Clinicopathologic Correlation of Leiomyoma With Clinical Findings and Secondary Changes in a Rural Population of North India

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ABSTRACT

Objectives: To examine the clinicopathologic profile of leiomyoma in surgically removed uteri in a rural tertiary care hospital of north India between January 2008 and August 2012.

Methods: Fibroids are the most common benign tumors of reproductive-age women, with the genital tract being the most common site for tumors. The type of fibroids and secondary changes were confirmed by histopathologic examination of excised uteri.

Results: Of the 200 patients with clinically suspected uterine fibroids, diagnosis was confirmed in 180. An intramural variant was most common (66.7%), followed by the subserosal (22.2%), submucosal (8.9%), and cervical (2.2%) varieties. Menorrhagia, abdominal mass, and abdominal pain were the most common clinical symptoms associated with intramural leiomyoma. Metrorrhagia was observed with submucosal leiomyoma. Secondary changes such as hyaline, mucoid, cystic, and fatty degeneration were also seen, most commonly in intramural leiomyoma.

Conclusions: This study examined the clinicopathologic profile of leiomyoma and is being presented on account of its rarity. To the best of the authors’ knowledge, such a study on a rural population of North India has not been done previously. It revealed that intramural leiomyoma was the most common variant and menorrhagia was the prime clinical symptom. Secondary changes such as hyaline, mucoid, cystic, and fatty degeneration were also seen, most commonly in intramural leiomyoma.

The genital tract is the most common site for tumors in females. Uterine leiomyomas are the most common female reproductive tract tumors, but most cases are asymptomatic. Leiomyomas are benign monoclonal tumors of the smooth muscles of the human uterus. They are also seen in the uterus of certain dogs and Baltic gray seals and are known as uterine leiomyoma, myoma, fibromyoma, fibroleiomyoma, and so on. These are typically found during the middle and late reproductive years. Fibroids have not been described in prepubertal girls, but they are occasionally noted in adolescents.

Myomas are clinically apparent in approximately 25% of reproductive-age women and noted on pathologic examination of approximately 80% surgically excised uteri. At least 20% of all women and 40% of women older than 40 years have uterine leiomyoma. The exact etiology is unknown, but there is considerable evidence that estrogen proliferates tumor growth since the tumors rarely appear before menarche and regress after menopause. Elevated estrogen level may cause its enlargement during pregnancy and shrink during puerperium. The tumors, composed of smooth muscle and fibrous tissue, are benign in nature. Based on their location within the uterine wall, leiomyomas are classified as submucosal/subendometrial, intramural/myometrial, or subserosal. The latter may be pedunculated and simulate adnexal masses. It is a useful classification system since it relates to the clinical presentation and treatment options. As leiomyomas enlarge, they may outgrow their blood supply, which results in various types of degeneration; these include hyaline, cystic, myxoid, or red degeneration and dystrophic calcification. Hyalinization is the most common type of degeneration, and cystic degeneration may be considered an extreme sequela of edema.
As per their anatomical location, leiomyomas are classified as follows:

1. Intramural fibroids, the most common, are within the wall of the uterus.
2. Subserosal fibroids are underneath the serosal surface of the uterus.
3. Submucosal fibroids are in the muscle beneath the endometrium of the uterus.
4. Cervical fibroids are in the wall of the cervix.

Fibroids may be single or multiple and mostly start in an intramural (in the muscle layer) location. With further growth, some lesions may develop toward the outside of the uterus or toward the internal cavity. Most fibroids are initially asymptomatic; as they grow, they cause menstrual irregularities (menorrhagia, metrorrhagia, and polymenorrhagia). The clinical diagnosis of myoma is usually based on the finding of an enlarged, mobile uterus with an irregular contour on bimanual examination or an incidental finding on transabdominal sonography. The objective of this study was to evaluate the clinicopathologic profile of leiomyoma in rural inhabitants.

The chief presenting symptoms with leiomyoma are menstrual irregularity (menorrhagia followed by metrorrhagia or polymenorrhagia), abdominal mass, abdominal pain, and other miscellaneous features. Menorrhagia is the most frequent clinical symptom seen with intramural leiomyoma since it interferes with myometrium contraction, whereas metrorrhagia is frequently associated with submucosal leiomyoma because of endometrial ulceration. Subserosal fibroids are usually asymptomatic. Other features are abdominal mass, abdominal pain, painful sexual intercourse, urinary frequency, and urgency. They may also interfere with pregnancy. Cystic changes and fatty degeneration are common findings in intramural leiomyoma. The trend and tradition of a clinical entity change with time. Considerable efforts have been devoted to studying uterine leiomyoma in the Indian population. However, to our knowledge, such an analysis of uterine fibroids in rural India has not been performed.

Materials and Methods

This work was carried out in the pathology department of the UP Rural Institute of Medical Sciences and Research, Saifai, India, a unique tertiary care hospital in a rural region of north India. It included all the surgically excised uteri and cervices sent for histopathologic examination between January 2008 and August 2012. We also incorporated all clinically suspective excised uterine fibroids and also excised uteri for other lesions such as prolapse and cervicitis, in which fibroid was an incidental finding and the confirmed diagnosis was made by histopathology. We have also included secondary changes seen in these excised fibroids along with the clinical findings observed in these patients. Excised uteri were grossly well circumscribed, and pink–white in color with whorling. The formalin-fixed excised uteri were routinely processed, and 4- to 5-µm-thick sections were made from paraffin blocks. On these sections, H&E was applied. Tumor cells were spindle shaped with an elongated nucleus that formed bundles with whorls.

The objective of this study is to evaluate the sociodemographic and clinicopathologic profile of uterine leiomyoma in a rural population of India. It is a retrospective review of all cases of uterine leiomyoma seen and managed surgically. The case records of these patients were retrieved, with relevant information extracted from the case records using a data capture form designed specifically for the study. Information extracted included sociodemographic data, clinical presentation and findings, management modality, operative findings, and treatment outcome. Predesigned pro forma questionnaires were filled at the time of presentation, and further findings of menstrual irregularity, pelvic mass by abdominal examination, bimanual examination, and other relevant results were entered on the questionnaire. Ethics approval was obtained from the ethics committee of the institute. Data were analyzed using Microsoft Office Excel 2007 (Microsoft, Redmond, WA).

Results

Patient ages ranged from 18 to 65 years (mostly 35-48 years). Of the 200 uteri, confirmed histopathologic diagnosis of uterine leiomyoma was obtained in 180 cases. Of these 180 cases, only 28 women were of postmenopausal age, and median parity was 4 (range, 2-7). None was on exogenous hormones, and most belonged to a lower socioeconomic status. The most common type of uterine leiomyoma was intramural (n = 120), followed by subserosal (n = 40), submucosal (n = 16), and cervical (n = 4). Multiple fibroids were seen in 108 cases.

The patients most commonly presented with menstrual irregularity, such as menorrhagia in 100, metrorrhagia in 30, and polymenorrhagia in 10 cases. The other presenting symptoms were abdominal mass (n = 40), followed by abdominal pain (n = 38) and other (n = 2). The most common clinical features seen with intramural leiomyoma (the most common variant) were menorrhagia (n = 89), abdominal mass (n = 36), abdominal pain (n = 34), polymenorrhagia (n = 3), metrorrhagia (n = 2), and miscellaneous (n = 1). Secondary changes were seen in 95 cases, including hyaline degeneration in 44, mucoid degeneration in 35, cystic changes in 12, and fatty changes in four. Secondary changes...
were most commonly seen with intramural leiomyoma, including hyaline degeneration in 28, mucoid degeneration in 20, cystic changes in six, and fatty changes in three.

Overall, menstrual disorders, abdominal mass, and abdominal pain were the most frequent clinical features and mostly associated with intramural leiomyoma. Table 1. Fibromyoma in the rural population follows a pattern that is fairly similar to the rest of India and other parts of the world. It is responsible for a number of gynecologic symptoms, and surgery still remains the main mode of treatment.

Discussion

Leiomyomas are the most common benign solid pelvic tumors in women, and they are present in about 80% of all hysterectomy specimens. Approximately 20% to 30% of women older than 35 years have clinically manifested uterine leiomyomas. In the present study, age of the patients ranged from 18 to 65 years. The mean age was 46 years, which is consistent with other international studies revealing uterine fibroids being more common in the third and fourth decades of life. In our study, 78% patients with fibroids presented between ages 31 and 50 years, and the youngest patient was 18 years old, which is very close to the study by Ashraf, who also observed that 80% of symptomatic patients with fibroids presented between ages 31 and 50 years, with the youngest patient age 20 years.

Leiomyomas may be single or multicentric. Cramer and Patel found 84% of uterine fibroids to be multicentric, whereas only 53.9% (n = 97) were multicentric in our study. Uterine fibroids are strongly dependent on estrogen, and thus their usual age distribution is from menarche to menopause. We also did not find any case during menarche, and most cases were of middle-aged woman. Some fibroids may interfere with pregnancy, although this appears to be very rare and usually is associated with submucosal myoma, which is responsible for recurrent pregnancy loss. According to Padubidri and Daftary, intramural (75%) fibroids are most common, followed by the submucosal (15%), subserosal (10%), and cervical (1%-4%) variants. Our results are fairly similar but have some variations. We also found intramural (n = 120; 66.7%) to be the most common variant, followed by subserosal (n = 40; 22.2%), submucosal (n = 16; 8.9%), and cervical (n = 4; 2.2%). We encountered 2.2% cervical fibroids, which is quite similar to Ibrar et al (3%).

The chief clinical features in our study were menorrhagia (n = 100; 55.6%), metrorrhagia (n = 30; 16.7%), and polymenorrhagia (n = 10; 5.5%). The other presenting symptoms were abdominal mass (n = 40; 22.2%) followed by abdominal pain (n = 38; 21.1%) and others (n = 2; 1.1%). Our study is comparable to those by Ibrar et al and Hafiz et al, who also found menorrhagia as the most common clinical symptom with leiomyomata. In our study, menorrhagia was the major clinical symptom seen with intramural leiomyoma (89%), which can be explained by interference with uterine contraction. Similarly, metrorrhagia (86.6%) is commonly seen with submucosal leiomyoma because of endometrial ulceration. Subserosal and cervical leiomyomas are usually asymptomatic but may cause symptoms such as abdominal mass and pain.

Attributing symptoms specifically to uterine fibroids is somewhat problematic because of their high incidence in the population, variable clinical presentation, and often asymptomatic nature. However, various studies showed that uterine fibroids are commonly identified in women who have menorrhagia, pelvic pain, obstructive symptoms, infertility, or recurrent pregnancy loss. Abnormal uterine bleeding was the commonest presenting symptom in these women with confirmed uterine fibroids. The incidence of abnormal uterine bleeding (77.8%) in our study was quite high. The cause of the increased uterine bleeding is not always clear but includes ulceration and hemorrhage of the endometrium overlying submucous fibroids, enlargement of the total surface area of endometrium due to mechanical distortion, and dilation of the venous plexuses draining the endometrium due to mechanical compression of the venous drainage by fibroid at any site.

Grossly, fibroids appear as round, well-circumscribed, solid nodules that are white or tan and show a whorled appearance on a histology section. We have also seen

**Table 1**

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<th>Variants of Leiomyoma and Their Correlation With the Presenting Symptom</th>
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<td><strong>Type of Fibroids</strong></td>
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<td>Intramural</td>
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leiomyomas well circumscribed, which, on cut section, appeared gray-white with whorling. On microscopic examination, tumor cells were seen as spindle shaped, with an elongated nucleus that formed bundles with whorls.

Secondary changes are described in approximately 65% of cases, while we found them in 50% in our study. Among them, hyaline degeneration is most common and reported in 63% of cases. In our study, it was seen in 44 (46.3%) cases and mostly attributed to intramural leiomyoma (63.6%; n = 28). According to Rosai, mucoid or myxomatous changes were seen in 19% of cases, but in our study, it was seen in 35 (36.8%) cases and again mostly with intramural leiomyoma (57%; n = 20). Microscopically, there have been reports of abundant amorphous myxoid material between smooth muscle, which was also noticed in our study.

Cystic changes, the end result of hyaline degeneration, were observed by Rosai and Zaloudek and Hendrikson in 4.1% of cases, while we reported them in 12 (12.6%) cases, most commonly the intramural variety (n = 6; 50%). Fat cells, skeletal muscle, and cartilage have been identified in leiomyoma. It is not uncommon to find scattered adipocytes in an otherwise typical leiomyoma. Leiomomas showing a striking amount of fat changes are called lipoleiomyomas. We have seen four cases of lipoleiomyoma, of which three were related to the intramural variety. Most secondary changes were attributed to intramural leiomyoma. This may be owing to the diminished vascularity in large leiomyomas, and most of the intramural leiomyomas were larger than an orange. The immediate cause of degeneration is an interference with the capsular circulation.

Akinyemi et al found that fibroids are the commonest benign tumors, contributing around 70% to 80% of new growths in the female genital tracts. Although almost never associated with death, it is an important cause of morbidity in reproductive-age women and, when complicated, could be a significant cause of mortality. They are mostly symptomless, especially when small and even when of considerable size. This is a big challenge to community health, especially in rural areas where health care facilities are sorely lacking. Moreover, it occurs mostly in women with a lower socioeconomic status in this region of India. In our study, only 2.8% of patients were from upper class I (Kuppuswami); the rest belonged to lower classes II, III, and IV (6.7%, 39.4%, and 51.1%, respectively).

The scenario is worse in villages, where females are the most neglected members of the family and their problems and illnesses are not given proper attention. They usually wait in agony before taking any medical advice. Most of the women who reported to our hospital were from the peripheral, rural, and remote areas. They belonged to the lower socioeconomic classes; most were illiterate and had been going to some local general practitioners, to primary health centers, and to local women (with some basic maternal and child health training) for their menstrual symptoms.

Diagnosis is made with confidence on clinical findings, but ultrasonography is a simple and effective diagnostic tool. Fibroids are associated with infertility, but their actual contribution is controversial. If fibroids were detected in time and properly managed, complicated surgeries and their adverse consequences could be avoided. In addition, the importance of preventive measures and public awareness also cannot be ignored in saving lives and should be implemented at different levels. Keeping in view these facts, this study is presented to add to the existing volume of knowledge regarding uterine fibroids.

### Conclusion

Uterine leiomyomas are the most common female reproductive tract tumors, and most cases are asymptomatic. Uterine leiomyomas are very common, but only a subset of women have had their fibroids clinically detected, is symptomatic, or warrants surgical treatment.

These tumors are found more frequently in the late reproductive and perimenopausal years. Menorrhagia is the most common clinical symptom, affecting a large number of females. Among the types of leiomyoma, intramural is the most common variant, with menorrhagia as the principal clinical symptom. Secondary changes such as hyaline degeneration, mucoid degeneration, cystic changes, and fatty changes also are seen mostly with intramural leiomyoma.

### References


