ORIGINAL RESEARCH

Sonography and Intraovarian Arterial Doppler Accuracy in Evaluating Polycystic Ovarian Syndrome

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ABSTRACT
BACKGROUND: Polycystic ovarian syndrome (PCOS) is a prevalent endocrine, metabolic, and reproductive condition in women that primarily affects those who are of reproductive age. Ultrasound plays an important part in the determination and diagnosis of polycystic ovaries. Hence, we explore the ultrasound features of this syndrome and try to improve its diagnostic criteria, providing an inexpensive, affordable diagnosis and establish guideline values of intra-ovarian arterial pulsatility and resistivity indices for diagnosing PCOS. The purpose of the current study is to describe the ultrasonographic features of polycystic ovaries & to assess the utility of intra-ovarian arterial Doppler study in diagnosing polycystic ovarian syndrome.
METHODS: A prospective case-control study was conducted in the Radiodiagnosis Department at R.L.J.H & R.C, Tamaka, Kolar in 20 months from December 2020 to July 2022. A total of 120 females out of which 60 patients formed the case group ,who presented with atleast 2 of the 3 features described as per “American society of reproductive medicine” or “European Society of Human Reproduction and Embryology criteria” and the remaining 60 females consisted of the control group who had no menstrual irregularities or ultrasonographic presence of polycystic ovaries. Ultrasonography and Doppler study were done in follicular phase of the menstrual cycle.
RESULTS: Most of cases and controls were below 25 years. Mean body mass index (BMI) and obesity among cases was significantly higher than those among controls. The mean ovarian volume and ovarian follicles were significantly higher among cases compared to controls. About 95 % of cases and 5 % of controls had echogenic stroma. There was increased peak systolic velocity (PSV) and end-diastolic volume (EDV) in cases when compared to controls. The mean resistive index (RI), pulsatility index (PI) and mean systolic/diastolic ratio (SDR) among cases were significantly lower than controls. Certain cut-offs for PI & RI were also be calculated from the data which can be used to diagnose polycystic ovarian syndrome.
CONCLUSION:
- Intraovarian arterial Doppler ultrasonography is an effective tool in diagnosing PCOS.
- Pulsatility index, systolic/diastolic ratio and end diastolic volume are the most sensitive

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and pulsatility index is the most specific Doppler indices for the diagnosis of PCOS.

- Pulsatility index, followed by end diastolic volume were the most reliable indicators for the diagnosis of PCOS
- Cut-off values for PI and RI which were derived in this study can be used to diagnose polycystic ovarian syndrome.
- Findings from this study have demonstrated that ovarian artery Doppler examination may be utilised in conjunction with conventional endocrinological and ultrasonographic criteria to diagnose PCOS.

KEYWORDS: Intraovarian Arterial Doppler, Polycystic Ovarian Syndrome, Resistive Index, Pulsatility Index, Ovarian Volume

INTRODUCTION

Leventhal and Stein disease, often known as polycystic ovarian syndrome (PCOS), is a metabolic and endocrine illness primarily affecting women of reproductive age. According to a 2010 World Health Organization report, PCOS is a growing problem that affects more than a 100 million women worldwide. [1] The majority of European women diagnosed with PCOS are between the ages of 35 and 44.[2] **March WA et al**. conducted a study in 2010 in which Rotterdam criteria was used for the diagnosis of PCOS. It was discovered that 18% of women had the condition & that 70% had never received a diagnosis. Additionally, type 2 diabetes, inflammation, dyslipidaemia, hirsutism, menstrual problems, abdominal obesity, pelvic discomfort, anovulation, acne and dark, velvety skin patches are all more common in women with PCOS.[3] PCOS can be identified by three signs: oligo-anovulation, hyperandrogenism, and polycystic ovaries (twelve follicles having a length of 2 to 9 millimeter and/or an ovarian volume higher than 10 mL in at least one ovary). [4]

The diagnostic standards for PCOS have evolved over time. In the consensus meeting of the National Institutes of Health, the basic diagnostic standards were developed. After identifying the four primary PCOS traits several years ago, these criteria were expanded.[5] If no other cause for hyperandrogenism and chronic oligo-anovulation are found then the diagnosis of PCOS can be made. [6] Furthermore, the two existing criteria were expanded to include polycystic ovarian morphology on ultrasound for the diagnosis of PCOS.

If an ovary has an ovarian volume (OV) larger than 10 cm^3 or twelve or more follicles which measures 2 to 9 millimeters per ovary, it was deemed to be polycystic. [7]

The determination of PCOS diagnostic criteria is critical in the early diagnosis and treatment of this illness. As a result, we conducted this study to look into the ultrasound criteria of this syndrome in order to improve its diagnostic criteria and offer a cost - efficient, affordably priced diagnosis, as well as define guideline values for resistive and pulsatility indices of ovarian arteries in PCOS. These guideline values can be utilised as auxiliary Doppler guidelines for diagnosing polycystic ovary.

OBJECTIVES

1. To describe the ultrasonographic features of polycystic ovaries.
2. To assess the utility of intra-ovarian arterial Doppler study in diagnosing PCOS.
3. To compare different parameters of Doppler haemodynamics in the ovarian artery of polycystic ovarian syndrome patients with normal patients and determine the best predictor for the diagnosis of PCOS in colour Doppler study of the ovarian artery.

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MATERIALS & METHODS

Source of Data

This was a prospective case-control study conducted in the Radio-diagnosis department at RLJH & R.C, Tamaka, Kolar, following approval from the Institutional Ethical Committee. This study was conducted from December 2020 to July 2022.

After receiving clearance from the ethics committee at RLJH & R.C, Tamaka, Kolar, the study was initiated. Before the study began, all patients who met the inclusion criteria were given a pre-printed consent form after the objective, technique, and expected outcome were thoroughly explained.

Methodology

A combined total of 120 patients were taken up for the study and grouped into case and control groups. The case group included 60 individuals who exhibited two of the following three symptoms on ultrasound examination: clinical and/or bio-chemical evidence of increased androgen, oligo or anovulation and polycystic ovaries (twelve or greater follicles of 2 - 9 mm in diameter and/or ovarian volume >10 cm^3), as per "European Society of Human Reproduction and Embryology (ESHRE)/ American Society for Reproductive Medicine (ASRM)" criteria. The control group had 60 patients not having signs/symptoms of PCOS with reference to "European Society of Human Reproduction and Embryology (ESHRE)/ American Society for Reproductive Medicine (ASRM)" criteria, having a normal menstrual cycle. The inclusion and exclusion criteria are as follows: -

Inclusion Criteria

1. Patients clinically suspicious of PCOS as per "the European Society of Human Reproduction and Embryology (ESHRE)/ American Society for Reproductive Medicine (ASRM)" criteria.
2. Patients above 18 years of age.

Exclusion Criteria

1. Women on hormonal birth control.
2. Fertility treatment within 3 months prior to enrolment.
3. Pregnancy.
4. Thyroid dysfunction.
5. Presence of local uterine or adnexal conditions apart from PCOS.
6. History of tubal or ovarian surgery.
7. Patient below the age of 18

Sample Size Calculation

Dwivedi et al. reported that the specificity & sensitivity of different parameters of Doppler haemodynamics in the ovarian artery as shown in the table below.[8] Assuming an alpha error of 5 % (95 % confidence limit) and a relative precision (d) of 15 %, the minimum required sample size to estimate the sensitivity of these parameters in detecting PCOS is calculated as shown below:

Parameter	Sensitivity	Absolute Precision	Sample Size Required
OA- PSV	70	12 %	57
OA-EDV	85	10 %	49
OA-RI	82	10 %	57
OA-PI	91	10 %	32
OA-S/D	94	10 %	22

The sample size was derived from the following formula:

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Sample size (n) = Z^2 (P x Q) / d^2
Z is the value for Confidence Interval
d is the absolute precision
P is the expected sensitivity and q = 1 – p
Hence, a total sample size of 57 cases and 57 controls were to be selected for the study purpose, giving a total sample size of 114; however, we have taken 60 cases and 60 controls.

Methodology

All participants provided a complete medical history, which included information on their reproductive and menstrual histories, weight gain in the past, thyroid disease in the past, galactorrhea in the past, and any other relevant symptoms. The following measurements were taken: weight height, and body mass index. For the investigation, a PHILIPS EPIQ 5Q ultrasound machine with C5-1 & C10-3v curvi-linear & endocavitatory probes was employed. Patients were told to have a full bladder before being evaluated. Ultrasound and Doppler studies were done during the follicular phase.

Figure 1: PHILIPS EPIQ 5G Ultrasound Machine

The number of follicles with diameters ranging from 2 to 9 mm in the ovary's periphery was counted. The ovarian artery situated lateral to the ovary's superior pole was evaluated and at least 3 acceptable waveforms were acquired & used to statistically analyse the average of the three waveforms. When enough colour signal was noted, blood flow waveforms were captured by putting the sample volume and utilising the pulsed Doppler mode. The resistive index (RI), pulsatility index (PI) and other measurements was determined using calculation software.

Statistical Analysis

The data was collected and entered into a pre-designed excel spreadsheet. The Statistical Package for Social Sciences (SPSS) application for Windows, version 20, was used. Ratios, proportions, and percentages were utilised as statistical indexes. The Chi-square test and odds ratio were employed to evaluate the statistical relationship. P < 0.005 was deemed statistically significant.

RESULTS

A prospective case-control research was conducted in the Radiodiagnosis department at RLJH & R.C, Tamaka, Kolar during the course of 20 months, from December 2020 to July 2022. This study was aimed to assess the utility of intra-ovarian arterial Doppler study in diagnosing polycystic ovarian syndrome. 60 cases and 60 controls were taken for the study exceeding the required sample size which was 57 cases & 57 controls

Age wise distribution

Table 1: Age Wise Distribution of Patients			
Age Group	**Cases (%)**	**Controls(%)**	**Total (%)**
< 25	32 (53.3)	33 (55.0)	60 (50.0)
26 and above	28 (46.7)	27 (45.0)	60 (50.0)
Total	60	60	120
Mean age	26.7 ± 4.36	26.00 ± 3.85	
P value	0.349		
Odds ratio	1.374		

It can be noted from the table that most of the cases and controls were below 25 years.

Distribution of cases and controls as per BMI

Table 2: Body Mass Index			
BMI	**Cases**	**Controls**	**Total**
Underweight (<18.5)	1 (1.7)	4 (6.7)	5 (4.2)
Normal (18.5–24.9)	23 (38.3)	44 (73.3)	67 (55.8)
Overweight (≥ 25)	36 (60.0)	12 (20.0)	48 (40.0)
Pre obese(25.0-29.9)	27 (45.0)	11 (18.3)	38 (31.7)
Obese I(30.0-34.9)	7 (11.7)	1 (1.7)	8 (6.7)
Obese II(35.0-39.9)	2(3.3)	0	2 (1.7)
Total	60	60	120
Mean BMI	26.07 ± 3.61	22.89 ± 2.64	
P value	<0.001		
Odds ratio	3.5		

It can be seen from the table that 60 % of the cases and 20 % of controls were overweight. Among those who were overweight, 45 % among cases and 18.3 % among controls were pre-obese, 11.7 % in cases and 1.7 % in controls were obese I category.
The mean BMI among cases was significantly higher than those among controls.

Distribution of cases and controls as per ovarian volume

Table 3: Overall Ovarian Volume			
Ovarian Volume	**Cases (%)**	**Controls (%)**	**Total (%)**
1-9 cc	0	116 (95.0)	116 (48.3)
10- 19 cc	101 (83.3)	4 (5.0)	105 (43.8)
20 – 29 cc	15 (13.3)	0 (0)	15 (6.3)
≥30 cc	4 (3.4)	0 (0)	4 (1.7)
Total	120	120	240
Mean age	16.13 ± 4.62	7.26 ± 0.99	
P value	<0.001		

It can be noted from the table that overall, most of the cases had their ovarian follicles between 11 to 15. On the other hand, the majority of controls had 0 - 5 follicles. The mean number of ovarian follicles among cases was significantly higher than among controls.

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Table 4: Overall Number of Follicles			
Number of Follicles	**Cases (%)**	**Controls (%)**	**Total (%)**
0-5	0 (0)	115 (95.0)	115 (47.9)
6-10	0 (0)	5 (5.0)	5 (2.1)
11-15	91 (80.0)	0 (0)	91 (37.9)
16-20	29 (20.0)	0 (0)	29 (12.1)
Total	120	120	240
Mean Number	13.90 ± 2.28	4.00 ± 1.08	
P value	< 0.001		

It can be noted from the table that overall, most of the cases had their ovarian follicles between 11 to 15. On the other hand, the majority of controls had 0 - 5 follicles. The mean number of ovarian follicles among cases was significantly higher than among controls.

Table 5: PSV			
PSV	**Cases (%)**	**Controls (%)**	**Total (%)**
≤ 10 cm/s	12 (10.0)	36 (30.0)	48 (20.0)
11-20	25 (20.0)	52 (43.3)	77 (32.1)
21-30	63 (50.0)	30 (25.0)	93 (38.8)
31-40	15 (15.0)	2 (1.7)	17 (7.1)
41-50	4 (3.3)	0 (0)	4 (1.7)
≥ 51	1 (1.7)	0 (0)	1 (0.4)
Total	120	120	240
Odds ratio	7.2		
Mean	24.17± 8.13	18.97± 7.68	
P value	<0.001		

It can be noted from the table that overall, most of the cases had their PSV between 21 to 30 cm/s. On the other hand, the majority of controls had their PSV between 11 - 20 cm/s. The mean PSV among cases was significantly higher than among controls.

End-diastolic volume

Table 6: EDV			
EDV	**Cases (%)**	**Controls (%)**	**Total (%)**
<10cm/s	55 (45.8)	116 (96.7)	171 (71.2)
11-20	64 (53.4)	4 (3.3)	68 (28.3)
21-30	1 (0.8)	0 (0)	1 (0.4)
Total	120	120	240
Odds ratio	37		
Mean	11.24± 3.36	5.54 ± 1.71	
P value	<0.001		

It can be noted from the table that overall, most of the cases had their EDV between 11 to 20 cm/s. On the other hand, the majority of controls had < 10 cm/s. The mean EDV among cases was significantly higher than among controls.

Resistivity index

Table 7: RI			
RI	**Cases (%)**	**Controls (%)**	**Total (%)**
<0.40	14 (11.7)	0 (0)	14 (5.8)
0.41-0.50	47 (39.2)	3 (2.5)	50 (20.8)
0.51-0.60	34 (28.3)	18 (15.0)	52 (21.7)

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0.61-0.70	22 (18.3)	46 (38.3)	68 (28.3)
0.71-0.80	3 (2.5)	44 (36.7)	47 (19.6)
≥0.81	0 (0)	9 (7.5)	9 (3.8)
Total	120	120	240
Odds ratio	27		
Mean	0.51 ± 0.10	0.68 ± 0.08	
P value	<0.001		

It can be noted from the table that overall, most of the cases had their RI between 0.41-0.50. On the other hand, the majority of controls had 0.61 - 0.70. The mean RI among controls was significantly higher than among cases.

Resistivity index with a cut-off of 0.6

Table 8: RI <0.60 Overall			
RI	**Cases**	**Controls**	**Total**
≤0.60	95	18	113
>0.60	25	102	127
TOTAL	120	120	

It can be noted from the table that overall, most of the cases had RI < 0.60 with sensitivity, specificity, PPV, NPV of RI at 0.60 cut off was 75 %, 90 %, 88 %, and 78 %, respect

Pulsatility index

Table 9: PI - Overall			
PI	**Cases (%)**	**Controls (%)**	**Total (%)**
0.1-1.0	65 (54.2)	0 (0)	65 (27.1)
1.1-2.0	47 (39.2)	4 (3.3)	51 (21.3)
2.1-3.0	8 (6.7)	6 (5.0)	14 (5.8)
3.1-4.0	0 (0)	42 (35.0)	42 (17.5)
≥4.1	0 (0)	68 (56.7)	68 (28.3)
Total	120	120	240
Mean	1.16 ± 0.45	4.17 ± 0.84	
P value	<0.001		

It can be noted from the table that overall, most of the cases had their PI between 0.1 - 1.0. On the other hand, the majority of controls had their PI>4.1. The mean PI among controls was significantly higher than among cases.

Pulsatility index with a cut-off of 2

Table 10: PI <2 overall			
PI	**Cases**	**Controls**	**Total**
<2	112	4	116
>2	8	116	124
Total	120	120	240

It can be noted from the table that the sensitivity, specificity, PPV, NPV of PI at cut off of 2 was 93 %, 97 %, 96 %, 93 %, respectively.

Systolic/Diastolic ratio

Table 11: Systolic/ Diastolic (S/D) Ratio – Overall			
SDR	**Cases (%)**	**Controls (%)**	**Total (%)**
1.1-2.0	61 (50.8)	4 (3.3)	65 (27.0)
2.1-3.0	49 (40.8)	51 (42.5)	100 (41.6)

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3.1-4.0	8 (6.7)	41 (34.2)	49 (40.8)
>4.0	2 (1.7)	24 (20.0)	26 (10.8)
Total	120	120	240
Odds ratio	27		
Mean	2.17 ± 0.55	3.40 ± 0.98	
P value	<0.001		

It can be noted from the table that overall, most of the cases had their SDR between 1.1-2.0. On the other hand, the majority of controls had their SDR between 2.1 - 3.0. The mean SDR among controls was significantly higher than among cases.

(N=120)

Overall sensitivity & specificity of various Doppler parameters

Table 12: Different Doppler Parameter – Overall								
Doppler Indices	**Number of findings**				**Sensitivity**	**Specificity**	**Predictive value**	
	TP (a)	**FP (b)**	**FN (c)**	**TN (d)**			**Positive**	**Negative**
PSV	84	32	36	88	70 %	73 %	72 %	71 %
EDV	107	10	13	110	90 %	92 %	92 %	89 %
RI	95	18	25	102	75 %	90 %	82 %	82 %
PI	112	4	8	116	93 %	97 %	97 %	94 %
S/D	110	56	10	64	93 %	52 %	95 %	52 %

From the above table, it can be concluded that the pulsatility index is the best indicator for the diagnosis of polycystic ovaries with maximum sensitivity and specificity of 93 % & 97% respectively. EDV is also a good indicator to diagnose PCOS with a sensitivity of 90% & specificity of 92 %.

Figure 2 – Ultrasound grey-scale image showing normal ovaries

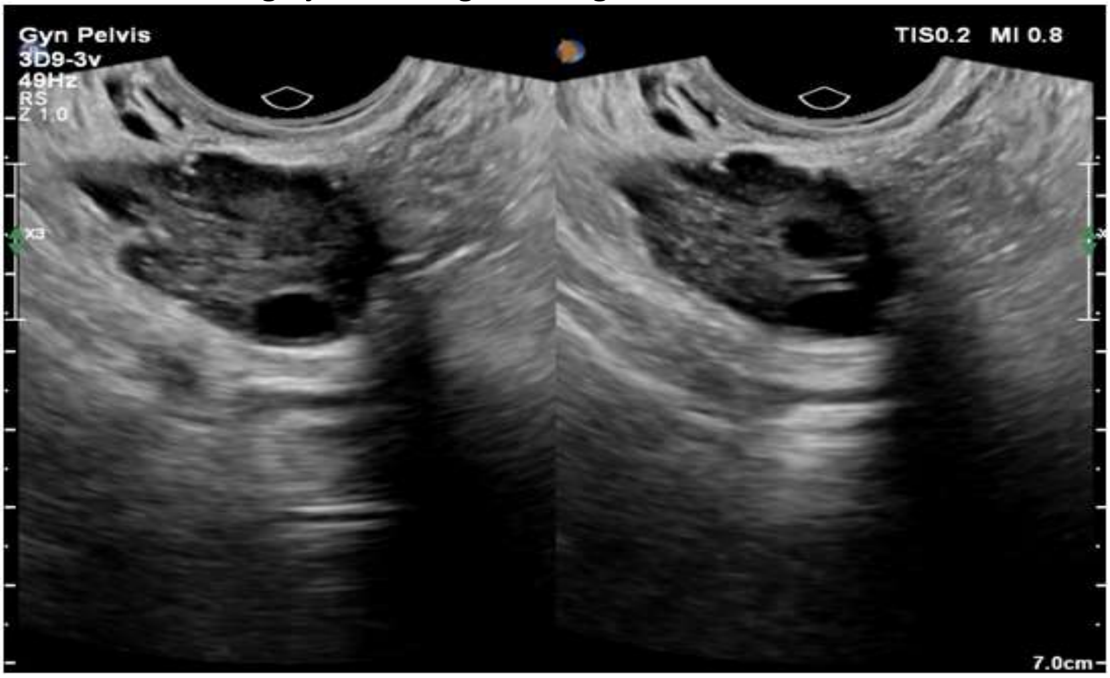

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Figure 3 – Spectral Doppler Image showing typical ovarian artery waveform

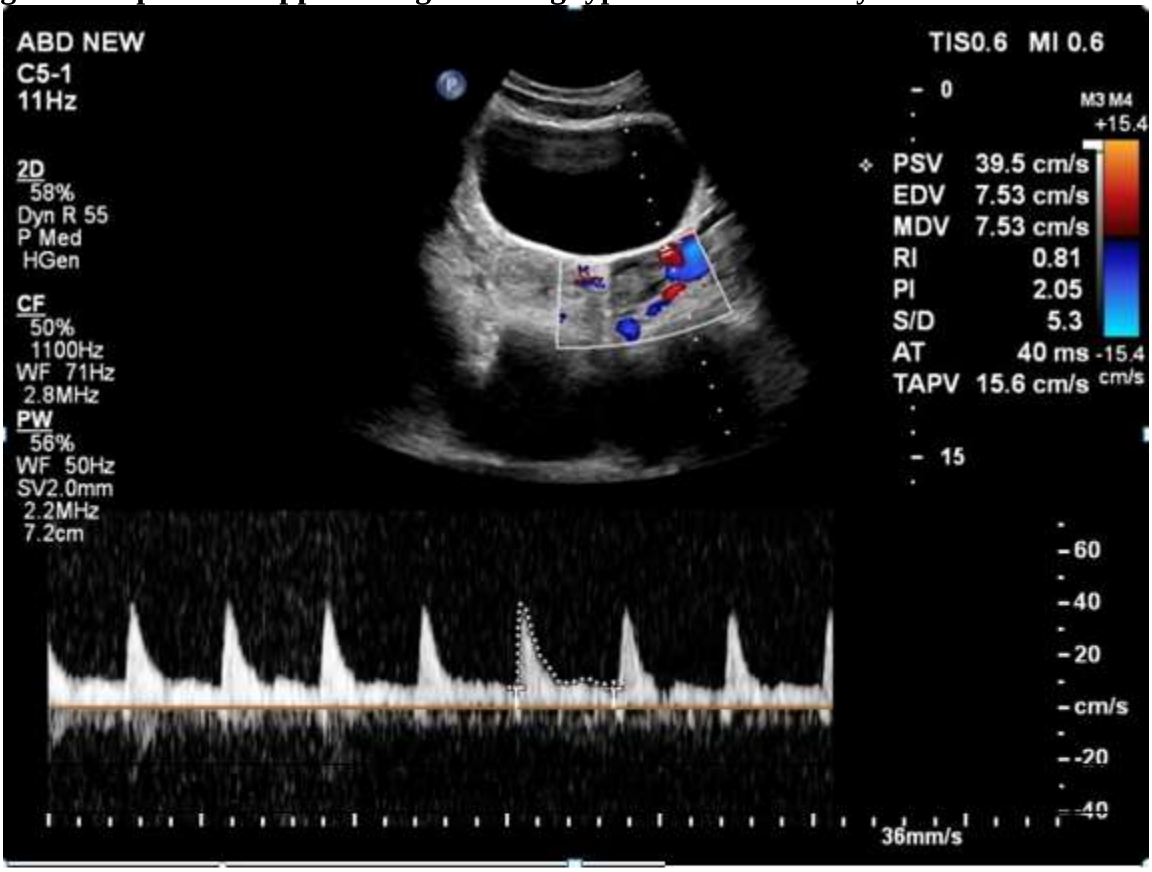

Figure 4 – Transvaginal ultrasound image showing polycystic ovarian morphology

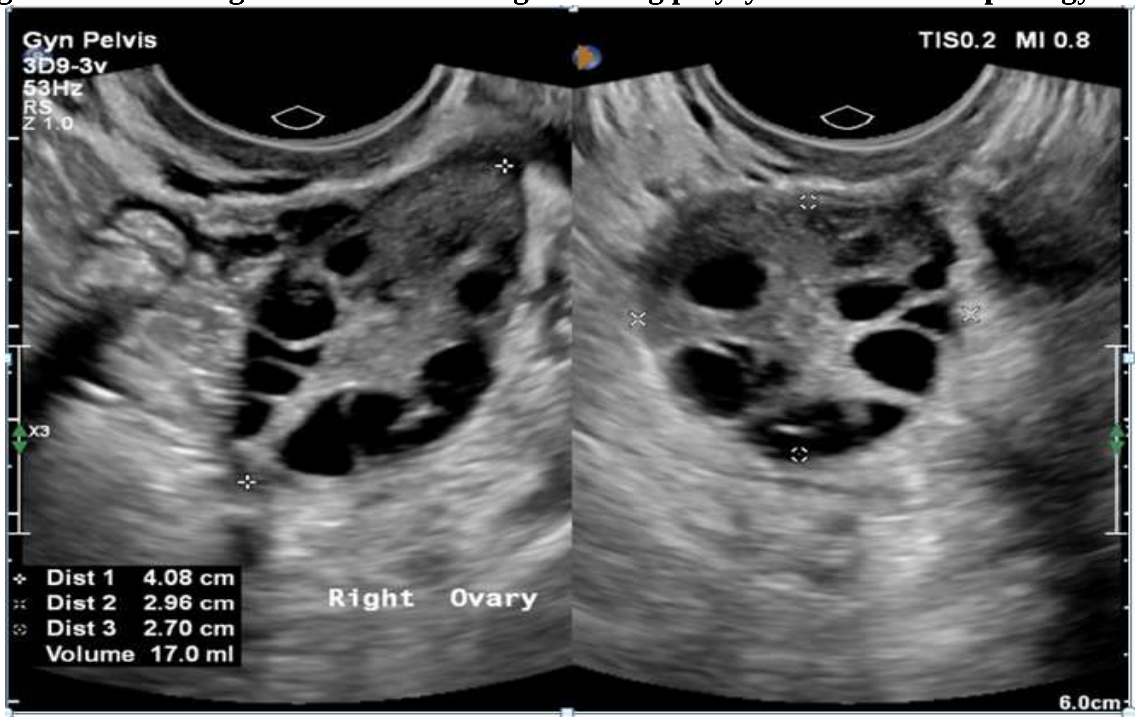

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Figure 5 – Transvaginal ultrasound image showing polycystic ovary

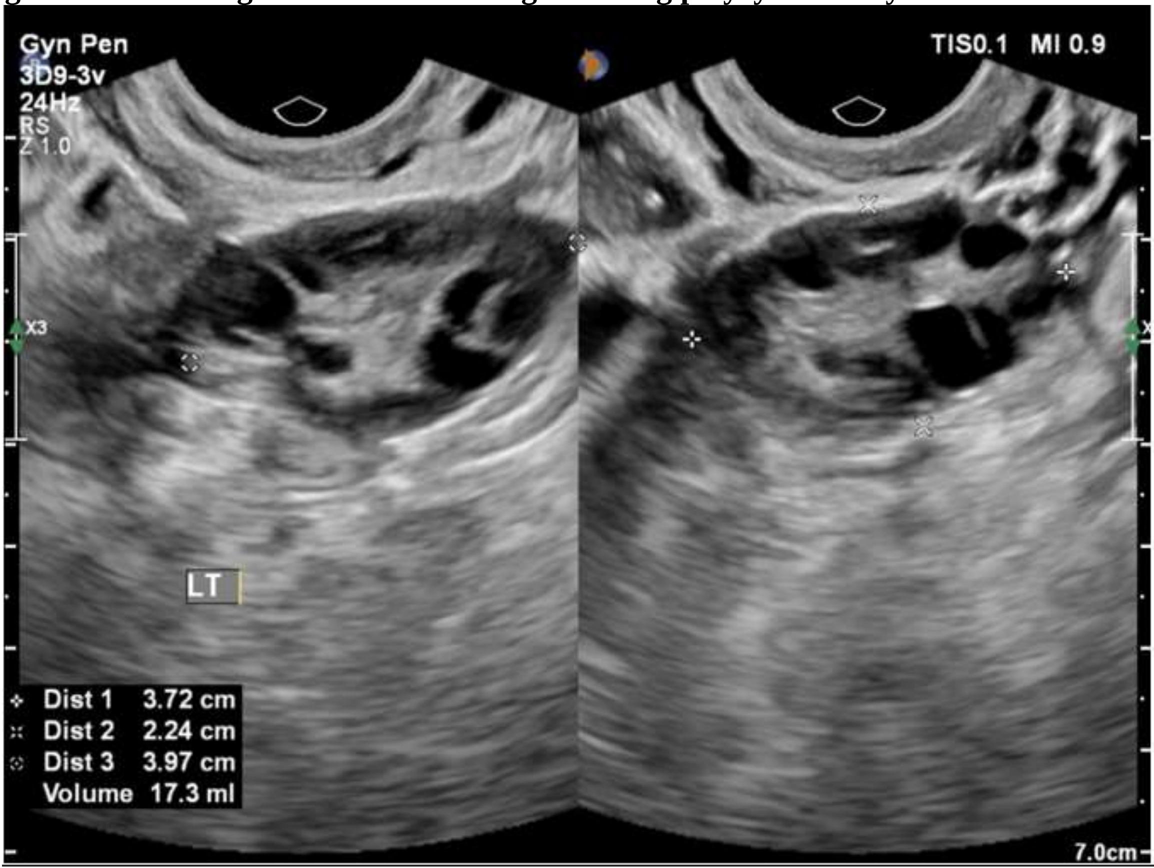

Figure 6 - Spectral Doppler image showing abnormal wave pattern in polycystic ovary with reduced RI and PI

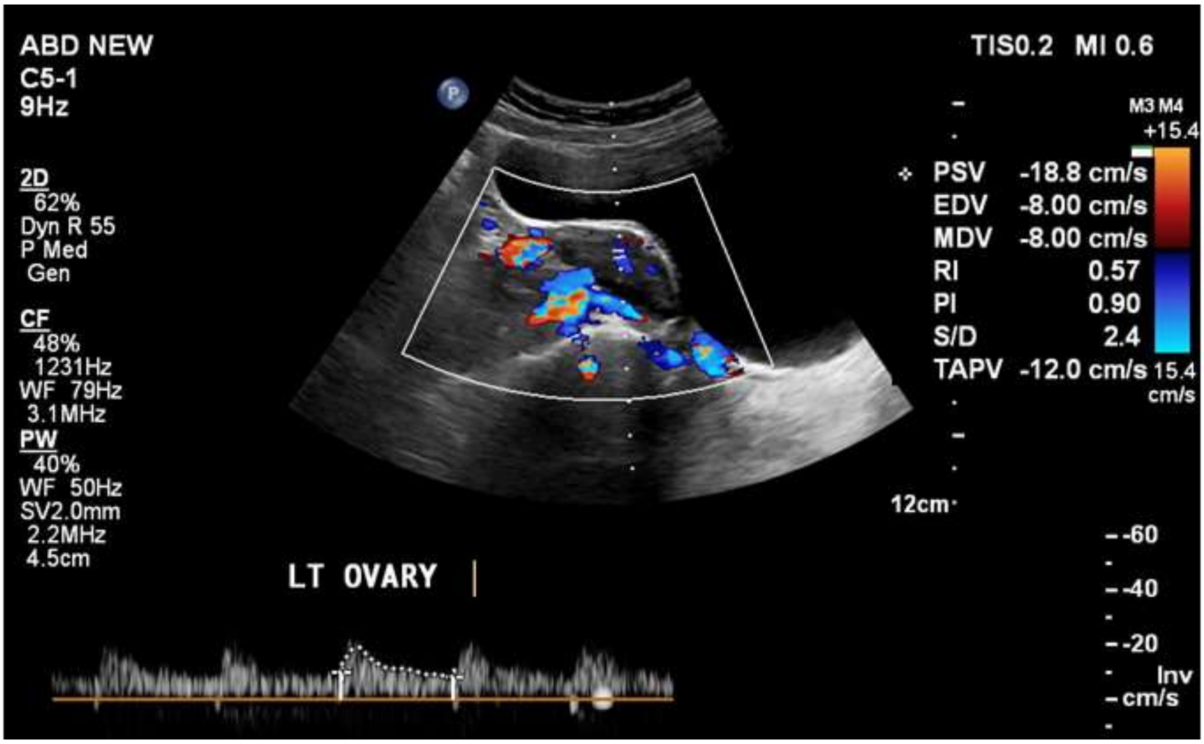

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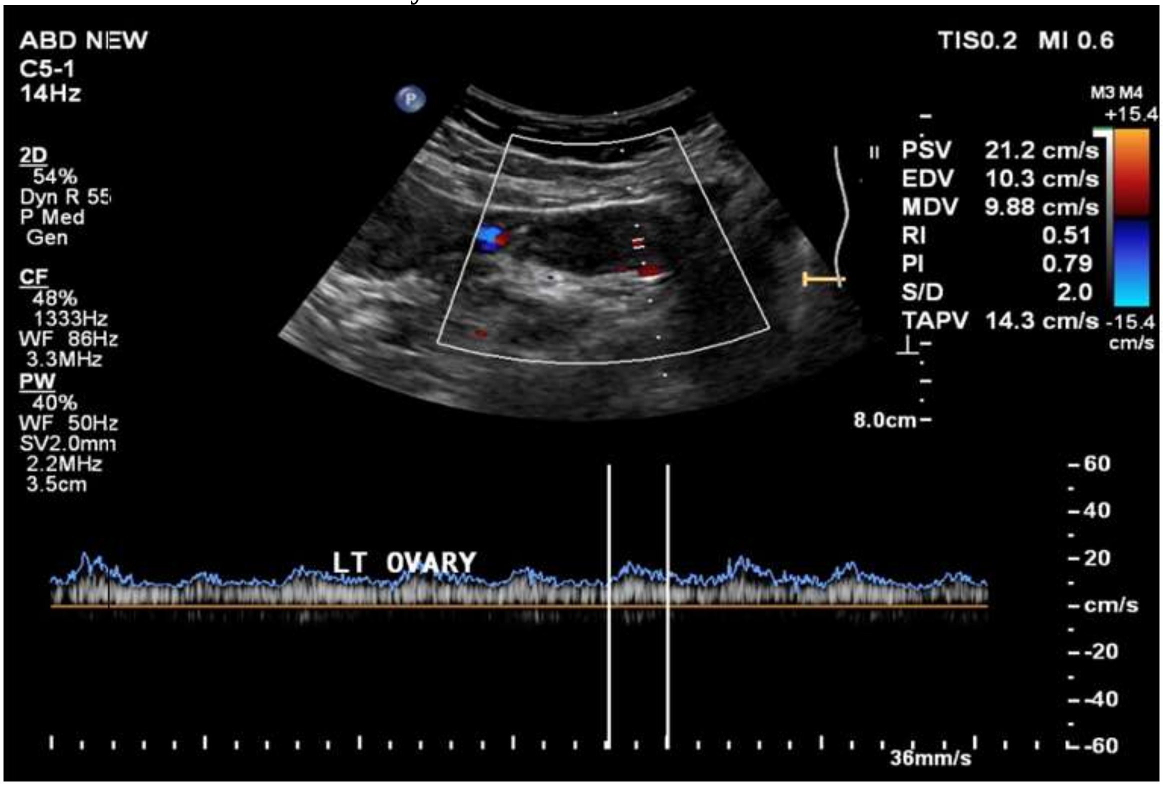
Figure 7 – Spectral Doppler image showing abnormal wave pattern in polycystic ovary with reduced RI and PI in a 27-year-old female



DISCUSSION

We began our investigation on ultrasonographic & Doppler assessment of polycystic ovaries and correlation of various Doppler indices between normal women & women suffering from PCOS as PCOS is a common endocrine illness that results in majority of infertility cases. Anovulation develops in PCOS due to the immaturity of the follicles. Typically, a few primary follicles begin to grow into secondary follicles, & one of these becomes the Graafian follicle, ovulating on the fourteenth day of menstrual cycle; however In PCOS, follicle development slows and many immature follicles are placed in the periphery of the ovary, with increased ovarian stroma. Blood flow in the ovarian stroma appears to be augmented, and vascular impedance decreases. Ultrasound is often regarded as the gold standard for the diagnosis of PCOS.[9,10] Previous studies on 3D ultrasound components of PCO have demonstrated a polycystic ovary's characteristics, such as an increased follicle count and volume of the ovary. [10,11] “Lam et al. conducted a study in 2007 with the goal of evaluating the ultrasound characteristics of ovaries in women with PCOS. For this purpose, 40 women with the disease and 40 normal women were enrolled & the results showed that follicular count, the volume of the ovary & its stroma and stromal vascularisation were increased in women with PCOS but there was no statistically significant difference in the ovarian stromal echogenicity and Doppler indices between the PCOS and control groups.” [12] “Bostanci et al. conducted a research in Turkey in 2013 to compare the ovarian stromal arteries in patients diagnosed with PCOS to patients with ultra-sonographic evidence of PCO alone, and the results suggest that the ovarian artery in the PCOS group had lower PI and RI when compared to the PCO only group.”[13] Another study published in 2014 in Taiwan by Ozdemir et al. compared intraovarian arterial blood flow of polycystic ovary syndrome patients and healthy women with polycystic ovarian image in ultrasonography and found that the Doppler

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indices in PCOS patients were significantly different from healthy women with polycystic ovarian morphology on ultrasound (p 0.05).[14] Dolz et al. published a study in 2014 that compared the ovaries of women with polycystic ovary syndrome to controls using colour and power Doppler. The results showed that women with polycystic ovary syndrome had larger ovaries and thicker stroma, increased stromal vascularity, and decreased impedance. [15]

This study's major premise is that ultrasonography is useful for detecting PCOS and that Doppler study is vital for measuring blood flow characteristics which can be used as an aid for diagnosis. In this study, the majority of the cases had their PSV between 21 to 30 cm/s, and the majority of controls had their PSV between 11 - 20cm/s. Most of the cases had their EDV between 11 to 20 cm/s, and the majority of controls had < 10cm/s. Majority of cases had their RI between 0.41-0.50. On the other hand, the majority of controls had 0.61 - 0.70. The mean RI among controls was significantly higher than among cases. Most of cases had their PI between 0.1 - 1.0. On the other hand, majority of controls had their PI>4.1. The mean PI among controls was significantly higher than among cases. Majority of cases had their SDR between 1.1-2.0. On the other hand, majority of controls had their SDR between 2.1 - 3.0. The mean SDR among controls was significantly higher than among cases, hence it can said that ovarian artery Doppler is a valuable tool which helps in distinguishing normal ovaries from polycystic ovaries. Also, it can be noted that the pulsatility index is the best indicator for the diagnosis of polycystic ovaries, with maximum sensitivity and specificity of 93 % & 97%, respectively. EDV is also a good indicator to diagnose PCOS, with a sensitivity of 90% & specificity of 92 %. Specific cut-off values can also be calculated for the diagnosis of PCOS; setting the cut-off value as <2.0 for pulsatility index gave sensitivity, specificity, PPV, NPV of 93 %, 97 %, 96 %, 93 % respectively and setting the cut-off of <0.60 for Resistivity index gave sensitivity, specificity, PPV, NPV of 75 %, 90 %, 88 %, and 78 % respectively, Hence these cut-off values can be used to diagnose PCOS.

CONCLUSION

- The following conclusions might be taken from the current study's findings.
- It is suggested that intraovarian arterial Doppler ultrasonography is an important diagnostic tool for PCOS.
- The pulsatility index, systolic/diastolic ratio and end-diastolic volume are the most sensitive Doppler indicators for diagnosing PCOS and the pulsatility index is the most specific Doppler indicator for diagnosing PCOS.
- Pulsatility index, followed by end-diastolic volume were the most reliable indicators for diagnosing PCOS.
- Cut-off values for PI and RI which were derived in this study can be used to diagnose polycystic ovarian syndrome.
- This study's findings showed that Doppler examination of ovarian arteries can be employed in addition to the usual endocrinological and ultrasonographic measures routinely used to diagnose PCOS.

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