

FIBROIDS AND FERTILITY: A LITERATURE REVIEW***M. Sebti, M. C. Fourati, F. Zidane, P. R. M. Yousfi and P. R S. Bargach**

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I-INTRODUCTION

Leiomyoma, more commonly known as uterine myoma or fibroma, is a benign tumor of the human uterus that grows at the expense of smooth muscle cells. These tumors consist of smooth muscle fibers with elongated nuclei, surrounded by collagen fibers and a pseudocapsule formed by smooth muscle cells, and are poorly vascularized. Myomas are extremely variable in form, each characterized by their size, consistency and position relative to the myometrium, and are mostly multiple within the same uterus. Fibroids are classified ultrasonographically into different types based on the position of their largest transverse diameter according to the FIGO classification. Fibroids are the most common uterine tumors in women of childbearing age and are present in 20% to 50% of these women, and their controversial relationship to infertility remains a matter of debate. The management of a woman with a fibroid and a desire for pregnancy is discussed. It is reported that 5% to 10% of infertility cases prior to medical management are associated with the presence of uterine fibroids. Uterine fibroids are considered to be the sole infertility factor in only 1-3% of cases.

KEYWORDS: fibroids, infertility, fertility, myomas, myomectomy, hysteroscopy, laparoscopy and ART.**II-MATERIAL AND METHODS**

Evidence of the relationship between these fibroids and infertility is complex, based on over-representation of observational data and a lack of randomized controlled trials.

In addition, the heterogeneity of patient populations, fibromatous pathology, and multiple etiologies of infertility make it difficult to design and implement large-scale, multicentric randomised controlled trials.

In order to assess the link between fibroids and infertility, a review of the literature was carried out using meta-analyses, clinical trials and other articles from different medical databases up to April 2020, using the keywords fibroids, infertility, fertility, myomas, myomectomy, hysteroscopy, laparoscopy and ART.

Only infertile patients were considered, and the criterion for judgment was the clinical pregnancy rate obtained.

Publications reporting an analysis of the factors influencing the pregnancy rate after myomectomy were also included.

Studies in which the proportion of infertile women was not determined were excluded from our analysis.

Studies involving non-surgical treatment, such as embolization of the uterine fibroid were not considered in our review because they are considered to be additional infertility factors.

The aim of our work is to answer two important questions in the study of fibroids and fertility, namely whether the presence of fibroids reduces implantation and thus pregnancy rates, and whether their treatment has a real benefit in terms of pregnancy rates and, if so, which treatment is the most optimal.

All of the data collected are gathered in our results and the discussion will help answer our questions.

Furthermore, we will first address the subject in a context of spontaneous procreation and then in medically assisted procreation.

III-RESULTS**A/ Natural Procreation**

We selected 44 studies, all based on Poncelet's 2001 meta-analysis reporting the rate of spontaneous pregnancy after myomectomy.

Intrinsic information on myomas helped to refine the study.

1/ Myoma and natural fertility

As described above no comparative study between patients with myomas and infertility has been published with a control population without myomas.

However, Bullettini *et al.*^[1] compare the rate of spontaneous pregnancy in infertile women with and without myomas who are neither tubal nor hormonally induced infertile.

The rate for the infertile group with myoma is 11% versus 25% for the control group.

However, the methodology of this study is imprecise and patient follow-up was brief, less than one year.

2) Myomectomy and pregnancy rate

Even if the real impact of myomas in natural reproduction on fertility remains poorly evaluated, data exist on the results of myomectomy, regardless of the type of myoma and the type of approach.

Fernandez *et al.*^[1] in 2001, evaluated the results of hysteroscopic treatment of submucosal myomas, and reported from a series of 200 patients, 35 of whom had infertility isolated or associated with menometrorrhagia, a pregnancy rate of 28% (n = 10) with only 6% full-term birth (n = 2).

The number of spontaneous childbearing pregnancies was three out of ten. A literature review by Ponce *et al.*^[27] in 2001 reported the following results

Table 1: Summarizes the main studies on the subject.

AUTHORS	TYPE OF STUDY	NUMBER OF PATIENTS	MYOMA TYPE	TYPE OF SURGERY	PREGNANCY RATE (%)
BERNARD	RP	31	SM	HSC	35,5
VERCELLINI	RP	40	SM	HSC	41,2
VARASTEH	RP	36	SM	HSC	53
GIATRAS	RP	41	SM	HSC	61
GOLDENBERG	RP	15	SM	HSC	46,6
BALLEZ	RP	32	SM	HSC	56,2
CRAVELLO	RP	16	SM	HSC	25

Table 1: Pregnancy rate in spontaneous procreation in women with SM myomas.^[2]
(RP: retrospective; SM: submucous; HSC: hysteroscopy)

For patients with exclusively submucosal myomas after hysteroscopic myomectomy, the spontaneous pregnancy rate ranged from 25% to 61%.

For subserous and intramural myomas, after analysis of six studies, the pregnancy rate ranges from 30.8% to 61.5%.

The routes were either laparotomies or laparoscopies.

For myomas larger than 5 cm with a largest diameter that was not submucosal, operated on by laparotomy or laparoscopy after analysis of the 3 publications, the pregnancy rate ranged from 33.3% to 64.3% (**Table 2**).

Table 2: Pregnancy rate in spontaneous procreation in women with SM >5cm.^[2]

AUTHORS	TYPE OF STUDY	NUMBER OF PATIENTS	MYOMA TYPE	TYPE OF SURGERY	PREGNANCY RATE (%)
SERRACCHIOLI	RP	115	>5 cm	LPT/LPS	54,8
RIBEIRO	RP	28	>5 cm	LPS	64,3
DUBUISSON	PP	21	>5 cm	LPS	33,3

PP : prospective ; LPS/LPT : laparoscopy/laparotomy)

Studies that did not distinguish or specify the position of the myomas prior to laparotomic or laparoscopic conservative surgery had a pregnancy rate between 9.6% and 75%.

The overall pregnancy rate regardless of type, size, and type of surgical management of the myoma was between 9.6% and 76.9%.

These results are consistent with data from Vercellini *et al.*^[3] who, in a 1999 meta-analysis, found an overall pregnancy rate after myomectomy by 61%.

In 2002, Donnez and Jadoul^[4] analyzed 46 infertile women with myoma.

After myomectomy the pregnancy rate was 48%.

In 2004, Chaker *et al.*^[5] conducted a retrospective study of 41 infertile women and 19 of them achieved a clinical pregnancy, i.e. 46.34%.

In 2006, Casini *et al.*^[6] on the basis of a prospective controlled study in spontaneous reproduction, compared 42 patients with submucosal and intramural fibroids treated surgically with 40 patients with non-operated

myomas; the reported pregnancy rate was respectively 40.5% and 38.5%.

In 2013, Chigbu *et al.*,^[7] published a prospective study of 40 infertile women with myoma showing a pregnancy rate of 60% after myomectomy.

The relationship between uterine myoma/myomectomy and infertility is only indirectly established and the surgical management of these patients must therefore be multifactorial.

The main determinants associated with a poor prognosis and causing an alteration in the pregnancy rate after myomectomy with statistically significant results are.^[3,8]

an age greater than 35 years, a duration of infertility greater than 2 years, an association with other male or female infertility factors and a myoma responsible for menometrorrhagia.

B/Fibrome And Art

Fourteen publications were retrieved for our analysis and all were retained.

All patients were included in an ART protocol with or without ICSI.

Research has focused on the influence of myomas on fertility in the context of medically assisted reproduction, while also looking at the impact of myomas according to their location.

1/All myomas combined

Seoud *et al.*,^[9] in 1992, based on a retrospective series of infertile patients, studied the effects of myomas and myomectomy on in vitro fertilization (IVF) outcomes without distinguishing between surgical approaches.

Patients who had myomectomy prior to IVF were compared to infertile patients with myoma. Pregnancy rates were not different.

The authors concluded that myomas and myomectomy did not affect fertility before IVF.

These results were contradicted by the work of Farhi *et al.*^[10] Indeed, he reports :

- A pregnancy rate of 9% for the 18 patients whose uterine cavity was deformed by the presence of myomas after 55 cycles of IVF;
- For the 28 patients with an interstitial myoma that did not deform the uterine cavity (86 IVF cycles), the pregnancy rate was 29.1%;
- For the 50 patients with infertility of tubal origin (127 IVF cycles), the pregnancy rate was 25,1%.

In this study, the effect of myomas deforming the cavity in terms of reduced IVF outcome was significant.

In a continuation of this work, Eldar-Geva *et al.*^[11], using a comparative retrospective series, studied the effect of submucosal, subserous, intramural myomas without deformation of the uterine cavity on IVF outcomes.

Thus, the pregnancy and implantation rates of 88 infertile patients (106 cycles) with at least one myoma were compared with those of 249 patients without myoma (318 cycles) and without a history of myomectomy:

- Submucosal and interstitial myomas statistically decreased the pregnancy rate, which was 10% and 16.4% respectively;
- For sub-serous locations, the pregnancy rate was 34.1%.
- For infertility without myoma, the observed pregnancy rate was 30.1%.

Ramzy *et al.*,^[12] in a retrospective case-control series compared 39 patients a uterine myoma greater than 7cm but not deforming the cavity in 367 patients without myoma.

All the patients were infertile and included in an IVF protocol with or without intracytoplasmic sperm injection (ICSI).

In this study, Ramzy found no difference in the implantation rate and pregnancy rate (39% versus 34%) that contradicted the results of previous studies.

Many studies have attempted to answer these different questions.

Stovall *et al.*,^[13] report a prospective case-control study in a population of infertile patients undergoing IVF.

They compared 91 patients with interstitial or subserous myoma with 91 control patients without fibroids.

The authors observed a statistically significant decrease in all the infertility factors combined: pregnancy rate, implantation rate and live birth rate.

These results are contradicted by Jun *et al.*,^[14] who in a retrospective cohort series compared 141 patients with 406 control myomas. The authors found no significant difference in the implantation rate between women with a myoma less than 7 cm in size that did not deform the cavity and women free of myomatous lesions, respectively 30.5% versus 41.6%.

Surrey,^[15] based on a retrospective study of IVF pregnancies, reported a live birth rate that was not influenced by the presence of interstitial myomas with a uterine cavity of normal appearance on hysteroscopy.

Oliveira *et al.*,^[16] in 2004, based on a retrospective controlled study of 408 first cycle IVF patients with subserous and intramural myomas, reported pregnancy rates of 47.8% and 44.9% respectively.

Analysis of the literature data concerning the consequences of all myomas combined on fertility in ART programs, without distinguishing the route of approach, shows results in favour of a deleterious effect of the myomas.

These data were confirmed by Somigliana in 2006,^[17] who performed a meta-analysis of the work that evaluated the influence of the position of myomas on patients undergoing ART for infertility.

Two fertility parameters are selected: the conception rate and the birth rate.

The results of this meta-analysis show that myomas, all locations combined, alter the pregnancy rate and the birth rate with an (OR)=0.8 (95% CI [0.7 -1.0]) and OR=0.8 (95% CI [0.6 -0.9]).

These results are confirmed by a second meta-analysis, that of Pritts *et al* (18) which shows in 2009 (**Table 3**), based on numerous publications, albeit heterogeneous, that fertility parameters such as the pregnancy rate, the implantation rate, the rate of live birth and the rate of fetal loss are significantly altered by the presence of myoma.

The only parameter not significantly altered is the rate of preterm delivery (Table 4).

It should be noted, however, that not all the studies analysed in this meta-analysis involved ART patients and of the 23 studies included in the statistical analysis, only 4 were in natural childbirth.

Table 3: Effect of fibroids on fertility in all uterine locations (Pritts Meta Analysis).

RATES	NUMBER OF STUDIES	RELATIVE RISK	CONFIDENCE INTERVAL	P
PREGNANCY RATE	18	0,849	0,734-0,983	0,029
IMPLANTATION RATE	14	0,821	0,722-0,932	0,02
LIVE BIRTH RATE	17	0,697	0,589-0,826	<0,001
FOETAL LOSS RATE	18	1,678	1,37-2,051	<0,001
EARLY DELIVERY RATE	3	1,357	0,607-3,036	_____

2/Submucosal myomas

In 2001, a study by Pritts,^[19] followed by a meta-analysis, documented a 70% reduction in pregnancy rates in 24 infertile patients with submucosal myomas after 86 cycles of IVF compared with infertile patients without submucosal myomas.

The results of the meta-analysis demonstrated a deleterious effect of submucosal myomas on the pregnancy rate with an RR of 0.3 (95% CI [0.1-0.7]).

In 2009, a second meta-analysis by Pritts *et al*,^[18] evaluated the alteration of fertility parameters related to the presence of submucosal myomas in patients undergoing ART compared with infertile patients without myomas.

This study found statistically significant results in favor of the deleterious effect of submucosal myomas on pregnancy rate, implantation rate, live birth rate, and rate of fetal loss. (Table 4)

Table 4: effect of sub-mucosal fibroids on fertility (PRITTS META ANALYSIS)

RATES	NUMBER OF STUDIES	RELATIVE RISK	CONFIDENCE INTERVAL	P
PREGNANCY RATE	4	0,363	0,179-0,737	0,005
IMPLANTATION RATE	2	0,283	0,123-0,649	0,003
LIVE BIRTH RATE	2	0,318	0,119-0,850	<0,001
FOETAL LOSS RATE	2	1,678	1,373-2,051	<0,022
EARLY DELIVERY RATE	0	1,357	0,607-3,036	_____

3/Sub serous myoma

All of the available results are part of broader work in which these myomas are associated with interstitial and submucosal fibroids.

Pritts' meta-analysis found no deleterious effect of the latter on fertility.

4/Interstitial myoma

After an exhaustive literature review, 19 studies were selected and analyzed.

On the main judgment criterion of this meta-analysis which is the live birth rate, the results of the comparison of patients with intramural myomas without distortion of the uterine cavity to patients without myomas are as follows: the live birth reduction rate is 21% with

statistically significant RR results of 0.79 (95% CI [0.70-0.88]) (p = 0.0001);

In an analysis of eight studies in which patients were younger than 37 years of age and four studies in which patients received their first cycle of IVF, the live birth rate was reduced by 25%, RR 0.75 (95% CI [0.62-0.89]) (p = 0.001) and 23%, RR 0.77, respectively. (95% CI a95% [0.69-1.0]) (p = 0.05) ; - analysis of the only two prospective studies showed a reduction in the rate of live birth 40%, RR 0.60 (95% CI [0.41-0.87]) (p = 0.007). On secondary endpoints, they report the following results : - regarding the pregnancy rate: after analysis of all studies (18/19), the reduction in pregnancy rate in infertile patients with intramural myomas without distortion of the uterine cavity compared to infertile patients without myomas after ART cycle was 15%, RR 0.85 (95% CI [0.77-0.94]) (p=0.002).

Analysis of the 13 studies in which the age of the patients was less than 37 years showed a reduction of 18%, RR of 0.82 (95% CI [0.73-0.92]) (p=0.0005).

Analysis of the 6 studies in which patients benefited from their first cycle of ART showed a 16% reduction in pregnancy rate, RR of 0.84 (95% CI [0.73-0.96]) (p=0.009).

Analysis of the four prospective studies showed an 11% reduction in the pregnancy rate, RR of 0.89 (95% CI [0.68-1.17]) (p=0.41). -regarding the Implantation rate: after analysis of all studies, the reduction in the implantation rate was 13%, RR 0.87 (95% CI [0.73-1.03]) (p=0.11).

Analysis of the 6 studies in which the age of the patients was less than 37 years showed a reduction of 28%, RR 0.72 (95% CI [0.59-0.87]) (p=0.0006).

Analysis of the 2 studies in which patients benefited from their first IVF cycle showed a 16% reduction in the pregnancy rate. RR of 0.84 (95% CI [0.55-1.29]) (p = 0.42).

Table 5: ART's results with or without myomas (main studies).

AUTHORS	MYOMA+ OR MYOMA -	NUMBER OF PATIENTS	PREGNANCY RATE	IMPLANTATION RATE
SEOUD AND AL ^[9]	+ -	11 1415	20,8% 19%	-----
FARHI AND AL ^[10]	+ DC +NC -	18 28 50	9% 25,1% 29,1%	2,7% 9,7% 8,9%
ELDAR -GEVA AND AL ^[11]	+SS +I +SM -	33 46 9 249	34,1% 16,4% 10% 30,8%	15,1% 6,4% 4,3% 15,7%
RAMZY AND AL ^[12]	+ -	39 367	45% 42%	12,5% 13,8%
STOVALL AND AL ^[13]	+ -	91 91	37,4% 52,7%	13,8% 19,7%
JUN AND AL ^[14]	+ -	141 406	30,5% 41,6%	-----
KLATSKY ^[21]	+ -	-----	36,9% 41,1%	18,2% 22,1%
PRITTS ^[18]	+SM -	META ANALYSIS	-70% -----	-----
OLIVEIRA AND AL ^[14]	+SS +SM	408 SM AND SS	47,8% 44,9%	-----
SUNKARA AND AL ^[22]	+SM (NC)	META ANALYSIS	-15%	-13%

(DC/NC : deformation of the uterine cavity/normal cavity ; SM : submucosal ; SS : subserous ; I : interstitial)

IV-DISCUSSION

Uterine fibroids would be recognized as the sole cause of infertility in only 1-2% of cases of infertile patent women.^[20,23-24-25]

An alteration in the upward movement of the sperm or the phenomenon of nidation by compression of the tubal ostium on the one hand and by deformation of the uterine

cavity on the other would probably be the two main mechanisms responsible.

The latter also modify the vascularisation of the endometrium, are involved in certain endometrial dystrophies and in the quantitative and qualitative changes in physiological uterine contractions and in the decrease in the production of the Heparin Binding-

Epidermal Growth Factor (HB-EGF), thus preventing embryonic implantation.^[26, 27-28]

A/CAUSE AND EFFECT: does the presence of fibroids reduce implantation ?

1/ In natural procreation

It is now accepted that submucosal fibroids have a negative impact on fertility through their presence within the uterine cavity.

Pritts et al. concluded that submucosal fibroids (FIGO 0-2) that cause deformation of the uterine cavity result in a decrease in the clinical rate of pregnancy, implantation and live birth, and an increase in the rate of spontaneous miscarriage.^[18]

With regard to fibroids that do not cause any modification of the uterine cavity, there is much controversy.

Pritts et al. found that women with pure intramural fibroids with no submucosal component (FIGO 3-4) also have decreased implantation and live birth rates, and an increased rate of spontaneous miscarriage compared with the fibroid-free control groups. However, the Pritts study appears to have underestimated the submucosal component of some fibroids and therefore these results may have been influenced by underdiagnosis.^[18]

What is clear from this study, however, is that there is no evidence to suggest that subserous fibroids (FIGO 5-7) are involved in the reduction of different fertility rates.

Ultimately, in order to guide infertile women and to explain the relationship between myoma and infertility and the possible benefit of myomectomy, other factors need to be taken into consideration. The intrinsic parameters of the myomas (size...) would seem to have no influence on the pregnancy rate after myomectomy.^[18]

The posterior location of the myomas, particularly in the case of uterine sutures, would reduce the pregnancy rate.

2/ In ART

The deleterious role of submucosal and intramural myomas on the pregnancy rate has been demonstrated.^[11,29,30]

The study by Ramzy et al^[12] showed no difference in terms of implantation and pregnancy after ART/ICSI in two groups of infertile patients with or without myomas. The methodological choices of this study made it questionable and unreliable.

A synthesis of available data showed a 21% reduction in the rate of live births after in vitro fertilization in women with intramural fibroids without deformation of the uterine cavity, compared with a control group without fibroids.^[18]

The weakness of this study results from the heterogeneity of the patient populations.

A major co-factor of infertility is access to care. Indeed, treatment received early will lead to better results.

There is a wealth of data showing that women of African and Caribbean origin in whom fibroids are frequent and severe have a deleterious access to care and are therefore under-represented in the databases relating to infertility, in vitro fertilization.^[31]

Feinberg et al. examined this disparity by studying the results of the first cycle of ART between African-American and Caucasian patients in conditions for access to equitable care.^[32]

Fertility outcomes between the two groups were found to be similar.

In both groups of women, the presence of fibroids reduced the ART implantation rate and the live birth rate (18% vs. 27%).

The treatment of these fibroids seems to be done judiciously before any attempt at ART.

B/ BENEFIT OF TREATMENT: Does fibroids treatment improve results and fertility rates ?

1/Hysteroscopy

Hysteroscopic myomectomy seems to be the method of reference in cases of intracavitary myoma (FIGO 0/1) and allows to restore the dimensions of the cavity and consequently improve fertility results.

The risk of endometrial lesions and intrauterine adhesions and their consequences on conception and possible pregnancy should be discussed with the patient prior to surgery.

Intrauterine adhesions during hysteroscopic myomectomies are of the order of 7.5%.^[33]

Valle et al. have shown that the severity of these adhesions is directly correlated with a decrease in fertility rates.

Rates of delivery after hysteroscopic resection of submucosal myoma vary in the literature from 10% to 69%.^[34]

With the exception of Goldenberg's work,^[34] all the other studies did not take into account the other factors of infertility, which makes the involvement of submucosal myomas difficult to interpret. In practice, the advantage is that they can be easily resected by hysteroscopy at the cost of low morbidity compared to other forms of myomectomy.

The consensus indications for hysteroscopic surgical management are submucosal myomas with a diameter of less than 4-5 cm and intramural myomas with more than 50% of their diameter in the uterine cavity.

As shown in Table 8, improvement in the pregnancy rate after submucosal myoma resection has been reported by many authors; however, there is no evidence that the rate of pregnancy after resection of submucosal myomas has improved.

There are no randomized controlled trials.

For submucosa classified as type 2 or less than 50% is intracavitary, their hysteroscopic approach is more complicated and usually requires a two-step procedure, especially if the size is greater than 3 cm.

Cammani et al have shown that the hysteroscopic approach is possible for fibroids larger than 5 cm in diameter.^[35]

For infertility, however, it is more prudent to proceed with Japaroscopic resection of these fibroids, despite the presumed increased risk of uterine rupture during future pregnancy and obstetric labour.

In practice, the low morbidity of hysteroscopic myomectomy and the demonstrated benefit on the pregnancy rate are strong reasons for recommending this procedure. procedure at an infertile patient with submucosal myoma.^[36]

Table 6 : fertility parameters after hysteroscopic myomectomy of SM fibroids.

AUTHORS	NUMBER OF PATIENTS	PREGNANCY RATE	DELIVERY RATE
NARAYAN AND AL	27	48,2%	-----
BERNARDAND AL	31	35,5%	69,3%
VARASTEH AND AL	36	53%	36%
VERCELLINI AND AL	108	38%	35%
GOLDENBERG	15	47%	40%
FERNANDEZ AND AL	59	27%	10%
SHOKEIR AND AL 2005	26	49%	63%
SHOKEIR AND AL 2009	216	63,4%	-----

2/Laproscopy or laparotomy

All fibroids classified as FIGO type 3 and above and large type 2 are best treated laparoscopically or laparotomically.

Fertility results appear to be similar with these two approaches.

Combined data from 267 women from two randomized controlled studies comparing the laparoscopic and laparotomic approach showed similar results in both groups (64).

For the first study, 131 patients scheduled for myomectomy on infertility with at least one fibroid greater than 5 cm, had a similar pregnancy rate, i.e. 53.6% for the laparoscopy group versus 55.9% for the laparotomy group.

Febrile morbidity was reduced in the laparoscopy group with a better hemoglobin level and a shorter hospital stay.^[37]

For the second study including 132 women with fibroids, while the cumulative results in the first 12 months after surgery were consistent (52.9% vs 38.2%), the outcome per cycle such as the pregnancy rate per cycle (6.5% vs 3.9%) and the time to conceive the first pregnancy were significantly better in the laparoscopy group.

All these data seem to suggest comparability in terms of fertility of laparoscopy and laparotomy.

Laparoscopy makes it possible to obtain better haemoglobin levels and to reduce the hospital stay.

Nevertheless, the conclusions of a meta-analysis by Pritts et al^[18] are much more nuanced with regard to the general benefit of intramural and subserous myoma surgery for patients with a desire to conceive.

The author stresses the morbidity associated with surgical treatment either by laparotomy or laparoscopy in infertile patients.

Indeed, none of the parameters evaluated is improved by surgical management as shown in **Table 7**.

Other factors, not directly involved in the surgical procedure, could influence the pregnancy rate after myomectomy.

Thus age, particularly over 35 years, a duration of infertility of more than two years, the association with other infertility factors (tubal or ovarian pathologies, or spermatoc factors), and the posterior location of the myoma(s) decreased. pregnancy rates.^[3,8]

On the other hand, resection of myomas causing menometrorrhagia would increase the pregnancy rate.^[33]

Finally, certain factors inherent to myomas, such as the size of the largest one, the total number of fibroids resected, and the imprint of the myoma on the

endometrial cavity did not seem to have an influence on the pregnancy rate post resection.^[3,8,37]

Table 7: fertility parameters after LPS/LPT myomectomy of I/SS fibroids (Pritts meta analysis).

RATES	NUMBER OF STUDIES	RELATIVE RISK	CONFIDENCE INTERVAL	P
Pregnancy rate	2	3,765	0,179-0,737	NS
Implantation rate	0	---	---	---
Live birth rate	1	1,671	0,750-3,723	NS
Foetal loss rate	1	0,758	0,296-1,943	NS
Early Delivery Rate	0	1,357	0,607-3,036	---

IV- CONCLUSION

In conclusion, the impact of myomas and their consequences on fertility are the subject of numerous studies.

The concordance of the results of the different studies is a strong element in favour of the involvement of these myomas in the alteration of fertility mechanisms.

Therapeutic management must be early and take several parameters into account.

In the context of medically assisted reproduction, submucosal uterine fibroids. And interstitial are infertility factors and their resection is therefore justified.

The therapeutic decision is based on the patient's age, the expected time of ART treatment, the results of ART and the delay caused by a possible myomectomy in the context of ART treatment.

Similarly, it is necessary to take into consideration the ART pregnancy rate in women with fibroids.

In natural procreation, given the lack of randomized, multicentric studies, it is difficult to establish a direct link between myomas and infertility, although in the absence of any other infertility factors, a myomectomy appears to be appropriate.

On the contrary, in the presence of other infertility factors, the involvement of the myoma is less obvious and the decision for myomectomy must be the subject of multidisciplinary consultation.

In the end, although many authors have taken an interest in this subject, apart from submucosal fibroids and those causing distortion of the uterine cavity which require myomectomy, no direct link can be clearly established between myoma and infertility.

All our data suggest at best an indirect link.

VI-BIBLIOGRAPHIC REFERENCES

1. Fernandez H, Kadoch O, Capella-Allouc S, Gervaise A, Taylor S, Frydman R. Hysteroscopic resection of

- submucous myomas: longterm results. *Ann Chir*, 2001; 126: 58-64.
- Poncelet C, Benifla JL, Batallan A, Darai E, Madelenat P. Myoma and infertility: analysis of the literature. *Gynecol Obstet Fertil*, 2001; 29: 413-21.
 - Vercellini P, Maddalena S, De Giorgio O, Pesole A, Ferrari L, Crosignani PG. J eterminants of reproductive outcome after abdommal myomectomy for mfertlhty.Fertil Steril, 1999; 72: 109-14.
 - Donnez J, Jadoul P. What are the implications of myomas on fertility? A need for a debate?, *Hum Reprod*, 2002 Jun; 17(6): 1424-30.
 - Chaker, A., et al. "[Uterine fibromyomas: fertility after myomectomy. (About 41 cases)]." *Tunis Med*. 82.12, 2004; 1075-81
 - Casini ML, Rossi F, Agostini R, Unfer V. Effects ofthe position of fibroids on fertility. *Gynecol Endocrinol*, 2006; 22: 106-9.
 - Chigbu B, Aluka C, Onwere S, Kamanu C, Feyi-Waboso P, Okoro O, et al. Fertility following myomectomy at Aba, South Eastern Nigeria. *J Med Invest Pract*, 2014; 10: 135.
 - Fauconnier A, Dubuisson J, Ancel P, Chapron C, Prognostic factors of reproductive outcome after myomectomy in infertile patients. *Hum Reprod*, 2000; 15: 1751-7.
 - Seoud MA, Patterson R, Muasher SJ, Coddington CC. Effects of myomas or prior myomectomy on in vitro fertilization performance. *J Assist Reprod Genet*, 1992; 9: 217-21.
 - Farhi J, Ashkenazi J, Feldberg D, Dicker D, Orvieto R, Ben Rafael Z. Effect of uterine leiomyomata on the results of in vitro fertilization treatment. *Hum Reprod*, 1995; 10: 2576-8.
 - Eldar-Geva T, Meagher S, Healy DL, MacLachlan V, Breheny S, Wood C. Effect of intramural, subserosal, and submucosal uterine fibroids on the outcome of assisted reproductive technology treatment. *Fertil Steril*, 1998; 70: 687-91.
 - Ramzy AM, Sattat M, Amin Y, Mansour RT, Seror CI, Aboulghar MA. Uterine myomata and outcome of assisted reproduction. *Hum Reprod*, 1998; 13: 198-202.
 - Stovall DW, Parrish SB, Van Voorhis BJ, ~ahn SJ, Sparks AE, Syrop CH, et al. uterine leiomyomas reduce the efficacy of assisted reproduction cycles:

- results of a matched follow-up study. *Hum Reprod*, 1998; 13: 192-7.
14. Jun SH, Gin-urg ES, Racowsky C, Wise LA, Homstein MD. Uterine leiomyomas and their effect on in vitro fertilization outcome. *J Assist Reprod Genet*, 2001; 18: 139-43.
 15. Surrey ES, Liez AK, Schoolcraft WB. Impact of intramural leiomyomata in patients with a normal endometrial cavity on in vitro fertilization-embryo transfer cycle outcome. *Fertil Steril*, 2001; 75: 405-10.
 16. Oliveira FG, Abdelmassih VG, Diamond MP, Dozortsev D, Melo NR, J Abdelmassih R, et al. Impact of subserosal and intramural uterine fibroids that do not distort the endometrial cavity on the outcome of in vitro fertilization-intracytoplasmic sperm injection. *Fertil Steril*, 2004; 81: 582-7.
 17. Somigliana E, Vercellini P, Daguati R, Pasin R, De Giorgi O, Crosignani PG. Fibroids and female reproduction: a critical analysis of the evidence. *Hum Reprod Update*, 2007; 13: 465-76.
 18. Pritts EA, Parker WH, Olive DL. Fibroids and infertility: an updated systematic review of the evidence. *Fertil Steril*, 2009; 91: 1215-23.
 19. Pritts EA. Fibroids and infertility: a systematic review. *Obstet Gynecol Surv*, 2001; 56: 483-91.
 20. Narayan R, Rajat, Goswamy K. Treatment of submucous fibroids, and outcome of assisted conception. *J Am Assoc Gynecol Laparosc*, 1994; 1: 307-11.
 21. Klatsky PC, Tran ND, Caughey AB, Fujimoto VY. Fibroids and reproductive Outcomes : a systematic literature review from conception to delivery *Am J Obstet Gynecol*, 2008; 198: 357-66.
 22. Sunkara SK, Khairy M, El-Toukhy T, Khalaf Y, Coomarasamy A, The effect of intramural fibroids without uterine cavity involvement on the outcome of IVF treatment a systematic review and meta-analysis. *Hum Reprod*, 2010; 25: 418-29.
 23. Zepiridis LI, Grimbizis GF, Tarlatzis BC, "Infertility and Uterine Fibroids" *Best Practice & Research Clinical Obstetrics & Gynaecology*, 2016. doi: 10.1016/j.bpobgyn.2015.12.001.
 24. CNGOF, le « texte long » des recommandations pour la pratique clinique incluant les communications des experts et les références bibliographiques est publié dans le numéro du *Journal de gynécologie, obstétrique et biologie de la reproduction* (Volume 40 - Décembre 2011 - no8) sous la référence : *J Gynecol Obstet Biol (Reprod)*, 2011; 40: 693-962.
 25. Buttram VC, Reiter RC. Uterine leiomyomata: etiology, symptomatology, and management. *Fertil Steril*, 1981; 36: 433-45
 26. Lopez P. Chez une femme infertile, la présence d'un ou plusieurs myomes de moins de trois centimètres de diamètre justifie-t-elle une myomectomie ? *Contracept Fertil Sex*, 1997; 25: 350-1.
 27. Lyons EA, Taylor PJ, Zheng XH, Ballard G, Levi CS, Kredentser JV. Characterization of subendometrial myometrial contractions throughout the menstrual cycle in normal fertile women. *Fertil Steril* 1991.55.771-4.
 28. Ali A, Fateen B, Ezzet A, Badawy H, Ramadan A, El-Tobge A. A new mechanism of infertility associated with myoma : decreased production of heparin-binding epidermal growth factor un the endometrium. *Obstet Gynecol*, 2000; 95: 49.
 29. Hugh S. Taylor, M.D Fibroids: when should they be removed to improve in vitro fertilization success?, *May 2018 109(5): 784-785*
 30. Thomson M, Carr B, Intramural myomas: to treat or not to treat, *May, 2016 ; 8 : 145-149.*
 31. Grainger D, Seifer D, Frazier ~' RallM, Tjaden B, Me~ll J. Racial disparity in chmcal outcomes from women usIng advanced reproductive technologies (ART): analysis of 80,196 ART cycles from the SART database 1999 and 2000. *Fertil Steril*, 2004; 82: S37-8.
 32. Feinberg EC, Larsen FW, Catherino WH, Zhang J, Armstrong AY. Comparison of assisted reproductive technology utilization and outcome~ betwee~ Caucasian and African American patients in an equal-access-to-care settJ.ng. *Fertil Steril*, 2006; 85(4): 888-94.
 33. Valle RF, Sciarra JJ. Intrauterine adhesions: hysteroscopic diagnosis, classification, treatment, and reproductive outcome. *Am J Obstet Gynecol*, 1988; 161(6 Pt 1): 1459-70.
 34. Goldenberg M, Sivan E, Sharabi Z, Bider D, Rabinovici J, Seidman DS. Oútcome of hysteroscopic resection of submucous myomas for infertility. *Fertil Steril*, 1995; 64: 714-6.
 35. Camanni M, Bonino L, Delpiano EM, Ferrero B, Migliaretti G, Deltetto F. Hysteroscopic management of large symptomatic submucous uterine myomas. *J Minim Invasive Gynecol*, 2010; 17: 59-65.
 36. Erdirn:; Sandoganl, Ertan Sandogan, Management of fibroids prior to in vitro fertilization/ intracytoplasmic sperm injection: A pragmatic approach, *J Turk Ger Gynecol Assoc*, 2019; 20: 55-9
 37. Seracchioli R, Rossi S, Govoni F, Rossi E, Venturoli S, Bulletti C, et al. Fertility and obstetric outcome after laparoscopic myomectomy of large myomata: a randomized comparison with abdominal myomectomy. *Hum Reprod*, 2000; 15: 2663-8.