

## Research Article

# SONOGRAPHIC IDENTIFICATION OF UTERINE LEIOMYOMAS (FIBROIDS) AND THEIR IMPACT ON FERTILITY – A SYSTEMATIC REVIEW

<sup>1</sup>Anum Sarwar, <sup>2</sup>Syeda Khadija, <sup>3</sup>Muhammad Ateeb Ali Khan, <sup>4</sup>Nazeeha Waseem and <sup>5</sup>Waqas Ali Ghouri

<sup>1</sup>Medical Imaging Doctor, Department of Radiological sciences and Medical Imaging, The University of Lahore, Lahore

<sup>2</sup>Assistant Professor, Department of Radiological Sciences and Medical Imaging, The University of Lahore, Lahore

<sup>3</sup>Technical Engineer, SGS Lahore

<sup>4</sup>Medical Imaging Doctor, Department of Radiological Sciences and Medical Imaging, The University of Lahore, Gujrat

<sup>5</sup>Assistant Director, Pace Groups Pvt. Pakistan

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### ABSTRACT

Fibroids are known to be most common tumors of the female genital tract. These are benign tumours developed in wall of the uterus primarily composed of smooth muscles. Fibroids are having different other names like leiomyoma, leiomyomata, myomas and fibro myomas. Located in different uterine parts and named them according to location in uterus. There is variation in their size from a pea to 10 inches large. The relationship of uterine fibroids with fertility outcomes and their impact on female fertility is still controversial. For identification of uterine fibroids ultrasound can be used as a gold standard. This study is conducted to review different types of fibroids and their impact on fertility. Fibroids effect every age and race of females but its incidence increases with increasing age and according to their type its management is necessary. **Aim:** This review is assembled by different retrospective studies on sonographic identification of uterine leiomyomas and their impact on fertility. **Methods:** All archive Data appropriate to uterine fibroid identification and their impact on fertility from time duration 2005 to 2020 was collected from MEDLINE, PubMed and Cochrane Library. **Results:** There are total 2451 abstracts and 480 full-text articles are studied and accessed. There was a high risk of bias and low-quality evidence but high-quality evidence support that the uterine leiomyomas impact on infertility is still controversial. A lot of studies conducted on it but all these studies provide controversial results. : Leiomyomas impact on fertility but it seems to be that all leiomyomas don't cause infertility and different kind of interventions like myomectomy, uterine fibroids embolization. **Conclusion:** there is an absolute impact of uterine fibroid impact on fertility and its frequency increase with age. Sub mucosal fibroid causes infertility. The relation of intramural fibroid with fertility is controversial and sub serosal fibroid doesn't cause infertility.

**Keywords:** UF, infertility, per abdominal ultrasound, TVS, Myomectomy.

### INTRODUCTION

Fibroids are the most common benign tumors of the female genital track.1 Prevalence of uterine fibroids varies in females based on age, race and method which is used to diagnose it like Ultrasound, MRI etc.2 Fibroids are most commonly diagnosed in females come for investigation of infertility and often diagnosed with uterine fibroids.3 They are mostly asymptomatic and rarely found before menarche and on menopause and regress because they found to be hormonal sensitive and estrogen stimulates its growth.4,5 Sub mucosal fibroids are more hormonal responsive than subserosal.6 7 to 8 out of 10 females having fibroids in their lifetime.7 Fibroids induce chronic inflammation of myometrium and influence its contractility and a hindrance in implantation.8-12 The prevalence rate according to literature is 20 to 50% prevalence varies with age and race. The current study tells that prevalence of uterine fibroid increases with age and also tendency of getting pregnant become lower with increased age and more complicated with family history of fibroids and infertility.13 Majority of fibroids are asymptomatic. Symptoms which attributed to uterine fibroids are pelvic pain, tenderness, bloating, pelvic pressure, heavy menstrual bleeding and infertility. Females which become pregnant in presence of uterine fibroids it significantly effect on fibroid growth.14 Fibroids are composed of cells belong to class of smooth muscles 15 and it arises due to mutation in a single cell of myometrium .16The hormone which is responsible for the growth of fibroid is Estrogen and also there are other growth factors and progesterone which boosted its development.17-18 There are different mechanical factors that influence on fertility with respect

to uterine fibroids like tubal ostia might be due to fibroid present in uterine cavity impact obstruction result in hindrance in sperm and embryo transport. Physiopathological changes in myometrium and endometrium and pressure effect due to fibroid on endometrium elongation and distortion effect the window of implantation.19 In rare cases the uterine fibroids are of different types depends on their location and origin in uterus. Fibroids are found in myometrium while sub mucosal fibroids are found inside the uterus. one type of fibroid which is Intramural found in the wall of uterus on ultrasound and it gives to be a bulging appearance on uterine wall. Fig 1 is showing a trans abdominal ultrasound showing a pelvic scan of uterus in which a subserosal fibroid is evaluated. Sub serosal fibroid cause deterioration in serosal wall of uterus and impact a lot on fertility. Its location is important because management and treatment of fibroid is based on its type and location.20 Grey scale ultrasonography is a Gold standard for the evaluation and diagnosis of uterine fibroids. First step to evaluate and diagnose uterine fibroid is ultrasound in which 2D, 3D, color Doppler and sono hystero-graphy plays their additional part. 2D or grey scale ultrasound helps to evaluate fibroids according to their sonographic features while color Doppler ultrasound help to access blood flow. It is helpful to differentiate it from malignant tumors.21 Different patterns of echogenicity of UF due to different internal composition and degenerations add to diagnostic confusion. Some uterine fibroids having variable features on ultrasound examination like hypo echogenicity and heterogeneous disjunctive mass with posterior shadowing and attenuation, distortion of uterine boundary, calcification, necrosis and degeneration of mass. One of fibroids, known as intramural fibroid grown up in the uterus and expand in size intimate the lining of uterus. On physical gynecological exam it gives feel of bulgy and large uterus Fig 2 showing a trans abdominal image of uterine cavity showing 2 fibroids

\*Corresponding Author: Anum Sarwar,

first image describing sub mucosal and second image is showing intramural fibroid .22 Uterine fibroids evaluation on ultrasound is accurate but some time misdiagnosed by other pelvic pathologies like adnexal masses. Sub serosal pedunculated or exophytic fibroids which have small stalk misdiagnosed as adnexal mass. A laterally bulging fibroid giving appearance of symmetrically bilobed uterus and misdiagnosed as bicorn ute uterus.23 Interstitial fibroids gave confusion about ectopic pregnancy.24 Different patterns of echogenicity of UF due to different internal composition and degenerations add to diagnostic confusion. Uterine leiomyomas are characterized on sonography as antonyms appearance, hypo and heterogeneous echogenicity, distortion and disruption in uterine wall, disconnected mass giving acoustic enhancement and shadowing and degenerative changes. 24 According to different studies the uterine fibroids impact on infertility is controversial like sub serosal fibroids have no impact on fertility. Mostly these are pedunculated having stalk cause abdominal pressure and distention. Intramural fibroid impact on fertility is not described completely it depends on their location and interfaces with endometrium so it may and may not cause infertility. Submucosal fibroid impact endometrial cavity and distort it having impact on fertility and cause infertility. .As shown in fig no 3 in a longitudinal image of uterus taken per abdominally showing a submucosal fibroid 25 for fibroids different methods of management and treatment are used these days myomectomy is gold standard for UF and success rate is considerable in females with submucosal fibroids. Other methods include uterine artery embolization (UAE), hysterectomy, hysteroscopy resection of uterine fibroids, endometrial ablation, MRI guided procedures. There is figure 4 elaborating the uterine fibroid in uterus on different locations.

## SYSTEMATIC REVIEW

Uterine leiomyomas are benign tumors of female genital tract but its impact on fertility is still controversial .hundreds of studies conducted on their relationship. A study was made on the Uterine Leiomyomas impact on female Reproduction by Heather Cook in 2010 by using secondary data on correlation of fibroids and reproduction. They concluded that age and race having relation with fibroids as incidence of fibroids increased by age. Submucosal and intramural myomas are associated with reduced fertility.<sup>1</sup> A study was conducted by Belina Carranza-Mamane on the topic of Uterine Fibroid management in Women if not done result in Infertility in 2015. Literature published by them was retrieved through PubMed, MEDLINE in November 2013 by Cochrane Library. Results of this study was confined to systematic reviews, Randomized observational, Clinical and Control trails. Authenticity of data was identified by using health technology agencies related websites clinical practice guidelines, Clinical trials and national and international medical societies. They concluded by this study that different type of fibroids shows different impact on fertility submucosal fibroid have impact on fertility whereas sub serosal don't have an impact on fertility and intramural might have an impact on fertility.<sup>2</sup> In 2015, Leonidas I. Zepiridis conducted a study on Infertility and Uterine Fibroids by using Secondary data based on meta-analysis made by different authors on using centennial researches on infertility and fibroid relation and they concluded that sub mucosal fibroid of any size and intramural fibroids of size more than 4cm impact fertility and sub serosal fibroid having little or almost no impact on fertility.<sup>27</sup> A research was conducted by P. Puro hit in 2016 on fibroids and infertility and used 42 articles and by their systematic review on basis of evidence he concluded that the relationship between fibroid and infertility is weak. According to him, for getting conclusive results on correlation of fibroids with infertility and impact of uterine leiomyomas on fertility, the types and location of myomas and Impact on endometrium is important. Submucosal fibroids should be treated hysteroscopically. Intramural fibroids

management vary case to case and sub serosal fibroids don't have any major impact on infertility.<sup>28</sup> A review based study was made by Aradhana Khaund on influence of fibroid on reproduction in 2008. A study was conducted for evaluate correlation of fibroids and infertility. For this 2 groups were made of case and control and randomized trials were made on it. Submucosal and intramural fibroids which impede the endometrial cavity cause infertility and by ART rate of successful pregnancy increases and miscarriages decreases.<sup>29</sup> In 2007, Neelan Jana Mukhopadhaya conducted research on UF Impact on Fertility and loss of Pregnancy. It was a systematic review made by using previous studies and elaborate this data in form of charts, tables and summary. At present, fibroids which cause infertility their ratio is 5-10 %. Submucosal fibroids are associated with infertility and cause miscarriages and hysteroscopy is beneficial for pregnancy outcomes. Intramural fibroids impede successful outcomes of ART. Sub serosal fibroids have no impact on pregnancy loss and fertility.<sup>30</sup> Pankaj Desai conducted research on Fibroids in 2011, Infertility and Laparoscopic Myomectomy by using electronic data searched for articles published between 1980 and 2010. They concluded that females with submucosal fibroids having infertility and myomectomy are fruitful for fertility outcomes in these females. Sub serosal fibroids have negative influence on fertility outcomes and its removal is not necessary. Intramural fibroids appear to decrease fertility. Pregnancy rates in females with leiomyomata's are similar in females who gone under process of laparotomy and management of UF through endoscope.<sup>31</sup> Andrew Horne conducted a study on uterine fibroid impact on implantation of embryo in 2007. This research gave a conclusion that there is decisive relation between fibroids and failure in embryo implantation due to variability in size, location and no of fibroids impact on fertility and infertility. This research don't give satisfactory results and recommend more research to evaluate mechanism of fertility with and without fibroids.<sup>32</sup>

A research review was made by C. Benecke on impact of fibroid on fertility in patient experience assisted reproduction in 2005 data was collected by internet sources and Cochrane Library infertility and in vitro fertilization in human in 1990–2002. According to in vitro fertilization, one group of IM with no cavitary distortion and other control groups without myomas. According to their results a significant negative impact on implantation rate in the intramural fibroids groups versus the control groups.<sup>33</sup> Rachel M. Why Nott made a review in 2017 on Uterine Fibroids impact by using authentic reports and guidelines on systematic review and meta-analysis through electronic search of data from 1996 till February 2017. A total of 558 articles were identified, or summary analyses of fertility outcomes were included. In this review, concluded that the uterine fibroids having variability in size and shape and its presence affects fertility. Surgical interventions are beneficial as compare to non-invasive medical treatment. In management of uterine fibroids the myomectomy is Gold Standard, in management of infertility Submucosal fibroids should be treated IM fibroids more than 3 cm may cause infertility and SS fibroids usually do not influence female fertility.<sup>34</sup> Barbara S. Levy conducted a study in 2008 on the Modern management of uterine fibroids, a deep research was made by using PubMed. Most of the references which are included are already published in 2018 and some material was obtained from online women's health resources provided by OBGYN.net. Numerous modalities for the management of uterine fibroids are available but many methods having some drawback so by considering all these things new modalities and methods were valuable. Many females who want to be pregnant while suffering from uterine fibroids for them uterine sparing approach is beneficial. The choice of used modality depends on female clinical presentation their need and approach which is used must be effective, safe and minimally invasive.<sup>35</sup>

In 2012, P. Gambadauro had a study on Dealing with Uterine Fibroids in Reproductive Medicine by using secondary data and get results that the impact and interference of uterine leiomyomas largely depend on their size and location sub mucosal fibroids have an impact on fertility and embryo implantation and its management are necessary for infertility treatment by considering their sign and symptoms. Intramural fibroids which distorted cavity impact on fertility and those who don't distort cavity their impact is controversial on fertility because distortion in cavity impact receptivity of endometrial and embryo implantation. No evidence in asymptomatic and infertile patients support the removal of subserosal fibroids.<sup>36</sup> Marek Lisiecki made a literature review on uterine fibroid association with fertility impairment in 2017. Data was extracted from different search engines and impressive data is collected on fertility in link with UF. According to existing literature, the relationship between infertility and uterine leiomyomas was described. According to them sub mucosal and intramural fibroid have an impact on fertility and receptivity and gene expression of endometrial especially sub mucosal fibroids which distort endometrial cavity. There was a study gap about intramural fibroid and they recommended further study on intramural fibroids impact on fertility.<sup>37</sup> Elizabeth A. Pritts made evidence based updated systematic in 2009 on uterine Fibroids and infertility. It was a control study made in a private reproductive endocrinology and infertility center. Female patients with fibroids and infertility were taken. According to these evidence-based strong study women with sub serosal fibroids have no impact on their fertility as compare to females with infertility and no myomas. Females with intramural fibroids showed an impact on their fertility with less fertility and increased pregnancy loss but quality and authenticity was poor. Sub mucosal fibroids have an impact on fertility and after myomectomy its fertility outcomes increases.<sup>38</sup>

Ayman Al-Hendy made a research on Uterine Fibroids: Burden and Unmet Medical Needs in 2017 by using previous data review that UF affect a large population of black women as compare to white and affect their daily routine, living standard and specially impact their professional life. They met with high cost treatment and consultations and treatment may result in partially and for life loss of fertility. There is little success rate of surgical and pharmacological procedure in use.<sup>39</sup> Fabio Parazzini conducted a research in 2015 on pregnancy outcomes and uterine fibroid relation. For evaluation of effectiveness of different modalities for treatment of IM fibroids a randomized trial were made. That which modality and intervention improves fertility outcomes and got conclusive results that experimental and some observational studies shows negative impact of sub mucosal fibroid on pregnancy while IM and SS fibroids role in fertility is less clear not conformed and confined but large in size fibroid have negative impact on fertility outcomes.<sup>40</sup> Tariqu Salman made a conclusive study on Uterine fibroids, Management and Effect on fertility in 2010 by using previous articles on fibroids and fertility relation and concluded that submucosal fibroids having no impact on fertility and intramural fibroids also doesn't impact fertility but it's controversial without strong evidence after studying the results of IV fertilization that SM and IM fibroids are not associated with lower insertion, pregnancy and rate of birth. Fibroids more than 5cm and distort endometrial cavity needs management of uterine fibroids after considering safety and efficacy.<sup>41</sup>

Elizabeth A. Stewart made a study in 2013 on The Burden of Uterine Fibroids for African American Women: Results of a National Survey by using An online survey and concluded that as compare to American white women the African American women having unique concerns regarding fibroid behavior, more severe symptoms, and unique different information regarding UF behaviour.<sup>42</sup> Bijan J. Borah conducted a study in 2013 on uterine leiomyomas influence: it was a

National Survey on affected females. This comparative study was based on national survey in females on age group 29-59 years who presented symptoms of uterine fibroid by self. According to their research results, uterine fibroids cause morbidity in females who want to conceive specially in age 40. It's supported the evidence that age impact fertility with complication of myomas.<sup>43</sup> Javier Monleón make a case report study in 2014 on For Uterine Fibroids use of Ulipristal Acetate as a treatment result in successful pregnancy by using variables, ulipristal acetate, pregnancy. Patient with uterine fibroid introduce ulipristal acetate result in a regression in uterine fibroid and progressive intrauterine pregnancy result in successful delivery.<sup>44</sup>

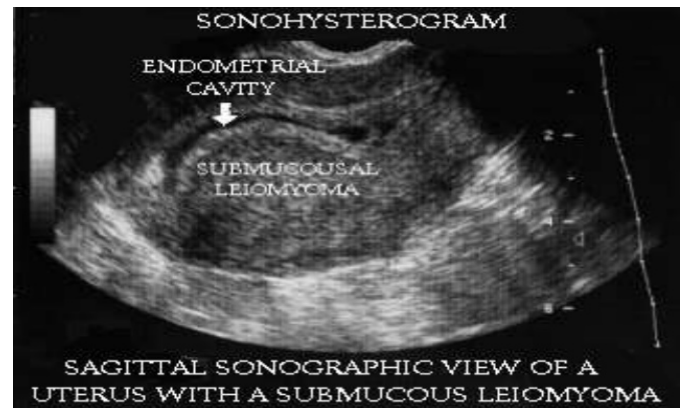
David L. Olive made a study in 2010 on Fibroids and Reproduction by using secondary data and concluded that uterine fibroids impact on infertility. Sub mucosal myoma cause infertility, intramural fibroids may decrease fertility and subserosal having no authentic evidence to influence on fertility.<sup>25</sup> M. David made research in 2013 on Uterine Fibroid Embolization the topic was Potential Impact on Fertility and Pregnancy Outcomes by previous literature reviews they concluded that UAE should not be a treatment of choice for women who want to conceive. at present there is little supportive evidential data on UAE impact on fertility outcomes. On basis of this article review there are increased fertility outcomes in females with myomas undergone operative myomectomy as compare to UAE. Study recommend more work and collection of evidences needed for UAE because according to this UAE increase the chance of spontaneous abortion.<sup>45</sup> Sotirios H. Saravelos made a study in 2011 on topic the prevalence and impact of fibroids and their treatment on the outcome of pregnancy in women with recurrent miscarriages couples were investigated according to established protocols by using TV ultrasound and hysteroscopy and diagnosed UF. They used 2 groups of females. One group was included that females who gone with surgery in which UF was distorting and impeding uterine cavity and the other group was in which UF was not impeding uterine cavity and by this they concluded that first group females met with midterm miscarriages as compare to other group.<sup>46</sup> Ertan Saridogan made research in 2006 on endoscopic management of uterine fibroids by using secondary data and concluded that Endoscopic management of uterine fibroids in women both with menstrual disorders and/or subfertility has become an established and widely used technique in the last few decades. Hysteroscopic myomectomy is now the standard treatment for the majority of women with submucosal fibroids. Laparoscopic myomectomy is suitable for a selected group of women with intramural and sub serosal fibroids but requires considerable experience in advanced laparoscopic surgery.<sup>47</sup>

Giovanna Tropeano made a study in 2008 on Non-Surgical Management of Uterine Fibroids by using internet sources and data was collected up to 2007. Different studies having good quality shows that UAE in symptomatic patients with fibroid having effectiveness and safe procedure. In symptomatic patients newer treatments are still investigational.<sup>48</sup> William H. Parker made a literature review on Etiology, Symptomatology and Diagnosis of Uterine Myomas in 2007 with help of 220 articles review and summaries that biology, symptoms and aetiology of UF is not understand properly but only UF and their type is understand.<sup>49</sup> Ben Kroon made research in 2011 on Fibroids in infertility consensus statement from ACCEPT by using previous articles and data according to these review UF effect females in their reproductive years. The fibroid relation with fertility based on female age, race, and family history their location in uterine part and interaction with endometrium. Sub serosal fibroid don't impede fertility and its removal surgery is made for only patients with symptoms. IM fibroid impact fertility but its surgical removal is not supported by adequate evidences. SM fibroids impede fertility and increased MR surgery depends on size of fibroids large size fibroid favors surgical removal and removal of sub mucosal fibroid improves

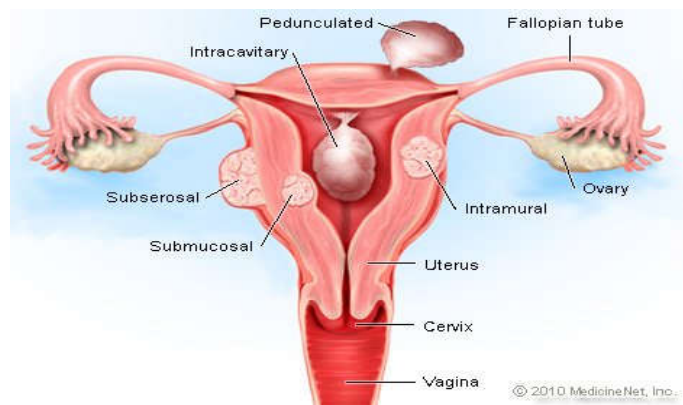
fertility.<sup>50</sup> Aamir T Khan made a review in 2014 on uterine fibroids: by using secondary data on 205 review articles by current aspects UF are benign tumors and cause morbidity and mortality about 40 % females in their fertile age window and after menopause. Females need to treat it without surgical procedures like hysterectomy and myomectomy and vascular embolization a noninvasive procedure improve their fertility outcomes.<sup>51</sup> E. Somigliana made a review in 2007 on Female Reproduction and fibroids: by using secondary data a caviling analyzation was made and got results that submucosal , intramural and sub serosal fibroids have impact on fertility but their incidence depend on different factors like age ,race, location, size, number and their interaction with.<sup>52</sup> In 2014, Kristin Van Heertum made a review-based study on uterine fibroids associated with infertility and concluded that uterine fibroids incidence increases with age.<sup>53</sup>

**RESULTS**

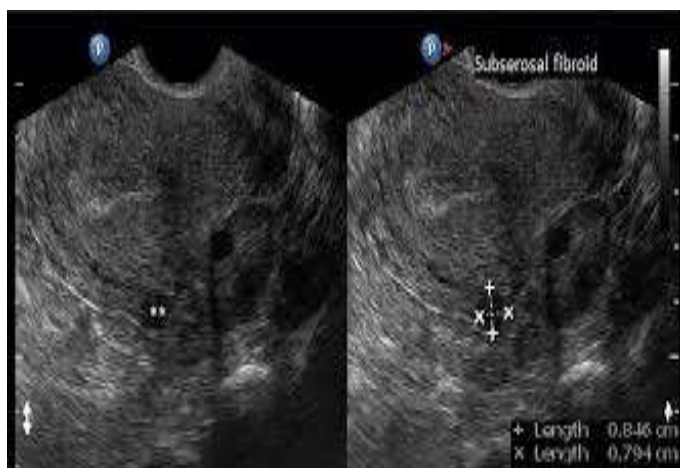
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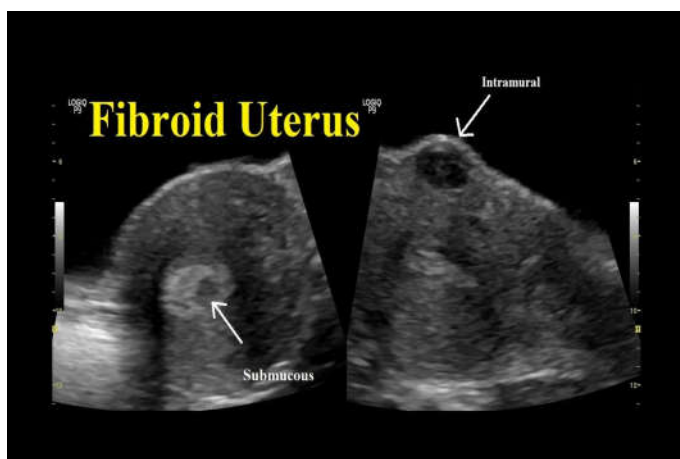
**Fig 3. A sonogram showing sub mucosal fibroid in a longitudinal view**



**Fig 4. is showing all types of uterine leiomyomas and their positions**



**Fig. 1. A transabdominal ultrasound showing a pelvic scan of uterus in which a subserosal fibroid is evaluated**



**Fig 2. a transabdominal image of uterine cavity is showing 2 fibroids sub mucosal and intramural fibroids**

**CONCLUSION**

Leiomyomas are highly prevalent and vary by age and race with an incidence in females of every age group but increase with increased age. Fibroids in pregnancy are also very common. The impact of uterine fibroid on fertility depends on their type, size and location. Most commonly with high impact factor sub mucosal fibroid impede implantation and cause infertility. Myomectomy improves fertility outcomes and recommended for females want to conceive relation of intramural fibroids with infertility is controversial it may and may not impact on fertility depends on their interface with an endometrial cavity if it invades endometrial cavity may cause infertility and if cavity is intact than there is no impact on fertility. The sub serosal fibroids don't impact on fertility.

**RECOMMENDATIONS**

Different management and treatment methods are valid and implemented in medical gynecological practice. There should be an authentic research work on invasive and non-invasive methods of treatment for UF for their type.

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**Ethical statement:** I stated that during this study all ethical parameters are fulfilled and there is no violation of human and animal's right was made.

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## REFERENCES

1. Heather Cook, Mohammad Ezzati, James H. Segars, Desiree McCarthy; "The Impact of Uterine Leiomyomas on Reproductive Outcomes"; *Minerva Ginecol.*; 2010; 62(3), pp. 225–236
2. Belina Carranza-Mamane, Sherbrooke, Jon Havelock, Vancouver BC, Robert Hemmings, Montreal; "The Management of Uterine Fibroids in Women With Otherwise Unexplained Infertility"; *SOGC Clinical Practice Guideline*; 2015; No-321, pp. 2787-285
3. Katarina Englund, Agneta Blanck, Inger Gustavsson, Ulrika Lundkvist, Peter Sjöblom, Allan Norgren, Bo Lindblom; "Sex Steroid Receptors in Human Myometrium and Fibroids: Changes during the Menstrual Cycle and Gonadotropin-Releasing Hormone Treatment"; *The Journal of Clinical Endocrinology & Metabolism*; 1998; Vol-83, Iss-11, pp. 4092-4096
4. Edward E. Wallach, Veasy C. Buttram, Robert C. Reiter; "Uterine leiomyomata: etiology, symptomatology, and management"; *Fertility and Sterility*; 1981; Vol-36, Iss-4, pp. 433-445
5. Erica E. Marsh, Serdar E. Bulun; "Steroid Hormones and Leiomyomas"; *Obstetrics and Gynecology Clinics of North America*; 2006; Vol-33, Iss-1, pp. 59-67
6. Mario Marugo Michele Centonze Donatella Bernasconi Laura Fazzuoli Silvia Berta Giulio Giordano; "Estrogen and Progesterone Receptors in Uterine Leiomyomas"; *Acta Obstetrica et Gynecologica*; 1989; Vol-68, Iss-8, pp. 731-735
7. Serdar E. Bulun; "Uterine Fibroids"; *The New England Journal of Medicine*; 2013; Vol-369(14), pp. 1344-1355
8. PA Richards, PDG Richards, AJ Tiltman; "The ultrastructure of fibromyomatous myometrium and its relationship to infertility"; *Human Reproduction Update*; 1998; Vol-4, Iss-5, pp. 520–525
9. Beth W Rackow, Hugh S Taylor; "Submucosal uterine leiomyomas have a global effect on molecular determinants of endometrial receptivity"; *Fertility and Sterility*; 2010; Vol-93, Iss-6, pp. 2027-2034
10. Aki Kido, Susan M Ascher, Keiko Kishimoto, Winnie Hahn, Reena C Jha, Kaori Togashi, James B Spies; "Comparison of uterine peristalsis before and after uterine artery embolization at 3-T MRI"; *AJR Am J Roentgenology*; 2011; Vol-196, No-6, pp. 1431-1435
11. Osamu Yoshino, Osamu Nishii, Yutaka Osuga, Hisanori Asada, Shigeo Okuda, Makoto Orisaka, Masaaki Hori, Toshihiro Fujiwara, Toshihiko Hayashi; "Myomectomy decreases abnormal uterine peristalsis and increases pregnancy rate"; *The Journal of Minimally Invasive Gynecology*; 2012; Vol-19, Iss-1, pp. 63-67
12. O Yoshino, T Hayashi, Y Osuga, M Orisaka, H Asada, S Okuda, M Hori, M Furuya, H Onuki, Y Sadoshima, H Hiroi, T Fujiwara, F Kotsuji, Y Yoshimura, O Nishii, Y Taketani; "Decreased pregnancy rate is linked to abnormal uterine peristalsis caused by intramural fibroids"; *Human Reproduction Update*; 2010; Vol-25, Iss-10, pp. 2475–2479
13. Maria Luisa Casini, Federica Rossi, Riccardo Agostini, Vittorio Unfer; "Effects of the position of fibroids on fertility"; *Gynecological Endocrinology*; 2006; Vol-22, Iss-2, pp. 106-109
14. Dr Elizabeth A Stewart; "Uterine fibroids"; *E A Stewart*; 2001; Vol-357, Iss-9295, pp. 293-298
15. D E Townsend, R S Sparkes, M C Baluda, G McClelland; "Unicellular histogenesis of uterine leiomyomas as determined by electrophoresis by glucose-6-phosphate dehydrogenase"; *American Journal of Obstetrics & Gynecology*; 1970; Vol-107, Iss-8, pp. 1168-1173
16. M S Rein, A J Friedman, R L Barbieri, K Pavelka, J A Fletcher, C C Morton; "Cytogenetic abnormalities in uterine leiomyomata"; *Obstet Gynecol*; 1991; Vol-77(6), pp. 923-6
17. D Linder, S M Gartler; "Glucose-6-phosphate dehydrogenase mosaicism: utilization as a cell marker in the study of leiomyomas"; *Science*; 1965; Vol-150, Iss-3692, pp. 67-69
18. [18] R D Mashal, M L Fejzo, A J Friedman, N Mitchner, R A Nowak, M S Rein, C C Morton, J Sklar; "Analysis of androgen receptor DNA reveals the independent clonal origins of uterine leiomyomata and the secondary nature of cytogenetic aberrations in the development of leiomyomata"; *Genes Chromosomes Cancer*; 1994; Vol-11, Iss-1, pp. 1-6
19. L Deligdisch, M Loewenthal; "Endometrial changes associated with myomata of the uterus"; *Journal of Clinical Pathology*; 1970; Vol-23, Iss-8, pp. 676-680
20. Elizabeth A Stewart; "Uterine fibroids"; *The Lancet*; 2001; Vol-357, Iss-9252, pp. 293-298
21. Oksana H. Baltarowich, Alfred B. Kurtz, Rebecca G. Pennell, Laurence Needleman, Maria M. Vilaro, Barry B. Goldberg; "Pitfalls in the Sonographic Diagnosis of Uterine Fibroids"; *American Journal of Roentgenology*; 1988; Vol-151, Iss-4, pp. 725-728
22. Sabrina Q. Rashid, Yi-Hong Chou, Chui-Mei Tiu; "Ultrasonography of Uterine Leiomyomas"; *Journal of Medical Ultrasound*; 2016; Vol-24, Iss-1, pp. 3-12
23. Mary Graham, Peter L. Cooperberg; "Ultrasound diagnosis of interstitial pregnancy: findings and pitfalls"; *Journal of Clinical Ultrasound*; 1979; Vol-7, Iss-6, pp. 433-437
24. V Persaud, P D Arjoon; "Uterine leiomyoma. Incidence of degenerative change and a correlation of associated symptoms"; *Journal of Clinical Ultrasound*; 1970; Vol-35(3), pp. 432-6
25. David L. Olive, Elizabeth A. Pritts; "Fibroids and Reproduction"; *Seminars In Reproductive Medicine*; 2010; Vol-28, Num-3, pp. 218-227
26. Fascilla FD, Cramarossa P, Cannone R, Olivieri C, Vimercati A, Exacoustos C; "Ultrasound diagnosis of uterine myomas"; *Minerva Ginecologica*; 2016; Vol-68(3), pp. 297-312
27. Leonidas I. Zepiridis, Grigoris F. Grimbizis, Basil C. Tarlatzis; "Infertility and Uterine Fibroids"; *Best Practice & Research Clinical Obstetrics & Gynaecology*; 2015; S1521-6934(15)00235-7, pp. 1-16
28. P. Purohit, K. Vigneswaran; "Fibroids and Infertility"; *Curr Obstet Gynecol Rep*; 2016; DOI 10.1007/s13669-016-0162-2, pp. 81-88
29. Aradhana Khaund, Aradhana Khaund; "Impact of fibroids on reproductive function"; *Best Practice & Research Clinical Obstetrics and Gynaecology*; 2008; Vol-22, No-4, pp. 749–760
30. Neelanjana Mukhopadhyaya, Grace Pokuah Asante, Isaac T Manyonda; "Uterine fibroids: impact on fertility and pregnancy loss"; *Obstetrics, Gynaecology and Reproductive Medicine*; 2007; 17:11, pp. 311-317
31. Pankaj Desai, Purvi Patel; "Fibroids, Infertility and Laparoscopic Myomectomy"; *Journal of Gynecological Endoscopy and Surgery*; 2011; Vol-2, Issue-1, pp. 36-42
32. Andrew W. Horne, Hilary O.D. Critchley; "The Effect of Uterine Fibroids on Embryo Implantation"; *Seminars In Reproductive Medicine*; 2007; Vol-25, Num-6, pp. 483-489
33. C. Benecke, T.F. Kruger, T.I. Siebert, J.P. Van der Merwe, D.W. Steyn; "Effect of Fibroids on Fertility in Patients Undergoing

- Assisted Reproduction"; *Gynecol Obstet Invest*; 2005; DOI: 10.1159/000084513, 59: pp. 225–230
34. Rachel M. Whynott, Kamaria C. Cayton Vaught, James H. Segars; "The Effect of Uterine Fibroids on Infertility: A Systematic Review"; *Seminars in Reproductive Medicine*; 2017; Vol-35, Num-6, pp. 523-532
35. Barbara S. Levy; "Modern management of uterine fibroids"; *Acta Obstetrica et Gynecologica*; 2008; DOI: 10.1080/00016340802146912, 87: pp. 812-823
36. P. Gambadauro; "Dealing with uterine fibroids in reproductive medicine"; *Journal of Obstetrics and Gynaecology*; 2012; DOI: 10.3109/01443615.2011.644357, 32: pp. 210–216
37. Marek Lisiecki, Maciej Paszkowski, Sławomir Woźniak; "Fertility impairment associated with uterine fibroids – a review of literature"; *Menopause Review/Przegląd Menopauzalny*; 2017; DOI: <https://doi.org/10.5114/pm.2017.72759>, 16(4): pp. 137-140
38. Elizabeth A. Pritts, William H. Parker, David L. Olive; "Fibroids and infertility: an updated systematic review of the evidence"; *American Society for Reproductive Medicine*; 2009; Vol. 91, No. 4, pp. 1215-1223
39. Ayman Al-Hendy, Evan Robert Myers, Elizabeth Stewart; "Uterine Fibroids: Burden and Unmet Medical Need"; *Seminars in Reproductive Medicine*; 2017; Vol-35, No-6, pp. 473–480
40. Fabio Parazzini, Dr. Luca Tozzi, and Stefano Bianchi; "Pregnancy outcome and uterine fibroids"; *Best Practice & Research Clinical Obstetrics & Gynaecology*; 2015; DOI: 10.1016/j.bpobgyn.2015.11.017, pp. 1-26
41. Tariqu Salman, Colin Davis; "Uterine fibroids, management and effect on fertility"; *Current Opinion in Obstetrics and Gynecology*; 2010; DOI:10.1097/GCO.0b013e32833d3606, 22: pp. 295–303
42. Elizabeth A. Stewart, Wanda K. Nicholson, Linda Bradley, Bijan J. Borah; "The Burden of Uterine Fibroids for African-American Women: Results of a National Survey"; *Journal Of Women's Health*; 2013; Vol-22, Num-10, pp. 807-816.
43. Bijan J. Borah, Wanda K. Nicholson, Linda Bradley, Elizabeth A. Stewart; "The impact of uterine leiomyomas: a national survey of affected women"; *American Journal of Obstetrics & Gynecology*; 2013; DOI:10.1016/j.ajog.2013.07.017, 209: pp. 319.e1-20
44. Javier Monleón, Alicia Martínez-Varea, Daniela Galliano, and Antonio Pellicer; "Successful Pregnancy after Treatment with Ulipristal Acetate for Uterine Fibroids"; *Hindawi Publishing Corporation*; 2014; Vol-2014, dx.doi.org/10.1155/2014/314587, pp. 1-3
45. M. David, T. Kröncke; "Uterine Fibroid Embolisation – Potential Impact on Fertility and Pregnancy Outcome"; *Geburtsh Frauenheilk* ; 2013; DOI:10.1055/s-0032-1328318, 73: pp. 247–255
46. Sotirios H. Saravelos, Junhao Yan, Hassan Rehmani, Tin-Chiu Li; "The prevalence and impact of fibroids and their treatment on the outcome of pregnancy in women with recurrent miscarriage"; *Human Reproduction Update*; 2011; Vol-26, No-12, pp. 3274–3279
47. Ertan Saridogan & Alfred Cutner; "Endoscopic management of uterine fibroids"; *Informa Healthcare Human Fertility*; 2006; Vol-9(4), pp. 201 – 208
48. Giovanna Tropeano, Sonia Amoroso and Giovanni Scambia; "Non-surgical management of uterine fibroids"; *Human Reproduction Update*; 2008; Vol-14, No-3, pp. 259–274
49. William H. Parker; "Etiology, symptomatology, and diagnosis of uterine myomas"; *American Society for Reproductive Medicine*; 2007; Vol-87, No-4, pp.725-736
50. Ben Kroon, Neil Johnson, Michael Chapman, Anusch Yazdani, Roger Hart; "Fibroids in infertility – consensus statement from ACCEPT"; *Australian and New Zealand Journal of Obstetrics and Gynaecology*; 2011; Vol-51, pp. 289–295
51. Aamir T Khan, Manjeet Shehmar, Janesh K Gupta; "Uterine fibroids: current perspectives"; *International Journal of Women's Health*; 2014; Vol-20, No. 14:6, pp. 95-114
52. E. Somigliana, P. Vercellini, R. Daguati, R. Pasin, O. De Giorgi and P.G. Crosignani; "Fibroids and female reproduction: a critical analysis of the evidence"; *Human Reproduction Update*; 2007; Vol-13, No-5, pp. 465–476
53. Kristin Van Heertum, Larry Barmat; "Uterine fibroids associated with infertility"; *Journal Of women's Health*; 2014; Vol-10(6), pp. 645–653

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