

Research Article

Sonographic Correlation Of Polycystic Ovarian Syndrome (PCOS) With Uterine Artery Resistive Index (RI)

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Abstract: Objective: Polycystic ovarian syndrome is a very common female endocrine, metabolic and reproductive disorder mainly affects females of reproductive age. It is multiple organ disorder affects 5 to 10 % female population. The world occurrence of PCOS is 105 million in the age ranges from 15 to 45. The polycystic ovarian syndrome is a set of disorders like amenorrhea, infertility, polycystic ovaries, hyperinsulinemia, hirsutism, acne vulgaris and other symptoms of hyperandrogenism. Ultrasound plays an important part in the determination and diagnosis of polycystic ovaries. Colour Doppler and Pulse Doppler play a major role in evaluation of uterine artery Resistive index for access correlation with PCOS. PCOS patients suffer from primary and secondary infertility. The aim of the current study was to find correlation between polycystic ovarian syndrome and blood perfusion of uterus by measuring changes in hemodynamic of uterine arteries by help of Colour Doppler Ultrasound. A cross-sectional analytical study was conducted in Gillani ultrasound centre Lahore in 3 months from March 2019 to May 2019. A total of 138 females were taken according to prevalence of PCOS based on AE-PCOS society. 69 patients with PCOS and 69 normal individuals were scanned. Per abdominal and Transvaginal ultrasonography was used and Ultrasound Machines of Mindray Z5 and Toshiba Xario 100 with convex transducer probe of 2.5-7.5 MHZ was used. According to the comparison of mean resistive index in PCOS patients and normal females the Mean RI of right and left uterine artery was 0.886 ± 0.065 in PCOS patients and 0.879 ± 0.06 in normal individuals and 0.877 ± 0.05 in the patients of PCOS and 0.868 ± 0.068 in normal individuals so we find no significant difference in resistive index of right and left uterine arteries in normal females and polycystic ovarian syndrome patients on Colour Doppler and Pulse Wave Doppler. It is concluded that there is no significant difference of uterine artery resistive index in polycystic ovarian syndrome patients and normal females.

Keywords: Colour Doppler ultrasound, Polycystic ovarian syndrome, Pulse wave Doppler, Resistive index, Trans abdominal ultrasonography, Transvaginal scan.

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is a common endocrine disorder of females at their reproductive age. PCOS is a very common and more complex metabolic endocrine disorder of premenopausal women of reproductive age which affects approximately 5-10% of female population (Asma, B. *et al.*, 2016). PCOS is characterized by chronic anovulation/oligo-ovulation, infertility, menstruation irregularities, hirsutism, acne vulgaris, and obesity. PCOS associated with psychological impairments included depression anxiety and other mood disorders. A patient diagnosed with PCOS are on the great risk of Type 2 diabetes due to hyperinsulinemia and increased symptoms of obesity with increased secretion of

interleukins, chemokines and adipokines due to body inflammatory state. PCOS can be divided into three divisions clinical, metabolic and endocrine disorders and abnormalities. PCOS is considered as a multi-organ disorder because it affects multiple organs not only ovaries but also affects adrenal and sex hormones. It has a deep influence on pituitary hormones including adrenocorticotrophic hormone (ACTH), gonadotropin and growth hormones (Gul, S. *et al.*, 2014). PCOS may result in abnormally functioned hypothalamic-pituitary-ovarian (HPO) axis and also associate with a raised level of a biochemical marker of plasma testosterone (Barber, T.M., & Franks, S. 2010). PCOS is a prevalent disorder with variable phenotypes and underlying pathophysiology which is not completely understood

Quick Response Code



Journal homepage:

<http://www.easpublisher.com/easjrit/>

Article History

Received: 15.09.2019

Accepted: 26.09.2019

Published: 05.10.2019

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yet. It is also associated with insulin resistance which results in obesity, Type 2 diabetes, dyslipidaemia, metabolic syndrome, hypertension, cardiac and vascular diseases, hyperplasia and endometrial carcinoma (Havelock, J. 2018). PCOS is genetic basis runs in family and patients diagnosed with PCOS having a family history of PCOS and infertility that is the reason high numbers of female relatives are affected. The features of PCOS don't remain consistent in all patients. PCOS symptoms are consistently variable among patient as clinical features in some females noted consistently variable and indeed some women with PCOS don't show any of the common symptoms; likewise, associated biochemical features with PCOS are not consistent so there is heterogeneity in sign and symptoms of PCOS and it may be changed for individuals over time (Legro, R. S. *et al.*, 1998).

Uterine artery blood flow remodelling occurs from time to time according to the state of the uterus. In the gravid state, there must be low resistive blood flow to supply nutrients and oxygen to the indwelling baby. But during non-gravid uterus, there is high resistive blood flow. As PCOs cause infertility that is why it is hypothesized that high resistive blood flow is expected in the uterine artery. At the level of 4th lumbar vertebrae abdominal aorta divides into right iliac artery and left iliac arteries. The right iliac artery divides into anterior and posterior iliac arteries. The left iliac artery divides into left anterior and posterior iliac arteries. Right and left anterior and posterior arteries give rise to many parietal and visceral arteries and supply their respective organs. Anterior iliac artery gives rise to ovarian and uterine artery also which supplies ovaries and uterus (Pelage, J. P. *et al.*, 1999). Uterine artery contains normal low resistance flow in normal young females but its flow may vary in pregnant females with their gestation trimesters (Clemente, Carmine. (1985). Doppler ultrasound plays an important part in evaluation, detection and measurements of uterine artery blood flow and supply to uterus after histological, anatomical, pathophysiological, clinical sign and symptoms and laboratory tests in 1970 KRATOCHWIL *et al.*, studied pelvic organs like uterus and ovaries by ultrasonography and explain changes which occur in uterus and ovaries with menstruation cycle changes (Kratowchwil, A. *et al.*, 1972). Ultrasonography is an essential and descriptive method for examination of different pelvic organs. It also plays an important part in diagnosis and evaluation of polycystic ovaries.

Important features of PCOS on ultrasound is multiple, anechoic ($n > 10$) small (2-8mm) cysts in enlarged ovaries (> 8 ml) which are arranged on periphery around a dense core of thick echogenic stroma (Battaglia, C. 2003). A trans-abdominal ultrasound shows enlarged ovaries (8-14ml) in 70% symptomatic patients and follicles may be scattered throughout the hyperechogenic stroma (Adams, J. *et al.*, 1985). Some females with PCOS may contain normal

ovarian volume on ultrasound it can be evaluated or diagnosed by clinical, histological and biochemical studies. The real anatomy of ovaries with maximum accuracy cannot be claimed by sonography, no of follicles, size and shape may be changed on histo-anatomical resection (Yee, B. *et al.*, 1987). Because of full bladder, underlying fat tissues in form of obesity, low resolution of ultrasound probe, bowel loops which is filled with bowel gases which covered underlying ovaries, to overcome all these hindrances in diagnostic importance of ultrasound transvaginal approach is used which is called transvaginal ultrasound (TVS) by using a special high frequency transvaginal probe in which no need of bladder filling. A full bladder and it overcomes the attenuation problem and artefacts due to obesity. High frequency provides better resolution of pelvic organs (Timor-Tritsch, I. E. *et al.*, 1988; Pache, T. D. *et al.*, 1992). Women with PCOS have markable changes in hemodynamic of ovaries and uterus in comparison of normal ovaries. According to Stein and Leventhal 5 - 10% of females have classical features of PCOS (obesity, infertility, and amenorrhea). For better diagnosis of PCOS all disorders which may cause hyper androgen and hyperinsulinemia must be excluded. On ultrasound ovaries which contain 12 and more than 12 follicles measuring 2-9 mm and increased ovarian volume (10 cm³) documented as polycystic ovary. Female should not evaluate for PCOS diagnosis in the follicular phase (day 3-5 of periods). In amenorrhea patient's blood flow of uterine arteries and ovarian artery shows modified hemodynamic profile. Peak systolic velocity and end-diastolic velocities underwent modifications and become significantly lower as compared to normal females with amenorrhea patients (Stein, I. F. 1935).

Ultrasound is a non-invasive, less time-consuming approach, easy availability of Doppler ultrasound and their great importance and sensitivity in the diagnosis of PCOS. Literature shows that Doppler ultrasound shows variability in blood flow PI and RI, of the ovarian and uterine artery in patient with PCOS. So it is acceptable that hormonal level is no more reliable for diagnosis of PCOS. Tran's abdominal Doppler ultrasound is an easy approach for uterine artery, and uterine artery Doppler indices give a strong recommendation for PCOS. Due to patient and disease variability in patient plain pelvic ultrasound findings shows the difference when compared with hormonal profile (Battaglia, C., & Volpe, A. 2000). Main rationale of this study is that ultrasound is very useful in the diagnosis of PCOS and Doppler capability is important for the evaluation of vascularity and blood flow characteristics. It is expected that there must be change in spectral waveform and other characteristics of blood flow in the uterine artery due to PCOS. This research is therefore aimed to note changes in uterine artery Doppler indices to be used as an additional parameter to be incorporated in Doppler findings of PCOs (Abbasi, T. A. *et al.*, 2018).

MATERIAL AND METHODS:

A cross-sectional analytical study was conducted in Gillani Ultrasound Center; Lahore from March 2019 to May 2019 after approval from the hospital ethical review committee was taken. A sample size of 138 patients was taken by using convenient sampling technique. The non-probability sampling procedure was used. 138 patients were included after the approval of synopsis by institutional review board (IRB). In this study 69 normal females at their menstrual cycle day 6-14 was taken and 69 females diagnosed with PCOS according to ROTTERDAM criteria ESHRE/ASRM sponsored PCOS consensus workshop group (2004) was taken. Where a corpus lutein seen that patient excluded. When two out of 3 criteria's were present (1) oligomenorrhea/anovulation (2) clinical and biochemical sign of hyperandrogenism (3) polycystic ovaries (ovarian volume more than 10 cm³). More than 12 follicles measuring 2-9 mm was taken. Females taking contraceptive pills, infertility treatment, uterine abnormalities, functional and nonfunctional ovarian cyst, pregnant females, thyroid disease, congenital hyperplasia and biochemical evidence of hyper prolactinemia were excluded from study. We used gel and extra compression for better resolution. Toshiba Xario machine was used for a Trans abdominal and transvaginal ultrasound. A trans abdominal probe of frequency 3/3.5 MHZ and Endo vaginal probe of 5/7.5 MHZ was used uterus was evaluated for any pathology and abnormality right and left ovaries evaluated and determine as normal and PCOS, ovarian volume is taken by measuring three dimensions of ovary by simplified formula 0.5 + length + width + thickness. The resistive index was taken as it is an indicator of resistance of perfusion to an organ on ultrasound. It is taken from peak systolic velocity and end-diastolic velocity of blood flow. The resistive index was taken as it is an indicator of resistance of perfusion

to an organ on ultrasound RI is taken from peak systolic and end-diastolic blood flow velocity. The uterine artery was visualized laterally to the cervix in longitudinal plane at the level of internal oss. The sample volume was placed across the vessel in pulse Doppler and the angle was kept close to 0 between ultrasound beam and the vessel. Acquired data was tabulated and analyzed by SPSS version 21.0.

RESULTS AND DISCUSSION:

Total of 138 participants included PCOS and normal individuals were recruited in this study. Out of them 108 (78%) having negative family history of PCOS and the rest of 30 (21.7%) with positive family history for PCOS. Equal no of patients 69 (50%) with PCOS and equal no 69 (50%) of normal females were taken. there were 40 (29%) patients with negative results of infertility and 98 (71%) patients with positive results of infertility. Patients with history of Amenorrhea 41 (29.7%) with irregular Menstruation 54 (39.1%) and with regular Menstruation were 43 (31.2%). A number of patients with hirsutism 88 (63.8%) and negative results of hirsutism was 50 (36.2%). Patients with Negative results of Acne vulgaris 100 (72.5%) and number of patients 38 (27.5%) with positive result of acne vulgaris. According to this study there were 46 (33.3%) patients with no weight gain and 92 (66.7%) with weight gain history. Mean age of the participants was 27.65±5.28 years, ranging from 20 to 45 years. Mean resistive index of right uterine artery was 0.8828±0.06277cm/s, ranging from 0.74 to 1.0 cm/s. The mean volume of right ovary was 10.31±5.57 cm³, ranging from 2.90 to 30.70 cm³. The mean volume of left ovary was 9.30 ±4.71cm³, ranging from 2.50 to 25.1 cm³. Mean velocity of left uterine artery resistive index was 0.87±0.08 cm/s, ranging from 0.48 to 1.10 cm/s. (Table 1).

Table 1: 138 patients Mean, Standard Deviation and Range of Age, RT Uterine RI, vol. of RT ovary, vol. of LT Ovary and LT Uterine RI

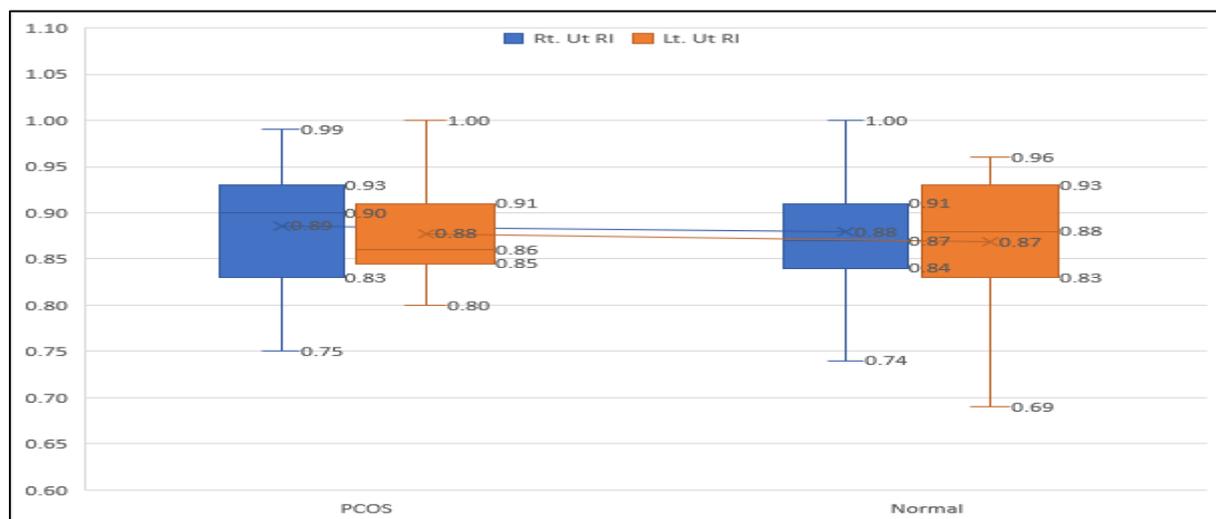
Description	N	Minimum	Maximum	Mean	Std. Deviation
AGE	138	20.00	45.00	27.6522	5.28412
RT Uterine RI	138	.74	1.00	.8828	.06277
Vol. RT Ovary	138	2.90	30.70	10.3123	5.57886
Vol. LT Ovary	138	2.50	25.10	9.3058	4.71241
LT uterine RI	138	.48	1.10	.8707	.08043

Comparison of the means of Resistive index between PCOS patients and normal individuals was done with an independent sample of t-test. Mean and standard deviation of right uterine artery resistive index was 0.886±0.065 in PCOS patients and 0.879±0.06 in

normal individuals. Mean and standard deviation of left uterine artery resistive index was 0.877±0.05 in patient with PCOS and 0.868±0.068 in normal individuals (Table 2, Graph 1).

Table 2: Comparison of Mean standard and deviation calculated with independent sample t-test among 69 patients of PCOS and 69 normal individuals

Group Statistics				
	PCOS	Mean	Std. Deviation	Std. Error Mean
RT uterine artery RI	PCOS	0.8861	0.06531	0.00786
	Normal	0.8794	0.06041	0.00727
LT uterine artery RI	PCOS	0.8775	0.04912	0.00591
	Normal	0.8687	0.06815	0.0082



Graph 1: Box and whisker's plot shows RI of uterine arteries of Mean standard and deviation calculated with independent sample t-test among 69 patients of PCOS and 69 normal individuals.

There was no significant effect seen of PCOS on uterine artery resistive index. The purpose of this study was to get a link, influence or a correlation of PCOS with uterine artery resistive index by ultrasound. PCOS is a worldwide health threat to females of reproductive age and a lead to primary and secondary infertility purpose of the current study was to evaluate that either PCOS affect the blood supply of uterus or not. For this purpose, two groups of equal no of females were scanned one group with PCOS and other was normal females at ovulatory phase from age group 20-50 years. It was quite challenging to diagnose a female as PCOS because it's a complex disease which is a combination of multiple organ disorders and different metabolic and endocrine abnormalities and all females diagnosed with PCOS do not contain all typical signs and symptoms of PCOS. For this purpose Rotterdam 1 criteria were used according to ROTTERDAM criteria ESHRE/ASRM sponsored PCOS consensus workshop group (2004), when 2 out of 3 criteria fulfil, (1) oligomenorrhea and /or anovulation, (2) clinical and biochemical sign of hyperandrogenism, (3) polycystic ovaries on ultrasound. We diagnosed it as a PCOS patient. It was a challenging task to determine both right and left uterine arteries and then calculate and access blood flow resistive index. For this purpose a lot of skills and expertise was needed and vigorous compression and angle correction technique was used for uterine artery blood flow. Ultrasound is a Gold standard for polycystic ovaries. Results show that there

is no significant correlation between PCOS and uterine artery resistive index.

According to different studies, there are a lot of variations in the pulsatility index and Resistive index of uterine arteries in PCOS patients.

Another similar study was conducted in combined military hospital Lahore on PCOS; they were searching for PCOS by using doppler ultrasound and doppler indices of uterine artery (RI and PI). Purpose of their study was to evaluate that either colour doppler ultrasound correctly diagnosed PCOS with uterine artery resistive index and pulsatility index. They concluded that by colour doppler pelvic ultrasound correctly diagnose cases of PCOS was 84.2% and mean values of pulsatility index of uterine arteries bilaterally were High in PCOS -patients and low Resistive index was noted (Asma, B. *et al.*, 2016).

Another study was conducted to evaluate blood flow changes in uterine arteries in females with PCOS are typically associated with endocrine findings of PCOS by the help of transvaginal colour doppler ultrasound and they observed elevated pulsatility index of uterine arteries in females with PCOS (Maciołek-Blewniewska, G. *et al.*, 1999).

A study “polycystic ovarian syndrome assessment with colour doppler angiography and three-dimensional ultrasonography” concluded that PCOS

had greater values of uterine artery pulsatility index and Resistive index (Dolz, M. *et al.*, 1999).

Another study which was conducted on “Polycystic ovarian syndrome: Relationship between insulin sensitivity, sex hormones level and ovarian stromal blood flow” concluded that mean resistive index and pulsatility index of uterine arteries having lower values in polycystic ovarian syndrome patients: (Loverro, G. *et al.*, 2001).

Doppler ultrasound plays an important part in the diagnosis of PCOS and uterine artery Doppler indices as in the current study. Colour doppler ultrasound was used in current study 69 (50%) patients with PCOS and 69 (50%) normal females were correctly scanned with colour doppler ultrasound. According to another study the frequency of correctly diagnosed cases (84.2%) of PCOS by colour doppler also was similar study by Battaglia C, *et al.*, which used power Doppler for correctly detect 83% cases. These both studies like our study used cutoff value of > 1.02 for PCOS. According to the current study the mean resistive index among PCOS and normal individuals. Mean and standard deviation of right uterine artery resistive index was 0.886 ± 0.065 in PCOS patients and 0.879 ± 0.06 in normal individuals. Mean and standard deviation of left uterine artery resistive index was 0.877 ± 0.05 in patient with PCOS and 0.868 ± 0.068 in normal individuals. In the current study, there was no significant difference in RI of uterine arteries. According to another study the mean pulsatility index was high (3.89 ± 0.76) and resistive index was on lower side i.e. 0.93 ± 0.10 . Dolz M, *et al.*, 17 also conducted a similar study to determine whether any difference in pulsatility index and resistive index according to their study a high PI in patients with PCOS i.e. $3.56 \pm 0.93 < 2.55 \pm 0.63$ 0.001 They determined that RI in patients with PCOS was 0.94 ± 0.06 and in controls it was 0.86 ± 0.06 and this was a statistically significant difference ($P < 0.05$). Goswamy and Steptoe 18 were the first to report significantly elevated RI and PI values in the uterine arteries of infertile females (Goswamy, R. K., & Steptoe, P. C. 1988).

A study is done on 124 PCOS patients and 118 controls to determine that either fat or adipose tissue accumulation is more in which females. As polycystic ovarian syndrome is endocrinological and metabolic disorder adipose tissues was more in PCOS patients. This study concluded that PCOS patients have more adipose/fat accumulation which increased risk of atherosclerosis result in cardiovascular diseases. Patient with PCOS on great risk of CV diseases due to excessive fat accumulation and also affect hemodynamics of uterine arteries (Tripathy, P. *et al.*, 2017). A study relative to current study was conducted by Faculty Allied Health Sciences (FAHS) on “Sonographic association of polycystic ovaries with Intra ovariaarterial pulsatility index and Resistive

index”. According to this study they want to find correlation between polycystic ovary and intraovarian hemodynamics. 100 females at ovulatory phase were taken in which 50 females with polycystic ovaries and 50 normal females were taken and by intraovarian approach through ultrasound and Tran’s vaginal scan. They examined that polycystic ovaries were hyper stimulate and hypervascular as compare to normal females (Rafiq, M. *et al.*, 2019).

Another similar study on “Sonographic correlation of polycystic ovarian syndrome with suprapubic subcutaneous fat” was conducted in Gosh-e-Shifa hospital Lahore. This study was to evaluate that either PCOS have link with suprapubic subcutaneous fat because PCOS result in hyperinsulinemia and metabolic disorders result in obesity. 128 patients were taken 69 females with PCOS and 69 normal females were taken and their fat deposition was measured with ultrasound and they concluded that PCOS and suprapubic subcutaneous fat thickness correlate with each other (Iqra, M. *et al.*, 2019).

This systematic review showed that the result of current study is unique and add information in scientific knowledge that there is no significant impact of PCOS on blood supply of uterus and ultrasound is very beneficial modality for evaluation of PCOS as it is reliable, less time consuming, low cost, non-invasive and easily available non ionizing modality.

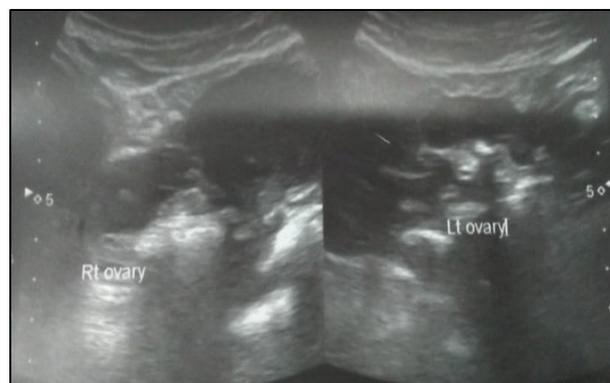


Figure 1 (a): Tran’s abdominal image of normal bilateral ovaries of a 21 years old married female.

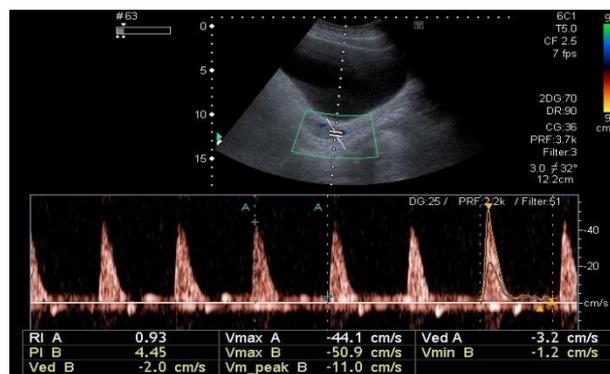


Figure 1 (b): Doppler ultrasound of right uterine artery shows pulsatility index and Resistive index

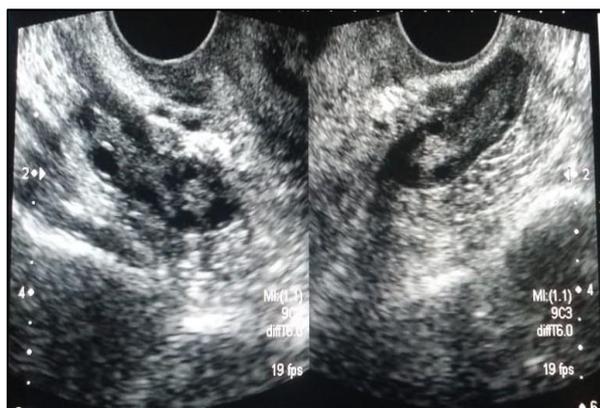


Figure 2 (a): A typical polycystic ovaries in a young female showing multiple immature follicles arranged on periphery with thick echogenic stroma.

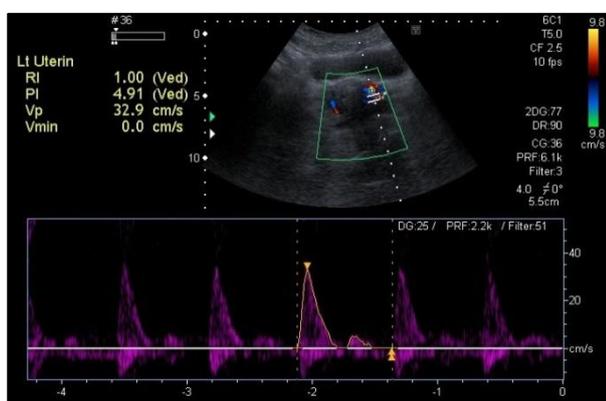


Figure 2 (b): Showing blood flow pattern and Doppler indices of Left uterine artery in a married female of 24 years with polycystic ovaries

CONCLUSION

It is concluded that there is no significant difference of uterine artery Resistive index in polycystic ovarian syndrome patients and Normal females.

Acknowledgment

In the name of Allah, the most beneficent and merciful. First and all praises be Allah, the Almighty, and the Glorious who has bestowed upon the faculties of thinking, searching and learning. I would like to express my gratitude to my supervisor Dr Raham Bacha, for his meticulous, stupendous supervision.

I would like to thank s Dr Khawaja Khursheed my co-supervisor for his guidance. I am also thankful to Syed Yousaf Gillani (biostatistician) for study and analysis of the data, Department of Radiological sciences and medical imaging Technology (UIRSMIT) and also thankful to Mr Ateeb Ali khan for assistance to bring this data in final shape and assisting in typing and handling all data in technical aspects.

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