

Correlation of Uterine Artery Resistive Index with Endometrial Thickness among the Patients of Primary Infertility

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Abstract:

Infertility is a worldwide social, economic, and psychological problem. It can be caused by various factors including age, mental health, polycystic ovarian syndrome, ovarian failure, and defective endometrial receptivity. Endometrial receptivity is the preparation and thickening of the endometrium.

Objective:

To correlate the uterine artery resistive index with endometrial thickness among the females of primary infertility.

Methods:

A cross-sectional analytical study was conducted at Gilani ultrasound center from December 2017 to May 2018. A total number of 104 women including, 52 fertile and 52 infertile, aged between 18-50 years were selected. Statistical analysis was performed through SPSS version 25.0.

Results:

Among 52 fertile women, mean endometrial thickness was 8.29 ± 0.63 mm while the mean resistive index of the uterine artery was 0.78 ± 0.070 . Among 52 infertile women, mean endometrial thickness was 7.42 ± 2.65 mm while the mean RI of uterine artery was 0.78 ± 0.047 . A non-significant association was found between RI of uterine artery and endometrial thickness of infertile participants ($p=0.100$).

Conclusions:

Hence, the study concluded that there was non-significant correlation found between

endometrial thickness and resistive index of the uterine artery among infertile participants.

Keywords:

Infertility, endometrial thickness, uterine artery, resistive index, doppler

Introduction:

Infertility is a worldwide issue leading to social, economic and psychological problems; it is estimated that it affects approximately 10-15% of couples¹. According to world health organization (WHO), infertility is defined as "Failure to succeed in a clinical pregnancy after 12 months of unprotected sexual intercourse". Infertility is classified into two types: primary infertility and secondary infertility. "Women who can't carry any child, whether the women are unable to become pregnant or unable to carry a pregnancy to a live birth (which includes spontaneous abortion or giving birth to a stillborn)", this type of infertility refers to as primary infertility. While secondary infertility is defined as "Couples who are unable to have another child afterward previous pregnancy even after with one year of unprotected intercourse and not using contraceptives"¹. In Pakistan, the prevalence of infertility is 21.9%: while the influence of primary infertility is 3.9% and secondary infertility is 18.0%^{2,3}. Among developing countries, Africa records some of the highest secondary infertility rates in the world with less primary infertility rates, Asia records highest primary infertility rates and lowest secondary infertility rates⁴. Among developed

countries, in United States of America total 10% of women age ranging between 15 to 44 years are reported to have complications to get pregnant or continuing pregnancy⁵, total rate of infertility in the Australian community was 26.3%; 8.2% for primary infertility and 18.1 % for secondary infertility⁶, estimates of the prevalence of infertility in Canada ranged from 11.5% to 15.7%⁷. Female infertility has a vast number of causes. Maternal age, smoking, obesity, diet, the sexually transmitted infections (STIs), exposure to some chemicals, alcohol, mental stress, ovulation disorders, chronic diseases, problems with the uterus and fallopian tube, and previous sterilization treatment are all the causes leading towards infertility⁸. However, there are complications which can occur due to infertility or due to the treatment of infertility such as ovarian hyperstimulation syndrome, while infertility for many years can also lead to stress and possibly depression⁹. Endometrial thickness plays an important role in the female fertility. The thick endometrium is considered good for implantation, whereas, thin endometrium corresponds to lower implantation rates¹⁰. "Endometrial thickness is defined as the distance from the highly reflective echogenic interfaces at the endometrium to myometrium junction, which is measured in the midsagittal plane"¹¹. Sonographically, there are three criteria used to describe changes in the endometrium throughout the menstrual cycle: 1. the echotexture of stratum functionalis is examined in contrast to the myometrium. 2. A morphology of "triple-line" is generally monitored throughout the follicular phase of the menstrual cycle. 3. Endometrial thickness is evaluated. In a triple-line pattern of the endometrium, the hypo-echoic endometrium is surrounded by a hyperechoic zone, which is basically a zone of vascularity¹². Several authors have described an increased likelihood of pregnancy when the endometrium reached a threshold thickness. Although others found no representative relationship between the

endometrial thickness and pregnancy rates¹³. Some other authors defined discriminatory zones of <7mm with no pregnancies¹⁴, and >14mm with a decline in implantation rate and pregnancy rates¹⁵.

Uterine receptivity is probably thought to be regulated by many factors which include uterine perfusion and its crucial role in the achievement of a successful normal pregnancy^{16,17}.

Endovaginal color Doppler provides an opportunity for non-invasive assessment of uterine arteries¹⁸. Doppler is the best imaging technique to assess uterine abnormalities, intrauterine pathologies, tubal patency, polycystic ovaries, ovarian follicular observation, failed ectopic pregnancy, endometrial receptivity and endometrial uterine and ovarian vascularity. In order to determine uterine receptivity, presence or absence of end-diastolic blood flow in uterine arteries, endometrial morphology and endometrial thickness are the best combinations to seek¹⁸. Schild RL, described that pregnancy rates are low when uterine pulsatility index (PI) was 3.3-3.5 and the uterine resistance index was 0.95¹⁹. Razik M A *et al.*, conducted a cross sectional study, highlighted that infertility is related to higher resistance to blood flow in the uterine artery throughout luteal phase²⁰. A Prospective study conducted by Son JB *et al.*, concluded that endometrial thickness and the measurement of blood flow index of endometrium and uterus are not effective in predicting pregnancy outcome²¹. Retrospective study performed by Strowitzki T *et al.*, highlighted that endometrium is an important fertility-determining factor but in future more therapeutic options are required to understand about endometrium as a fertility determining factor¹⁰.

Few studies were dedicated to determine association between RI of uterine artery and endometrial thickness of infertile participants. It is therefore justified to conduct study on uterine artery RI and endometrial thickness in infertility cases and compare it with the uterine artery RI

and endometrial thickness of fertile women.

Methods:

It was a cross-sectional study. Women were recruited clinically at Gilani ultrasound center Lahore, from December 2017 to May 2018, after taking approval from board of studies (BOS) and institutional review board (IRB) of The University of Lahore. A written informed consent was taken from the patients. A total of 104 females were recruited for this study (Age range 18-50 years), 52 infertile females and 52 fertile females. Exclusion criteria for both groups was females with co-morbidities. American Institute of Ultrasound in Medicine (AIUM) gynecological Ultrasound guidelines were observed, during this study for examination techniques²². Ultrasound data were collected from the machine using Mindray DC7

and Toshiba xairo, with convex transducer 3-6 MHz and Micro-convex transvaginal transducer 5-7.5 MHz and demographic data were collected directly from the patient. Statistical analysis was performed through SPSS version 25.0. The sample size was estimated by using sample power formulae, with variance: 0.135.

Results:

Among fertile females age range was 18-50 years mean 30.21 ± 6.73 years, endometrial thickness and RI of the uterine artery of fertile females was 8.29 ± 2.63 mm and 0.78 ± 0.07 respectively. Among infertile females age range was also 18-50 years mean 27 ± 7.02 years, endometrial thickness and RI of the uterine artery of fertile females was 7.42 ± 2.65 mm and 0.78 ± 0.04 respectively, Table 1.

Fertile females				Infertile females		
	Minimum	Maximum	Mean $\pm$ S.D	Minimum	Maximum	Mean $\pm$ S.D
Age in Years	18	50	30.21 ± 6.73	18	42	27.00 ± 7.02
Endometrial thickness (mm)	3.30	19.40	8.29 ± 2.63	3.10	16.00	7.42 ± 2.65
RI of Uterine Artery	0.63	0.92	0.78 ± 0.07	0.63	0.87	0.78 ± 0.04

Table 1: Participants' age, mean uterine artery RI and endometrial thickness

30 fertile participants were lying within the interval of 1-10 years, 21 fertile participants were within the interval of 11-20 years, no fertile participant was within the interval of 21-30 years, and 1 fertile participants was lying within the interval of 31-40 years. Whereas, 41 infertile participants were within the interval of 1-10 years, 10 infertile participants were within the interval of 11-20 years, 1 infertile participants was within the interval of 21-30 years, and 0 infertile participants were within the interval of 31-40 years, Table 2.

Fertility	Lapse of years of marriage				Total
	1-10	11-20	21-30	31-40	
Fertile	30	21	0	1	52
Infertile	41	10	1	0	52
Total	71	31	1	1	104

Table 2: Participants with lapse of years of marriage

According to results, insignificant association was found between RI of uterine artery and the endometrial thickness among infertile females, $p=0.100$. Whereas, association between RI of uterine artery and the endometrial thickness

among fertile females was also insignificant $p=0.687$, shown in Table 3.

Groups	Endometrial thickness	RI of Uterine Artery	pvalue
	Mean $\pm$ SD	Mean $\pm$ SD	
Infertile	7.42 $\pm$ 2.65	0.78 $\pm$ 0.04	0.100
Fertile	8.29 $\pm$ 2.63	0.78 $\pm$ 0.07	0.687

Table 3: Association between fertile and infertile groups with respective mean $\pm$ SD of uterine artery RI and endometrial thickness

Discussion:

Endometrial thickness plays a crucial role in the female fertility. In a retrospective study performed by Paulson RJ *et al.*, indicated that the thickness of the endometrium is highly related with the functional receptivity of the endometrium. Patients who successfully achieved pregnancy had 10.24mm $\pm$ 2.63mm S/D mean thickness of the endometrium, while patients who were not pregnant having 8.62mm $\pm$ 3.49mm S/D mean thickness of the endometrium. Whereas, endometrial thickness of <5mm was not considered good for implantation, study by Paulson RJ²³. Results of current study were similar to the study described above. A retrospective study performed by Esmailzadeh S *et al.*,²⁴ indicated that a successful pregnancy was achieved when meaning endometrial thickness was 10.1mm $\pm$ 3.0mm S/D. Parsad S *et al.*, also suggested that increased endometrial thickness was reported among fertile women as compared to infertile women, with a mid-cycle endometrial thickness of 9.72mm $\pm$ 1.47mm, fertile women and mid-cycle thickness of endometrium as 7.78mm $\pm$ 1.87 in infertile women. The late cycle endometrial thickness of 13.44mm $\pm$ 1.20mm, fertile women and late cycle endometrial thickness of 10.44mm $\pm$ 2.70mm among infertile women.²⁵ Findings of current study were found almost similar, as mean endometrial thickness in the fertile group was 8.29mm $\pm$ 2.63mm and infertile group was 7.42mm $\pm$ 2.65mm. Endometrial thickness among infertile women was 7.8mm

during proliferative phase. Amir W *et al.*, provided measurements on endometrial thickness, which is an important step. The researcher measured endometrial thickness and correlated it with the age of women, advised that thickest endometrium (11.9mm $\pm$ 2.5mm) was denoted in patients with the age of <25 years and was correlated with increased pregnancy rates as compared to women with the age >40 years having thinnest endometrium (9.6mm $\pm$ 2.3mm)²⁶. A study performed by Dietterich C *et al.*, also suggested that there is no impact of a thickened endometrium determined by implantation, pregnancy, or abortion rates²⁷. Results of current study were found almost closely similar with the study described above, as only small difference was found between the mean endometrial thickness of fertile and infertile women. It was also reported that improper uterine arteries perfusion, may be a cause leading to infertility²⁸. Many reports indicated that high resistance to blood flow is correlated with decreased conception rates. The results of this study were found contradictory to the findings of the study described above by Lazzarin N *et al.*, and Ferreira A *et al.*,^{29,30}. Studies conducted by Kupesic S and Kupesic S, Kurjak A, performed on 150 women documented resistive index RI of 0.88 $\pm$ 0.04 till day 13th of the 28-day menstrual cycle^{31,32}. Results of present study were found related with the study designated above. Khan *et al.*, suggested that highest pregnancy rates were related to women having thick endometrium, whereas reversal or absence of end-diastolic blood flow indicates no successful pregnancy rates³³. Increased uterine blood flow resistance was found in infertile women; nonpregnant women³⁴. Current findings revealed that no increased resistance was found in infertile women i.e. RI of anterior uterine artery was 0.79 during proliferative phase. Where as, there are several studies which also suggested that there was no correlation found between blood flow and endometrial thickness and relation with pregnancy rates, patients who successfully

conceived were found to have (RI) of (0.563 ± 0.1) . While, the non-pregnant patients were found to have a (RI) of (0.603 ± 0.1) , in a study conducted by Strowitzki T *et al.*,¹⁰. Findings of current study were inconsistent with their results.

Conclusions:

Hence, the study concluded that there is non-significant correlation found between endometrial thickness and resistive index of the uterine artery among infertile participants.

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