Original Article

The Effect of Twisted Uterus Caused by Endometriosis or Myomatosis on Reproductive Treatment Outcomes

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Received December 2020; Revised and accepted April 2021

Abstract

Objective: Twisted uterus is detected when the body of the uterus is rotated from the cervical canal. This anomaly may be due to different causes, such as uterine fibroids, endometriosis or the presence of both. The study has aimed to compare the effect of the twisted uterus cause in terms of reproductive treatment outcomes.

Materials and methods: It consisted of a retrospective study of twisted uterus cases with repeated implantation failure (more than three embryo transfers or four blastocysts transferred unsuccessfully) in our ultrasound department. The twisted uterus was defined when the vaginal probe needed to be rotated to assess the endometrial line thoroughly or when the coronal view was seen by 2D scan. From 2017 to 2020, 879 gynecological ultrasounds were performed. For statistical analysis, we carried out a logistical regression analysis adjusted by confounding factors.

Results: From 145 patients included only 92 patients underwent reproductive treatments. With the known cause of uterine torsion. 56 patients with endometriosis, 18 with uterine myoma and the remaining 18 suffered from both. After assisted reproductive treatment, the endometriosis group showed the highest clinical pregnancy rate (53.57%) compared to myoma (22.22%) and endometriosis and myoma (38.89%) groups.

Conclusion: Uterine myoma capable of causing uterine torsion may affect embryo implantation more than endometriosis. Prospective randomized studies with a larger number of patients would be needed to confirm these findings.

Keywords: Leiomyoma; Endometriosis; Assisted Reproductive Techniques; Ultrasonography; Diagnostic Imaging

Introduction

Despite excellent success rates in current assisted reproductive treatments, there is a challenge of recurrent implantation failures (RIF). The concept of repeated implantation malfunction has been widely discussed under a variety of definitions (1,2). It seems necessary that after the failure of three good quality embryo transfers, we evaluate all the possible risk factors influencing the expected success of subsequent treatments. Therefore, uterine pathologies such as polyps, various types of fibroids, congenital anomalies and endometriosis must also be ruled out

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as a possible factor of implantation failure (3).

Although hysteroscopy has been the procedure of choice for studying uterine factors (4), an ultrasound examination is a definitive method for a correct diagnosis.

The three significant positions of the uterus are version, flexion and rotation. The angle of rotation of the uterine body concerning its cervix could vary from 0º to 90º. The angle is 0º when the uterine body and cervix are wholly aligned without any rotation, and it is 90º when the uterine body rotates by 90º on its vertical axis with respect to the cervix leading to a twist between them. In such cases, it is possible to visualize the coronal section of the uterus in a two-dimensional (2D) ultrasound view. This rotation can be towards the right or left sides in anteflexed or retroflexed uteri (5).

Uterine torsion is a situation that causes concern in reproductive treatments; first because it avoids a proper evaluation of the endometrial thickness and pattern, which is fundamental to evaluate an excellent endometrial preparation (6), second because it has not been yet assessed whether it affects pregnancy outcomes. Furthermore, this situation is increasingly common in reproduction departments and is usually associated with pathologies such as endometriosis, uterine myoma or pelvic adhesions from diverse origins. To our knowledge, no reports are evaluating the cause of uterine torsion and the reproductive treatment outcomes.

Our study aimed to compare whether the cause of uterine torsion could influence the results of reproductive treatments in a specific population with repeated implantation failures.

Materials and methods

This study had approval from the Institutional Review Board of Instituto Bernabeu on 2nd July 2020 (reference: MR 26-2020), which waved the requirement for informed consent. A retrospective study has been performed, in which 145 patients with repeated implantation failure (RIF) and a diagnosis of the twisted uterus were included. Recurrent implantation failure has been defined after three embryo transfers or four blastocysts transferred without success. These patients were evaluated with both 2D and 3D ultrasounds for a correct diagnosis.

All ultrasounds were performed using the same BM operator, with the Voluson E10 (General Electric Healthcare) ultrasound system, equipped with a 5-9 MHz transvaginal volumetric probe. For a 2D ultrasound, we applied the frequency with harmonics at an angle of 180º. In the case of a 3D ultrasound, we applied a scanning angle of 120º for maximum quality. Both HD Live and Tomographic Ultrasound Imaging (TUI) had been used to visualize the coronal section of the uterus after the capture, and to establish uterine torsion that was noted in two dimensions.

The twisted uterus was defined using only 2D scan. The 3D scan was performed after 2D to confirm the torsion of the uterus (Figure 1).

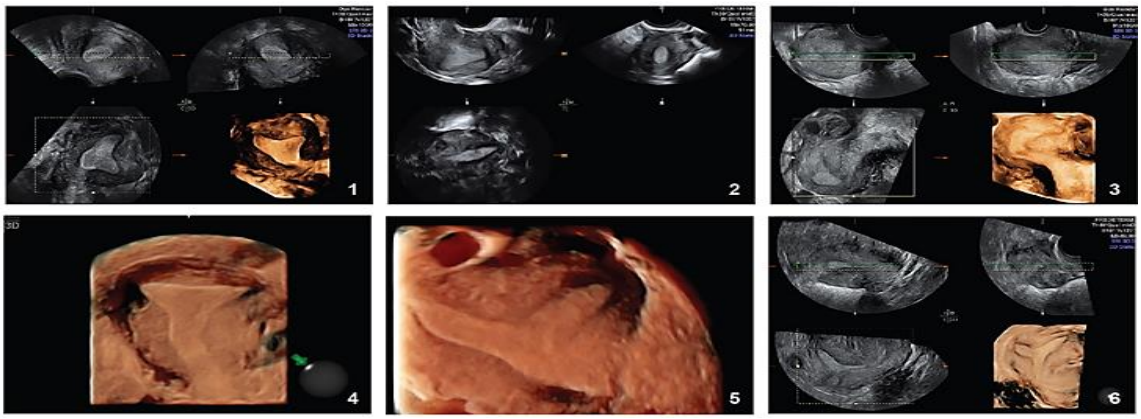

Figure 1: 3D images of a rotated uterus. 1. Full rotation with 90º angle of the uterine body with respect to the cervical canal. 2. Plane A represents the 2D vision of the uterus, in which its coronal vision can be seen, plane C would represent the longitudinal cut with the endometrial thickness. 3. Double angulation of the cervical canal with final rotation of the uterine body 4. Minimal uterine rotation. 5. Complete uterine rotation with the cervical canal in another plane with respect to the body. 6. Complete uterine rotation. In this case the C and 3D planes represent the vision obtained in 2D.

The standard angle of uterus (without torsion) was considered to be 0º, and it was capable of seeing the endometrial line correctly from the cervix to the fundus. When a uterus is twisted, the vaginal probe needs to be rotated to visualize the endometrial sequence completely. This rotation has been considered as the angle of rotation of the twisted uterus, and can be in anteflexion or retroflexion, to the right or the left and from 0º to 90º.

We analyzed 879 2D/3D ultrasound scans performed from 2017 to 2020. Of these, 145 met the criteria for twisted uterus. From these 145 scans, 25 had no apparent cause for uterine torsion, so they were considered as not real torsion, because it was thought that it may turn to an untwisted situation spontaneously. Ninety-two patients of the remaining 120, underwent reproductive treatments after an ultrasound. Among these 92 patients with uterine torsion, 18 were diagnosed with endometriosis and myoma, 18 had only myoma and 56 had only endometriosis (Figure 2).

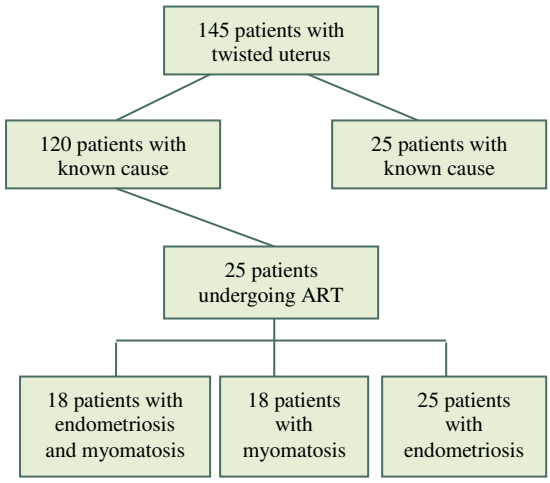

Figure 2: Flow chart of the study

All patients with myomas had previously undergone a hysteroscopy, ruling out the presence of submucosal fibroids. On the other hand, all patients had three or more intramural and subserousal myomas as the cause of uterine torsion, and at least one intramural myoma was over 3 cm in size.

Of the 56 patients with endometriosis, 18 (32.1%) had been diagnosed by ultrasound, while 36 (67.9%) had undergone previous surgery. The diagnosis of added adenomyosis was yielded in 8 patients (14.3%) of those diagnosed with endometriosis. Only the integrity of the junctional zone was taken into account in the 3D ultrasound scan for determination of adenomyosis,

We have followed STATA 14 for statistical analysis. Quantitative variables are shown as means and categorical variables as percentages. Fisher's exact test for categorical variables and the ANOVA test for quantitative variables were used to assess the difference between groups.

A logistic regression analysis was carried out adjusted by confounding variables. The level of statistical significance was defined as $p < 0.05$.

Results

Eight hundred seventy-nine 3D ultrasound scans were performed on patients referred to the repeated implantation failure unit at Instituto Bernabeu from 2017 to 2020. Of these, 145 patients met the diagnostic criteria established for twisted uterus, thus giving a prevalence of the phenomenon of 16.5%. Twenty-five were excluded since there was no known cause of uterine torsion. Consequently, the torsion diagnosed at that moment was not verifiable later. Twenty-eight more patients were excluded for the reason that no reproductive treatment was performed after the ultrasound scan.

Patients with endometriosis were younger and had fewer previous treatments than those in the other two groups. On the contrary, patients with endometriosis and myoma had suffered a long period of sterility than the others (Table 1).

Table 1: Baseline characteristics of patients

	Endometriosis (n=56)	Myomas (n=18)	Endometriosis & Myomas (n=18)	P
Age (years)	39,8	42.2	42.9	0.0063
Sperm factor (%)	39.8	55%	40%	0.356
Infertility period (years)	36.07%	5.1	7.1	0.005
Previous ART* (n)	5.1	5.8	6.3	0.05
Previous ET (n)	4.4	7	7.3	0.21
Previous live birth (n)	5.4	0.05	0.1	0.861
Previous Miscarriage	0.12	1.2	1	0.213
Egg donation (%)	0.64	52.63%	68.43%	0.244

*ART. Assisted reproductive treatments; **ET: embryo transplantation

However, the three groups did not differ significantly in terms of sperm factor, the number of total embryos previously transferred, term pregnancies conceived before treatments, clinical abortions or types of treatment (egg donation vs intracytoplasmic sperm injection with own oocyte).

Patients diagnosed with only myoma showed a lower percentage of clinical pregnancy (Myoma: 22.22% vs Myoma and endometriosis: 38.89% vs Endometriosis: 56.57%) than the other two groups. We also observed linearity between the groups (Figure 3). Conversely, despite the clinical differences, no statistically significant differences were found in the probability of a positive biochemical pregnancy test (Myoma: 33.33% vs Myoma and endometriosis: 44.44% vs Endometriosis: 60.61%) or an abortion (Myoma: 5.56% vs Myoma and endometriosis: 16.67% vs Endometriosis: 10.91%).

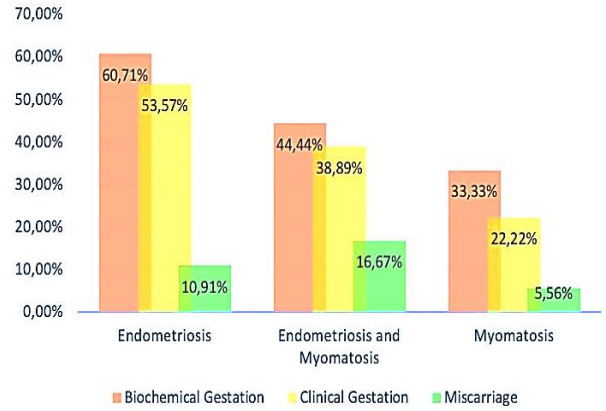

Figure 3: Reproductive Treatment outcomes. Biochemical pregnancy rate, clinical pregnancy rate and miscarriage rate.

To control possible confounding factors of the woman's age, time of sterility and number of treatments performed, we performed a binomial logistic regression analysis with the Endometriosis group as the reference group. Following this study, we observed a lower rate of biochemical pregnancy and clinical pregnancy in the Myoma group than in the Endometriosis group (aOR 3.29, 95% CI [1.03, 10.5]; aOR 4.14, 95% CI [1.2, 14.7] respectively). However, there was no increased likelihood of abortion when compared with endometriosis patients in myoma group (aOR 2.14, 95% CI [0.2, 19.9]) or in endometriosis and myoma group (aOR 0.85, 95% CI [0.2, 4.4]) (Table 2).

Table 2: Logistical analysis regression adjusted by confounding factors

	OR**	IC 95%	p
Biochemical gestation*			
Myomas	3.01	1.91 a 7.24	0.0591
Endometriosis & myomas	2.04	1.29 a 4.9	0.2193
Clinical Gestation*			
Myomas	3.86	2.35 a 10.64	0.0347
Endometriosis & myomas	1.81	1.14 a 4.37	0.3117
Miscarriage*			
Endometriosis & Myomas	2.13	0.46 a 5.3	0.505
Myomas	0.84	-16.6 a 1	0.838

* Adjusted analysis by age, infertility period and number of previous reproductive treatments

** OR with endometriosis group as reference

Discussion

We found the twisted uterus prevalence of 16.5% in RIF patients. Endometriosis patients were younger and with shorter periods attempting to conceive, while endometriosis and myoma group achieved the longest time of sterility. Therefore, we carried out an adjusted analysis with the endometriosis group as a reference group. It has been observed the lowest biochemical pregnancy rate and clinical pregnancy rate in myoma group.

Our study results were unexpected compared to previous published studies posing that endometriosis is related to a higher percentage of abortions, lower percentage of implantation (7) and a poorer prognosis compared to other infertility causes. On the other hand, there is a consensus on promising results in fertility treatments in cases of fibroids that do not distort the endometrial cavity (8).

It is unknown whether twisted uterus impairs embryo implantation. Nevertheless, it is a situation that avoids a correct evaluation of the uterus. Globally, a sonographer cannot assess properly the whole uterus in this situation, and specifically endometrial line. Therefore, it makes it difficult to rule out several endometrial pathologies such as polyps or even submucosal fibroids.

In many studies, the relationship between the presence of myomas and the results of reproductive treatments has been controversial, as many researchers may not have taken into account the location and size of these fibroids (3). Greater cohesion exists in the presence of submucosal fibroids, i.e. those that invade the endometrial cavity worsen the reproductive prognosis.

However, a recent study showed that fibroids

near the uterine cavity, defined as type 3 according to the FIGO classification, with a size greater than 2 cm also affect the results of reproductive treatments, thus proving that invasion of the cavity is not the only effect caused by fibroids (9). Some reports state that it could be associated cytokine elevation in patients with fibroids with repeated implantation failure or repeated miscarriages (10, 11). Even today, researchers continue to study the cellular origin of fibroids with the influence of stem cells (12). There is increasing evidence that intramural fibroids can affect the functionality of endometrium over time, causing an alteration in gene expression of different molecules involved in embryo implantation (13, 14).

A recent study hypothesized that large intramural leiomyomas decrease the expression of endometrial implantation factors during the implantation window (15). Other authors confirm that genetic favoring of endometrial receptivity increases after intramural myomectomy, even when they do not distort the cavity (16).

Furthermore, an increase in the expression of neurogenic factors in the presence of fibroids has also been reported (17). Besides, an increase in uterine peristalsis that may be caused by fibroids can influence the outcomes of fertility treatments (18).

There is a controversy regarding whether the most appropriate treatment for fibroids for better fertility results is surgical (myomectomy), medical or radiological (19, 20).

Therefore, we hypothesized that the effect caused by the myomas capable of rotating the uterus might affect myometrium functionality being able to affect uterine peristalsis during embryo implantation as well as endometrium functionality.

Our findings suggest that myomas able to rotate the uterus may affect the outcomes after assisted reproductive treatments. Future researches could take account of it to assess whether twisted uterus could be an added criterion for surgery intervention to improve the reproductive outcomes.

Nevertheless, further prospective studies analyzing the effect of twisted uterus regarding reproductive outcomes in suitable prognosis patients should be performed to confirm our findings.

The strengths of our study are a strict definition to diagnose the pathology and only one operator performing the scans. The limitations are the nature of the retrospective study and the number of patients included.

Conclusion

In conclusion, our study indicates that patients with uterine torsion and myoma have poorer clinical and biochemical pregnancy rates as compared to those with uterine torsion and endometriosis and those with uterine torsion and endometriosis and myoma. These results were contrary to the results of some studies indicating that endometriosis has a poorer pregnancy outcome. With these findings, new research can be carried out assessing the implication of twisted uterus in reproductive effects and whether myomas capable of rotating uterus achieved worse prognosis than others.

Acknowledgments

Authors have no conflict of interests.

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Citation: Moliner B, Sellers F, Bernabeu A, Fuentes A, Castillo JC, Llacer J, et al. **The Effect of Twisted Uterus Caused by Endometriosis or Myomatosis on Reproductive Treatment Outcomes.** J Fam Reprod Health 2021; 15(2): 106-11.