Evaluation of different diagnostic and therapeutic modalities in the treatment of uterine fibroids: from the present to the future

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Abstract

Benign tumors that form from the uterine muscle tissue are known as uterine leiomyomas, often known as uterine fibroids. Approximately 70% of the Fibroids are asymptomatic while only 30% of the fibroids presents symptoms such as pelvic discomfort, abnormal uterine bleeding, infertility, menorrhagia and dysmenorrhea. This objective of this study is to evaluate the different diagnostic as well as therapeutic modalities present in the healthcare industry for controlling uterine fibroids. Current treatment strategies are mostly surgical as well as expensive. An alternative to the surgical procedures i.e. the pharmacological treatment is extremely limited. Developing an alternative to the surgical procedures will reduce both cost as well as increases the safety of the patients. An alternative is necessary because surgical methods are not preferred in women who want to maintain their fertility. This evaluation aims to compare all the treatment strategies and look out for the better future of disease management. This study focuses more on therapeutic options available for uterine Fibroids and future prospects for effective management

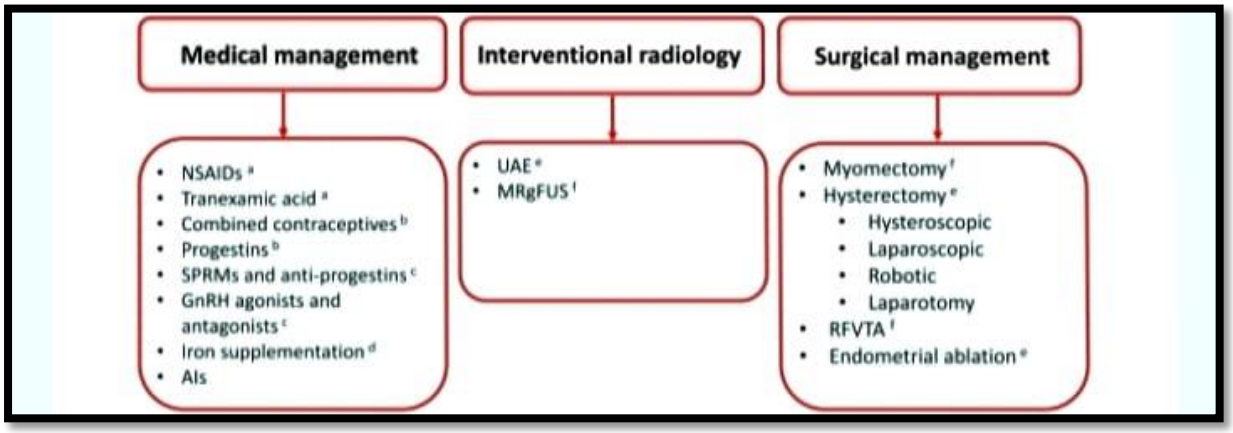
Keywords: Uterine Fibroids, Gynecology, Hysterectomy, Myomectomy.

1. Introduction:

Uterine fibroids, also called uterine leiomyomas or myomas, are benign growths in the uterus made up mainly of smooth muscle cells and fibroblasts. These fibroids are hormonally reactive, particularly to estrogen and progesterone, and typically develop between menarche and menopause. They are the most common cause of hysterectomy and one of the leading reasons for gynecological hospitalizations due to symptoms like heavy menstrual bleeding, abdominal pain, frequent urination, and gastrointestinal issues. While fibroids can cause severe symptoms in some women, many remain asymptomatic and are often found incidentally.

Around 70% of women may develop fibroids by menopause, making them one of the most prevalent uterine conditions. Clinical symptoms include abnormal bleeding, pelvic pressure, urinary problems, and back pain. In some cases, fibroids can lead to infertility or pregnancy complications. About 25% of women of reproductive age show clinically significant symptoms requiring treatment.

Diagnosis often involves ultrasonography, and treatment options vary depending on factors like symptom severity, patient age, and fertility concerns. Options include medications, myomectomy (fibroid removal), uterine artery embolization, and hysterectomy. Fibroids can impact fertility, and the costs associated with the condition, including medical treatment and lost work productivity, are substantial. Despite the availability of treatment options, there is a lack of high-quality data on the best practices for managing fibroids, highlighting the need for improved diagnostic tools and access to early treatment.



2. Methodology

STUDY DESIGN

Retro-prospective study.

STUDY SITE

The study was conducted at Shadan institute of medical sciences and research centre.

DURATION OF THE STUDY
The study was conducted for a period of 6 months.

SAMPLE SIZE
80

CRITERIA FOR THE STUDY

Inclusion criteria:

1. Age group: 18 years and above.
2. Patients diagnosed with uterine fibroids.
3. Patients who understood the need for the study and gave consent.

Exclusion criteria:

1. Patient below 18years of age.
2. Patients who were not comfortable with sharing their data

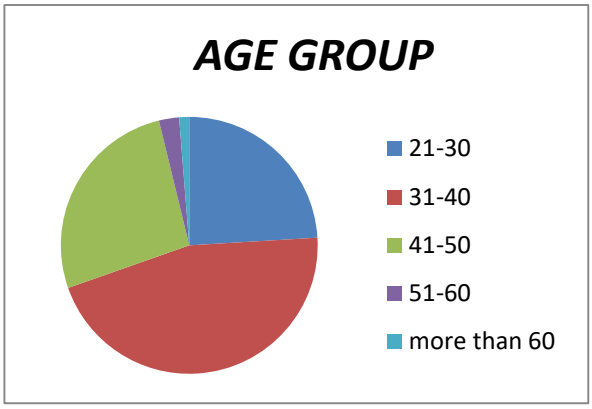
3. Results

Total of 80 patients participated in this study. the data was collected from the patients that includetheir demographic details, menstrual history, medical history,ultrasonography and other diagnostic reports along with their treatment plan. Follow up of the patients included the scans as well as symptomatic changes observed by the patients.

1. The most commonly employed diagnostic tool was found to be**Ultrasonography**followed by **MRI.** CT scans were not used in any of the patient. **Ultrasonography** is most commonlyused because of its low cost and higher safety. Many women were diagnosed with uterine fibroids following their symptoms such as menorrhagia, infertility, etc. Signs and symptoms of uterine fibroids depend on the location of the myoma. Menorrhagia is the most common symptom in intramural and submucosal fibroid while pain and pressure symptoms are common in subserosal fibroids. Differential diagnosis includes adhesions from prior surgeries, pelvic inflammatory disease, endometriosis etc.

Age group

AGE	NO.OF PATIENTS:
LESS THAN 20	0 (0%)
20 – 30	19 (23.25%)
31 – 40	37 (46.25%)
41 – 50	21 (26.25%)
51 – 60	2 (2.5%)
MORE THAN 60	1 (1.25%)



The participants in the study were of the age group **21-65**. Highest prevalence of uterine fibroids was found in the age group **31-40**(46.25%) followed by 41-50 (26.25%), then 20-30 (23.75%), 51-60 (2.5%) and lastly greater than 60 (1.25%). No patients were noted below the age of 20.

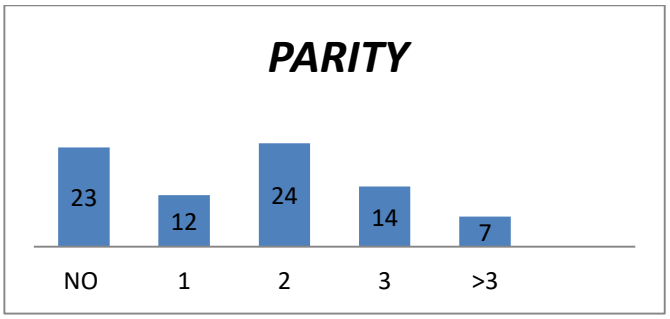
MARITAL STATUS

MARRIED	**76**
UNMARRIED	4

Most of the patients were married (n=76) while only few of them were unmarried (n=4).

PARITY:

PARITY	NO OF PARICIPANTS
NULLIPAROUS	23
ONE CHILD	12
TWO	24
THREE	14
MORE THAN 3	7



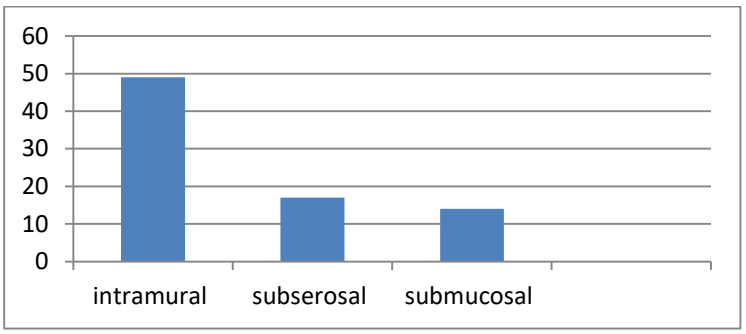
CO-MORBIDITIES

CO MORBIDITY	PATIENTS
PCOS	**12**
DM	**4**
HTN	**3**
HYPOTHYROIDISM	**5**
OTHERS	**15**

The highest comorbid condition was found to be **PCOS** (n=12). other co morbidities apart from the above mentioned were **pelvic inflammatory disease**(n=3), **hepatomegaly** (n=2) **fatty liver** (n=2), **Nabothian cysts** (n=2), **cholelithiasis** (n=2), **UTI** (n=1) and **seizures** (n=1).

TYPE OF FIBROID

FIBROID TYPE	n=
INTRAMURAL	49
SUBSEROSAL	17
SUBMUCOSAL	14



The most common type of fibroid was found to be **intramural fibroid** (n=49) which accounts for **62%** of the total study population followed by **subserosal fibroids** (n=17) which is **21%** and **submucosal fibroid** (n=14) which is **17%** of the total study population.

PATIENTS GETTING TREATED FOR INFERTILITY:

31%(n=25) of women with fibroids were undergoing treatment for infertility caused by fibroids. Out of these 25 women 12 had intramural fibroids, 10 had submucosal fibroids and 3 had subserosal fibroids. The age group affected by infertility in our study was found to be 26 – 39. Fibroids can also increase the chances of abortion/miscarriage. In our study, 17 women had one abortion, 3 had 2 abortions while 5 women never conceived.

Intramural and **submucosal** are found to have more effect on fertility than **subserosal fibroids**. in addition to the location, multiple fibroids can also have negative impact on fertility.Similarly, co-morbid conditions such as polycystic ovarian syndrome/disease (PCOS/PCOD), pelvic inflammatory disease (PID), hypothyroidism, Nabothian cysts can increase the chances of infertility. Age alsohas a significant impact on fertility. Women of younger age can conceive faster than women of older age with fibroids.

The fibroids can affect fertility by:

- Reducing the number of sperms entering the uterus.
- Effect the movement of sperms.
- Reducing the chances of implantation.
- Changing the shape of the uterus and blocking the oviducts.

TREATMENT PREFERRED

TREATMENT	n=
HYSTERECTOMY	31
MYOMECTOMY	23
DRUGS	20
DRUGS +MYOMECTOMY	6

Our study shows that the most preferred treatment was **hysterectomy** followed by **myomectomy** and drugs. Although drugs significantly decrease the fibroid size and have greater reduction in menstrual blood flow still many participants preferred surgical procedures. This can be again due to the age, lack of education and support.In addition to this, our study being based in the rural area, proved it to be difficult for the patients to purchase medications of higher costs and follow the prescribed regimen.

MOST PREFERRED DRUG CLASS

DRUG	n=	Only drug	With myomectomy
Mifepristone	20	16	4
Ulipristal acetate	6	4	2

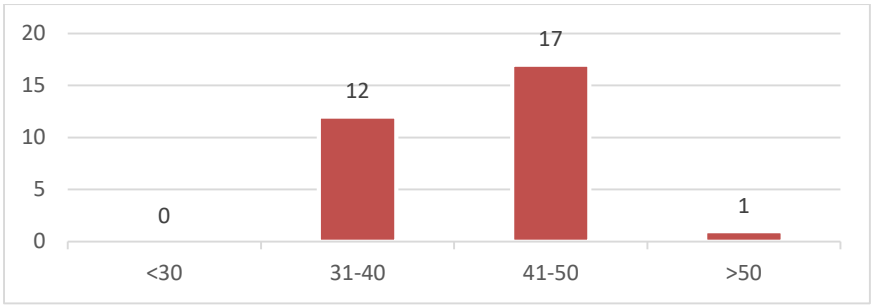
Mifepristone (brand: FIBROEASE 25mg) was found to be a more preferrable drug than **Ulipristal acetate** (brand: FEMIPRISTAL 10 Mg). Although both mifepristone and ulipristal acetate are progestin antagonists, mifepristone is preferred more than ulipristal acetate.This can be attributed to low cost, general availability and the efficacy of mifepristone over ulipristal acetate.

Mifepristone was found to be effective in decreasing the size of fibroid to an extent of **60%** in majority of the cases while the ulipristal acetate showed only **30-40%** decrease in the fibroid size. Hence, health care professionals preferred mifepristone over ulipristal acetate.

Patients opting myomectomy **after being treated with drugs were** being treated for infertility and were anxious to conceive.Using drugs before myomectomy reduces the fibroid size, supresses the neo vascularization and cell proliferation of the leiomyoma cells.

AGE GROUP UNDERGOING HYSTERECTOMY

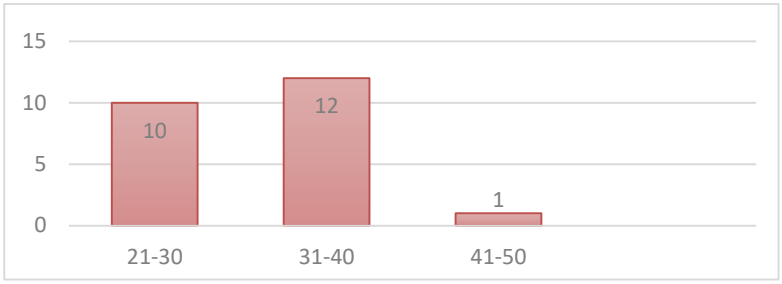
AGE:	n=
<30	0
31 – 40	12
41 – 50	17
>50	1



The age group that preferred hysterectomy more was found to be between **41-50**. This can be attributed to the fact that fertility preservation is not necessary in this age group and hence is easy for patients to undergo this surgical procedure.

AGE GROUP UNDERGOING MYOMECTOMY

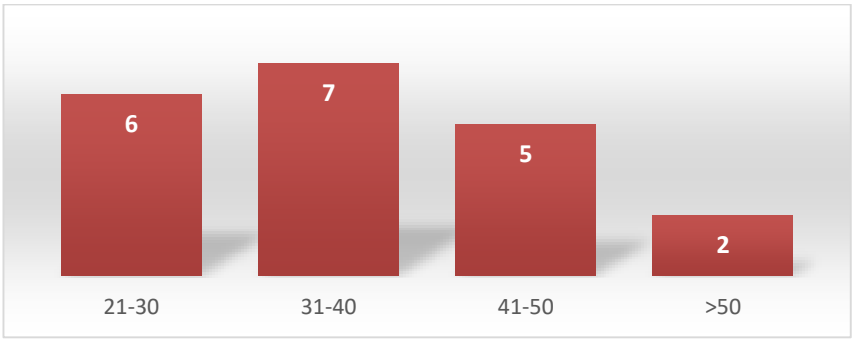
AGE	n=
21-30	10
31-40	12
41-50	1



Most of the women opted myomectomy as it preserves fertility and removes fibroid completely to an extent. However, In3 instances there were cases of the fibroid relapseeven after myomectomy.

AGE GROUP USING DRUGS

AGE	n=
21 – 30	6
31 – 40	7
41 – 50	5
>50	2



Drugs were mostly used in nulliparous and infertile patients. As discussed above, **Mifepristone** was the most preferred drug followed by **Ulipristal acetate**. These drugs provided symptomatic relief in addition to decreasing the size of the fibroid but were not commonly prescribed as they were a lot more expensive.Patients residing in poorly developed areasoften find it difficult to purchase medications of higher costs.As a result, the frequency of hysterectomy and myomectomy can also be greatly reduced by lowering the cost of medicine.

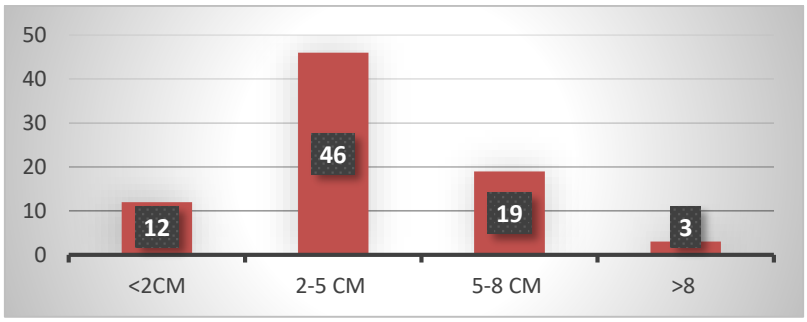
AGE GROUP FOR DRUGS + MYOMECTOMY

AGE	n=
21-30	3
31-40	3

As discussed above patients opting myomectomy after being treated with drugs were seeking treatments for infertility and were anxious to conceive. Using drugs before myomectomy reduces the fibroid size, supresses the neo vascularization and cell proliferation of the leiomyoma cells.

SIZE OF FIBROID

SIZE (in cm)	n=
< 2CM	12
2 – 5 CM	46
5 – 8 CM	19
>8 CM	3



The size of the fibroid alsoaffects the treatment strategy. Larger fibroids need to be removed while the smaller fibroids can be treated by drugs, it is also believed that the greater the size of the fibroid, greater is its effect on fertility. Asymptomatic fibroids are usually single and of smaller size.

4. Discussion

Uterine fibroids are highly prevalent and they pose a high health risk and burden on health care cost. As many of the leiomyomas are asymptomatic, no intervention or treatment is requiredDue to symptoms like menorrhagia, dysmenorrhea, infertility, and pelvic pain, most women seek treatment for leiomyomas. Nulliparous and infertile women are found to be more keen to seek treatment than women with parity. Our study focused on the treatment evaluation of symptomatic fibroids in a tertiary care hospital located in a rural area to demonstrate the effect of other factors such as education, financial background, medication adherence, etc.

A **retro-prospective study** was conducted at Shadan institute of medical sciences and research centre to evaluate different diagnostic and treatment strategies in management of

uterine fibroids.Our study, which involved 80 patients in all, reveals that hysterectomy was the procedure that patients preferred the most, followed by myomectomy and drugs.

The highest prevalence of hysterectomy was found to be in the age group **41-50**(58%).The youngest individual to undergo hysterectomy was **36**years old and the oldest was found to be **65** years old.Although a hysterectomy is a definitive surgical option, it has a number of long-term side effects, including vaginal dryness, mood swings, hot flashes, and increased osteoporosis.Our research revealed that those who choose hysterectomy did not feel the need to maintain their fertility.Higher prevalence of hysterectomy and poor medication adherence were caused by variables such as**lack of education** and **financial support.**

On the other hand, the majority of individuals undergoing myomectomy were doing so to alleviate fibroid-related infertility.Highest prevalence of myomectomy was found in the age group **31-40** (52.17%).Although myomectomy leaves the uterus intact, chances of reoccurrence of fibroids is high.

According to a study conducted during myomectomysurgery,the myometrial thickness increases when myoma slices are removed, leading to protrusion of intramural component into the uterine cavity.

Our study witnessed that patients who were using drugs noted significant relief from symptoms as well as decrease in the size of myoma as evidenced by the ultrasounds and MRI reports. But the drawback of the medications was found to be their higher costs which hindered the patients from following the treatment regimen. Many women in our study confessed that it was difficult for them to purchase the medications even though they noticeda difference in their disease condition. Older women opted surgical procedures after taking drugs for few months following its cost and slower reduction in the symptoms. Medication non-adherence can be due to many factors such as the cost of the drugs, lack of knowledge of dosage regimen, etc. Proper counselling about the disease, drugs and dosage can improve the use of medications and help in delivering better health care in the future.

The last group of our study were patients who used drugs initially for a certain period of time then proceeded to undergomyomectomy. All the patients of this group were seeking treatment for infertility. The age group of patients with drugs followed by myomectomy was **21 – 30** (n=3, 50%) and **31 – 40** (n=3, 50%). 4 patients used drugs for more than 6 months while 2 patients used only for 2 months. The reason for opting myomectomy can be slower reduction of size of fibroid, medication non-adherence, lack of education and financial issues, increasing age (as fertility decreases with increase in age), keen for conceiving, etc. The data about the women who conceived after myomectomy is not present in our study hence we cannot demonstrate the fertility chances following this type of treatment.

Our study concluded that surgical proceduresare still preferred over pharmacological treatment. We tried to mention all the factors affecting the treatment choice. This evaluation will further help the health care professionals in managing leiomyomas considering all the

factors affecting it. The demonstrations in our study will also help the manufacturers to provide an alternative which can be cost effective as well have good clinical efficacy. In this evaluation we focused on the factors affecting the treatment selection and patient compliance for the management. During the sample size collection, we came across many women who were diagnosed with uterine fibroids but were not seeking any kind of treatment due to their **financial condition, absence of symptoms, negligence** and **lack of support**. Proper counselling to these patients can preventdisease progression, help in choosing better treatment approach and avoiding further complications.

Our study had few limitations. In our study we failed to interpret the effect of fibroid size on infertility, the drug selection criteria, chances of conceiving after the treatment, reasons for variations in treatment efficacy, side effects and late complications of the treatment opted. This may be due due to short duration of the study, location of the study, and small sample size

FUTURE PROSPECTS:

To date factors such as extracellular matrix components, cytokines, chemokines, hormones, etc were being implicated in the development of fibroids. But recent studies have shown that development of fibroids is dependent on mRNAregulation and the first event in fibrogenesis is somatic mutation.

Studies are being conducted to understand the effect of genes as well as role of progesterone in fibrogenesis. This can help in targeting genes through gene therapy and development of accurate progesterone antagonists that may treat fibroids at their initial stages in order to avoid surgical procedures. Also, it was noted that certain interventional radiologic procedures such as the **uterine artery embolization, MRgFUS**, endometrial ablation techniques are extremely limited in a developing country like INDIA. Introducing these procedures can reduce the number of hysterectomies, deliver more appropriate and affordable treatment, and reduce the health care costs. Additionally, providing proper counselling to the patient about the disease, drugs and the treatment can also avoid problems arising due to the medication non-adherence, improper dosage, etc.

5. Conclusion

Our study aimed to evaluate the diagnostic and therapeutic modalities in the management of uterine fibroids in patients visiting the gynaecology and obstetrics department of shadan institute of medical sciences and research centre. This evaluation revealed that surgical procedures such as hysterectomy and myomectomy are more preferred than pharmacological management in a rural area. Drugs were found to have good efficacy but were still not commonly used because of their costs, patient compliance, severity of symptoms, age, lack of knowledge and support. Higher prevalence of fibroids was found in the age group 31 – 40 (46.25%), followed by 40 – 50 (26.25%). Hysterectomy (39%, n=31) was found to be the most preferred treatment followed by myomectomy (29%, n=23), pharmacological (25%,

n=20) and myomectomy after drugs (7%, n=6). Mifepristone (n=20) was found to be the most preferred drug followed by ulipristal acetate (n=6). 31 % of women (n=25) were seeking treatment for infertility caused by fibroids. 6 patients who underwent myomectomy after using drugs took pharmacological therapy for an average of 8 months (<6months n = 2) (>6months n= 4).

Several factors were recognised in the treatment selection such as age, parity, financial condition, patient's compliance, willing to preserve fertility, cost of medications, improper knowledge of the disease, medication non–adherence. Removing these barriers can deliver more appropriate management of the disease with minimal complications.

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