

Post-laparoscopy predictive factors of achieving pregnancy in patients treated for infertility

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Abstract

Introduction: Laparoscopy is a long-established diagnostic and therapeutic method for treating women suffering from infertility. The application of this method of treatment can help achieve pregnancy only if there is correct classification of patients and evaluation of their partner's reproductive capacity. The main predictors of achieving pregnancy in a couple treated for infertility are the woman's age, her ovarian reserve, tubal patency, the presence of endometriosis and quality of sperm parameters.

Aim: To evaluate the effect of endometriosis, ovarian reserve and selected parameters of semen on the effect of achieving pregnancy in patients undergoing laparoscopy.

Material and methods: The most significant predictor of pregnancy in patients undergoing laparoscopy due to infertility was found to be anti-Mullerian hormone (AMH) level after laparoscopy, and the main parameters of semen partners were density, motility and morphology. The number of achieved pregnancies after the laparoscopic treatment of infertility was lower in patients diagnosed with endometriosis, and depended on the severity of the condition.

Results: As a result of laparoscopic treatment of endometriosis, we found a decrease in ovarian reserve measured by means of AMH.

Conclusions: The most important predictors of pregnancy in patients who underwent laparoscopy due to infertility are post-laparoscopy AMH levels and the main parameters of the partner's semen: density, motility and morphology. The number of pregnancies after laparoscopic treatment is lower in patients diagnosed with endometriosis, and depends on the severity of the condition.

Key words: infertility, sperm, laparoscopy, endometriosis.

Introduction

Disorders of human reproduction affect a growing number of couples in our society [1]. In some cases, the therapeutic process leading to pregnancy requires laparoscopy. It is a long-established diagnostic and therapeutic method for women treated for infertility

[2]. By using laparoscopy, we can remove the fibroids, ovarian tumors, endometriosis, and adhesions, and evaluate the functionality of the fallopian tubes in a minimally invasive way [3]. The application of this treatment method may contribute to a pregnancy only when there is correct classification and evaluation of the partner's reproductive capacity [4, 5].

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The main predictors of achieving pregnancy in a couple treated for infertility are the woman's age, her ovarian reserve, tubal patency, the presence of endometriosis and quality of sperm parameters [2, 4, 6]. Proper assessment of the chance of getting pregnant gives the opportunity to choose the appropriate method of treatment, so as not to lead to unnecessary waste of reproduction time [7]. Algorithms with a pair suffering from reduced fertility, as well as the diagnostic minimum, are not fully specified. They depend on the availability, and acceptance by the pair, of selected diagnostic and therapeutic methods.

In most countries, the adopted course of action with a couple who after a year of natural means cannot obtain any offspring comprises the execution of six intrauterine inseminations (IUI), if the male factor allows it. In a situation where it has no effect or sperm parameters have no chance of fertilization, patients are made eligible for *in vitro* fertilization (IVF). Eligibility for IVF is also accelerated in the case of an elderly patient, fallopian tube obstruction and the presence of advanced endometriosis [8, 9].

During the management of the infertile couple, it is also reasonable to perform laparoscopy, especially in a situation when there is suspected presence of endometriosis, adhesions, or there is a need for the fenestration of ovaries. The literature suggests that laparoscopy, in appropriate indications, increases the chance of getting pregnant [2, 3].

Aim

The aim of the study was to evaluate the influence of endometriosis, ovarian reserve and selected parameters of semen on achieving pregnancy in patients undergoing laparoscopy.

Material and methods

The study was conducted by making a retrospective analysis of medical records of patients treated for inability to obtain offspring in 2011–2016 at the Ovum center for infertility in Lublin. We analyzed the records of treatment of 258 patients undergoing first-time laparoscopic surgery aged 30–34, trying to become pregnant for the first time. We analyzed the medical records, from within +6 months after undergoing laparoscopy, of couples trying to achieve pregnancy as a result of intra-uterine insemination. We excluded women with blocked fallopian tubes and those

who, due to complications, underwent laparotomy, as well as with a body mass index (BMI) > 35 kg/m², urgent and chronic metabolic diseases. The stage of endometriosis was classified in four stages by means of the ASRM staging (American Society of Reproductive Medicine) [10]. Sperm analysis was assessed manually under a microscope in accordance with the WHO criteria of 2010 after 3–5 days of sexual and alcohol abstinence [11]. Levels of follicle-stimulating hormone mIU/ml (FSH) and anti-Mullerian hormone (AMH) ng/ml were determined on the third day of the cycle preceding ovulation to 3 months before and after laparoscopy in an approved laboratory. The presence of pregnancy was determined by means of ultrasound performed in the sixth week of its duration.

Consent to the study was issued by the Bioethics Committee at the Institute of Agricultural Medicine in Lublin.

Statistical analysis

The results were statistically analyzed. The values of the analyzed measurable parameters are presented as the mean, median, minimum and maximum values, lower and upper quartile and standard deviation, and the categorical parameters are presented as the number and percentage. In terms of qualitative characteristics, the χ^2 test was used to detect the existence of differences between the compared groups. Checking the normal distribution of variables between groups was performed using the Shapiro-Wilk normality test. Testing differences between the two groups was performed by means of the Mann-Whitney non-parametric test. To evaluate the significance of changes in AMH and FSH before and after laparoscopy, Student's *t*-test was used for dependent samples. Determinants of getting pregnant were performed using logistic regression. The level of significance was established at $p < 0.05$, indicating the existence of statistically significant differences or relationships. Database and statistical surveys were carried out on the basis of the Statistica 9.1 computer software (StatSoft, Poland).

Results

In the studied group of patients, 136 pregnancies were achieved in up to half a year after the performed laparoscopy as a result of intrauterine insemination (group A), while 122 did not become pregnant (group B). Couples whose treatment was

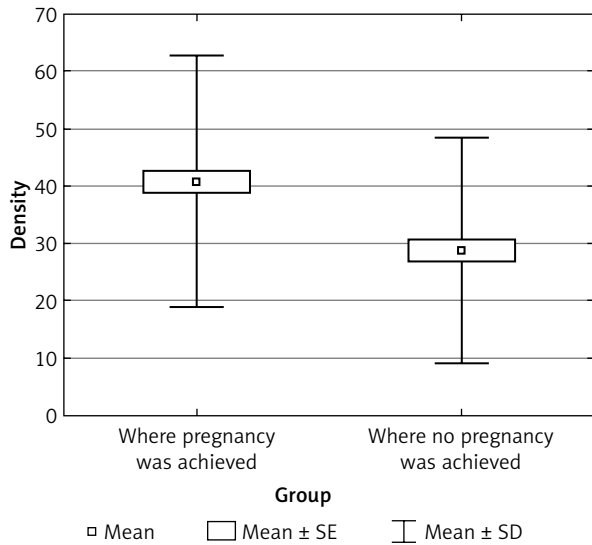


Figure 1. Comparison of partners' medium sperm density for patients with and without pregnancy

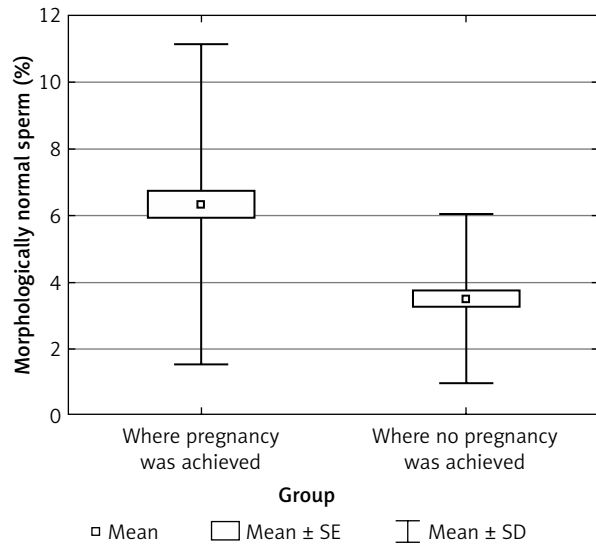


Figure 2. Comparison of the medium percentage of morphologically normal spermatozoa in the sperm of partners of patients with and without pregnancy

successful tried to become pregnant for 3.46 years, while the rest did so for 3.54 years. The difference was not statistically significant ($Z = 0.363; p = 0.716$).

The average age of patients' partners was 33.79 in group A, while in group B it was 34.75, the difference not being statistically significant ($Z = 1.31; p = 0.188$). Partners of patients who underwent laparoscopy, after which pregnancy was achieved, had higher average sperm density (40.69 million/ml) than patients who did not achieve pregnancy (33.79 million/ml). This difference was statistically significant ($Z = -5.166; p = 0.000$) (Figure 1). Furthermore, the average percentage of sperm showing progressive motility was significantly higher among couples where treatment was successful (37.15%) compared to those who failed to get pregnant (28.42%) ($Z = -5.155; p = 0.000$) (Figure 2). Men's ejaculates from group A had a higher percentage of morphologically normal sperm (6.33%) than in group B (3.49%), with this difference being statistically significant ($Z = -5.026; p < 0.001$) (Figure 3). We did not observe significant differences between the two groups in men's ejaculates in the case of the percentage of the viability (VIAB) average values ($Z = -1.418; p = 0.156$), mixed antiglobulin reaction (MAR) IgA ($Z = 0.261, p = 0.794$) or MAR IgG ($Z = -0.498; p = 0.618$).

The average level of AMH before laparoscopy among pregnant patients was 3.92 ng/ml, while in

women who failed the treatment it was 3.36 ng/ml. These values were significantly different ($Z = -2.439; p = 0.014$) (Figure 4). A similar relationship involved the average level of this hormone after laparoscopy, where women from group A scored 3.83 ng/ml, whereas those from group B scored 3.83 ng/ml ($Z = -2.48, p = 0.013$) (Figure 2). We found no statistically significant difference between the treated groups in the average

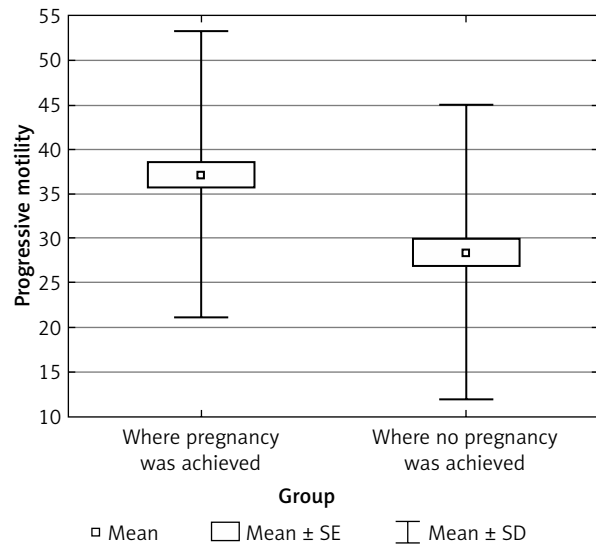


Figure 3. Comparison of medium progressive motility and medium sperm density of patients with and without pregnancy

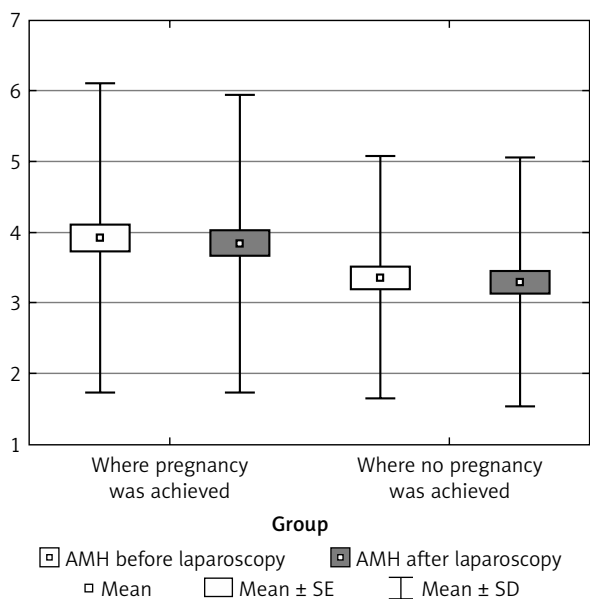


Figure 4. Comparison of patients' AMH levels before and after laparoscopy in the examined groups

FSH levels either before performing the procedure ($Z = -1.000$; $p = 0.317$) or after it ($Z = -1.116$; $p = 0.264$). The observed statistically significant differences have no clinical significance.

42.65% of the women successfully concluding the treatment of infertility and 59.84% of those who did not become pregnant were diagnosed with endometriosis. In the group of patients who became pregnant, we noted significantly fewer cases of endometriosis than in the group of women who did not become pregnant ($\chi^2 = 7.602$, $df = 1$, $p = 0.006$) (Figure 5).

Analyzing the severity of endometriosis, we observed a statistically significant difference in severity between the group of women of who became pregnant and the group of women who did not become pregnant ($Z = -3.215$, $p = 0.001$). In the group with the resulting pregnancy, a significantly lower severity of endometriosis was noted ($M = 0.90$, $Me = 0$) than in non-pregnant patients ($M = 1.47$, $Me = 1$) (Table I).

Table I. Comparison of severity of endometriosis in group with and without pregnancy

Group	N	Mean	Median	Lower quartile	Upper quartile	Standard deviation	Z, p
Where pregnancy was achieved	136	0.90	0.0	0.00	2.0	1.26	-3.215, 0.001
Where no pregnancy was achieved	122	1.47	1.0	0.00	3.0	1.46	

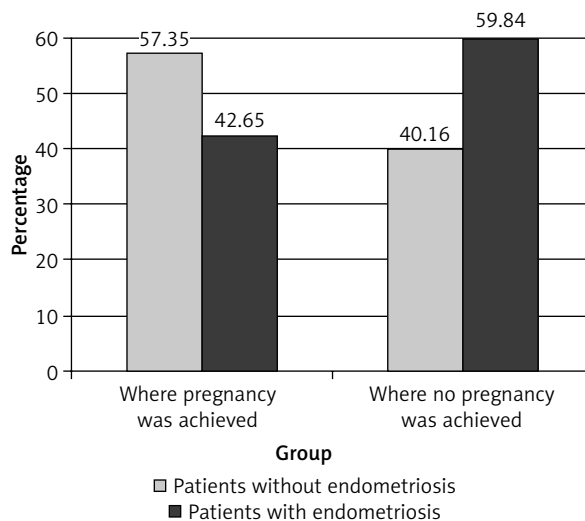


Figure 5. Presence of endometriosis in both groups

Based on the logistic regression analysis, it was found that with increasing variables – such as sperm density, the percentage of normal sperm cells, the percentage of sperm in progressive movement in the ejaculate, and the level of AMH in patients after laparoscopic surgery – the chance of getting pregnant increases, with these relationships being statistically significant (Table II). In the case of partner's age, VIAB, MAR, IgA and IgG tests, time of trying to become pregnant and FSH in women after laparoscopy, there was no association with the occurrence of pregnancy after laparoscopic treatment.

Discussion

The analysis showed that the main factors for achieving pregnancy in women undergoing laparoscopy are the level of AMH of the patient after surgery and the presence of endometriosis, as well as basic semen parameters of her partner (density, the percentage of correct form and progressive movement).

The significance of AMH levels for prediction of pregnancy is confirmed by examinations we carried

Table II. Model of logistic regression of pregnancy predictive factors

Analyzed variable	B	Wald	P-value	OR	-95% CI	+95% CI
Partner's age	-0.025	0.661	0.416	0.976	0.920	1.035
Density [mln]	0.028	13.001	< 0.001	1.028	1.013	1.043
% correct	0.222	21.969	< 0.001	1.248	1.138	1.369
% progressive movement	0.029	10.851	0.001	1.030	1.012	1.048
% VIAB	0.013	1.349	0.246	1.013	0.991	1.036
% MAR test IgA	0.021	0.564	0.453	1.021	0.967	1.077
% MAR test IgG	-0.033	0.871	0.351	0.968	0.903	1.037
Post-laparoscopy AMH	0.149	3.952	0.047	1.160	1.002	1.344
Post-laparoscopy FSH	0.013	0.028	0.868	1.013	0.870	1.180
Years of trying to become pregnant	-0.047	0.290	0.590	0.954	0.804	1.132
Constant	-3.356	4.498	0.034	0.035		

$\chi^2 = 73.757$, $df = 10$, $p < 0.001$, $R^2_{Nagelkerke} = 0.249$, $R^2_{Cox-Snell} = 0.332$; Hosmer-Lemeshow test: $\chi^2 = 6.558$, $df = 8$, $p = 0.585$.

out previously among women aged 25–35 in whom intra-cytoplasmic sperm injection was performed [12]. The accuracy of using AMH and FSH levels to predict pregnancy after IVF was determined by ROC curve analysis. An FSH level of 4.7 provided maximum discrimination between whether or not pregnancy will be achieved, with 28.57% sensitivity and 93.75% specificity. Similarly, an AMH level of 3.5 has 46.75% sensitivity and 86.11% specificity for indicating whether pregnancy will be achieved. The value of area under the curve (AUC) for FSH was 0.692, while the AUC value for AMH was 0.705. The assumed level for α was 0.05 and the obtained value for p was 0.597. There were no statistically significant differences between the curves for FSH or AMH ($Z = 383$, $p = 0.702$). The obtained results are consistent with those conducted among women undergoing the IVF procedure only as far as the significance of AMH level for prediction of pregnancy is concerned. The importance of AMH to predict the chance of impregnation is also confirmed by numerous other reports by various authors, which were summed up by Grynepur *et al.* in their meta-analysis [13].

There are no reports describing the value of the parameter of semen used in artificial insemination to predict the chance of impregnation after laparoscopy. The importance of correct morphology, density and sperm motility for the treatment of infertility by artificial insemination have been, similarly to ours, confirmed by the analysis of Coetzee *et al.* and Alamaneni *et al.* [14, 15]. Undoubtedly, the issue of

male factor and its presence with the severity of endometriosis will require further research.

In our study, endometriosis was present in 50.78% of patients having undergone laparoscopy. This is a result similar to the one obtained by Mishra *et al.*, who diagnosed endometriosis in 48.38% of 372 women who underwent laparoscopy [16].

The analysis shows that the proportion of pregnancies resulting from post-laparoscopy artificial insemination was 52.71%. It is most similar to the efficiency described by Keresztúri *et al.*, who used a similar treatment strategy and achieved a 53.4% rate of pregnancies [17]. In their studies, as well as in our, the treatment effect (impregnation) was dependent on the severity of endometriosis. Another pregnancy rate after laparoscopic treatment of endometriosis was obtained by Słabuszewska-Jozwiak *et al.*, who confirmed pregnancies in 32% of 53 women in 6 months; 11 out of 53 (20.75%) women became pregnant spontaneously, and 6 out of 53 (11.32%) patients became pregnant as a result of assisted reproductive technology (ART) (5 IVF and IUI 1). In conclusion of the efficacy of treatment conducted by Angioni *et al.*, the percentage of pregnancies achieved after laparoscopic treatment of endometriosis ranges from 34% to 84.5% for different authors. These differences most likely result from a variety of test models and other methods for impregnation after surgery.

Our study shows the legitimacy of the laparoscopic treatment of endometriosis in patients with

problems in obtaining offspring, which is also confirmed by the Cochran analysis performed by Jacobson *et al.* [18]. Recommendations developed for the European Society of Human Reproduction and Embryology (ESHRE) by Dunselman *et al.* do not give a clear answer as to the validity of using laparoscopy in the treatment of infertility [19]. The lack of a firm stance on the laparoscopic treatment of endometriosis can undoubtedly be caused by problems in finding an appropriate research model that takes into account a number of predictors of pregnancy. The search for the conditions of becoming pregnant in those patients will undoubtedly constitute the target of future research in reproductive medicine.

Conclusions

The most important predictors of pregnancy in patients who underwent laparoscopy due to infertility are post-laparoscopy AMH levels and the main parameters of the partner's semen: density, motility and morphology. The number of pregnancies after laparoscopic treatment is lower in patients diagnosed with endometriosis, and depends on the severity of the condition. As a result of laparoscopic treatment of endometriosis, one can determine a decrease of the ovarian reserve measured by means of AMH.

Conflict of interest

The authors declare no conflict of interest.

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