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The consequences of cesarean section and vaginal delivery on ovarian reserve in infertile women

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Abstract

According to the data of the World Health Organization (WHO), although the rate of cesarean section is increasing worldwide, one out of every five births is performed by cesarean section. Cesarean section is life saving for both mother and baby depending on the situation. However, it also brings some complications. Its effect on fertility also raises concerns. The aim of the present study was to investigate the consequences of cesarean section on ovarian reserve. Anti-Mullerian hormone, Follicle-Stimulating Hormone, Luteinizing Hormone, Estradiol, antral follicle count, ovarian volume, and ovarian elastography results of 120 patients under the age of 30 who were not obese and were compatible with the criteria for unexplained infertility of the American Society for Reproductive Medicine were analyzed in both pre-pregnancy and postpartum period. There were 57 patients with vaginal delivery and 63 patients with cesarean section. Differences between the groups according to the mode of delivery and between the pre-pregnancy and postpartum groups were investigated. There was no statistically significant difference for the vaginal birth group in terms of AFC, AMH, FSH, LH, E2, SWE and ovarian volumes between pre-pregnancy and postpartum. In the cesarean section group, AFC, AMH and ovarian volumes were found to be significantly lower in the postpartum period than before pregnancy. As a result, cesarean delivery may have negative consequences for ovarian reserve tests.

Keywords: AMH, cesarean, elastography, ovarian reserve, vaginal birth

1. Introduction

Modern cesarean section techniques started with the Sänger technique in the early 1900s, and the Pfannenstiel-Kerr technique formed the infrastructure of today's technique as a double layer closure with a lower segment transverse incision (1). Cesarean section is life saving for both mother and baby depending on the situation (2). However, it also brings some complications. Some of these are infection, fever, excessive blood loss, injury to other intra-abdominal organs, endometriosis, urinary retention, and anesthesia-related side effects (3–5). While the rate predicted by the World Health Organization for cesarean section was between 10% and 15% in the 1980s, it is over 40% in some regions today (6). Today, the increasing frequency of cesarean section raises concerns with the studies showing some negative effects on fertility (7–9). However, these studies had limitations, such as the older age of the cesarean section group, the co-morbidities of the cesarean section group, and the non-homogeneous distribution of the groups (10, 11).

The most important indicator of female fertility is the ovarian reserve, and it is directly related to the number of antral follicles in the ovary (12). Anti-Mullerian hormone (AMH), antral follicle count (AFC), Follicle-Stimulating Hormone (FSH), Luteinizing Hormone (LH), and Estradiol (E2) are tests used to evaluate ovarian reserve (13). AMH blood level is not affected by the menstrual cycle like FSH, LH, and E2 (14).

Ultrasound elastography, which has become widespread in recent years, shows the elasticity of soft tissues and is also used in the ovary's evaluation in gynecology practice (15).

The aim of this prospective study was to observe the consequences of cesarean section on ovarian reserve tests in infertile women.

2. Material and Methods

After obtaining the approval of the local ethics committee, patients who applied to the obstetrics and gynecology outpatient clinic of our tertiary hospital because of unexplained infertility were evaluated for this study. The criteria for unexplained infertility were compatible with the criteria of the American Society for Reproductive Medicine (16). Patients who gave birth before, over 30 years of age and obese (Body Mass Index ≥ 30) were not included in the study.

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AMH, FSH, LH, and E2 blood levels were analyzed on the 3rd day of the participants' menstruation. FSH, LH, and E2 tests were carried out by a chemiluminescence immunoassay method (Abbott®). Reference ranges were in follicular phase 3.03-8.8 IU/L for FSH, 1.8-11.78 IU/L for LH, and 21-251 ng/L for E2. AMH levels were determined by another chemiluminescence immunoassay method (Beckman-Coulter®), its reference ranges were 0.07 -7.35 ng/ml.

Antral follicle count was performed by Samsung HS70A ultrasound device® via 2D imaging for both ovaries transvaginally. Follicles with a diameter of 2-10 mm were antral follicles. Length (L), height (H), and width (W) measurements were made for each ovary. The volume of the ovaries was calculated using the formula L x H x W x 0.523 (Figure 1). Shear wave elastography (SWE) evaluation was also performed (Figure 2). Participants' age, height, and weight data were recorded. Body mass index (BMI) was calculated with weight (kilogram)/height(meter)². Data of 240 participants were recorded for the study. Pregnancy occurred in 182 of these participants within 1 year. 151 of 182 pregnancies resulted in live births. In the study, 31 patients who did not continue their follow-up for various reasons were dropped out. In order to ensure standardization and to comply with the recommendations of the Ministry of Health, 400 micrograms of folic acid in the first trimester of pregnancy and Decavit Pronatal® (Kocak Farma) once a day from the third month to delivery were recommended. Ultrasound measurements and hormone measurements were repeated on the 3rd day of menstruation when the 120 participants included in the study had menstruation at least 6 months after live birth.

Participants using postpartum hormonal contraceptive methods were not included in the study. The data of the participants constituted two groups who gave birth by cesarean (CS) and delivered vaginally (VB).

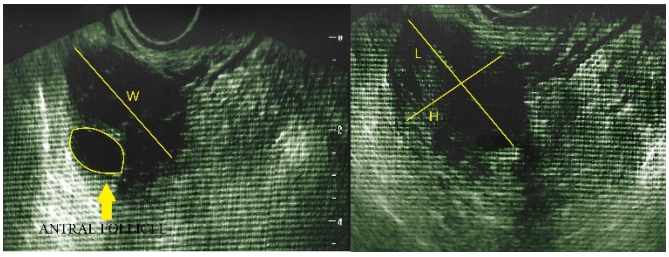

Fig. 1. Calculation of the volume of the ovaries (L x H x W x 0.523) and antral follicle

G* Power software version 3.01 (Franz Foul, Kiel, Germany) was used for sample size calculation. In a study published in 2017, it is estimated that there are approximately 1.7 million infertile women in Turkey (17). Power analysis was performed using the mean and number of study participants in the study of Gurol-Urganci et al. (10). All data obtained were analyzed with IBM SPSS Statistics for Windows, Version 23.0, and $p \leq 0.05$ was significant. Compatibility with the normal distribution was evaluated using the Kolmogorov-Smirnov test. The difference between the CS and VB groups was analyzed using the Independent-T test for normally distributed data, and the Mann-Whitney U test for non-normally distributed data. The changes in pre-pregnancy and postpartum data for VB and CS were analyzed with the paired T-test for data with normal distribution, and with the Wilcoxon Signed test for data without normal distribution. Correlation between data was analyzed by a Pearson Correlation test.

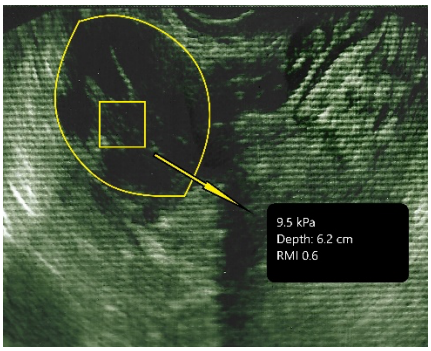

Fig. 2. Evaluation of the ovary with Shear Wave Elastography

Ethical permission for the study was obtained from the Clinical Research Ethics Committee of Kanuni Training and Research Hospital (2019/47).

3. Results

There were 120 primiparous pregnant women included in the present study. While 63 (52.5%) of the participants gave birth vaginally, 57 (47.5%) gave birth by cesarean section. The ages of the participants ranged from 19.2-28.8 years, and their BMI ranged between 19-28.9 kg/m2. There was no difference between the groups in terms of age, BMI and duration of conception (Table 1).

Table 1. Descriptive characteristics of patients according to delivery type

	Vaginal delivery (*n* = 57) (mean ± SD)	**Cesarean section (*n* = 63)** (mean ± SD)	***p***
Age (year)	24.1 ± 3.1	23.6 ± 2.7	0.423*
BMI (kg/m²)	23.4 ± 3.2	23.7 ± 3.4	0.512*
Duration of conception (month)	7.0 ± 2.7	7.3 ± 3.1	0.315**

BMI: Body Mass Index * Independent-T test ** Mann-Whitney U test

There was no significant difference for the VB group in terms of AFC, AMH, FSH, LH, E2, SWE and ovarian volumes between before pregnancy and postpartum period. In the cesarean section group, AFC, AMH and ovarian volumes were found to be significantly lower in the postpartum period than before pregnancy. In the postpartum period, a significant difference was found between the VB and CS groups in terms of AFC, AMH, ovarian volumes and SWE in the left ovary (Table 2).

According to the method of conception, patients were

classified as spontaneous, intrauterine insemination (IUI), in vitro fertilization (IVF). There was no difference between CS and VB groups in terms of conception method (Table 3).

Table 2. Laboratory results and ultrasound findings of patients according to delivery type

	Vaginal delivery (n = 57)	Cesarean section (n = 63)	p value
[b]AFC in the right ovary	7.6 ± 1.4	7.8 ± 1.2	0.808[*]
[a]AFC in the right ovary	7.4 ± 1.6	6.1 ± 1.1	**0.431**[*]
p value[i]	0.512	**0.145**	
[b]AFC in the left ovary	7.6 ± 1.5	7.3 ± 1.4	0.380[*]
[a]AFC in the left ovary	7.6 ± 1.4	6.0 ± 1.0	**0.027**[*]
p value[i]	0.716	**0.044**	
[b]AMH (ng/ml)	2.2 ± 0.7	2.3 ± 0.7	0.292[**]
[a]AMH (ng/ml)	2.2 ± 0.7	1.7 ± 0.5	**0.033**[**]
p value[ii]	0.746	**0.025**	
[b]FSH (IU/L)	6.8 ± 1.5	6.7 ± 1.8	0.452[**]
[a]FSH (IU/L)	7.0 ± 1.7	6.8 ± 1.3	0.528[**]
p value[ii]	0.253	0.439	
[b]LH (IU/L)	7.6 ± 2.8	7.3 ± 2.7	0.509[**]
[a]LH (IU/L)	6.9 ± 2.5	8.2 ± 2.6	0.054[**]
p value[ii]	0.343	0.278	
[b]E2 (ng/L)	42.7 ± 11.6	36.7 ± 14.9	0.064[**]
[a]E2 (ng/L)	37.6 ± 12.2	34.3 ± 13.9	0.302[**]
p value[ii]	0.189	0.248	
[b]SWE in the right ovary (kPa)	8.3 ± 1.9	8.2 ± 2.1	0.540[**]
[a]SWE in the right ovary (kPa)	8.4 ± 2.0	8.9 ± 1.6	0.304[**]
p value[ii]	0.618	0.057	
[b]SWE in the left ovary (kPa)	8.4 ± 2.0	9.3 ± 1.9	0.056[**]
[a]SWE in the left ovary (kPa)	8.2 ± 1.8	9.3 ± 1.9	**0.039**[**]
p value[ii]	0.056	0.612	
[b]Right ovarian volume (mm^3)	9.5 ± 1.7	9.6 ± 1.7	0.421[**]
[a]Right ovarian volume (mm^3)	9.7 ± 1.7	7.6 ± 1.2	**0.028**[**]
p value[ii]	0.415	**0.031**	
[b]Left ovarian volume (mm^3)	10.0 ± 1.9	10.0 ± 2.0	0.462[**]
[a]Left ovarian volume (mm^3)	9.7 ± 1.5	7.9 ± 1.3	**0.043**[**]
p value[ii]	0.415	**0.029**	

AFC: Antral Follicle Count, AMH: Anti-Mullerian Hormone, FSH: Follicle Stimulating Hormone, LH: Luteinizing Hormone, E2: Estradiol SWE: Shear Wave Elastography
[a]after birth; [b]before pregnancy; [*] Mann-Whitney U test; [**] Independent-T test;
[i] Wilcoxon Signed test; [ii] paired T-test

Table 3. Distribution of conception types according to delivery type

	Vaginal delivery (n = 57)	Cesarean section (n = 63)	p [*]
Spontaneous	8 (14%)	9 (14.3%)	0.359
IUI	38 (66.7%)	41 (65%)	0.432
IVF	11 (19.3%)	13 (20.7%)	0.248

IUI: Intrauterine insemination, IVF: In vitro fertilization [*] Chi-square test

4. Discussion

Although there are studies on the consequences of a mode of delivery on ovarian reserve in the literature, there is no comparative study covering the pre-pregnancy period. Ovarian reserve tests during pregnancy differ between pre-pregnancy and trimesters (18). Therefore, the current study provides new information on this aspect. Past studies either did not include a standardized group or the analysis was carried out using retrospective data. In some studies, it has been indirectly associated with some factors, such as intra-abdominal adhesions and vascular injury, that may affect ovarian reserve (10).

Today, with the change in the obstetric population, there have also been changes in obstetric practices. The average age of women at first pregnancy was increasing, and the number of women with additional diseases who achieve pregnancy with assisted reproductive techniques was also increasing (1). The incidence of cesarean is high in advanced maternal age and in pregnancies with assisted reproductive techniques (19,20). In addition, the frequency of cesarean section varied during the first birth due to legal problems (21). The thought that cesarean delivery may have a negative consequence for ovarian reserve worries both physicians and patients (7).

In the present study, AMH, AFC, FSH, LH, E2, ovarian volume, and SWE were analyzed both in the pre-pregnancy and postpartum period. There was no significant difference in ovarian reserve tests in the vaginal delivery group. However, AMH, ovarian volume and AFC were significantly adversely affected in the CS group. The present

study showed that cesarean section may adversely affect ovarian reserve tests.

With the increasing cesarean rate, the consequences of the mode of delivery on fertility is a more striking issue, and some studies have suggested that cesarean section may cause negative reproductive outcomes (7–9). However, some studies suggest that there was no such relationship (10,11, 22). These studies on the consequences of cesarean section on ovarian reserve were not in the infertile patient group, but included a patient population that could cause bias. In our study, prospective follow-up was performed in the unexplained infertile patient group and the groups were similar to each other in terms of descriptive characteristics.

AMH measurement is widely used in determining ovarian reserve, however, the lack of an international standard and being affected by many factors are its handicaps (23). One of these factors is age and with increasing age, serum AMH level decreases, especially after 35 years of age (23). In our study, there was no difference in age between the groups and the mean age was also found to be 23.9 ± 2.9 years.

Although there are studies suggesting the evaluation of ovarian reserve by looking at serum FSH, LH and E2 levels on the 3rd day of menstruation (24), the combination of AFC, AMH, FSH, LH gave more reliable results (25). Therefore, ovarian reserve tests were evaluated in combination in our study. Although ovarian volume was not a stand-alone ovarian reserve test, it might correlate with AFC (26). Ovarian volumes were also evaluated in our study, and a significant decrease was observed in postpartum ovarian volume in the CS group.

The deterioration of ovarian reserve tests with the increase in BMI should be considered (27). In the present study, patients considered obese according to the World Health Organization were not included (BMI ≥ 30), and the participants' BMI ranged from 19 to 28.9 kg/m2.

Evaluation of the ovaries using SWE has been studied in patients with polycystic ovary syndrome, and it has been shown that SWE values increase in the polycystic group. In the study in which the elasticity of the ovaries was evaluated, the SWE value was found to be approximately 8 kPa in the non-patient control group (28). In the present study, the SWE results of the ovaries were approximately 8.6 kPa, and the results of delivery and elasticity did not show a significant difference in both the VB and CS groups.

In the study of Romanski et al., it was reported that IVF cycles had no effect on the ovarian reserve (29). Pregnancy was achieved by various methods, and the methods were similar between the CS and VB groups in the current study.

Limitations

There were approximately two years between the time the patients were first evaluated and the time they were evaluated postnatally. The decrease in age-related ovarian reserve is observed especially over the age of 30 (30). Since the mean age of the patients in our study was 23.9 at the beginning, no significant decrease was observed in ovarian reserve tests with advancing age.

As a result, cesarean delivery may have negative consequences for ovarian reserve tests. There is a need for further studies investigating the consequences for long-term outcomes and clinical pregnancy rates.

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Conflict of interest

The authors declared none.

Authors' contributions

Concept: K.B.E., Design: K.B.E., D.K., Data Collection or Processing: K.B.E., D.K., Analysis or Interpretation: K.B.E., D.K., Literature Search: K.B.E., D.K., Writing: K.B.E., D.K.

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