Clinicopathological Study of Uterine Leiomyomas: A Multicentric Study in Rural Population

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Abstract

Background and Objectives Leiomyoma of uterus forms the most common type of benign tumor of uterus and also the most common pelvic tumor in women. The symptomatology continues to be variable. Surgery has for long

been the main mode of therapy for the myomas. For women who wish to retain the uterus for future pregnancies or other reasons, myomectomy is preferred. Recent trend has been toward nonsurgical approaches like GnRH hormone analogs/agonists, RU 486, or selective uterine artery embolization, laparoscopic cryoablation, radiofrequency thermal ablation, and MRGUs. This multicentric study was an attempt to analyze the clinicopathological spectrum in cases of leiomyoma of the uterus at Cheluvamba Hospital, Adichunchanagiri Institute of Medical Sciences, and to know regarding the pattern of presentation, pathological correlation, with type of fibroid, and endometrial and ovarian changes.

Methods A clinical study of 100 cases of fibroid uterus was conducted in the Cheluvamba Hospital, attached to Mysore Medical College and Research Institute, Mysore, and Adichunchanagiri Institute of medical sciences, BG Nagara, Mandya from November 2008 to August 2012. The cases are selected by random allocation. On admission,

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detailed history, clinical examination, and investigations were recorded.

Results Leiomyoma is the most common benign tumor of the uterus and commonly affects the women of child-bearing age, most commonly in the third decade, 55 %. The most common mode of presentation was menstrual disturbances (76 %), among which menorrhagia was seen in 54 % of the cases. Primary infertility was seen in 15 % of the patients. Intramural fibroids were the most common variety occurring in 60 % of the cases. Endometrial pattern was proliferative in 66.3 %. Cystic ovaries were seen in 8 % of the patients, adenomyosis in 16 % indicating hyperestrogenism.

Conclusion Fibromyoma (leiomyoma) is the most common benign tumor of the pelvis. It commonly affects the women of child-bearing age, mostly in the third decade and is most commonly seen in multipara. The most common mode of presentation is menstrual disturbances. Intramural fibroid is the most common variety. The proliferative and hyperplastic endometrium was commonly reported. The presence of proliferative endometrium, adenomyosis, and cystic ovaries all are indicative of hyperestrogenic state associated with development of fibroids.

Keywords Fibroid · Leiomyoma · Myomectomy · GnRH analogs · Uterine artery embolization · Hysterectomy · Menorrhagia

Introduction

Leiomyoma of uterus forms the most common type of benign tumor of uterus and also the most common pelvic tumor in women. It occurs one in every four or five women of reproductive age. The incidence is around 5–20 %. These tumors develop in a high proportion of women by fifth decade, >45 %. Despite being the most common tumor, the etiology still remains a speculation. Genetic and hormonal factors have been implicated. Although estrogen, growth hormone, and possibly human placental lactogen have been implicated, the role of estrogen in their growth is significant. Studies using glucose-6-phosphate dehydrogenase isoenzyme suggest that each fibroid apparently arises from a single cell within the myometrium.

Risk Factors

Ethnicity The incidence rates of these leiomyomata are higher among blacks at all ages, and the rates peak earlier among blacks (35–39 years) than among whites (40–44 years) [1, 2]. **Menstrual history** The risk of uterine leiomyomata increases as a woman's age at menarche decreases. There is 70–90 % reduced risk in

postmenopausal women. **Child-bearing history** Most studies have found 20–50 % reduced risk of developing leiomyomata, but unfortunately symptomatology continues to be variable. Women with live-born child were compared to nulliparous women. Most studies also suggest that the woman's risk of these tumors increases, as the time from her most recent birth increases [3]. History of infertility has been reported to be risk factors in uterine leiomyomata. It is believed that symptomatology depends on number, size, and location of tumor, although most leiomyomas are believed to be asymptomatic and progress slowly.

Due to their wide spectrum of clinical symptoms such as menstrual irregularities, pelvic pain, and infertility, they represent tremendous public health burden on women and economic costs to the society. They assume to be important particularly in our country as they are an important cause for anemia. So strategies are needed to prevent their formation, to limit their growth, and to treat them nonsurgically. Surgery has for long been the main mode of therapy for myomas. For women who have completed childbearing, hysterectomy forms an attractive option as it eliminates both symptoms and chances of recurrence. For women who wish to retain the uterus for future pregnancies or other reasons, myomectomy is preferred.

Recent trend has been toward nonsurgical approaches such as GnRH hormone analogs/agonists, RU 486 [4] or selective uterine artery embolization [5], laparoscopic cryoablation [6, 7], radiofrequency thermal ablation [8], and MRGUs [9, 10]. Cervical fibroids are a separate class by themselves and account for 2–8 % of cases usually single. They are either interstitial or serous, and rarely they are of submucous variety. Because of their extraperitoneal situation, they remain in the pelvis and produce pressure symptoms.

This study is an attempt to analyze the clinicopathological spectrum in cases of leiomyoma of the uterus (at Cheluvamba Hospital, Adichunchanagiri Institute of medical sciences) and to know regarding the pattern of presentation, mode of treatment, and associated conditions in this region.

Methodology

A clinical study of 100 cases of fibroid uterus was conducted in the Cheluvamba Hospital, attached to Mysore Medical College and Research Institute, Mysore, Adichunchanagiri Institute of medical sciences from November 2008 to August 2012. The cases are selected by random allocation. On admission, a detailed history, clinical examination, and investigations were made. Various investigations such as routine Hb, blood group, ESR, FBS, and USG scan were done.

At laparotomy, the size of uterus, number and situation of fibroids, and condition of tubes and ovaries were noted. In cases undergoing for myomectomy, tubal patency test was made by utilizing methylene blue. The ovaries were conserved in cases of hysterectomies unless associated with pathology and in elderly patients. The removed specimen was cut anteriorly in the midline and near the cornu to inspect the cavity and seedling fibroids. The specimen was sent for histopathological examination of endometrium and myometrium.

Microscopic examination was done to confirm the lesions for degenerative changes, associated endometrial pathology, associated with adenomyosis, and for changes in the ovaries, tubes, and cervix.

Results

Regarding the incidence of leiomyoma in relation to age, it was evident that leiomyomas are most commonly seen in women of child-bearing age, most commonly occurring in the third decade. The mean age is 39 years. Incidence of leiomyoma in relation to parity was seen in Para 3 women (44 %). Interval between the last child birth and development of symptoms shows that there is a long period of secondary infertility before the symptoms could develop, i.e., the interval between last delivery and development of symptoms in most of the cases is significantly long, which in 32 % of the cases was 16–20 years and in 23 % of the cases was more than 20 years. There was no cases detected within 5 years of last child birth. Considering the interval between sterilization and development of symptoms, the mean age of sterilization is -22.37 ± 4.84 . Early age at marriage and early sterilization also play a role. The mean age at which the patients were sterilized was 22 years. In 38.2 % of the patients, the duration between sterilization and development of symptoms was 16–20 years.

Regarding distribution of menstrual symptoms, menstrual disturbances were noted as the most common modality of presentation (76 %), among which menorrhagia (54 %) was seen most commonly (Table 1). Considering the incidence of various operations performed, 50 % patients underwent total abdominal hysterectomy (TAH): 22 % TAH with bilateral salpingo-oophorectomy, 18 % TAH with unilateral salpingo-oophorectomy, 8 % myomectomy, and 2 % vaginal hysterectomy. In our series, it was noted that the size of the fibroid uterus varied from a few centimeters to 30 weeks of gravid uterus. It is seen that, about 68 % were of the size of 16 weeks gravid uterus, 23 % were of the size between 16 and 20 weeks. Among the uterine, about 93.9 % of the fibroid were in the body of the uterus and 6.1 % were cervical, intramural

Table 1 Incidence of various symptoms in combination in the present study

Symptoms	Percentage	X ²
Menstrual disturbances	76	27.04
Dysmenorrhoea	20	36.00
White discharge	12	57.76
Pain abdomen	33	11.56
Mass/abdomen	13	54.76
Mass/vagina	2	92.16
Urinary symptoms	15	81.00
Bowel disturbances	0	–
Infertility	15	81.00
Asymptomatic	2	92.16
Others	5	–

Table 2 Incidence of various degenerations in the cases studied

Degenerations	%
Hyaline degeneration	2
Myxoid degeneration	3
Cystic degeneration	1
Calcareous degeneration	1
Sarcomatous change	1
Fatty degeneration	0

Table 3 Incidence of histopathological pattern of endometrium

Endometrial pattern	%
Proliferative	66.3
Secretory	12
Hyperplasia	4.3
Cystic glandular hyperplasia	2.1
Atrophic	8.7
Unknown	6.5

fibroid was the commonest variety comprising about 60.6 % of the cases, 9.1 % submucous, 5.1 % subserous.

Myxoid degeneration was the most common degeneration, seen in 3 % of the patients, followed by hyaline degeneration, which was found in 2 % of the patients (Table 2).

Histopathological pattern of endometrium was studied. It showed proliferative endometrium in 66.6 %, secretory changes were noted in 12 %, endometrial hyperplasia was seen in 4.3 % cases, cystic glandular hypertrophy was seen in 2.1 %, and atrophic endometrium occurred in 8.7 % (Table 3).

Table 4 Histopathological abnormalities in combination with myoma

Associated pelvic pathology	%	χ^2
Cystic ovaries	8	61.82
Chronic cervicitis	85	68.58
Adenomyosis	16	38.25
Endometriosis	2	
Pelvic inflammatory disease	4	

Table 5 Associated medical or surgical conditions

Associated medical/surgical conditions	%
Hypothyroidism	7
DM	4
DM and HTN	4
HTN	8
Cholelithiasis	2
Fibroadenoma of breast	1

The associated pathology in the adnexa and other pelvic structures was studied, which showed cystic ovaries in 8 % of the cases. A variety of cysts were noted such as simple serous cyst, follicular cyst, serous/papillary cystadenoma, dermoid cyst, and corpus luteal cyst. Adenomyosis was found in 16 % of the cases, chronic cervicitis in 85 % of the cases, endometriosis in 2 %, and PID in 4 % of the cases (Table 4).

Subclinical hypothyroidism was found in 7 %, of which only 2 had overt hypothyroidism, which may be because of the regional variation, as our state is endemic for hypothyroidism. Diabetes was found in 8 % and hypertension in 12 %. Cholelithiasis was reported only in 2 % (Table 5).

Table 6 Incidence of various symptoms in the present study

Symptoms	Present series %	Poddar [13]	Bhaskar Reddy [11]	Pinto [14]	Usha et al. [12]	Chhabra et al. [15]
Menstrual disturbances	76	55.9	59	72.8	94	63
Dysmenorrhoea	20	16.3	–	4.2	42	–
White discharge	12	10.0	9.5	6.7	–	13
Pain abdomen	33	32.5	25	19.4	45	–
Mass/abdomen	13	31.5	27.5	17.7	21	23
Mass/vagina	1	–	–	5.9	–	10
Urinary symptoms	15	–	–	6.7	–	6
Bowel symptoms	–	–	–	–	–	–
Infertility	15	–	–	–	6	16
Asymptomatic	2	–	–	–	15	13
Others	4	–	–	–	15	13

Discussion

The incidence of leiomyoma is the highest in the third decade; this is similar to the incidence from old statistics from our hospital, and the incidence is quoted by other investigators, Bhaskar Reddy [11] and Usha et al. [12], indicating that leiomyoma is a disease seen in women of child-bearing age; they are rarely found before puberty and cease to grow after menopause. Similarly, the incidence of leiomyoma was the highest among the multiparous group in most of the studies, as depicted in Table 6. Although the literature states that leiomyoma is a disease of low parity, this is probably due to early age at marriage and long gap between the last child birth and development of symptoms.

The analysis of symptoms shows that the menstrual complaints were predominant among all the study groups with comparable results. Other complaints such as pain/abdomen and mass/abdomen were also found. The incidence of urinary complaints was the highest in our series (15 %). Primary infertility due to fibroid has been seen in 15–16 % of the patients by different authors. But western authors like Khaund and Vilos have reported an infertility rate of 1–3 % associated with fibroids.

About 60 % were intramural fibroids which is the most common variety. Similar results were obtained by Usha et al. (77 %), Chhabra et al. (47 %), and Shaw (73 %). About 15 % of the cases had multiple fibroids in our series. Although the incidence of cervical fibroid has been as low as 4 % (Shaw) and 0.6 % (Tiltman), the incidence in our study is comparatively as high as 6 % (Table 7).

Compared to the older statistics from our institute, it has been seen that the number of myomectomies has increased, indicating the need for conserving uterus in young woman. The histological pattern of endometrium observed was of proliferative type in 66.3 % of the cases, and these results are comparable to those quoted by Udawat (68 %) and

Table 7 Incidence of various operations performed

Operation	Present series %	Old statistics
Total abdominal hysterectomy	50	23
Total abdominal hysterectomy with bilateral salpingo-oophorectomy	22	45
Total abdominal hysterectomy with unilateral salpingo-oophorectomy	18	23
Myomectomy	8	3
Vaginal hysterectomy	1	1

Chhabra et al. (40 %). This indicates the hyperestrogenic states associated with fibroids, and endometrium was secretory in 12 % of the cases. The association with cystic ovaries and adenomyosis also indicates hyperestrogenism. Only 2 % had hyaline degeneration, and the presence of hyaline degeneration depends on the size of the specimen and the number of samples from each sample studied. There was one case of leiomyosarcoma, giving an incidence of 1 %, which is similar to the incidence quoted by others.

Conclusion

Fibromyoma (leiomyoma) is the most common benign tumor of the pelvis. The trends in the age and incidence have remained the same, and the occurrence of fibroid is rare before 20 years of age, and they cease to grow after menopause. Therefore, it commonly affects women of child-bearing age, mostly in the third decade. Although fibroid is a disease of low parity, it was most commonly observed in multipara, a significantly long period of no fertility following last child birth predispose to the development of fibroids. The most common mode of presentation is menstrual disturbances. Since most of the patients were referred by local doctors, the patients ascribed any symptoms to the presence of fibroid, retrospectively. Therefore, the incidence of asymptomatic cases is very low (2 %). Primary infertility was seen in 15 %. Intramural fibroid is the most common variety, followed by combination leading to multiple fibroids, then submucous and subserous fibroids. The proliferative and hyperplastic endometrium was commonly reported. The presence of proliferative endometrium, adenomyosis, and cystic ovaries all are indicative of hyperestrogenic state associated with the development of fibroids.

Compliance with Ethical Standards

Conflict of interest Maitri Raghavendra Kulkarni, Indranil Dutta, Dilip Kumar Dutta declare that they have no conflicts of interest.

Informed consent All procedure followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Informed consent was obtained from all patients for being included in the study.

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