

FREQUENCY OF UTERINE LEIOMYOMA WITH ITS RELATED RISK FACTORS OBSERVED AT A TERTIARY CARE CENTRE IN KARACHI

Talat Zehra¹, Khadija Bano², Syeda Sakeena Raza², Mahin Shams³, Tajwar Fatima², Amna Qadri⁴

¹Jinnah Sindh Medical University, Karachi Pakistan

²Jinnah Postgraduate Medical Center, Karachi Pakistan

³United Medical and Dental College, Karachi Pakistan

⁴Dr Ziauddin Hospital North Nazimabad, Karachi Pakistan

ABSTRACT

Objective: To study the frequency of uterine leiomyoma with its risk factors.

Material and Methods: A cross-sectional study was carried out between January 2020 to June 2020 including women who were diagnosed with uterine leiomyomas in the Department of Gynecology, Jinnah Postgraduate Medical Center (JPMC), Karachi. All the major risk factors including demographic details, family history, marital status, parity, use of oral contraceptives and co-morbidities were studied in 300 females using a questionnaire. The data was analyzed with the statistical program Statistical Package for the Social Sciences (SPSS) version 21.0.

Results: A total number of 300 patients having uterine leiomyomas were included in the study. The mean and standard deviation of the patients' age was 42.52±7.98 and patients' weight was 59.8±9.12. The mean and standard deviation of the patients' BMI was 23.4±3.85 and patients' height was 63.01±2.23. The demographic and clinical characteristics of the patients are presented in Table-I and II. Leiomyomas were reported mostly in women between the ages of 36-40 years (28%), followed by 46-50 years (20%) and 51-55 years (14.3%). 10% of the women reported hypertension as a co-morbid. 3.8% were both hypertensive and diabetic. 76.9% females presented with abnormal uterine bleeding and 69.8% had anemia. Most of the women with leiomyomas were para 3+ (36.9%) and para 3 (20.9%). 22.2% women were nulliparous. 72.2% women had a single fibroid and 21.6% had two or more fibroids. 5.7% women had a family history of fibroids. 5.4% women were using some form of hormonal contraception.

Conclusion: Risk factors for uterine leiomyomas were identified and prevalence of these risk factors in patients with leiomyomas was observed.

Key Words: Leiomyoma, Risk factors, Uterine fibroid.

This article can be cited as: Zehra T, Bano K, Raza SS, Shams M, Fatima T, Qadri A. Frequency of uterine leiomyoma with its related risk factors observed at a tertiary care centre in Karachi. Pak J Pathol. 2022; 33(4): 139-142.

DOI: 10.55629/pakjpathol.v33i4.732

INTRODUCTION

Uterine leiomyomas or fibroids are smooth muscles tumors of the uterus that are benign in nature. They usually affect women in the reproductive age group. They occur in 20% of all women of reproductive age [1-3]. They may cause a variety of symptoms or remain asymptomatic. Heavy menstrual bleeding is the most usual complaint that women present with and this leads to anemia along with painful periods [4-7]. Other symptoms include pain in the pelvic area, abdominal discomfort, pelvic pressure, painful intercourse and dysfunctional bladder or bowel. This leads to constipation, urinary retention or urinary incontinence [5-8]. Leiomyomas can also be associated with problems in reproductive life. These include infertility, complications in pregnancy, miscarriages and poor obstetric outcomes [9-15]. The incidence of leiomyoma varies

between 20–40% in Pakistan according to different studies [16]. It is one of the major causes of hospital admissions for gynecological problems in USA, and also the most frequent reason for hysterectomy [17-20]. It has been postulated that over 70% of women develop leiomyomas by the onset of menopause [21-23].

In 25% of women of reproductive age they become clinically evident and approximately 25% of women with leiomyoma develop severe symptoms that require treatment [4,24,25].

The exact cause of leiomyomas is still unknown but some of the risk factors have been identified which are attributed to the occurrence of these tumors. Older women have a higher risk of developing these tumors than younger women. Race is an important contributor in the development of leiomyoma. African American women are the most frequently affected population. Other factors include low parity, unopposed/ increased estrogen exposure, obesity, family history of these tumors, high blood pressure and no history of pregnancy [26-30]. Factors that may decrease the risk of leiomyomas

Correspondence: Dr Mahin Shams, Assistant Professor, Department of Pathology, United Medical and Dental College, Karachi Pakistan.

Email: mahin.16@gmail.com

Received: 28 Sep 2022; Revised: 11 Dec 2022; Accepted: 27 Dec 2022

include increasing number of term pregnancies (live births and still births). While on the other hand, incomplete pregnancies have not been associated with risk reduction. Infact, according to literature it is associated with slight increase in the risk of fibroids [31, 32]. Gonadotropin releasing hormone agonist (GnRHa) or leuprolide acetate drastically lowers estrogen level by causing pituitary desensitization which contributes in shrinkage of leiomyomas, hence supporting the notion that increased estrogen levels or unopposed estrogen may be the risk factor for these smooth muscle lesions [33].

Women who are going through menopause or had menopause have significantly low risks for fibroids. Use of oral contraceptive for a longer duration has a steady decrease in the risk of developing fibroids. There is a reduction of around 17% in the risk of fibroids with every five years of oral contraceptive use. Body weight has a direct relation with the risk of fibroids. According to some studies, there is a 17% increase in the risk of fibroids with every 10kg of bodyweight. This is particularly important for post-menopausal women in whom the major source of estrogen is fat cells where androstenedione is converted to estrogen. Cigarette smoking is also associated with reduction in the risk of uterine leiomyomas [31, 32].

In Pakistan, few studies have been conducted on the prevalence of leiomyoma and their association with clinical features like uterine bleeding, pelvic pain and pelvic pressure. In this study we identified the major risk factors in our population including age, weight, BMI, family history, parity, contraception and co morbid. The results of this study will help to identify the prevalence of these risk factors with leiomyomas in our population and help to correct the modifiable risk factors resulting in reduced incidence of leiomyomas.

MATERIAL AND METHODS

This cross sectional study was conducted at the Department of Gynecology, Jinnah Postgraduate Medical Center (JPMC), Karachi. Sample size was calculated using the formula: $Z_{1-\alpha/2} \sqrt{p(1-p)} / d^2 Z = 1.96$ ($p < 0.05$), $P = 0.2$, $d = 5\%$. The ethical clearance was obtained from the Ethics Committee NO. F.2-81/2020-GENL/43938. By using non probability convenient sampling technique and using the sample size formula for cross sectional study, we calculated the sample size. We used the reference prevalence as 20% from previous literature [2]. We selected patients between 20-60 years who were diagnosed with uterine leiomyomas and were willing to participate in the study. The pregnant women were

omitted from this study. Sample size of three hundred patients with uterine fibroids was asked the questions in the proforma as per study guidelines.

The data was collected and then recorded in a pre-designed proforma. It was analyzed using Statistical Package for the Social Sciences (SPSS) version 21.0. Mean and standard deviation was calculated for continuous variables. Frequency and percentages were calculated for categorical variables.

RESULTS

A total number of 300 patients having uterine leiomyomas were included in the study. The mean and standard deviation of the patients' age was 42.52 ± 7.98 years. The mean and standard deviation of the patients' weight was 59.8 ± 9.12 years. The mean and standard deviation of the patients' BMI was 23.4 ± 3.85 . The mean and standard deviation of the patients' height was 63.01 ± 2.23 . The demographic and gynaecological characteristics of the patients are presented in the Table-I and II.

Fibroids were reported the most in women between the ages of 36-40 years (28), 46-50 years (20%) and 51-55 years (14.3%). 10% of the women reported hypertension as a co-morbid. 3.8% were both hypertensive and diabetic. 76.9% females presented with abnormal uterine bleeding and 69.8% had anemia. Most of the women with leiomyomas were para 3+ (36.9%) and para 3 (20.9%). 22.2% women were nulliparous. 72.2% women had a single fibroid. 5.7% women had a family history of leiomyomas. 5.4% women were using some form of hormonal contraception.

Table-I: Age distribution of patients with uterine fibroids.

Age group of patients in years	Number of patients (n=300)	Percentage (%)
20-25	1	0.3
26-30	23	7.7
31-35	36	12
36-40	84	28
41-45	42	14
46-50	60	20
51-55	43	14.3
56-60	11	3.7

Table-II: Gynecological data of patients.

Uterine Leiomyoma	Parity	Number of patients	Percentage (%)
	Nulliparous	71	22.2
1	18	5.6	
2	26	8.1	
3	67	20.9	
>3	118	36.9	

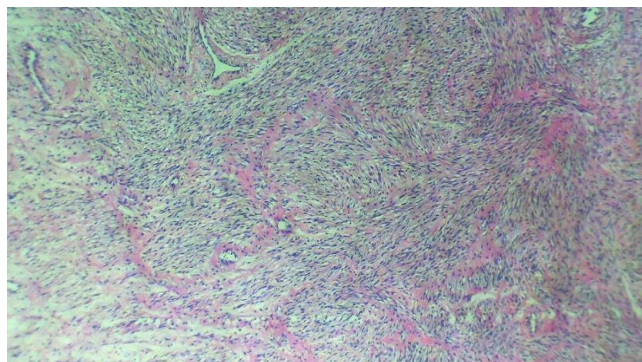


Figure-I: Leiomyoma at 4X magnification.

DISCUSSION

Uterine leiomyomas are the most common benign smooth muscle tumors in women of child bearing age (Figure-I). In our study the most common age group in which women had leiomyomas was 36-40 years (28%) followed by 46-50 years (20%) and 51-55 years (14.3%). This difference may be attributed to the different hormonal levels among different age groups. In a study carried out at Haiti in 2021 the mean age of the women having fibroids was 41.3 [34]. The mean age of the patients with fibroids in our study was 42.52 ± 7.98 . The average age of patients with uterine leiomyomas in a cross sectional study in United States was 43.4 years [35].

Age is an important predictor for uterine fibroid in women. Most of the uterine fibroids are asymptomatic and shrink with menopause [2]. In our present study, we found a decrease in the occurrence of leiomyomas with increasing age after 35 years (Table-I).

Majority (36.9%) of the women having fibroids were para 3+ (Table-II) in our study compared to a study carried out at Ghana in 2016 in which parity had a negative association with fibroids and these tumors were seen more in nulliparous as compared to women with children [36] probably due to the differences in the study sample size and demographic characteristics. 10% of the women with leiomyomas had hypertension as a co-morbid in this study. In another study, women with fibroids reported medical conditions like hypertension and diabetes (24.4% and 8.5% respectively) [35]. The most common presenting symptom was abnormal uterine bleeding (AUB) in our study. 76.9% females having fibroids presented with AUB.. 72.2% women had a single leiomyoma. 5.7% women had a positive family history of leiomyomas. A study carried out in Haiti in 2021 reported risk factors associated with leiomyomas which included family history.

In our study, 5.4% of the women with fibroid had used contraceptives at some time. A study conducted at England and Scotland showed that 53%

women with leiomyomas had used oral contraceptives and also observed that risk decreases with increasing duration of the oral contraceptive use [37].

The mean and standard deviation of the patients' BMI was 23.4 ± 3.85 in this study. A study in 2016 at Poland showed that an increase in body mass index (BMI) by one unit increases the risk of uterine fibroids 1.1 [38,39]. In our study, 69.8% women had anemia with fibroids. Anemia was observed to be the most common complication (52.6%) in a similar study conducted in rural Haiti [34].

CONCLUSION

This study identified the frequency of risk factors in patients with uterine leiomyomas observed at a tertiary care center in Karachi. Various factors were taken into consideration and it was found that these tumors were more prevalent in patients aged 36-40 years, women who were para 3+, women who had a family history of fibroids or had a co-morbidity like diabetes mellitus or hypertension. Further studies should be continued to evaluate the risk and association of fibroids with each risk factor separately in different races and ethnicities.

AUTHOR CONTRIBUTION

Talat Zehra: Conceived the idea, wrote the synopsis and manuscript.

Khadija Bano: Facilitated in data collection.

Syeda Sakeena Raza: Collected the data from the patients.

Mahin Shams: Wrote the manuscript and analysed the results.

Tajwar Fatima: Collected the data from the patients.

Amna Qadri: Wrote the manuscript and analysed the results.

REFERENCES

1. Geethamala K, Murthy VS, Vani BR, Rao S. Uterine leiomyomas: An ENIGMA. *J Midlife Health.* 2016; 7(1): 22-7. DOI: 10.4103/0976-7800.179170
2. Malik SN. Management of uterine leiomyoma. *JRMC.* 2012; 16(2): 168-70.
3. Barjon K, Mikhail LN. Uterine Leiomyomata. [Updated 2022 Aug 8]. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK546680>.
4. Mathew RP, Francis S, Jayaram V, Anvarsadath S. Uterine leiomyomas revisited with review of literature. *Abdom Radiol (NY).* 2021; 46(10): 4908-26. DOI: 10.1007/s00261-021-03126-4.
5. Segars JH, Al-Hendy A. Uterine leiomyoma: New Perspectives on an old disease. *Semin Reprod Med.* 2017;35(6): 471-72. DOI: 10.1055/s-0037-1606569.
6. Al-Hendy A, Myers ER, Stewart E. Uterine fibroids: Burden and unmet medical need. *Semin Reprod Med.* 2017; 35(6): 473-80. DOI: 10.1055/s-0037-1607264.

7. McWilliams MM, Chennathukuzhi VM. Recent advances in uterine fibroid etiology. *Semin Reprod Med.* 2017; 35(2): 181-89. DOI: 10.1055/s-0037-1599090.
8. World Health Organization. Coronavirus COVID-19 Dashboard (<https://COVID19.who.int/>, 2020).
9. Abid K, Bari YA, Younas M, Tahir Javaid S, Imran A. Progress of COVID-19 epidemic in Pakistan. *Asia Pac J Public Health.* 2020; 32(4): 154-56.
10. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Gynecology. Management of Symptomatic Uterine Leiomyomas: ACOG Practice Bulletin, Number 228. *Obstet Gynecol.* 2021; 137(6): e100-e115. DOI: 10.1097/AOG.0000000000004401.
11. Farris M, Bastianelli C, Rosato E, Brosens I, Benagiano G. Uterine fibroids: An update on current and emerging medical treatment options. *Ther Clin Risk Manag.* 2019; 15: 157-78. DOI: 10.2147/TCRM.S147318
12. Juvvadi S, Verabelly M. Prevalence of fibroids: A study in semi urban area in Telangana India. *Int J Reprod Contracept Obstet Gynecol.* 2017; 6(12): 5247-50. DOI: <http://dx.doi.org/10.18203/2320-1770.ijrcog.201750.59>
13. Zehra T, Anjum S, Mahmood T, Shams M, Sultan BA, Ahmad Z, et al., A novel deep learning-based mitosis recognition approach and dataset for uterine leiomyosarcoma histopathology. *Cancers.* 2022; 14(15):3785. DOI: 10.3390/cancers14153785
13. De La Cruz MS, Buchanan EM. Uterine fibroids: diagnosis and treatment. *Am Fam Physician.* 2017; 95(2): 100-107.
14. Ghosh S, Naftalin J, Imrie R, Hoo WL. Natural History of Uterine Fibroids: A Radiological Perspective. *Curr Obstet Gynecol Rep.* 2018; 7(3): 117-21. DOI: 10.1007/s13669-018-0243-5.
15. Nougaret S, Vargas HA, Sala E. *BJR* female genitourinary oncology special feature: introductory editorial. *Br J Radiol.* 2021; 94(1125): 20219003. DOI: 10.1259/bjr.20219003.
16. Awiji MO, Badawy M, Shaaban AM, Menias CO, Horowitz JM, Soliman M, et al. Review of uterine fibroids: Imaging of typical and atypical features, variants, and mimics with emphasis on workup and FIGO classification. *Abdom Radiol (NY).* 2022; 47(7): 2468-85. DOI: 10.1007/s00261-022-03545-x.
17. Naz S, Naeem S, Riyaz A, Jehangir F, Rehman A, Iqbal T. Leiomyoma: Its variants and secondary changes-A five-year study. *J Ayub Med Coll Abbottabad* 2019; 31(2): 192-5.
18. Manuel EC, Plowden TC, Valbuena FM Jr, Bryce RL, Barick AA, Ramakrishnan A, et al. the environment, leiomyomas, latinas, and adiposity Study: Rationale and design. *Am J Obstet Gynecol.* 2022; 226(3): 392.e1-392.e12. DOI: 10.1016/j.ajog.2021.05.005.
19. Shaikh F, Memon F P, Hingoro R, Rani K, Daudpota U F. Clinical pattern and management of patients presented with uterine fibroids. *J Soc Obstet Gynaecol Pak.* 2020; 10(3): 190-94.
20. Giuliani E, As-Sanie S, Marsh EE. Epidemiology and management of uterine fibroids. *Int J Gynaecol Obstet.* 2020; 149(1): 3-9. DOI: 10.1002/ijgo.13102.
21. Marsh EE, Al-Hendy A, Kappus D, Galitsky A, Stewart EA, Kerolous M. Burden, prevalence, and treatment of uterine fibroids: A survey of U.S. Women. *J Women Health (Larchmt).* 2018; 27(11): 1359-1367. DOI: 10.1089/jwh.2018.7076.
22. Fortin C, Flyckt R, Falcone T. Alternatives to hysterectomy: The burden of fibroids and the quality of life. *Best Pract Res Clin Obstet Gynaecol.* 2018 Jan; 46: 31-42. DOI: 10.1016/j.bpobgyn.2017.10.001.
23. Munusamy MM, Sheelaa WG, Lakshmi VP. Clinical presentation and prevalence of uterine fibroids: A 3-year study in 3-decade rural South Indian women. *Int J Reprod Contracept Obstet Gynecol.* 2017; 6: 5596-601. DOI: <https://dx.doi.org/10.18203/2320-1770.ijrcog20175.288>
24. Raza AM, Tazri SA, Ahmed M, Nahar S, Afroz D, Barua D. A study on uterine leiomyoma with clinicopathological spectrum. *J Histopathol Cytopathol.* 2018; 2(1): 41-6.
25. Yu O, Scholes D, Schulze-Rath R, Grafton J, Hansen K, Reed SD. A US population-based study of uterine fibroid diagnosis incidence, trends, and prevalence: 2005 through 2014. *Am J Obstetrics Gynecol.* 2018; 219 (6): 591-e1. DOI: 10.1016/j.ajog.2018.09.039
26. Machado-Lopez A, Simón C, Mas A. Molecular and cellular insights into the development of uterine fibroids. *Int J Mol Sci.* 2021; 22(16): 8483. DOI: 10.3390/ijms22168483.
27. Stewart EA. Uterine fibroids. *New England J Medicine.* 2015; 372, 1646-55. Retrieved October 25,2018, from <https://www.nejm.org/doi/full/10.1056/NEJMcp1411029?page=&sort=oldest>
28. Stewart EA, Cookson CL, Gandolfo RA, Schulze R. Epidemiology of uterine fibroids: A systematic review. *BJOG: An Int J Obstetrics Gynaecol.* 2017; 124(10): 1501-12.
29. Pavone D, Clemenza S, Sorbi F, Fambrini M, Petraglia F. Epidemiology and risk factors of uterine fibroids. *Best Pract Res Clin Obstet Gynaecol.* 2018; 46: 3-11.
30. Yang Q, Ciebiera M, Bariani MC, Ali M, Elkafas H, Boyer TG, et al. Comprehensive review of uterine fibroids: Developmental origin, pathogenesis, and treatment. *Endocr Rev.* 2022; 43(4): 678-719. DOI: <https://doi.org/10.1210/edrv/bnab039>
31. Kwas K, Nowakowska A, Fornalczyk A, Krzycka M, Nowak A, Wilczyński J, et al. Impact of contraception on uterine fibroids. *Medicina (Kaunas).* 2021; 57(7): 717. DOI: 10.3390/medicina57070717
32. Ross RK, Pike MC, Vessey MP, Bull D, Yeates D, Casagrande JT. Risk factors for uterine fibroids: Reduced risk associated with oral contraceptives. *BMJ.* 1986; 293: 359-62. DOI:10.1136/bmj.293.6543.359
33. Kwas K, Nowakowska A, Fornalczyk A, Krzycka M, Nowak A, Wilczyński J, et al. Impact of contraception on uterine fibroids. *Medicina (Kaunas).* 2021; 57(7): 717. DOI: 10.3390/medicina57070717.
34. Kurman RJ, Ellenson LH, Ronnett BM. *Blaustein's Pathology of the female genital tract.* Publisher: Springer International Publishing Imprint, Springer, Cham, 2019.
35. Millien C, Manzi A, Katz AM, Gilbert H. Assessing burden, risk factors, and perceived impact of uterine fibroids on women's lives in rural Haiti: Implications for advancing a health equity agenda, a mixed methods study. *Int J Equity Health.* 2021; 20(1): 1. DOI:10.21203/rs.3.rs-35994/v3
36. Fuldeore MJ, Soliman AM. Patient-reported prevalence and symptomatic burden of uterine fibroids among women in the United States: findings from a cross-sectional survey analysis. *Int J Women Health.* 2017; 9: 403-11. DOI: <https://doi.org/10.2147/IJWH.S133212>
37. Sardokie BD, Botwe BO, Adjei DN, Ofori E. Factors associated with uterine fibroid in Ghanaian women undergoing pelvic scans with suspected uterine fibroid. *Fertil Res Pract.* 2016; 2: 9. DOI:10.1186/s40738-016-0022-9.
38. Laberge PY, Murji A, Vilos GA, Allaire C, Leyland N. Guideline no. 389-medical management of symptomatic uterine leiomyomas—an addendum. *J Obstet Gynaecol Can.* 2019; 41(10): 1521-24. DOI: 10.1016/j.jogc.2019.01.010.
39. Ciebiera M, Włodarczyk M, Stabuszewska-Jóźwiak A, Nowicka G, Jakiel G. Influence of vitamin D and transforming growth factor β 3 serum concentrations, obesity, and family history on the risk for uterine fibroids. *Fertil Steril.* 2016; 106(7): 1787-92. DOI: 10.1016/j.fertnstert.2016.09.007.
40. Datir SG, Bhake A. Management of uterine fibroids and its complications during pregnancy: A review of literature. *Cureus.* 2022; 14(11). e31080 DOI: 10.7759/cureus.31080