Association between Infertility and Uterine Fibroid: A Cross Sectional Study

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ABSTRACT
Background: The most frequent gynecological tumors in women are uterine fibroids. The purpose of this study is to determine the prevalence of fibroid among infertile women visiting an outpatient clinic for infertility and to investigate the effects of various myoma types on fertility.
Patients and method: The infertility outpatient clinic, Obstetrics and Gynecology Department, Faculty of Medicine, Zagazig University, was the site of this cross-sectional study. The study group consisted of 108 women, whose ages varied from 22 to 40 years and had uterine fibroids. Patients were examined thoroughly and transvaginal ultrasound examination was done for the assessment of pathological state and uterine fibroids (number, place, and size).
Result: The uterus of 31.5% of infertile women contained numerous fibroid tumors. Patients with numerous fibroids had significantly higher odds ratio of being infertile (3.24, confidence interval: 1.28–7.24). Infertile women had a significantly higher percentage of intramural fibroid despite having a significantly lower percentage of sub-serous fibroid. According to the classification of The International Federation of Gynecology and Obstetrics (FIGO), 27.8% of the patients had FIGO 5, 28.7% had FIGO 6, and 7.6% had FIGO 7. Infertile women had a significantly greater percentage of FIGO classes 2 to 5. With odds ratio of 6.6 and a confidence range of 1.34 to 32.5, patients had a significantly increased risk of infertility based on FIGO 2–5.
Conclusion: Though the significance of uterine fibroids is still up for debate, it would seem that myomas lessen the chance of conception.
Keywords: Pregnancy rates, Uterine fibroids, Infertility

INTRODUCTION

The most frequent gynecological tumors in women are uterine fibroids, which affect 25–30% of all women at some point throughout their reproductive years. Since they tend to expand during adolescence and retract after menopause, studies have suggested that estrogen helps them develop [1].

Researchers have connected fibroid formation to both a genetic predisposition and hormone stimulation, however the specific cause of this relationship is yet unknown. This would explain why some racial groups have a higher risk of developing fibroids and why some families tend to have a hereditary predisposition [2].

Women with fibroids typically have symptoms between 20 and 50 percent of the time, such as irregular uterine bleeding, pelvic pain, pressure feelings, spontaneous abortion, and infertility [3].

Obstetric consequences of co-existing uterine fibroids in pregnancy include miscarriages, premature labor, antepartum hemorrhage, malpresentation, malposition, obstructed labor, postpartum hemorrhage, uterine inversion, and puerperal infection in addition to menstrual irregularities and infertility. There is a rise in surgical deliveries as a result of uterine fibroids. If left untreated, these problems may result in maternal mortality either singly or in combination [3].

Myomas frequently have an association with infertility. The majority of patients are either nulliparous or of poor parity, and 27% of infertile women have been documented to have fibroids. After myomectomy, about 50% of infertile women with myomas become pregnant [4].

Numerous theories have been put out to explain how myomas affect fertility, but the precise cause and association between fibroids and infertility remain unknown. Myomas can alter the shape and surface area of the uterine cavity, causing it to become larger and elongated as well as submucosal or intramural with an intracavitary component. By obstructing the tubal ostia, changing uterine contractility and peristalsis, and perhaps affecting sperm migration and ovum transport, a deformed uterine cavity reduces implantation and raises the risk of miscarriage [4]. In more than half of patients with intramural myomas, MRI has revealed abnormal uterine contractility during the mid-luteal phase (window of implantation) [5].

Leiomyomas can compress and deform the endometrium that lies above it, which reduces the embryo's window of receptivity for implantation. Initial phases of implantation and subsequent placentation may suffer from junctional zone disruption within the myometrium [6].

Additionally, aberrant expression of endometrial growth factors and cytokines, such as those that control cell differentiation, proliferation, and angiogenesis, has been linked to leiomyomas [7]. Additionally, leiomyoma-related endometrial fibrosis and inflammation may lower implantation rates [8].

First pregnancies are increasingly occurring in women in their late twenties, thirties, and forties [9]. The increased occurrence of leiomyomas among these age groups and the altered age at which women have their first child served as the backdrop for this investigation. This study aims to assess the prevalence of infertility in fibroid-affected women.

PATIENTS AND METHODS

The study group consisted of 108 women, whose ages varied from 22 to 40 years and had uterine fibroids. The infertility outpatient clinic, Obstetrics and Gynecology Department, Faculty of Medicine, Zagazig University, was the site of this cross-sectional study.

Inclusion criteria: Must be between 18 and 40. All females who had fibroid uteri.

Other reasons of female infertility as well as male factors were exclusion criteria.

All of the women in this study had a thorough history taking process of clinical importance, which included obtaining information from the patient and her spouse about any potential etiologies of infertility as well as a thorough medical history. The patients were asked about their personal history, which included their age, place of residence, marital status, occupation, exposure to known environmental risks, and usage of nicotine products, alcohol, and illicit or legal substances.

The female partner underwent a targeted physical examination that focused on vital signs and included a thyroid, breast, and pelvic examination.

Imaging and laboratory tests were part of the infertility workup. Tests on the female partner's ovarian reserve, ovulatory function, and anatomical anomalies were the main focus. Imaging of the reproductive system could reveal important details about ailments that impaired fertility. Imaging techniques could evaluate ovarian reserve, find pelvic disease, and check tubal patency. Standard infertility tests such FSH, LH, serum prolactin, TSH, AMH, E2, and examination of the husband's sperm were done. Employing a Mindray DP-15 Digital Ultrasonic Diagnostic Imaging System (China) to image transvaginal ultrasound examination was done for the assessment of pathological state and uterine fibroids (number, place, and size).

Ethics approval:

All patients gave signed informed permission after being fully informed about the specifics and aim of the current investigation. Patients had the right to leave the research at any time without having their access to medical treatment negatively impacted. Institutional Research Board Approval Number (IRB # 9743) of Obstetrics and Gynecology Department and Faculty of Medicine, Zagazig University, authorized the study protocol. The Helsinki Declaration, the World Medical Association's rule of ethics for human research, was followed throughout the study's procedure.

Statistical analysis

IBM SPSS statistic was used to examine the data. The normality of the distribution was evaluated using the Kolmogorov-Smirnov test. For categorical variables, the appropriate test was the chi-square test, the Fisher exact test or Mann whitnney test. *(p value less than 0.05 was considered significant).*

RESULTS

Studied group included 108 women, their ages ranged from 18- 40 years with a mean of 33.1±5.08 years. Out of 108 women harboring uterine fibroid 55.6% had infertility. Duration of infertility ranged from 1- 15 years with a mean of 5±3.5 years. Women had primary infertility were 46.7% (table 1).

Table (1): Demography data (n.108)

Variables			
Age (years)	**Mean ±SD**	33.1±5.08	
		n.	**%**
Age category	**18-25**	10	9.3
	26-32	35	32.4
	33-40	63	58.3
Infertility	**Yes**	60	55.6
	No	48	44.4
Duration of infertility	Mean ±SD Range		5±3.5 1-15
	<5 years	35	58.3
	≥5 years	25	41.7
Infertility	Primary	28	46.7
	Secondary	32	53.3

Table 2 shows that there was significant higher percent of multiple fibroids in infertile women.

Table 2: Fibroid multiplicity in studied women

Fibroid number	total n.108		Infertility n.60		Fertile n.48		χ^2	p
	n	%	n	%	n	%		
Single	74	68.5	36	60.0	38	79.2		
Multiple	34	31.5	24	40.0	10	20.8	4.54	0.033*

χ^2: Chi square test, *: Significant

Table 3 shows that there was significant larger fibroid size in infertile women.

Table 3: Fibroid volume in studied women

	Total n.108	Infertility n.60	Fertile n.48	U	p
Size (mm) Mean ±SD Median (range)	54.1±23.9 50(16-109)	59.2±26.8 55.5(16-109)	47.6±18 45(16-93)	2.21	0.034*

U: Mann whitnney U test, ***: Significant**

Table 4 shows that there was significant higher percent of intramural fibroid in infertile women. While there was significant lower percent of sub-serous fibroid in infertile women.

Table 4: Site of fibroid in studied women

Site	Total n.108		Infertility n.60		Fertile n.48		χ^2	p
	n	%	n	%	n	%		
Intramural	55	50.9	37	61.7	18	37.5	6.23	0.013*
Sub-serous	50	46.3	22	36.7	28	58.3	5.03	0.025*
Pedunculated intra cavity	3	2.8	1	1.7	2	4.2	f	0.584

χ^2: Chi square test, *: Significant

Table 5 shows that there was significant higher percent of FIGO class 2-5 in infertile women.

Table 5: FIGO in studied women

	total n.108		Infertility n.60		Fertile n.48		χ^2	p
	n	%	n	%	n	%		
FIGO 0	3	2.8	1	1.7	2	4.2	f	0.584
FIGO 1	3	2.8	2	3.3	1	2.1	f	1
FIGO 2	2	1.9	1	1.7	1	2.1	f	1
FIGO 3	3	2.8	2	3.3	1	2.1	f	1
FIGO 4	2	1.9	2	3.3	0	.0	f	0.502
FIGO 5	30	27.8	17	28.3	13	27.1	0.02	0.885
FIGO 6	31	28.7	17	28.3	14	29.2	0.009	0.924
FIGO2-5	15	13.9	13	21.7	2	4.2	6.83	0.008*
FIGO 7	19	17.6	5	8.3	14	29.1	7.98	0.005*

χ^2: Chi square test, f: Fisher exact test, FIGO: The International Federation of Gynecology and Obstetrics, *: Significant

Size of fibroid, multiple fibroids, intramural fibroid, and FIGO2-5 were significant predictors of infertility (Table 6).

Table 6: Univariate logistic regression for predictors infertility in women with uterus harbor fibroid

	Sig.	Exp(B)	95% C.I. for EXP(B)	
			Lower	Upper
Size of fibroid	0.014	1.022	1.004	1.04
Multiple fibroid	0.036	2.53	1.06	6.03
Intramural fibroid	0.013	2.68	1.23	5.86
FIGO2-5	0.019	6.36	1.36	29.77

Exp(B): Odds ratio (OR), C.I.: Confidence interval, *: Significant.

Patients who had large size of fibroid, multiple fibroids, or FIGO 2-5 were at significant risk of infertility (Table 7).

Table 7: Multiple logistic regression for predictors of infertility in women with uterus harbor fibroid

	B	SE	Sig.	Exp (B)	95% C.I. for EXP(B)	
					Lower	Upper
Size (mm)	0.023	0.010	0.017	1.02	1.004	1.043
Multiple fibroid	1.176	0.476	0.014	3.24	1.27	8.24
FIGO 2-5	1.887	0.814	0.020	6.6	1.34	32.5

Exp(B): Odds ratio (OR), C.I.: Confidence interval, *: Significant

DISCUSSION

The mean age of the study group, which consisted of 108 women with fibroid uteri, was 33.1±5.08 years and 41.7% of the women in this group had an infertility duration of less than five years. Among them, 58.3% of the women were equal to or older than 33 years old, and the duration of infertility ranged from 1 to 15 years with a mean of 5±3.5 years. 55.6% of 108 women who had uterine fibroid were infertile. Primary infertility affected 46.7% of women, whereas secondary infertility affected 53.3% of them.

Grannaz et al. [10] in order to assess the risk of infertility with fibroid in the reproductive age range, a study with 203 individuals was conducted. The age range was between 18 and 40 years. 12.8% of the population was under 18, 45.3% were between 26 and 32, and 41.9% were between 33 and 40. Only 9.9% of the 203 patients had infertility, leaving the other 90.1% to have a healthy reproductive life. The average length of infertility was between 2 and 10 years for women, and between 11 and 20 years for men.

In a study by **Aggarwal et al.** [11], the average age of the study population, which consisted of 100 patients, was 33±4.5 years. The bulk of the population was between the ages of 28 and 36, and 14% of the population had primary infertility.

In the current study, 31.5% of the women who were examined had multiple fibroids; however, the percentage of infertile women who had multiple fibroids was substantially higher. With a mean of 54.1±23.9 (mm), the fibroid size ranged from 16 to 109 mm. The size of the fibroid was noticeably greater in the infertile group than the fertile women group.

In a different investigation by **Abinaya and Narayanan** [12] 35 patients who were infertile were included; 12 women (34.3%) and 23 women (65.7%) both have multiple fibroids. The average number of fibroids per patient was 1.4±0.6, with the largest myoma in 23 (65.7%) of the women measuring less than 5 cm. And 12 (34.3%) of the ladies developed myomas that were at least 5 cm in size. The largest myoma's average size was 4.4±1.19 cm.

Aggarwal et al. [11] in 100 patient prospective observational research, 22% of cases had numerous fibroids, while 78% had just one.

Infertile women had considerably lower percentages of sub-serous fibroid (46.3%) and intramural fibroid (50.9%), according to our research (p=0.03 and p=0.013, respectively).

Additionally, we noted that a higher percentage of infertile women belonged to FIGO classes 2 to 5. Infertility is significantly more likely in patients with FIGO 2–5 fibroids, with odds ratio of 6.6 and a confidence interval of 1.34–32.5.

Research by **Akinola et al.** [13], aimed to assess the prevalence of uterine fibroids using the FIGO categorization system in a cohort of women in Nigeria. Transvaginal ultrasonography was used to determine the presence of uterine fibroids in 436 of the study's participants. According to the study's findings, intramural fibroids were present in 75.5% of the women, followed by subserosal (16.7%), submucosal (5.5%), and pedunculated (2.3%) fibroids.

Another investigation looked at uterine fibroids according to the FIGO classification in a group of women receiving hysteroscopic myomectomy. The majority of women in the population had submucosal fibroids, which were followed by intramural fibroids (26%) and subserosal fibroids (15%), according to the study. The prevalence of pedunculated fibroids in the women was extremely low (about 2%) [14].

According to our research, patients with large fibroid sizes had a significant risk of infertility with odds ratio of 1.02 and a confidence interval of 1.04 to 1.043, patients with multiple fibroid sizes had a significant risk of infertility with odds ratio of 3.24 and a range of 1.28 to 8.24, and patients with FIGO 2-5 sizes had a significant risk of infertility with odds ratio of 6.6 and a range of 1.34 to 32.5.

CONCLUSION

Thoughts on the function of uterine fibroids are still divided, it would seem that myomas lessen the chance of pregnancy. Therefore, more research is needed to confirm the relationship between fibroids and primary infertility, particularly studies with larger patient groups and samples.

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