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Article

Assessment of the risk of subclinical atherosclerosis in women with polycystic ovary syndrome

Noor Mohammed Fadhil[1,*], Rana Ali Hamdi[1], Khitam Malik Abdulhameed[2], liqaa Ali Jaber[3]
[1]Department of Clinical Biochemistry, College of Medicine, University of Baghdad.
[2]Infertility and clinical reproduction.
[3]Medical laboratory technologist.
*Correspondence: nnoormmohamad@gmail.com
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Abstract: Polycystic ovarian syndrome (PCOS) is one of the most prevalent endocrinal disorders affecting women of reproductive age, which has been linked to an enlarged risk of cardiovascular disease and premature atherosclerosis. Atherosclerosis is a persistent inflammatory and lipid-depositing disease that starts from endothelial response to injury, ultimately leading to critical cardiovascular events. Podocalyxin, a cell surface sialomucin, is found on endothelial cells covering blood vessels. Objectives: Measuring serum podocalyxin to predict early atherosclerosis in PCOS women, also measuring lipid panel including the Atherogenic Index of Plasma (AIP), which is a powerful marker that can accurately predict the likelihood of developing theє risk of atherosclerosis even when other atherogenic risk factors appear within normal limits. Materials and Method: This case-control study included 124 age-matched women divided into 63 women diagnosed with PCOS (patients) and 61 healthy women (controls). Lipid panel and serum podocalyxin were measured. Results: There is a significant elevation in the mean value of serum podocalyxin (P=0.000), TG (P=0.39), TC (P=0.002), VLDL-C (P=0.039), LDL-C (P=0.001), a Risk ratio of TC/HDL-C (P=0.000), Risk ratio of LDL/HDL-C (P=0.000), and AIP (P=0.013) with significant decrease in mean value of HDL-C (P=0.000) in PCOS women as compared to healthy control. Conclusion: Higher levels of serum podocalyxin and atherogenic index of plasma were found in PCOS women; a positive correlation was also found between serum podocalyxin and atherogenic index of plasma. Therefore, serum podocalyxin appears to be a predictive marker to detect early atherosclerosis in women with PCOS.

Keywords: polycystic ovary syndrome, atherosclerosis, podocalyxin, lipid profile, AIP.

Introduction

Polycystic ovarian syndromeє (PCOS) is the most prevalent gynecological endocrinopathy [1,2]. PCOS Women are more likely to experience reproductive difficulties such as infertility, endometrial malignancy, late menopauseє [3,4] and also metabolic irregularities such as insulin resistanceє (IR), type 2 diabetes mellitus (T2D), dyslipidemia and cardiovascular diseases (CVD) [5,6]. The physiological function in uterine endometrium related to endometrial receptivity is disturbed by IR, a typical metabolic characteristic of PCOS. Changes in endometrial function 7 may also cause low fertility in PCOS-afflicted women. Dyslipidemia is the most

common metabolic disorder in females with PCOS [8] and is a central cause of atherosclerosis. This chronic inflammatory and lipid-depositing condition eventually results in acute cardiovascular events [9]. Raised serum total cholesterol (TC), triglycerides (TG), low-density lipoprotein-cholesterol (LDL-C), very low-density lipoprotein cholesterol (VLDL-C), and reduced serum high-density lipoprotein-cholesterol (HDL-C) are all signs of dyslipidemia [10]. Triglyceride-rich lipoprotein remnants (TRLs) quickly accumulate on the walls of the artery, which may harm the endothelium and move into the arterial intima as a result of endothelium impairment and develop enrollment and attachment of monocytes to persuade formation of foam cells at the same time, TRLs take part in the improvement and advancement of atherosclerosis [11]. The Atherogenic index of plasma (AIP) is an essential guide that can beе utilized as a separate index for cardiac risk assessment. It is intensely interrelated to CVD risks and can act as a supporter of the individual lipid profileе. When the other atherogenic risk parameters seem normal, AIP can be utilized as a diagnostic indicator [12]. Cardiovascular disease occurrence has been on the rise worldwide, affected by atherosclerosis, and is a primary reason for death. Therefore, it is essential to look for biomarkers that can detect early-stage atherosclerosis [13]. Podocalyxin (PODXL) is a CD34 sialomucin family type I transmembrane protein [14]. It is a sialomucin on the cell surface found in glomerular podocytes and vascular endothelial cells, hematopoietic stem cells and platelets. PODXL regulates the adhesion of cells, migration, and polarity of cells, among other functions [13]. As a universal marker for the vasculature, PODXL has been reported to be pro-adhesive in endothelial cells [14]. This study aimed to measure serum podocalyxin to predict early atherosclerosis in PCOS women, also measuring lipid panel including the Atherogenic Index of Plasma (AIP), which is a powerful marker that can accurately predict the likelihood of developing theе risk of atherosclerosis even when the other atherogenic risk parameters appear normal.

Materials and Methods

One hundred and twenty-four (124) women between 18 and 38 years participated in this case-control study. From November 2021 to March 2022, women visited the infertility center and Consulting Clinic Department at Baghdad Teaching Hospital. Informed consent was taken from all participants. This study was approved by the Ethical Committee of the College of Medicine/ University of Baghdad. Two groups of women were created: Group 1- included sixty-three (63) women diagnosed with PCOS, and Group 2- included sixty-one (61) healthy women (as controls). According to the Rotterdam 2003 criteria, PCOS can be diagnosed when two symptoms are submitted: oligo/anovulation, clinical and biochemical hyperandrogenism, and polycystic ovaries as detected by gynecological ultrasonography [15]. Women with primary causes of dyslipidemia, hyperprolactinemia, congenital adrenal hyperplasia, Cushing's syndrome, androgen-secreting tumors, smoking, hypertension, or chronic renal failure were excluded from the study. Serum podocalyxin and lipid profiles, including total cholesterol, triglycerides, and HDL-C, were studied biochemically. The following equations were used to measure VLDL-C, LDL-C, and AIP:

$$\text{VLDL-C} = \text{TG}/5 \quad (1)$$

$$\text{LDL} - \text{C} = \text{Total Cholesterol} - (\text{VLDL-C} + \text{HDL-C}) \quad (2)$$

$$\text{AIP} = \log (\text{TG} / \text{HDL-C}) \quad (3)$$

AIP readings below 0.11 are linked to low risk of CVD, but those between 0.11 and 0.21 and over 0.21 are linked to intermediate and higher risks, respectively [16]. Additionally, the risk ratios of TG/HDL-C and LDL-C/HDL-C were calculated.

Statistical analysis

Data were inserted into a computer and analyzed using the computer facility of SPSS-23 "PASW Statistics." The results were expressed as numbers, range and mean ± SD (standard deviation). The Significance of the difference was assessed using the Student-t test for two independent means. Correlation and regression were applied for the relationship between two quantitative variables, taking $P \leq 0.05$ as the lowest significance limit.

Results

There is a significant increase in the mean value of serum TG (P=0.39), TC (P=0.002), VLDL-C (P=0.039), LDL-C (P=0.001), AIP (P=0.013), Risk ratio of TC/HDL-C (P=0.000), Risk ratio of LDL-C/HDL-C (P=0.000), and s-Podxl (P=0.000) with significant decrease in mean value of HDL-C (P=0.000) for patients as compared to controls as shown in Table (1).

Parameters	Patients (N= 63)		Control (N=60)		P_ value
	Mean ± SD	Range	Mean ± SD	Range	
TG(mg/dl)	174.24 ± 22.68	(138- 204)	76.30 ± 22.28	(56 – 157)	0.039*
TC(mg/dl)	206.94 ± 13.87	(187 – 231)	127.37 ± 22.72	(98 – 200)	0.002**
HDL-C(mg/dl)	38.13 ± 3.36	(30-46)	53.90 ± 3.53	(45 – 61)	0.000**
VLDL-C(mg/dl)	34.85 ± 4.54	(27.60 – 40.80)	15.26 ± 4.46	(11.20 – 31.40)	0.039*
LDL-C(mg/dl)	133.96 ± 12.66	(112.60-165.00	58.21 ± 20.59	(28.80 – 113.4)	0.001**
AIP	0.66 ± 0.06	(0.53-0.79)	0.14 ± 0.10	(0.14- 0.45)	0.013**
Risk Ratio of TC/HDL	5.46 ± 0.59	(4.70 – 7.33)	2.37 ± 0.45	(1.79 – 3.82)	0.000**
Risk Ratio of LDL/HDL	3.54 ± 0.53	(3.01 – 5.15)	1.08 ± 0.41	(0.51 – 2.52)	0.000**
Podocalyxin	10.63 ± 1.18	(9.03- 12.88)	6.37 ± 0.71	(4.22- 7.59)	0.000**

Table 1. Mean value lipid panel and serum podocalyxin in patients and controls.

The data of this study revealed a significant positive correlation between serum PODXL level and serum TG (r=0.597, P=0.000), as well as serum PODXL and AIP (r=0.863, P=0.000). However, a significant negative correlation exists between serum PODXL level and serum HDL-C (r=-0.498, P=0.000), as shown in Figures 1,2 and 3, respectively.

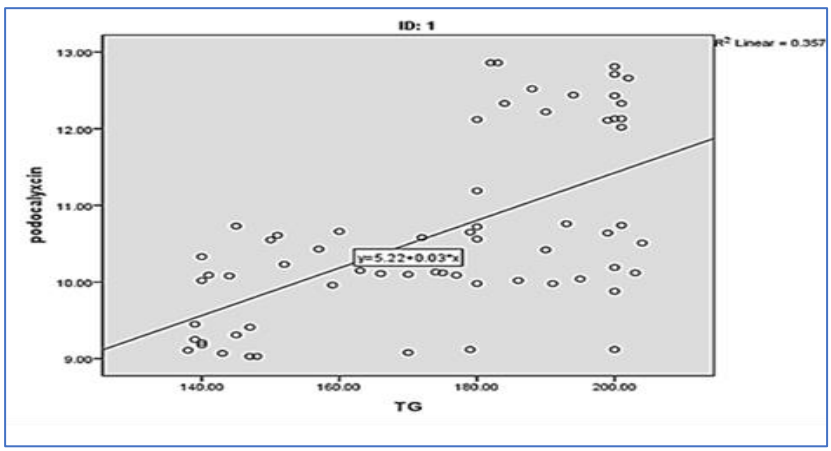

Figure 1: Significant positive correlation between PODXL and TG (r=0.597, P0.000).

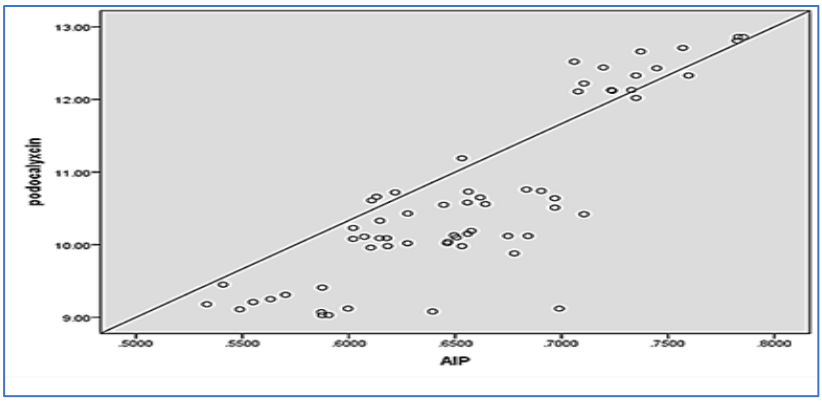

Figure 2. Significant positivee correlation between PODXL and AIP (r=0.863, P=0.000).

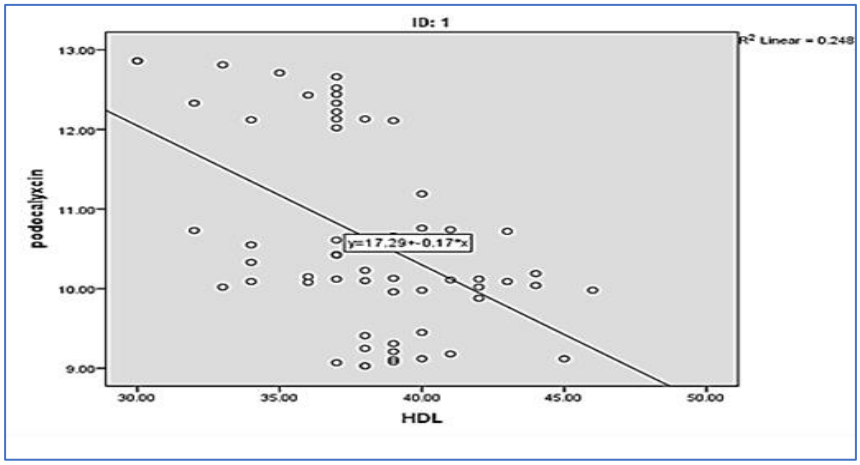

Figure 3. Significant negativee correlation between PODXL and HDL-C (r=-0.498 P=0.000).

Discussion

Up to 18% of females of reproductivee agee aree affected by polycystic ovarian syndromee (PCOS), a complex disorder with psychological (depression, anxiety, and emotional distress), reproductivee (hyperandrogenism, ovulatory dysfunction and subfertility) as well as metabolic features (insulin resistancee, impaired glucosee tolerancee, diabetes mellitus, dyslipidemia, and cardiovascular diseasee) [17]. This study showed that women with PCOS had higher lipid panels than healthy controls, similar to other studies [18, 19]. Additionally, these results are consistent with a previous study, which found that the incidencee rate of CVD, including hypertension and dyslipidemia, was higher in PCOS compared to controls [20]. Wekker and colleagues also found that women with PCOS aree significantly more likely to develop futuree hypertension and type 2 diabetes mellitus. PCOS could lead to adverse lipid serum concentrations and an increase in non-fatal cerebrovascular events [21].

Additionally, Kim and Min discovered that dyslipidemia is significantly moree common in Korean women with PCOS [22]. This study also showed that women with PCOS had higher AIP than healthy controls, similar to other studies [16]. A longstanding study also found that AIP values increasee with increasing CV risk [23]. Moreover, a previous study noted that AIP was a significant and independent predictor for coronary artery disease risk and might bee better than traditional lipid parameters and other lipid ratios [24]. It has been shown that AIP is a reliable indicator of atherosclerosis risk. When the other atherogenic risk markers seem normal, AIP can be utilized as a diagnostic sign [12]. Because vascular endothelial cells express PODXL, researchers focused on it because it was assumed that its presence

in the bloodstream would indicate vascular damage [13]. This study supported the previous assumption by showing higher levels of serum PODXL in women with PCOS compared to healthy controls. Similar to a recent study [25]. In addition, a previous study reported that diabetic patients with higher levels of lipids had higher levels of serum PODXL, too, compared to controls [26]. Additionally, a study by Shoji et al. showed that serum PODXL levels were significantly related to Intima Mediated Thickness even after controlling the common cardiovascular disease risk factors [13].

Conclusion

Higher levels of serum podocalyxin and atherogenic index of plasma were found in PCOS women; a positive correlation was also found between serum podocalyxin and atherogenic index of plasma. Therefore, since serum podocalyxin is expressed in vascular endothelial cells and is related to vascular injury, it is a predictive marker to detect early atherosclerosis in women with PCOS.

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