

Understanding metabolic patterns in polycystic ovary syndrome: Comparing lean and obese women at a family medicine clinic

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ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is a heterogeneous disorder and various phenotypes have been described. While most women with PCOS are obese, women who are lean also suffer from PCOS. Metabolic derangements often accompany this syndrome. Family physicians, being the first point of contact in the healthcare system, play a vital role in the early diagnosis and management of this condition through diet and lifestyle modifications. The present study was conducted at the Diet and Lifestyle Diseases Management Division of a Family Medicine Clinic. **Methods:** We conducted a retrospective analysis of the correlation between body mass index (BMI) and metabolic parameters in women diagnosed with PCOS. The case records of women with PCOS, diagnosed as per modified Rotterdam criteria and who attended the outpatient clinic from January 2020 to December 2022, were chosen. Data on BMI and metabolic parameters were retrieved and statistically analyzed. **Results:** Upon analysis of 51 case records, 25.49% of women were in the lean group and 74.51% were overweight or obese. Triglycerides/HDL ratio (1.91 ± 0.47 vs 3.97 ± 5.89) and Vitamin D levels (Median 14.12 vs 16.10 ng/ml) were abnormal in both the obese and the lean women groups. However, there was no significant difference between the groups. Other metabolic parameters were within normal ranges. **Conclusion:** The present study indicates that metabolic derangements are associated with PCOS, irrespective of BMI. More robust studies in larger population samples are needed to elucidate the role of metabolic derangements and mainly insulin resistance in the pathophysiology of PCOS and its different phenotypes.

Keywords: Body mass index, family physician, polycystic ovary syndrome

Introduction

Polycystic ovary syndrome (PCOS) is a heterogeneous endocrine disorder commonly found in women of reproductive age group.

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The prevalence of PCOS among Indian women has been reported as high as 10% and is one of the common causes of female infertility.^[1] Polycystic ovary syndrome is characterized by both reproductive and metabolic derangements. Ovarian dysfunction is the underlying pathology with hyperandrogenism, anovulation, and polycystic ovarian morphology being the main features seen in these women.^[2] Clinical manifestations may include menstrual irregularities, features of androgen excess like hirsutism, and obesity. Most of these women exhibit

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various metabolic abnormalities. Dyslipidemia, abnormal glucose metabolism, hypertension, and obesity are some of the metabolic abnormalities commonly found in women with PCOS. Insulin resistance is considered to be the underlying cause of these metabolic derangements.^[3] In fact, PCOS is considered as the ovarian manifestation of insulin resistance syndrome or metabolic syndrome.^[4] There is also an associated increased risk of type 2 diabetes and early onset of abnormal cardiovascular risk profile in this group of women.^[5,6]

The European Society for Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Medicine (ASRM) arrived at the Rotterdam consensus on diagnostic criteria for PCOS in 2003 and it was updated in 2018. The criteria specify that to diagnose PCOS, two or more of the features, namely, oligo/anovulation, signs of clinical or biochemical hyperandrogenism, and ultrasonographic evidence of polycystic ovaries need to be present, and other related endocrine and gynecological disorders should have been excluded before.^[7,8] The workshop, convened by the National Institute of Health in the year 2012, specified the four different phenotypes observed among women population with PCOS.^[9]

Apart from these phenotypic varieties described, the population of women with PCOS typically exhibits variations in their body mass index (BMI). The majority (80%) of them are overweight and obese and the remaining have a normal BMI or sometimes even lower BMI values. It is widely debated whether women with PCOS with these differing BMI values share a common or a different underlying pathophysiological process. Studies on the hormonal, metabolic, and biochemical profiles in these differing phenotypes and the applicability of treatment modalities show contradicting results.^[10]

With the prevalence of PCOS creeping up alarmingly in recent times and with major metabolic diseases often being part of this condition, the role of family physicians assumes greater importance in addressing this health issue in the community. A recent article underscores the importance of the family physician developing a thorough understanding of this endocrine–metabolic disorder and the barriers to treatment adherence by patients.^[11] The current study was conducted at the diet and lifestyle management division of a family medicine clinic to understand the key differences in metabolic parameters between lean and obese PCOS women.

Materials and Methods

This retrospective study was conducted by analyzing the medical records available at the Diet and Lifestyle Management division of our Family Medicine Clinic. We included 51 case records of women with PCOS who attended the clinic during the period from January 2020 to December 2022.

Women of age 18–35 years, diagnosed with PCOS according to the modified Rotterdam criteria of ESHRE and ASRM, were

included in the study. Case records of patients who had reported a history of Cushing syndrome, or other related endocrine disorders, and those who were already on medications for the management of PCOS or other related disorders were excluded. Those records which were incomplete with regard to the data being collected were also excluded.

The study was approved by the Institutional Ethics Committee [Ref: GMKMC and H/114/IEC/2023]. Written informed consent had been already obtained from the patients for the use of medical data after due anonymization. Anthropometric data on height, weight, and BMI of all patients were tabulated. Metabolic parameters including fasting blood sugar, fasting insulin, HbA1C, calculated HOMA-IR, fasting lipid parameters including total cholesterol (TC), triglycerides (TGL), low-density lipoproteins (LDL), high-density lipoproteins (HDL), calculated TGL/HDL ratio, and Vitamin D values were recorded. The collected data were submitted for statistical analysis.^[11]

Statistical workup

Sample size

The sample size was calculated assuming the correlation between BMI and metabolic parameters as 0.75. The other parameters considered for sample size calculation were 80% power and 95% confidence level. The sample size was calculated using G-power software.^[12] The required sample size as per the above-mentioned data was 46. To account for a nonparticipation (incomplete case records) rate of about 10%, another five subjects were added to the sample size. Hence, the final required sample size was taken as 51.

Statistical analysis

Metabolic parameters were considered as primary outcome variables. BMI was considered a primary explanatory variable. The association between obesity categories and normally distributed numerical outcome variables was assessed by comparing the mean values using an unpaired *t* test. Mean differences along with 95% CI were presented. The association between the two categorical variables was assessed by the Chi-square test/Fisher's exact test. The correlation between BMI and metabolic variables was assessed by Pearson's correlation/Spearman's rank correlation based on data distribution. *P* value < 0.05 was considered statistically significant. Data were analyzed by using coGuide software, V.1.0.3.^[13]

Results

A total of 51 case records of women with PCOS, who attended the clinic during the period from January 2020 to December 2022, were included in the study. The demographic profile of the study subjects is shown in Table 1. The majority of the study population was obese, 74.51% (*n* = 38) and 25.49% (*n* = 13) were lean with a Mean ± SD BMI of 29.12 ± 6.48 (kg/m²). The Mean ± SD of age were 24.88 ± 4.28 (years) with a range of 18 to 35 years. The (Mean±SD) levels of Total Cholesterol was 190.67 ± 34.29 mg/

dL; that of Triglyceride was (118.50 ± 57.31 mg/dL) and that of HDL cholesterol was (46.03 ± 10.36 mg/dL). The levels of LDL cholesterol level was (111.96 ± 28.79 mg/dL) and that of triglycerides/HDL ratio was (2.87 ± 1.95).[Table 1].

The Mean ± SD of laboratory parameters such as fasting blood sugar, HOMA-IR, HbA1c, fasting insulin, thyroid stimulation hormone and Vitamin D were 90.37 ± 26.73 (mg/dl), 2.35 ± 2.76, 5.39 ± 0.81 (%), 11.17 ± 11.71 (mIU/L), 3.05 ± 1.29 (mIU/mL), and 16.97 ± 7.87 (ng/ml), respectively [Table 2]

Table 3 shows the lipid profile parameters in lean and obese groups. There was a statistically insignificant difference in total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol, and triglycerides/HDL ratio in both the groups ($P > 0.05$)

Table 4 shows the laboratory parameters in both the groups. Obese women had high-fasting blood sugar ($P = 0.036$) and HbA1c ($P = 0.002$ Mean difference -0.79 (95% CI -1.27 to 0.31)) than lean women. However, the values of these parameters were within normal limits in both the groups, and hence, the statistical difference was not considered clinically relevant. The rest of the laboratory parameters, like fasting insulin, HOMA-IR, thyroid stimulation hormone, and Vitamin D, were similar in both the groups.

Figure 1 depicts the correlation between BMI and Lipid profile parameters. There was a significantly negative and moderate correlation of BMI with high-density lipoprotein ($r = -0.318$, $P = 0.023$), and there was a statistically weak and insignificant correlation of BMI with triglycerides ($r = 0.226$, $P = 0.111$), low-density lipoprotein ($r = 0.220$, $P = 0.120$), and total cholesterol ($r = 0.150$, $P = 0.294$), respectively.

Discussion

In the current scenario of changing disease patterns, noncommunicable diseases, mainly metabolic syndrome, contribute to higher morbidity and mortality than infectious and communicable illnesses. Even during the Global COVID-19 pandemic, metabolic syndrome was one of the major contributors to mortality worldwide.^[14] General practitioners and family physicians, who serve as the point of first and frequent contact for patients, have a crucial role to play in the early diagnosis of metabolic syndrome and in alleviating the negative consequences. Many of the adolescents and young women presenting to primary care clinics with features of PCOS are coexisting various facets of the metabolic syndrome like elevated blood sugar, blood pressure, etc., In 1988, Gerald Reaven was the first to put forth the idea that insulin resistance was a central component of the cluster of abnormalities comprising the metabolic syndrome and that hyperinsulinemia is an accompanying feature.^[15] PCOS is considered the ovarian manifestation of this insulin-resistance condition.^[4]

In our patient groups, serum triglyceride value was within the normal range in both the obese and the lean patients. Previous

Table 1: Descriptive analysis of demographic parameters and Lipid profile parameters in the study population (n=51)

Demographic parameters	Summary
Age (years)	24.88±4.28 (Range 18 to 35)
Height (cm)	159.12±5.12 (Range 147 to 170)
Weight (kg)	73.72±16.80 (Range 40 to 123)
BMI (kg/m ²)	29.12±6.48 (Range 16.02 to 48.65)
BMI group	
Lean	13 (25.49%)
Obese	38 (74.51%)
Lipid profile parameters	
Total cholesterol (mg/dl)	190.67±34.29 (Range 121.60 to 293.10)
Triglycerides (mg/dl)	118.50±57.31 (Range 39.35 to 301.10)
HDL cholesterol (mg/dl)	46.03±10.36 (Range 22.10 to 72.55)
LDL cholesterol (mg/dl)	111.96±28.79 (Range 64.63 to 209.53)
Triglycerides/HDL ratio	2.87±1.95 (Range 0.62 to 9.60)

Table 2: Descriptive analysis of laboratory parameters in the study population (n=51)

Laboratory parameters	Summary
Fasting blood sugar (mg/dl)	90.37±26.73 (Range 63.85 to 208.19)
HOMA-IR	2.35±2.76 (Range 0.12 to 16.59)
HbA1c (%)	5.39±0.81 (Range 4.10 to 9.20)
Fasting insulin (mIU/L)	11.17±11.71 (Range 0.56 to 75.61)
Thyroid stimulation hormone (mIU/mL)	3.05±1.29 (Range 0.71 to 6.16)
Vitamin D (ng/ml)	16.97±7.87 (Range 6.59 to 42.64)

studies have shown contrasting results. Makhija N *et al.*,^[16] while studying the clinical-metabolic profile in lean versus obese women with PCOS, noted elevated triglycerides in both the groups. Similar studies by Gupta *et al.*^[17] and Kar^[18] have shown higher triglyceride values in the obese when compared with the lean women with PCOS.

In our study population, the HDL values were 43.60 ± 12.25 mg/dL in the obese group and 50.67 ± 7.70 mg/dL in the lean group, with no statistical difference between the groups. One previous study has quoted lower mean HDL values in both obese and lean groups.^[16] In another study, the number of women with low HDL was equally distributed between both the groups.^[17]

Homeostatic Model of Assessment—IR (HOMA-IR) is one of the commonly used tools in research studies for quantifying insulin resistance indirectly. A cutoff value of 2.5 is taken as an indicator of insulin resistance in adults.^[19] In our study population, the HOMA-IR value was below this cutoff in both the obese and lean patients with PCOS. However, a study by Makhija N *et al.*^[16] has shown elevations of HOMA-IR in both lean and obese PCOS women with those in the obese group showing higher values.

Study articles have described the triglyceride/HDL ratio (TG/HDL) as a marker of insulin resistance and a predictor of

Table 3: Comparison of lipid profile parameters with BMI group

Lipid profile parameters	BMI group		Mean difference	95% CI	P
	Lean (n=13)	Obese (n=38)			
Total cholesterol (mg/dl) (Median (IQR))	170.9 (150.5–217.4)	194.1 (170–211.3)	–	–	0.358 [†]
Triglycerides (mg/dl) (Mean±SD)	94.12±15.48	126.84±63.88	–32.72	(–68.90, 3.46)	0.075*
HDL cholesterol (mg/dl) (Mean±SD)	50.67±7.70	43.60±12.25	7.07	(–0.23, 14.37)	0.057*
LDL cholesterol (mg/dl) (Mean±SD)	106.85±43.93	110.92±26.07	–4.07	(–24.35, 16.2)	0.688*
Triglycerides/HDL ratio (Mean±SD)	1.91±0.47	3.97±5.89	–2.06	(–5.37, 1.25)	0.217*

*=Independent sample *t* test *P* value; [†]=Mann–Whitney *U* test *P* value

Table 4: Comparison of laboratory parameters with BMI group

Laboratory parameters	BMI group		P
	Lean (n=13)	Obese (n=38)	
Fasting blood sugar (mg/dl) (Median (IQR))	77.59 (75.5–80.8)	88.915 (78.62–96.5)	0.036 [†]
Fasting insulin (mIU/L) (Median (IQR))	7.53 (4.06–9.92)	9.15 (4.76–16.3)	0.456 [†]
HbA1C (%) (Mean±SD)	4.81±0.43	5.59±0.82	0.002*
HOMA-IR (Median (IQR))	1.311 (0.71–1.98)	1.6239 (0.91–2.78)	0.424 [†]
Thyroid stimulation hormone (mIU/mL) (Median (IQR))	2.57 (1.98–3.16)	2.79 (2.23–3.8)	0.611 [†]
Vitamin D (ng/ml) (Median (IQR))	14.12 (11.35–15.98)	16.095 (11.9–20.69)	0.275 [†]

*=Independent sample *t* test *P* value; [†]=Mann–Whitney *U* test *P* value

increased cardiovascular risk.^[20] The cutoff value for this ratio has been debated in various articles. A study by Lelis DF *et al.*^[21] in a mixed adult population has specified the cutoff value for the TG/HDL ratio as 2.6 for men and 1.7 for women to detect cardiometabolic conditions. In our present study, both lean and obese PCOS women had values of TG/HDL more than this cutoff value. The values were higher in obese women, but the difference was not statistically significant.

Vitamin D deficiency has been implicated in metabolic syndrome and Vitamin D supplementation has been proposed as a treatment strategy in metabolic syndrome.^[22] Vitamin D deficiency is very common in women with PCOS and one study mentions the prevalence as high as 67 to 85% in this patient group. Low Vitamin D levels have been associated with exacerbation of symptoms of PCOS including insulin resistance, ovulatory and menstrual irregularities, infertility, hyperandrogenism, and obesity, and have been shown to increase the risk of cardiovascular diseases.^[23] In our study, we observed low levels of Vitamin D in both obese and lean women with PCOS with no statistical difference between the groups.

Carmina and Lobo^[24] in their study comparing lean and obese PCOS women in different PCOS phenotypes point out the influence of body weight on the metabolic patterns in the women in the four PCOS phenotypes. They point out that the existing Rotterdam criteria take only the ovulatory pattern and androgen secretion into consideration, ignoring the phenotypic difference in the body mass index of the patients. We observed that our study did not bring out any significant differences in the overall metabolic parameters between the obese and the lean women with PCOS. Two other research articles had also noted no difference in the thyroid and reproductive hormone levels with respect to PCOS patients' body weight.^[25,26] A recent review questioned whether lean PCOS actually has any unique

characteristics compared to obese women with PCOS and concluded that further studies are needed to resolve this debate.^[10]

To conclude, in our study on the retrospective analysis of data on women diagnosed with PCOS, we noted that the TG/HDL ratio and the Vitamin D levels were deranged in both the obese and the lean women groups with no significant difference between the groups. Other metabolic parameters were within the normal ranges.

PCOS is one of the common manifestations of metabolic syndrome and family physicians, being the first point of contact in a medical system, have a crucial role to play in early identification of the endocrine and metabolic derangements in this group of patients. Proper medical record keeping of patient profiles and conducting research helps in improving our understanding of this largely heterogeneous disorder with varied presentations. The novelty in the present study and its strength lies in the fact that this study was conducted in the Diet and Lifestyle Diseases Division of a Family Medicine Clinic. The clinic conducts structured screening and health education programs focusing on dietary modifications to manage PCOS and other lifestyle diseases. As a part of research activities, we looked at the correlation between their BMI and their metabolic parameters in women with PCOS.

A key limitation of the study is the smaller sample size, which can be one of the reasons for the lack of statistical significance between the study groups. We also could not adjust for the potential confounders for the same reason. Considering all the study parameters are objective measurements and were done in an accredited institution, the probability of ascertainment bias is very minimal. More extensive studies may throw light on the underlying mechanisms operating in these groups of women with PCOS who seem to have strikingly different body habitus.

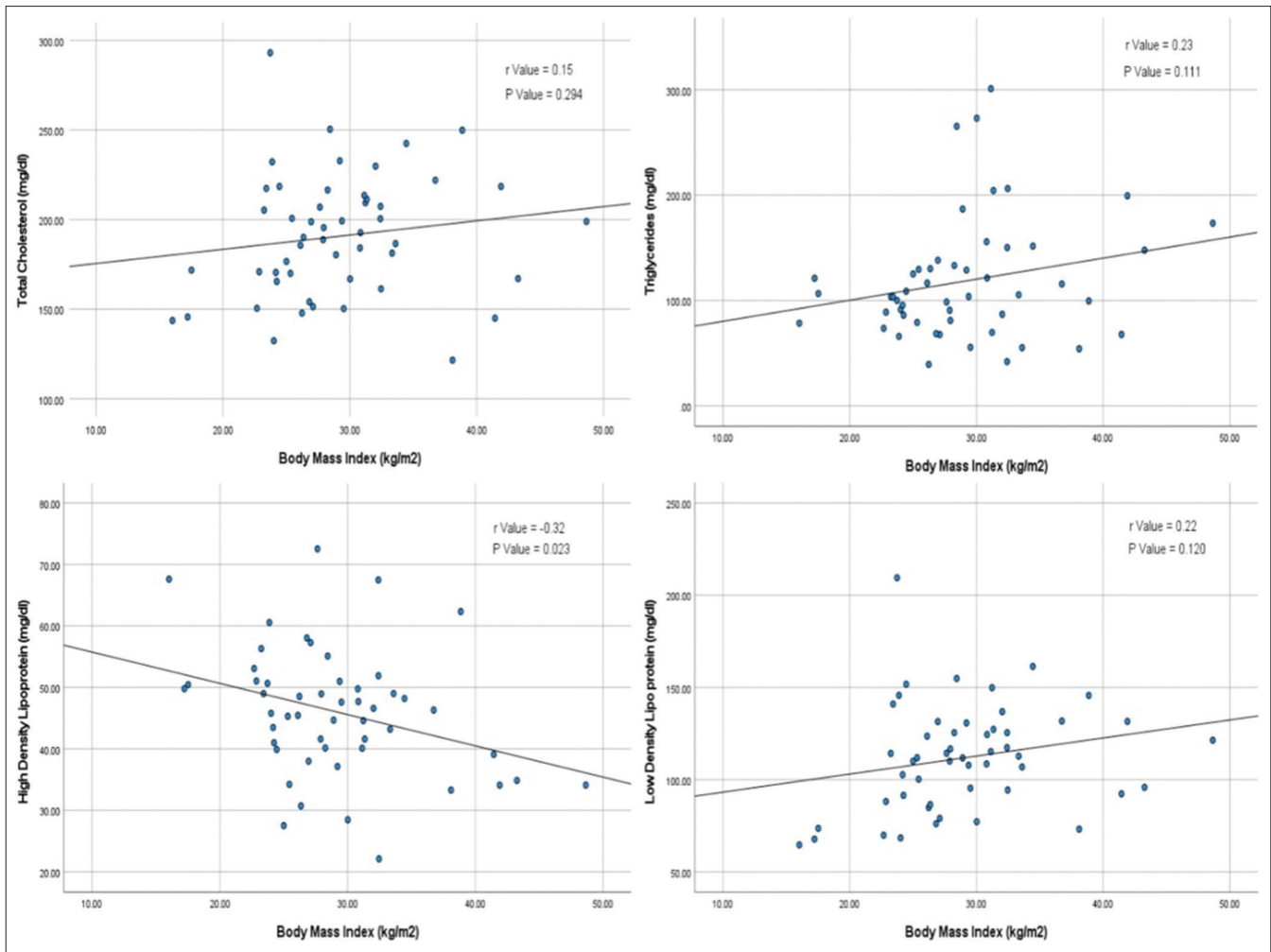


Figure 1: Scatterplot diagram of a correlation between BMI (kg/m^2) with total cholesterol (mg/dl), triglycerides (mg/dl), high-density lipoprotein (mg/dl), and low-density lipoprotein (mg/dl)

Key Points

- Polycystic ovary syndrome is an endocrine–metabolic disorder seen commonly in the outpatient setting in young women in the reproductive age group
- Primary care physicians have a crucial role in identifying the condition at an early stage and instituting lifestyle changes
- Research in family medicine practice helps in developing a better understanding of medical conditions and in the delivery of appropriate care.

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Conflicts of interest

There are no conflicts of interest.

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