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Levels of adiponectin, malondialdehyde and lipid profile in women with polycystic ovary syndrome

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ABSTRACT

Polycystic ovary syndrome (PCOS) is a heterogeneous disease affects about 4-18% of women of reproductive age worldwide, with associated increased risk of endocrine, metabolic, and reproductive defects. Adiponectin (ADP), the most abundantly secreted adipokine, is a homeostatic regulating factor for insulin, lipid, and glucose through its antioxidant, anti-fibrotic, and anti-inflammatory effects. Serum levels of adiponectin, malondialdehyde (MDA), and lipid profile were evaluated in the fasting sample in 30 healthy underweight women as a control group, and 30 females with PCOS, age, and body mass index (BMI) matched with the healthy control. Compared with the healthy control, serum levels of adiponectin were significantly lower in females with PCOS. Additionally, total cholesterol (TC) levels were significantly higher in concomitant women compared to the control group. Interestingly, no significant variations were observed in the serum levels of MDA, LDL, TG, VLDL, and HDL. However, no significant correlations were found between the study groups. In conclusion, findings of our study revealed that low adiponectin and high total cholesterol levels could serve as predictive markers of PCOS risk in lean women with a family history of PCOS, or women with fewer symptoms.

Keywords: PCOS, lipids, malondialdehyde, adiponectin, BMI

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is a complex and heterogeneous endocrine disease affecting women of reproductive age, with a prevalence rates ranged from 4-20% using the applied criterion[1]. The presence of two out of the following three criteria is required for the diagnosis of PCOS: polycystic ovaries, ovulatory dysfunction, and hyperandrogenism[2]. PCOS is not only a reproductive disorder but also a metabolic disorder, with affected women being at an increased risk of developing insulin resistance, dyslipidemia, obesity, type 2 diabetes, and cardiovascular disorder[3-6]. Adiponectin is an adipose tissue-derived adipokine and a hormone that influences multiple metabolic processes through its anti-atherogenic, anti-inflammatory, and insulin-sensitizing properties[7]. Adiponectin has been shown to decrease in females with PCOS, and this decrease has been attributed to the insulin resistance which is a characteristic of PCOS[8,9]. Insulin resistance leads to decreased production of adiponectin, which in turn aggravates insulin resistance and contributes to the metabolic abnormalities associated with PCOS[7]. Moreover, adiponectin has a direct effect on ovarian function. Adiponectin receptors are expressed in the ovary, and studies have shown that adiponectin can stimulate steroidogenesis and follicular growth[10-12]. Adiponectin also reduces the production of androgens in the ovary, which is a key feature of PCOS[13]. The decrease in adiponectin levels in PCOS contributes to the hyperandrogenism and ovulatory dysfunction associated with this disorder[14].

Oxidative stress play a significant role in the pathophysiology of several diseases, including PCOS[15]. The underlying mechanisms linking PCOS with oxidative stress are not fully understood. It is believed that oxidative stress may lead to the development of insulin resistance by impairing insulin signaling pathways and promoting inflammation[16]. Furthermore, oxidative stress may lead to the hyperandrogenism seen in PCOS by promoting the production of androgens by the ovaries and adrenal glands[17]. Moreover, it has been shown that adiponectin has antioxidant properties and protects against oxidative stress, and the decline in adiponectin levels may be a factor in PCOS patients' increased oxidative stress[18]. Malondialdehyde (MDA) is a byproduct of lipid peroxidation that is often used as a marker for the presence of oxidative stress in the body[19,20]. Several studies have reported increased levels of MDA in females with PCOS and is related with insulin resistance and dyslipidemia[15, 16, 21]. The elevated levels of MDA in females with PCOS suggest the presence of oxidative stress in this population.

Dyslipidemia is a common metabolic abnormality PCOS, and females with PCOS are more likely to have dyslipidemia including, decreased high-density lipoprotein (HDL) levels and increased triglyceride, low-density lipoprotein

(LDL) levels, compared to women without PCOS[22,23]. The mechanisms underlying the relationship between dyslipidemia and PCOS are thought to be related to insulin resistance, androgen excess, and obesity[22]. Dyslipidemia is a significant risk factor for the development of cardiovascular disease (CVD) in women with PCOS.

Previous studies have shown that adiponectin, MDA, and lipid profile are altered in women with PCOS[9,15,16,21]. However, the relationship between these biomarkers and the metabolic disturbances associated with PCOS is not well understood. Therefore, this study aimed to assess the serum levels of adiponectin, MDA, and lipid profile in females with PCOS and compare them with those of healthy controls. We hypothesize that women with PCOS will have lower levels of adiponectin, higher levels of MDA, and dyslipidemia compared to healthy controls.

METHODOLOGY

Subjects

This cross-sectional study involved 60 females with an age range between (16-35) years, from August 2022 to September 2022. Thirty women with polycystic ovary syndrome and thirty healthy underweight women as a control group. For all participants, the body mass index (BMI) was calculated from the measured weight and height.

Biochemical measurements

All blood samples were obtained from women after overnight fasting and incubated for 10 mins at 37°C in a water bath, and then centrifuged at 3500 rpm for 12 mins. Sera were obtained and stored at -20°C for estimation of adiponectin, malondialdehyde, TC, LDL, TG, VLDL and HDL.

ELISA was applied to determine the concentration of adiponectin using a kit provided by USBIOLOGICAL (USA)[24]. The modified method, in which MDA and thiobarbituric acid (TBA) react to form a pink compound detectable at 532 nm, was used to determine the serum malondialdehyde concentration[25].

An enzymatic colorimetric method was used to measure fasting serum TG[26], TC, and HDL using BIOLABO kit while, VLDL and LDL levels were determined using Friedewald's equation[27].

Data analysis

All values are set as mean ± standard deviation (SD). Unpaired t-tests were used for comparisons between PCOS and control groups, using GraphPad Prism software version 8.0.2, California, USA.

RESULTS and DISCUSSION

The demographic characteristics of the control and PCOS groups are described in Table 1. Sixty women included in this study, of which 30 were healthy women and 30 had PCOS. No significant variations in mean age were observed between the control and the PCOS group (p-value 0.29). However, there was a significant difference in body mass index (BMI) between the women with PCOS and control groups (p-value 0.0012). PCOS women had significantly higher BMI (mean difference 1.81) (Figure 1).

Table 1. Demographic characteristics of the control and PCOS groups

Parameters	Control (n=30)	PCOS (n=30)
Age (years)	23.67 ± 6.126	21.97 ± 4.478
BMI (Kg/m^2)	17.74 ± 0.7032	19.55 ± 1.956*

PCOS: polycystic ovary syndrome. BMI: body mass index. Values set as mean ± standard deviation (SD). Unpaired t-test was used, where *p < 0.05 sets as statistically significant

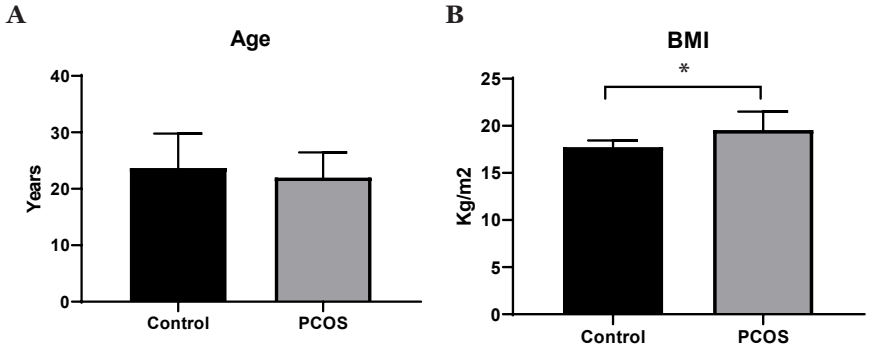

Figure 1. Demographic characteristics of the control and PCOS groups. (A) Age, (B) BMI. PCOS: polycystic ovary syndrome. BMI: body mass index. Values set as mean ± standard deviation (SD). Unpaired t-test was used, where *p < 0.05 sets as statistically significant.

Validation of serum levels of adiponectin, malondialdehyde and lipid profile

Women with PCOS had significantly lower serum adiponectin levels (Figure 2), and significantly higher total cholesterol levels than the control group (Figure 3). However, no significant variations in the levels of MDA (Figure 4), LDL, VLDL, TG, and HDL (Figure 3) were observed between the study groups Table 2.

Table 2. Serum levels of adiponectin, malondialdehyde and lipid profile

Parameters	Control (n=30)	PCOS (n=30)
Adiponectin (µg/ml)	11.24 ± 1.140	10.12 ± 1.403*
Malondialdehyde (µmol/L)	0.3953 ± 0.1802	0.6647 ± 0.5970
TC (mmol/L)	120.8 ± 16.56	144.6 ± 37.08*
LDL (mmol/L)	52.13 ± 22.39	66.01 ± 35.66
TG (mmol/L)	89.33 ± 17.45	106.4 ± 34.00
VLDL (mmol/L)	17.89 ± 3.500	21.31 ± 6.778
HDL (mmol/L)	49.67 ± 10.95	53.90 ± 11.42

TC: total cholesterol. LDL: low-density lipoprotein. TG: triglyceride. VLDL: very low-density lipoprotein. HDL: high-density lipoprotein. Values set as mean ± standard deviation (SD). *p < 0.05 represents statistically significant differences, as set by unpaired t-test

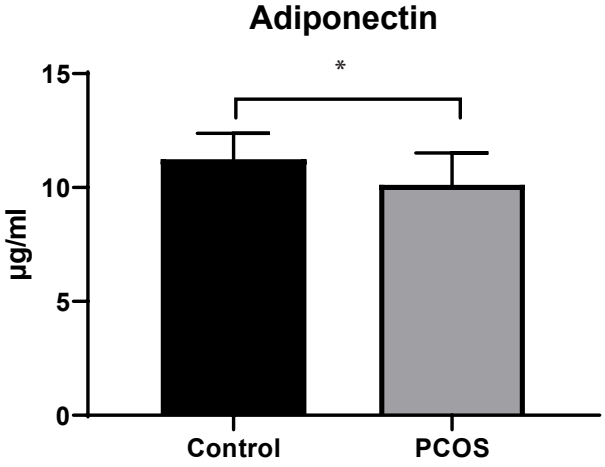

Figure 2. Serum levels of adiponectin. Values set as mean ± standard deviation (SD). *p < 0.05 represents statistically significant differences, as set by unpaired t-test.

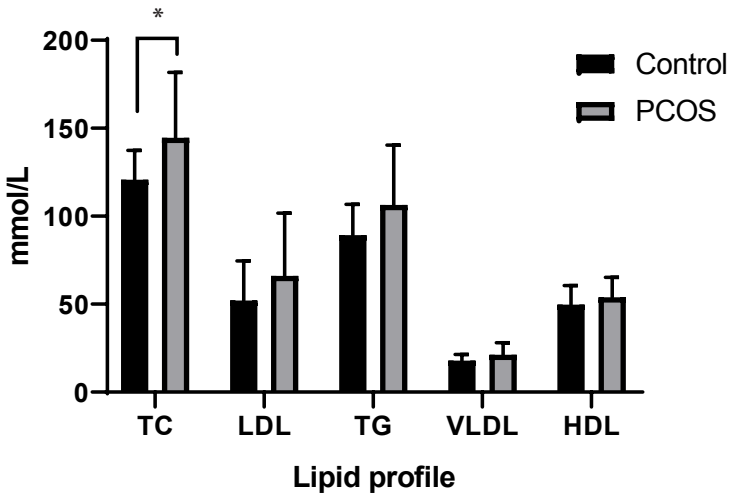

Figure 3. Lipid profile. TC: total cholesterol. LDL: low-density lipoprotein. TG: triglyceride. VLDL: very low-density lipoprotein. HDL: high-density lipoprotein. Values set as mean ± standard deviation (SD). *$p < 0.05$ represents statistically significant differences, as set by unpaired t-test.

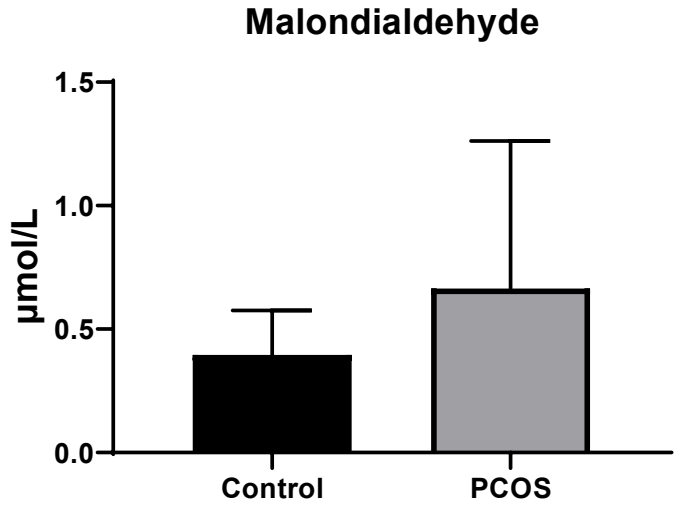

Figure 4. Serum levels of malondialdehyde. Values set as mean ± standard deviation (SD).

The complicated nature of PCOS makes it extremely challenging for physicians to trace the underlying cause and identify the key signs to aid in the diagnosis of illness and the associated metabolic repercussions[28]. One of the principal alterations in PCOS is dyslipidemia, which is primarily caused by insulin resist-

ance and glucose intolerance and has an impact on other potential biomarkers including adiponectin[29,30]. Thus, reduced adiponectin level could indicate the persistence of PCOS[31]. The current study focused on lean women with PCOS, indicated by BMI, to reveal an average reduced level of adiponectin. Physiologically, decreased adiponectin level is a feature in obese individuals which reversed with reduced body weight[32,33]. Although women involved in the current study are not apparently obese, they indicated significant increase in BMI compared to their corresponding control. It is known that adiponectin level is negatively correlated with BMI[32]. Consequently, the present results may reflect normal findings as the adiponectin level in tested individuals with PCOS were inversely related to BMI. This was in agreement with certain studies that indicated reduced adiponectin production with increased obesity, and this is well correlated also with the dyslipideamia associated with PCOS[34-36]. However, the fact that these women are considered underweight, indicated by BMI, may highlight the metabolic abnormality arises from PCOS's pathophysiological changes spotted by lower adiponectin and increased cholesterol levels. This is an important characteristic of PCOS where there are changes in the circulating levels of adipokines, including adiponectin, causing disturbed lipid metabolism which may even be observed in non-obese women[37]. This was consistent with Mirza S. et al. whom conducted a case control study to explore the level of adiponectin in PCOS non-obese females[38]. The study indicated lower levels of adiponectin in PCOS women compared to their healthy controls of the same age and weight range. The study also claimed the usefulness of adiponectin as a biomarker for PCOS in lean young women. Beyazit et al. investigated the levels of adipokines, including adiponectin, and their correlation with obesity in PCOS women[39]. The study reveals reduced levels of adiponectin in PCOS women with averaged BMI below than 25 and concluded that adiponectin may serve as a significant biomarker in the diagnosis of PCOS which may support the findings from the current study. However, in a study by Arikan et al. to evaluate the variations in the resistin and adiponectin levels in non-obese PCOS young women, the results where contrary with that of the current study[40]. It reveals significantly elevated adiponectin levels in PCOS women compared to their controls. Geloneze B et al. raised another claim demanding that the level of adiponectin is positively correlated with that of HDL independently from obesity or BMI[34]. The latter may partially correlate with the present results in highlighting decreased levels of adiponectin in PCOS and dyslipidaemia changes. However, the current study disagreed with the results from Geloneze B et al. in revealing no significant variations between HDL levels in PCOS women compared to their controls[41]. In fact, only total cholesterol in the current results, out of other

lipid profile markers, was significantly elevated in PCOS women. This is possibly because of the younger age and below averaged weight of women included in the study which could limit the chances of showing advanced pathological changes normally observed in older and obese PCOS patients. This could be the same reason why malonaldehyde level was not significant compared to controls showing no indication of altered oxidative stress. Chen et al. evaluated the levels of adiponectin and leptin and their association with lipid profile in obese and lean women with PCOS[37]. the study results revealed no significant changes in the level of adiponectin in lean PCOS women compared to controls which disagreed with the results from the current study. The results also were not consistent with the present study in showing significant elevation in serum levels of LDL, and triglyceride in lean women with PCOS. Uçkan et al. studied the relationship between oxidative stress markers and metabolic abnormalities in PCOS women, and indicated strong correlation between oxidative stress and metabolic changes in PCOS[42]. The study disagreed with the results of the current research as it revealed significant changes in MDA, LDL, and HDL levels in non-obese women with PCOS compared to controls.

Gözüküçük et al., also investigated the levels of adiponectin and leptin along with lipid profile in normal weight PCOS women[43]. The results were consistent with the results of the current study as it revealed no significant variations in lipid profile including serum triglycerides, LDL, and HDL between PCOS women and control subjects. Karadeniz et al. explored oxidative stress markers and lipid profile in young non-obese PCOS patients[41]. The study concluded no significant variations between PCOS patients with controls owing to the younger age of the patients and being non-obese. This was consistent with the results from the current work and may thus support the claims that adiponectin and total cholesterol levels could serve as useful markers in PCOS. This was evident as these indices showed significant difference in PCOS patients compared to other markers even in younger non-obese individuals.

Findings from the current study revealed statistical difference in the serum levels of both adiponectin and total cholesterol spotted in lean young women with PCOS. These markers may serve as early predictive markers of PCOS in these individuals even when other indicators are not evident or yet significant.

STATEMENT OF ETHICS

The approval was obtained from the University of Mosul/ Ethics Committee (25.04.2021-No. 5/5/7044).

CONFLICT OF INTEREST STATEMENT

No conflict of interest was declared by the authors.

AUTHOR CONTRIBUTIONS

Surgical and Medical Practices: Z.M.Y., Z.H.F. Concept: Z.M.Y., Z.H.F. Design: J.A.M., Z.H.F. Data Collection or Processing: S.M.M., Z.M.Y. Analysis or Interpretation: Z.H.F., Z.M.Y. Literature Search: J.A.M., S.M.M., Z.M.Y., Z.H.F. Writing: J.A.M., S.M.M., Z.M.Y., Z.H.F.

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