Role of BMI in PCOS Towards Cardiovascular Risk Factors

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Abstract

Background: Polycystic ovary syndrome (PCOS) is a prevalent disorder in which blood markers of cardiac disorders have been frequently established. However, the impact of obesity on PCOS is still to be discovered. This study was designed to determine if cardiac disorder in PCOS women may explain by altered BMI and biochemical parameters.

Methods: A prospective study was carried out by having 100 samples of obese (50) and non-obese (50) PCOS patients. Blood samples (<5ml) were collected, statistical analysis and correlation of BMI were done with hormonal and lipid profile.

Results: On Pearson correlation analysis of BMI with lipid and hormonal profile, cholesterol showed a positive correlation in obese PCOS. Spearman correlation analysis of BMI showed positive significant correlation with testosterone in non-obese PCOS. Obese and non-obese groups were further subdivided into married (obese, non-obese), unmarried (obese and non-obese) groups. Negative correlation with LH in married obese, while none of the significant results had been found in married non-obese. In the case of unmarried obese, testosterone showed negative and estradiol showed a positive correlation in unmarried non-obese.

Conclusions: The data from this study concluded that young PCOS women have evidence for altered endocrine functions along with elevated BMI. Furthermore correlation of BMI and testosterone might be one of the major factors of developing adiposity and infertility that further causes cardiac diseases. Lifestyle modifications are also beneficial for lessen the ovarian cysts and promote fertility in pubertal females. However, the evidence is limited and more investigations are still needed.

1: Introduction:

Polycystic ovary syndrome is a metabolic and endocrine multifactorial as well as congenital disorder stimulated by the environmental factors. The diagnosis of this disease is menstrual irregularities, hyperandrogenism, abdominal adiposity [1, 2]. [3, 4]. [1, 5], obesity [5], hirsutism, acne, and alopecia due to high circulating levels of androgens, anovulatory cycle and obesity [6–9] but its exact pathogenicity is still to be investigated. Environmental factors such as weight loss and obesity orientation are also the risk factor of PCOS that affects the female's prenatal and postnatal life. [10, 11].

Stein-Leventhal syndrome which is now being recognized as (PCOS) Polycystic Ovarian Syndrome is the most frequently developing endocrine women syndrome. According to the National Institute of Health (NIH), this syndrome has been testified to be 6.5–6.8% among the reproductive-aged females. [12–14]. About 30–70% of PCOS women are obese, although PCOS also exists in normal BMI females but in lesser ratio. World Health Organization (WHO) and the National Institute of Health (NIH) have defined standard criteria of BMI for underweight, normal weight and overweight. Further studies show that BMI is correlated with hirsutism and obesity while FSH is associated with obesity and infertility [15].

Obesity is a chronic state of accumulated body fat. From the last few years, the fertility issues in the obese population have become a threatening fecundity (subfertility and infertility) concern [16{Bolúmar, 2000 #160, 17–20}] resulting in oligoovulation or anovulation. Some investigations illustrated that obese women are more exposed to longer ovarian stimulation problems and have more gonadotropin ampoules requirement[21]with a decreased number of oocytes[21–23].

Higher mortality and morbidity rate is very common in a Western population due to the association of obesity with diabetes and cardiovascular disorders; moreover, obesity is also a risk factor towards gynecological and obstetrical issues [24]; [25–32]. Moreover, lipid abnormalities are the leading cause of atherosclerosis and cardiovascular disorder in PCOS as compare to the healthy female [33] [34] and this abnormality may affect 60–80% of PCOS females and 95% of obese women with this syndrome [35, 36].

PCOS is a chronic condition from the pubertal stage [37–40] and is characterized by baldness, enlargement of the ovary, infertility, central obesity that gives roots to cardiovascular disorders and type 2 diabetes [37, 38, 41, 42]. Lipid profile (cholesterol, triglycerides, LDL, HDL) fluctuations frequently occur in female PCOS that leads to a cardiovascular risk factor. Premature atherosclerosis may occur if remain untreated [42],[43]. The last few decades of investigation illustrated the susceptibility of PCOS females towards CVDS with elevated insulin resistance, hypertension, triglycerides, and LDL and decreased HDL [39, 44–48]. Therefore we conducted this study in polycystic ovary syndrome (PCOS) females and assessed the effects of isolated BMI in them by hormonal and biochemical analysis along with their correlation.

2: Materials And Methods

100 samples of non-pregnant PCOS patients were enrolled in our prospective cohort study during September 2018- February 2019, out of which 50 were obese and 50 were non-obese PCOS with age ranging 18–35. Each patient had provided written consent performa before participating in the study, which was approved by the Ethical Committee of the Zoology, department of Women University Multan, Pakistan.

According to the exclusion and inclusion selection criteria (pregnancy was excluded while acne, obesity, hirsutism, oligomenorrhea, amenorrhea were included), PCOS volunteers were included in this study. The height and weight of each patient were obtained to calculate the BMI immediately before drawing the blood. With respect to BMI, Patients were categorized as follows: underweight ($BMI < 18.5 \text{ kg/m}^2$), normal weight ($18.5 \leq BMI < 24 \text{ kg/m}^2$), overweight ($24 \leq BMI < 28 \text{ kg/m}^2$), and obese ($BMI \geq 28 \text{ kg/m}^2$). The study protocol was started with the venipuncture of 3 ml blood drawn by each patient and dispensed into the red top vial (plain). After centrifugation, blood serum had been stored at -20°C .

All samples were consecutively processed for hormonal and lipid profile analysis. Cholesterol, triglycerides, low-density lipoprotein (LDL), high-density lipoprotein (HDL), luteinizing hormone (LH), follicle-stimulating hormone (FSH), estradiol, testosterone, and progesterone parameters were measured by Selectra junior (Kinetic techniques), Cobas and vitros (Chemiluminescence techniques). Mean $\pm$ SD

range and the ratios of lipid and hormonal profile was calculated on the word excel file while testosterone was measured by radioimmunoassay (RIA) [49].

To compare the variables, statistical analysis was assessed by students t' test. Correlation of BMI with hormonal and lipid profile was done by Pearson (parameters which have normal distribution) and Spearmen correlation (for non-normal distribution) analysis on. The significance level was set at $P < 0.05$.

3: Results:

50 obese and 50 non-obese PCOS were recruited in our study with 18–35 years old females. The mean $\pm$ SD value of biochemical and hormonal profile parameters is mentioned in table no.1. Statistical analysis (student's t-test) has proved no significant results in obese vs. non-obese.

Table 1

Comprehensive Results of lipid and hormonal profile of PCOS (obese, non-obese married obese and non-obese)

Parameters	Overall		Group:1 Married		Group:2 Unmarried	
(lipid & hormonal profile)	Obese	non-obese	1a: obese	1b: non obese	2a: obese	2b: non-obese
BMI	30.03 ± 4.40	21.45 ± 3.58	30.51 ± 4.59	21.14 ± 3.39	27.86 ± 3.58	20.82 ± 2.04
Cholesterol	188.38 ± 58.56	193.84 ± 57.44	190.4 ± 59.63	197.74 ± 54.00	181.64 ± 56.79	172 ± 85.92
Triglycerides	170.68 ± 67.27	168.10 ± 73.58	176.26 ± 69.43	178.42 ± 71.74	142.73 ± 61.55	104.24 ± 56.22
LDL	161. 68 ± 63.84	106.51 ± 44.04	159.56 ± 105.85	111.06 ± 43.65	91.73 ± 43.73	85 ± 37.11
HDL	34.41 ± 22.14	70.31 ± 31.80	34.55 ± 14.70	73.20 ± 32.42	73.37 ± 35.40	56.4 ± 20.50
Cho/HDL	7.77 ± 9.46	3.36 ± 1.89	6.22 ± 2.85	3.33 ± 1.96	3.14 ± 2.18	3.21 ± 1.44
Tg/HDL	6.98 ± 9.37	2.90 ± 2.01	5.93 ± 3.46	3.01 ± 2.11	2.37 ± 1.61	2.01 ± 1.04
HDL/LDL	0.25 ± 0.16	0.78 ± 0.48	0.29 ± 0.19	0.78 ± 0.50	1.22 ± 1.46	0.74 ± 0.41
LH	15.20 ± 2.58	15.82 ± 2.86	15.28 ± 2.60	15.75 ± 3.06	15.25 ± 2.59	13.43 ± 6.38
FSH	6.29 ± 1.12	6.17 ± 1.22	6.40 ± 1.21	6.11 ± 1.22	5.91 ± 0.85	13.52 ± 15.39
Estradiol	115.01 ± 88.0	150.14 ± 126.07	126.35 ± 92.16	154.09 ± 127.38	78.38 ± 62.92	128.30 ± 140.02
Testosterone	43.68 ± 44.64	41.33 ± 47.73	35.56 ± 36.25	36.34 ± 41.93	76.41 ± 60.35	72.40 ± 80.56
Progesterone	1.37 ± 2.16	2.11 ± 3.79	1.51 ± 2.43	2.08 ± 3.84	0.82 ± 0.18	2.57 ± 4.17
LH/FSH	2.48 ± 0.59	2. 64 ± 0.62	2.46 ± 0.59	2.64 ± 0.60	2.63 ± 0.63	2.11 ± 1.38

biochemical parameters (lipid, hormonal profile and their ratios) and non-obese PCOS Pearson correlation showed positive correlation with (p = 0.03, r = 0.297) in obese (Figure:1) whereas on applying spearman correlation, only testosterone (p = 0.04, r = 0.3) showed correlation with BMI in non-obese PCOS, (Figure:2).

PCOS was further divided into two main subgroups i.e., group:1 married PCOS and group: 2 unmarried PCOS which were then further categorized into 1a: married obese PCOS and 1b: married non-obese PCOS, 2a: unmarried obese PCOS, 2b: unmarried non-obese PCOS.

On applying Spearman correlation analysis, none of the correlation had been recorded between BMI and lipid, hormonal profile in group 1b (married non-obese) but in case of group 1a (married obese), BMI showed a negative correlation with LH ($p = 0.04$, $r = -0.32$) as shown in figure:3.

In case of groups 2a (unmarried obese) and 2b (unmarried non-obese), BMI showed negative correlation with testosterone in unmarried obese ($p = 0.02$, $r = -0.655$) (figure:4) while strong positive correlation with estradiol had been recorded in unmarried non-obese ($p = 0.03$, $r = 0.90$) (figure:5).

Table 2
Spearman correlation of BMI with lipid & hormonal Profile (P Value Summary)

Parameters (lipid & hormonal profile)	Overall		Group:1 Married		Group:2 Un – married	
	Obese	non-Obese	1a: Obese	1b: non-Obese	2a: Obese	2b: non-Obese
Cholesterol	0.737	0.799	0.676	0.794	0.658	0.624
Triglycerides	0.619	0.908	0.972	0.765	0.179	0.624
LDL	0.71	0.325	0.75	0.394	0.989	0.285
HDL	0.64	0.844	0.89	0.613	0.669	0.285
Cho/HDL	0.76	0.685	0.35	0.840	0.709	0.873
Tg/HDL	0.92	0.503	0.91	0.927	0.384	0.624
HDL/LDL	0.99	0.749	0.93	0.335	0.729	0.391
LH	0.08	0.583	$p = 0.04^*$, $r = -0.3$	0.610	0.572	0.873
FSH	0.952	0.389	0.653	0.527	0.232	0.747
Estradiol	0.374	0.246	0.146	0.385	0.989	$p = 0.03^*$, $r = 0.9$
Testosterone	0.309	$p = 0.04^*$, $r = 0.3$	0.996	0.330	$p = 0.02^*$, $r = -0.6$	0.104
Progesterone	0.652	0.893	0.344	0.995	0.606	0.870
LH/FSH	0.197	0.279	0.08	0.294	0.527	0.747
(P-value represents significance from Pearson correlation statistical analysis)						
*correlation is Significant at the < 0.05 level(2tailed).						

4: Discussion:

The Polycystic ovarian syndrome is a metabolic gynecological endocrine disorder and about 4–7% of premenopausal females are suffering from this syndrome [12, 13, 41, 50]. 60–80% of patients have a complaint of hyperandrogenism and are obese [4, 37]. Ratajczak *et al.*, 2016 [51] elaborated in his study that PCOS may or may not be congenital. Post-term births are also a major factor in developing PCOS. Despite the mother's BMI, elevated daughter's BMI can be a major risk factor of PCOS.

PCOS is symptomized by the cluster of risk factors e.g., waist to hip ratio, obesity, increased BMI, diabetes and insulin resistance, higher blood pressure with disturbed lipid profile [52–55],[56–58]. In the present study, BMI correlates with a potential marker for developing cardiovascular risk factors (CVDs) in obese and non-obese PCOS patients. Our study investigates that BMI has a strong relation with CVDs in PCOS females similar several recent investigations that have strongly proved the correlation of BMI, weight, waist with cardiovascular diseases (atherosclerosis) similar to Talbott [59]. Potential association of CVDs and PCOS is basically obesity[34] [57, 58, 60, 61].

Deepthi et al.,(group 2004) illustrated strong evidence of developing cardiac diseases in PCOS by the analyses of various biochemical parameters from the serum i.e., lipid profiles (cholesterol), blood sugar and hormones such as Follicle Stimulating Hormone (FSH) and Luteinizing Hormone (LH) and suggested a controlled diet and lifestyle modification (increasing physical exercise) to lessen the risk of CVDs[34].

However, insulin, hormonal disruption (irregular testosterone), and BMI attenuated the relationship of PCOS and CVDs in the pubertal aged PCOS female (18–35 years old) that may be driven by hyperinsulinemia and obesity. While insulin accelerates the transport of cholesterol into the arteries by proliferating the cells [62].

Students't test was applied to our present study groups. BMI was correlated with lipid and hormonal profile along with their ratios in all the above-said groups. Lipid levels of obese PCOS were more statistically significant as compared to non-obese. According to the [63, 64] BMI correlates with the lipid profile that is accordance with our present investigation. BMI correlation is further married and unmarried (obese and non-obese) were also reported in our study while higher means of BMI and WHR were reported by [63].

Due to lipid abnormalities and insulin resistance in PCOS females, susceptibility of atherosclerosis and cardiovascular diseases are more as compared to the healthy ones [65], these abnormalities may affect 60–80% of PCOS and, 95% of obese PCOS [35, 36].

As [66, 67] could not found any statistical significance between FSH and BMI, likewise our study also does not show a correlation of BMI with FSH in any of the above-mentioned groups. Moreover, BMI did not correlate with the LH/FSH ratio in any of the groups similar to [68]. Our respective study shows BMI-LH negative correlation in the married obese groups as compare to Lefebvre [69, 70]. Testosterone showed a positive and negative correlation with BMI in non-obese and unmarried obese groups

respectively while the majority of the studies do not show testosterone-BMI correlation anywhere. According to our findings in the unmarried non-obese group, BMI shows a correlation with estradiol which is controversial to Mendonca [66].

Conclusions:

The worth of this present investigation includes PCOS of younger pubertal aged women before menopause from risk factor analysis to disease assessments. These pubertal females present an extremely unique group to diagnose and monitor disease prognosis. In clinical practice, PCOS females have menstrual irregularities, obesity, accelerated BMI, hormonal imbalance, and sterility complaints. Immediate cure for such complaints is targeted traditionally. No further treatments are needed after taking the immediate action of complaints. The conclusion of such study is the excess BMI, lipid (cholesterol) and hormonal imbalance (especially the testosterone) of obese and lean PCOS that might be elaborated by the identified traditional risk factors. Correlation of BMI and testosterone might be one of the major factors of developing adiposity and infertility that further causes cardiac diseases. Elevated BMI, more weight, less physical activity, interrupted hormonal and lipid profile may be monitored and treated to reduce the risk factor of cardiovascular risk factor especially in PCOS. Such lifestyle modifications are also beneficial for lessen the ovarian cysts and promote fertility in pubertal females.

Abbreviations:

BMI: body mass index

Cho: Cholesterol

HDL: High density lipoproteins

LDL: Low density lipoproteins

Tg: triglycerides

LH: Luteinizing hormone

FSH: Follicle stimulating hormone

CVDs: Cardiovascular disorders

Declarations:

Ethics approval and consent to participate:

The authors took ethical approval from the ethical Committee of Zoology department of Women University and Nishtar Hospital Multan, Pakistan.

Consent for publication:

Consent forms were also signed by the participants and can be provided on demand.

Availability of data and materials:

All data and material generated or analysed during this study are included in this published article in the form of tables and graphs.

Competing interests:

The authors declare that they have no competing interests.

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Authors' contributions:

1: Farhatul-Ain Arshad drafted the manuscript, interpreted the data and performed statistical analysis of data. 2: Rubaida Mehmood designed the study. 3: Dr. Nahid Kausar and 4: Dr. Asia Bibi supervised the team and the study. 5: Dr. Annus Khan participated in the data collection. All authors read and approved the final manuscript.

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Conflict of interest:

There is no conflict of interest to any of the author in this study.

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Figures

Figure 1

positive correlation of BMI with cholesterol $p=0.03$, $r=0.297$

Figure 2

p=0.04, r=0.3, BMI with testosterone in non-obese.

Figure 3

BMI with LH in married obese

Figure 4

BMI with testosterone in unmarried obese.

Figure 5

BMI with estradiol in unmarried non-obese