

EVALUATION OF LEIOMYOMA: A CLINICOPATHOLOGICAL STUDY IN A TERTIARY CARE CENTER IN KATHMANDU

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ABSTRACT

Uterine leiomyoma is one of the common gynecological benign tumors. It is usually observed in female of reproductive age group and often presented with symptoms like abdominal pain, dysmenorrhea and fertility disorders. Hysterectomy and myomectomy are the procedure for management of uterine leiomyoma. The prime objective of our study was to evaluate the demographic distribution and clinicopathological changes in hysterectomy and myomectomy specimens with leiomyomas. A descriptive hospital based cross-sectional study was conducted in the Department of Pathology, Nepal Medical College Teaching Hospital (NMCTH), Nepal from May 2023 to October 2023. A total of 57 uterine leiomyoma samples received in the department of Pathology for histopathological examination were included in the study. Ethical approval for the study was obtained from Institutional Review Committee of NMCTH and informed consent was taken from each patient. The tissue biopsies were routinely processed and stained with Hematoxylin and Eosin (H and E). The observed findings were managed in MS Excel sheet and later analyzed using SPSS-17. The most common age group diagnosed with uterine leiomyoma was 41 to 50 years (64.9%). The leiomyomas were highly prevalent in women from *Adibashi-Janajati* community (47.4%). Pelvic pain, menorrhagia and bleeding disorders were the most frequent clinical manifestations. Intramural was the commonest site (77.2%) and the hyalinization was the most usual secondary changes (19.2%) found. The correlation between age distribution, site of leiomyoma and secondary changes were statistically not significant. However, detailed histopathological examination gives many information related to leiomyoma and it is necessary for the effective management.

KEYWORDS

Uterine leiomyoma, clinical features, histopathological examination, degenerative changes

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INTRODUCTION

Uterine leiomyoma, also known as uterine fibroids, fibroma, or leiomyoma are the most common solid gynecological benign tumors of the female genital tract that originate from the mesenchymal or connective tissues of the myometrium.¹ The complex interactions of local growth hormones and sex steroid hormones induce mutations in normal myometrium and the requirement of hormonal environment for the leiomyoma growth is demonstrated by the molecular studies with the tissues exhibiting more receptors for estrogen hormones as compared to normal myometrium.² Due to their hormone-responsive nature, fibroids mainly affect women of reproductive age (15-49 years) which are exceptionally rare before menarche and usually degenerates after menopause.³ Several observations suggest that progesterone, estrogen, null parity and genetic predisposition play a vital role in their growth, however, the majority of the lesions are asymptomatic.⁴ Approximately 30% of women having fibroid manifest with severe symptoms, including pelvic pain, back pain and urinary symptoms (such as frequent urination, urinary retention, nocturia), gastrointestinal symptoms, dysmenorrhea, infertility, abnormal uterine bleeding and iron-deficiency anemia that need immediate intervention.⁵

In women with complete childbearing, hysterectomy is considered as a permanent remedy for symptomatic leiomyoma, abnormal bleeding, endometriosis, adenomyosis, uterine prolapse and cancer of reproductive organs whereas, for asymptomatic fibroids without any malignancy, hysterectomy is not required.⁶ Similarly, myomectomy-uterine sparing procedure involving removal of fibroids and leaving the uterus intact, is offered to patients who desire future fertility.⁷

Cut surface of leiomyoma is gray white to tan with a whorled trabecular pattern consisting interlacing fascicles of consistent fusiform smooth muscles cells and the degenerative changes like calcification, cystic, hyaline, myxoid and fatty are observed, thus requires histopathological examination for differential diagnosis of leiomyosarcoma and the suitable patient management.^{8,9} The aim of our study was to find out the frequency, site, demography, morphological changes and clinical manifestations associated with uterine leiomyoma.

MATERIALS AND METHODS

The present study was conducted in the Department of Pathology, Nepal Medical College Teaching Hospital (NMCTH),

Kathmandu over a period of six months from May 2023 to October 2023. A total of 57 uterine leiomyoma samples were received in our department for histopathological examination. Ethical approval for the study was obtained from Institutional Review Committee (IRC) of NMCTH and informed consent was taken from the patients. The detail demographic and clinical data were retrieved. Women who underwent hysterectomy procedure other than uterine leiomyoma, unlabelled and improper specimens were excluded from the study.

After receiving hysterectomy and myomectomy specimens, they were fixed in 10% neutral buffered formalin for 24-48 hours and gross examination was carried out. The number of pieces received and the appearance of the specimens were noted. The tissues were processed in automated tissue processor (Yorco, 2L) for 16 hours. Then the tissue blocks were prepared by embedding the tissue chunks in paraffin wax and the tissue sections of 4 um thick were obtained using microtome (Slee Mainz). The sections were stained with Hematoxylin and Eosin (H and E) stain, mounted with dibutylphthalate polystyrene xylene (DPX) and examined under the microscope. The clinical data and histopathological findings were recorded and managed in Microsoft Excel sheet. The data were later analyzed using SPSS-17 and represented with frequency and percentage.

RESULTS

A total of 57 uterine leiomyoma were studied, among which 49 cases were hysterectomy specimen whereas 8 cases were myomectomy specimen. The leiomyomas was seen in women over age ranging from 21 years to 60 years with mean age of 42.84 ± 7.2 years and median age of 44 years. Out of 57 cases of leiomyoma, more patients (85.9%) were in reproductive age group (≤ 49 years) compared to very few patients (13.9%) in non reproductive age group (> 49 years). Females of age 41 to 50 years was the most common age group with 37 cases (64.9%) followed by age group 31-40 years with 11 cases (19.3%) (Table 1).

Table 1: Age wise distribution (n=57)

Age group (years)	cases (n)	%	Mean \pm S.D (years)	Median (years)
21 - 30	2	3.5		
31 - 40	11	19.3		
41 - 50	37	64.9	42.84 ± 7.2	44
51 - 60	7	12.3		
Total	57	100.0		

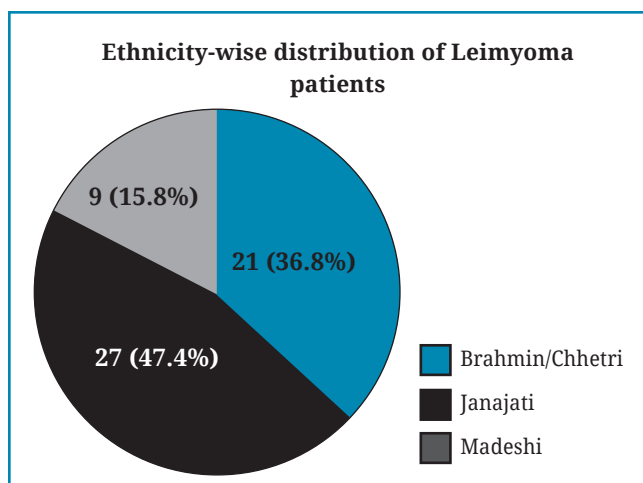


Fig. 1: Distribution of the patients based on ethnicity (n=57)

Patients from multiple ethnic diversity were diagnosed with uterine leiomyoma. The maximum number of women presented with leiomyoma were from *Adibashi-Janajati* ethnicity 27 cases (47.4%) followed by *Brahmin-Chhetri* with 21 cases (36.8%) and *Madhesi* with 9 cases (15.8%). The patient distribution based on ethnicity is shown in Fig. 1.

Patients with uterine leiomyoma presented with multiple clinical features. Pelvic pain was the most common complaint (87.7%) followed by menorrhagia (80.7%), urinary symptoms (52.6%), infertility (21.0%) and irregular

Table 2: Clinical findings/ features of leiomyoma (n=57)

Clinical findings	n	%
Pelvic pain	50	87.7
Dysmenorrhea / menorrhagia	46	80.7
Urinary symptoms	30	52.6
Infertility / subfertility	12	21
Irregular menstruation	10	17.5

menstruation (17.5%). Most of the patients were presented with more than one clinical finding. (Table 2).

Leiomyomas were found to be distributed in different sites. The most common site of leiomyoma was intramural with 44 case (77.2%) followed by 13 cases (22.8%) of others. Others include subserosal and both cases (intramural and subserosal). In the subserosal and both category, 10 cases (17.5%) were seen in subserosal site whereas 3 cases (5.3%) were seen in both (intramural and subserosal) site. However, leiomyoma in submucosal location was not seen. More than one-third of the

Table 3: Site and number of leiomyomas (n=57)

Site of lesion	Number of cases			%
	Single	Multiple	Total (n)	
Intramural	27	17	44	77.2
Others	10	3	13	22.8
Total	37	20	57	100.0

patients with 17 cases (35.0%) present with multiple leiomyomas, and the most of multiple lesions was obtained from intramural region (Table 3).

In this study leiomyoma without any degenerative changes were seen in 32 cases (56.1%) while leiomyoma with degenerative changes were seen in 25 cases (43.9%). Leiomyoma with hyalinization was seen in 11 cases (19.2%) followed by leiomyoma with sclerosis in 8 cases (14.0%) and leiomyoma with adenomyosis in

Table 4: Secondary changes within uterine leiomyoma (n=57)

Secondary changes	n	%
Absent	32	56.1
Present	25	43.9
Hyalinization	11	19.2
Sclerosis	8	14
Adenomyosis	3	5.2
Cellular leiomyoma	2	3.5
Infarct type necrosis	1	1.7

3 cases (5.2%) respectively. There are 2 cases (5.2%) of cellular leiomyoma and 1 case (1.7%) of leiomyoma with infarct type of necrosis. (Table 4). None of the uterine leiomyoma was found to be associated with malignancy.

Table 5: Reproductive age and site of leiomyoma correlation (n=57)

Site	Age (Years)		Total
	≤ 49	>49	
Intramural	39 (88.6%)	5 (11.3%)	44 (100.0%)
Others	10 (76.9%)	3 (23.0%)	13 (100.0%)
Total	49 (85.9%)	8 (13.9%)	57 (100.0%)
P value	0.365		

Correlation of reproductive age (≤ 49 and >49 years) of the patients and site of leiomyoma is tabulated in table 5. The correlation between reproductive age of patient and site of leiomyoma was statistically not significant (P = 0.365) (Table 5).

Correlation of mean age (≤ 43 and >43 years) of the patients and site of leiomyoma is tabulated in table 6. However, the correlation between

Table 6: Mean age and site of leiomyoma correlation (n=57)

Site	Age (years)		Total
	≤ 43	>43	
Intramural	17 (38.6%)	27 (61.3%)	44 (100.0%)
Others	4 (30.7%)	9 (69.2%)	13 (100.0%)
Total	21 (36.8%)	36 (63.1%)	57 (100.0%)
P value	0.748		

Table 7: Reproductive age and secondary changes in leiomyoma correlation (n=57)

Secondary changes	Age (years)		Total
	≤ 49	>49	
Present	21 (84.0%)	4 (16.0%)	25 (100.0%)
Absent	28 (87.5%)	4 (12.5%)	32 (100.0%)
Total	49 (85.9%)	8 (14.0%)	57 (100.0%)
P value	0.706		

age of patient and site of leiomyoma was statistically not significant (P = 0.748) (Table 6).

Correlation of reproductive age (≤ 49 and >49 years) of the patients and secondary changes in leiomyoma is tabulated in table 7. This shows there is no statistically significant correlation (P = 0.706) (Table 7).

Table 8: Mean age and secondary changes in leiomyoma correlation (n=57)

Secondary changes	Age (years)		Total
	≤ 43	>43	
Present	9 (36.0%)	16 (64.0%)	25 (100.0%)
Absent	12 (37.5%)	20 (62.5%)	32 (100.0%)
Total	21 (36.8%)	36 (63.1%)	57 (100.0%)
P value	0.907		

Correlation of mean age (≤ 43 and >43 years) of the patients and secondary changes in leiomyoma is tabulated in table 8. This shows

Table 9: Secondary changes in leiomyoma and site of leiomyoma correlation (n=57)

Site	Secondary changes		Total
	Present	Absent	
Intramural	17 (38.6%)	27 (61.3%)	44 (100.0%)
Others	8 (61.5%)	5 (38.4%)	13 (100.0%)
Total	25 (43.8%)	32 (56.1%)	57 (100.0%)
P value	0.205		

there is no statistically significant correlation (P = 0.907) (Table 8).

Correlation of site and secondary changes in leiomyoma is tabulated in table 9. However, the correlation between secondary changes and site of leiomyoma was statistically not significant (P = 0.205) (Table 9).

DISCUSSION

Leiomyomas are the benign type of uterine neoplasm for which hysterectomy or myomectomy is performed. Leiomyomas are mostly seen in premenopausal women. In the present study, the maximum cases of uterine leiomyoma were seen in the age group 41 to 50 years (64.9%). The finding is similar to that observed by Gupta *et al*⁶ (51.4%), Kaur *et al*⁸ (61.5%), Bhatta *et al*¹⁰ (54.8%), Priyadarshani *et al*¹¹ (51.0%) and Lahori *et al*¹² (46.8%).

In this study, the women from varied ethnicity were presented with uterine leiomyomas. The majority of the leiomyomas specimens were received from women of *Adibashi-Janajati* community (47.4%) followed by *Brahmin-Chhetri* community (36.8%) and *Madhesi* community (15.8%). Our result is comparable to a study by Steward *et al*¹³ and mentioned that black race was recurrently reported factor responsible for increasing the uterine fibroids by two-three times as compared to white race, but there are other factors like age, premenopausal state, contraceptives, smoking, reduced parity affecting uterine fibroids risk similar or greater in magnitude than race.

In our study, the common complaint of patients with uterine leiomyoma was pelvic pain (87.7%) followed by menorrhagia (80.7%), urinary symptoms, infertility and irregular menstruation. In contrast to our finding, other studies by Ramteerthakar *et al*,² Kaur *et al*,⁸ Priyadarshani *et al*¹¹ and Lahori *et al*¹² reported menorrhagia as major clinical manifestation accounting 38.0%, 51.5%, 38.0% and 37.9% respectively whereas, Kulkarni *et al*¹⁴ observed menstrual disturbances as the most common symptom of leiomyomas.

In the present study, out of 57 cases of leiomyomas, 37 (65.0%) were single and 20 (35.0%) were multiple. In a study by Priyadarshani *et al*¹¹ single leiomyoma lesion was seen in 59.0% cases and multiple in 41.0% cases. In contrast to our result, Safaraz *et al*⁹ observed multiple leiomyomas in 42 (61.0%) cases out of 69 cases and single lesion in remaining 27 (39.0%) cases. The leiomyoma

is found to be originated from two main sites of uterus; intramural and subserosal. The most frequent site of leiomyoma was intramural. Out of total 57 cases, 44 (77.2%) cases were intramural. Similar to our study Ramteerthakar *et al*,² Kaur *et al*,⁸ Sarfaraz *et al*,⁹ Priyadarshani *et al*,¹¹ and Lahori *et al*,¹² reported intramural was the most common site of leiomyoma comprising 58.0%, 62.9%, 67.0%, 67.0% and 57.4% of total cases, respectively. Likewise, subserosal was the second common site of leiomyoma accounting 10 (17.5%) cases and remaining 3 (5.3%) cases were combined intramural and subserosal. Similar to our study, few other studies observed subserosal as the second frequent site of leiomyoma.^{2,11,12}

In this study, we didn't observe any submucosal uterine lesion. In contrast to our finding, other studies by Ramteerthakar *et al*,² Kaur *et al*,⁸ Priyadarshani *et al*¹¹ and Lahori *et al*¹² reported submucosal leiomyoma accounting 14.0%, 21.8%, 11.0% and 8.8% of total cases, respectively.

In the present study, leiomyoma with hyalinization was seen in 19.2% cases and leiomyoma with sclerosis was seen in 14.0%. Similar to our finding, several other studies also observed hyaline changes as the most frequent degenerative change in leiomyoma.^{2,8,12,15}

In addition, adenomyosis was seen in 5.2%, cellular leiomyoma in 3.5% and infarct type of necrosis in 1.7% cases in the present study. A study conducted by Kaur *et al*⁸ observed adenomyosis in myometrium along with leiomyoma in 27.7% cases whereas, Rani *et al*¹⁶ reported 20.0% of hysterectomy specimens had adenomyosis with leiomyoma. In contrast to our finding, Ramteerthakar *et al*² and Lahori *et al*¹² observed cystic change, calcification, red

(carneous) degeneration, myxoid change and lipoleiomyoma as secondary changes.

Not a single uterine leiomyoma was found to be associated with malignancy in our study. Singh *et al*¹⁵ also observed that malignant change in leiomyoma was very rare. In a study done by Rani *et al*¹⁶ they noted 2.0% of malignancy among hysterectomy specimens.

In this study, leiomyomas in intramural and other site along with secondary changes were seen in 17 cases (38.6%) out of 44 cases and 8 cases (61.5%) out of 13 cases respectively. Similarly, leiomyomas in intramural and other site without secondary changes were seen in 27 cases (61.3%) out of 44 cases and 5 cases (38.4%) out of 13 cases respectively. In the study done by Dayal *et al*¹⁷ secondary changes in intramural, subserosal and submucosal site of uterus were seen in 60.0%, 6.3% and 32.5% cases, respectively.

In conclusion, leiomyoma is the common benign uterine neoplasm for which gynecological procedures; hysterectomy or myomectomy is performed for its effective management. Perimenopausal women presented with abdominal pain, menorrhagia, dysmenorrhea, abnormal bleeding and other urinary symptoms are more prone to uterine leiomyoma. Intramural is the most frequent location and hyalinization is the most common degenerative change. Degenerative changes may pose diagnostic differences. A complete histopathological examination is must to rule out malignant transformation and to confirm the diagnosis.

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