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Obesity as an Early Clinical Marker for Predicting Polycystic Ovarian Syndrome

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KEYWORDS

BMI, Polycystic Ovarian Syndrome, Obesity

ABSTRACT:

Introduction: PCOS is a heterogeneous endocrine disorder seen in women of reproductive age. It causes abnormality like polycystic ovaries, hyperandrogenism and signs of amenorrhea, oligomenorrhea, hirsutism and obesity. PCOS is significantly associated with risk factors like glucose intolerance, diabetes mellitus, hypertension, dyslipidemia and cardiovascular disease.

Aim: The aim of the study was to analyze and correlate BMI and biochemical parameters of women with PCOS and to identify the significance of BMI in early detection of PCOS among obese women.

Material & Methods: Group-I with 70 women without PCOS and Group-II comprising of 70 women with PCOS in the age group of 18-40 years were included in the present study. Blood samples from participants of both groups were assessed for biochemical parameters like FBS, T.Cholesterol, HDL and Uric acid. Anthropometric measurements such as height and weight were measured. The BMI was calculated based on the formula of weight divided by the square of height in meter. Patients with diabetes mellitus, hypertension, thyroid disorders, cardiovascular disease, Cushing's syndrome, pregnant or lactating women and women on medication for oral contraception, hypoglycemics, lipid lowering drugs, hormonal medications within previous 6 weeks were excluded from the study.

Results: The participants of the study were 100% females in the age group of 18-40 years. Among Group-I and Group-II, there was significant positive correlation of Glucose with T.Cholesterol and HDL with p-value of <0.05. And significant positive correlation of BMI with Glucose, T.Cholesterol and HDL with p-value of <0.05 and there was no significant correlation of BMI and glucose with uric acid with p-value of >0.05.

Conclusion: Obesity seen in PCOS women indicates multiple risk factors like early onset of diabetes, hypertension and cardiovascular complications. The findings of our study have indicated that there is an association of BMI with Glucose, Total cholesterol and HDL. However, the inter-relationship between BMI and biochemical parameters seen in the study indicates, overlapping and multifaceted association with PCOS. Therefore, use of cost effective parameters might prove to be risk markers in early detection of PCOS in obese women. The limitations of the study are, only few risk factors like obesity and dyslipidemia were assessed. Hence, studies with larger sample size, longer duration and follow up is essential.

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INTRODUCTION

Polycystic Ovarian Syndrome (PCOS) is the most common female endocrine disorder affecting about 5 to 10 % of women of reproductive age. PCOS results from a functional derangement rather than a specific central or local defect. PCOS is considered to be a heterogeneous disorder with multifactorial causes [1].

PCOS is characterized by increased ovarian and adrenal androgen secretion, hyperandrogenic symptoms such as hirsutism, acne and/or alopecia, menstrual irregularity and polycystic ovaries. One of the most significant discoveries regarding the pathophysiology of PCOS was the demonstration of a unique form of insulin resistance associated with Hyperinsulinemia and Impaired glucose tolerance. PCOS is diagnosed based on modified Rotterdam criteria-2003 in which PCOS may be diagnosed if any two of the following are present: (1) clinical or biochemical hyperandrogenism, (2) evidence of oligo-anovulation, (3) polycystic appearing-ovarian morphology on ultrasound, with exclusion of other relevant disorders.

With the advent of newer laboratory techniques, diagnostic modalities like sonography and routine laparoscopic evaluation, incidence of PCOS has increased drastically [3]. Women with PCOS are at higher risk of developing diabetes, hypertension, dyslipidemia, infertility, obesity and cardiovascular disease [4]. Thus the aim of the study was to analyze and correlate BMI and biochemical parameters of women with PCOS and to identify the significance of BMI in early detection of PCOS among obese women.

MATERIALS AND METHODS

This prospective comparative study was conducted in the Department of Biochemistry, SCB Medical College and Hospital, Cuttack. The current study was conducted as a thesis research for partial fulfillment of requirement for the degree of MD affiliated to the UTKAL University, Odisha. The study was conducted over a period of one year on a sample size of 140 participants divided into 2 Groups.

Group-I comprised of 70 healthy female volunteers with regular menstrual cycle and no clinical or biochemical features of hyperandrogenism, thus excluding the diagnosis of PCOS. Participants with diabetes mellitus, hypertension, thyroid disorders, cardiovascular disease, cushing's syndrome, pregnant or lactating women and women on medication for oral contraception, hypoglycemics, lipid lowering drugs, hormonal medications within previous 6 weeks were excluded from the present study.

Group-II comprised of 70 premenopausal women in the age group of 18-40 years diagnosed with PCOS in Department of Obstetrics and Gynecology, S.C.B. Medical College and Hospital, Cuttack were included in the study. Patients were selected based on modified Rotterdam criteria (2003) for diagnosis of PCOS along with their history, physical examination, biochemical investigation and ultrasound ovaries.

All the participants of the study were given a questionnaire containing details of age, medical history, menstrual history, family history of diabetes or PCOS. The study was conducted after obtaining ethical approval from the Institutional Ethical Committee. The procedure was explained and informed consent were obtained from all the participants.

Sample collection and testing

5ml of venous blood sample was collected from participants in Group-I and Group-II after overnight fasting. 2ml of blood was collected in a sodium fluoride tube and the plasma was analyzed for Fasting Blood Sugar (FBS). And 4ml of sample was collected in a plain tube and the serum was analysed for T.cholesterol, HDL and Uric acid using commercial available kits. Anthropometric measurements such as height and weight were measured. The BMI was calculated based on the formula of weight divided by the square of height in meter. Patients with diabetes mellitus, hypertension, thyroid disorders, cardiovascular disease, cushing's syndrome, pregnant or lactating women and women on medication for oral contraception, hypoglycemics, lipid lowering drugs, hormonal medications within previous 6 weeks were excluded from the study.

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The biochemical assays are done based on the principles mentioned in **Table 1**.

Table 1: Showing the various biochemical assay done and their principle in the present study

	Biochemical Assay	Principle
1	Fasting Blood Glucose	GOD-POD method
2	**LIPID PROFILE**	
	Serum Total Cholesterol	CHOD-POD method
	Serum HDL (High Density Lipoprotein)	Immunoturdibometry assay method
3	Uric acid	Uricase method

The values were expressed as Mean±Standard deviation. Deviation and the findings were analyzed by using student t-test. Pearson's correlation coefficients were calculated to assess the correlation between the biochemical parameters in the study Group-I and Group-II. A p-value of <0.05 was considered statistically significant.

Results:

The participants of the study were 100% females in the age group of 18-40 years. Among Group-I and Group-II, there was significant positive correlation of Glucose with T. Cholesterol and HDL with p-value of <0.05. And significant positive correlation of BMI with Glucose, T. Cholesterol and HDL with p-value of <0.05 and there was no significant correlation of BMI and glucose with uric acid with p-value of >0.05.

Anthropometric parameters

The mean age and its standard deviation in Group-I was 27.35±5.3 and Group-II was 29.4±4.37. The correlation of age between Group-I and Group-II the p-value obtained was 0.715 (not significant) **(Table 2).**

Table 2: Showing mean, standard deviation & p-value of age and BMI in Group-I and Group-II

PARAMETER	Group-I [n=70] Mean ± S.D	Group-II [n=70] Mean ± S.D	p-value
Age [Years]	27.35±5.3	29.4±4.37	0.715
BMI [Kg/m²]	22.16±1.88	28.17±2.47	<0.001*
<0.001- highly statistically significant			

Biochemical parameters

The comparison of biochemical parameters among participants of Group-I and Group-II results were as follows. The mean, standard deviation of Group-I and Group-II were compared and the p-value noted was **<0.001** for Glucose and HDL and **<0.0001** for T.Cholesterol. There was no significant correlation in Uric acid levels **(p=0.606)** between Group-I and Group-II **(Table 3).**

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Table 3: Showing mean, standard deviation and p-value of biochemical parameters in Group I and Group II.

PARAMETERS	Group-I [n=70] Mean ± S.D	Group-II [n=70] Mean ±S.D	p-value
Glucose (mg/dl)	85.7±9	98±15	**<0.001***
T.Cholesterol (mg/dl)	164±9.1	189±25.3	**<0.0001****
HDL (mg/dl)	46±4.9	41±5.5	**<0.001***
Uric Acid (mg/dl)	4.7±1.2	4.6±1.5	0.606
<0.001 & <0.0001 - Highly statistically significant			

In the present study, BMI was correlated with other biochemical parameters and found that the p- value of Glucose, T.Cholesterol and HDL were <0.05 whereas Uric acid showed a p-value of >0.05. **(Table 4) (Fig 1 & 2)**

Table 4: Showing correlation coefficient and p-values of BMI with biochemical parameters in patients with PCOS.

PARAMETERS	BMI (kg/m²)	
	r-value	p-value
Glucose (mg/dl)	0.181	**0.033***
T. Cholesterol(mg/dl)	0.263	**0.002****
HDL (mg/dl)	-0.195	**0.021***
Uric Acid (mg/dl)	0.129	0.12

In the present study, Glucose was correlated with other biochemical parameters and found p-value of <0.05 with T.Cholesterol whereas with HDL p-value was >0.05. Correlation of T.Cholesterol with Glucose and HDL showed p-value of <0.05 (significant) and with uric acid p-value was >0.05 (no significant correlation) **(Table 5) (Fig 3 & 4).**

Table 5: Showing correlation co-efficient and p-values of Glucose and T. Cholesterol with biochemical parameters in patients with PCOS.

PARAMETERS	**Glucose (mg/dl)**		**T. Cholesterol (mg/dl)**	
	r-value	p-value	r-value	p-value
Glucose (mg/dl)	-	-	**0.240**	**0.004****

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T. Cholesterol (mg/dl)	0.240	**0.004****	-	-
HDL (mg/dl)	-0.114	0.179	-0.176	**0.037****
Uric acid	-0.053	0.533	0.043	0.615

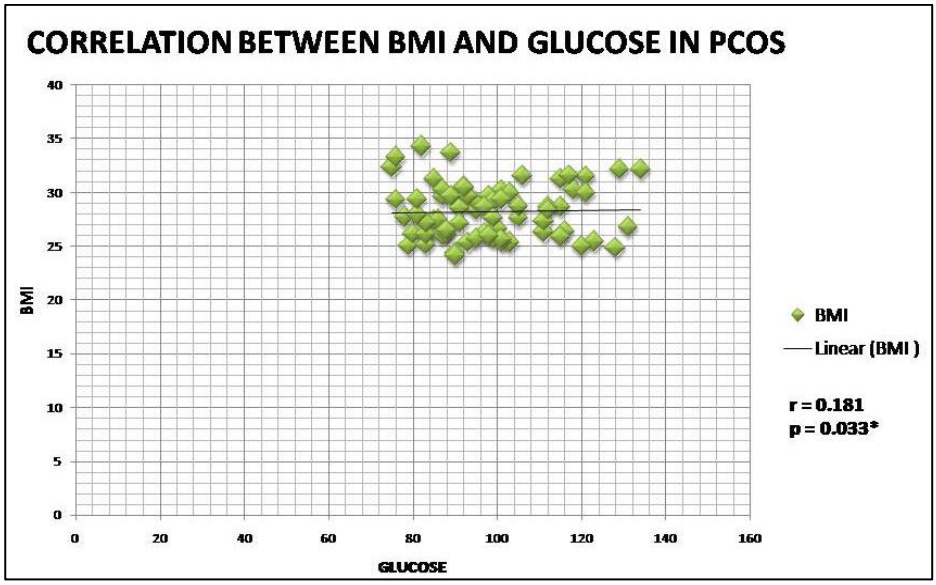

Figure 1: Linear graph showing positive correlation of BMI and Glucose in PCOS patients

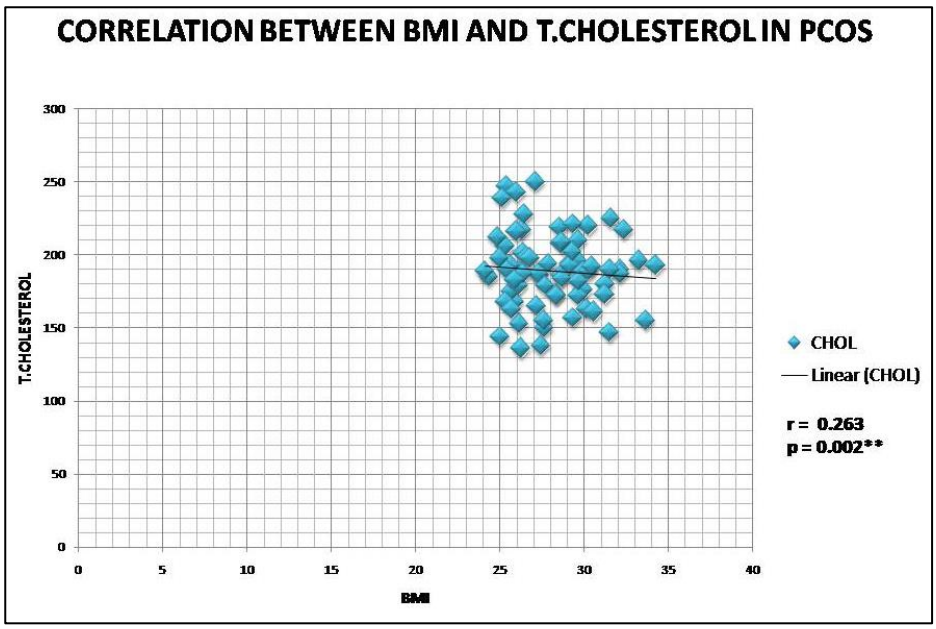

Figure 2: Linear graph showing positive correlation of BMI and T. Cholesterol in PCOS patients.

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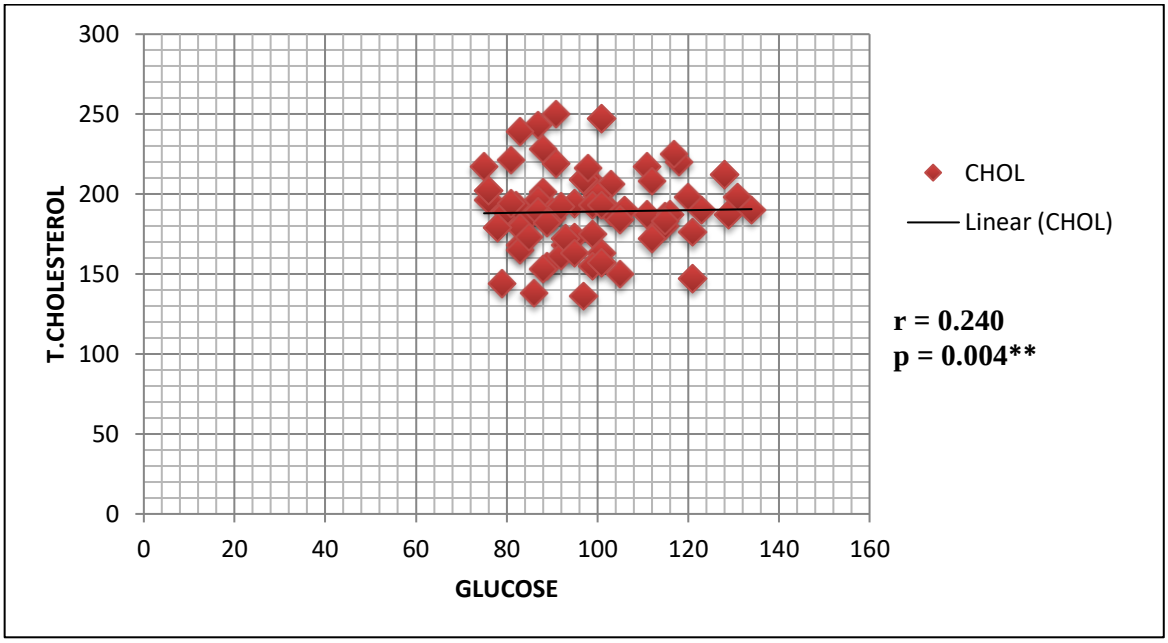

Figure 3: Linear graph showing positive correlation between T. Cholesterol and Glucose in PCOS patients

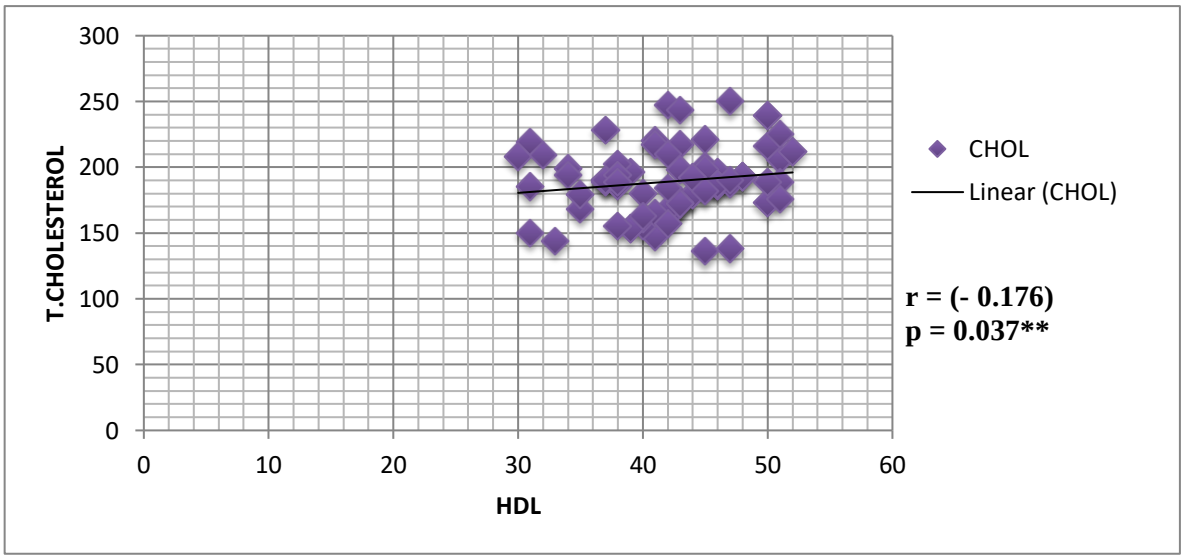

Figure 4: Linear graph showing significant negative correlation between T. Cholesterol and HDL in PCOS patients

Discussion

The most common cause of menstrual disturbance during reproductive age in females is Polycystic Ovarian Cyst (PCOS) and it is also the most prevalent endocrine disorder. In mid-18th century, multicystic or sclerocystic ovaries were recognized as pelvic pain or menorrhagia. In the early 20th century, prevailing hypotheses viewed them as resulting from inflammation due to infection, congestion due to pressure or partial torsion that disrupted normal blood flow to the ovary, or from dystrophy due to abnormalities in ovarian nutrition [5]. Irving F.Stein and Michael L. Leventhal were the

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first to describe a symptom complex associated with anovulation [6].

Women with PCOS are at higher risk of developing hypertension, lipid disorders, diabetes, osteoporosis and cancer [3]. The aim of the study was to analyze and correlate BMI and biochemical parameters of women with PCOS and to identify the significance of BMI in early detection of PCOS among obese women.

This prospective study was done on 140 subjects; 70 healthy controls without PCOS in Group-I and 70 patients diagnosed with PCOS in Group-II. Blood sample was analyzed for biochemical parameters like FBS, T.Cholesterol, HDL and Uric acid. And BMI was calculated based on the formula of weight divided by the square of height in meter. The values obtained in Group-I was compared with Group-II. The results of comparison were correlated with Pearson correlation and p-value of <0.05 was considered as statistically significant.

PCOS is diagnosed based on modified Rotterdam criteria-2003 in which PCOS may be diagnosed if any two of the following are present: (1) clinical or biochemical hyperandrogenism, (2) evidence of oligo-anovulation, (3) polycystic appearing-ovarian morphology on ultrasound, with exclusion of other relevant disorders. Thus aid in intervention and early management of PCOS [7].

The participants of this study in Group-I and Group-II were females. The mean age noted in Group-II was 29.4 years and in Group-I it was 27.35 years. However, their comparison was not statistically significant.

In the present study, FBS was used as an indirect method for detection of insulin resistance which is the most significant metabolic feature of PCOS. The plasma FBS levels were highly statistically significant in PCOS patients than healthy controls. This finding was similar to the studies of Polak AM et al 2020. However, the findings of our study contradict to findings of VM Vinodhini et al 2004 who found no statistically significant association of FBS in PCOS patients and healthy subjects. Legro et al 2005 and Talbott et al 2007 showed that the conversion rates of normal glucose tolerance to impaired glucose tolerance was higher but statistically insignificant in women with PCOS compared to healthy controls. Women with PCOS are known to show high prevalence of impaired glucose tolerance and Type-2 diabetes. The study findings showed that PCOS is associated with glucose intolerance resulting from defects in insulin action and β-cell dysfunction [9-11].

In the present study, serum lipid profile was estimated among PCOS patients and healthy controls. It was found that T.cholesterol and HDL were significantly higher in PCOS patients than healthy controls. The results of the study were consistent with findings of Olivier Valkenburg et al 2008 [12]. Abnormal lipid metabolism is one of the main metabolic characteristics of PCOS patients. Dyslipidemia is a very common metabolic abnormality in women with PCOS and obesity can alter the glucose and lipid metabolism. Decrease in HDL level is one of the characteristics biochemical finding in women with PCOS [13].

It was further noted that when glucose was correlated with total cholesterol, HDL and uric acid in PCOS patients it was found that glucose showed a significant positive correlation with total cholesterol and non-significant negative correlation with HDL and uric acid. Similarly, when total cholesterol was correlated with glucose, HDL and uric acid in PCOS patients it showed a significant positive correlation with glucose, significant negative correlation with HDL and no significant correlation with uric acid. JarosławKozakowski 2013 in their study showed significant positive correlation of Glucose with Body Weight, BMI, Total Cholesterol, Glucose and Abdominal fat [14]. However, Anuradha Kalra 2006 found no correlation between BMI with various lipid parameters [15].

Studies have shown that obese women with PCOS have 3-7-fold higher risk of developing Type-2 diabetes compared to normal controls. Obesity associated with impaired insulin signaling and certain patterns of fat deposition (eg; central or intra-abdominal obesity) are highly related to insulin resistance in PCOS. Correlation of obesity with insulin resistance in PCOS offers the potential to identify factors influencing the early development of infertility, cardiovascular risk and Type-2 DM even before the onset of disease [16,17].

In this present study, BMI levels were significantly elevated in women with PCOS than in normal controls and is similar to the study of Xioli Chen 2010 [21]. Hind Beydoun 2010 found no significant effects of PCOS or BMI on the number of mature

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oocytes fertilized per mature oocyte as well as on the odds of pregnancy, miscarriage or live birth through multiple regression analysis [22]. BMI was correlated with glucose, Total cholesterol, HDL and uric acid in PCOS patients and it was noted that BMI showed a significant positive correlation with glucose and total cholesterol,significant negative correlation with HDL and no significant correlation with uric acid. Elevated levels of FBS, insulin, lipid parameters with decreased levels of HDL were also noted in studies by Douchi 1995 [23]. Interestingly, Pergialiotis 2018 showed that PCOS women with mild elevation of cholesterol have a higher BMI, fasting insulin levels and insulin resistance when compared to PCOS women with normal cholesterol [24]. The risk for developing glucose intolerance increases with increasing body mass index (BMI); the prevalence of impaired glucose tolerance and Type-2 diabetes were much lower in non-obese women with PCOS (10.3% and 1.5% respectively) compared to obese and the overall population [25]. It appears to be 3 to 7 fold higher in women with polycystic ovary syndrome (PCOS) compared with the normal female population [17,25]. Though in the present study, waist circumference was not recorded, Baillargeon et al 2008 in his study showed positive significant correlation between BMI and waist circumference in PCOS cases [26]. Women with PCOS have a higher prevalence of upper body obesity which causes increased waist circumference. This is related to high exposure to testosterone levels in women with PCOS [27].

Uric acid is the metabolic end product of purine metabolism. In the present study, the levels of serum uric acid were not significant in PCOS women and healthy controls and is similar to the findings of Antilla 1996 [18]. However, this finding was in contrast to the findings of Fouzi 2017 who found that serum uric acid was significantly increased in women with PCOS suggesting that androgens may increase the metabolic purines [19]. Studies showed inverse correlation between serum uric acid concentration and insulin sensitivity in patients with metabolic syndrome and concluded that hyperuricaemia is an inherent biochemical feature of metabolic syndrome. Vuorinen Markkola & Yki Jarvinen 1995 suggested hyperuricaemia to be a simple marker of insulin resistance thus associated with increased mortality and morbidity due to coronary artery diseases [20].

Conclusion

Obesity seen in PCOS women indicates multiple risk factors like early onset of diabetes and cardiovascular complications. Obesity in turn can exacerbate the symptoms of PCOS such as further metabolic issues and reproductive abnormalities. The findings of our study have indicated that there is an association of BMI with Glucose, Total Cholesterol and HDL. However, the inter-relationship between BMI and biochemical parameters seen in this study indicates overlapping and multifaceted association with PCOS. Therefore, use of cost-effective parameters prove to be the risk marker in early detection of PCOS in obese women. The limitations of the study are, only few risk factors like obesity and dyslipidemia were assessed. Hence, studies with larger sample size, longer duration and follow up is essential.

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