

## Colour Doppler Sonographic Analysis of Ovarian Stromal Blood Flow Between Women with Normal Ovaries and Women with Polycystic Ovarian Syndrome

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### Abstract

The highest incidence of polycystic ovarian syndrome found in 21-25 years age group followed by 25-30 years with mean ( $\pm$ SD) of patient  $26.27 \pm 5.4$  years. The burden of obesity is more in PCOS patients than normal fertile females. PCOS patients have increased ovarian volume with majority of patients lying in range of 10-19cc. The number of follicles increases in PCOS patients with maximum patients lying in range of 11-15 and mean of 14 and 3 in PCOS patient & normal patient respectively. Increased stromal echogenicity is very sensitive and specific criteria for differentiating PCOS and normal patients. Vascularity is significantly increased in ovarian artery and stroma with reduction in resistance to blood flow in PCOS cases as compared to normal women. Setting the criteria of velocity 20cm/sec for PSV allows maximum sensitivity (80 %) and specificity (85.45 %). We recommend setting the velocity threshold of 8cm/sec for end diastolic velocity (EDV) as it gave maximum sensitivity (90.91 %) and specificity (90.91 %). For resistive index (RI), most of the patients of PCOS fell in the group of 0.51. Setting the criteria at RI 0.6 gave a decent sensitivity and specificity of 83 % and 92.73 % respectively. The pulsatility index (PI) is reduced in PCOS patients, with 49 of patients having  $PI < 2.0$  with a sensitivity of 89.09 % and specificity of 98.18 %. If the value of PI is revised to  $< 1.0$ , then the sensitivity becomes 60 % specificity becomes 98.28%. Setting the cut off value as  $< 3.0$  for systolic/diastolic velocity (S/D ratio) gave high sensitivity of 86.54 % but poor specificity of 43.64%. Thus the ovarian artery pulsatility index & systolic/diastolic ratio are the most sensitive tests. The pulsatility index is the most specific test in diagnosing polycystic ovarian syndrome. The overall best indicator is the Pulsatility index followed by end diastolic velocity.

**Keywords:** Polycystic Ovarian syndrome Pulsativity Index Resistive Index End Diastolic Velocity Color Doppler.

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### Introduction

PCOS is an abbreviation of polycystic ovary syndrome. It is an endocrine ovary disorder. The present study aims to find the relationship between color Doppler ultrasonography in normal women and PCOS women. Study has 110 patients in

total. Perform Doppler ultrasonography and evaluate the results on the gray scale. Use Doppler of the ovarian vessels to record the ovarian volume based index and follicles. There is a higher Doppler index in the

females with PCOS as compared to normal and healthy females.

### Outline:

Out of commonly existing anovulatory infertilities, PCOS (polycystic ovarian syndrome) is considered as the commonest problem. On ultrasound, it has been observed that 16 to 25 percent of normal women have this condition. This is suggestive not a diagnostic case for PCOS as considered by the specialists. The workshop on PCOS based on Rotterdam needs the specific criteria for the detection and diagnosis of polycystic ovarian syndrome. These conditions include, anovulation also known as oligo-ovulation, hyperandrogenism (clinical or any biochemical symptoms and signs), the ultrasound indicating PCOS. [1]

It has been observed that nearly half of the women suffering from polycystic ovary syndrome are obese or overweight, also as compared to normal females, they have some metabolic differences as well.[2]

The android fat distribution is characteristic of cases associated with increased insulin levels in the blood, impaired glucose level tolerance, increased androgen level production rates, decreased SHBG (abbreviation of sex hormone level binding globulins, increased or elevated level of testosterone and elevation in the level of estradiol.[3]

To determine the insulin resistant state in this disease, obesity is considered as an important factor, with the possibility that a component of resistance of insulin in the women with polycystic ovarian syndrome regardless of their obesity status. [4]

Regarding the role of transvaginal ultrasound and Doppler ultrasound, it is always significant to find out and determine the condition of female ovaries and flow of blood in uterus especially during this disease. [5]

Investigators would agree that for an organ, the pattern of flow of blood is often linked to the organ function and morphology.[5]

Color Doppler ultrasound studies have shown that polycystic ovarian syndrome patients have often shown considerable changes in the vascular functioning of ovaries especially at intraovarian artery level. Though it is very much clear and well known fact that before 8-10 of the cycle of 28 days, the intraovarian vascularization is known seen.[7]

The intraovarian vascularity in cases of PCOS is localized mainly within the hyperechogenic ovarian stroma. From the tissues of ovaries, waveforms are obtained and they exhibit the mean RI (resistance index) of 0.54 in the absence of cyclic changes between subsequent examinations. Therefore, the high resistance to flow and its maintained value with no cyclic changes are established characteristics of an-ovulatory cycles. [8]

In women with polycystic ovarian syndrome the ovarian stromal blood flow was considerably higher and it was P 0.01 and perfusion of uterus was lower and it was P 0.01. The normal women had lower ranges of these factors. The pulsatility index PI, the ovarian stromal artery was correlated inversely with the DHEAS levels. The DHEAS stands for dehydroepiandrosterone and growth factor like insulin and factor 1 and ratio of follicle stimulating hormone and luteinizing hormone. Between uterine artery PI and DHEAS levels, a positive correlation was seen. [11].

As per outcomes, the ovarian arteries PI and RI at the time of polycystic ovarian syndrome were seen decreasing with the PI and RI contrasting values of normal females especially at the follicular stage. In polycystic ovarian syndrome, hyperstimulation is undergone by stroma as a result of hyper-vascularity and vascular remodeling. The Doppler analysis is highly significant as concluded for polycystic

ovarian syndrome detection and for offering the detailed data about the diseased ovaries and their hemodynamics.[12]

With polycystic ovarian syndrome, the subjects were seen to have higher baseline values as compared to the controls for all the ovarian disease markers. It has been demonstrated with models that are univariate experience faster rate of decline in AFC and AMH. The OV changes were not different as well. No significant difference in AFC reduction was seen in the patients with PCOS as shown by adjusted models as compared to controls but in AMH the reduction was faster P 0.1 and reduction in OV was slower P.01.[13]

In Polycystic Ovarian syndrome patients, the PI and RI values were higher for uterine artery as compared to the normal ovary condition.

To the level of androstenedione, the ovarian stromal artery R1 value is seen to be related inversely, at the same time for uterine artery p1 the exchange value varies to the serum androstenedione directly to the PCOS level in the patients. [14]

In polycystic Ovarian syndrome adjustments, there is an overestimated interstitium on the basis of hyper vascularity and remodeling. The PSV is higher in PCOS patients with ovarian interstitial vessels along with higher pulsatility index PI, lower resistance RI. The uterine arteries and their PSV was lower significantly and in the same way increased values of PI and RI were seen. The polycystic ovarian syndrome is a heterogeneous disorder causing the multiple system endocrine derangements. For the detection of polycystic ovarian syndrome, the ultrasounds are significant. In the same way, we can use Doppler, small vessels and hemodynamic changes for the circulation of blood in ovaries and uterus and responsive evaluations [15].

### **Aim and Objectives**

#### **Aim**

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To assess the polycystic ovarian syndrome and ovarian stromal flow of blood pattern in females and normal, healthy women using color Doppler analysis.

#### **Objective**

**Primary objective** – To estimate the difference between total antral follicle count and total ovarian colour doppler indices of women with polycystic ovarian syndrome and women with normal ovaries.

**The secondary objective** is to estimate the correlation between age, index of body mass, count of overall antral follicles, color of Doppler in ovaries.

#### **Material and Method**

Cross sectional investigation on total of 110 females was conducted. Their reproductive age was recorded as 15-49 years. This study was conducted at Department of Gynecology, OPD section in HIMS in Safedabad, Barabanki (U.P.) for 14 months. The ovarian artery color Doppler parameter was taken through transabdominal ultrasound, and the data were analyzed by statistical methods. The patient came for ultrasonography of either the whole abdomen or the pelvis from the Department of Obstetrics and Gynaecology. Now look for ovarian stroma and ovarian volume and count the number of follicles in bilateral ovaries. If the number of follicles is > 10, the ovarian volume is > 10 cc, and the stroma is echogenic, Take the Doppler parameter of the ovarian artery. Now we have PSV (abbreviation of peak systolic velocity), EDV (abbreviation of end diastolic velocity), PI (abbreviation of the pulsatility index), RI (abbreviation of resistive index) for ovarian artery. After obtaining all the data, they compare parameters and analyze the results using the "t" test.

#### **Inclusion criteria:**

1. All newly diagnosed various cases of PCOS as per criteria of Rotterdam in Obstetrics and Gynecology department in the reproductive age group (15-49 years)
2. In ultrasonography, 12 or more follicles were present in one of the ovaries. The range of size of these follicles is 2-9 mm and ovarian volume was higher as well. (>10 cm<sup>3</sup>) (20)
3. No induction of ovulation in the current cycle and at least for one cycle before enrollment.

**Exclusion criteria:**

1. All females who were already diagnosed with polycystic ovary syndrome and were currently on hormonal treatment for the last 6 months
2. The presence of hypertension, diabetes mellitus, autoimmune disease, anemia (hemoglobin 11 g/dl), cardiovascular

disorders, or any other conditions that may affect the circulatory system

3. Presence of local uterine or adnexal conditions apart from polycystic ovarian syndrome
4. Presence of a follicular cyst >20 mm in the early follicular phase
5. History of tubal or ovarian surgery or pathology
6. Other aetiologies of anovulation, like hyperprolactinemia

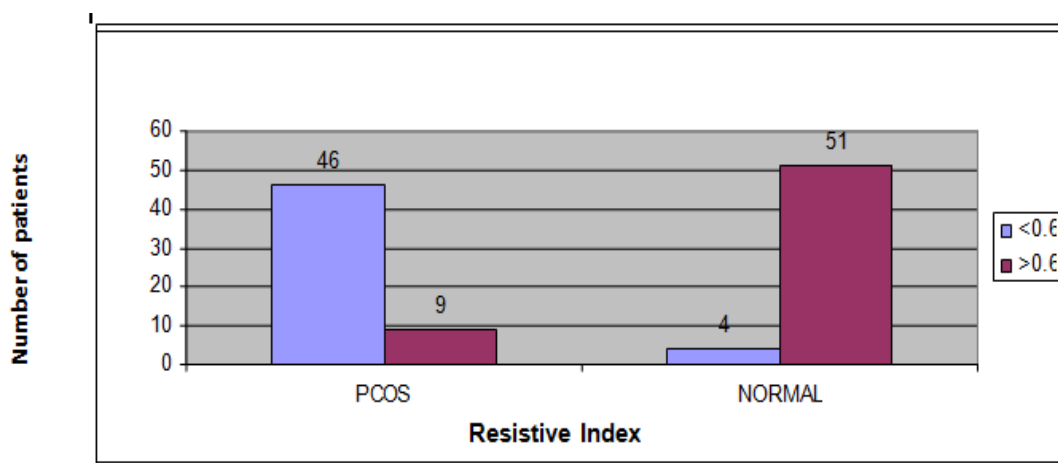
**Data compilation and analysis:**

IBMS PSS Statistics Version 26.0  
 Microsoft Excel Advanced Version Office 365 201 (16.0.13426.20274) November 23, 2020, EpiInfo (EpiInfo 3.5.4 or EpiInfo 7.1.5: www.cdc.gov/epiinfo) will be used. Operational Definitions GE Logiq F8 Expert machine was used. Acuson NX3 Elite Siemens GE Logiq V5 The probe used: a curvilinear probe with a maximum frequency of 4–7 MHz.

**Results**

**Table 1: RI Values in Different Patients**

Ri Value	PCOS	Normal
<0.6	46	4
>0.6	9	51
Mean ± Sd	0.61 ± 0.14	
Significance P Value	<0.00001 (S)	
Sensitivity	83.64	
Specificity	92.73	



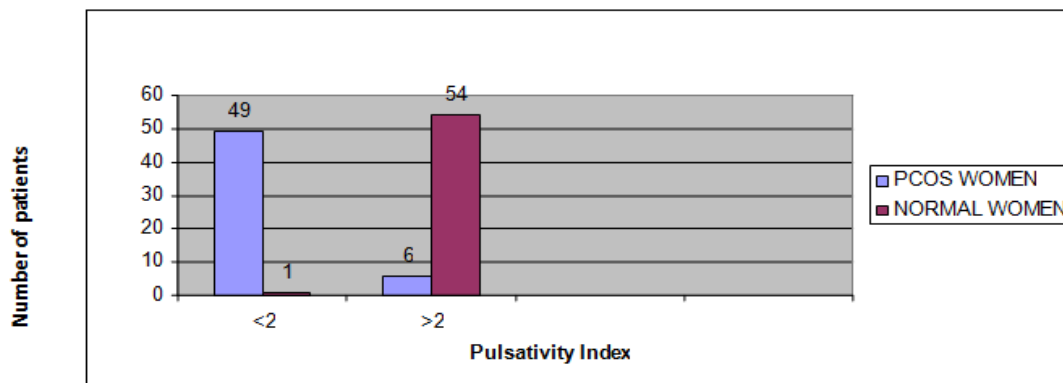
**Figure 1: Ovarian Artery Resistance Index**

Table 1 and figure 1 : RI < 0.6 in women with PCOS, RI > 0.6 in normal women .

PCOS patients had a lower resistance index (0.52) than controls (0.71). The p value is 0.0001 which is very sensitive. Setting the cutoff to 0.6 gave the best sensitivity (83.64%) and specificity (92.73%).

**Table 2: PI value in different patients**

Pi Value	PCOS Women	Normal Women
<2	49	1
>2	6	54
Mean ± Sd	2.89 ± 1.7	
Significance P Value	<0.00001 (S)	
Sensitivity	89.09	
Specificity	98.18	



**Figure 2: Ovarian artery pulsativity index**

Table 2 and Figure 2: PI values <2 in women with PCOS and PI values >2 in normal women.

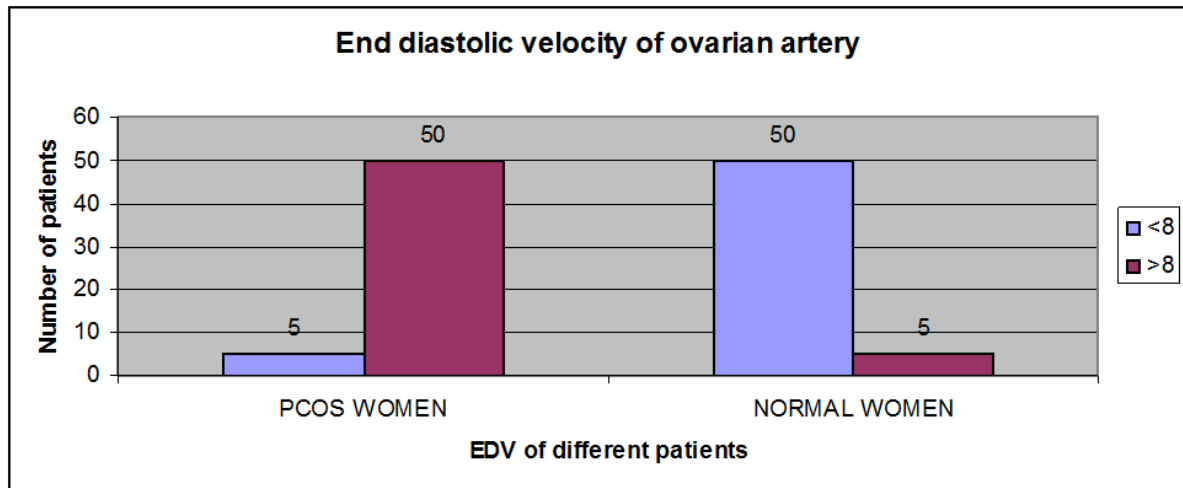
PCOS patients with a P value of 0.0001 had lower PI values than normal women. The mean PI for PCOS and normal women is 1.35 and 4.4 respectively. PI less than 2 has

a sensitivity of 89.09% and a specificity of 98.10% for the diagnosis of PCOS.

If the cut-off value is taken as less than 1 , the sensitivity drops to 60% , but the specificity and good predictive value are 98.21%.

**3: Patient ovarian end-diastolic velocity**

Edv	PCOS Women	Normal Women
<8	5	50
>8	50	5
Sensitivity	90.91	
Specificity	90.91	



**Figure 5: Ovarian Arteries End Diastolic Rate**

Table 3 and Figure 3: 05 women with PCOS with EDV <08 cm/sec and 50 with EDVs>08 cm/s were found, EDVs of normal women were mostly <8 cm/sec. The mean end-diastolic velocity was  $11.73 \pm 2.7$  cm/sec for patients versus 5.5 cm/sec for controls.

This difference is very important. If velocity>10cm/sec pattern is obtained, the sensitivity of the diagnosis of PCOS is 54.55% and the specificity is 98.18%. Setting the threshold to EDV > 8cm/sec gave the best compromise between sensitivity (90.91%) and specificity (90.91%).

### Discussion

There is an increased flow of blood in the patients with PCOS (polycystic Ovarian syndrome). In females, this disease is regarded as one of the commonest endocrinopathy and it affects 6-8 percent of females at the phase of their reproductive cycle. On the other hand, etiology of the disease is still unknown. The recent studies reveal that, PCOS prevalence has hiked in the past few years. The indices of colored Doppler ultrasound were used in this study for detection and diagnosis of PCOS. For the flow of blood determination, it is a non-invasive assessment. On the other hand, conflicting values have been shown by different studies especially for RI, PI and PCOS detection in the ovarian artery.

The glucose intolerance is also reportedly linked with polycystic ovarian syndrome. This also ends up in producing various defects in the functioning of B cells and insulin action. These kinds of defects increase substantially with obesity. Hence, we can say that obese women are at higher risk of polycystic ovarian syndrome. The condition increases with conditions like glucose intolerance [22]. In this investigation, for the women, the mean BMI was 24.33, and for normal women, it was 22.4. This concurs with a study done previously, where the mean BMI of PCOS women was 25.89 and that of normal women was 21.80 for normal women. In previous studies, the mean BMI was 24.4 for PCOS women. OVARIAN VOLUME AGE: 25.4 years was the mean age of patients selected in this investigation. In the previous studies, the mean age was recorded as 26.38 years [11]. In between 15-30 years, there was a main burden of this disease.

### Body mass Index:

In obese or overweight women, there are more reproductive disturbances. There are more irregularities of menstrual cycles and an-ovulatory infertility issues in overweight and obese women as compared to normal women. Women, in the age of reproductive phase, have higher risk of anovulatory infertility with the increase of BMI from 24 kg/m<sup>2</sup> and with increasing BMI it increases as well.

The ovarian volume increase is regarded as an essential feature for polycystic ovarian syndrome diagnosis. As per investigation conducted in the past, to define polycystic ovarian syndrome, a criterion is there to fulfil the sufficient specificity and sensitivity and it is to have one of the following, 12 to more follicles with 2-9mm diameter and increased mass of ovaries, to be specific it is more than 10 cm<sup>3</sup>. The patients in this study have higher volumes that are greater than 10.

In my study, the mean ovarian volume of PCOS women was 17.4+ 4.96 cc, and for normal women, it was 7.3 +1.9 cc. This concurs with a previous study. [11], in which he found the ovarian volume to be 16.04+ 4.18 for PCOS women and 8.28+ 1.28 for normal women.

**NUMBER OF FOLLICLES** In polycystic ovarian syndrome, the number of follicles increases and their size variations are likely to happen. On the other hand, for the minimum number of follicles, different studies have given different values as well. In this investigation,[14] was the mean follicle number in polycystic ovarian syndrome was 14.7 +2.1 and in normal or healthy females it was 4.8+ 2.4. We also took help from the study in past that 12 or higher threshold is needed to distinguish between polycystic and normal ovaries adequately. The follicles present measuring 2-9mm is an indication of PCOS with an increased ovarian mass, greater than 5.5 cm<sup>2</sup> and the volume of the ovary greater than 11 ml indicates PCOS. The specificity is 99 percent while sensitivity is 75 percent. As mentioned in the studies in past, 13.91 was the total follicles with +/-4.11 in PCOS women, where as it was 5.55 +/- 2.34 in normal women (p 0.05).

**ECHOGENIC STROMA:** In polycystic Ovarian syndrome, there is an apparent increase in stromal echogenicity and this is due to the raised ovarian stroma volume and lower echogenicity at mean value for the ovaries in the females suffering from polycystic ovarian syndrome. In the

maintenance of perifollicular flow of blood, VEGF (vascular endothelial growth factor) plays a significant role and a positive correlation has been indicated by recent evidence between the blood flow in ovarian stroma and VEGF. There is an increased flow of blood, VEGF mediate this and hence the formation of increased stroma is seen in polycystic ovarian syndrome with ultimate phenotype which is often linked to the stromal echogenicity.

As per studies conducted in the past, presence of 10 or more follicles is perhaps the most sensitive feature in the disease. 82 percent follicles in left and 69 percent follicles in right ovary. The peripheral follicular distribution was studied as well and it was recorded to be 81.8 percent for left, while 71.9 percent for right ovary. As in previous criteria, the ovarian enlargement and stromal brightness was not much sensitive but the most specific condition here was the brightness of stroma. The diagnosis of PCOS was accurately made by combining all the above mentioned criteria and the accuracy was over 86.4 percent. US based criteria for the detection of PCOS was considered to be more accurate as concluded. In the investigation being conducted here, in 98 percent of females' echogenic stroma was seen while it was only 4 percent in normal women. (p 0.00001).

**PCOS AND PEAK SYSTOLIC VELOCITY:** in the patients suffering from polycystic ovarian syndrome, the ovarian vessels are often seen engorged and as a result, the vascularity of these increases. The PSV increases as well. The overall PSV of the women suffering from polycystic ovarian syndrome was 24.5 and it was 15.4 for the normal females. As indicated in the studies conducted previously, the stromal vascularity increases and PI and RI reduces in the women suffering from polycystic ovarian syndrome. In women to be 30.7cm/sec there is a peak systolic velocity in PCOS. For PCOS, the diagnostic sensitivity was

more than 80 percent especially in the condition where PSV was higher than 20cm/sec and 85.45 percent specificity.

**PCOS & END DIASTOLIC VELOCITY:** in polycystic ovarian syndrome, the vascularity of the ovaries increased. End diastolic velocity increases out of proportion to the peak systolic velocity and as a result of it, the RI decreases and also there is a decline in PI. In the present study, for the women suffering from polycystic ovarian syndrome, the end diastolic velocity was 11.7 and when contrasted with normal females, the corresponding value was 5.5. EDV was 2.64-1.75 in normal females in previous studies. 54.5 percent was the sensitivity of diagnosis of polycystic ovarian syndrome with 98.18 percent specificity. If EDV is adjusted to be greater than 8cm/sec, sensitivity and specificity are best compromised and their respective values are 90.91 percent and 90.91 percent.

**PCOS AND RESISTIVE INDEX:** In the flow of blood in ovaries, the impedance was lesser significantly in the females suffering from polycystic ovarian syndrome. RI was lower in this group of patients. It was 0.52 in women with PCOS while in normal women it was 0.71. when the settings are cut off to 0.6, the best sensitivity is obtained and it is 83.64 percent while the specificity obtained was 92.73 percent.

**PCOS & PULSATILITY INDEX:** Inside the ovaries, it was seen that vascularity increases and it was on the color Doppler imaging and also with the help of analysis of Doppler spectrum. In the present investigation, for ovarian stroma, the PI value was lesser. In the women suffering from PCOS it was 1.35 and it was 4.4 in case of normal females. In PCOS patients, the flow of blood in stromal artery is much more as compared to the normal or healthy females. As per investigation the values obtained were (Ovarian PI, 1.40 in PCOS women and 2.90 in normal women) and another study. (9) (0.96 +.19 in PCOS women and 2.6 +.26 in normal women). For

PI the sensitivity in the PCOS detection and diagnosis was 89.09 percent and the specificity was 98.18 percent. If 1 is the value of cut off, there is a reduction in sensitivity by 60 percent while specificity was 98.21 percent.

**PCOS & SYSTOLIC/DIASTOLIC INDEX:** in the patients of PCOS, there is a decrease in the ration of S/D especially when contrasted with the same ratio in normal females. As per investigation in the past, in the S/D ration of both left and right ovaries, there was a statistically significant decrease. The previous investigations and this outcome align well in this regard. If the cut off value is adjusted to be 3.0, higher sensitivity is obtained and it is 86.54 while the specificity was poor and it was recorded to be 43.64 percent.

Sensitivity and specificity of various doppler indices- Thus, PI for ovarian artery and SR and DR are sensitive mostly, for the diagnosis of PCOS, the pulsality index is regarded as highly specific test for the PCOS diagnosis. The PI and end diastolic velocity are considered as best indicators for the PCOS diagnosis.

### Conclusion

In the age of 21 to 25, the higher incidences were reported for the polycystic ovarian syndrome. This value was followed by the next age range of 25 to 30 years; the mean SD was recorded as 26.27+ 5.4 years. The ovarian volume of PCOS patients increases. In the same way, in PCOS patients, the number of follicles increase as well with the patients in maximum range located between 11-15. The stromal echogenicity was increased and also it was considered as highly sensitive factor for various criteria in PCOS and normal people differentiation. The increase in vascularity is prominent in PCOS patients especially in the stroma and ovarian artery. The velocity was 20 cm/sec for PSV and this allows the sensitivity to be over 80 percent while specificity was (85.45%). We recommend setting the velocity threshold at 8 cm/sec for end-



diastolic velocity (EDV) as it gives maximum sensitivity (90.91%) and specificity (90.91%). For the resistive index (RI), most of the patients with PCOS fell into the group of 0.51. Setting the criteria at RI 0.6 gave a decent sensitivity and specificity of 83% and 92.73%, respectively. The pulsatility index (PI) is decreased in patients with PCOS, of which 49 had a When PI > 2.0, we record the specificity and sensitivity and values obtained were approximately, 80.9 percent sensitivity and for specificity the value was 98.18 percent. PI value if adjusted to 1.0, 60 percent is the sensitivity and 98.2 percent is the specificity. When the cut off value is adjusted as 3.0 for the S/D ratio for systolic and diastolic velocity we can get adjustments in specificity (43.64 percent) while sensitivity can be adjusted to as 86.54 percent. The index of pulsatility of ovarian artery and ratio of systolic and diastolic velocity are marked as highly sensitive tests. The best marker for this disease, PCOS is pulsatility index and this is followed by end diastolic velocity. In diagnosis of hemodynamic alteration with accuracy, these markers are considered significant.

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