

Value of transvaginal ultrasound doppler in uterine and ovarian arteries during mid luteal phase in women with unexplained infertility

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Abstract: **Abstract:** **Objective:** Altered utero-ovarian blood flow and uterine receptivity has been found to be a cause of unexplained infertility. the aim of this study was to evaluate the role of trans vaginal ultra sound Doppler in determination of uterine and ovarian arteries blood flow in unexplained infertile women during the window phase of implantation and to detect any uterine abnormality that may affect embryo implantation. Study design: observational, cross section, controlled study done at department of obstetrics and gynecology Alzhraa hospital and bahtem hospital during the period of May 2015 to October 2017. **Outcome measure:** Element of uterine scoring system of infertility and mean uterine and ovarian arteries resistance and pulsation indices in both groups and their values in the diagnosis of altered blood flow in unexplained infertility were measured. **Result:** women with unexplained infertility had significantly higher uterine and ovarian arteries pulsating index ($P < .001$) Uterine artery pulsating index of >1.2 was a good test for the diagnosis of decreased uterine artery blood flow in unexplained infertility. With a sensitivity of 68.00%, specificity of 92.00% for uterine artery and a sensitivity of 96.00, specificity of 100.00% for ovarian artery. **Conclusion:** Unexplained infertility is associated with increase resistance to blood flow in the utero-ovarian circulation during the mid-luteal phase uterine artery PI of 1.2 indicated decreased utero ovarian blood flow. More studies are needed to support this Conclusion and to evaluate the possible role of perfusion Enhancer drugs in increasing blood flow and enhancing pregnancy in women with unexplained infertility. [Iman Bayoumi Abd –Rabou, Doaa Mahmoud Effat, Samar Salah–Elden Mohammed. **Value of transvaginal ultrasound doppler in uterine and ovarian arteries during mid luteal phase in women with unexplained infertility.** *Nat Sci* 2018;16(10):44-47]. ISSN 1545-0740 (print); ISSN 2375-7167 (online). <http://www.sciencepub.net/nature>. 7. doi:10.7537/marsnsj161018.07.

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1. Introduction

Infertility is defined as one year of unprotected intercourse without conception and affects about 15% of couples. Unexplained infertility is diagnosed when basic infertility evaluation fails to reveal an obvious abnormality and it represents about 15% of infertility causes (1). Basic investigations include normal semen analysis, normal ovulation with a mid luteal serum progesterone ≥ 10 ng/ml, patent fallopian tubes and normal pelvic cavity diagnosed by hysterosalpingography and laparoscopy. In 1988 Goswamy et al. (3) suggested that women with unexplained infertility may have an impaired uterine blood flow and subsequent studies (4) found that unexplained infertility was associated with aberrant uterine artery blood flow and intermittently absent end-diastolic flow. Trans-vaginal color Doppler ultrasonography is used to assess utero-ovarian blood flow and to evaluate the functional capacity and receptivity of the endometrium (5) and in the prediction of successful implantation and revealing unexplained infertility problems (6). Some investigators (7) found that good uterine blood flow is necessary for embryo implantation and good pregnancy rates and that higher uterine arterial resistance was associated with low pregnancy rate and

poor outcome. Ovarian hemodynamic was claimed to be responsible for selection and maturation of the follicles and quality of the corpus luteum and that measurement of the ovarian artery blood flow correlated with the number and quality of harvested oocytes (8), while other authors did not find this association (9).

2. Patients and methods

The study was approved by the ethics committee of the department of Obstetrics and Gynecology, Alzhraa hospital and consent was taken from every woman before enrolling in the study. Two groups each of 25 cases aged 20–35 years were studied during the period from May 2015 to October 2017. A control group of fertile women who got pregnant within one year of marriage and a study group of women with unexplained infertility were included according to the following criteria (2): 1- Unprotected regular intercourse. 2- Normal semen analysis. 3- Serum progesterone at the mid luteal phase ≥ 10 ng/ml. 4- Patent fallopian tubes and normal pelvic cavity diagnosed by hysterosalpingography and laparoscopy. Exclusion criteria included 1- Patients treated with vasodilator drugs. 2- Women who received hormonal therapy or ovarian stimulation during the cycle of the

study. Two dimension trans-vaginal color Doppler ultrasound (Voluson 730 PRO, GE, Healthcare, USA) with 7.5 MZ vaginal probe, was done at 21–23 days of the cycle between 10 am and 12 pm to avoid circadian changes in blood flow. Each parameter of uterine scoring system is recoded, The uterus was scanned in the sagittal plane and the probe was directed to the lateral fornix to identify the ascending branch of the uterine artery in the para-cervical area at the level of the internal os. The pulsed Doppler wave was activated and the angle of insonation was adjusted to obtain three consequent similar waves. The probe was then moved to the posterior fornix and the ovaries visualized and the obtained color flow was explored until the typical low-amplitude ovarian artery signals were obtained. The blood flow resistant and pulsation indices of the uterine and ovarian arteries were visualized. The resistant and pulsation indices of the both uterine and ovarian arteries were displayed on the monitor and the mean calculated.

2.1. Statistical analysis

Data entry and analysis were performed using statistical package for the social science (SPSS) version 10 (SPSS, Inc., Chicago, IL, USA). Quantitative data were presented as mean and standard deviation. Student's *t*-test was used to compare means of two independent groups. The Receiver Operator Characteristic (ROC) curve was used to evaluate the value of resistant and pulsation indices in diagnosis of decreased blood flow in unexplained infertility patients. An area under the ROC curve from 0.9 to 1 represents excellent test, from 0.8 to 0.9 good tests, from 0.7 to 0.8 fair tests, from 0.6 to 0.7 poor test and from 0.5 to 0.6 fail test. Validity of the test at a certain cutoff point was represented by sensitivity, specificity and accuracy of the test. Result was considered significant at a *P* value of ≤ 0.05 .

3. Results

Table 1 shows no significant differences between infertile and fertile women as regards mean age, BMI and MAP.

Table 1. Demographic characteristics of the infertile and fertile women.

Data	Group			
	Infertile mean \pm SD	Fertile mean \pm SD	<i>t</i>	<i>P</i>
Age	28.52 \pm 3.61	29.72 \pm 2.32	1.6	NS
BMI	21.44 \pm 1.83	22.20 \pm 1.55	1.2	NS
MAP	95 \pm 6.38	92 \pm 5.2	1.3	NS

BMI: body mass index; MAP: mean arterial pressure.

Table 2 shows that infertile women had a significantly higher mean uterine and ovarian arteries PI than fertile women ($P < 0.001$ – 0.003), and no significant difference was found between the two groups as regards the RI of the ovarian artery.

Table 2. Comparison between uterine and ovarian arteries Doppler indices in the infertile and fertile women.

Indices	Groups			
	Infertile mean \pm SD	Fertile mean \pm SD	Test of significance	
			<i>t</i>	<i>P</i>
Uterine RI	0.85 \pm 0.09	0.79 \pm 0.10	0.35	0.72
Uterine PI	1.25 \pm 0.20	1.02 \pm 0.09	5.28	0.001
Ovarian RI	0.65 \pm 0.08	0.64 \pm 0.12	0.59	0.55
Ovarian PI	0.62 \pm 0.10	1.00 \pm 0.10	3.11	0.003

RI: resistance index; PI: pulsation index.

Table 3. Area under the curve, cutoff points, sensitivity, specificity and accuracy of the uterine and ovarian arteries RI and PI for diagnosis of decreased blood flow in unexplained infertility patients.

Indices	AUC (95%CI) ^a	<i>P</i> value	Cutoff points	Sensitivity	Specificity	Accuracy
Uterine RI	0.71(0.68–0.75)	0.29	0.77	80%	65%	42%
Uterine PI	0.85(0.84–0.97)	0.001	1.15	68%	92%	89%
Ovarian PI	0.97 (0.83–0.97)	0.02	.97	96%	100%	67%

Fig. 1 shows the ROC curves of the uterine artery indices. The pulsation index was a good test and the

resistant index was a poor test for the diagnosis of decreased uterine artery blood flow in women with

unexplained infertility (AUC #95% CI) = 0.89 and 0.42, respectively.

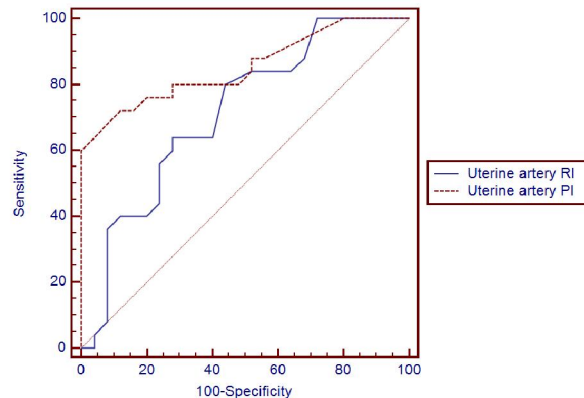


Figure 1. The ROC curves of the uterine artery indices. The pulsation index was a good test and the resistant index was a poor test for the diagnosis of decreased uterine artery blood flow in women with unexplained infertility (AUC # 95% CI) = 0.89 and 0.42 respectively.

The test result variable (s); mean uterine artery PI and RI have at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

b. Null hypothesis is: true area = 0.5.

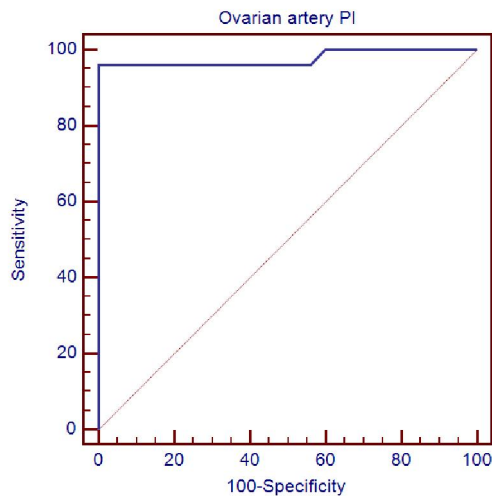


Fig. 2 shows the ROC curves of the ovarian artery indices. The pulsation index was a poor test and the resistant index was a fail test for the diagnosis of decreased ovarian artery blood flow in women with unexplained infertility (AUC #95% CI) = 0.71 and 0.85, respectively.

Figure 2. The ROC curves of the ovarian artery indices. The pulsation index was a poor test and the resistant index was a fail test for the diagnosis of

decreased ovarian artery blood flow in women with unexplained infertility (AUC # 95% CI) = 0.97.

Table 3 shows the performance of the uterine and ovarian arteries blood flow indices in the diagnosis of decreased blood flow in women with unexplained infertility. Uterine artery PI at a cutoff point of ≥ 1.21 was the only good and significant test ($P < 0.001$) with a sensitivity and specificity of 68. % and an accuracy of 92%.

4. Discussion

Trans-vaginal color Doppler ultrasonography is a noninvasive and efficient method for visualizing small vessels and study of blood flow changes (10). Changes in flow velocity waveforms of the uterine and ovarian arteries during the normal ovulatory cycle are related to ovulation with the lowest flow indices being found in the mid-luteal phase (11,12). In the present study, there was significantly higher PI during the luteal phase in unexplained infertility compared to fertile women ($P < 0.001$), while there was no significant difference as regards the RI. The cutoff value of the uterine artery PI for the diagnosis of decreased blood flow in unexplained infertility was ≥ 1.21 with a sensitivity and specificity of 83.3% and an accuracy of 89%. These results agree with previous studies (6) that demonstrated significantly high PI on the day of ovulation in non conception cycles compared to conception cycles and suggested that high impedance to blood flow in the luteal phase may be a cause of unexplained infertility. The mechanism mediating this increased uterine impedance in infertile patients was suggested to be secondary to attenuation in the uterine arterial response to the circulating ovarian hormones (13). Previous studies (7) found that good uterine blood flow is necessary for good pregnancy rates and that higher uterine arterial resistance was associated with low pregnancy rate and poor outcome, while others (9) did not find any association between uterine artery blood flow indices and endometrial receptivity or pregnancy outcome association. Ovarian hemodynamic during spontaneous and/or stimulated cycles may be responsible for selection and maturation of the follicles and quality of the corpus luteum(8). In the present study, there was a significantly higher ovarian artery PI in the infertile compared to fertile women ($P < 0.003$) and no significant difference was found between the two groups as regards the RI. This result agrees with that previously reported (14,15) of high PI in uterine and ovarian arteries in the luteal phase in infertile compared to fertile women. In another study (16) high vascular resistance was found in the uterine and ovarian arteries in infertile patients and suggested to be due to peri-vascular fibrosis arising from subtle infection or endometriosis and liberation of vaso-active factors such as

prostaglandins. Studies (17) found that in ART, the mean uterine arterial RI and PI values were significantly lower in the pregnant than in the non-pregnant group before embryo transfer while the mean ovarian arterial indices values were similar and that measurement of the blood flow correlated to the number and quality of harvested oocytes. The authors added that follicle hypoxia may impair chromosomal organization and separation within the oocyte and that increase in blood flow was important for embryo implantation. On the contrary, other authors (18) found that in IVF or IVF/ICSI and embryo transfer, serial Doppler ultrasound examination of the uterine artery did not discriminate between cycles resulting in ongoing pregnancy, miscarriage and no pregnancy. Treatments of unexplained infertility are empirical and all are designed, one way or another, to increase gamete density, bringing together more than the usual numbers of eggs and sperm in a timely way as in ovarian stimulation and intrauterine insemination (2). A new approach was suggested that unexplained infertility is associated with a profound impairment of endometrial perfusion that might be amenable to treatment by perfusion enhancer drugs (19).

5. Conclusions

Unexplained infertility is associated with increased resistance to blood flow in the utero-ovarian circulation during the luteal phase. Uterine artery PI of ≥ 1.2 indicated decreased utero-ovarian blood flow. More studies are needed to support this conclusion and to evaluate the possible role of perfusion enhancer drugs in increasing blood flow and enhancing pregnancy in women with unexplained infertility.

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