Original Article

Patients with unexplained primary infertility have similar uterine and ovarian blood flow parameters compared with fertile cases: A prospective cross-sectional study

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Abstract

Aim: In this prospective cross-sectional study, we compared the uterine and ovarian artery blood flow parameters in patients diagnosed with unexplained primary infertility with fertile cases.

Materials and Methods: Thirty female patients previously diagnosed as unexplained primary infertility aged 20-40 years were selected. The control group consisted of 30 fertile patients. To evaluate uterus and ovaries, all participants underwent ultrasonographic examination on the third day of the mestrual cycle. Also, blood samples were taken to evaluate the basal hormonal profile. Participants were re-evaluated on the 21st day of the menstrual cycle. Blood samples were taken for the measurement of progesterone level. Maximum endometrial thickness in the sagittal plane on both sides of the endometrial line was measured using transvaginal ultrasonography. Also, blood flows in uterine and ovarian arteries were measured via transvaginal Doppler ultrasonography. Resistance index and pulsatility index values in both uterine and ovarian arteries were recorded and averaged.

Results: Both groups had similar clinical features and endometrial thickness values (P > 0.05). Patients with unexplained primary infertility had similar uterine and ovarian blood flow parameters compared to fertile patients (P > 0.05). There was no correlation between uterine and ovarian Doppler findings and demographic-clinical data.

Conclusion: Patients with unexplained primary infertility have similar uterine and ovarian blood flow values compared with fertile patients.

Keywords: Doppler ultrasonography; ovarian artery; uterine artery; unexplained infertility

INTRODUCTION

Infertility is the failure to achieve a clinical pregnancy despite 1 year or more of regular unprotected sexual intercourse. Unexplained infertility is diagnosed when the etiology cannot be determined by standard diagnostic tests used in the evaluation of infertility (1). It's prevalence ranges from 8% to 37% of infertile couples (2,3). Standard diagnostic tests include the evaluation of ovulatory function, investigation of tubal pattern, and semen analysis (1). Researches speculated many theories such as hormonal factors, altered endometrial function, gamete dysfunction and ovarian antibodies on the etiology of unexplained infertility (4-7). Despite numerous research, unexplained infertility remains a mystery (1).

Doppler ultrasonography is a safe and noninvasive technique, and it is used used in obstetrics and gynecology (8,9). Doppler studies have shown that the measurement of uterine blood flow is important in determining endometrial receptivity and predicting the success of pregnancy (10,11). There are studies in the literature investigating the uterine perfusion abnormalities in women diagnosed with unexplained infertility, but these are few (12,13). Moramezi et al. (12) reported a higher impedance in uterine artery blood flow in patients diagnosed with unexplained infertility compared with fertile women. In another study, Raine-Fenning et al. (13) reported impaired endometrial and subendometrial perfusion in unexplained infertility patients. In both studies (12,13), the case group included patients with unexplained infertility either primary or secondary, and unexplained primary infertile patients were not evaluated separately.

We hypothesized that the patients diagnosed with unexplained primary infertility may have reduced uterine

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and ovarian blood flow parameters compared with fertile women. Thus, the aim of this prospective cross-sectional study was to compare the uterine and ovarian artery blood flow parameters in patients diagnosed with unexplained primary infertility with fertile cases.

MATERIALS and METHODS

This prospective cross-sectional study was designed according to the Hel¬sinki Declaration. The study protocol was approved by the Ethical Committee of Atatürk University, Medical Faculty, Erzurum, Turkey (Protocol number: B.30.2.ATA.0.01.00/159). Prior to enrollment, all participants were informed about the study. Written consent form was obtained from all patients who agreed to participate in the study. The study was performed in the Gynecology Clinic of Erzurum Nenehatun Maternity Hospital. Thirty female patients previously diagnosed as unexplained primary infertility (normal semen analysis, normal basal hormonal profile, normal ovulatory function detected by transvaginal ultrasound or midluteal phase progesterone value, normal uterine cavity and tubal pattern detected by the hysterosalpingography) aged 20-40 years were included in the study. Thirty fertile patients had at least a vaginal live birth, had regular menstrual cycle, normal physical and pelvic examinations and did not use hormonal contraception or intra uterine device were included in the control group. Patients with body mass index (BMI) ≥ 30 kg/m^2, who had delivered by cesarean section, and smokers or alcohol users were excluded from the study. To evaluate uterus and ovaries, all participants underwent ultrasonographic examination on the third day of the mestrual cycle. Also, blood samples were taken to evaluate the basal hormonal profile. Patients with pathological conditions such as fibroids, endometrioma, ovarian cysts were excluded from the study. Participants were re-evaluated on the 21st day of the menstrual cycle. Blood samples were taken for the measurement of progesterone level. Maximum endometrial thickness in the sagittal plane on both sides of the endometrial line was measured using transvaginal ultrasonography. Also, blood flows in uterine and ovarian arteries were measured via transvaginal Doppler ultrasonography. At the level of the internal os, the uterine artery was defined and the ascending main branch of the uterine artery on both sides was used to measure blood flow parameters. The ovarian blood flow was measured from the largest artery in the ovary hilus. Resistance index (RI) and pulsatility index (PI) values in both uterine and ovarian arteries were recorded and averaged. Data was obtained by averaging the value of three consecutive measurements and all measurements were performed by an experienced radiologist (E.G.G.). All Doppler examinations were performed using Aplio 300 ultrasound (Toshiba Medical Systems, Tokyo, Japan).

Power analysis was done using Russ Lenth's Power and sample size calculation application (14). To detect a mean difference between the two groups at least as 1 SD on Doppler index values, the number of patients required in every group was found as 25, based on the power of 90% at 5% significance level. Data were shown as number or means ± error standards. The data were recorded in SPSS 13.0 program and independent T test was used for statistical analyses. A Pearson correlation analysis was performed to detect the relationship between blood flow parameters and demographic-clinical data. The P value less than 0.05 was considered statistically significant.

RESULTS

During the study period, 200 women (40 patients with unexplained primary infertility and 160 fertile patients) were eligible and 120 patients had inclusion criteria. Thirty five patients were included in the unexplained primary infertility group and were matched with 35 patients in the control group. The Doppler scan was unsuccessful in 5 patients in each group. Thus, 30 women in each group were included in the final statistical analyses. Demographic and clinical data were presented in Table 1. There were no statistically significant differences between groups in terms of clinical features and endometrial thickness (Table 1, P > 0.05). Uterine and ovarian blood flow parameters in patients with unexplained primary infertility were observed to be similar to those of fertile patients (Table 2, Figure 1). There was no correlation between uterine and ovarian Doppler findings and demographic-clinical data.

Table 1. Comparison of the groups in terms of demographic and clinical characteristics			
	Patients with unexplained infertility (n=30)	Control group (n=30)	P value
Age (years)	28.60±3.66	27.90±4.56	0.511
BMI (kg/m2)	24.65±1.29	24.19±1.11	0.146
Basal FSH value (mIU/mL)	5.32±1.63	5.64±1.33	0.405
Bazal LH value (mIU/mL)	5.91±0.44	5.97±1.10	0.795
Midluteal serum progesterone value (ng/mL)	11.84±1.22	11.51±1.41	0.281
Endometrial thickness (mm)	13.20±1.49	12.96±1.43	0.533
Parity		2.10±1.09	
Duration of infertility (years)	3.20±0.99		
Mentrual cycle (day)	24.43±2.88	24.90±2.50	0.507

Table 2. Ovarian and uterine blood flow parameters in groups			
	Patients with unexplained primary infertility (n=30)	Control group (n=30)	P value
Uterine artery PI	1.47±0.21	1.48±0.37	0.952
Uterine artery RI	0.78±0.83	0.76±0.11	0.387
Ovarian artery PI	0.96±0.27	1.08±0.46	0.242
Ovarian artery RI	0.56±0.95	0.57±0.98	0.701
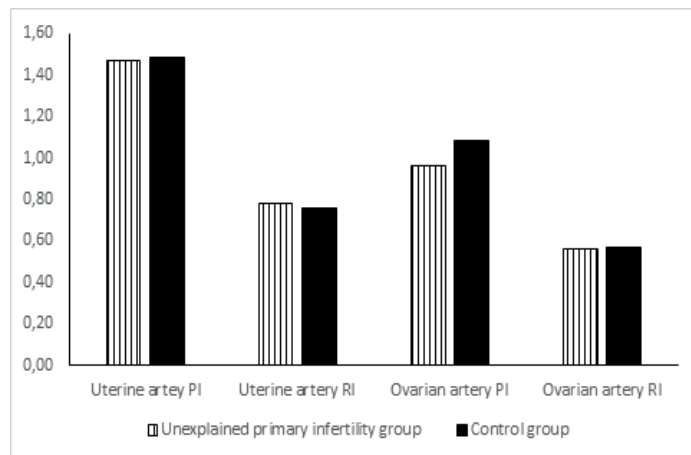
Figure 1. The comparison of uterine and ovarian blood flow parameters in groups

DISCUSSION

This study aimed to compare the uterine and ovarian artery blood flow parameters in patients diagnosed with unexplained primary infertility with fertile cases. Uterine and ovarian blood flow parameters in patients diagnosed with unexplained primary infertility were found to be similar to those of fertile patients.

Infertility is the failure to achieve a clinical pregnancy despite 1 year or more of regular unprotected sexual intercourse (1). The incidence of infertility has been increasing in recent years due to the postponement of childbearing, increasing pelvic infections and increasing sperm function disorders (15). Factors related to men, women or both may play a role in the etiology of infertility. Standard diagnostic tests including the evaluation of ovulatory function, investigation of tubal pattern and semen analysis are used to investigate the cause of infertility (1-3). When there is no reason to explain the cause of infertility, unexplained infertility is diagnosed. The prevalence of unexplained infertility ranges from 8% to 37% of infertile couples (1-3).

Transvaginal Doppler ultrasound is a non-invasive method and it is usually used to assess the uterine perfusion in infertile patients. There are studies in the literature evaluating uterine perfusion changes in unexplained infertile patients (16-19). Uysal et al. (16) investigated the mid-luteal phase endometrial spiral artery blood flow parameters in patients diagnosed with unexplained infertility. They reported higher spiral artery PI and RI values in patients with unexplained infertility compared with fertile group. El-Mazny et al. (17) observed increased uterine artery PI and RI values and impaired peri-implantation endometrial perfusion in women with unexplained infertility compared to fertile parous controls. In another study, Zebitay et al. (18) compared serum estradiol and progesterone levels, endometrial thickness and ovarian, uterine and spiral artery PI, and also RI values in fertile, unexplained infertility and tubal factor infertility patients. They reported higher ovarian, uterine and spiral artery PI and RI values in patients with unexplained

infertility compared with other groups. In a recent study, Alı et al. (19) compared mid-luteal phase progesterone levels, RI and PI values of uterine and ovarian arteries in unexplained infertility patients with fertile controls. They reported lower uterine and ovarian perfusion parameters in addition to lower progesterone levels in unexplained infertility patients than in control group. In constrat to their results (16-19), we observed similar uterine and ovarian PI and RI values and mid-luteal phase progesterone levels in patients with unexplained infertility compared with fertile patients. The reason for these differences may be due to the differences in the clinical characteristics of the patients selected for this current study. While this study was performed in patients diagnosed with unexplained primary infertility. In above studies (16-19), the case group included participants presented with unexplained infertility either primary or secondary, and unexplained primary infertile patients were not evaluated separately. We hypothesized that impaired uterine and ovarian blood flow may be an important factor in women diagnosed with unexplained primary infertility. Also, we speculated that uterine and ovarian blood flow may have been negatively affected in secondary unexplained infertile patients due to the medical interventions during previous pregnancy, births or abortions. Therefore, only patients diagnosed with unexplained primary infertility were included in this current study.

CONCLUSION

In conclusion, patients with unexplained primary infertility have similar uterine and ovarian blood flow parameters compared with fertile patients. To the best of our knowledge, this is the first study comparing uterine and ovarian blood flow parameters in patients diagnosed with unexplained primary infertility with fertile cases. A limitation was our relatively small patient population. Large prospective clinical studies are required investigating the changes in uterine and ovarian hemodynamics in patients with unexplained primary infertility.

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