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Original Research Paper

Histopathology

"HISTOPATHOLOGICAL STUDY OF UTERINE FIBROID AND ENDOMETRIAL CHANGES ASSOCIATED WITH FIBROID UTERUS – A TWO YEAR PROSPECTIVE STUDY".

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ABSTRACT

Introduction: Uterine fibroids, or leiomyomas, are benign tumors from uterine smooth muscle, predominantly affecting reproductive and peri-menopausal women. They cause significant morbidity, with menorrhagia as the most common symptom. Approximately 33% of women with severe dysmenorrhea and bleeding also have adenomyosis, exacerbating symptoms even with small fibroids. **Aim And Objectives:** To analyze the incidence of uterine fibroids in hysterectomy specimens at JMC&H, Jhalawar, and the histomorphological patterns of endometrium in fibroid uterus, including the association with fibroid location and adenomyosis. **Materials And Methods:** This prospective study analyzed hysterectomy specimens at the Pathology department, Jhalawar Medical College, from August 2022 to July 2024. Standard histopathological procedures were used. **Observation And Results:** Among 554 hysterectomy specimens, 189 (34.11%) had leiomyomas, mostly in multiparous women aged 41-50, with menorrhagia as the most frequent symptom. Intramural fibroids accounted for 73% of cases, with significant endometrial changes linked to fibroid location ($p < 0.05$). Adenomyosis was present in 43.9% of cases, predominantly in women aged 31-50. **Conclusion:** Uterine leiomyomas are the commonest neoplasms in women, with a 34.11% incidence in this study. Menorrhagia was the leading symptom, likely due to tumor-induced vascularity and hormonal effects. Endometrial phases were mainly proliferative (40.7%) and secretory (39.7%), indicating a hyper-estrogenic state. These findings highlight specific clinical and pathological features of uterine fibroids, aiding in diagnosis and management.

KEYWORDS : Uterine leiomyoma, Degeneration, Endometrium, Oestrogen, Proliferative, Hyperplasia, Adenomyosis.

INTRODUCTION

Uterine fibroids, or leiomyomas, are benign tumours originating from the uterus's smooth muscle, mainly found in the myometrium. They are a leading cause of hysterectomy in women of reproductive and peri-menopausal age.[1,2] Although often asymptomatic, fibroids can cause menstrual irregularities and other symptoms, mainly due to high estrogen levels.[3]

About one-third of gynaecological admissions involve symptoms like menorrhagia, anaemia, and abdominal pain with a lump. Uterine fibroids, influenced by sustained estrogen without pregnancy or lactation, affect 20%-40% of women in their reproductive years and 11%-19% during perimenopause. They are often found incidentally during routine exams or pelvic imaging for unrelated issues.[4,5]

About 33% of women with severe dysmenorrhea and vaginal bleeding have adenomyosis, which exacerbates pain even with small fibroids. This is common in women aged 30-40. Those with heavy bleeding often have adenomyosis, and subfertility cases often involve uterine myomas, needing myomectomy if treatments fail. Frequent hospital visits due to persistent symptoms impact emotional and socioeconomic well-being.[6,7]

The endometrium undergoes structural reorganization during menstrual cycle influenced by hormonal effect (mainly estrogen and progesterone), preparing for potential implantation. If implantation doesn't occur, the superficial layer is shed and remodelled for the next cycle. Various compounds, including hormones like estrogen and progesterone, play crucial roles in maintaining endometrial integrity and supporting implantation.[8] Leiomyomas likely originate from the sub-endometrial myometrium, showing cyclical hormone receptor changes during menstrual cycle. This suggests they grow in coordination with endometrial changes and depend on steroid hormones.[9]

This dissertation deals with the study of histopathological study of uterine fibroid and changes in endometrium associated with fibroid uterus with special reference to sub-mucous, intramural and sub-serous fibroid in all hysterectomy specimens come to pathology department of Jhalawar Medical College and Hospitals, Jhalawar for the duration of two years.

Aims And Objectives

1. To analyze the spectrum of uterine fibroid in uterus according to its site/location in hysterectomy specimens received at pathology department, JMC, Jhalawar (Raj.).
2. To analyze the histomorphological pattern of endometrium in fibroid uterus.
3. To study pattern of endometrial changes associated with fibroid uterus on the basis of location of fibroid.
4. To analyze incidence and occurrence of adenomyosis associated with fibroid uterus.

MATERIALS AND METHODS

Source of Data

A total of 554 hysterectomy specimens were received for various diseases were received at department of pathology, Jhalawar Medical College and Hospitals, Jhalawar from obstetrics and gynaecology department, SHKBM Hospital who underwent hysterectomy and specimens sent from nearby Private/Government hospitals in and around Jhalawar, from 1st August 2022 to 31st July 2024. Among the hysterectomy specimen received during the period of 2 years (from 1st August 2022 to 31st July 2024), only those specimens with fibroid were taken up for the study. A total of 189 cases

were studied in which leiomyoma was present.

Inclusion Criteria

All hysterectomy specimens of respective cases received during the period of 2 years (from 1st August 2022 to 31st July 2024) at the department of histopathology, JMC&H, Jhalawar.

Exclusion Criteria

Myomectomy specimens, endometrial biopsies, endocervical biopsies, endometrial curetting and Women with pregnancy with fibroids will be excluded from the study.

Method of Collection of Data

Brief clinical data was obtained from patients or patient records with respect to age, clinical presentation, parity and menstrual phase. Tissue fixation and gross examination, Tissue processing, Sectioning, and staining (Hematoxylin and eosin stain) will be done for histopathological examination of specimens. Further, the obtained parameters (endometrial and myometrial) were evaluated using descriptive statistical analysis. Significance was assessed at 5% level of significance. Chi-square/Fisher Exact test have been used to find the significance of study parameters on categorical scale between two or more groups. 95% Confidence Interval has been computed to find the significant features. Confidence Interval with lower limit more than 50% is associated with statistical significance.

OBSERVATIONS AND RESULTS

In this study, out of 554 hysterectomy specimens received in two years (from 1st August 2022 to 31st July 2024) at the department of histopathology, JMC&H, Jhalawar, 189 (34.11%) had leiomyomas. Majority of the patients (90%) were in 4th - 6th decades of life. Most common age group affected was 41-50 years (51.9%). The mean age was 47 years [Table-1]. Multiparous women constituted 99.5% of the cases. Menorrhagia was the commonest symptom among patients with leiomyoma. It constituted for 71.43%, followed by pain abdomen (43.92%), mass per vagina (22.75%) and mass per abdomen (18.52%). In the present study, uterine fibroid was the commonest clinical diagnosis (51.9%), followed by 3' UV prolapse (16.9%), uterine fibroid with DUB (11.6%), dysfunctional uterine bleeding (9.0%), fibroid with pelvic inflammatory disease (4.2%), 2' UV prolapse (3.7%) etc. Most of the patients were in secretory phase (33.3%), 20.1% of the patients were post menopausal, 7.9% were to be in menstrual phase and 6.3% were in proliferative phase.

Table 1: Age Distribution

		Frequency	Percentage
AGE GROUPS (In years)	21-30	4	2.1%
	31-40	35	18.5%
	41-50	98	51.9%
	51-60	37	19.6%
	61-70	12	6.3%
	71-80	3	1.6%
	Total	189	100%

Data regarding the last menstrual phase was not available in 32.3% of the cases. It was observed that majority of the uteri weighed between 100–400 grams, which accounted for 80.4% of the cases. In this study most of the uteri showed a multiple fibroid, accounting for 54%. It was observed that 73% of the cases had intramural leiomyoma, 10.1% had subserosal leiomyoma and 6.3% had submucosal leiomyoma. The remaining 20 cases had Leiomyomas in more than one location [Table-2].

On gross examination of the cut surface of the leiomyomatous uteri, endometrial polyp was seen in 11 cases out of the 189 cases (5.8%) and the largest polyp measures 5.4 cm in maximum diameter. It was observed that 26 out of the 189 (13.76%) leiomyomatous uteri showed secondary or degenerative changes within the fibroids, of which hyaline degeneration was seen in 17 cases (9%), calcification with hyaline change found in 4 cases (2.1%), calcification seen in 3 cases (1.6%), hemorrhage seen in 1 case and focal necrosis was seen in 2 cases.

Table 2: Location Of Fibroids

Location of Fibroids	Frequency	Percentage
Intramural	138	73.0%
Subserosal	19	10.1%
Submucosal	12	6.3%
Intramural + Subserosal	11	5.8%
Intramural + Submucosal	5	2.6%
Subserosal + Submucosal	2	1.1%
Intramural + Subserosal + Submucosal	2	1.1%
Total	189	100%

Out of the 189 cases, proliferative endometrium was noted in 40.7%, followed by secretory endometrium in 39.7%, atrophic endometrium in 14.8% and endometrial hyperplasia in 4.2% of the cases [Table-3].

Out of 138 cases of intramural fibroid, the incidence of proliferative phase was 39.8% and early secretory phase, mid secretory phase, late secretory phase and atrophic endometrium were 6.5%, 3.6%, 34.05% and 11.6% respectively. The incidence of hyperplasia without atypia was 1.4% and with atypia was 2.2%. Out of 19 cases of subserosal fibroid, the incidence of proliferative Phase, secretory phase and atrophic endometrium were 52.6%, 29.6% and 15.8% respectively.

Out of 12 cases of submucous fibroid, the incidence of atrophy was 33.3%, proliferative phase was 50% and secretory phase was 16.7% [Table-4]. It was observed that the association of endometrial changes with fibroid on the basis of location was found statistically significant [p- Value = 0.0002(<0.05)].

Table 3: Endometrial Phase On Microscopy

Endometrial Phase	Frequency	Percentage
Proliferative Phase	77	40.7%
Disordered Proliferative	1	0.5%
Early Secretory Phase	10	5.3%
Mid Secretory Phase	6	3.2%
Late Secretory Phase	59	31.2%
Hyperplasia Without Atypia	5	2.6%
Hyperplasia With Atypia	3	1.6%
Atrophy	17	9.0%
Cystic Atrophy	3	1.6%
Senile Cystic Atrophy	8	4.2%
Total	189	100%

The patients who were mostly in secretory phase as per their LMP (63 cases), their endometrial findings on microscopy mostly was secretory phase and proliferative, 53.9% and 41.3% respectively. In post-menopausal as per their LMP (38 cases), their endometrial findings on microscopy were found mostly proliferative and atrophied, 50% and 39.4% respectively. In 32.2% (61 cases out of 189) of the patients who were not aware of their LMP, the endometrium was secretory phase (40.9%)[Table-5]. On the basis of available information about LMP given by patients, the association between LMP and microscopic finding of endometrium changes were found significant [p-Value – 0.0001(<0.05)].

Table 4: Endometrial Changes Associated With Location Of Fibroids

ENDOMETRAL PHASE	LOCATION OF FIBROIDS							Total
	INTRAMURAL	SUB SEROSA	SUB MUCOSAL	INTRAMURAL +	INTRAMURAL +	SUB SEROSA	INTRAMURAL +	

		L		SUBSEROSAL	SUBMUCOSAL	L + SUBMUCOSAL	SUBSEROSAL + SUBMUCOSAL	
PROLIFERATIVE PHASE	55 (39.8%)	10 (52.6%)	6 (50%)	4 (36.4%)	2 (40%)	0	0	77
DISORDERED PROLIFERATIVE	1 (0.7%)	0	0	0	0	0	0	1
EARLY SECRETORY PHASE	9 (6.5%)	0	0	1 (9.1%)	0	0	0	10
MID SECRETORY PHASE	5 (3.6%)	1 (5.3%)	0	0	0	0	0	6
LATE SECRETORY PHASE	47 (34.0%)	5 (26.3%)	2 (16.7%)	4 (36.4%)	0	1 (50%)	0	59
HYPERPLASIA WITHOUT ATYPIA	2 (1.4%)	0	0	2 (18.2%)	0	1 (50%)	0	5
HYPERPLASIA WITH ATYPIA	3 (2.2%)	0	0	0	0	0	0	3
ATROPHY	8 (5.8%)	3 (15.8%)	4 (33.3%)	0	1 (20%)	0	1 (50%)	17
CYSTIC ATROPHY	1 (0.7%)	0	0	0	2 (40%)	0	0	3
SENILE CYSTIC ATROPHY	7 (5.1%)	0	0	0	0	0	1 (50%)	8
Total	138 (100%)	19 (100%)	12 (100%)	11 (100%)	5 (100%)	2 (100%)	2 (100%)	189

Adenomyosis was seen on microscopic examination of the myometrium in 43.9% (83 out of 189) of the cases. 3 (3.6%) cases were found in age group between 21 to 30 years, 12 cases (14.4%) in 31 to 40 years age group, 40 cases (48.2%) in 41 to 50 years age group, 20 cases (24.1%) 51 to 60 years age group, 7 cases (8.4%) in 61 to 70 years age group and there was only 1 case seen above 71 years. Maximum number of adenomyosis cases (62.6%) occurred between the age group 31 to 50 years. Association between presence of adenomyosis according to age were found not significant [p-Value = 0.310(>0.05)].

Table 5: Comparison Of Menstrual Phase As Per Lm P With Microscopic Endometrial Phase

ENDOMETRIAL PHASE	MENSTRUAL PHASE as per LMP					Total
	NOT AVAILABLE	SECRETORY PHASE	MENOPAUSE	MENSTRUAL PHASE	PROLIFERATIVE PHASE	
PROLIFERATIVE PHASE	23 (37.7%)	26 (41.3%)	19 (50%)	1 (6.7%)	8 (66.7%)	77
DISORDERED PROLIFERATIVE	0	0	0	1 (6.7%)	0	1
EARLY SECRETORY PHASE	4 (6.5%)	4 (6.3%)	0	2 (13.3%)	0	10
MID SECRETORY PHASE	3 (4.9%)	2 (3.2%)	0	1 (6.7%)	0	6
LATE SECRETORY PHASE	18 (29.5%)	28 (44.4%)	4 (10.5%)	7 (46.7%)	2 (16.7%)	59
HYPERPLASIA WITHOUT ATYPIA	3 (4.9%)	1 (1.6%)	0	1 (6.7%)	0	5
HYPERPLASIA WITH ATYPIA	2 (3.3%)	0	0	0	1 (8.3%)	3
ATROPHY	8 (13.1%)	2 (3.2%)	4 (10.5%)	2 (13.3%)	1 (8.3%)	17
CYSTIC ATROPHY	0	0	3 (7.9%)	0	0	3
SENILE CYSTIC ATROPHY	0	0	8 (21.0%)	0	0	8
Total	61 (100%)	63 (100%)	38 (100%)	15 (100%)	12 (100%)	189

DISCUSSION

A. Discussion On Clinical Details

Incidence of Leiomyoma:

Leiomyoma of the uterus is an extremely common neoplasm. In the current study total 554 hysterectomy specimen were received of which 189 (34.11%) revealed leiomyomas. Ackerman et al did a meticulous study of 100 consecutive hysterectomy specimens of which 77 revealed leiomyomas [10]. The low incidence in our study can be partly explained by conservative management of leiomyoma by gynaecologists.

Age: Leiomyomas are the most prevalent tumors in the female pelvis, with an overall incidence ranging from 4% to 11%, which increases to almost 40% in women over 50 years old. In this study, leiomyomas were most commonly observed in females aged 31-40 years (18.5%), 41-50 years (51.9%), and 51-60 years (19.6%). The development of fibroids in females aged between 20-30 years and during later reproductive years is influenced by cumulative estrogen and progesterone stimulation, as well as hormonal changes related to perimenopause.

Parity: In this study, multiparous women (99.5%) had more leiomyomas compared to primipara and nullipara, aligning with findings from Chhabra & Jaiswal et al.[11], Rosario Pinto et al.[12], and Anusha Babu Rajendran et al.[13] This trend is likely due to higher levels of estrogen, progesterone, and receptors (ER/PR) in multiparous women. Most patients with leiomyomas experienced menorrhagia (71.43%), followed by abdominal pain in 43.92% of cases. Menorrhagia was also the most common symptom reported by Anusha Babu Rajendran et al.[13], Buttram and Reiter et al.[14], Chhabra and Jaiswal et al.[11], and Manjula et al.[15] The predominance of menstrual symptoms may be due to increased vascularity, a larger endometrial surface, altered endometrial contractility, and the hormonal effects of the tumor.

B. Discussion On Gross Pathology

Number of Fibroids: We have noted an increase in occurrence of multiple leiomyoma accounting for 54% as is against the other studies wherein the occurrence of a single fibroid per uteri is high (Rosario Pinto et al[12] and Dr. Chethana Mannem et al.[16] These findings are in concurrence with the study conducted by Ksheera Cariappa. A et al[17].

Location of Fibroids: In the present study, majority of leiomyomas were intra-mural in location constituting 73.0%, followed by subserosal (10.1%) and submucosal leiomyomas (6.3%). Chhabra and Ohri et al[18], Rosario Pinto et al[12], Dr. Chethana Mannem et al[16] and Ramesh et al[19] also reported intramural leiomyomas as the commonest type observed in their study with an incidence of 47.5%, 73.5%, 73.0 and 55.09% respectively.

C. Discussion On Microscopy

Comparison Of The Endometrial Phases In Uterus With Fibroid:

In the present study, proliferative and secretory endometrium accounted for 40.7% and 39.7% of the cases respectively, accounting together for 80.4%. These findings compared with the findings of other studies {Rosario Pinto et al[12], Purandare & Jhalam et al[20], Sanyal et al[21] and Dr. Chethana Mannem et al[16]}. The probable cause may be the hyper-estrogenic state responsible for the proliferative phase and hyperplastic lesions which may also be the causative factor of the organic lesion as well[14]. The atrophic endometrium associated with leiomyoma was probably due to the pressor effect and hormonal factors [22]. The explanation for endometrial hyperplasia (4.2%), is a possible protective role of leiomyoma as a target tissue which capture estrogens[23]. Hence the incidence of hyperplasia with or without atypia is less.

Comparison of Menstrual Phase as per Last Menstrual Period with Microscopic Endometrial Phase: However, in a proportion of the patients who were in secretory phase as per LMP, the endometrium showed persistence of proliferative endometrium (41.3%). Similarly, persistent proliferative phase was also noted by Pavic et al. [24]

Incidence of Adenomyosis:

There is wide agreement that the incidence of adenomyosis is raised in the presence of myomata. Laitinen reported the association between adenomyosis in the cornua and sterility in women with myomata. The study found an adenomyosis incidence of 43.9%, aligning with the findings reported by Deligdish and Loewenthal et al[22]. In the present study, adenomyosis was found to be more common among multiparous women. This finding is similar to other studies[24].

Degenerative Changes in Leiomyomas:

In the present study, degenerative changes were observed in 26 leiomyomas (13.76%). Of the various degenerative changes, hyaline degeneration accounted for the highest number (17 out of 26 cases, 65.38%). similarly, Ksheera Cariappa. A et al.[17], Dr. Chethana Mannem et al[16], Manjula et al[15] and Geethamala, et al[25] noted higher incidence of hyaline change. Degeneration in fibroids occurs secondary to inadequate blood supply, which may be hyaline (commonest), myxomatous, cystic, fatty, haemorrhagic or malignant in nature [25].

CONCLUSION

The research aims to examine the endometrial characteristics of females diagnosed with uterine leiomyomas. Uterine leiomyomas represent the predominant tumours affecting the female genitourinary system, causing substantial morbidity among premenopausal women, with menorrhagia being the most frequent clinical manifestation. In our investigation, a majority of the women exhibited multiparity, contrary to the assertion that uterine leiomyomas are more prevalent in women with lower parity. This observation can be elucidated by the dependence of uterine leiomyomas on both estrogen and progesterone for their development and sustenance, with progesterone levels typically elevated during each pregnancy. Proliferative endometrium and endometrial hyperplasia, both of which represent estrogenic phase accounted for 44.9% of the endometrial phase, suggesting a prevalence of estrogenic activity in the leiomyomatous uteri. The incidence of hyperplasia with atypia was only 1.6%, which substantiates for the higher content of estrogen and progesterone receptors in the myometrium than in the endometrium. Thereby, the brunt of excess hormones was borne by the myometrium in the form of leiomyoma, while endometrium mostly showed proliferative phase. The above findings suggest that if endometrial curettings obtained show a mixed picture of glandular atrophy, endometrial hyperplasia or polyposis, together with many distorted, elongated or dilated glands and muscle fibres between glands, one can suggest the presence of uterine leiomyoma.

Limitation and Recommendations

One limitation of this study is the absence of immunohistochemistry (IHC) testing for estrogen receptors (ER), progesterone receptors (PR), and an in-depth examination of the sub-endometrial myometrium. Such analyses could provide a clearer understanding of the hormonal dependency and pathogenesis of leiomyomas. Future research could explore these aspects to confirm whether leiomyomas consume steroid hormones, thereby mitigating their impact on the endometrium.

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