



A REVIEW ON UTERINE FIBROID

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ABSTRACT:

Uterine fibroids are a major cause of morbidity in women of a reproductive age (and sometimes even after menopause). Uterine fibroids (also known as leiomyomas or myomas) are the most common form of benign uterine tumors. Clinical presentations include abnormal bleeding, pelvic masses, pelvic pain, infertility, bulk symptoms and obstetric complications. According to the studies, uterine fibroids are more commonly observed in women of African ancestry than white women. This article aims to educate readers on some fundamental concepts regarding uterine fibroids, such as the different types of fibroids according to various classification schemes, as well as their etiology, epidemiology, pathogenesis, management, and treatment, all of which must be understood by anyone studying medicine or working in the medical field.

Keywords: Myomas, Leiomyomas, pain, Surgery and Treatment.

1.INTRODUCTION

The “fibroid” term was introduced by Rokitansky (1860) and Klob (1863), while Virchow, the famous German pathologist, demonstrated that those tumors originated from the uterine smooth muscles. The most prevalent type of benign tumor in smooth muscle cells of the uterus or the female reproductive organ is uterine fibroids. They are monoclonal tumors of uterine smooth muscle, thus originating from the myometrium. They are composed of large amounts of extracellular matrix (ECM) containing collagen, fibronectin and proteoglycans. They may be asymptomatic or cause a range of severe and chronic symptoms. Uterine fibroids are the most common neoplasm affecting women, and it has been postulated that they occur in over 70% of women by the onset of menopause. Even though their pathogenesis is not clearly known, there is considerable evidence that estrogens and progestogens proliferate tumor growth.

They are classified by their location relative to the layers of the uterus and can be single or multiple; (Subserous, intramural or submucous). In the postpartum period, women with fibroids have an increased risk of postpartum hemorrhage secondary to an increased risk of uterine atony.²⁰ The risk of malignancy for uterine fibroids is very low; the prevalence of leiomyosarcoma is estimated at about one in 400 (0.25%) women undergoing surgery for fibroids.²¹ Because the natural course of fibroids involves growth and regression, enlarging fibroids are not an indication for removal. They are more common in obese women and probably have some genetic determinant and they are less common in smokers. Majority of fibroids grow as women gets older, and tend to shrink after menopause.

II. EPIDEMIOLOGY:

The prevalence of fibroids has been historically underestimated by epidemiologic studies which focused mainly on symptomatic women, leaving behind a large population of asymptomatic women and women who underreport their symptoms. The prevalence of fibroids varies among different studies and countries (4.5%–68.6%) based on the type of investigation, method of diagnosis, and racial ethnic demographics of the population studied. Fibroids are rare before puberty, increase in prevalence during the reproductive years, and decrease in size after menopause. Aromatase in fibroid tissue allows for endogenous production of estradiol, and fibroid stem cells express estrogen and progesterone receptors that facilitate tumor growth in the presence of these hormones.

III. ETIOLOGY

3.1 Race and Age

A study carried out in USA with randomly selected women between the age of 35 and 49 years (who were screened by self-report, medical record and sonography) showed that the incidence of uterine fibroids by age 35 was 60% among African-American women, increasing to 80% by age 50, whereas Caucasian women showed an incidence of 40% by age 35, and almost 70% by age 50. Moreover, delaying the first pregnancy until the third decade of life also places women at higher risk of uterine fibroids.

3.2 Early Menarche

Early age of menarche is also a risk factor for other hormonally mediated conditions such as endometrial and breast cancers. The biological mechanisms are not understood, and they may or may not be the same for the different hormonally mediated conditions.

3.3 Parity and Pregnancy

Pregnancy has been found to have a protective effect on the development of uterine fibroids, but the mechanism remains unclear. Ischemia during parturition has also been proposed as a mechanism. Thus, it may be implied that fibroid tissue could be highly susceptible to ischemia during both parturition and remodeling.

3.4 Caffeine and Alcohol

An association has been reported between alcohol and caffeine intake and an increased risk of developing uterine fibroids in a study concerning the health of women of African origin. Current drinkers had significantly higher risks than women who had never consumed alcohol, and there appears to be a dose response for both duration of alcohol consumption and number of drinks per day. With regards to caffeine, among women, 35 years of age, the highest categories of caffeinated coffee (3 cups/day) and caffeine intake (500 mg/day) were both associated with increased fibroid risk.

3.5 Other Factors

There is contemporary interest in the influence of dynamics encompassing the likes of uterine infection, hormonal, metabolic, dietary, stress, and environmental factors.

General health status may also be predictive of leiomyoma growth, with factors such as obesity and high blood pressure playing a role. A diet rich in red meat appears to increase the risk of developing leiomyomas, while smoking decreases the risk, for unknown reasons.

IV. TYPES OF UTERINE FIBROIDS

Growth and location are the main factors that determine if a fibroid leads to symptoms and problems. When the receptors are present in the fibroid, the growth of the fibroid will be stimulated by these hormones. The cause of fibroid development is not fully understood. All cells of one fibroid are the same and different to the cells of another fibroid of the same woman (this is called monoclonal cells). Classification of fibroids is according to their site in the uterine wall:

- Subserosal fibroids are found superficially under the outer lining of the uterus, the serosa. They can grow to the interior part of the wall or completely under the serosa and become pedunculated with only a thin bridge to the myometrium.
- Intramural fibroids are the most common. They are situated in the middle layer of the uterine muscle.
- Submucosal fibroids grow in the myometrium near the inner lining of the uterus, called endometrium. Like the subserous fibroids, they can become pedunculated and protrude into the uterine cavity.
- Uncommon sites are the ligaments of the uterus. These fibroids are difficult to manage surgically as they are often near other structures such as the ureters, vessels and nerves and should only be attempted by experienced surgeons.

V. THEORIES OF FIBROID FORMATION

Despite the major public health impact of leiomyomas, little is known about their cause. The most important aspect of the etiology of

fibroids - the initiator(s)-remains unknown. Several theories have been advanced. One hypothesis states that increased levels of estrogen and progesterone result in an increased mitotic rate that may contribute to myoma formation by increasing the likelihood of somatic mutations. Another favors an inherent abnormality in the myometrium of individuals who develop fibroids, based upon the finding of significantly increased levels of estrogen receptors (ER) in the myometrium of fibroid. More recently, growth factors have been shown to mediate the growth-promoting effects of estrogen and play an important role in the development of fibroid tumors. Growth factors, proteins/ polypeptides produced locally by smooth muscle cells and fibroblasts control the proliferation of cells and appear to stimulate myoma growth, primarily by increasing the extracellular matrix. Some of the identified myoma-related growth factors are transforming growth factor- β (TGF- β), basic fibroblast growth factor (bFGF), epidermal growth factor (EGF), platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), insulin-like growth factor (IGF), and prolactin. Growth factors affect cells in complex ways, and the response to combinations of growth factors may be different from the response to an individual factor. Many of these growth factors are overexpressed in myomas and either increase smooth muscle proliferation (TGF β , bFGF), increase DNA synthesis (EGF, PDGF), stimulate synthesis of extracellular matrix (TGF- β), promote mitogenesis (TGF- β , EGF, IGF, prolactin), or promote angiogenesis(bFGF, VEGF). The steroid hormones, estrogen and progesterone, are considered the most important regulators of leiomyoma growth. Leiomyomas grossly appear as round, well circumscribed (but not encapsulated), solid nodules that are white or tan and show whorled appearance on histological section. Microscopically, tumor cells resemble normal cells (elongated, spindle shaped, with a cigar shaped nucleus) and form bundles with different .these cells are uniform in size and shape with scarce mitosis

5.1 Clinical Features

Approximately 50% cases of uterine fibroids are symptomless, however in symptomatic women, the symptoms differ on the basis of size, situation and number of the tumors. Submucosal fibroids usually present with maximum symptoms. In symptomatic females the most common presentation is menorrhagia. Menorrhagia in Indian setting can be life threatening as owing to the low socioeconomic status; the patient is usually anemic which gets further aggravated by menorrhagia.

Pain in fibroids may be indicative of degeneration. Dysmenorrhea and pelvic pain impair the quality of life of the patient. Fibroid also gives rise to pressure symptoms like bowel abnormality, urinary frequency, pain in lower back, constipation, pressure in the pelvic region, urinary retention, etc. Uterine fibroids most commonly submucous fibroids can also lead to infertility and recurrent abortions. Various mechanisms have been suggested for infertility caused by uterine fibroids like by altering the anatomy of the uterus, impairment of the blood supply of endometrium and myometrium as well as increased contractility of uterus. Leiomyomas are also considered to significantly accentuate the risk of cesarean delivery to 33.1% from 24.2 % when compared to a control group in a large retrospective study. The study also proved a greater risk of breech delivery upto 5.3%, preterm delivery upto 15.1%, intrauterine fetal demise and growth retardation up to 3.9% as well as increased risk of premature rupture of membranes up to 3.3%. The chance of undergoing malignant transformation for a uterine fibroid is very low.

VI. SYMPTOMS

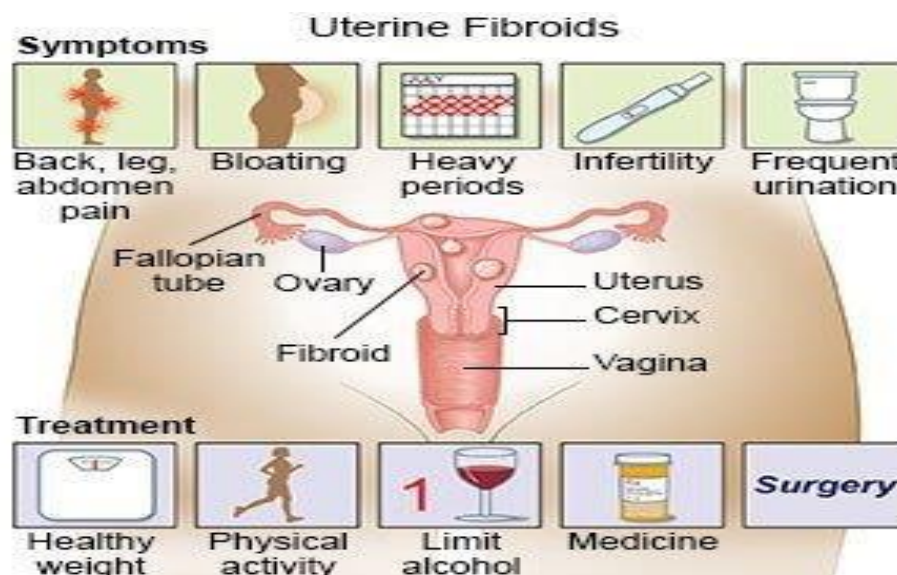


Fig. 1 Symptoms of uterine fibroid

The most common symptoms of women with fibroids are pressure symptoms and heavy periods. An enlarged womb will place pressure on the bladder giving increased symptoms. Up to 70% of fibroids are asymptomatic and may be incidentally diagnosed during radiologic procedures conducted for other indications.

Asymptomatic fibroids do not require treatment or frequent follow-up. Symptomatic fibroids, based on their size and location in the uterus, can manifest with bulk symptoms

- Heavy menstrual bleeding or painful periods.
- Longer or more frequent periods.
- Pelvic pressure or pain.
- Frequent urination or trouble urinating.
- Growing stomach area.
- Constipation.
- Infertility.
- Pain in the stomach area or lower back, or pain during sex.

Pregnancy-associated symptoms: spontaneous abortion, recurrent abortion, abdominal pain and pressure signs in pregnancy, premature rupture of membranes, dystocia and post-partum hemorrhage. Several studies have shown that women with fibroids, as a result of their associated symptomatology, have a higher risk of developing emotional distress, depression, and anxiety, which can strongly impact their quality of life.

VII. DIAGNOSIS

The evaluation of fibroids is based mainly on the patient's presenting symptoms abnormal menstrual bleeding, bulk symptoms, pelvic pain, or findings suggestive of anemia. The diagnosis is likely if bimanual pelvic examination detect an enlarged, mobile, irregular uterus that is palpable above the pelvic symphysis. Confirmation requires imaging. Gynecologic ultrasonography (ULTRASOUND) has evolved as the standard tool to evaluate the uterus for fibroids.

- Ultrasound
- Lab test
- Magnetic resonance imaging (MRI)
- Hysterosonography
- Hysterosalpinogography
- Hysteroscopic myomectomy
- Laparoscopic myomectomy
- Laparoscopic hysterectomy

7.1 Ultrasonography

Ultrasonography using the trans abdominal and trans vaginal routes has been employed most frequently, due to its accessibility and relatively low cost. While cost-effective instrument, ultra sound has been criticized for its significant operator-dependence, resulting in inferior reproducibility when compared to MRI. Ideally, both trans abdominal and trans vaginal scans should be performed. Therefore ultrasound examination should include the urinary tract whenever a large pelvic mass is identified. The diagnosis of fibroids on ultrasound is usually reasonably straightforward though focal adenomyosis can mimic a fibroid and a pedunculated uterine fibroid can sometimes be mistaken for an adnexal mass. When there is doubt about the origin of a pelvic mass at ultrasound further evaluation with MRI should be performed

7.2 Lab Test

There might be a routine investigation standards setup in your laboratory for certain conditions or likely operations. For patients with uterine fibroids make sure they contain at the minimum the following.

- Hb to assess the amount of anemia which will help you to decide whether the patient needs an operation or not and whether

you may need a blood transfusion.

- Erythrocyte sedimentation rate (ESR) or white blood cell (WBC) count to know if there is preexisting infection.
- Blood grouping and cross-matching for operation or to correct anemia prior to operation.
- Urinalysis to detect UTI as a source of postoperative infection prior to operation.

7.3 Magnetic Resonance Imaging (MRI)

Thus, MRI is more sensitive in identifying uterine fibroids than ultrasound, does not involve the use of ionizing radiation, and it can readily demonstrate the uterine zonal anatomy. Submucosal, intramural, and subserosal fibroids are usually easily differentiated with MRI, and fibroids as small as 5 mm in diameter can be demonstrated. Fibroids in relatively unusual locations, such as within the cervix, can also be identified. MRI can be very helpful when investigating suspected acute fibroid complications when the patient presents to the emergency department, and it is also a valuable tool that can be used to both predict and assess the response of fibroids to uterine artery embolization (UAE). Uterine fibroids are composed of a combination of smooth muscle cells and fibrous connective tissue. As these masses enlarge, they commonly outgrow their blood supply and undergo varying degrees of necrosis, which accounts for their variable signal intensities on MRI.

7.4 Hysteroscopic Myomectomy:

Over the last 30 years, advances in instruments and techniques have promoted hysteroscopic myomectomy to the rank of a standard minimally invasive surgical procedure for submucous myomas. Small fibroids (<2cm) are now routinely removed in an outpatient setting according to the technique described by Bettocchi. Depending on personal experience and available equipment, the gynecologist has a choice of several alternative procedures. The first involves cutting the base of pedunculated fibroids with either the resectoscopic loop or laser fiber. The second alternative is a complete excision of fibroids by a one-step procedure. The most commonly used approach is the slicing technique. Repeated and progressive passage of the cutting loop allows the surgeon to cut the myoma into small chips. The operation is considered complete when the fasciculate fibers of the myometrium are visualized. Hysteroscopic resection is effective and safe and should be considered the technique of choice for type 1 myomas. The development of intrauterine morcellators has facilitated the implementation of hysteroscopic myomectomy. If the myoma is large (>3 cm in diameter), there is an increased risk of operative complications (perforation, bleeding and fluid extravasation) and damage to surrounding myometrium due to use of electrosurgery. Interestingly, Casadio et al., (2011) demonstrated that during surgery, myometrial thickness increases when myoma slices are removed, leading to protrusion of the intramural component into the uterine cavity.

7.5 Hysterosalpinography

Hysterosalpingography (his-tur-o-sal-ping-GOG-ruh-fee) uses a dye to highlight the uterine cavity and fallopian tubes on X-ray images. Your doctor may recommend it if infertility is a concern. This test can help find out if your fallopian tubes are open or are blocked, and it can show some submucosal fibroids. A doctor or technician places a slender catheter inside your cervix. It releases a liquid contrast material that flows into your uterus. The dye traces the shape of your uterine cavity and fallopian tubes.

7.6 Hysterosonography

Hysterosonography (his-tur-o-suh-NOG-ruh-fee) uses sterile salt water called saline to expand the space inside the uterus, called the uterine cavity. This makes it easier to get images of submucosal fibroids and the lining of the uterus if you're trying to get pregnant or if you have heavy menstrual bleeding. Another name for hysterosonography is a saline infusion sonogram. Hysterosonography distinguishes normal cavities from pathologic ones, endometrial atrophy from mucosal anomalies, polyps from myomas. Conversely, endometrial biopsy is still necessary for diagnosis of hyperplasia or cancer. Hysterosonography can also be proposed for first trimester bleedings, trophoblast retention or ectopic pregnancy.

7.7 Laparoscopic Myomectomy (LM)

Laparoscopic myomectomy is perceived by many gynecological surgeons to be more difficult, but the advantages are real: less severe post-operative morbidity, faster recovery with laparoscopic procedures and no significant difference between reproductive outcomes. Laparoscopic myomectomy is a minimally invasive treatment for patients, especially those wishing to maintain their fertility sparing potential. While this surgery requires intensive training in surgical skills such as intracorporeal suturing and specimen extraction, patients can also expect less adhesion and a quick return to normal activity. This surgery can be broken into three stages, each presenting its own specific and unique challenges- enucleation, reapproximation of the myoma bed, and specimen extraction. Recently,

minimally invasive surgery is becoming a more popular intervention and the number of myomectomy surgeries using laparoscopy are increasing. There are two types of such surgeries. One is laparoscopic myomectomy (LM), the other is Laparoscopically-Assisted Myomectomy (LAM).

LM is defined as the enucleation and preparation of the myoma bed and extraction, all being performed totally laparoscopically. With LAM, a small incision, around 3 to 6 cm, is made in the lower abdomen and the suturing of the myoma bed and extraction are performed via this opening. In LAM, an abdominal incision retractor or Lap Disc Mini is used. In LM, intracorporeal suturing is necessary, resulting in an increase in the difficulty of this surgery.

7.8 Laparoscopic Hysterectomy

Laparoscopic hysterectomy is a vaginal hysterectomy performed with aid of a laparoscope, a thin, flexible tube containing a video camera. Thin tubes are inserted through tiny incisions in the abdomen near the navel. The uterus is then removed in sections through the laparoscope tube or through the vagina. Hysterectomy has long been considered standard surgical treatment for symptomatic intramural and submucous fibroids, particularly for women not wishing to conceive or those of premenopausal age (40–50 years). It is a minimally invasive procedure that is designed to replace abdominal hysterectomy. It has been well established that patients who have a laparoscopic hysterectomy have less pain, less bleeding, less risk of infection and are quicker to return to work and normal activities than women who have an abdominal hysterectomy.

VIII. TREATMENT

The treatment of fibroids should not only be directed toward improving symptomatology, but also influenced by the patient's desire for future fertility, desire to retain the uterus, likelihood of achieving treatment goals, and overall health status. Treatment options improve fibroid-associated symptomatology by reducing the size of the fibroids, controlling fibroid-related AUB, or definitively curing the fibroids. Treatment of uterine fibroids should be tailored to the size and location of the tumors; the patient's age, symptoms, desire to maintain fertility, and access to treatment; and the physician's experience.

There are three basically treatment options:

- Expectant therapy
- Medical treatment
- Surgical treatment

8.1 Expectant Therapy

Medical therapies-Gonadotropin-releasing hormone agonists, Preoperative treatment to decrease size of tumors before surgery or in women approaching menopause Decrease blood loss, operative time, and recovery time.

- Levonorgestrel-releasing intrauterine system (Mirena), Treats abnormal uterine bleeding, likely by stabilization of endometrium Most effective medical treatment for reducing blood loss; decrease fibroid volume.
- Nonsteroidal antiinflammatory drugs, Anti-inflammatories and prostaglandin inhibitors Reduce pain and blood loss from fibroid.
- Oral contraceptives, Treat abnormal uterine bleeding, likely by stabilization of endometrium Reduce blood loss from fibroids; ease of conversion to alternate therapy if not successful.
- Tranexamic acid (Cyklokapron) Antifibrinolytic therapy Reduces blood loss from fibroids; ease of conversion to alternate therapy.

8.2 Surgical therapies

Hysterectomy³⁹ - Surgical removal of the uterus (transabdominally, transvaginally, or laparoscopically) Definitive treatment for women who do not wish to preserve fertility; transvaginal and laparoscopic approach associated with decreased pain, blood loss, and recovery time compared with transabdominal surgery.

- Myomectomy⁴¹- Surgical or endoscopic excision of tumors Resolution of symptoms with preservation of fertility.
- Uterine artery embolization⁴²- Interventional radiologic procedure to occlude uterine arteries. Minimally invasive; avoids surgery; short hospitalization Recurrence rate > 17% at 30 months.

8.3 Medical Treatment

Medical treatments may decrease symptoms potentially related to fibroids. Although most of them are not capable of treating the tumor

itself and lead to marked decreases in fibroid volume, symptomatic control may still be achieved in many patients, who may prefer treating their conditions medically rather than resorting to invasive procedures.

Table 8.1 Medical Treatment for Uterine Fibroid

Drug class	Action	Benefits	Risks	Side-effects (%)	Authors
COC	Inhibits ovulation; inhibits sex steroid secretion	17% decrease in the risk of leiomyoma growth; decreases bleeding and increases hematocrit	Thromboembolic events; hepatocellular adenoma (rare)	Spotting; mastalgia; headache; gastrointestinal upset	Qin <i>et al.</i> ; Orsini <i>et al.</i>
Progestogens	May inhibit ovulation and sex steroid synthesis; decidualizes endometrium, inducing a "pseudopregnancy" state	Improves bleeding in up to 70%; amenorrhea in up to 30%; may decrease uterine volume in up to 50%	Loss of bone mass (prolonged use of depot MPA)	Irregular bleeding/spotting; ovarian follicular cysts	Venkatachalam <i>et al.</i> ; Ichigo <i>et al.</i>
LNG-IUS	Endometrial atrophy	Reduces bleeding intensity in up to 99%; decreases uterine volume in about 40%	Device expulsion	Ovarian cysts; acne	Kriplani <i>et al.</i> ; Sayed <i>et al.</i>
GnRH-a	Hypoestrogenism due to gonadotrophin secretion inhibition	Uterine volume decrease in up to 50%; high rates of amenorrhea	Loss of bone mass with prolonged use	Hot flashes (>90%); vaginal atrophy; headache; mood disorders	Friedman <i>et al.</i> ; Tummon <i>et al.</i> ; Dawood <i>et al.</i>
SPRM	Inhibits ovulation; inhibits progesterone action on fibroid tissue	Improves bleeding in up to 98% of patients; decreases fibroid volume in up to 53%	Long term endometrial safety is unknown	Benign endometrial changes after short term use	Donnez <i>et al.</i> ; Williams <i>et al.</i>

NSAID: Non-steroid anti-inflammatory drugs, LNG-IUS: Levonorgestrel releasing intrauterine system, COC: Combined oral contraceptive, GnRH-a: Gonadotropin-releasing hormone analog, SPRM: Selective progesterone receptor modulators, MPA: Medroxyprogesterone acetate

8.4 Gonadotropin-releasing hormone (GnRH) agonists and antagonist

Among the GnRH agonists, leuprolide acetate is the most commonly used as a 3.75 mg monthly or 11.25 mg every 3 months intramuscular injection for 3–6 months for the pre-operative treatment of uterine fibroids. . These treat fibroids by blocking the body from making the hormones estrogen and progesterone. This puts you into a temporary menopause-like state. As a result, menstrual periods stop, fibroids shrink and anemia often gets better. GnRH agonists lead to amenorrhea in most women (>98%) and are associated with a 35%–65% decrease in fibroid size within 3 months of treatment initiation. In some cases, this may allow for a minimally invasive surgical approach and may increase preoperative haemoglobin levels. GnRH agonists include leuprolide (Lupron Depot, Eligard, others), goserelin (Zoladex) and triptorelin (Trelstar, Triptodur Kit). Many people have hot flashes while using GnRH agonists. Often, these medicines are used for no more than six months. That's because symptoms return when the medicine is stopped, and long-term use can cause loss of bone. GnRH antagonists include elagolix (Oriahnn) and relugolix (Myfembree). These medicines can treat heavy menstrual bleeding in people with uterine fibroids who haven't gone through menopause. But they don't shrink fibroids. GnRH antagonists can be used for up to two years. Taking them along with add-back therapy can lessen side effects such as hot flashes and bone loss. At the present time, the use of GnRH antagonists such as cetrorelix and ganirelix acetate is uncommon. Despite their immediate clinical response, they are more expensive than GnRH agonists, and have a shorter half-life requiring daily injections. However, a new orally administered GnRH antagonist (elagolix), which was approved in the United States as a drug for the treatment of moderate to severe endometriosis-associated pain, has been shown to be also effective in reducing menstrual bleeding and uterine volume in women with fibroids in a recently published clinical trial.

8.5 Selective progesterone receptor modulators and anti-progestins

SPRMs and anti-progestins act at the level of the peripheral progesterone receptors by inducing apoptosis, inhibiting cellular proliferation of the fibroid and thinning the endometrial lining. Ulipristal acetate (5–10 mg orally once a day) has been associated with 25%–50% fibroid shrinkage, and greater than 90% uterine bleeding control in initial studies based in Europe (PEARL trial). SPRM that has been approved and commercialized as a 3-month pre-operative adjuvant therapy and, more recently, as intermittent treatment of moderate to severe fibroid symptoms for up to four courses. However, it is not currently available in other countries such as the United States, in part because of concerns over rare but severe cases of liver toxicity.

8.6 Progestin-releasing intrauterine device (IUD)

A progestin-releasing IUD can relieve heavy bleeding caused by fibroids. It only relieves symptoms, though. It doesn't shrink fibroids or make them go away. It also prevents pregnancy.

8.7 Non-steroidal anti-inflammatory agents

Dysmenorrhea induced by fibroids involves the use of NSAIDs due to their low cost, limited adverse effects, and general availability.¹⁹ The most commonly used agents are ibuprofen (600–1800 mg daily) or naproxen (550–1100 mg daily) which are most efficacious when started a day or two before the onset of menses and continued for the duration of menstruation. NSAIDs work by inhibiting the enzyme cyclooxygenase and lowering the production of pro-inflammatory prostaglandins and have been shown to improve dysmenorrhea and menorrhagia. NSAIDs should be avoided in women with known hypersensitivity to this class of medications, active gastric or peptic ulcers, or renal disease.

8.8 Tranexamic acid

The synthetic lysine derivative, tranexamic acid, is an antifibrinolytic agent and promoter of blood clot formation. Tranexamic acid (lysteda, cyklokapron). This nonhormonal medicine can ease heavy menstrual periods. You take it only on heavy bleeding days. Most commonly, it is administered at a dose of two 650 mg tablets orally three times a day for up to 5 days. It is associated with rare and mild adverse effects including gastrointestinal and musculoskeletal symptoms, and it is contraindicated for patients with color blindness, active bleeding and history of intravascular clotting or hypersensitivity to the medication.

8.9 Combined hormonal contraceptives

Combined estrogen–progesterone contraceptives, in the form of pills, vaginal devices, or transdermal patches, used cyclically or continuously, are commonly used for the treatment of AUB, including in women with uterine fibroids. They mainly tend to keep the endometrium thin and decrease the amount of endometrial shedding during the menstrual cycle. Fibroid-associated AUB, haemoglobin concentration, and quality of life were found to be improved in women who used combined oral contraceptives compared to placebo, however they performed less well than progestin-releasing intrauterine devices (IUD).²² Medical eligibility criteria such as age, smoking, history of venous thrombosis, and migraines with aura should be reviewed with the patient before recommending the use of any combined hormonal contraceptives as well as adverse effects including nausea, headaches, and irregular bleeding.

8.10 Iron supplementation

Since fibroids are often associated with heavy and prolonged menstrual bleeding, they can cause iron-deficiency anaemia for which iron supplementation is a justified adjuvant treatment. Several oral formulations (150–200 mg of elemental iron daily) are available containing iron dextran, iron sucrose, or ferric gluconate.²⁸ In severe or unresponsive cases, or in cases where the patient is unable to tolerate oral iron, intravenous iron can be an option although significantly more expensive and potentially unavailable in low-resource settings.²⁸ The most common adverse effects of oral iron are gastrointestinal symptoms, while intravenous administration can cause allergic reaction (urticaria and pruritus) and musculoskeletal pain. Blood transfusion may be used as a last resort in unstable patients or after failed iron treatment.

8.11 Aromatase inhibitors

These agents suppress the activity of the enzyme aromatase, responsible for the conversion of androgens into estrogens. It has been observed that UF cells may carry an intrinsic capacity of secreting estrogens due to the expression of aromatase, leading to the experimental use of this class of drugs in the treatment of UF. A promising class of agents for the treatment of uterine fibroids in premenopausal women includes aromatase inhibitors such as letrozole and anastrozole. s. Aromatase inhibitors such as letrozole (2.5 or 5 mg orally once a day) and anastrozole (10 mg orally once a day) induce a hypoestrogenic state by inhibiting the aromatization of androgens to estrogens which results in thinning of the endometrial lining and reduced menstrual bleeding.

8.12 Danazol

Danazol is a synthetic steroid, structurally similar to testosterone, which has an inhibitory action over sex-steroids synthesis and directly inhibits the progesterone receptor. It was more frequently used in the treatment of endometriosis, but its efficacy in the treatment of UF was assessed by some studies. A small study involving 20 women has demonstrated significant tumor volume reduction (23.6% ± 5%) and partial to complete symptomatic improvement, which persisted after 6 months of treatment withdrawal. Danazol has significant adverse effects due to its androgenic action, including weight gain, acne and hirsutism.

8.13 Surgical Treatment

Surgical management options include myomectomies, hysterectomies, laparoscopic radiofrequency volumetric thermal ablation, and

endometrial ablation.

8.14 Myomectomy

Myomectomy is a uterine-sparing procedure that involves removing the fibroids but leaving the uterus intact. It is most often offered to patients who desire future fertility but is also considered by those who have completed childbearing and wish to retain their uterus.

Myomectomy is a uterine-sparing procedure that involves removing the fibroids but leaving the uterus intact. It is most often offered to patients who desire future fertility but is also considered by those who have completed childbearing and wish to retain their uterus.

Myomectomy provides temporary reduction in uterine volume and improvement of symptoms in up to 80% of women but is associated with an approximately 27% risk of recurrence after removal of a single fibroid, and greater than 50% in the case of multiple fibroids.

Women who undergo myomectomy report improvement in fibroid symptoms, including decreased heavy menstrual bleeding and pelvic pressure. For women who desire future childbearing and have significant uterine wall disruption during surgery, cesarean delivery prior to the onset of labor is recommended over vaginal delivery because of its association with an increased risk of a devastating maternal and neonatal consequence such as uterine rupture (approximate risk <2%).

8.15 Hysterectomy:

Hysterectomy is the surgical removal of the uterus. The ovaries may also be removed, although this is not necessary for fibroid treatment. Hysterectomy remains the only definitive surgical treatment for symptomatic fibroids. This is not an appropriate procedure for women who have not completed childbearing and/or who simply wish to retain their uterus. Following hysterectomy, the majority of women report a significant improvement in quality of life and symptomatology as early as 3 months after surgery. 7 During minimally invasive myomectomies and hysterectomies, sharp morcellation techniques can be used to remove fibroids and/or myomatous uteri in well counseled women.

Types of Hysterectomy Procedures:

- Abdominal hysterectomy
- Vaginal hysterectomy
- Laparoscopically assisted vaginal hysterectomy (LAVH)
- Total laparoscopic hysterectomy
- Robotic-assisted laparoscopic hysterectomy

8.16 Total Abdominal Hysterectomy

Total abdominal hysterectomy (TAH) has been the traditional procedure. It is an invasive procedure that is best suited for women with large fibroids, when the ovaries also need to be removed, or when cancer or pelvic disease is present. The surgeon makes a 5- to 7-inch incision in the lower part of the belly. The cut may either be vertical, or it may go horizontally across the abdomen, just above the pubic hair (a bikini cut). The bikini cut incision heals faster and is less noticeable than a vertical incision, which is used in more complicated cases or with very large fibroids. The patient may need to remain in the hospital for 3 to 4 days, and recuperation at home takes about 4 to 6 weeks.

8.17 Vaginal Hysterectomy

The American College of Obstetricians and Gynecologists (ACOG) recommends vaginal hysterectomy as the first choice, when possible. Vaginal hysterectomy requires only a vaginal incision through which the uterus is removed. The vaginal incision is closed with stitches.

8.18 Robotic Hysterectomy:

Robotic-assisted hysterectomy is a type of laparoscopic hysterectomy, but the surgical instruments are attached to a robot. The surgeon uses a computer console in the operating room to guide the robot's movements. The American College of Obstetricians and Gynecologists (ACOG) advises that robotic hysterectomy is best suited for complex hysterectomies. Before choosing robotic hysterectomy, it is important to find a surgeon who has extensive training and experience with this technique.

8.19 Laparoscopic radiofrequency volumetric thermal ablation:

Radiofrequency volumetric thermal ablation (RFVTA) is a laparoscopic outpatient procedure performed under ultrasound guidance

which uses an electro-surgical probe, inserted within the fibroid, to induce coagulative myolysis. Available data demonstrate promising results indicating improvement in symptom severity and shrinkage of the fibroids (up to 77% volume reduction at 6 months) with a relatively low rate of reintervention (11%), shorter hospital stay, and lower blood loss compared to laparoscopic myomectomies. However, there is still limited information regarding subsequent pregnancy or long-term outcomes and only few centers are currently offering this treatment option.

8.20 Endometrial ablation:

Endometrial ablation destroys the lining of the uterus. The treatment does not shrink the fibroid(s) but can help to decrease heavy menstrual bleeding caused by fibroids. Good candidates for endometrial ablation, as an option for the management of fibroid-associated AUB, are pre-menopausal women who have completed childbearing. Thermal balloon, microwave, hydrothermablation, bipolar radiofrequency endometrial ablation, or endometrial cryotherapy devices are used to achieve endometrial destruction. Desire for future fertility, active pelvic infections, endometrial cancer, and uterine congenital anomalies are contraindications for endometrial ablation. Since this procedure does not prevent future pregnancy and pregnancy after ablation can be associated with abnormal implantation/placentation and several obstetrical complications.

IX. CONCLUSION

In Conclusion, substantial advancement has been achieved in past 10 years, in our understanding of the interaction between steroid hormones, danger issues, stem cells, genetics and epigenetics that affect the pathophysiology and progressive some of uterine fibroids. The systematic review of epidemiology of UFs to analyses the incidence and prevalence of UFs and evaluate the risk factors with large effect. The most practical investigative modality has always been gray scale ultrasonography but with the development of innovative method of treatment, it's not just enough to diagnose the presence of fibroid but also its dynamic relation with surrounding tissue as well. In asymptomatic fibroids do not require treatment once the diagnosis is confirmed by ultrasonography or MRI. Women should be made aware of all available treatment option (medical, radiological and surgical) and why they may or may not be appropriate. The current needs in this population include methods to enhance diagnosis and associated disease, enhance fertility preserving treatment and enhance patients and participation; even its epidemiology has not been fully understood. Future research into prevalent female condition that has significant impact on common health state will undoubtedly find this area to be exciting.

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