Original Article

A Study of Serum Adiponectin Levels in Patients with Polycystic Ovarian Syndrome and its Correlation with Various Cardiometabolic Risk Markers

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Abstract

Background: Polycystic ovarian syndrome (PCOS) is the most common metabolic disorder in the reproductive age group, the pathogenesis of which is constantly evolving with the discovery of novel molecules and the lookout for potential therapeutic targets. **Aims:** The aim of the present study was to estimate the circulating levels of serum adiponectin in patients with PCOS compared to controls and to find its correlation with markers of cardiovascular risk, with special emphasis on circulating levels of oxidised low-density lipoprotein (oxLDL). **Settings and Design:** In this cross-sectional observational study recently diagnosed, PCOS subjects were compared with age- and body mass index (BMI)-matched controls. **Materials and Methods:** All the included subjects underwent detailed clinical, biochemical and hormonal evaluation, including lipid profile, 75 g oral glucose tolerance test, fasting serum insulin, fasting serum adiponectin, oxLDL, total testosterone and anti-Mullerian hormone. **Statistical Analysis Used:** Appropriate statistical methods were performed using SPSS (version 21) and Microsoft Excel (2019). **Results:** A total of 56 PCOS cases and 32 controls were included in the study. Mean values of serum adiponectin (μg/mL) in our study were found to be significantly lower in PCOS cases (11.53 ± 4.74) versus controls (14.73 ± 5.61) irrespective of BMI. Mean values of serum oxLDL (μg/dL) were found to be higher in PCOS cases (157.96 ± 53.89) versus controls (117.52 ± 45.44), with a significant negative correlation between adiponectin and oxLDL in cases. No difference in levels of adiponectin was found between the different PCOS phenotypes. **Conclusion:** Hypoadiponectinaemia was found to be associated with PCOS irrespective of obesity in PCOS subjects. Serum oxLDL can complement adiponectin as early predictor of CV risk in PCOS.

Keywords: *Adiponectin, cardiovascular risk, oxidised low-density lipoprotein, polycystic ovarian syndrome, polycystic ovarian syndrome phenotypes*

Introduction

Polycystic ovarian syndrome (PCOS) at any age is characterised by greater odds for elevated cardiovascular risk markers.[1] PCOS patients are more prone to abnormal production of some regulatory proteins secreted from the adipose tissue. Adiponectin, one such adipokine, has direct insulin sensitising and anti-atherosclerotic effects and has been reported to be lower in PCOS patients.[2] Oxidised low-density lipoprotein (oxLDL) is defined as a particle derived from circulating LDL that may have peroxides or

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their degradation products generated within the LDL molecule or elsewhere in the body associated with the particle.[3] oxLDL has been established in the initiation and progression of atherosclerosis in patients with coronary artery disease.[4]

The aim of the present study was to estimate the circulating levels of adiponectin in patients with PCOS and controls in both lean and obese subjects and to correlate it with markers of cardiovascular (CV) risk with special emphasis on circulating levels of oxLDL.

Subjects and Methods

This cross-sectional observational study was conducted in a tertiary centre in the department of endocrinology, from March 2020 to November 2021. Informed written consent was obtained from all the enroled study subjects after explaining the study particulars. The study was approved by the institutional ethical committee.

Ethical policy and institutional review board statement

The study was approved by institutional ethics committee Gauhati Medical College and Hospital, vide letter no 190/2007/Pt-11/March-2020/38 on 19th March 2020. Written Informed consent was obtained for participation in the study and use of the patient data for research and educational purposes. The procedures follow the guidelines laid down in the Declaration of Helsinki 2013.

Subjects

A total of 56 subjects with recently diagnosed PCOS in the age group of 16–30 years and not on any pharmacotherapy were enroled in the study. PCOS was diagnosed using the Rotterdam criteria,[5] i.e., the presence of at least any two of three features of oligo-ovulation or anovulation (O), biochemical and/or or clinical signs of hyperandrogenism (H) and polycystic ovaries (P) (by ultrasound). The cases were classified into two subgroups according to their body mass index (BMI): lean (BMI: 17.5–22.9 kg/m^2) and overweight (BMI: 23–27.4 kg/m^2)/obese (BMI ≥27.5 kg/m^2). PCOS subjects were also classified into four phenotypes based on the National Institute of Health consensus panel criteria.[6] Phenotype A (n = 20): H + O + P (classic phenotype); B (n = 17): H + O (classic phenotype but normal ovaries); C (n = 15): H + P (ovulatory phenotype) and D (n = 17): O + P (normoandrogenic phenotype). Age- and BMI-matched individuals with normal ovulation cycles, neither clinical nor biochemical hyperandrogenism and normal ovaries under ultrasound examination were included as controls. The controls were classified into two subgroups according to their BMI-like cases. None of the participants had concomitant thyroid dysfunction, hyperprolactinaemia, any significant drug history for at least 3 months or any other acute or chronic inflammatory conditions before entering the study.

Methods

Subjects were compared with age- and BMI-matched controls. Detailed menstrual history, hyperandrogenism symptoms and signs were recorded. Anthropometric measurements such as BMI (kg/m^2), waist circumference, hip circumference and waist/hip ratio (WHR) were measured. Clinical measurements such as systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured, and modified Ferriman–Gallwey score was recorded. All laboratory evaluations were performed in the morning after an overnight fast of 8–10 h during the early follicular phase up to day 7 of a spontaneous menstrual cycle, except in subjects with amenorrhoea who were examined on random day in fasting state. A 75 g oral glucose tolerance test (OGTT) was performed, and measurement of serum glucose in fasting and at 120 min after intake of oral glucose solution was done. Serum levels of total cholesterol (TC), triglyceride (TG), LDL cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) were measured on the same day. Samples for fasting insulin, adiponectin, oxLDL, testosterone and anti-Mullerian hormone (AMH) were drawn along with the fasting sample of OGTT. Serum was allowed to clot for 10–20 min at room temperature and later centrifuged at 2000–3000 rpm for 20 min. These aliquots of serum were prepared for the analysis of the biochemical markers being studied. Serum samples were stored at − 80° centigrade until measurements of adiponectin, oxLDL, insulin, testosterone and AMH were done. Baseline ultrasonography of pelvic scan was also done on the same visit for ovarian volume and antral follicle count using a Samsung Prestige RS80A ultrasound machine (probe frequency range: 5–7 MHz). Homeostasis model assessment for insulin resistance (HOMA-IR) score was calculated according to the equation: (Fasting insulin [mU/mL] × Fasting glucose [mmol/mL])/22.5. IR was defined by a HOMA-IR score ≥2.5.

Assays

TC, TGs and HDL-C were measured by routine enzymatic methods (VITROS 5600 integrated system). LDL-C was derived using the Friedewald equation LDL-C (mg/dL) = TC-HDL-(TG/5). Blood glucose including fasting blood glucose and 2 h OGTT was measured by a glucose oxidase method. Serum insulin (intra-assay coefficient of variation [CoV] <5% and inter-assay CoV <10%), serum adiponectin (intra-assay CoV <7.5% and inter-assay CoV < 8%) and oxLDL levels (intra-assay CoV <6%

and inter-assay CoV <10%) were measured using the enzyme-linked immunosorbent assay (ELISA) kits in accordance with the manufacturer's instructions. Thermoscientific ELISA reader was used for the same. Testosterone (intra-assay CoV <5% and inter-assay CoV <8%) and AMH (intra-assay CoV <2% and inter assay CoV <5%) were measured using electrochemiluminescent immunoassay (Roche Cobas e411 analyser).

Statistical analysis

Frequency, percentage, mean and standard deviation were used for all quantitative data. Data were checked for normality using the Kolmogorov–Smirnov and Shapiro–Wilk tests. For determining statistical significance between continuous variables, independent Student's *t*-test and ANOVA were used for data following normality and for non-normal data. Mann–Whitney *U*-test and Kruskal–Wallis tests were used. Pearson's correlation was used to find the strength of association between variables. The statistical analysis was performed using SPSS version 21 (IBM Corp., Armonk, NY, USA).

To detect 90% power of the study at a 95% confidence interval and a clinically significant difference of 5 units between the groups with expected population standard deviation of 5, with ratio of samples between the groups taken as 2 and considering a 10% non-response rate, the minimum required sample calculated in the first group (cases) was 56 and second group (controls) was 28, with a total sample size of 84 using below statistical formula. In our study, we had taken 88 samples including 56 cases and 32 controls.

$$n = \frac{2\,(Z_1 - \frac{\alpha}{2} + Z_1 - \beta)^2 \sigma^2}{d^2}$$

Results

The present study included a total of 88 subjects consisting of 56 cases of PCOS (including 24 lean and 32 overweight/obese PCOS) and 32 age- and BMI-matched controls (including 16 lean and overweight/obese control each). All the included subjects underwent complete clinical, biochemical and hormonal evaluation.

The data for women with PCOS and normal controls are summarised in Table 1. Mean values of serum adiponectin (μg/mL) in our study were found to be significantly ($P < 0.05$) lower in PCOS cases (11.53 ± 4.74) versus controls (14.73 ± 5.61). Mean values of serum oxLDL (μg/dL) in our study were

Table 1: Comparison of clinical, biochemical and hormonal data between women with polycystic ovarian syndrome and control subjects

Clinical parameters	Mean±SD		*P*
	PCOS (*n*=56)	Control (*n*=32)	
Age (years)	21.96±3.87	22.19±3.47	0.788
Onset of menarche (years)	12.83±1.14	12.66±0.65	0.431
BMI (kg/m^2)	25.28±3.98	25.19±4.38	0.919
WC (cm)	90.88±8.79	83.81±5.95	<0.001
WHR	0.92±0.07	0.85±0.05	<0.001
SBP (mmHg)	117.86±7.57	115.75±4.09	0.149
DBP (mmHg)	78.96±5.45	78.63±4.26	0.763
Biochemical parameters			
FPG (mg/dL)	89.27±9.04	78.75±4.27	<0.001
2 h PG post-OGTT (mg/dL)	125.57±17.73	115.25±18.41	0.011
Cholesterol (mg/dL)	168.05±24.74	155.16±26.04	0.023
HDL (mg/dL)	48.79±4.82	50.5±4.64	0.107
LDL (mg/dL)	86.99±24.13	76.29±25.59	0.054
TG (mg/dL)	161.38±57.04	141.81±35	0.082
Hormonal parameters			
Fasting insulin (mIU/mL)	12.08±6.03	10.33±3.88	0.144
HOMA IR	2.69±1.47	2.02±0.77	0.018
Oxidised LDL (μg/dL)	157.96±53.89	117.52±45.44	0.001
Adiponectin (μg/mL)	11.53±4.74	14.73±5.61	0.005
Total testosterone (ng/dL)	50.79±18.16	31.75±16.75	<0.001
AMH (ng/mL)	9.16±5.1	6.41±3.12	0.007

BMI=Body mass index, WC=Waist circumference, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, FPG=Fasting plasma glucose, OGTT=Oral glucose tolerance test, HDL=High-density lipoprotein, LDL=Low-density lipoprotein, HOMA IR=Homeostasis model assessment for insulin resistance, AMH=Anti-Mullerian hormone, SD=Standard deviation, PCOS=Polycystic ovarian syndrome, TG=Triglyceride, WHR=Waist/hip ratio

found to be higher in PCOS cases (157.96 ± 53.89) than in controls (117.52 ± 45.44) [Table 1]. We also analysed all variables after the classification of PCOS women and controls according to BMI, i.e., overweight/obese PCOS women, lean PCOS women, overweight/obese controls and lean controls [Tables 2 and 3]. We also analysed the data between different PCOS phenotypes, including normoandrogenic (Phenotype D) and hyperandrogenic phenotype (A + B + C) [Table 4].

In our study, amongst the cases, a significant negative correlation was found between serum adiponectin levels and oxLDL levels. The correlation of serum adiponectin levels with various CV risk variables is depicted in Table 5.

Discussion

In the present study, we estimated serum adiponectin levels and then correlated with various clinical, hormonal and metabolic parameters. Serum oxLDL levels were also measured as one of the important biochemical markers of increased CV risk in both cases and controls. Our study on serum adiponectin levels and simultaneous measurement of oxLDL levels in PCOS subjects is the first of its kind in this region.

In the present study, adiponectin levels (µg/mL) were lower in the PCOS group compared to the control group [Table 1] and lean PCOS patients had lower serum adiponectin levels compared to lean controls [Table 2], but there was no statistically significant difference in adiponectin levels between obese PCOS patients and obese controls [Table 2] implying that not only obesity itself leads to decreased adiponectin levels but also PCOS can itself be a determining factor for lower adiponectin levels irrespective of obesity. Possible mechanisms include higher trunk-to-peripheral fat ratio,[7] increased visceral adiposity, decreased expression of adiponectin messenger RNA in both subcutaneous and visceral fat tissue[8] and certain unexplained factors, including genetic predisposition as suggested by various research studies.

Our study is in concordance with various other studies conducted by Gowthami *et al*.,[9] Mirza *et al*.,[10] Ardawi and Rouzi,[11] Barber *et al*.,[12] Carmina *et al*.,[13] etc., where they have demonstrated reduced levels of serum adiponectin in women with PCOS. A few of them (Aroda *et al*.,[14] Ardawi *et al*.,[11] Mirza *et al*.[10] and Carmina *et al*.[13]) have also shown that lower adiponectin

Table 2: Comparison of clinical, biochemical and hormonal data between subgroups of polycystic ovarian syndrome and control subjects

Clinical parameters	Mean±SD		*P*	Mean±SD		*P*
	Lean PCOS (*n*=24)	Lean control (*n*=16)		Overweight/obese PCOS (*n*=32)	Overweight/obese control (*n*=16)	
Age (years)	21.46±3.09	21.25±3.34	0.84	22.34±4.37	23.13±3.44	0.536
Onset of menarche (years)	12.96±0.95	12.75±0.58	0.44	12.73±1.27	12.56±0.73	0.619
BMI (kg/m^2)	21.63±0.98	21.4±1.2	0.52	28.02±3.06	28.97±2.75	0.3
WC (cm)	83.13±3.86	79±3.67	0.002	96.69±6.69	88.63±3.22	<0.001
WHR	0.86±0.04	0.82±0.04	0.001	0.96±0.06	0.88±0.02	<0.001
SBP (mmHg)	114.58±6.76	112.88±3.58	0.36	120.31±7.29	118.63±2.03	0.371
DBP (mmHg)	77±5.37	76.38±3.12	0.67	80.44±5.1	80.88±4.13	0.767
Biochemical parameters						
FPG (mg/dL)	87.04±8.13	77.5±4.91	<0.001	90.94±9.44	80±3.18	<0.001
2 h post-OGTT (mg/dL)	120.17±16.01	101.81±11.86	<0.001	129.63±18.1	128.69±13.21	0.855
Cholesterol (mg/dL)	162.04±27	144.63±15.81	0.02	172.56±22.27	165.69±30.25	0.377
HDL (mg/dL)	50.04±3.98	51.94±4.25	0.15	47.84±5.22	49.06±4.68	0.435
LDL (mg/dL)	81.66±24.03	67.69±17.65	0.058	90.99±23.78	84.9±29.73	0.446
TG (mg/dL)	151.71±43.93	125±31.63	0.04	168.63±64.91	158.63±30.45	0.563
Hormonal parameters						
Fasting insulin (mIU/mL)	8.94±4.34	8.3±3.64	0.629	14.43±6.09	12.35±3.01	0.206
HOMA IR	1.93±1	1.6±0.73	0.266	3.26±1.51	2.43±0.57	0.04
Oxidised LDL (µg/dL)	130.65±44.57	90.1±31.29	0.003	178.44±51.66	144.94±41.03	0.029
Adiponectin (µg/mL)	14.01±4.31	17.35±5.47	0.037	9.67±4.21	12.11±4.53	0.072
Total testosterone (ng/dL)	47.85±18.88	29.57±11.63	0.001	53±17.57	33.93±20.85	0.002
AMH (ng/mL)	8.24±5	6.42±2.98	0.2	9.86±5.14	6.4±3.35	0.019

BMI=Body mass index, WC=Waist circumference, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, FPG=Fasting plasma glucose, OGTT=Oral glucose tolerance test, HDL=High-density lipoprotein, LDL=Low-density lipoprotein, HOMA IR=Homeostasis model assessment for insulin resistance, AMH=Anti-Mullerian hormone, SD=Standard deviation, PCOS=Polycystic ovarian syndrome, TG=Triglyceride, WHR=Waist/hip ratio

Table 3: Comparison of clinical, biochemical and hormonal data between lean and overweight/obese polycystic ovarian syndrome subjects

Clinical parameters	Mean±SD		*P*
	Overweight/obese PCOS (*n*=32)	Lean PCOS (*n*=24)	
Age (years)	22.34±4.37	21.46±3.09	0.401
Menstrual cycles/year	6.25±2.45	5.04±3.38	0.127
Onset of menarche	12.73±1.27	12.96±0.95	0.472
BMI (kg/m^2)	28.02±3.06	21.63±0.98	<0.001
WC (cm)	96.69±6.69	83.13±3.86	<0.001
WHR	0.96±0.06	0.86±0.04	<0.001
mFGS	5.25±3.32	4.92±2.89	0.696
SBP (mmHg)	120.31±7.29	114.58±6.76	0.004
DBP (mmHg)	80.44±5.1	77±5.37	0.018
Biochemical parameters			
FPG (mg/dL)	90.94±9.44	87.04±8.13	0.111
2 h post-OGTT (mg/dL)	129.63±18.1	120.17±16.01	0.047
Cholesterol (mg/dL)	172.56±22.27	162.04±27	0.116
HDL (mg/dL)	47.84±5.22	50.04±3.98	0.091
LDL (mg/dL)	90.99±23.78	81.66±24.03	0.154
TG (mg/dL)	168.63±64.91	151.71±43.93	0.276
Hormonal and imaging parameters			
Fasting insulin (mIU/mL)	14.43±6.09	8.94±4.34	<0.001
HOMA IR	3.26±1.51	1.93±1	<0.001
Oxidised LDL (µg/dL)	178.44±51.66	130.65±44.57	0.001
Adiponectin (µg/mL)	9.67±4.21	14.01±4.31	<0.001
Total testosterone (ng/dL)	53±17.57	47.85±18.88	0.298
AMH (ng/mL)	9.86±5.14	8.24±5	0.243
MOV (CC)	10.51±2.96	10.73±3.49	0.797

BMI=Body mass index, WC=Waist circumference, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, FPG=Fasting plasma glucose, OGTT=Oral glucose tolerance test, HDL=High density lipoprotein, LDL=Low density lipoprotein, HOMA IR=Homeostasis model assessment for insulin resistance, AMH=Anti-Mullerian hormone, SD=Standard deviation, PCOS=Polycystic ovarian syndrome, mFGS=Modified Ferriman-Gallwey score, MOV=Mean ovarian volume, TG=Triglyceride, WHR=Waist/hip ratio

levels in PCOS were independent of the weight and/or BMI of the study subjects. On the contrary, a study conducted in the North Indian population by Talat *et al*. did not find a significant association between cases and controls with respect to adiponectin when matched to BMI.[15] Another study conducted by Chen *et al*. showed that only obese PCOS subjects had significantly low adiponectin levels but not in lean PCOS subjects compared to controls.[16]

In the present study, adiponectin levels were lower in overweight/obese PCOS subgroup compared to lean PCOS subgroup [Table 3] which could be due to higher degree of adiposity as well as IR in overweight/obese subjects. Similar findings were shown in studies conducted by Ramanand *et al*.[17] and Panidis *et al*.[18] However, the very first study on serum adiponectin levels in patients with PCOS conducted by Orio *et al*. in a study of 60 PCOS subjects did not find any significant difference in the levels of adiponectin between obese and lean PCOS subjects.[19]

Only a few studies have examined and compared serum adiponectin levels within the PCOS phenotypes. In our study, we did not find significant difference in adiponectin levels between different phenotypes and between hyperandrogenic and normoandrogenic group [Table 4]. This might be due to similar WHR in both the groups and hence similar distribution of abdominal/visceral body fat. In discordance, a study by Otta *et al*. observed higher adiponectin levels in ovulatory PCOS phenotype, followed by normoandrogenic phenotype and the lowest in classic PCOS.[20]

In our study, adiponectin levels were negatively correlated biochemical indices of IR including HOMA IR, fasting insulin levels and fasting glucose in cases but not in controls [Table 5]. This could be due to hypoadiponectinaemia causing reduced activation of AMPK and PPARα in the liver and skeletal muscle, thereby resulting in decreased fatty-acid oxidation, increased tissue TG content and decreased glucose uptake, leading to increase in the IR. Similar findings were reported by Chen *et al*. in their study of 422 subjects (224 PCOS cases and 198 controls).[16] A study conducted by Ramanand *et al*. in 49 newly diagnosed Indian women with PCOS found an inverse correlation only with signs

Table 4: Comparison of clinical, biochemical and hormonal data between hyperandrogenic and normoandrogenic phenotype of polycystic ovarian syndrome

Clinical parameters	Mean±SD		*P*
	Hyperandrogenic phenotype (*n*=38)	Normoandrogenic phenotype (*n*=18)	
Age (years)	22.29±3.68	21.28±4.25	0.365
Menstrual cycles/year	5.84±3.15	5.5±2.43	0.686
Onset of menarche	12.86±1.26	12.78±0.88	0.815
BMI (kg/m^2)	25.55±4.03	24.72±3.94	0.475
WC (cm)	91.42±9.09	89.72±8.25	0.505
WHR	0.92±0.07	0.92±0.07	0.863
mFGS	7.05±1.21	1±1.41	<0.001
SBP (mmHg)	118.21±7.08	117.11±8.68	0.616
DBP (mmHg)	79.58±5.24	77.67±5.79	0.223
Biochemical parameters			
FPG (mg/dL)	90.39±9.34	86.89±8.1	0.178
2 h post-OGTT (mg/dL)	127.13±14.98	122.28±22.61	0.343
Cholesterol (mg/dL)	170.53±25.77	162.83±22.18	0.281
HDL (mg/dL)	48.79±4.6	48.78±5.39	0.993
LDL (mg/dL)	88.28±25.28	84.27±21.91	0.565
TG (mg/dL)	167.26±64.39	148.94±35.48	0.265
Hormonal and imaging parameters			
Fasting insulin (mIU/mL)	12.72±6.34	10.71±5.21	0.248
HOMA IR	2.86±1.55	2.33±1.25	0.211
Oxidised LDL (µg/dL)	166.05±58.3	140.86±39.27	0.103
Adiponectin (µg/mL)	11.12±4.03	12.39±6.01	0.352
Total testosterone (ng/dL)	60.69±11.62	29.89±9.55	<0.001
AMH (ng/mL)	8.93±5.31	9.65±4.73	0.625
MOV (CC)	9.82±3.5	12.26±1.23	0.006

BMI=Body mass index, WC=Waist circumference, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, FPG=Fasting plasma glucose, OGTT=Oral glucose tolerance test, HDL=High density lipoprotein, LDL=Low density lipoprotein, HOMA IR=Homeostasis model assessment for insulin resistance, AMH=Anti Mullerian hormone, SD=Standard deviation, PCOS=Polycystic ovarian syndrome, mFGS=Modified Ferriman–Gallwey score, MOV=Mean ovarian volume, hyperandrogenemic phenotype (phenotype A + B + C), normoandrogenic phenotype - phenotype D, TG=Triglyceride, WHR=Waist/hip ratio

of insulin resistance (IR), rather than with HOMA IR and fasting insulin.[17] On the contrary, the studies conducted by Gowthami *et al*.[9] from South India and Orio *et al*.[19] did not show the correlation between these parameters.

In the present study, we did not find the correlation between serum adiponectin levels and total testosterone levels [Table 5], though free testosterone levels were not estimated. This is in accordance with studies by Ramanand *et al*.[17] and Orio *et al*.[19] However, a study by Escobar-Morreale *et al*. in 66 PCOS subjects diagnosed by Androgen Excess Society criteria found a significant inverse relationship between adiponectin and free testosterone levels, suggesting that hyperandrogenism and abdominal adiposity, by reducing serum levels of insulin sensitiser adiponectin might contribute to IR in PCOS.[21]

In the present study, we observed no significant correlation between serum adiponectin levels and ovarian reserve parameters, including AMH and ovarian volume, in both cases and controls [Table 5]. This finding aligns with the results of a study by Kohzadi *et al*., which reported a similar outcome.[22] However, a study by Woo *et al*. found a significant correlation between AMH and adiponectin levels only in controls but not in cases.[23] Hypoadiponectinaemia can lead to increased IR and insulin levels. Insulin is one of the effective factors in increasing the number of antral follicles and ultimately increased AMH and ovarian volume. However, there might be other independent factors in determining AMH levels in PCOS that could be reason of not finding the correlation between adiponectin and AMH in our study.

Blood pressure (SBP and DBP) negatively correlated with adiponectin levels in both cases and controls in our study [Table 5]. It has been shown that hypoadiponectinaemia results in endothelial dysfunction due to a decrease in endothelial nitric oxide synthase, leading to impaired vasodilatation,[24] impairment of renin–angiotensin system secondary to overproduction of angiotensin II associated with obesity as well as disproportionate activation of sympathetic nervous system secondary to obesity.[25] In accordance with our findings, a study by Shin *et al*. in 60 PCOS subjects

Table 5: Correlation of serum adiponectin (µg/mL) with clinical, biochemical and hormonal variables

Parameters	Adiponectin (µg/mL)			
	PCOS (*n*=56)		Control (*n*=32)	
	r	*P*	*r*	*P*
Age (years)	−0.083	0.543	−0.206	0.257
BMI (kg/m^2)	−0.649	<0.001	−0.636	<0.001
WC (cm)	−0.655	<0.001	−0.546	0.001
WHR	−0.522	<0.001	−0.414	0.018
mFGS	−0.074	0.587		
SBP (mmHg)	−0.310	0.02	−0.678	<0.001
DBP (mmHg)	−0.290	0.03	−0.478	0.006
Fasting insulin (mIU/mL)	−0.535	<0.001	−0.206	0.258
FPG (mg/dL)	−0.296	0.027	−0.416	0.018
HOMA-IR	−0.543	<0.001	−0.237	0.191
2 h post-OGTT (mg/dL)	−0.435	0.001	−0.500	0.004
Cholesterol (mg/dL)	−0.165	0.225	−0.085	0.642
HDL (mg/dL)	0.320	0.016	0.198	0.277
LDL (mg/dL)	−0.132	0.332	−0.068	0.71
TG (mg/dL)	−0.213	0.115	−0.199	0.274
Oxidised LDL (ug/dL)	−0.454	<0.001	−0.467	0.007
Testosterone (ng/dL)	−0.229	0.089	0.036	0.845
AMH (ng/mL)	−0.109	0.425	0.163	0.373
MOV (CC)	0.162	0.231	−0.182	0.312

BMI=Body mass index, WC=Waist circumference, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, FPG=Fasting plasma glucose, OGTT=Oral glucose tolerance test, HDL=High-density lipoprotein, LDL=Low-density lipoprotein, HOMA IR=Homeostasis model assessment for insulin resistance, AMH=Anti-Mullerian hormone, PCOS=Polycystic ovarian syndrome, mFGS=Modified Ferriman–Gallwey score, MOV=Mean ovarian volume, TG=Triglyceride, WHR=Waist/hip ratio

showed similar findings.[26] In another study by Gulcelik *et al*., adiponectin levels were inversely correlated with DBP but not with SBP.[27]

Serum adiponectin levels in our study showed a significant positive correlation with HDL levels in PCOS but not in controls, whereas no correlation was observed between adiponectin levels and other lipid parameters, including cholesterol, TGs and LDL [Table 5]. As per recent literature, adiponectin has been shown to increase HDL-C through an increase in the hepatic production of Apolipoprotein-A1, ATP-binding cassette transporter A1, activation of lipoprotein lipase and downregulation of hepatic lipase activity.[28] In concordance with our study, Yadav *et al*. found a significant positive correlation between adiponectin and HDL.[29]

In this study, we found that higher levels of serum adiponectin are linked to lower levels of oxLDL. This connection suggests that when IR, high androgen levels and hyperlipidaemia are present, it leads to more oxidative stress and, consequently more production of oxLDL. This might be caused by increased abdominal obesity and markers of IR in the studied cases. If we can confirm that oxLDL is an early indicator of cardiovascular risk in PCOS, it would complement the role of adiponectin.[30]

Conclusion

Hypoadiponectinaemia was found to be associated with PCOS irrespective of obesity in PCOS subjects. There was a consistent correlation between adiponectin with various CV risk markers, including BMI, IR indices, systolic and DBP, lipid profile, and oxLDL. Further studies in larger population are needed on adiponectin and oxLDL to establish their role in PCOS as early markers of CV risk and hence, potential targets of therapy.

Author's contributions

GSP - Concept, design, literature search, data acquisition and analysis, manuscript preparation, editing and review. UKS - Concept, design, statistical analysis, manuscript editing and review; AKB - Concept, design, data analysis, manuscript. editing and review; AB - Design, literature search, data acquisition and analysis, manuscript preparation, editing and review.

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Conflicts of interest

There are no conflicts of interest.

Data availability statement

The data set used in the study is available with corresponding author.

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