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Serum Resistin and Adiponectin Levels in Relation with Metabolic Changes in PCO Patients

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Abstract

Background:
With a 5%–10% global incidence rate, polycystic ovarian syndrome (PCOS) is one of the most prevalent endocrinal illnesses affecting premenopausal women. Understanding the pathophysiology of the condition and how to treat it by inhibiting or controlling associated pathways may need research into the inflammatory processes and mediators that contribute to the onset and progression of PCOS.

Aim of study:
The current study aims to determine the relationship between serum levels of resistin and adiponectin and metabolic alterations in PCO patients.

Methods:
Fasting blood samples were collected from 100 PCO married infertile women (23.30±4.66 years) attending Bint AL-Hoda and Al-Shatra hospitals in Thi- Qar province - Iraq, in addition to 50 healthy age matched (23.84±4.80 years) control.
According to BMI and fasting serum glucose level, the patients of PCO were classified into four groups: normal weight nondiabetic patients, normal weight diabetic patients, overweight non-diabetic patients and overweight diabetic patients compared with healthy control.

Results:
Adiponectin considerably decreased in all PCO subgroups compared to healthy controls, but resistin significantly rose in all PCO patients. However, its level was more substantially ($P<0.05$) elevated in overweight diabetics. All PCOS patients had

significantly higher levels of triglycerides, total cholesterol, LDL, and VLDL as compared to healthy controls. While HDL was not significantly changed in all subgroups of PCO patients except it significantly declined in overweight diabetic PCO patients.

Conclusion:
PCOS patients had dramatically changed adiponectin, or resistin levels compared to healthy women. PCOS patients showed low adiponectin levels and high serum resistin levels, indicating that the pathophysiology of PCOS may be influenced by serum adiponectin levels. However, in PCOS patients, resistin levels had a separate relationship with insulin resistance and BMI.

Keywords: Polycystic ovary, Resistin, Adiponectin, lipid profile

Introduction

Polycystic ovarian syndrome (PCO) is one of the most common endocrine disorders of females. After excluding other causes of hyperandrogenism and ovulatory dysfunction, PCOS individuals were selected based on Rotterdam consensus criteria. Even if it is only necessary to take into account two of the following three criteria to diagnose PCOS disease, we did so to achieve optimal homogeneity[1]. identification of oligo- and/or anovulation, identification of biochemical and/or clinical symptoms of hyperandrogenism, and application of the Ferriman-Gallwey (FG) for hirsutism determination were the aforementioned criteria [2]. As only one ovary is required for diagnosis, the presence of 12 follicles with a diameter of 2–9 mm or an ovary volume of >10 ml (without a cyst or dominant follicle in the two ovaries) allows for the assessment of the usual ultrasonographic symptoms of polycystic ovaries.

Oligo-/anovulation, hyperandrogenism, and polycystic ovaries are the hallmarks of polycystic ovarian syndrome (PCOS), a multisystem, endocrinological, reproductive, and metabolic illness[3, 4]. Concurrent obesity exacerbates several of the metabolic abnormalities that appear in PCOS, most notably insulin resistance (IR), poor tolerance for glucose, T2DM, and dyslipidemia[5]. However, several of these metabolic abnormalities may be found in PCOS patients who are slim, and as a result, they are appropriately acknowledged as being part and parcel of PCOS[6, 7]. Even in PCOS individuals who are normal weight, many of these findings can be substantially explained by the rising prevalence of abdominal obesity [8], According to some evidence, the symptoms of the metabolic syndrome seen in PCOS patients are preceded by the disruption of adipokine and ghrelin release from adipose tissue[7]. It is still don't know if the malfunction of adipokines and ghrelin is a result of the interplay between obesity, the distribution of visceral fat, hyperandrogenemia, and hyperinsulinemia, or if it is a fundamental aspect of PCOS. So, the purpose of this study was to determine if altered

adipose tissue production of different adipokines is a result of obesity, hyperandrogenism, or hyperinsulinemia or whether it is a result of PCOS itself.
The adiponectin levels in serum are considerably lower in people with type-2 diabetes mellitus and obesity compared to healthy people[9]. Additionally, it was suggested that lower adiponectin levels relative to matched controls were associated with coronary artery disease (CAD)[10] Adiponectin may act as an anti-inflammatory and vasoprotective adipokine [11]. Many studied showed that serum adiponectin levels in PCOS groups were significantly lower than in control groups [12, 13].

Patients and Methods

Blood samples (after 12 hrs fasting) were collected by venipuncture from hundred PCO married infertile women (23.30±4.66 years) visiting Al-Shatra and Bint AL-Hoda hospitals in Thi-Qar province- Iraq, they were diagnosed by gynecologists according to Rotterdam criteria, from September 2021 to the November 2022. The patients with suspicion of androgen-secreting tumor, Cushing syndrome, thyroid dysfunction, congenital adrenal hyperplasia, hyperprolactinemia, women used antidiabetic, contraceptives, hormonal, and hypolipidemic drugs were excluded. Blood samples were also taken from 50 healthy, age matched (23.84±4.80 years), with regular menstrual cycle, non-pregnant, to serve as control. The research was confirmed by an ethical committee of health directorate of Thi-Qar governorate Iraq. Furthermore, written consents were signed by all participants. Pro-inflammatory markers resistin and adiponectin were determined by using Enzyme-Linked Immunoassay (BIO TEK 800 analysis instrument, USA). Glucose and lipid profile were determined by using spectrophotometer (Apel analysis instrument, Japan), while the equation (VLDL=TG (mg)/5) was used to determine the level of VLDL.

Statistical analysis:

The significancy between PCO and healthy control groups for each parameter was determined by using student t-test (Spss version 26). P-value 0.05 or lower, is considered as significant.

Results

According to BMI and fasting serum glucose level, in comparison with the group of healthy control, the patients of PCO were classified into four groups: normal weight nondiabetic patients [BMI: 22.03±4.82 kg/m^2 NS and serum glucose: 99.45±10.62 mg/dl (NS)], normal weight diabetic patients [(BMI: 22.58±4.74 kg/m^2 NS and serum glucose: 128.93±16.34 mg/dl (P<0.01)], overweight non-diabetic patients [BMI: 30.27±5.22 kg/m^2 (P<0.001) and serum glucose: 100.45±12.54 mg/dl (NS)] and overweight diabetic patients (BMI: 34±6.28 kg/m^2 (P<0.001) and serum glucose: 130.88±18.22 mg/dl

(P<0.001)] compared with healthy control (BMI: 22.84±4.63kg/m^2 and serum glucose: 96.14±10.23 mg/dl).

Resistin was significantly increased in normal weight nondiabetic (442±70 ng/ml, P<0.05), normal weight diabetic (470±65 ng/ml, P<0.05), overweight non-diabetic (458±64 ng/ml, P<0.05) and overweight diabetic (510±22, P<0.01) compared with healthy control (350±60 ng/ml /ml). However, its level was more significantly (P<0.05) increased in overweight diabetic than other PCO subgroups.

Adiponectin was significantly declined in all PCO subgroups, in normal weight nondiabetic (5.7±3.5 mg/l, P<0.05), normal weight diabetic (6.4±4.5 mg/l, P<0.05), overweight non-diabetic (4.3±2.6 mg/l, P<0.05) and overweight diabetic (4.1±2.8 mg/l, P<0.05) compared with healthy control (11.0±4.2 mg/l), with no significant variation among PCO groups .

Triglycerides, total cholesterol, HDL, LDL and VLDL were not significantly changed in normal weight nondiabetic (143±62, 213±18, 34±16,202±25 and 28±13 mg/dl, respectively) and in normal weight diabetic PCO patients (175±46, 218±16,29±15, 215±36 and 37±9 mg/dl, respectively) compared with healthy control (150±64, 206±16, 36±20, 205±23 and 30±13 mg/dl, respectively). However, triglycerides, total cholesterol, LDL and VLDL were significantly elevated in overweight non-diabetic (458±164, P<0.01; 191±56.2, P<0.05; 214±29, P<0.05; and 35.2±11, P<0.05), respectively and in overweight diabetic PCO patients (228±66, P<0.01; 215±19, P<0.05; 232±30, P<0.01; and 46±13, P<0.01) respectively compared with healthy control. While HDL was not significantly changed in both subgroups of PCO patients in comparison with control.

Variables	Control N=50	PCO Patients (N=100)			
		Normal Weight Nondiabetic N=16	Normal Weight Diabetic N=8	Overweight Non-Diabetic N=50	Overweight Diabetic N=26
BMI (Kg/M^2)	22.84±4.63^a	22.03±4.82^a	22.58±4.74^a	30.27±5.22^b	34±6.28^b
Glucose Mg/Dl	96.14±10.23^a	99.45±10.62^a	128.93±16.34^b	100.45±12.54^a	130.88±18.22^b
Resistin (Ng/Ml)	350±60 ^{A}	442±70^b	470±65^b	458±64^b	510±22^c
Adiponectin (Mg/L)	11.0±4.2^a	5.7±3.5^b	6.4±4.5^b	4.3±2.6 ^{B}	4.1±2.8^b
TG (Mg/Dl)	150±64^a	143±62^a	175±46^a	191±56.2^b	228±66^c
Cholesterol (Mg/Dl)	206±16^a	213±18^a	218±16^a	216±16^a	215±19^a
HDL-C (Mg/Dl)	36±20^a	34±16^a	29±15^a	32±18^a	28±17^b
LDL-C (Mg/Dl)	205±23^a	202±25^a	215±36^a	214±29^a	232±30^b
VLDL-C (Mg/Dl)	30±13^a	28±13^a	37±9^a	35.2±11^a	46±13^b

Table (1): Serum levels of resistin and adiponectin in relation with weight and hyperglycemia in PCO patients

Discussion

The prevalence of infertility among women is continually rising globally, and PCOS has recently been established as the main factor contributing to anovulatory infertility. PCOS is associated with a decline in the serum adipokine level [14], but it is unclear whether these alterations occurred as a result of PCOS itself or of obesity, hyperandrogenism, or hyperinsulinemia. This study was carried out to explain the contradictory findings of earlier researches.

In the current study, the level of adiponectin was decreased in all subgroup (Normal weight nondiabetic, normal weight diabetic, overweight non-diabetic and overweight diabetic PCO patients), with no significant variation amoing PCO subgroups. The involvement of adipokines in the etiology of PCOS has recently received more attention. PCOS is characterised by resistance to insulin and obesity. Adiponectin is the prominent adipocytokine in the adipose tissue, so only cytokines, which have well-documented antiatherogenic, anti-inflammatory in nature, and insulin sensitizer characteristics, are produced at and released from adipose tissue. It is well known that obese persons' adiponectin levels are much lower than those of normal-weight subjects [15]. Additionally, it was shown that the degree of insulin resistance is inversely associated with serum adiponectin concentrations [16]. The significance of adiponectin in the etiology of PCOS and whether there is a relationship with resistance to insulin in PCOS trigger our interest because of the relationship between PCOS and obesity and insulin resistance. Hypoadiponectinemia is typically seen in PCOS patients which may attributed to overweight, insulin resistance, or hyperandrogenemia. Escobar-Morreale *et al*., found that abdominal obesity-related hyperandrogenism in PCOS patients participated in their hypoadiponectinemia [17]. Additionally, studies show that high androgens secretion lower blood levels of adiponectin [18]. Adiponectin levels are connected with HDL cholesterol and adversely correlated with triglyceride levels [19] . Similar results were recorded in our study.

However, resistance was significantly elevated in all PCOS subgroups, but it highly elevated in overweight diabetic PCOS patients. These results were in agreement with many studies [20-21]. Resistin was discovered in 2001 and it entirely generated in adipose tissue [20-21]. It worked as an insulin antagonistic that raises blood glucose levels [22]. It contributes in the pathophysiology of diabetes, IR and cardiovascular disorders. Resistin could represent a key relationship between increasing fat mass and IR. In PCOS patients, the blood resistin level and resistin genes expression were linked with BMI [23-24] . Resistin concentration in PCOS patients fluctuated according to BMI values, indicating that resistin may be linked to fatness in PCOS patients [24]. PCOS patients' adipocyte resistin mRNA levels were two times greater than controls[25].

Resistin caused insulin resistance and poor glucose tolerance. Its levels in the blood and its expression in fat cells were rised in people with T2DM and obesity [26].
Triglycerides, total cholesterol, HDL, LDL and VLDL were not significantly changed in normal weight nondiabetic and in normal weight diabetic PCO patients compared with healthy control. However, triglycerides, total cholesterol, LDL and VLDL were significantly elevated in overweight non-diabetic ($P<0.05$) and in overweight diabetic PCO patients ($P<0.01$) compared with healthy control. While HDL was not significantly changed in both subgroups of PCO patients.

This study evaluated the prevalence, distribution, and risk factors for dyslipidemia in PCOS patients. Women with PCOS frequently have dyslipidemia, although its severity and kind might vary[27-28]. According to previous investigations, the dyslipidemia (a decline in HDL-C levels and a rise in LDL-C and TG levels) in PCO patients was comparable to that found in the cases of insulin resistance [29-30].
The potential relationship between serum lipids and plasma adiponectin has attracted attention in light of recent discoveries. Plasma adiponectin and levels of lipids have been demonstrated in several studies to be correlated [31-33]. In the current study, we discovered no association between adiponectin and HDL-C levels, and a negative correlation between adiponectin and total-cholesterol.

Conclusion

Regardless of obesity criteria, the findings of our investigation clearly show that PCOS patients have dramatically changed adiponectin, or resistin levels compared to healthy women. In the current research, subjects with PCOS had low adiponectin levels whereas high serum resistin levels. These findings imply that the pathophysiology of PCOS may be influenced by serum adiponectin levels. However, in PCOS patients, resistin levels had a separate relationship with insulin resistance and BMI. However, larger-scale studies on this matter must be conducted.

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