

# Evaluation of serum Podocalyxin in Iraqi women with Polycystic Ovary Syndrome

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## Abstract:

**Background:** Polycystic ovarian syndrome is the most common endocrine disease in females of childbearing time of life. Women with polycystic ovarian syndrome have a higher chance of developing complications such as dyslipidemia, hypertension, and obesity. Obesity is a state of extreme fat buildup which leads to the development of multiple complications involving non-alcoholic fatty liver disease, cardiovascular disease and type2 diabetes mellitus. Podocalyxin is an element of the endothelial cells plasma membranes that is widely spread, it is limited to the luminal membrane area and is irregularly located on the surface of endothelial cells lining blood vessels.

**Objectives:** To estimate serum Podocalyxin in polycystic ovarian syndrome women and compare its level with healthy controls. Also, to find the correlation between serum Podocalyxin and anthropometrics parameters which are (body mass index, waist circumference, waist to hip ratio).

**Methods:** This case control study included 124 women who were grouped into 2 groups: group 1 included 63 females diagnosed with PCOS (patients) and group 2 included 61 healthy women (controls). Serum podocalyxin was measured by Enzyme-linked immunosorbent assay technique and anthropometrics measures (“body mass index (BMI), waist circumference (WC) and waist to hip ratio WHR”) were done.

**Results:** The results of this study showed significantly high mean BMI(P=0.001), WC(P=0.002) and WHR(P=0.001) in patients as compared to healthy controls. The results also showed a significant increase in mean value of serum PODXL (P=0.001) in PCOS females when compared with healthy controls. In patients group, significant positive correlations were found between serum PODXL and BMI (r=0.395, p=0.001), waist circumference (WC) (r=0.433, p=0.001) and waist to hip ratio (WHR) (r=0.427, p=0.001).

**Conclusion:** PCOS women have greater body mass represented by BMI, WC and WHR which reflect the risk of multiple complications like hypertension, dyslipidemia and cardiovascular disease. Moreover, PCOS women have higher serum PODXL which is considered as a marker for the vasculature thus might be a potential marker for prediction of early atherosclerosis.

**Keywords:** Atherosclerosis, body mass index, obesity, podocalyxin, polycystic ovary syndrome.

## Introduction:

Polycystic ovarian syndrome (PCOS) is a complicated disorder described by high androgen amounts, irregular menstrual cycle, and/or small subcapsular ovarian cysts on one or both ovaries (1,2). PCOS affects women’s health and their quality of life (1), females with PCOS have a greater chance of developing complications for example hypertension (HTN), type 2 diabetes mellitus (T2DM), cardiovascular disease (CVD), dyslipidemia besides obesity (3). Obesity is a state of excessive fat accumulation (4), it promotes cardiovascular risk factors involving: T2DM, HTN, dyslipidemia and sleep disturbances. It also leads to the progress of CVD mortality independently of other cardiovascular risk factors (5). Podocalyxin (PODXL), identified as “podocalyxin-like protein-1, PCLP1 or PCX, is a type I” transmembrane

“protein of the sialomucin family of CD34. Human PODXL is a 558-amino-acid long protein that” undergoes significant post translational modification to produce an outcome with a molecular weight of 140–200 kDa (6). PODXL is a component of endothelial plasma membranes that is widely spread, it is limited to the luminal membrane area and is irregularly located on the surface of endothelial cells (7). The high endothelial venules, which line blood arteries, have a high expression of PODXL. The negatively charged sialoprotein surface that covers the endothelium is primarily comprised of PODXL, just like podocytes. PODXL is said to promote adhesion in endothelial cells (6).

## Materials and Methods

One hundred and twenty-four female participants with age from 18 to 38 years were divided into two groups: group 1 included 63 PCOS women and group 2 included 61 healthy women (as controls) participated in this case-control research. The

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participants visited the infertility center and consulting clinic department of Baghdad Teaching Hospital between November 2021 and March 2022. Each participant gave her agreement after being informed. This study, was approved by the Ethical Committee of the College of Medicine/ University of Baghdad.

Corresponding to Rotterdam criteria, women are considered to have PCOS if two out of three of the following conditions are present: clinical and/or biochemical hyperandrogenism, oligoovulation and/or anovulation (described by the existence of oligomenorrhea or secondary amenorrhea), and polycystic ovaries morphology as determined by ultrasound (8). Furthermore, women who had primary causes of dyslipidemia, congenital adrenal hyperplasia, hyperprolactinemia, smoking, Cushing's syndrome, hypertension, androgen-secreting tumors, or chronic renal failure were excluded from the study. Each serum sample was analyzed for assessing serum PODXL. Also, anthropometric measurements were done for each participant including:

1. Body mass index (BMI): is a screening method for determining if a person is underweight, normal or overweight (9) as shown in the next formula: "[BMI = weight (kg) / (height (m))<sup>2</sup> ]".
2. Waist Circumference (WC): one way to identify persons who are more likely to develop diseases associated with obesity because of a buildup of abdominal fat. It is a straightforward anthropometric indicator for abdominal adiposity that measures visceral obesity more accurately than BMI (9).
3. Waist to Hip Ratio (WHR): Due to its inclusion of measuring hip circumference, the WHR may serve as a favored risk factor for foretelling MI. WHR ( $\geq 0.1$ ) rises the risk of heart disease and other illnesses related to obesity in both men and women.

### Statistical analysis

Information was input into computer and analyzed using computer software of SPSS-18 (Statistical Package for Social Science – version 23)"PASW Statistics". The outcomes were expressed as numbers, range and mean  $\pm$  SD (standard deviation). Significance of difference was assessed using Student's-*t* test for two independent means. Correlation and regression were applied for the relationship between two quantitative variables, taking  $P \leq 0.05$  lowest limit of significance.

### Results

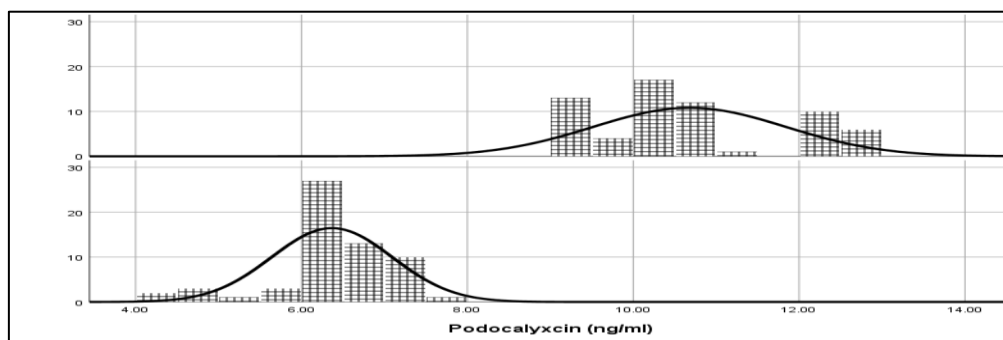
Patients and controls were matching for age. However significant difference in mean value of BMI ( $P=0.001$ ), WC( $P=0.002$ ) and WHR( $P=0.001$ ) between patients and control as shown in Table (1)

**Table (1): Mean values of age, BMI, waist circumference and waist to hip ratio in patients and controls**

Parameter	Patients (N= 63)		Control (N=60)		P value
	Mean $\pm$ SD	Range	Mean $\pm$ SD	Range	
Age (Year)	26.94 $\pm$ 6.15	(18-38)	27.43 $\pm$ 6.21	(18 - 38)	0.810
BMI (Kg/m <sup>2</sup> )	31.15 $\pm$ 6.81	(17.25 - 43.81)	25.66 $\pm$ 3.19	(17.46 - 32.17)	0.001**
WC (cm)	96.30 $\pm$ 12.01	(70- 112)	82.27 $\pm$ 8.62	(70 - 105)	0.002**
WHR	1.03 $\pm$ 0.22	(0.76 - 1.42)	0.78 $\pm$ 0.08	(0.62 - 0.98)	0.001**

\*Significant difference between two independent means via Student's-t-test at 0.05 level.

Additionally, considerable elevation in mean value of serum PODXL in patients group as compared to control group ( $P = 0.001$ ) as demonstrated in Figure (1).



**Figure (1): Distribution of serum PODXL in patients (a) and controls(b).**

Moreover, significant positive correlations were found between serum PODXL level and anthropometric measures [BMI. ( $r=0.395$ ,  $p=0.001$ ), WC.( $r=0.433$ ,  $p=0.001$ ), and WHR ( $r=0.427$ ,  $p=0.001$ )] in patients group as shown in Figure 2A, 2B and 2C, respectively.

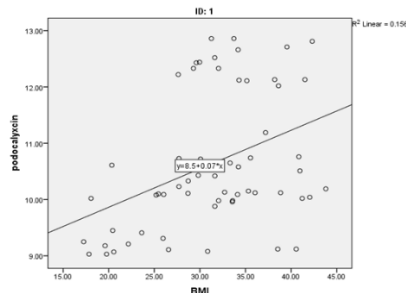


Figure: 2A

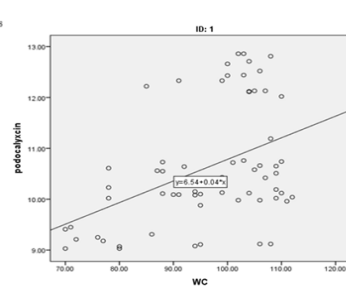


Figure: 2B

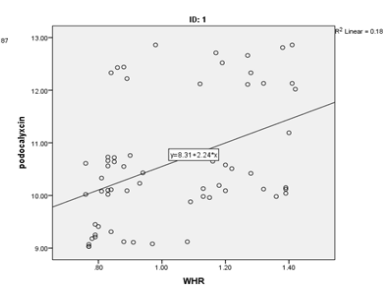


Figure: 2C

Figure (2): Significant positive correlations between serum PODXL level and anthropometric measures.

**Discussion:**

Polycystic ovary syndrome reveals the interfaces among several proteins and genes influenced by genetic and environmental factors (10). It is accompanied with a range of difficulties that involve endometrial cancer, infertility, high risk of CVD and increased body weight (11). A lot of these women develop unusual glucose and fat metabolism, hypertension, obesity, resistance of insulin and other traits that suggests systemic inflammatory responses (12,13). The current study showed that women with PCOS had higher weight characterized by BMI, WC and WHR as compared to healthy controls, similar to recent study which found that obese group had notably higher weight, BMI, WC, mean arterial pressure, diastolic blood pressure, systolic blood pressure and pulse pressure as compared to non-obese. In addition, obesity has a considerable association with dyslipidemia which may elevate the potential risk for CVD development (14). Additionally, in 2016 a study by Mandviwala and partners have reviewed the data that takes obesity as both a risk marker and an independent risk factor for progression of heart failure, arterial fibrillation and asymptomatic and symptomatic coronary artery disease (15). Serum PODXL, a cell surface sialomucin, was also discovered in blood vessels other than capillaries. For instance, it was discovered in the endothelium of all coronary artery branches, kidney arterioles and the abdominal aorta. It was also discovered in an irregular pattern similar to that of capillaries (7). This study revealed higher levels of serum PODXL in females with PCOS as compared to healthy controls. In agreement with a recent study which found that women with PCOS have higher PODXL levels as compared to controls (16). Researches focused on serum PODXL which was detected in the blood because it is expressed in vascular endothelial cells, and is thought to be related to vascular injury (17).

**Conclusion:**

PCOS women have higher body weight represented by BMI, WC and WHR which reflect the risk of multiple complications like high blood pressure, type 2 diabetes mellitus, hyperlipidemia and cardiovascular disease. Moreover, PCOS women have higher serum PODXL which considered as a

marker for the vasculature thus might be a potential marker for prediction of early atherosclerosis.

**Authors' Contributions:**

Study conception, study design and critical revision: Noor Mohammed Fadhil and Rana Ali Hamdi  
Acquisition of data analysis, drafting of manuscript and interpretation of data: Noor Mohammed Fadhil and Rana Ali Hamdi.

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## قياس البودوكاليكسين في مصل الدم لدى النساء العراقيات المصابات بمتلازمة تكيس المبايض

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#### الخلاصة:

**الخلفية:** متلازمة تكيس المبايض هي اضطراب الغدد الصماء الأكثر شيوعاً لدى النساء في سن الإنجاب. النساء المصابات بهذه المتلازمة أكثر عرضاً للإصابة بمضاعفات مثل ارتفاع مستوى الدهون في الدم وارتفاع ضغط الدم والسمنة. السمنة هي حالة من تراكم الدهون المفرط الذي يؤدي إلى تطور مضاعفات متعددة بما في ذلك داء السكري من النوع ٢ ومرض الكبد الدهني غير الكحولي وأمراض القلب والأوعية الدموية. بودوكاليكسين هو أحد البروتينات المكونة لأغشية البلازما البطانية التي تنتشر على نطاق واسع، ويتم توزيعها بشكل غير منتظم على سطح الخلايا المبطن للأوعية الدموية.

**الأهداف:** لتقدير البودوكاليكسين في مصل دم النساء المصابات بمتلازمة تكيس المبايض ومقارنة تركيزه في النساء السليمات، وكذلك لإيجاد العلاقة بين البودوكاليكسين في المصل (مؤشر كتلة الجسم ومحيط الخصر ونسبة الخصر إلى الورك).

**المواد وطرق العمل:** تضمنت هذه الدراسة ١٢٤ امرأة وتم تقسيمهن إلى مجموعتين: المجموعة الأولى تضمنت ٦٣ امرأة تم تشخيصهن بمرض متلازمة تكيس المبايض (مجموعة المرضى) و المجموعة الثانية تضمنت ٦١ امرأة يتمتعن بصحة جيدة. تم قياس بروتين البودوكاليكسين في المصل وايضا تم قياس مؤشر كتلة الجسم، محيط الخصر و نسبة محيط الخصر الى الورك.

**النتائج:** أظهرت نتائج هذه الدراسة ارتفاع واضح في متوسط قيمة مؤشر كتلة الجسم ( $P=0,001$ )، محيط الخصر ( $P=0,002$ ) ونسبة محيط الخصر الى الورك ( $P=0,001$ ) بين المرضى مقارنة بالأصحاء. كما أظهرت النتائج زيادة واضحة في متوسط قيمة بروتين البودوكاليكسين في المصل ( $P=0,001$ ) في النساء المصابات بهذه المتلازمة مقارنة بالنساء السليمات. ايضا، وجد في مجموعة المرضى علاقة إيجابية بين بروتين البودوكاليكسين في المصل و بين مؤشر كتلة الجسم ( $r=0.395$ ,  $p=0.001$ )، محيط الخصر ( $r=0.433$ ,  $p=0.001$ ) ونسبة محيط الخصر إلى الورك ( $P=0,001$ ,  $r=0,427$ )

**الاستنتاجات:** ان النساء المصابات بمتلازمة تكيس المبايض لديهن وزن عالي متمثل بمؤشر كتلة الجسم، محيط الخصر، و نسبة محيط الخصر الى الورك مما يعكس خطر حدوث مضاعفات متعددة مثل ارتفاع ضغط الدم ومرض السكري من النوع ٢ وخلل في مستوى الدهون بالدم وأمراض القلب والأوعية الدموية. علاوة على ذلك، وجد أعلى مستويات لبروتين البودوكاليكسين لدى النساء المصابات بمتلازمة تكيس المبايض والذي يعتبر علامة للأوعية الدموية وبالتالي قد يكون دليل محتمل للتنبؤ بالإصابة بتصلب الشرايين المبكر.

**الكلمات المفتاحية:** السمنة، بودوكاليكسين، تصلب الشرايين، متلازمة تكيس المبايض، مؤشر كتلة الجسم.