Preterm delivery in infertile women after reproductive surgery: should we encourage spontaneous conception?

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Abstract

Objective: To evaluate an association between the mode of conception and preterm delivery in women after reproductive surgery, and to explore an effect of reproductive surgery on preterm delivery. Design: Prospective cohort study and historical case-control study. Setting: Division of Obstetrics and Gynecology, Ljubljana, Slovenia. Population or sample: A cohort of 761 infertile women after reproductive surgery. Methods: In infertile women, we evaluated the association between the mode of conception and preterm delivery using logistic regression adjusted for relevant co-variables. In a case-control study, we evaluated the effect of reproductive surgery on preterm delivery using propensity score method. We calculated the adjusted odds ratios with a 95% confidence interval with a two-way test. Main Outcome Measure: Preterm delivery. Results: Among 761 infertile women, 428 (56.2%) conceived spontaneously, and 333 (43.8%) conceived after IVF/ICSI. The incidence of twin pregnancies was significantly lower after spontaneous conception (2.6% vs. 14.1%; p <0.000). Adjusted logistic regression analysis in singleton pregnancies disclosed no significant association between the mode of conception and preterm delivery. Compared with fertile women, the incidences of preterm deliveries < 37, and < 32 gestational weeks were higher in infertile women (11.2% vs. 14.2%, and 1.7% vs. 2.6%, respectively). However, the differences did not reach a statistical significance (p=0.076 and p=0.218, respectively). Conclusion: In selected infertile women after reproductive surgery, a high rate of spontaneous conception, a low rate of multiple pregnancies, and no treatment-related adverse effect on preterm delivery should be the reasons to encourage spontaneous conception after reproductive surgery.

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Abstract

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Design : Prospective cohort study and historical case-control study.

Setting : Division of Obstetrics and Gynecology, Ljubljana, Slovenia.

Population or sample : A cohort of 761 infertile women after reproductive surgery.

Methods : In infertile women, we evaluated the association between the mode of conception and preterm delivery using logistic regression adjusted for relevant co-variables. In a case-control study we evaluated the effect of reproductive surgery on preterm delivery using propensity score method. We calculated the adjusted odds ratios with a 95% confidence interval with a two-way test.

Main Outcome Measure : Preterm delivery.

Results : Among 761 infertile women, 428 (56.2%) conceived spontaneously, and 333 (43.8%) conceived after IVF/ICSI. The incidence of twin pregnancies was significantly lower after spontaneous conception (2.6% vs. 14.1%; $p < 0.000$). Adjusted logistic regression analysis in singleton pregnancies disclosed no significant association between the mode of conception and preterm delivery. Compared with fertile women, the incidences of preterm deliveries < 37, and < 32 gestational weeks were higher in infertile women (11.2% vs. 14.2%, and 1.7% vs. 2.6%, respectively). However, the differences did not reach a statistical significance ($p = 0.076$ and $p = 0.218$, respectively).

Conclusion: In selected infertile women after reproductive surgery, a high rate of spontaneous conception, a low rate of multiple pregnancies, and no treatment-related adverse effect on preterm delivery should be the reasons to encourage spontaneous conception after reproductive surgery.

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Keywords : reproductive surgery, preterm delivery, spontaneous conception, IVF/ICSI, infertile women

Tweetable abstract

In selected infertile women, spontaneous conception after reproductive surgery should be encouraged.

Introduction

Preterm birth is one of the leading causes of neonatal morbidity, mortality, and severe long-term disability[1]. With the advance in infertility treatment, conception after in vitro fertilization (IVF) procedures has been recognized as a substantial increase in preterm delivery risk[2]. The increase in preterm delivery risk after IVF is found mainly due to the higher rate of multiple pregnancies, but also due to advanced maternal age, nulliparity, and co-morbidity[2-6]. However, some data demonstrate that adverse outcomes, preterm delivery included, occur in infertile women regardless of the mode of conception, IVF, or spontaneous, suggesting that infertility may be the underlying cause[7].

While the body of studies exists on pregnancy rate and outcome in infertile women after IVF conception, there are scarce studies on pregnancy outcome of spontaneous conception after reproductive surgery[8]. The main reason exists in the opinion that reproductive surgery should only be performed as an initial part of infertility evaluation to increase implantation and pregnancy rates after IVF[9]. However, evidence shows that careful selection of patients for reproductive surgery enables couples to conceive spontaneously and yields high cumulative pregnancy rates and good outcomes[8-10].

In the absence of obvious indication for IVF/ISCI procedure (like a male factor of infertility, bilateral tubal factor, or need for preimplantation genetic diagnostic), the usual approach to infertility treatment at our institution is, firstly, to restore fertility with reproductive surgery. Thus, every woman without any clear indication for IVF/ICSI undergo diagnostic or operative laparoscopy and, in the case of pathology found on transvaginal ultrasound, also a hysteroscopy. The usual overall pregnancy rate after reproductive surgery has been around 50%[10]. Women, who do not conceive spontaneously after reproductive surgery are advised to undergo IVF procedure.

Since the IVF/ICSI procedure has been supposed to be the known factor for preterm delivery[4], we aimed to explore an association between the mode of conception, spontaneous or IVF/ICSI, and preterm delivery in a cohort of infertile women after reproductive surgery. We hypothesized that in infertile women after reproductive surgery, the mode of conception is not associated with preterm delivery risk. Also, the opinion is that any infertility treatment is associated with a higher risk of preterm delivery[6]. Thus, we aimed to explore the effect of reproductive surgery on preterm delivery as a treatment-related adverse outcome. We hypothesized that preterm delivery in infertile women is not a reproductive surgery treatment-related adverse outcome.

Material and Methods

Study population

Firstly, we conducted a prospective observational study of a cohort of 761 infertile women who underwent reproductive surgery and delivered at the Division of Obstetrics and Gynecology, University Medical Centre Ljubljana, Slovenia, from 1st July 2012 to 31st December 2015. Further on, a historical case-control study for evaluating preterm delivery as a reproductive surgery treatment-related side effect, a control group was selected among fertile women who delivered in Slovenia in the same period. In Slovenia, 99.9% of deliveries are in-hospital.

There was no patient and public involvement in the study.

Data collection

The anonymized data on women's demographic and clinical data, an indication and type of surgical treatment, pregnancy and delivery were obtained by linking three computerized databases: Computerized database of reproductive surgery at the Department of Human Reproduction, National Register of Assisted Reproduction Technology (NRART) and National Perinatal Information System (NPIS). The data included in databases are collected during the hospital stay by attending doctors, nurses, and midwives. The Computerized database of reproductive surgery was described in detail elsewhere (10). The NRART was introduced in 1983 at the Ministry of Health of Republic of Slovenia, and from 1999 the data are also sent to the IVF

Monitoring (EIM) Consortium of the European Society of Human Reproduction and Embryology regularly. The data from NPIS, which also serves as a birth registry, are sent to the Slovenian National Institute of Public Health yearly where they go through statistical quality checks, are edited, and form the basis for the official perinatal Statistics of Slovenia. The data from NPIS are also sent to the Vermont Oxford Network and Euro-Peristat.

Dependent variables

Dependent variables were a preterm delivery < 37, and < 32 gestational weeks. Gestational age was derived from the day of ovarian punction or embryo transfer for IVF/ICSI pregnancies, and the measurement of the fetal crown-rump length in the first trimester for spontaneous pregnancies[11].

Independent variables

The main independent variables were the mode of conception (spontaneous / IVF/ICSI) in the observational study, and infertility with reproductive surgery in the case-control study (yes / no).

Independent co-variables were maternal age (continuous), maternal age at delivery >35 years, pre-pregnancy body mass index (BMI) (continuous), BMI [?] 30 kg/m2 (yes / no), BMI < 18.5 kg/m2 (yes / no), gestational weight gain (GWG) z-score (continuous), GWG z-score > -2 (yes / no), GWG z-score > 2 (yes / no), pre-pregnancy hypertension (yes / no), pre-pregnancy diabetes (yes / no), previous conization (yes / no), uterine anomalies (yes / no), chronic kidney disease (yes / no), other chronic diseases (heart, thyroid and/or mental disease) (yes / no), previous preterm delivery (yes / no), previous miscarriage (yes / no), smoking (yes / no), preeclampsia/eclampsia (yes / no), gestational diabetes (yes / no), small-for-gestational age neonate (birthweight < 10th percentile) (yes / no), nulliparous (yes / no).

BMI was defined as the woman's body mass divided by the square of body stature (kg/m2). The pregravid BMI was categorized according to the Institute of Medicine criteria as underweight (< 18.5 kg/m2), normal weight (18.5–24.9 kg/m2), and overweight (15.0-29.9 9 kg/m2), and obese ([?] 30 kg/m2)[12]. In Slovenia, maternal weight is recorded at the first appointment in pregnancy and all appointments after. The mean gestational week at the first appointment in pregnancy was nine weeks. For the calculation of the GWG z-score, we used the same method as described before[13]. Preeclampsia was defined as the presence of hypertension (blood pressure [?] 140 and/or 90 mmHg) and any other end-organ dysfunction after the 20th week of gestation[14]. National guidelines for screening and diagnosing GDM changed during the study period. Until 2012, GDM was diagnosed in Slovenia using the two-step approach: screening with 50 g oral glucose load and, when indicated, performing a 100 g oral glucose tolerance test (OGTT) using the Carpenter and Coustan criteria[15]. Since 2012, we diagnose GDM using the one-step approach by a 75-g OGTT according to the 2010 International Association of Diabetes and Pregnancy Study Groups Consensus[16]. SGA was a neonate with birthweight below the 10th percentile for gestational age and gender-based on a Slovenian Birth Weight Standards[17]. A nulliparous woman was defined as a pregnant woman who had no previous viable pregnancies.

Statistics

A descriptive analysis was performed using absolute and relative frequencies for categorical variables and mean value with standard deviation for continuous variables. Then, we performed Pearson's Chi-Square and t-test, as appropriate, of clinical and demographic characteristics of women between the groups. We used logistic regression to evaluate an association between the mode of conception and preterm delivery in infertile women after reproductive surgery. The logistic regression model was adjusted for variables which presented as significantly different between the spontaneous and IVF/ICSI group in descriptive analysis. The association was presented as adjusted odds ratio (aOR) with 95 % confidence interval (95% CI).

For the case-control study of the effect of reproductive surgery on preterm delivery, we used the propensity score (PS) method. Controls were selected from among all fertile women (n=100765) who delivered in the same period using PS matching. In the PS model, we included maternal age as a continuous variable, BMI as a categorical variable (underweight, normal weight, obese), and dichotomous variables: previous conization,

chronic diseases (pre-pregnancy hypertension, pre-pregnancy diabetes, kidney, heart, thyroid and/or mental disease), previous preterm delivery, smoking, and multiple pregnancies. We performed 1:1 matching with an optimal matching algorithm with a calliper width of the linear predictor of 0.1 standard deviations. The balance between the control and treated group was considered well when the value of the standardized difference was <0.1. The effect of reproductive surgery on preterm delivery was evaluated in the PS-matched sample by Pearson's Chi-Square test and presented as the odds ratio (OR) with 95% confidential interval (95% CI).

Considering an increase in preterm delivery rate by 30% in infertile women, within the limit of the number of treated women, the study's power was 0.78 at a 5% Type I error rate.

For statistical calculations, we used statistical program IBM SPSS Statistics v25 and R[18] with R-package "MatchIt"[19]. For all calculations, a two-sided probability (p) value < 0.05 was considered statistically significant.

Ethical approval

The study of infertile women was approved by the National Medical Ethics Committee at the Ministry of Health of the Republic of Slovenia (No. 0120-174/2018/6) and was conducted following the WMA Declaration of Helsinki. The retrospective analysis of anonymous entries of fertile women from NPIS was exempt from approval by the ethical committee by the Slovenian law (Personal Data Protection Act; Article 17). The Slovenian National Institute of Public Health as the data controller and the Division of Obstetrics and Gynecology of the University Medical Centre Ljubljana as the data processor signed the contract on NPIS data transmission according to the Personal Data Protection Act, Article 11, every five years. The last contract was signed on 25th July 2019.

Results

Among 761 infertile women with reproductive surgery, 428 (56.2%) women conceived spontaneously, and 333 (43.8%) conceived after IVF/ICSI. There were 58 pairs of twins (7.23%). The incidence of twin pregnancies was lower after spontaneous conception than after IVF/ICSI (11 (2.6%) vs. 47 (14.1%); P-value <0.001).

The most common indication for fertility treatment was endometriosis (228; 32.4%) with no significant difference between the spontaneous conception and IVF/ICSI group (Table S1).

Among 761 infertile women, 703 women had a singleton pregnancy. Compared with women who conceived spontaneously, women who conceived after IVF/ICSI were significantly older (33.08±3.13 vs. 31.81±2.24; P-value <0.001), more often older than 35 years (37.4% vs. 27.3%, P-value 0.005), and nulliparous (90.2% vs. 81.5%; P value 0.002) (Table S2). We found no significant differences between spontaneous and IVF/ICSI conception concerning the pre-gestational BMI, pre-gestational BMI < 18.5 kg/m2, pre-gestational BMI [?] 30 kg/m2, GWG z-score, GWG z-score >+2, or >-2, pre-gestational hypertension, pre-gestational diabetes, chronic kidney disease, other chronic diseases, conization, uterine anomalies, hysteroscopy (diagnostic/therapeutic), smoking during pregnancy, previous preterm delivery, preeclampsia/eclampsia, gestational diabetes and birth of an SGA neonate (Table S2). Univariate analysis showed that women who conceived after IVF/ICSI significantly more often delivered < 32 gestational weeks (3.8% vs. 1.4%; P value 0.041) (Table S2). However, logistic regression analysis adjusted for maternal age and nulliparity disclosed no significant association between the mode of conception and all preterm deliveries < 37 gestational weeks, spontaneous preterm deliveries < 37 weeks, as well as all preterm deliveries < 32 gestational weeks (Table 1).

In the second part of the study, we evaluated the effect of reproductive surgery on preterm delivery as a treatment-related adverse outcome. Almost half of the women in the infertility group conceived after IVF/ICSI (43.8%). Compared with fertile women before PS matching, infertile women were older at delivery, more often nulliparous, they more often suffer from chronic diseases, had uterine anomalies, and miscarriage previously, all of which may increase the risk of preterm delivery (Table 2). Also, among infertile women,

there were more of those who had numerous co-existent risk factors for preterm delivery (Figure 1). After PS matching, the fertile and infertile women were well balanced for the chosen possible risk factors for preterm delivery, also concerning the number of co-existent risk factors per woman (Figure 1, Table 2). In the PS matched sample, the incidences of preterm delivery < 37 and < 32 gestational weeks were higher in the infertile women. However, the differences did not reach a statistical significance (Table 3).

Using PS matching, we also calculated the odds of preterm delivery in the group of infertile women who conceived spontaneously and after IVF/ICSI separately and found no significant differences compared with fertile women. Compared with fertile women, the odds of preterm delivery < 37 weeks in infertile women who conceived spontaneously was 1.51 (95%CI 0.93-2.43; *p-value* 0.093), and < 32 weeks was 0.72 (95%CI 0.29-1.81; *p-value* 0.486). Compared with fertile women, the odds of preterm delivery < 37 weeks in infertile women who conceived after IVF/ET was 1.29 (95%CI 0.86-1.94; *p-value* 0.217), and < 32 weeks was 1.09 (95%CI 0.48-2.52; *p-value* 0.832).

Discussion

Main Findings

In the present study, we found that, in infertile women with singleton pregnancies who underwent reproductive surgery before conception, the risk of preterm delivery was not associated with the mode of conception. Also, we found that reproductive surgery in infertile women had no significant treatment-related side effects in terms of preterm delivery neither < 37 gestational weeks nor < 32 gestational weeks.

Strengths and Limitations

The main limitation of our study is its retrospective observational design in the second part of the study, which does not account for all potential co-founders. Secondly, despite incorporated automatic checkpoints, the computerized database is also prone to human errors. Thirdly, infertile women were heterogenous regarding indication for reproductive surgery which might influence the insignificant difference in preterm delivery in regard to the mode of conception. The main strength of our study is a novel approach to exploring the effect of fertility treatment on preterm delivery as a treatment-related adverse outcome. Using PS matching approach allowed us to balance the treated and untreated group for some of the main co-founders and also for the number of co-existing possible risk factors for preterm delivery per woman making the observational study close to a randomized study. Therefore, the PS matching approach enables higher control over cofounding, reduces bias, and adds to higher prediction estimation[20-21]. However, the number of outcomes in our study was low, especially of preterm deliveries < 32 weeks, which might influence the precision of estimation. For that reason, the result should be treated with caution.

Interpretation

Evidence shows that conception after IVF/ICSI increases the odds of preterm delivery when analysed in population-based cohorts[4,5,22-24]. Contrary to those findings, in our cohort of infertile women with singleton pregnancy after reproductive surgery, IVF/ICSI, compared to spontaneous conception, did not increase the odds of preterm delivery. Still, there are few reports on an outcome of spontaneous conception after reproductive surgery due to an opinion that reproductive surgery should only be performed as an initial part of infertility treatment before proceeding to IVF/ICSI[9]. Nevertheless, encouraging reports on a high spontaneous pregnancy rate after reproductive surgery, as in this study, emerged in the last years[8,10]. Similar to our finding, Boyle et al.[8] have found the low preterm delivery rate in women who conceived spontaneously after restorative reproductive medicine after failed IVF. Indeed, waiting for spontaneous conception in infertile women who are often at advanced reproductive age is discouraging. However, besides lower treatment burden for women and lower medical expenses, an essential advantage of a spontaneous conception after reproductive surgery is a lower rate of multiple pregnancies compared with IVF/ICSI, which was evident in our cohort. Precisely lowering the multiple pregnancy rate is the only preventive measure that we can take to reduce preterm delivery risk in women who need an infertility treatment[25].

We report that reproductive surgery in infertile women had no significant effect on preterm delivery, re-

gardless of the mode of conception. However, Valenzuela-Alcaraz et al.[26] have found the significantly higher prevalence of overall pregnancy complications in all studied infertility groups regardless of the infertility treatment, preterm delivery being the highest in the IVF/ICSI group. Also, Dunietz et al.[6], when compared spontaneous conception with assisted reproductive techniques (ART) conception in women with singleton pregnancy after infertility treatment, have reported an increased preterm delivery risk after ART within each of the treatment group. However, compared with women who had trouble conceiving but conceived without any assistance, Oberg et al.[27] had reported that when women received some fertility treatment, the odds of preterm delivery were higher through independent multiple gestations. All mentioned studies have evaluated a relative relationship between infertility treatment and preterm delivery using multivariate regression models, which have well-documented limitations as a means to explore causal relationships[28]. In our study, using the propensity score method, fertile women and women who received infertility treatment were well balanced not only for every single risk factor for preterm delivery but also for the number of co-existing risk factors per woman. Considering this, our finding that reproductive surgery had no significant effect on preterm delivery in the well-balanced sample suggests that the higher rate of women with co-existing risk factors in infertile women may be the main contributor to an increased risk of preterm delivery when compared with all fertile women.

In our study, the main indication for infertility treatment was endometriosis, in one-third of the women, which might contribute to our insignificant treatment-related side effect. Namely, Stern et al. have reported that among all ART deliveries, following singleton or multiple pregnancies, the increased preterm delivery risk was associated with male factor, ovulation disorders, tubal inflammation, but not with endometriosis[7].

Our findings do not contradict other findings that, compared with all fertile women, preterm deliveries are higher in women who conceived after IVF/ICSI or received any infertility treatment[29]. What our study pointed out is that not the mode of conception or reproductive surgery, but rather maternal risk factors for preterm delivery like high maternal age, nulliparity, and chronic diseases, which were more prevalent in women who received infertility treatment and even more prevalent in women who conceived after IVF/ICSI might contribute to the higher prevalence of preterm delivery when compared to all fertile women. Besides, to our finding, the higher prevalence of co-existing risk factors for preterm delivery per woman may be the most critical contributor to the higher rate of preterm delivery in women who received infertility treatment.

Conclusion

Our study highlighted that in infertile women with singleton pregnancies after reproductive surgery, the preterm delivery rate is comparable between spontaneous conception and conception after IVF/ICSI. The preterm delivery risk seems to be associated, preferably, with maternal risk factors and their co-existence rather than with the mode of conception as well as reproductive surgery. Thus, reproductive surgery has a valuable role in infertility treatment that enables a high ratio of spontaneous conceptions and should not be avoided before proceeding to IVF/ICSI. In selected infertile women with no obvious indication for IVF/ICSI or advanced age, we should encourage spontaneous conception after reproductive surgery. So, we can spare women of a psychosocial and medical treatment burden associated with IVF/ICSI procedure as well as decrease the risk of multiple pregnancies.

Disclosure of interest

The authors report no conflict of interest.

Contribution to authorship

TPS designed the study, reviewed the literature and wrote the manuscript. HBF contributed the data, designed the study, reviewed the literature and critically revised the manuscript. EBV and SK contributed the data and critically revised the manuscript. IV and TB analyzed the data and critically revised the manuscript.

Details of ethics approval

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Figure 1. Percentage of women with co-existing risk factors for preterm delivery per woman before (A) and after (B) propensity score matching.

Table 1. The adjusted odds of preterm delivery in infertile women with a singleton pregnancy after reproductive surgery by the mode of delivery (N=703).					
Outcome	Spontaneous conception N=417	IVF/ICSI (Referent) N=286	aOR*	95% CI	p-value
Preterm delivery < 37 weeks	37 (8.9)	29 (10.1)	1.07	0.63-1.81	0.793
Spontaneous preterm delivery < 37 weeks	28 (6.7)	21 (7.3)	1.04	0.57-1.89	0.912
Preterm delivery < 32 weeks	6 (1.4)	11 (3.8)	2.25	0.80-6.34	0.124
In the second and third culomn, the results are presented as a number (percent). *Adjusted for maternal age at delivery and nulliparity. Legend: IVF/ICSI – in vitro fertilization/intracytoplasmic sperm injection, aOR – Adjusted odds ratio, 95% CI – confidential interval.	In the second and third culomn, the results are presented as a number (percent). *Adjusted for maternal age at delivery and nulliparity. Legend: IVF/ICSI – in vitro fertilization/intracytoplasmic sperm injection, aOR – Adjusted odds ratio, 95% CI – confidential interval.	In the second and third culomn, the results are presented as a number (percent). *Adjusted for maternal age at delivery and nulliparity. Legend: IVF/ICSI – in vitro fertilization/intracytoplasmic sperm injection, aOR – Adjusted odds ratio, 95% CI – confidential interval.	In the second and third culomn, the results are presented as a number (percent). *Adjusted for maternal age at delivery and nulliparity. Legend: IVF/ICSI – in vitro fertilization/intracytoplasmic sperm injection, aOR – Adjusted odds ratio, 95% CI – confidential interval.	In the second and third culomn, the results are presented as a number (percent). *Adjusted for maternal age at delivery and nulliparity. Legend: IVF/ICSI – in vitro fertilization/intracytoplasmic sperm injection, aOR – Adjusted odds ratio, 95% CI – confidential interval.	In the second and third culomn, the results are presented as a number (percent). *Adjusted for maternal age at delivery and nulliparity. Legend: IVF/ICSI – in vitro fertilization/intracytoplasmic sperm injection, aOR – Adjusted odds ratio, 95% CI – confidential interval.

Table 2. Characteristics of fertile (controls) and infertile women after reproductive surgery before and after PS matching.						
Variable	All women (n=100 765)	All women (n=100 765)	All women (n=100 765)	PS matched sample (n=1516)	PS matched sample (n=1516)	PS matched sample (n=1516)
	Fertile women n=100 007	Infertile women n=758*	Std. Diff.	Fertile women n=758	Infertile women n=758	Std. Diff.
Maternal age at delivery (years)	30.2 ± 4.8	32.4 ± 4.2	0.537		32.4 ± 4.2	-0.017
BMI (kg/m^2)						
BMI < 18.5	4712 (4.7)	44 (5.8)	0.047	45 (5.9)	44 (5.8)	-0.006
BMI 18.5-24.99	66 205 (66.3)	501 (66.1)	-0.004	504 (66.5)	501 (66.1)	-0.008
BMI 25 – 29.99	19 169 (19.2)	131 (17.3)	-0.050	129 (17.0)	131 (17.3)	0.007
BMI > 30	9810 (9.8)	82 (10.8)	0.032	80 (10.6)	82 (10.8)	0.009
Nulliparous	48 312 (48.3)	646 (85.2)	1.040	644 (85.0)	646 (85.2)	0.007
Smoking	9486 (9.5)	57 (7.5)	-0.074	50 (6.6)	57 (7.5)	0.035
Chronic diseases	10 953 (11.0)	135 (17.8)	0.179	131 (17.3)	135 (17.8)	0.014
Previous miscarriage	18 155 (18.2)	184 (24.3)	0.142	181 (23.9)	184 (24.3)	0.009
Previous conization	3752 (3.8)	33 (4.4)	0.029	28 (3.7)	33 (4.4)	0.032
Uterine anomaly	4668 (4.7)	348 (45.9)	0.827	347 (45.8)	348 (45.9)	0.003
Previous preterm delivery	3081 (3.1)	13 (1.7)	-0.105	16 (2.1)	13 (1.7)	-0.031
Multiple pregnancy	1773 (1.8)	58 (7.7)	0.221	56 (7.4)	58 (7.7)	0.010

Table 2. Characteristics of fertile (controls) and infertile women after reproductive surgery before and after PS matching.	Table 2. Characteristics of fertile (controls) and infertile women after reproductive surgery before and after PS matching.	Table 2. Characteristics of fertile (controls) and infertile women after reproductive surgery before and after PS matching.	Table 2. Characteristics of fertile (controls) and infertile women after reproductive surgery before and after PS matching.	Table 2. Characteristics of fertile (controls) and infertile women after reproductive surgery before and after PS matching.	Table 2. Characteristics of fertile (controls) and infertile women after reproductive surgery before and after PS matching.	Table 2. Characteristics of fertile (controls) and infertile women after reproductive surgery before and after PS matching.
Results are presented as a mean ± SD or No. (%) as appropriate. *3 women droped out from propensity score calculation due to lack of all variables. Legend: BMI – body mass index	Results are presented as a mean ± SD or No. (%) as appropriate. *3 women droped out from propensity score calculation due to lack of all variables. Legend: BMI – body mass index	Results are presented as a mean ± SD or No. (%) as appropriate. *3 women droped out from propensity score calculation due to lack of all variables. Legend: BMI – body mass index	Results are presented as a mean ± SD or No. (%) as appropriate. *3 women droped out from propensity score calculation due to lack of all variables. Legend: BMI – body mass index	Results are presented as a mean ± SD or No. (%) as appropriate. *3 women droped out from propensity score calculation due to lack of all variables. Legend: BMI – body mass index	Results are presented as a mean ± SD or No. (%) as appropriate. *3 women droped out from propensity score calculation due to lack of all variables. Legend: BMI – body mass index	Results are presented as a mean ± SD or No. (%) as appropriate. *3 women droped out from propensity score calculation due to lack of all variables. Legend: BMI – body mass index

Table 3. The effect of reproductive surgery on preterm delivery in the PS-matched sample.	Table 3. The effect of reproductive surgery on preterm delivery in the PS-matched sample.	Table 3. The effect of reproductive surgery on preterm delivery in the PS-matched sample.	Table 3. The effect of reproductive surgery on preterm delivery in the PS-matched sample.	Table 3. The effect of reproductive surgery on preterm delivery in the PS-matched sample.	Table 3. The effect of reproductive surgery on preterm delivery in the PS-matched sample.
Outcome	Fertile women N=758	Infertile women (Referent) N=758	OR	95% CI	p-value
Preterm delivery < 37 weeks	85 (11.2)	108 (14.2)	1.31	$0.97 - 1.78$	0.076

Table 3. The effect of reproductive surgery on preterm delivery in the PS-matched sample.	Table 3. The effect of reproductive surgery on preterm delivery in the PS-matched sample.	Table 3. The effect of reproductive surgery on preterm delivery in the PS-matched sample.	Table 3. The effect of reproductive surgery on preterm delivery in the PS-matched sample.	Table 3. The effect of reproductive surgery on preterm delivery in the PS-matched sample.	Table 3. The effect of reproductive surgery on preterm delivery in the PS-matched sample.
Preterm delivery < 32 weeks	13 (1.7)	20 (2.6)	1.57	0.78 − 3.18	0.218
In the second nad third culomn, the results are presented as a number (percent). Legend: OR − Odds ratio, 95% CI − confidential interval.	In the second nad third culomn, the results are presented as a number (percent). Legend: OR − Odds ratio, 95% CI − confidential interval.	In the second nad third culomn, the results are presented as a number (percent). Legend: OR − Odds ratio, 95% CI − confidential interval.	In the second nad third culomn, the results are presented as a number (percent). Legend: OR − Odds ratio, 95% CI − confidential interval.	In the second nad third culomn, the results are presented as a number (percent). Legend: OR − Odds ratio, 95% CI − confidential interval.	In the second nad third culomn, the results are presented as a number (percent). Legend: OR − Odds ratio, 95% CI − confidential interval.