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Review Article

Factors Associated with Uterine Fibroids and their Impact on Women: A Systematic Review

Hitika¹, Shyam Prakash², SujataRawat³, Hanumanthrao C Patil⁴, Rajesh Kumari Patil^{5*}

^{1,2}Pharm.D Scholar, Adesh Institute of Pharmacy and Biomedical Sciences, Adesh University, Bathinda ³Assistant Professor. Department of Obstetrics and Gyneocology, Adesh Institute of Medical & Research Sciences, Adesh University, Bathinda

⁴Professor & Principal, Department of Pharmacy Practice, Adesh Institute of Pharmacy and Biomedical Sciences, Adesh University, Bathinda

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ABSTRACT

Objectives: The most frequent pelvic tumours in women are uterine fibroids, which have a prevalence of 21.4% worldwide. The aim of this study is to examine the associated risk factors in patients suffering from uterine fibroids and their impact on women lives.

Data Sources: MEDLINE, OVID, PubMed (1950–December 2015), Google scholar, individual article files, and bibliographies of found articles that addressed the issue of interest and original research.

Study Selection: The articles were chosen for their applicability to the associated risk factors of Uterine Fibroids and their economic impact on women. Patients who met the criteria had to undergo a transvaginal ultrasound.

Results: In 21.4% of them, uterine fibroids were found. Heavy bleeding, prolonged bleeding, bleeding between periods, frequent periods, irregular and regular periods were all symptoms that women with uterine fibroids reported reporting substantially more frequently than those without a diagnosis. Participants' ages ranged from 42.08±8.89 on average. According to BMI data, women with a weight between 18.5 kg/m2 and 24.9 kg/m2 (36.49%) and 25 kg/m2 to 29.9 kg/m2 (54.74%) and 30 kg/m2(8.75%) had a greater prevalence of fibroids. When compared to women who had previously taken oral contraceptives, those who hadn't had a higher prevalence of fibroids. Other risk variables previously mentioned did not seem to be significant.

Conclusion: Age and BMI had significant effects on the prevalence of fibroids. Due to their comparatively high incidence and potential negative effects on patients' quality of life, fibroids are a significant gynecologic pathology in women. Women with UF had to control their symptoms, receive treatments, and bear a heavier financial burden, to name a few issues.

Keywords: Uterine fibroids, Risk factors, Body Mass Index (BMI), oral contraceptives, age.

INTRODUCTION

The most frequent pelvic tumours in women are uterine fibroids, benign tumours of the uterus (also known as myomas or leiomyomas). An early 2003 study by Baird et al. predicted that by the age of 50, the prevalence of fibroids in women was over 80% for black women and over 70% for white women.[1] Fibroids originate from the cells of the smooth muscle of the uterus called the myometrium, and the level of estrogen in the blood has a significant impact on how they develop. More details

show that the pathophysiology of fibroids is poorly known. The majority of women who have uterine fibroids are asymptomatic, which results in less clinical attention being given to them and a high rate of fibroid tumours going misdiagnosed.[2,3] The three primary locations where uterine fibroids are usually found are subserosal (outside the uterus), intramural (within the myometrium), and submucosal (into the uterine cavity). Physical examinations and ultrasound imaging, which has a high sensitivity for

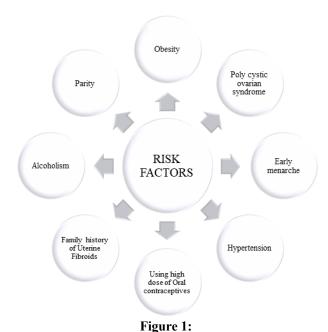
⁵Professor and HOD, Department of Pharmacy Practice, Adesh Institute of Pharmacy and Biomedical Sciences, Adesh University, Bathinda

this illness, are the traditional procedures for identifying fibroids. Most women will encounter the growth of one or more uterine fibroids during their reproductive years. The Italian Seveso Women's Health Study (SWHS) revealed that 21.4% of women between the ages of 30 and 60 have fibroids, making it one of the most reliable estimations of the condition's prevalence in a European population. In the United States, 26 million women between the ages of 15 and 50 are thought to have uterine fibroids. Although the specific aetiology of fibroids is still unknown, there is a lot of evidence to support the idea that oestrogens and progestogens promote the growth of tumours because fibroids virtually every appear before menarche and typically recede after menopause. Fibroids are a common condition that can cause abnormal uterine bleeding, pelvic pain or pressure, and may have an impact on a person's ability to conceive and have a poor pregnancy result. The most typical presenting symptom is excessive bleeding during menstruation, which can result in anaemia, tiredness, and painful periods. [4-9] Other symptoms of UF include non-cyclical discomfort, abdominal protuberance, painful erections or pelvic pressure, and bladder or bowel problems that result in pain, constipation, or urine incontinence or retention. Fibroids are a common disease that can result in abnormal uterine bleeding, pelvic pain or pressure, and may have reproductive implications such as infertility and poor pregnancy outcomes.[10] Why uterine fibroids develop is unknown. Age, reduced

fertility, frequent alcohol and caffeine use, obesity, intake of red meat, hypertension, diabetes mellitus, an earlier diagnosis of pelvic inflammatory disease, and heredity are only a few of the risk factors for fibroids that have been discovered in prior studies.[11-17] According to some estimates, UFs are the most common neoplasm infecting women by the time menopause sets in, affecting more than 70% of women. However, because it frequently goes undiagnosed in women because it is asymptomatic or emerges gradually over time, the condition's frequency is probably underestimated. Long menstrual cycles, (multi)parity, recurrent oral contraceptive usage, early maternal age, nursing, menopause after menopause, smoking, and vegan or vegetarian diets are protective factors.[17,18] Treatment for UFs is heavily influenced by the fibroid's symptoms, location, and size. The most frequent benign tumour in women, uterine fibroids are the main cause of hysterectomies. Realise that not all UF-affected women exhibit symptoms.

The prevalence of UF may be larger than previously believed, according to the NIH (2006), which found that many women are unaware they have the condition. Women with prominent UF symptoms usually seek treatment (HRQOL), as UF symptoms can be challenging to manage properly and can have a detrimental influence on health-related quality of life.

Risk Factors



• Early menarche

African ancestry and advancing age (till menopause) are the main risk factors for the development of fibroid.[7,8] In comparison to white women, black women had a greater lifelong incidence of fibroids and more serious symptoms, which could have an adverse effect on their quality of life.

• Hormonal imbalance (estrogen /progesterone)

Uterine fibroids or uterine enlargement are among the first symptoms of hormonal imbalance in the body to appear in the uterus. Higher estrogen levels than progesterone during your reproductive years cause the hormonal imbalance. The condition is oestrogen dominance. [1] This issue may lead to an enlarged uterus, which may put pressure on the bladder and make the patient uncomfortable. Fibroids in your uterus can form and grow as a result of oestrogen dominance. It has been demonstrated that high estrogen levels encourage the growth of fibroid. Increases in fibroid growth have also been linked to high progesterone levels.

• Hypertension

We conducted a cross-sectional study and meta-analysis to ascertain whether UFs are related to elevated blood pressure. Women who have fibroids are at an elevated risk for hypertension. Recently, we reproduced past studies that reported a high frequency of hypertension in women with fibroids and demonstrated that this connection was independent of age, BMI, and African ancestry. Women with uterine fibroids need to regularly manage their hypertension.

Family history of Uterine Fibroids

The likelihood of getting fibroids in your lifetime increases if a family member has them. In fact, the significant genetic component of this problem is shown by the fact that if your mother had fibroids, you are threefold more likely to get them than a woman who has no family history of them. To clarify the genetic components of this illness, more research is required.

Alcoholism

Estradiol and estrone levels are influenced by alcohol. According to recent studies, the body's estrogen levels are related to uterine fibroid growth. We frequently observe women developing fibroids when increased levels of estrogen are introduced into the body. Inflammation and immune system issues might result from excessive alcohol consumption.

• Parity

The medical term "nulliparous woman" refers to a person who has never given birth to a biological child. This condition is associated with an increase in uterine fibroids. The most significant risk

factors for uterine fibroid revealed to be delayed childbirth and nulliparity after the age of 36.

When you have several pregnancies, you are less likely to develop fibroids if you have high parity (multiparity). According to Baird and Dunson, remodelling that occurs during uterine involution after delivery explains why parity is protective. However, little is known about the hormonal alterations that take place during uterine involution.

Obesity

According to a thorough meta-analysis, obese women are 17% to 26% more probable to develop uterine fibroids, however it is unclear what causes one to cause the other. Another study found that women who are obese had a 2-3 times higher risk of developing fibroids than women who are ordinary weight. This is especially true for those with central obesity or significant abdominal fat. Fibroids grow because of estrogen, which is excessively produced when there is too much abdominal fat.

• Utilisation of high-dose oral contraceptives

However, when the progestogen dose increased, these oral contraceptives (OCs) have been linked to a reduction in uterine fibroids. Early high estrogen dose OCs contribute to the formation of uterine fibroids. Unopposed estrogen stimulation therefore seems to raise the chance of uterine fibroids.

A protective effect from OCs with an appropriate progesterone dosage is possible.

• Vitamin D deficiency

Vitamin D insufficiency is more common in women with darker skin tones, and some studies have linked it to a higher risk of uterine fibroid formation.

• Poly Cystic Ovary Syndrome

Concerns about women's reproductive health frequently centre on PCOS and uterine fibroids. Both can affect menstruation and are impacted by hormones.

High estrogen levels are associated with fibroids growing. Women with PCOS have been found to have high levels of estrogen (estrogen dominance).

Some other factors are:

- Anaemia
- Late menopause
- Subfertility

Symptoms of Uterine Fibroids

• Enlarged Uterus

Fibroids can cause abdominal swelling, which enlarges and distends your stomach. This can not only affect how you look, but it can also make it hard to locate clothes that fits. Nobody likes to

appear overweight, especially if the reason is a relatively treatable medical problem.

• Pelvic Pain

Although it is usually benign, a uterine fibroid is simply an abnormal growth of tissue. So it shouldn't be a surprise if you have symptoms like a feeling of fullness or bloating if you have fibroids in and on your uterus.

Particularly submucosal fibroids can cause the uterus to feel heavy. Due to the fact that they occupy space designated for your uterus or other organs, fibroids can also cause generalised pain. A fibroid that outgrows its blood supply or considerably impairs the proper operation of other organs may cause acute pain, which is uncommon.

Heavy Bleed

Submucosal fibroids, which develop on the inside of the uterus, and intramural fibroids, which embed themselves in the uterine wall's muscle, are typically associated with this symptom.

Long-term heavy bleeding can cause anaemia-related tiredness and other problems, in addition to the practical challenges involved in managing excessive flow and the passage of clots.

• Weight Gain

Uterine fibroids are the cause of fast weight gain in many women. Weight gain is one of the symptoms of fibroids, which affect 20% to 80% of women. This is especially true for people who have larger fibroids that grow quickly.

• Painful Sex

You may be aware that there are a variety of causes for a woman to feel discomfort during sexual activity, but did you also realise that uterine fibroids may play a role? The uterus is deformed by fibroids, particularly sub mucosal and intramural, which prevents it from operating correctly and makes pressure or contractions painful. The presence of fibroids near the cervix may cause sex-related issues, such as bleeding. The hormonal imbalance that fibroids cause can also negatively affect a woman's libido, lowering desire and reducing the pleasure of sex. If you've never had a problem having sex, but you've only recently noticed a decline in desire, pain, or bleeding, your sexual symptoms may be very instructive.

Infertility

Untreated fibroids can make getting pregnant difficult. A woman's pregnancy should be a joyful and exciting period in her life. Fibroids can complicate pregnancy, leading to more doctor visits, health issues for both the mother and the unborn child, and a six-times higher likelihood of requiring an emergency caesarean section. Fibroids can occupy vital womb space that a developing foetus needs if left untreated, making it hard or impossible for a

woman to become pregnant or continue her pregnancy.

• Back and Leg Pain

The most typical symptoms of subserosal uterine fibroids, which originate outside of the uterus, are leg and back pain. The spinal column is relatively nearby if the fibroid is found on the back of the uterus. If it grows large enough, it may press on or enclose nearby nerves, resulting in fibroid pain. A fibroid pressing against the sciatic nerve can also cause sciatica, which radiates pain down the backs of the legs.

• Frequent Urination or Constipation

The pelvic cavity is shared by the bladder and the uterine fibroid, which develops on top of the uterus. Because of this, the bladder's capacity is reduced, increasing the chance of urine incontinence and frequency of urinating. Urinary tract infections (UTIs) and blood in the urine might result from a bad bladder and a blocked urinary system. Similar to this, if the fibroid is near the colon, it may impair normal bowel movements and result in constipation in addition to obstructing the passage of faeces in a painful manner.

Majority of other symptoms include

- Menorrhagia (Regular periods with increased bleeding)
- Metrorrhagia (Irregular periods with increased bleeding)
- Dysmenorrhea (Menstrual cramps)
- Subfertility

Impact on Women's Life

Uterine fibroid, a benign tumour of the uterus, has a significant impact on quality of life.

The UF-related symptoms can have a direct impact on a woman's functional capacity, emotional state, implications of work performance, and self-perception of health. Numerous investigations have shown that increased tiredness, depressed symptoms, attention problems, and nervous feelings are frequently reported. The idea suggests that the health system's ability to treat fibroids is constrained by poverty. Uterine fibroids complicate as a result, causing women to lose their jobs and businesses. Women consequently lack money and savings and sink deeper into poverty.

This cycle can be applicable to diseases with symptoms that are similar to or worse than fibroids and is moving in the direction of morbidity, death, and detrimental societal effects. The significant number of surgical interventions carried out as a result of UF symptoms and the use of medical resources for UF therapy show that UF has a definite cost impact on the women diagnosed. Participants also stated that the severity of their symptoms did

have an adverse effect on their employment, resulting in days absent from work. The management of symptoms, available treatments, increased financial load, and disruption of everyday life are just a few of the problems that African American women with UF must deal with.

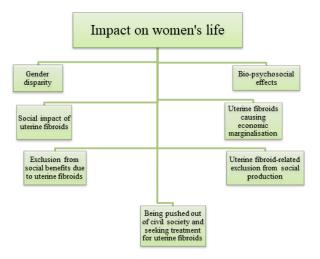


Figure 2:

• Gender disparity

According to the interviews, both the family members of women with fibroids and the women themselves feel that women in the community ought to be in charge of household responsibilities including food preparation, cleaning, and laundry. Even though they experience severe pain from uterine fibroids, women occasionally attempt to complete these tasks for their husband's approval. Sometimes, partners assume that women should become pregnant after marriage without realising that a pregnancy requires the fertile cooperation of both spouses. They sometimes become irate with their partners when they decline to engage in sexual activity with them due to the illness.

Bio-psychosocial effects

Because fibroids can occasionally cause emotional difficulties, bleeding, anaemia, atypical menstruation, infertility, and much more, women with fibroids conveyed their physical suffering across the majority of the transcripts. According to what was reported, women with fibroids appeared to be under a lot of stress, and their body language during the interviews supported this. Because it's culturally expected that families have children, and because fibroids prevent them from becoming pregnant, women worry a lot. Because fibroids make them so dependent, they occasionally felt depressed and had thoughts of suicide.

• Social impact of uterine fibroids

According to this study, fibroids can cause a family great suffering and even cause a breakup. Women with fibroids have reported that the condition prevents them from having sex with their husbands. Sometimes the biological effects of the sickness prevented them from doing housework, cooking, or washing their clothes, forcing them to live in unhygienic conditions. Other family members, including the spouse, mother, brothers, and sisters, were also impacted by the fibroids.

• Uterine fibroids causing economic marginalisation.

Women reported that the pain of the fibroids interferes with their ability to work and run their businesses, leaving them destitute. They claimed that occasionally the illness caused them to lose their jobs. Women with uterine fibroids described how they occasionally had small companies, but the fibroids forced them to give them up due to their incapacitating biological consequences, while they spent their few resources on traditional healers, tests, and private labs for treatment. Finally, they ran out of money and decided to stay home with the illness rather than seek care.

• Exclusion from social benefits due to uterine fibroids

Sometimes, women with fibroids are unable to send their children to school and afford the cost of transportation to the hospital for treatment. Additionally, the condition prevents them from affording a suitable place to live or food, which has

an adverse effect on their ability to exercise their fundamental rights. Women who have fibroids are denied access to necessary social services.

• Uterine fibroid-related exclusion from social production

Women with fibroids have reported that the condition makes it difficult for them to engage in social activities. They admitted that there were occasions when they were unable to attend temple or church to give God their prayers. One of the women who participated in the interviews indicated that she enjoyed football but was unable to attend a match because of her fibroids.

• Being pushed out of civil society and seeking treatment for uterine fibroids

Women claimed that they experienced excessive waiting times when attempting to receive treatment for uterine fibroids and wished that the hospital would treat their cases with greater importance. They mentioned how expensive it was to receive the care they required when they visited a private clinic and that they were unable to pay for it. According to what they said, medical staff did not give them enough time to communicate. It is clear that the ways in which the healthcare system now handles the treatment of fibroids is ineffective, and many women who have uterine fibroids are not included in this system.

CONCLUSION

Multiple bleeding and uncomfortable symptoms brought on by uterine fibroids can be harmful to women's health and negatively impact their sexual, social, and professional lives. In our female population, uterine fibroids were found to be present 21.4% of the time. We discovered that having a higher BMI and being between the ages of 35 and 50 were major risk factors for the development of fibroid, although taking oral contraceptives played a protective function. Multiple bleeding and pain sensations brought on by uterine fibroids may negatively affect a woman's sexual, social, and professional lives. This indicates that women with UF may experience financial hardship. These women bear an excessive financial burden as a result of the costs connected with the medications. In rural areas, health awareness campaigns and early management assistance might aid to lower morbidity.

REFERENCES

 Baird, D. D., Dunson, D. B., Hill, M. C., Cousins, D., &Schectman, J. M. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. American journal of obstetrics and gynecology, 2003;188(1): 100-107.

- Schwartz, S. M., Marshall, L. M., & Baird, D. D. Epidemiologic contributions to understanding the etiology of uterine leiomyomata. Environmental health perspectives, 2000:821-827.
- 3. Okolo, S. Incidence, aetiology and epidemiology of uterine fibroids. Best practice & research Clinical obstetrics & gynaecology, 2008;22(4), 571-588.
- 4. Subramaniyam, N. K., Kandluri, V., Chadeve, A., Modapu, D., Jyothi Dumpala, A., Gudise, B. R., & Pradeep, B. Prevalence of Risk Factors for Uterine Fibroids at Tertiary Care Teaching Hospital: A Cross-sectional Study. Journal of Young Pharmacists, 2020; 12(1): 86.
- 5. Stewart EA. Uterine fibroids. Lancet. 2001; 357(9252): 293-8.
- 6. Jr Buttram VC, Reiter RC. Uterine leiomyomata: Etiology, symptomatology and management. Fertil Steril. 1981;36(4):433-45.
- 7. Khan, A. T., Shehmar, M., & Gupta, J. K. Uterine fibroids: current perspectives. International journal of women's health, 2014;95-114.
- 8. Kjerulff, K. H., Langenberg, P., Seidman, J. D., Stolley, P. D., &Guzinski, G. M. Uterine leiomyomas. Racial differences in severity, symptoms and age at diagnosis. The Journal of reproductive medicine, 1996;41(7): 483-490.
- 9. Carlson, K. J., Miller, B. A., & Fowler Jr, F. J. The Maine Women's Health Study: II. Outcomes of nonsurgical management of leiomyomas, abnormal bleeding, and chronic pelvic pain. Obstetrics and Gynecology, 1994; 83(4): 566-572.
- Zimmermann, A., Bernuit, D., Gerlinger, C., Schaefers, M., &Geppert, K. Prevalence, symptoms and management of uterine fibroids: an international internet-based survey of 21,746 women. BMC women's health, 2012;12: 1-11.
- 11. Lippman, S. A., Warner, M., Samuels, S., Olive, D., Vercellini, P., &Eskenazi, B. Uterine fibroids and gynecologic pain symptoms in a population-based study. Fertility and sterility, 2003;80(6): 1488-1494.
- 12. Catherino, W. H., Eltoukhi, H. M., & Al-Hendy, A. Racial and ethnic differences in the pathogenesis and clinical manifestations of uterine leiomyoma. In Seminars in reproductive medicine. Thieme Medical Publishers. 2013, September; 31(05): 370-379.
- 13. Wise, L. A., Palmer, J. R., Harlow, B. L., Spiegelman, D., Stewart, E. A., Adams-Campbell, L. L., & Rosenberg, L. Risk of uterine leiomyomata in relation to tobacco, alcohol and caffeine consumption in the Black Women's

- Health Study. Human reproduction, 2004;19(8): 1746-1754.
- 14. Wise, L. A., Palmer, J. R., Harlow, B. L., Spiegelman, D., Stewart, E. A., Adams-Campbell, L. L., & Rosenberg, L. Reproductive factors, hormonal contraception, and risk of uterine leiomyomata in African American women: a prospective study. American journal of epidemiology, 2004;159(2): 113-123.
- Wise, L. A., Palmer, J. R., Spiegelman, D., Harlow, B. L., Stewart, E. A., Adams-Campbell, L. L., & Rosenberg, L. Influence of body size and body fat distribution on risk of uterine leiomyomata in US black women. Epidemiology (Cambridge, Mass.), 2005;16(3): 346.
- Lobel, M. K., Somasundaram, P., & Morton, C.
 C. The genetic heterogeneity of uterine leiomyomata. Obstetrics and Gynecology Clinics, 2006;33(1): 13-39.
- 17. Chiaffarino, F., Parazzini, F., La Vecchia, C., Chatenoud, L., Di Cintio, E., & Marsico, S. Diet and uterine myomas. Obstetrics & Gynecology, 1999;94(3): 395-398.
- 18. Evans, P., & Brunsell, S. Uterine fibroid tumors: diagnosis and treatment. American family physician, 2007;75(10): 1503-1508.
- Terry, K. L., De Vivo, I., Hankinson, S. E., & Missmer, S. A. Reproductive characteristics and risk of uterine leiomyomata. Fertility and sterility, 2010;94(7), 2703-2707.
- 20. Wilson, I. H., Yamey, G., & Yip, W. John G Meara, Andrew JM Leather, Lars Hagander, Blake C Alkire, Nivaldo Alonso, Emmanuel A Ameh, Stephen W Bickler, LesongConteh, Anna J Dare, Justine Davies, Eunice DérivoisMérisier, Shenaaz El-Halabi, Paul E Farmer, Atul

- Gawande, Rowan Gillies, Sarah LM Greenberg, Caris E Grimes, Russell L Gruen, Edna Adan Ismail, ThaimBuyaKamara, Chris Lavy, Ganbold Lundeg, Nyengo C Mkandawire, Nakul P Raykar, Johanna N Riesel, Edgar Rodas, John Rose, Nobhojit Roy, Mark G Shrime, Richard Sullivan, Stéphane
- Meara JG, Leather AJM, Hagander L, et al. Global Surgery 2030: evidence and solutions for achieving health, welfare, and economic development. The Lancet. 2015;386(9993):569-624.
- Kim, J. Y., Farmer, P., & Porter, M. E. Redefining global health-care delivery. The Lancet, 2013;382(9897): 1060-1069.
- 23. Atun R, de Andrade LOM, Almeida G, et al. Health-system reform and universal health coverage in Latin America. The Lancet. 2015;385(9974): 1230-1247.
- 24. Mullan, F. Health, equity, and political economy: a conversation with Paul Farmer. Health Affairs, 2007;26(4): 1062-1068.
- Grimes, C. E., Bowman, K. G., Dodgion, C. M., & Lavy, C. B. Systematic review of barriers to surgical care in low-income and middle-income countries. World journal of surgery, 2011;35: 941-950.
- 26. Anderson, M. W. The metrics of workforce planning. Public Personnel Management, 2004; 33(4): 363-378.
- 27. De Wolf, A. H., & Toebes, B. Assessing private sector involvement in health care and universal health coverage in light of the right to health. Health and Human Rights, 2016;18(2): 79.