



**ORIGINAL RESEARCH PAPER**

**Pathology**

**IMMUNOHISTOCHEMICAL EVALUATION OF ESTROGENRECEPTOR AND PROGESTERONE RECEPTOR IN UTERINESMOOTH MUSCLE CELLTUMORS**

**KEY WORDS:**

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**ABSTRACT**

**Objective:** To study the histo-morphological spectrum of uterine smooth cell tumors withimmunohistochemical expression of estrogen and progesterone receptor and to compare their expression with respect to that of surrounding myometrium. **Materials & Methods:** The study is conducted at a tertiary care hospital in northern India which included themyomectomy as well as hysterectomy specimens of the smooth muscle cell tumor. **Results:**This study found that the majority of leiomyoma tumors express positivity for estrogen and progesterone receptors, with one-third showing moderate expression and the rest showing strong expression. **Conclusion:**The study concludes that the majority of uterine smooth muscle tumors are benign and hormone receptor expression, particularly ER, may play a crucial role in their development and progression, highlighting the need for further research to improve diagnostic and treatment approaches. Additionally, a decrease in hormone receptor expression was observed as tumors progressed from benign to malignant, but the conclusion is limited due to the small number of tumors demonstrating atypical characteristics.

**Introduction**

Smooth muscle tumors are common in the uterine myometrium, affecting 20-40% of pre-menopausal women, and are classified based on their morphological features as leiomyomas, Smooth muscle tumor of uncertain malignant potential, atypical leiomyoma, and Leiomyosarcoma.1 The tumors are associated with symptoms such as excessive uterine bleeding, pelvic pain, and pressure sensation in the lower abdomen, and are believed to be primarily dependent on estrogen for growth, with both estrogen and progesterone exerting myogenic effects.<sup>3,4,5</sup>

**MATERIALS&METHODS**

The study was conducted at a tertiary care hospital in Northern India with all necessary institutional approvals in place. Myomectomy and hysterectomy specimens of smooth muscle cell tumors of the myometrium were processed according to the standard operating procedures of the histopathology laboratory, taking into account the inclusion and exclusion criteria. Written informed consent was obtained from participants, and a brief clinical history was recorded in a predesigned proforma. The histopathological specimens were grossly examined to observe macroscopic details. Slides thus prepared were stained with routine hematoxylin and eosin stains the one selected representative slide for each specimen was also stained immunohistochemically for estrogen and progesterone receptors.

**RESULTS**

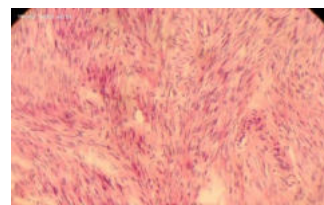
This study investigated the expression of estrogen and progesterone receptors in leiomyoma and leiomyosarcoma tumors, with the majority of patients being in their 4th or 5th decade and having intramural tumors. Immunohistochemical analysis using the Allred score showed positive expression of estrogen receptor in all cases of leiomyoma, with one-third showing moderate expression (4-6) and the rest showing strong expression (7-8). The Allred score for progesterone receptor was strong in almost all cases of leiomyoma, except for one case of leiomyosarcoma that showed negative

expression for both ER and PR. Additionally, the expression of surrounding myometrial tissue was taken as control, and its intensity was found to be lesser when compared with that of leiomyoma. These findings suggest that the majority of leiomyoma tumors express positivity for estrogen and progesterone receptors, which may have an etiological association and may be of use as a therapeutic modality. However, further studies with a sufficient sample size conducted over a period of time are required to establish these associations.

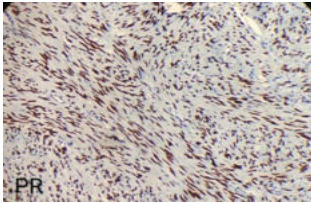
**Table 1: expression of ER and PR in tumor tissue using Allred score and H Score.**

ER expression			PR Expression		
AS	No of samples	H- Score (Mean)	AS	No of samples	H- Score (Mean)
0	0	0	0	0	0
1	1	10	1	1	15
2	0	0	2	0	0
3	0	0	3	0	0
4	11	91.8± 16	4	0	0
5	13	160± 0	5	0	0
6	17	223.5± 20.6	6	0	0
7	53	226.4± 43.9	7	17	238.2± 28.3
8	29	257.9±15.7	8	106	265.3± 18.9

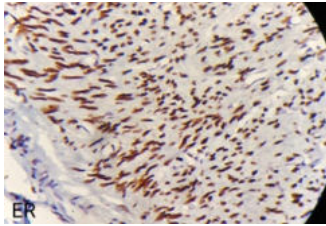
**Uterin**



**Fig 1: H&E stained slide at lower magnification showing Intersecting fascicles of smooth muscle fibers with bland nuclear features.**



**Strong nuclear Positivity for progesterone receptor**



**Strong nuclear Positivity for Estrogen receptor**

### DISCUSSION

Our study revealed that the majority of patients who underwent surgical removal for smooth muscle tumors were in their 4th decade (41.9%) or 5th decade (35.5%). Interestingly, we found a significantly lower incidence of surgery in patients in their 3rd decade (3.2%). These findings are consistent with those reported by Erdem H. et al., where 72% of cases were observed in the 30-50 age range and may reflect the natural progression of the disease, as smooth muscle tumors are uncommon in younger patients and are primarily managed conservatively. It is crucial to consider fertility and family expectations while choosing the management plan for younger patients.<sup>6</sup>

After analyzing our study population, we found that the majority of uterine fibroids were intramural (75.8%). Subserosal fibroids accounted for 23.4% of cases, while only 0.8% of cases involved submucosal fibroids. These findings are consistent with those reported by Horiuchi et al. In our study, necrosis was observed in only one case of leiomyosarcoma out of a sample size of 124, thus making it difficult to establish significant clinical implications based on this single case.<sup>7</sup>

Out of the total 124 leiomyoma examined, 56.5% showed no cellular atypia, while mild atypia was observed in 41.1% of cases. Only a single case (0.8%) showed significant atypia. These findings are consistent with the results reported by Gökaslan et al., who found atypia in only 1.2% of their study subjects.<sup>8</sup>

These results suggest that the majority of uterine smooth muscle tumour do not exhibit significant cellular atypia, and therefore may not be associated with a high risk of developing into cancer. However, close monitoring and further investigation may be warranted in cases with mild or significant atypia.

We also observed an association between age and ER expression, with 52% of cases falling into the age group of 31-40 years and showing strong positivity with an ALLRED score of 7 to 8. These results are similar to those reported by Chu et al., who found the highest number of ER- positive cases in the same age interval.<sup>9</sup>

These findings suggest that age may be a significant factor in the development and progression of ER-positive tumors. Further research is needed to explore the underlying mechanisms involved in the relationship between age and ER expression, as well as to develop more effective diagnostic and treatment strategies for women with ER-positive tumors. We found a significant association between ER expression and the absence of necrosis in our study, as significant

necrosis was absent in ER-positive cases. Interestingly, we also found that a single case exhibiting significant atypia, necrosis, and mitosis showed negative expression for estrogen receptor.

We also investigated the association between overall ER positivity and the mitotic index, which revealed that most cases (123) had a mitotic index of <10/hpf. These findings are consistent with those reported by researchers such as Giuseppa et al. and Nielsen et al., who also found similar positive and statistically significant associations<sup>10</sup>.

Taken together, these results suggest that ER expression may play an important role in the development and progression of uterine tumors, particularly those with atypical cellular features such as necrosis and mitosis. Further research is needed to better understand the underlying mechanisms involved in the relationship between ER expression and tumor characteristics, as well as to develop more effective diagnostic and treatment strategies for women with uterine tumors.

We found a significant association between PR and ER expression, as determined by the Allred score, which is consistent with the results reported by Raspollini et al. in their study<sup>11</sup>.

These findings suggest that the expression of PR and ER may be closely related in uterine tumors, and further research is needed to explore the underlying mechanisms involved in this relationship. Better understanding of the role of PR and ER in uterine tumors may lead to the development of more effective diagnostic and treatment strategies for women with these tumors.

In our study, the majority of leiomyoma cases showed strong positivity for ER, with approximately two-thirds exhibiting a strong expression pattern (Allred score 7 or 8), and close to one-third exhibiting moderate positivity. These results suggest that age had no significant impact on the expression pattern of estrogen receptors. Interestingly, we observed only one case of smooth muscle tumor with atypia and significant necrosis that exhibited negative staining for ER.

Our observations regarding the expression of PR receptors were almost identical to those for ER receptors. These findings are consistent with studies conducted by Eunhee Kim et al. and HavvaErdem et al., who reported significant expression of ER and PR in 73.9% of their cases.<sup>12,8</sup>

Taken together, our results suggest that ER and PR are significantly expressed in a majority of uterine tumors, and that their expression patterns are largely unaffected by age. These findings have important implications for the diagnosis and treatment of uterine tumors, and highlight the need for further research to better understand the underlying mechanisms involved in the expression of ER and PR in these tumors.

The comparison between the ER - Allred score and the difference in mean age was found to be remarkably small, with a difference of only 0.002 at a 95% confidence interval. These findings are consistent with previous studies by Gokalsa et al. and Hewedi et al., who also observed a significant association between mean age and ER categories.<sup>8,13</sup>

When comparing the ER - Allred score with the size of the tumor, we found that the difference in the mean tumor size was not significant, as it was 0.623 at a 95% confidence interval. These findings are consistent with a previous study by Rima et al., which also reported similar results.<sup>14</sup>

Upon further analysis, a notable association was observed

between the ER-ALLRED Score and the H-score, with a statistically significant difference in the mean values of the H-score at a 95% confidence interval (p-value=0.001).

The analysis of the PR-ALLRED Score comparison revealed a significant association between the difference in mean age, with a p-value of 0.059 at a 95% confidence interval. Similar results were observed by researchers such as Nisolle et al., who also reported a significant association.<sup>15</sup>

**CONCLUSION**

The study's findings indicate that the majority of smooth muscle tumors found in the uterus are benign, which is supported by the observed hormone receptor expression. Additionally, the expression of ER may be a crucial factor in the development and progression of uterine tumors, particularly those with atypical cellular features. The close relationship between PR and ER expression in uterine tumors is noteworthy. The study highlights the importance of conducting further research to enhance diagnostic and treatment approaches for women with uterine tumors.

Interestingly, the expression of ER and PR was not significantly influenced by the patient's age, tumor location, or size. As the tumors progressed from benign to malignant, a decrease in hormone receptor expression was observed. However, due to the limited number of tumors demonstrating atypical characteristics, the study's conclusion in this regard is restricted.

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