Section: Pathology

Original Research Article

DECODING MYOMETRIAL PATHOLOGY: A CLINICO-HISTOMORPHOLOGICAL AND IMMUNOHISTOCHEMICAL INSIGHT INTO SMOOTH MUSCLE NEOPLASMS, ESPECIALLY LEIOMYOMAS

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ABSTRACT

Background: Uterine myometrial lesions encompass a broad spectrum of non-neoplastic and neoplastic conditions and are a significant cause of gynecological morbidity in women. These lesions are among the most common indications for hysterectomy. Smooth muscle tumors, particularly leiomyomas, represent the most frequent benign neoplasms of the uterus. Histopathological examination plays a crucial role in identifying the spectrum of myometrial lesions and in differentiating benign from malignant smooth muscle tumors. The aim and objective is to analyze the clinico-histomorphological spectrum of uterine myometrial lesions in hysterectomy specimens with special reference to smooth muscle neoplasms. Immunohistochemical profile of leiomyomas also studied.

Materials and Methods: This descriptive study was conducted on 300 hysterectomy specimens received in the Department of Pathology. Relevant clinical details including age, presenting complaints, and indications for hysterectomy were recorded. All specimens were subjected to detailed gross examination followed by routine histopathological processing and microscopic evaluation using hematoxylin and eosin-stained sections. The lesions were categorized and analyzed according to their histomorphological features. Immunohistochemical profile of leiomyomas also studied for Estrogen receptor ER, Progesterone receptor PR and CD 34 was performed.

Results: Among the 300 cases studied, leiomyoma was the most common lesion observed, accounting for 46.3% of cases. Adenomyosis was the second most common lesion seen in 29.3% of cases, while coexistent leiomyoma with adenomyosis was noted in 22% of cases. Other rare myometrial lesions constituted 2.4% of the cases. Leiomyomas were predominantly observed in women of reproductive age group and commonly presented with symptoms such as menorrhagia, dysmenorrhea, and abdominal mass. Various histomorphological patterns of leiomyoma were identified, whereas malignant and other rare mesenchymal tumors were encountered infrequently. Immunohistochemical expressions of Estrogen Receptor (ER), Progesterone Receptor (PR) and mean blood vessels density assessed by CD-34 were also observed in cases of leiomyomas.

Conclusion: Leiomyoma remains the most common uterine myometrial lesion and a major indication for hysterectomy. Comprehensive histopathological evaluation is essential for identifying variant patterns and differentiating benign from malignant smooth muscle tumors, thereby ensuring accurate diagnosis and appropriate patient management.

Keywords: Adenomyosis; Histopathology; Hysterectomy; Immunohistochemistry, Leiomyoma; Smooth muscle tumors.

INTRODUCTION

The uterus is a hollow, muscular, pear-shaped organ whose primary function is to support implantation and sustain foetal development until birth. Anatomically, it is located within the female pelvis. Structurally, the uterus is divided into four main anatomical regions arranged from superior to inferior: the fundus, corpus (body), isthmus, and cervix.[1] Histologically, the uterine wall is composed of three distinct layers.[2] The innermost layer, the endometrium, is hormonally responsive and undergoes cyclical proliferation and shedding during menstruation, resulting in menstrual bleeding. The middle layer, the myometrium, forms the bulk of the uterine wall and consists predominantly of interlacing bundles of smooth muscle fibres. The outermost layer, the serosa or perimetrium, is a thin mesothelial covering composed of epithelial cells.

The myometrium, being entirely composed of smooth muscle tissue, is prone to a variety of pathological conditions, both neoplastic and non-neoplastic. Among the common non-neoplastic lesions, adenomyosis is frequently encountered. Uterine myometrial neoplasms are broadly classified into homologous tumours, composed exclusively of native uterine mesenchymal tissue, and heterologous sarcomas. Homologous tumours include pure mesenchymal neoplasms, of which leiomyomas are the most common, arising from the smooth muscle cells of the myometrium.[3,4]

Uterine leiomyomas represent a substantial public health burden due to increased outpatient visits and the high cost of surgical management. Leiomyomas occur in approximately 20–30% of women of reproductive age.[5,6] Grossly, they are well-circumscribed, firm, grey-white bulging masses with a whorled appearance on cut surface, and microscopically show cells arranged in crisscrossing fascicles. The gross appearance is often altered by secondary or degenerative changes, which are commonly seen. Menorrhagia is the most frequent clinical symptom associated with intramural leiomyoma, as it interferes with myometrial contraction. Subserosal fibroids are usually asymptomatic. The malignant counterpart of leiomyoma is leiomyosarcoma. Although relatively uncommon, leiomyosarcoma may present clinically in a manner similar to benign leiomyoma, making preoperative differentiation challenging. Therefore, histopathological examination is essential for accurate diagnosis and for distinguishing leiomyosarcoma from benign leiomyoma variants such as Symplastic (atypical), cellular, and mitotically active leiomyomas, as well as from low-grade and high-grade endometrial stromal sarcomas.[7-10]

The present study was designed to analyse the clinico-histomorphological spectrum of uterine smooth muscle neoplasms. Histomorphological analysis of secondary changes and variants of leiomyomas was also performed.

MATERIALS AND METHODS

The present study was a hospital-based observational study, conducted in the department of Pathology, in a tertiary teaching hospital in Western Uttar Pradesh, India. Approval was obtained from the Institutional Ethics Committee (Ref.No.MMC/IEC/2024/371). Informed consent was obtained from all patients and strictly following inclusion and exclusion criteria, 300 patients of uterine lesions were included in the study.

Sample size: 300 (Duration period for data collection according to inclusion criteria and last three years average.) Sampling technique was convenience sampling technique.

Inclusion Criteria

1. Cases of myometrial lesions were included in study in which adequate tissue material and clinical data is available and falling within specific time period.
2. Patients who agreed to participate

Exclusion Criteria

1. Autolyzed or poorly preserved tissue.
2. Non-availability of representative tissue in the slide and paraffin block in archives of Department of Pathology.

Detailed clinical history, investigations and gross features were collected for all the cases and recorded on the case proformas. The tissues were routinely fixed in buffered formalin, grossed and processed. Hematoxylin and eosin- stained sections were studied for their detailed histopathological features with special reference to the presence or absence of leiomyoma - its type or variant and other lesions or findings.

Immunohistochemical staining for Estrogen receptor ER, Progesterone receptor PR and CD 34 was performed using a monoclonal primary antibodies on PL coated sections. Citrate buffer at pH 6.0 was used for antigen retrieval. The Allred system of scoring was used to score the immuno-histochemical stain for Estrogen receptor and Progesterone receptor.

Table 1: Allred semi-quantitative system of scoring of IHC for ER and PR

Proportion score	Observation	Intensity score	Observation
0	None	0	None
1	1%	1	Weak
2	1-10%	2	Intermediate
3	10-33%	3	Strong
4	33-66%	Proportion score + Intensity score = Final Score	
5	66-100%		

Interpretation: Sum of proportion score and intensity score was taken to designate the section as positive or negative.
- 0-2 as Negative
- 3-8 as Positive.

CD34 Immunohistochemistry was done using antibodies. CD 34 was positive in the endothelium of the vascular channels.

Data were analyzed using Chi-square test. A p-value <0.05 was considered statistically significant at 95% confidence interval.

RESULTS

In this study, the average age of the participants was 44.58 ± 5.80 years (minimum age: 32 years; maximum: 67 years). Most of the patients (62.3%) were in 41–50 years age group followed by 30–40 years (24.7%).

Menorrhagia was the most common presenting complaint, reported by 50.2% of the study participants, highlighting abnormal uterine bleeding as the predominant symptom. This was followed by pain in the abdomen (18.99%) and dysmenorrhea (17.72%), reflecting a significant burden of pain-related symptoms. Heaviness in abdomen (16.46%) was also frequently reported, suggesting advanced or bulky uterine pathology in a subset of patients. As this was a multiple-response analysis many participants presented with more than one symptom.

Among the 300 study participants, leiomyoma was the most prevalent histopathological lesion, accounting for 46.3% of cases.

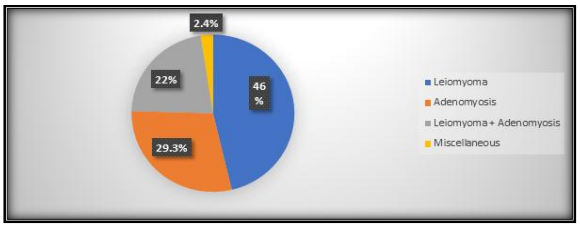

Figure 1: Distribution of pathological lesions among study participants (N=300)

Adenomyosis was observed in nearly 29.3% of the study participants. Notably, co-existence of adenomyosis and leiomyoma was present in 22% and miscellaneous in 2.4% of the study subjects. Miscellaneous cases are Adenofibroma, Endometrial stromal nodule, Endometrial stromal tumor, Leiomyosarcoma, PEComa.

Majority of the cases reported were single [59% (121)]. Totally 84 cases (41%) reported were multiple in number.

In the present study of 205 participants with leiomyoma lesions, intramural leiomyomas were the most common lesion type, accounting for nearly twothirds (64.8%) of cases. Lesions confined exclusively to the submucosal (6.3%) and subserous (4.8%) locations were relatively uncommon. A considerable proportion of women (17.8%) exhibited mixed-type leiomyomas, most frequently involving intramural components combined with submucous or subserous locations. The presence of leiomyomas involving all three layers (6.3%) highlights the tendency for multifocal and anatomically complex disease in a subset of patients.

Hyaline degeneration was the most common type of degenerative change, seen in 39 cases (19.02%), indicating it as the predominant pathological alteration in leiomyomas. Myxoid degeneration (0.97%) Calcification (1.45%) and Cystic degeneration (1.45%) were comparatively less common. This pattern aligns with the usual progression of fibroid degeneration, where hyaline change is typically the earliest and most frequent form. Variants of leiomyoma were identified in 22% of the total study population. Cellular leiomyoma was the most common variant, accounting for 12.19%, while other variants such as Symplastic, hydropic and Lipoleiomyoma were relatively infrequent. Rare variants including epithelioid and Cotyledonoid dissecting leiomyoma were observed only sporadically, indicating that uncommon histological subtypes constituted a small proportion of leiomyoma cases in the study population.

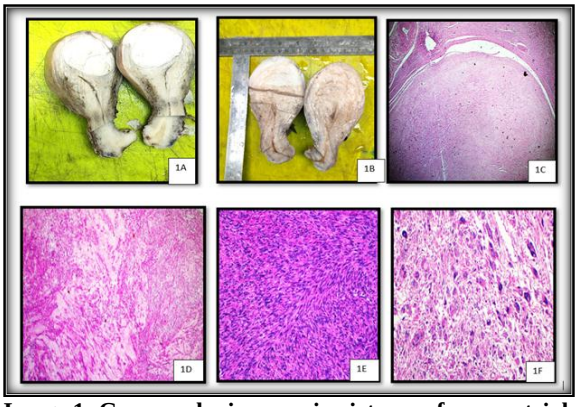

Image 1: Gross and microscopic pictures of myometrial lesions. 1A: Gross of uterine leiomyoma showing a well circumscribed growth. On cut surface- tan-white, whorled, firm and bulging. 1B: Gross of adenomyosis. The thickened and spongy appearing myometrial wall of the sectioned uterus typical of adenomyosis, a condition in which endometrial glands with stroma are located within the myometrium. 1C: Photomicrograph of Leiomyoma (H&E stained):Proliferation of uniform spindle –shaped smooth muscle cells and cells which show eosinophilic cytoplasm, elongated blunt-ended nuclei (cigar-shaped) (40X). 1D: Photomicrograph of Hyalinised Leiomyoma: The characteristic whorled fascicles of spindle cells are separated or replaced by homogeneous, acellular pink collagenous material. (40X). 1E: Photomicrograph of Cellular Leiomyoma: These are more cellular than the normal myometrium but lack nuclear atypia, tumour cell necrosis or increased mitotic activity. (100X). 1F:Photomicrograph of Leiomyoma with Hydropic changes with Bizarre Nuclei (Symplastic): There ispresence of bizarre, hyperchromatic, smudged nuclei. Multinucleated or multilobulated cells with eosinophilic cytoplasm. (100X).

Conventional leiomyomas are differentiated from the variants (like cellular or atypical leiomyomas) by their low cellularity and lack of bizarre cell nuclei. They are also distinguished from malignant smooth muscle tumors (leiomyosarcomas) by the absence of necrosis and low mitotic actiity.

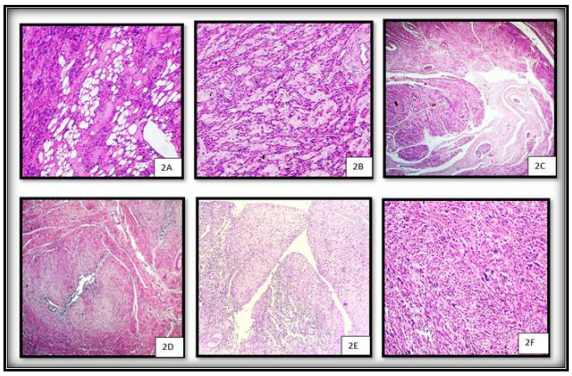

Image 2: Photo-micrographs of myometrial lesions. 2A: Photomicrograph of Lipoleiomyoma lack nuclear atypia, significant mitotic activity, or tumour cell necrosis. (100X).2B: Photomicrograph of Neurilemmoma like Leiomyoma: The tumour shows Biphasic pattern, a mixture of high-cell-density areas (Antoni A) and low-cell-density, myxoid areas (Antoni B). (100X).2C: Photomicrograph of Cotyledonoid Dissecting Leiomyoma: It extends outside the uterus. (40X).2D: Photomicrograph of Adenomyosis: Presence of islands of endometrial glands and stroma inside the myometrium with diffuse and poorly-circumscribed lesions. (40X).2E: Photomicrograph of Adenofibroma: BenignBiphasic Proliferation is seen of both epithelial (glandular) and stromal (fibrous) elements. (100X).2F: Photomicrograph of Leiomyosarcoma: Intersecting fascicles of spindle-shaped cells with cigar-shaped (elongated) blunt-ended nuclei and abundant eosinophilic cytoplasm. (100X)

Among the 154 participants diagnosed with adenomyosis, the majority had Grade 2 disease (67.6%), indicating moderate involvement as the most common presentation. Grade 1 (15.6%) and Grade 3 (16.8%) cases were comparatively less frequent and nearly similar in proportion. Overall, most women exhibited intermediate severity of adenomyosis. Across all grades, the early secretory phase was the most frequently observed endometrial pattern, accounting for half of cases in each grading.
Immunohistochemical expressions of Estrogen Receptor(ER), Progesterone Receptor (PR) and mean blood vessels density assessed by CD-34 were also observed in cases of leiomyomas. In the present study, Leiomyoma showing mean Allred scoring for Estrogen receptor as 5.00 and and for Progesterone receptor as 7.00.
The low mean blood vessels was found among leiomyoma (22.36±4.16) using CD-34.

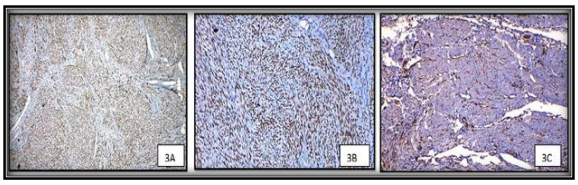

Image 3: Photomicrographs showing immunohitochemical profile of Leiomyomas 3A: Photomicrograph of Leiomyoma: Estrogen Receptor Immunoexpression, Allred Score- 5 (40X). 3B: Photomicrograph of Leiomyoma: Progesterone Receptor Immunoexpression, Allred Score- 7 (100x) 3C: Photomicrograph of Leiomyoma: CD-34 Immunoexpression in blood vessels (100X).

DISCUSSION

In this study histomorphological evaluation of uterine myometrial lesions with special reference to smooth muscle neoplasms was done. The average age of the participants was 44.58 ± 5.80 years (minimum age: 32 years; maximum: 67 years).

Table 2: Distribution of age among the study participants (N=300)

Study	Year	Predominant age group
Present study	2026	41–50 years (62.3%)
Tiwari & Sapkota,[11]	2025	40–49 years
Petanovski& Kurjak,[12]	2022	Perimenopausal age
Garg et al,[13]	2021	41-50
Sankar et al,[14]	2019	41–50 years
Anusha Babu Rajendran,[15]	2019	41-50 years
Mohanvir Kaur,[16]	2018	41-50 years
Sushama Bhatta,[17]	2017	41-50 years
Mega Lahori,[18]	2016	41-50 years
Seema Dayal,[19]	2014	35-48 years

Menorrhagia was the most frequent presenting symptom in our series (50.2% of patients) followed by abdominal pain, dysmenorrhea and feeling of heaviness in lower abdomen. The higher frequency of AUB as the leading symptom is in accordance with the clinical behavior of leiomyomas, mainly intramural and submucosal ones. Menorrhagia is still the most common symptom of uterine fibroids and it is frequently an indication for hysterectomy.[20] In the study by Tiwari and Sapkota,[11] menorrhagia was the most prevalent complaint in women with leiomyomas followed by Sankar et al. also found AUB to be the commonest symptom motivating presentation.
The present study confirms that leiomyoma is the dominant histopathological lesion in hysterectomy specimens, frequently occurring alone or in combination with adenomyosis.

Table 2: Distribution of pathological lesion among the study participants (N=300)

Study	Leiomyoma (%)	Adenomyosis (%)	Combined (%)
Present study (2026)	46.3	29.3	22.0
Tiwari & Sapkota (2025),[11]	52.4	21.7	NR
Parul Garg (2021),[13]	NR	100	39.60
Sonali Saraf (2020),[21]	90	NR	8.3
Sankar et al (2019),[14]	58.1	18.4	NR
Anusha Babu Rajendran (2019),[15]	22.62	NR	33.23
Mohan vir Kaur (2018),[16]	55.69	18.98	25.32

Majority of cases of leiomyomas were single in number (59%). These findings are in agreement with studies of Gowri M et al., and Velu ARK et al.[22,23] This finding is in contrast with Begum S et al., and Cramer SF et al. who found multiple leiomyomas to be more frequent than single leiomyomas.[24,25] In a study by LahoriMet al,[18] 56.96% were single and 43.04% were multiple. In Sarfraz et al (2010),[26] multiple leiomyomas were seen in 60.87% cases. Abraham and Saldanha et al,[27] observed solitary leiomyoma in 42.5% cases and multiple leiomyomas in 57.5%.

Of the 205 patients with leiomyomas, those found to have intramural fibroids (64.8%). Submucosal was rare and subserosal fibroids likewise; combined location of fibroid was found significantly high.

This distribution is quite consistent with the existing literature. Petanovski and Kurjak noted that intramural fibroids are the most common leiomyomas, with up to 60–70%.[12] Sankar et al. also reported intramural fibroids to be the dominant location.[14]

In the present study, degenerative changes were frequently observed in uterine leiomyomas, with hyaline degeneration emerging as the predominant type. Other forms of degeneration such as myxoid, cystic, calcific, and hemorrhagic changes were encountered less often. Murase et al. (1999),[28] identified hyaline degeneration as the most frequent secondary change in leiomyomas, attributing it primarily to compromised vascularity within enlarging fibroids. These findings closely parallel the observations in the present study. Gupta et al. (2024),[29] similarly reported hyaline degeneration as the commonest degenerative change, followed by cystic and calcific degeneration. Comparable results were also documented by AnushaBabuRajendran (2019),[15] SushamaBhatta (2017),[17] Mega Lahori (2016),[18] Gowri M (2013),[22] and Abraham J (2013),[27] all of whom identified hyaline degeneration as the dominant degenerative pattern in leiomyomas. Cellular leiomyoma was the most common variant, accounting for 12.19%. In a study by Saraf and Kanhe et al,[21] it was found 99.2% leiomyoma of usual type. Two variants of leiomyoma. One was cellular leiomyoma and other was mitotically active leiomyoma accounting for 0.4% each.

One of the interesting results obtained in this study was the high frequency of adenomyosis, which was observed in 52.3% of cases. This prevalence is in line with that of Krentel and De Wilde, who demonstrated adenomyosis in a significant number of women undergoing hysterectomy for abnormal uterine bleeding and pelvic pain.[30] Lonky et al. similarly found adenomyosis in almost 50% women undergoing hysterectomy for fibroid-related AUB.[31]

Rare myometrial neoplasms, such as adenofibroma, endometrial stromal nodule/tumor, PEComa, and leiomyosarcoma were not frequently encountered in this study. Their rare occurrence parallels what is found in the large hysterectomy series wherein they are a minuscule proportion of uterine masses.[29] The rarity of such lesions emphasizes the benign nature of most uterine masses seen in everyday practice and the importance of careful histopathological evaluation to rule out malignancy. Also, the pathologist needs to be cautious while diagnosing cases of atypical, mitotically active or bizarre leiomyoma's due to their morphologic homogeneity with STUMP and leiomyosarcoma.

The present study highlights the infrequent occurrence of rare myometrial lesions, with such entities accounting for ≤0.7% of uterine masses. This finding is consistent with previously published large hysterectomy series, including the study by Gupta et al,[29] which also reported these lesions as rare. Although rare myometrial lesions are uncommon, their potential clinical implications mandate heightened awareness among pathologists.

In our study, both ER and PR are typically overexpressed in leiomyoma tissue compared to the surrounding normal myometrium (uterine muscle).

Few researchers have highlighted that leiomyomas are often more progesterone-dependent than estrogen-dependent. Rajendran et al have showed higher PR positivity (up to 87%) compared to ER positivity (around 62%) in these tumors. It was observed that out of 102 cases 61.76% were positive for estrogen receptor and 87.30% positivity was seen for PR.[32]

The hormone receptor status of the leiomyoma shows that they are more progesterone dependant than estrogen dependant substantiating the fact that the growth of leiomyoma is dependent on the progesterone.

In a study by Khan et al, there was an observation that PR content was predominant in both SMM and SSM and their adjacent myometria. They did not find any change in the expression of ER in any type of these myomas.[33]

In concordance to the findings of the present study, Nisolle et al, also founded dominance of ER and PR in leiomyomata and their adjacent myometrium which was statistically significant.[34]

In our study we found very less expression of CD 34 in leiomyomas as compared to adjacent myometrium. Studies by other researchers analyzing vascular density in myomas compared with myometrium have used CD34 to stain blood vessels, generally showing lower microvessel density within the leiomyoma itself.[35,36]

CD34 is notably expressed in a subset of stem/progenitor cells (CD34+/CD49b+). While typical uterine leiomyomas are CD34-negative, specific types (like lipoleiomyoma) or particular cell populations within them can show focal CD34 positivity.[36]

Limitations: Single-centre study and lack of long-term follow-up.

CONCLUSION

This large clinicopathological study highlights that most uterine masses are benign, though meticulous histology is essential. Intramural leiomyomas remain the predominant myometrial lesion in women undergoing hysterectomy, with hyaline degeneration as the most frequent secondary change and adenomyosis as a common coexisting condition. These findings reinforce the importance of thorough histopathological evaluation of all uterine specimens, support current clinical understanding of fibroid-related pathology in mid-life women, and underline the need for multicentric, prospective studies to better elucidate clinical correlations and long-term outcomes. There was dominance of ER and PR in leiomyomata and their adjacent myometrium. Lesser expression of CD 34 in leiomyomas was noted in comparison to adjacent myometrium. It is recommended that further future studies should be conducted across multiple centers and diverse healthcare settings to improve the generalizability of findings and to better represent different demographic and clinical populations. Long-term follow-up of patients should also be incorporated in future research to correlate histopathological patterns with clinical presentation, treatment outcomes, and recurrence rates.

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