

Original Research Article

## BIOCHEMICAL EVALUTION OF PATIENTS WITH POLYCYSTIC OVARIAN SYNDROME

Dr. Manojit Chatterjee<sup>1\*</sup>, Dr. Saptarshi Chakraborty<sup>2</sup>

<sup>1\*</sup> Assistant Professor, Dept. of OBG, Dept. of OBG, ICARE Institute of Medical Sciences and Research & Dr. Bidhan Chandra Roy Hospital, Haldia

<sup>2</sup> Assistant Professor, Dept. of OBG, ICARE Institute of Medical Sciences and Research & Dr. Bidhan Chandra Roy Hospital, Haldia

**\*Corresponding author:** Dr. Manojit Chatterjee

\*Assistant Professor, Dept. of OBG, Dept. of OBG, ICARE Institute of Medical Sciences and Research & Dr. Bidhan Chandra Roy Hospital, Haldia

### ABSTRACT

**Introduction:** The Polycystic ovary syndrome (PCOS) is considered as a common disturbance of sexual hormonal system. The diagnosis of PCOS is based h/o chronic anovulation, hyperandrogenism and by ultrasonography. PCOS is the major cause of female infertility which increases the risk of development of metabolic syndrome, diabetes mellitus, cardiovascular diseases and some cancer. The studies conducted in the past has proven the association between hyperinsulinemia and development of PCOD. The insulin resistance in PCOS was higher in obese women without PCOS and is a common feature of PCOS in both normal and obese women.

**Aim and Objectives:** To estimate and compare the levels of testosterone, insulin, LDL cholesterol and HbA1c in patients with and without PCOD and to estimate and compare ovarian volume in patients with and without PCOD.

**Materials and Methods:** Detailed history regarding clinical symptoms of PCOs including irregular menstrual cycles and hirsutism, signs of hyperandrogenism and a constellation of oligomenorrhea, amenorrhea, or infertility were recorded. BMI was measured by noting the weight in kgs and height in metre square. After taking informed consent all the patients were subjected to transabdominal and transvaginal ultrasound examination.

**Ultrasound investigation:** The ultrasound instrument was a Voluson E6 (a 2–5 MHz abdominal probe and a 7.5-MHz transvaginal probe, all scans were performed in a private room after getting patient consent. Ultrasound investigation was done from 3th Day to 7th of the menstrual cycle. Using abdominal probe and transvaginal probe. Each ovary was scanned and anatomic observed with respect to the utero-ovarian ligament. The parameters should include (1) volume, (2)

number of follicle (3) diameter of each ovary. Fasting 12 hours blood sample were collected from all subjects. Serum samples were subjected for analysis of free testosterone, insulin, Glycosylated hemoglobin (HbA1c) and LDL-C. Statistical analysis were performed by entering the data into Microsoft excel sheet and the comparison between the groups was performed using student t test. P value less than  $<0.05$  is considered statistically significant. Insulin resistance was calculated by using HOMA-IR formula.

**Results:** In the present study, we included a total of 200 patients based on inclusion and exclusion criteria, we divided the patients into 4 groups as discussed above. The mean weight and BMI were significantly increased in obese PCOS in comparison to normal subjects. We measured biochemical parameters HbA1c, LDL-C, free testosterone, HOMA-IR were significantly elevated in women with PCOS compared to women without PCOS. We also compared ovarian volume by performing transabdominal ultrasound, we found significantly elevated ovarian volume in patients with PCOS compared to the women without PCOS.

**Discussion and Conclusion:** Hormonal changes in combination with clinical symptoms increased the accuracy and sensitivity of ultrasound and more reliability of using biochemical in combination with ultrasound for ovarian volume and morphology in early diagnosing of subjects suspected to develop PCOS for control and management.

**Key-words:** polycystic ovarian syndrome, hyperandrogenism, ultrasound examination, free testosterone, and insulin resistnace.

## **INTRODUCTION:**

The Polycystic ovary syndrome (PCOS) is considered as a common disturbance of sexual hormonal system [1]. The diagnosis of PCOS is based h/o chronic anovulation, hyperandrogenism and by ultrasonography. PCOS is the major cause of female infertility which increases the risk of development of metabolic syndrome, diabetes mellitus, cardiovascular diseases and some cancer [3]. The studies conducted in the past has proven the association between hyperinsulinemia and development of PCOD. The insulin resistance in PCOS was higher in obese women without PCOS [5] and is a common feature of PCOS in both normal and obese women.

The diagnosis of PCOS depends on the combination of clinical and laboratory investigation of specific sexual hormones including serum luteinizing hormone, testosterone, and reduction of sex hormone binding globulin [6-9].

The study conducted by Swanson et al. reported that, the ovary of PCOS showed enlarged and rounded, with a volume of 12 cm and high number of follicles (2–8 mm) encircling the ovarian cortex. However, ovarian size showed a significant overlap between normal and PCOS ovaries and limit normal has reduced from 1.0 to 5.0 cm.

Adams et al. stated that, trans abdominal ultrasound, showed 10 or more cysts of 2–7 mm arranged around an echo dense stromal. The assessment and management of PCOS provides a good index guidelines to physician on evidence based diagnosis and management [10-14].

The present study was undertaken to estimate biochemical markers in patients with and without radiologically diagnosed PCOS.

## **AIM AND OBJECTIVES:**

- 1) To estimate and compare the levels of testosterone, insulin, LDL cholesterol and HbA1c in patients with and without PCOD.
- 2) To estimate and compare ovarian volume in patients with and without PCOD.

## **MATERIALS AND METHODS:**

This is a cross-sectional observational study conducted at our tertiary care hospital in patients attending OG OPD.

The incidence of hypothyroidism in pregnancy is higher in Asian countries, with more observed in the Indian population being attributed to nutritional as well as immunological origins. Even subclinical hypothyroidism (SCH) with high thyroid-stimulating hormone (TSH) and a normal thyroxine level is commonly associated with endocrine abnormalities in pregnancy [15-19]. Anti-thyroperoxidase (anti-TPO) antibody having the ability to cross the placenta has been suggested to affect fetal growth [20,21]. Euthyroid pregnant women with high anti-TPO antibody titers have been registered with several adversities in obstetric and fetal outcomes [22-24].

Gestational diabetes mellitus (GDM) is a frequent occurrence in the second trimester of pregnancy, with the risk being greater with increasing age [25-27]. Autoimmune diseases like insulin-dependent diabetes mellitus (IDDM), Hashimoto's thyroiditis, pernicious anemia, etc., are more common in women and occur concomitantly. An association between hypothyroidism and different types of diabetes mellitus has been reported previously [The incidence of hypothyroidism in pregnancy is higher in Asian countries, with more observed in the Indian population being attributed to nutritional as well as immunological origins. Even subclinical hypothyroidism (SCH) with high thyroid-stimulating hormone (TSH) and a normal thyroxine level is commonly associated with endocrine abnormalities in pregnancy [15-19]. Anti-thyroperoxidase (anti-TPO) antibody having the ability to cross the placenta has been suggested to affect fetal growth [20,21]. Euthyroid pregnant women with high anti-TPO antibody titers have been registered with several adversities in obstetric and fetal outcomes [22-24].

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## **MATERIALS AND METHODS:**

This cross-sectional study was conducted in the Department of Obstetrics and Gynecology, at our tertiary care hospital.

**Study design:** Cross-sectional observational study.

**Sample size:** we included a total of 200 patients with and without PCOS, in the age group 20-40 years.

We divided the patients into 4 groups,

Group A: normal healthy women with BMI 18-24 kg/m<sup>2</sup>

Group B: obese women with BMI >30 kg/m<sup>2</sup>

Group C: PCOS women with BMI 18-24 kg/m<sup>2</sup>

Group D: PCOS women with BMI >30 kg/m<sup>2</sup>

**Inclusion Criteria:** we included the patients in the age group 20-40 years with and without PCOD. Radiologically confirmed cases of PCOD and those who are willing to participate in the study.

**Exclusion Criteria:** we excluded women with pregnancy and lactation, women with OCP, women with hormone replacement therapy, and patients who were on treatment for PCOD and Infertility and patients on thyroid hormone therapy.

**Data collection:** Detailed history regarding clinical symptoms of PCOs including irregular menstrual cycles and hirsutism, signs of hyperandrogenism and a constellation of oligomenorrhea, amenorrhea, or infertility were recorded. BMI was measured by noting the weight in kgs and height in metre square. After taking informed consent all the patients were subjected to transabdominal and transvaginal ultrasound examination.

**Ultrasound investigation:** The ultrasound instrument was a Voluson E6 (a 2–5 MHz abdominal probe and a 7.5-MHz transvaginal probe, all scans were performed in a private room after getting patient consent. Ultrasound investigation was done from 3th Day to 7th of the menstrual cycle. Using abdominal probe and transvaginal probe. Each ovary was scanned and anatomic observed with respect to the utero-ovarian ligament. The parameters should include (1) volume, (2) number of follicle (3) diameter of each ovary. Fasting 12 hours blood sample were collected from all subjects. Serum samples were subjected for analysis of free testosterone, insulin, Glycosylated hemoglobin (HbA1c) and LDL-C. Statistical analysis were performed by entering the data into Microsoft excel sheet and the comparison between the groups was performed using student t test. P value less than <0.05 is considered statistically significant. Insulin resistance was calculated by using HOMA-IR formula.

## RESULTS:

We included a total of 200 patients with and without PCOS. We divided the patients into 4 groups which includes,

Group A: normal healthy women with BMI 18-24 kg/m<sup>2</sup>

Group B: obese women with BMI >30 kg/m<sup>2</sup>

Group C: PCOS women with BMI 18-24 kg/m<sup>2</sup>

Group D: PCOS women with BMI >30 kg/m<sup>2</sup>

**Table 1: Shows demographic parameters and BMI in subjects with and without PCOS**

	Non-obese		Obese		p value
	Normal ovary (n=50)	PCOS (n=50)	Normal Ovary (n=50)	PCOS (n=50)	
Weight (Kg)	78.67±7.88	69.67±6.88	108.67±9.54	100.67±10.22	S
BMI (kg/m <sup>2</sup> )	23.88±3.56	22.78±5.88	27.86±3.46	29.88±2.88	S

**Table 2: Shows the comparison of HbA1c, LDL-C, free testosterone, fasting insulin and DHFA in patients with and without PCOS**

	Patients without PCOS		Patients with PCOS	
	Group A (n=50)	Group B (n=50)	Group C (n=50)	Group D (n=50)
HbA1c	5.46±0.68	5.58±8.98	6.12±1.22	6.22±2.8
LDL-C	140.44±10.2	144.82±9.88	168.23±9.88	172.88±10.22
Free testosterone (nmol/L)	0.66±0.23	0.71±0.69	2.2±1.8	2.6±2.24
HOMA-IR	1.33±0.87	2.22±1.34	3.98±1.46	4.23±1.98

**Table 3: Shows the comparison of ovarian volume in patients with and without PCOS**

	Patients without PCOS		Patients with PCOS	
	Group A (n=50)	Group B (n=50)	Group C (n=50)	Group D (n=50)
Ovarian volume	9.2±0.22	9.12±0.36	11.6±1.32	11.69±1.41

## DISCUSSION:

Polycystic ovarian syndrome (PCOS) is an extremely common disorder affecting 4% to 12% of women of reproductive age. Despite being heterogeneous in nature, the hallmarks of the disease are hyperandrogenism and chronic anovulation. Since its description in 1935 by Stein and Leventhal much has been learned about the pathophysiology of PCOS from its neuroendocrine underpinnings to an ever-growing understanding of the link between obesity, insulin resistance (IR) and PCOS. Based on this current understanding of PCOS, it is important that the patient and medical provider approach management not only toward improving the often troublesome hirsutism and infertility but also toward the long-term risks associated with IR. Indeed, the management of the PCOS patient often will vary over time as the patient enters different stages of life with different goals. In contrast, because of the long-term health implications of IR, the importance of lifestyle modification toward weight management and maintaining adequate physical activity should be the

one constant in the management of these patients. Despite the high prevalence of PCOS, the diagnosis and differential diagnosis remains confusing. This is in part due to the lack of a specific diagnostic test for the disorder. Oftentimes the clinical history and a few laboratory tests are enough to make the diagnosis and exclude other entities that may present in much the same way. Once the diagnosis is made, the management options can seem daunting at first. This has become especially true since the link between PCOS and IR has been made (i.e., adding the issue of if/when insulin sensitizers should be used). However, if approached from the standpoint of what the patient and/or medical provider is concerned about at any given time, the options seem more manageable. In the present study, we included a total of 200 patients based on inclusion and exclusion criteria, we divided the patients into 4 groups as discussed above. The mean weight and BMI were significantly increased in obese PCOS in comparison to normal subjects. We measured biochemical parameters HbA1c, LDL-C, free testosterone, HOMA-IR were significantly elevated in women with PCOS compared to women without PCOS. We also compared ovarian volume by performing transabdominal ultrasound, we found significantly elevated ovarian volume in patients with PCOS compared to the women without PCOS.

#### **CONCLUSION:**

Hormonal changes in combination with clinical symptoms increased the accuracy and sensitivity of ultrasound and more reliability of using biochemical in combination with ultrasound for ovarian volume and morphology in early diagnosing of subjects suspected to develop PCOS for control and management.

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This cross-sectional study was conducted in the Department of Biochemistry, in collaboration with the Department of Obstetrics and Gynecology, and 382 eligible pregnant women coming for their first antenatal checkup (ANC) were enrolled in the study.

Apparently healthy pregnant women, both primigravida and multi-gravida, with singleton pregnancies in their first ANC were included and written informed consent was obtained from the enrolled cases. Pregnant women with preexisting thyroid diseases or any other endocrine disorders, pre-existing diabetes, on any hormone replacement therapy, any other metabolic or chronic disorders, and bad obstetric history with a known cause were excluded from the study.

After general and gynecological examination, fasting, one-hour, and two-hour blood samples were collected for 75 g OGTT and estimation of thyroid profile (TSH, fT4, anti-TPO antibody). The biochemical parameters were performed on the Beckman Coulter AU5A00 auto analyzer with commercially available kits. Thyroid profiles were done by the chemiluminescence method in an Siemens Advia Centaur automated Immunoassay analyzer.

For this study, the trimester-specific upper limit value for TSH was taken as <2.5 mIU/mL for the first trimester and <3 mIU/mL for the second and third trimesters as per American Thyroid Association (ATA) 2011 criteria. Patients with TSH levels higher than the trimester specific level and normal fT4 levels were diagnosed with SCH. Anti-TPO level <60 U/L was taken as normal upper limit as per manufacturer's protocol.

Level more than 60U/L is considered a raised anti-TPO titer.

GDM was diagnosed using 75 g of glucose challenge test (GCT) with a fasting value of more than 92 mg/dl, a one-hour post-glucose value of more than 180 mg/dl, and a two-hour post-glucose value of more than 153mg

**RESULTS:** This cross-sectional observational study was conducted in the Department of Obstetrics and Gynecology at our hospital. A total of 400 eligible pregnant women coming for their first antenatal checkup (ANC) were enrolled in the study