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Correlation of dyslipidemia with HBA1c, fasting plasma glucose and BMI in patients with PCOS and Healthy women

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Abstract: *Background:* Polycystic ovary syndrome (PCOS) is a complicated endocrine ailment of unknown reason, it additionally impacts metabolic pathways. Obesity, insulin resistance (IR), and dyslipidemia are common in PCOS cases. Women with PCOS have a greater prevalence of atherosclerosis and cardiovascular illnesses. *Objective:* To determine the lipid profile and correlate with HBA1c levels in women with PCOS compared with non-PCOS women to identify the diabetic and cardiovascular risk. *Material and Methods:* A total of 55 subjects were recruited between, out of which 26 were cases (PCOS) and 29 were controls (healthy women). HBA1c, fasting plasma glucose (FBS), and lipid profile values were notes. Using SPSS software statically analysis were calculated. *Results:* The serum levels of TC, TAG, VLDL, and LDL cholesterol are significantly increased in women with PCOS compared with healthy women, except for the HDL level, which is significantly decreased. A statistically significant positive correlation was noticed between HBA1c, total cholesterol, triglycerides, and VLDL at a 5% p-value. *Conclusion:* Women with PCOS are more prone to dyslipidemia, which is the major determinant of cardiovascular diseases and other metabolic disorders; their reduction plays a significant role in the primary prevention of CVD. Hence they should be screened routinely for a lipid profile and hyperglycemic state to prevent cardiovascular complications and other metabolic syndromes.

Keywords: Polycystic ovary syndrome, Total cholesterol, Triglycerides, High Density Lipoprotein-Cholesterol (HDL-C), Low Density Lipoprotein Cholesterol (LDL-C).

Introduction

Polycystic ovary syndrome (PCOS) is a complex endocrine disorder of unknown etiology, which is characterized by oligomenorrhoea or anovulation and hyperandrogenic symptoms such as the presence of acne and hirsutism. It is the most common endocrinopathy in women of reproductive age [1] and the global prevalence varies from 5.5–12.6 in the age group 17–45 years women's, whereas the prevalence varies from 8.2–22.55 depending on the different diagnostic criteria [2]. PCOS is diagnosed based on the presence of at least two of the following criteria: hyperandrogenism, determined by the presence of total (TT) or free (FT) testosterone excess or hirsutism; ovarian dysfunction (OD), characterized by oligo-amenorrhea and chronic anovulation; and the detection of a specific polycystic ovarian morphology. That is an estimate of 10 small cysts of a diameter between 2 and 9 mm developing on one or both ovaries and/or the ovarian volume in at least one ovary exceeds 10 ml [3-5]. In addition to impaired ovulation, it affects metabolic pathways. Obesity, insulin resistance (IR), and dyslipidemia, which may predispose patients to metabolic syndrome, are common in PCOS.

Dyslipidemia is found in women with PCOS, independently of the excess weight. Women with PCOS have a greater prevalence of atherosclerosis and cardiovascular diseases and an estimated seven-fold increased risk for myocardial infarction [6]. Lipid abnormalities in PCOS include decreased levels of high-density lipoprotein (HDL) and HDL2-cholesterol (HDL2-C), increased levels of total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-C), very low-density lipoprotein-cholesterol (VLDL-C) and

triglycerides (TG)[7]. According to WHO (World health organization) prevalence of the metabolic syndrome in subjects with PCOS was 33% and 37% by NCEP-ATP-III and by IDF criteria it is 40%, compared with 10% by NCEP-ATP-III and 13% by IDF in controls at $P < 0.001$ [8].

In women with PCOS, due decreases in estrogen and SHBG (sex hormone binding globulin) and increased androgen levels lead to obesity and insulin resistance further, increased free fatty acid levels lead to dyslipidemia by the overproduction of VLDL, LDL, and TGs. We know that dyslipidemia increases the risk of cardiovascular disease by increasing coagulation and decreasing the fibrinolysis process. This study was planned to determine the lipid profile and correlate with HBA1c levels in women with PCOS compared with non-PCOS women to identify the diabetic and cardiovascular risk.

Material and Methods

Study population: We conducted a cross-sectional study in a tertiary care teaching hospital. We screened consecutive adult patients with PCOS attending the OBG outpatient department during the study period. Patients diagnosed with PCOS according to to2003- Rotterdam criteria [9] were included after obtaining written informed consent and age-matched healthy controls that were unrelated to patients (12–45 Years) were included in the study after obtaining written informed consent with their demographic data. Patients with diabetes mellitus, thyroid dysfunction, and endocrine disorders like Cushing's, congenital adrenal hyperplasia, ovarian/adrenal androgen-secreting tumors, and patients on anti-hypertensives, antiplatelets, lipid-lowering agents, and subjects unwilling to participate in the study were excluded from the study. Exclusion criteria for controls included a family history of PCOS and those who did not provide written informed consent.

Blood sampling and analysis: Blood was drawn (3ml) from PCOS cases and controls after overnight fasting to determine the HBA1c, FBS, and lipid profiles. The samples were analyzed for total cholesterol (TC), triglycerides (TG), and high-density lipoprotein (HDL) by direct enzymatic method using ERBA diagnostic kits in XL 640 automated analyzer. VLDL and LDL were calculated by the Friedewald formula ((VLDL = TG / 5, LDL = Total Cholesterol – (HDL+VLDL)).

Statistical analysis: Data analysis was performed using the SPSS software. All the results are expressed as Mean ± SD. Intergroup data were compared using the person's correlation coefficients with p-value <0 .05 using SPSS software.

Results

In this study, we randomly selected 26 PCOS cases and 29 controls from our tertiary care hospital. The mean age of the case and controls were found to be 28.5 ± 7.4 and 28.3 ±8.5 (Table 1). Cases (73%) and controls (70%) in the age group 21–40 years were dominant in our study population.

Table-1: Comparison of lipid profile and basic characterization between cases and controls.

Variables/ Group	Case (N=26)	Control (N=29)	p-Value
	Mean ± SD	Mean ± SD	
Age	28.5 ± 7.4	28.3 ± 8.5	0.957 (NS)
BMI	33.6 ± 5.9	22.3 ± 2.4	0.001*
FBS	106.2 ± 22	86.5 ± 10	0.001*
HBA1c	5.6 ± 0.8	4.9 ± 0.2	0.001*
Total cholesterol	181.3 ± 42.5	154.9 ± 15.6	0.03*
Triglycerides (TAG)	177.9 ± 90.6	89.3 ± 20.5	0.001*
HDL	41.9 ± 9.9	53.8 ± 5.8	0.001*
LDL	114.2 ± 27.7	74.8 ± 13.3	0.001*
VLDL	38 ± 16.2	26.8 ± 5.1	0.001*

HBA1c: Glycated hemoglobin, *HDL:* High-density lipoproteins, *LDL:* Low-density lipoproteins, *VLDL:* Very Low-density lipoproteins, *FBS:* Fasting plasma glucose, *BMI:* Body mass index**,** *SD:* standard deviation.

The mean BMI of cases was found to be higher compared to controls. In our study, out of 26 cases, 3.8% had normal weight, 23.1% were overweight and 73.1% were obese. The mean FBS and HBA1c c levels were elevated in cases compared with controls. Among the cases 11.5% were diabetic and 19.2% were pre-diabetic.

Expect HDL, other parameters such as total cholesterol, triglycerides, LDL and VLDL levels of cases were elevated compared to controls (Table 1). TC levels were elevated above the threshold value 200 mg/dl in five cases (19.2%). Total cholesterol and LDL levels were elevated above the threshold value of 130 mg/dl in 19 cases (73.1 %). Total HDL cholesterol levels were reduced below the threshold value of 50mg/dl in 19 cases (73.1%).Total VLDL cholesterol levels were above the threshold value of 40 mg/dl in 16 cases (61.5%). Total triglyceride levels were above the threshold value of 150mg/dl in 14 participants (53.8%). Concerning the lipid profile in our study, a statistical significance at a 5% p-value was noticed between the cases and control group.

Table-2: Correlation between lipid profile and basic characterization in total study population (N=55)

		Age	BMI	FBS	HBA1c	Total cholesterol	Triglycerides	HDL	LDL	VLDL
Age	Pearson Correlation	1	.094	.163	.181	.166	.115	.095	.154	.266*
	p-Value		.497	.234	.186	.226	.404	.491	.260	.050
BMI	Pearson Correlation	.094	1	.447**	.424**	.386**	.529**	-.461**	.578**	.521**
	p-Value	.497		.001	.001	.004	.000	.000	.000	.000
FBS	Pearson Correlation	.163	.447**	1	.821**	.423**	.559**	-.291*	.529**	.669**
	p-Value	.234	.001		.000	.001	.000	.031	.000	.000
HBA1c	Pearson Correlation	.181	.424**	.821**	1	.398**	.622**	-.301*	.533**	.639**
	p-Value)	.186	.001	.000		.003	.000	.026	.000	.000
Total cholesterol	Pearson Correlation	.166	.386**	.423**	.398**	1	.541**	.137	.868**	.405**
	p-Value	.226	.004	.001	.003		.000	.319	.000	.002
Triglycerides	Pearson Correlation	.115	.529**	.559**	.622**	.541**	1	-.428**	.620**	.657**
	p-Value	.404	.000	.000	.000	.000		.001	.000	.000
HDL	Pearson Correlation	.095	-.461**	-.291*	-.301*	.137	-.428**	1	-.237	-.227
	p-Value	.491	.000	.031	.026	.319	.001		.081	.096
LDL	Pearson Correlation	.154	.578**	.529**	.533**	.868**	.620**	-.237	1	.405**
	p-Value	.260	.000	.000	.000	.000	.000	.081		.002
VLDL	Pearson Correlation	.266*	.521**	.669**	.639**	.405**	.657**	-.227	.405**	1
	p-Value	.050	.000	.000	.000	.002	.000	.096	.002	

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

HBA1c: Glycated hemoglobin, HDL: High density lipoproteins, LDL: Low density lipoproteins, VLDL: Very Low density lipoproteins, FBS: Fasting plasma glucose, BMI: Body mass index, N: Number of participant.

In our study, statistically significant positive correlations were observed between BMI and FBS, HBA1c and with lipid profile at 5% p-value. While a statistically significant negative correlations were observed between HDL with BMI, FBS, HBA1c and triglycerides at 5% p-value (Table 2).

We calculated the Pearson's correlation coefficient in obese PCOS women between anthropometric parameters and lipid profile in our study. Statistically significant positive correlations were noticed between HBA1c, total cholesterol, triglycerides, and VLDL at a 5% p-value (Table 3).

Table-3: Correlation between lipid profile and basic characterization in only obese PCOS cases (N=25)

		HBA1c	total cholesterol	triglycerides	HDL	LDL	VLDL
BMI	Pearson Correlation	.046	-.089	.120	.078	-.088	.525**
	p-Value	.825	.671	.568	.711	.675	.007
HBA1c	Pearson Correlation	1	.285	.505*	.111	.313	.610**
	p-Value		.167	.010	.596	.127	.001
total cholesterol	Pearson Correlation	.285	1	.459*	.493*	.902**	.289
	p-Value	.167		.021	.012	.000	.161
triglycerides	Pearson Correlation	.505*	.459*	1	-.135	.425*	.570**
	p-Value	.010	.021		.519	.034	.003
HDL	Pearson Correlation	.111	.493*	-.135	1	.307	.036
	p-Value	.596	.012	.519		.136	.865
LDL	Pearson Correlation	.313	.902**	.425*	.307	1	.215
	p-Value	.127	.000	.034	.136		.303
VLDL	Pearson Correlation	.610**	.289	.570**	.036	.215	1
	p-Value	.001	.161	.003	.865	.303	

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

HBA1c: Glycated hemoglobin, HDL: High density lipoproteins, LDL: Low density lipoproteins, VLDL: Very Low density lipoproteins, N: Number of participant

Discussion

Although PCOS is diagnosed exclusively based on reproductive criteria, it is also a metabolic disorder associated with insulin resistance (IR), impaired glucose tolerance, type 2 diabetes mellitus, obesity, and dyslipidemia.

In our study 23.1% of cases were overweight and 73.1% were obese. Studies have reported that women with PCOS develop insulin resistance and type 2 diabetes compared with non-PCOS women [10-11]. A similar result was noticed in our study, where the FBS and HBA1c levels were elevated and 11.5% of cases were diabetic and 19.2% of cases were pre-diabetic. Studies have reported that elevated levels of HBA1c in PCOS cases are associated with high testosterone, estradiol, and inflammation marker concentrations and low concentrations of inhibin-A, FSH, LH, and prolactin, resulting in menstrual cycle disturbances, anovulation, and infertility [12].

The IR of PCOS is primarily a result of intrinsic factors. When insulin binds to the insulin receptor, there is a post-

binding decrease in the phosphorylation of tyrosine residues and an increase in the phosphorylation of the serine residues of the intracellular domain of the insulin receptor and causing resistance to insulin's metabolic actions. Also, Serine phosphorylation of the adaptor protein IRS-1 disrupts the intracellular signaling necessary for the translocation of GLUT4 into the plasma membrane, which explains the impaired glucose tolerance in patients with PCOS [13]. Therefore, it is necessary to diagnose the hyperglycemic condition and control the insulin resistance in all women with PCOS, irrespective of their BMI at the earliest.

IR has a dominant influence on women with PCOS. Insulin directly stimulates ovarian androgen secretion through its effects on steroidogenic enzymes. It has also been suggested that insulin augments adrenal androgen synthesis, hyperandrogenism that probably plays a role in these abnormalities, contributing to small HDL- cholesterol size by stimulating hepatic lipase activity. Dyslipidemia or altered lipid profile is considered as an added independent cardiovascular risk factor [14].

Dyslipidemia is contributed by insulin resistance in women with PCOS, and it is clinically characterized by elevated levels of triglycerides (TG), total cholesterol, small dense LDL-C, and decreased high-density lipoprotein cholesterol (HDL-C) [15]. In our study, a statistically significant positive correlation was noticed between HBA1c, total cholesterol, triglycerides, and VLDL, and a statistically significant negative correlation was noted with HDL at a 5% p-value in obese women with PCOS. Similar results have been reported by many studies and reported that the levels of serum triglycerides, cholesterol, LDL-C, and VLDL-C were significantly increased, whereas serum HDL-C levels were significantly decreased in patients with PCOS compared with normal menstruating women, and the study suggested that insulin resistance in PCOS is associated with dyslipidemia. They also suggested the presence of an atherogenic lipid profile in the PCOS group independent of obesity [16-18].

Banaszewska conducted a study in Poland of prospective evaluation of lipid profile in a PCOS cohort and evaluated only hyper-insulinemic subjects on a single dose of metformin at 3 and 6 months. He observed that a less favorable lipid profile was observed in hyper-insulinemic subjects with PCOS than in the normal-insulinemic subjects with PCOS. The use of metformin for treating hyper-insulinemic subjects has shown a progressive improvement in lipid profile comparable to the levels found in normal-insulinemic women with PCOS [19]. Studies have reported that both lean, as well as obese patients with PCOS, should be screened for a lipid profile to prevent cardiac complications [20-22].

Therefore, for all PCOS cases, the hyperglycemic state and lipid profile will be determined at the earliest, and proper treatment with a healthy diet and lifestyle should be maintained to d the infertility complication, and metabolic disorders which arise from PCOS.

Limitations of the study: The sample size is less and follow-up of participants with PCOS was not done. Hormone analyses were not included in the study.

Conclusion

From our study, we conclude that in PCOS cases to screening of IR, HBA1c may not be a sensitive and specific tool when compared to other tools, but it is a good indicator, inexpensive and informative biomarker of PCOS complications such as diabetes mellitus, cardiovascular disorders, and other metabolic abnormalities. Women with PCOS are more prone to dyslipidemia which is the major determinant of cardiovascular diseases; their reduction plays a major role in the primary prevention of CVD. Hence they should be screened routinely for lipid profile and hyperglycemic state to prevent metabolic disorders.

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References

1. Pasquali R, Stener-Victorin E, Yildiz BO et al. Forum: research in polycystic ovary syndrome today and tomorrow. *Clin Endocrinol (Oxf).* 2011; 74(4):424-433.
2. Mehreen TS, Ranjani H, Kamalesh R et al. Prevalence of polycystic ovarian syndrome among adolescents and young women in India. *J Diabetol*. 2021; 12:319-325.
3. Rasquin LI, Anastasopoulou C, Mayrin JV. Polycystic Ovarian Disease. 2022 Nov 15. In: StatPearls [Internet]. Treasure Island (FL): *StatPearls Publishing*. 2024 Jan. PMID: 29083730
4. Zueff LF, Martins WP, Vieira CS, Ferriani RA. Ultrasonographic and laboratory markers of metabolic and cardiovascular disease risk in obese women with polycystic ovary syndrome. *Ultrasound Obstet Gynecol.* 2012; 3993):341-347.
5. El Hayek S, Bitar L, Hamdar LH, Mirza FG, Daoud G. Poly Cystic Ovarian Syndrome: An Updated Overview. *Front Physiol.* 2016; 7:124.
6. Franks S. Polycystic ovary syndrome. *New England J Medicine.* 1995; 333(21):853-861.
7. Mallick S, Khatun S, Islam S. Dyslipidemia in Women with Polycystic Ovary Syndrome: Comparison between Obese Cases and Obese Controls in a Government Hospital in West Bengal. *Int J Sci Stud.*2018;6(4):34-38
8. Cussons AJ, Watts GF, BurkeV, et al. Cardiometabolic risk in polycystic ovary syndrome: A comparison ofdifferent approaches to defining the metabolic syndrome. *Hum Reprod.* 2008; 23(10): 2352-2358.
9. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. *Fertil Steril.* 2004; 81(1):19-25.
10. Persson S, Elenis E, Turkmen S, Kramer MS, Yong EL, Poromaa IS. Higher risk of type 2 diabetes in women with hyperandrogenic polycystic ovary syndrome. *Fertil Steril.* 2021; 116(3):862-871.
11. Kujanpää L, Arffman RK, Pesonen P et al. Women with polycystic ovary syndrome are burdened with multimorbidity and medication use independent of body mass index at late fertile age: A population-based cohort study. *Acta Obstet Gynecol Scand.* 2022; 101(7):728-736.
12. Numbi DK, Beya DT, Luzolo GM et al. Importance of the Glycated Hemoglobin Assay in Congolese Women with Polycystic Ovary Syndrome: A Case-Control Study in Kinshasa, DR Congo. *Open Journal of Obstetrics and Gynecology*. 2019; 9:1492-1509.
13. Pasquali R. Contemporary approaches to the management of polycysticovary syndrome. *Ther Adv Endocrinol Metab.* 2018; 9(4):123-134.
14. Baldani DP, Skrgatic L, Ougouag R. Polycystic Ovary Syndrome: Important Under recognized Cardiometabolic Risk Factor in Reproductive-Age Women. *IntJ Endocrinol.* 2015; 2015:786362.
15. Wilson EE. Polycystic ovarian syndrome and Hyperandrogenism. In: Schorge JO, Schaffer JI, Hairorson LM, Hoffman BL, Bradshaw KD and Cunningham FG. Williams Gynecoloy. *New York: MC Graw Hill.* 2008; 383-399.
16. Lath R, Shendye R, Jibhkate A. Insulin resistance and lipid profile in polycystic ovary syndrome. *Asian J Biomed Pharm Sci.* 2015;5(48):30-35.
17. Manjunatha S, Amruta SB, Shaktiprasad H, Veena HC. Effect of PCOS on Lipid Profile. *J App Med Sci.* 2014; 2(3D):1153-1155.
18. Ambiger S. Study of Insulin Resistance and Lipid Profile in Polycystic Ovarian Syndrome. *IJSRP*. 2016; 6(2):2250-2253.
19. Banaszewska B, Duleba AJ, Spaczynski RZ, Pawelczyk L. Lipids in polycystic ovary syndrome: role of hyperinsulinemia and effects of metformin. *Am J Obstet Gynecol.* 2006; 194(5):1266-1272.
20. Panda SR, Rout PK, Chandra C. A case control study of role of lipid profile in polycystic ovarian syndrome: is there any role in non-obese polycystic ovary syndrome?. *Int J Reprod Contracept ObstetGynecol.* 2016; 5(6):1981-1984.
21. Madhu M, Vijay M, Sharma B, Sumapreethi A. Markers of oxidative stress and serum lipids in patients with polycystic ovarian syndrome. *Journal of Evolution of Medical and Dental Sciences.* 2012; 1:769-774.
22. Glintborg D, Kolster ND, Ravn P, Andersen MS. Prospective Risk of Type 2 Diabetes in Normal Weight Women with Polycystic Ovary Syndrome. *Biomedicines.* 2022; 10(6):1455.

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