain and spinal cord. Among the various subtypes of meningiomas, meningothelial meningioma is the most prevalent and typically exhibits benign behavior. However, a subset of meningothelial meningiomas can display aggressive clinical features, necessitating a comprehensive understanding of the underlying molecular characteristics to aid in personalized treatment strategies.

The expression of hormone receptors, particularly the progesterone receptor (PR), has been extensively investigated in meningiomas due to its potential role in tumor progression and response to hormonal therapy. Progesterone is a key female sex

hormone involved in the regulation of the menstrual cycle and pregnancy. It exerts its effects by binding to PR, a ligand-activated transcription factor, and modulating gene expression patterns [1-4].

In meningiomas, the expression of PR has been reported in varying proportions, with some studies suggesting that it is more commonly observed in meningothelial meningiomas compared to other subtypes. This finding has raised intriguing questions about the potential involvement of PR in the development and progression of meningothelial meningioma, as well as its implications for therapeutic interventions [5].

Understanding the expression patterns of PR in meningothelial meningioma is of significant clinical importance. The presence or absence of PR in these tumors has been associated with variations in tumor growth, recurrence rates, and response to hormonal therapies such as progestin analogs. Identifying PR-positive meningothelial meningiomas may provide valuable information for clinicians to tailor treatment options and improve patient outcomes [6-8]

In this study, we aim to investigate the expression of PR in meningothelial meningioma using a comprehensive approach. We will analyze a cohort of meningothelial meningioma samples obtained from patients and evaluate the PR status using immunohistochemistry. Furthermore, we will explore potential correlations between PR expression and clinicopathological characteristics, including tumor grade, patient age, and recurrence rates.

## OBJECTIVE

To assess the expression of progesterone receptor in meningothelial meningioma.

## METHOD

This descriptive cross-sectional study was carried out at the Department of Pathology, Dhaka Medical College over a period of two years from January 2018 to December 2019. A total of 60 Patient of any age group with histologically diagnosed meningiomas of the central nervous system were included as a sample population. During the collection of specimen, all relevant information were recorded systematically in a prepared proforma. All the cases were numbered chronologically and the same number was given to H&E as well as in immunohistochemically stained slides.

Evaluation of immunostaining and scoring was performed by light microscopy. All slides were examined for positively stained tumor cell nuclei regardless of tumor grade. Distinct brown-stained nuclei were recorded as positive. PR receptor expression was evaluated on the basis of extent and intensity of immunolabelled tumor cells. The receptor status was determined by immunoreactivity scoring scale (IRS).

After meticulous checking and rechecking all data were recorded in a predesigned data collection sheet. Continuous variables were expressed as mean ± SD and were compared between groups of patients by student's 't' test. Categorical variables were compared using a chi-square test or Fischer's exact test as appropriate, and were presented as absolute frequencies with percentages. All P values were two-tailed with significance defined as $p<0.05$ at the level of 95% confidence interval (CI). All analysis was done using the SPSS 22.0 (Statistical Package for Social Science) package for windows.

## RESULTS

Figure-1 shows age of the study patients in meningioma. It was observed that majority of the cases were at fourth and fifth decade and the mean age was 46.78 (±15.56) years, ranging from 3to 75 years.

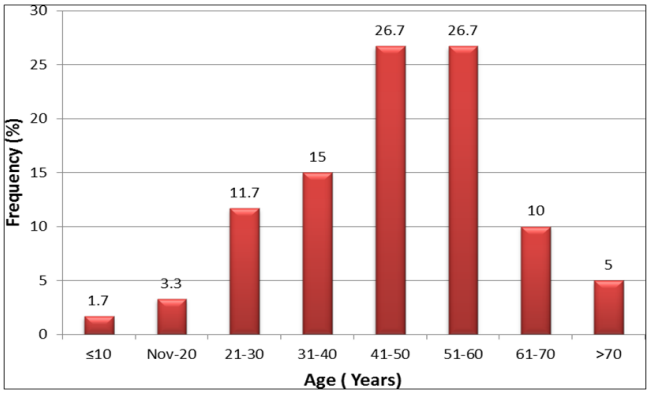


**Figure-1: Age of the study patients in meningioma.**

Table-1 shows distribution of study patients according to sex. Among them 30.0% were male and 70.0% were female. The male female ratio was 1: 2.32.

**Table-1: Distribution of the study patients according to sex (n=60):**

| a | Frequency | Percentage (%) |
|---|---|---|
| Male | 18 | 30.0 |
| Female | 42 | 70.0 |
| **Total** | **60** | **100.0** |

Male : Female = 1: 2.32

Table-2 mentions the distribution of the histomorphologic types of the study patients. It was observed that 55% cases were meningothelial meningioma, 8 (13.3%) patients had atypical meningioma, 5 (8.3%) patients had transitional meningioma, 4 (6.7%) patients had psammomatous meningioma and 1(1.7%) cases had anaplastic meningioma.

**Table-2: Distribution of the study patients according to histomorphologic type (n=60):**

| Histologic subtype | Frequency | Percentage (%) |
|---|---|---|
| Meningothelial | 33 | 55.0 |
| Fibrous | 2 | 3.3 |
| Transitional | 5 | 8.3 |
| Psammomatous | 4 | 6.7 |
| Angiomatous | 2 | 3.3 |
| Secretory | 1 | 1.7 |
| Lymphoplasmacyte-rich | 1 | 1.7 |
| Atypical | 8 | 13.3 |
| Chordoid | 2 | 3.3 |
| Clear cell type | 1 | 1.7 |
| Anaplastic | 1 | 1.7 |
| **Total** | 60 | 100.0 |

Figure-2 shows the distribution of the study patients according to PR expression. It was observed that 56.7% study patients had positive PR expression and 43.3% had negative PR expression.

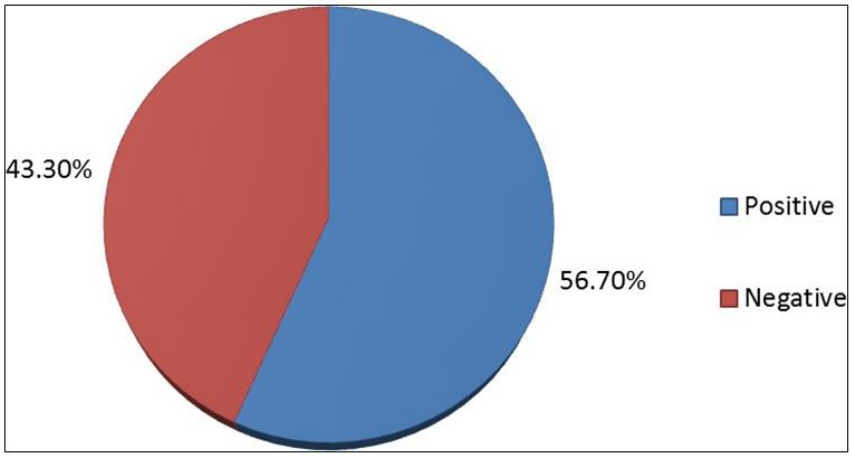


**Figure-2: Distribution of the study patients according to PR expression (n=60)**

Table-3 shows association of age and PR expressions. It was found that 68.8% patients with age group 51-60 years were found positive PR expression and 31.3% were found negative. The mean age was found 50.15±13.63 year in positive cases and the mean age was 42.38 ± 17.05 year in negative cases. These differences were found statistically significant (p value <0.05).

**Table-3: Association of age and PR expression (n=60):**

| Age (years) | PR Expression | | P value* |
|---|---|---|---|
| | **Positive (%)** | **Negative (%)** | |
| ≤10 | 0 (0.0) | 1 (100.0) | |
| 11-20 | 0 (0.0) | 2 (100.0) | |
| 21-30 | 3 (42.9) | 4 (57.1) | |
| 31-40 | 5 (55.6) | 4 (44.4) | |
| 41-50 | 9 (56.3) | 7 (43.8) | |
| 51-60 | 11 (68.8) | 5 (31.3) | |
| 61-70 | 4 (66.7) | 2 (33.3) | |
| >70 | 2 (66.7) | 1 (33.3) | |
| **Total** Mean ± SD | **34 (56.7)** 50.15 ± 13.63 | **26 (43.3)** 42.38 ± 17.05 | 0.048[s] |

*Unpaired t test was done to measure the level of significance. s= significant.

Table-4 shows association of sex and PR expression. It was found 50% male patients had positive PR expression and 50% male patients had negative PR expression. In female 59.5% cases showed positive and 43.3% showed negative PR expression. The differences were found statistically non-significant (p>0.05) between the two groups.

**Table-4: Association of sex and PR expression (n=60):**

| Age (years) | PR Expression | | P value* |
|---|---|---|---|
| | **Positive (%)** | **Negative (%)** | |
| Male | 9 (50.0) | 9 (50.0) | |
| Female | 25 (59.5) | 17 (40.5) | |
| **Total** | **34 (56.7)** | **26(43.3)** 0.495 [ns] | |

*Chi square test was done to measure the level of significance. ns=not significant.

Table-5 shows association of histomprphologic types and PR expression. It was found that in meningothelial subtype 72.7% cases were PR positive and 27.3% cases were PR negative. In atypical subtype 87.5% cases were PR negative and 12.5 % cases were PR positive.

**Table-5: Association of histomorphologic types and PR expression (n=60):**

| Age (years) | PR Expression | | P value* |
|---|---|---|---|
| | **Positive (%)** | **Negative (%)** | |
| Meningothelial | 24 (72.7) | 9 (27.3) | 0.006[a*] |
| Fibrous | 1 (50.0) | 1 (50.0) | 0.999[b] |
| Transitional | 2 (40.0) | 3 (60.0) | 0.644[b] |
| Psammomatous | 3 (75.0) | 1 (25.0) | 0.626[b] |
| Angiomatous | 1 (50.0) | 1 (50.0) | 0.999[b] |
| Secretory | 0 (0.0) | 1 (100.0) | 0.433[b] |
| Lymphoplasmacyte-rich | 0 (0.0) | 1 (100.0) | 0.433[b] |
| Atypical | 1 (12.5) | 7 (87.5) | 0.016[b*] |
| Chordoid | 2 (100.0) | 0 (0.0) | 0.501[b] |
| Clear cell type | 0 (0.0) | 1 (100.0) | 0.433[b] |
| Anaplastic | 0 (0.0) | 1 (100.0) | 0.433[b] |

[a*]Chi square test was done to measure the level of significance.

[b]Fisher's Exact test was done to measure the level of significance.

Table-6 shows association of histomorphologic subtypes and PR expression in both sexes. There was no significant (p > 0.05) differences were found in between histomorphologic subtype and PR expression in both sexes. But in female meningothelial cases showed 72.7% positive immunostaining for PR which was found statistically significant (P<0.05).

**Table-6: Association of histologic subtype and their PR expression in relation to sex (n=60):**

| Age (years) | PR Expression | | P value* |
|---|---|---|---|
| | Positive (%) | Negative (%) | |
| **Male** Meningothelial | 8 (72.7) | 3 (27.3) | 0.0498[b*] |
| Transitional | 0 (0.0) | 1 (100.0) | 0.999[b] |
| Atypical | 1 (16.7) | 5 (83.3) | 0.131[b] |
| **Female** Meningothelial | 16 (72.7) | 6 (27.3) | 0.001[a*] |
| Fibrous | 1 (50.0) | 1 (50.0) | 0.999[b] |
| Transitional | 2 (50.0) | 2 (50.0) | 0.999[b] |
| Psammomatous | 3 (75.0) | 1 (25.0) | 0.286[b] |
| Angiomatous | 1 (50.0) | 1 (50.0) | 0.999[b] |
| Secretory | 0 (0.0) | 1 (100.0) | 0.999[b] |
| Lymphoplasmacyte rich | 0 (0.0) | 1 (100.0) | 0.999[b] |
| Atypical | 0 (0.0) | 2 (100.0) | 0.506[b] |
| Chordoid | 2 (100.0) | 0 (0.0) | 0.158[b] |
| Clear cell type | 0 (0.0) | 1 (100.0) | 0.999[b] |
| Anaplastic | 0 (0.0) | 1 (100.0) | 0.999[b] |

[a]Chi square test was done to measure the level of significance.

[b]Fisher's Exact test was done to measure the level of significance.

## DISCUSSION

Meningioma possesses wide range of histomorphological varieties. Determinations of histomorhological subtypes are useful for grading. The current study showed various histomorphologic subtypes. Out of 76.7% grade I meningioma, meningothelial meningioma was the most common subtype (55%). Among grade II, atypical (13.3%) was the commonest. The study showed only 1 (1.7%) cases of anaplastic meningioma. Other subtypes of grade I were transitional (8.3%), psammomatous (6.7%), fibrous (3.3%), angiomatous (3.3%), secretory (1.7%) and lymphoplasmacyte rich (1.7%). Other grade II meningiomas were chordoid (3.3%) and clear cell type (1.7%). In India Mukherjee *et al.,* (2011) showed most common histologic subtype is meningothelial meningioma (36.7%). The study revealed 8.3% atypical meningioma and 1.7% anaplastic meningioma which almost match the current study. One study showed meningothelial meningioma as the most common subtype and it was 50% of the total study population [9]. whereas other studies all showed that most common histomorphological subtype of meningioma was meningothelial meningioma (76-82%) [10-12].

In a research study byone study, tumors were found atypical in 10% cases while in another study, found 19.1% atypical meningioma. 11-12 Various study revealed most common histomorphological type is Transitional meningioma (about 32%). 10-13 The variation resulted probably due to the lack of strict criteria employed in categorising meningiomas into these subtypes.

Out of 60 cases of meningiomas 34 cases (56.7%) showed positive expression for progesterone receptor and 26(43.3%) cases showed negative expression. Among 588 patients observed in one study found that positive PR expression in 56.1% cases. In other study Al-Nuaimy *et al.,* (2012) 0bserved positive PR expression in 72% cases [14].

The association between age distribution and PR expression was done. The current study showed patients' ages ranged from 51-60 years were mostly positive for PR (68.8%). The association of age and PR expressions was statistically significant. One study showed significant association between PR expression and patients' age while other study did not found any significant association [15-16].

The study revealed that PR expression was more in females (59.5%) than in males (50%). No significant association was found between PR expression and gender. The result is consistent with the other study [17].

In the current study PR expression was positive in 24 (72.7%) out of 33 meningothelial cases. In other subtypes it was found positive in 50% fibrous, 40% transitional, 1/2 cases of angiomatous, 1/8 cases of atypical, 2 cases of chordoid and 1 case of microcystic meningioma. In atypical meningioma, PR was positive in 7/8 cases while all cases of secretory, lympholasmacyte rich, clear cell type and anaplastic type were negative for PR. In meningothelial and atypical subtype the differences were found significant ($p<0.05$). In other histomorphologic subtypes the differences were non-significant. Another study

revealed that there was association between PR immunostaining and histomorphologic subtypes (p=0.0023) [18]. In other studies showed that there were significant associations in PR expression in meningothelial, transitional and fibrous subtypes. Study done by one report found no relation between PR and histological types of meningioma. This variation may be due to variation in patient population included in the study [16].

The current study revealed that among the female patients the most common histomorphologic subtype was meningothelial and 72.7% of it revealed positive PR expression. According to histomorphologic subtype and PR expression significant association was seen. The study found significant association in meningothelial meningioma and PR expression in female patients. In other subtypes no significant association was noted. The result was similar to the study done [10].

## CONCLUSION

In our study, a significant correlation was found between immunohistochemical expressions of PR with WHO 2016 grades of meningiomas. So as a marker, they can be used in assessing high grade meningiomas. It can help us to estimate the accurate biological behavior of meningiomas to select the appropriate treatment protocol. Appropriate patient screening for PR status may yield important insights into patient response and may guide the development of useful therapies for high-risk patient.

## REFERENCE


1. Abry, E., Thomassen, I. Ø., Salvesen, Ø. O., & Torp, S. H. (2010). The significance of Ki-67/MIB-1 labeling index in human meningiomas: a literature study. *Pathology-Research and Practice*, *206*(12), 810-815.
2. Al-Nuaimy, W. M. T., Jalal, J. A., & Mohammed, B. B. (2012). Ki-67 (MIB-1) and progesterone receptor in meningioma: an immunohistochemical study. *Iraqi Postgrad Med J*, *11*(2), 157-167.
3. Ayoubi, S., Dunn, I.F. & Al-Mefty, O., (2012). Meningiomas.In Brain Tumors (pp. 600-629). WB Saunders.
4. Blankenstein, M. A., Verheijen, F. M., Jacobs, J. M., Donker, T. H., van Duijnhoven, M. W., & Thijssen, J. H. (2000). Occurrence, regulation, and significance of progesterone receptors in human meningioma. *Steroids*, *65*(10-11), 795-800.
5. Blitshteyn, S., Crook, J. E., & Jaeckle, K. A. (2008). Is there an association between meningioma and hormone replacement therapy?. *Journal of Clinical Oncology*, *26*(2), 279-282.
6. Bray, F., Ferlay, J., Soerjomataram, I., Siegel, R. L., Torre, L. A., & Jemal, A. (2018). Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: a cancer journal for clinicians*, *68*(6), 394-424.
7. Carroll, R.S., Glowacka, D., Dashner, K. & Black, P.M., (1993). Progesterone receptor expression in meningiomas. *Cancer research*, 53(6), 1312-1316.
8. CBTRUS (2009–2010) CBTRUS Statistical Report: promary brain and central nervous system tumors diagnosed in eighteeen states in 2002–2006.
9. Chargari, C., Vedrine, L., Bauduceau, O., Le Moulec, S., Ceccaldi, B., & Magne, N. (2008). Reapprasial of the role of endocrine therapy in meningioma management. *Endocrine-related cancer*, *15*(4), 931-941.
10. Cetin, A., Lacin, S., & Sogutcu, N. (2019). Progesterone receptor status may be the most important prognostic factor for meningiomas. *International Journal of Hematology and Oncology*, *33*(1), 038-045.
11. Claus, E. B., Park, P. J., Carroll, R., Chan, J., & Black, P. M. (2008). Specific genes expressed in association with progesterone receptors in meningioma. *Cancer research*, *68*(1), 314-322.
12. Commins, D. L., Atkinson, R. D., & Burnett, M. E. (2007). Review of meningioma histopathology. *Neurosurgical focus*, *23*(4), E3.
13. Cossu, G., Messere, M., Parker, F., Levivier, M., & Daniel, R. T. (2016). Meningiomas' management: an update of the literature. *Neurooncology Newer Dev*, *15*, 361-79.
14. Cossu, G., Levivier, M., Daniel, R. T., & Messerer, M. (2015). The role of mifepristone in meningiomas management: a systematic review of the literature. *BioMed research international*, *2015*.
15. Custer, B. S., Koepsell, T. D., & Mueller, B. A. (2002). The association between breast carcinoma and meningioma in women. *Cancer*, *94*(6), 1626-1635.
16. Dolecek, T.A., Propp, J.M., Stroup, N.E. & Kruchko, C., (2012). CBTRUS statistical report: primary brain and central nervous system tumors diagnosed in the United States in 2005–2009. *Neuro-oncology*, 14(suppl_5), v1-v49.
17. El-Badawy, N.M., Farid, R.M., Nagib, L.N. & Ibrahim, R.A., (2013). Role of progesterone receptor expression and proliferative activity in predicting the recurrence of meningioma. *Egyptian Journal of Pathology*, 33(1), 76-81.