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Correlation between Serum Uric Acid, Vitamin D and HbA1c in Polycystic Ovary Syndrome

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Abstract

Background: Polycystic ovary syndrome (PCOS), is the most common endocrine disorder in reproductive-aged women.
Patients and methods: two hundred patients with symptoms and signs of PCOS seek medical advice in two hospitals in Basrah provenience in southern Iraq during the period from 1st of September 2023 to 1st of February 2024 in an obstetrics and gynecology outpatient clinic of Al - Fayhaa teaching hospital and Al-Mawani teaching hospital. Anthropometric study done for each and fasting sample were drawn and sent for vitamin D3, uric acid, HbA1c levels in addition two hundred normal women without complains were chosen for comparisons.
Results: all parameters of this study showed statistically significant differences between patients' sample and control, with Conf. interval (CI) 6.93 - 4.48 for Vitamin D, 0.14 -0.47 for Uric acid and 0.28 -0.61 for HbA1c, body mass index as well, significantly correlated (CI) 0.52-1.81. While (CI) for age is 0.14- 2.19 which is not significant between both groups.
Conclusion: all parameter of metabolic abnormalities of POCS are significantly correlated with patients suffering from this syndrome but not for non-modifiable risk factor (age).

Introduction

Women at reproductive age are facing many problems which annoying their life and affects their physical activities, one of these problems and consider to be famous problem are Polycystic ovary syndrome (PCOS). It is endocrine problem and represent single most endocrine metabolic problem in female. [1]

Polycystic ovary syndrome (PCOS) is a genetically complex endocrine disorder that its etiology is unclear with a complex pathophysiology. According to the estimation of the World Health Organization, (116) million women (3.4%) worldwide have been affected by PCOS. [2] The global prevalence of PCOS is estimated between 4% and 20%. [3] According to a systematic screening of women using the National Institutes of Health (NIH) diagnostic standards, 4-10% of reproductive-age women are predicted to have PCOS worldwide. [4]

Many women with PCOS are characterized by disturbances in reproductive hormones, including androgen, the luteinizing/follicle-stimulating hormone (LH/FSH) ratio and estrogens. [5-7] Polycystic ovary syndrome (PCOS) is a leading cause of infertility among women throughout the world. PCOS is an endocrine abnormality that presents as hyperandrogenemia, anovulation, and/or polycystic ovaries. [8] There is a dynamic relationship between activities of hypothalamic-pituitary- (adrenal/and or ovarian axis) and metabolic diseases such as obesity, with involvement of compensatory hyperinsulinemia and insulin resistance. [9,10] Vitamin D has an essential role in calcium homeostasis and bone metabolism. However, its

role in a wide range of biological actions has been revealed over the past two decades. The roles include cell differentiation, cell growth inhibition, immunomodulation, and control of other hormonal systems. Vitamin D deficiency is a common health condition in the reproductive period of women life. [11] Vitamin D deficiency is common in women with PCOS ranged between 67% and 85% as defined serum concentrations of 25-hydroxyvitamin D (25OHD) < 20 ng/ml. Vitamin D deficiency may escalate the symptoms of PCOS in women. The lower Vitamin D in PCOS patients has been shown to associate with insulin resistance (IR), lower pregnancy rate, ovulatory and menstrual irregularities, hirsutism, obesity, and hyperandrogenism. [12] Currently, there is limited evidence on the association of Vitamin D levels with PCOS disease. [12,13]

PCOS patients have an increased chance of developing impaired glucose tolerance and suffer from T2DM. [14] As insulin directly mimics the action of LH and indirectly raises GnRH, hyperinsulinemia is the primary cause of excessive androgen production. Sex hormone binding globulin (SHBG), a key circulatory protein that regulates testosterone levels, is decreased by insulin. Therefore, lower SHBG levels would lead to higher levels of free androgens, which cause clinical symptoms of PCOS, such as hirsutism, alopecia, and acne. [15] Numerous studies have shown that lowering insulin resistance will ultimately result in reduced androgens and an improvement in the disease condition. [16 -17]

Although lean PCOS women undergo IR; obesity aggravates IR. [18] PCOS pubescent girls with normal-weight undergo peripheral IR and fatty liver compared with control girls with normal-weight. [19]

Uric acid (UA) is an organic acid that is produced during purine nucleotide metabolism. Elevated serum uric acid (SUA) is closely associated with metabolic disorders. [20]

Increased levels of Estradiol and progesterone are related to a decreased SUA level; in contrast, follicle-stimulating hormone (FSH) was positively associated with the SUA concentration. In addition, a higher SUA level was correlated with an increased probability of anovulation. [21]

The aim of current study is to correlate the factors modifiable and non-modifiable that predispose to polycystic disease of ovaries occurrences in our society.

Patients and Method

This study was carried out between 1st of September 2023 and 1st of February 2024 in an obstetrics and gynecology outpatient clinic of Al - Fayhaa teaching hospital and Al- Mawani teaching hospital.

A case-control study design use in this study, of four hundred women at child-bearing age, (200) was diagnosed with PCOS and (200) without PCOS were participate in this study.

The diagnosis of PCOS can be performed by using various guidelines/criteria as recommended by the National Institute of Health (NIH), Rotterdam criteria, and the Androgen Excess PCOS Society (AE-PCOS) criteria. [22] Recently, the international evidence-based guidelines suggested that the Rotterdam criteria are superior to others in diagnosing PCOS [23], when two (or more) of the three of the following criteria were found: oligo- and/or anovulation. Polycystic ovaries were defined as the presence of 12 or more follicles in each ovary measuring 2-9 mm in diameter and /or increased ovarian volume (>10 ml; calculated using the formula 0.5 × length × width × thickness), clinical and/or biochemical hyperandrogenism, polycystic ovaries (PCO), and exclusion of other etiologies.

The women with PCOS consulted outpatient clinic for PCOS-related symptoms such as hirsutism, acne, obesity, infertility or menstrual irregularities.

Assuming the following parameters for your study:

Prevalence of Vitamin D deficiency in controls: 20%

Expected odds ratio: 2.0

Significance level (alpha): 0.05

Power (1-beta): 0.80

Ratio of cases to controls: 1:1

Using these assumptions, a sample size formula for case-control studies was chosen as follows: [24]

$$n = \frac{(Z_{\alpha/2}+Z_{\beta})^2 \times (p_1(1-p_1)+p_2(1-p_2))}{(p_1-p_2)^2}$$

Where

- Zα/2 is the critical value for a two-tailed test (1.96 for alpha = 0.05).
- Zβ is the critical value for the desired power (0.84 for 80% power).
- p1(1-p1) is the prevalence of the exposure in controls.
- p2 (1-p2) is the prevalence of the exposure in cases.

This calculation suggests a sample size of approximately 169 cases and 169 controls for your study, assuming the above parameters. The sample size was increased to 200.

The participants were divided into two groups. The cases group comprised (200 women) with PCOS (age ranged 18-45 years) and control group (200 women) without PCOS (age ranged 18-45 years). We exclude Patients who had known to be diabetes mellitus, osteomalacia and gout.

Anthropometric measures (body weight (Kg) and height (cm) were taken. Weight and height were measured in light clothing without shoes. The BMI was calculated as weight in kilograms divided by the square of height in meters [25]. The studied PCOS patients classified according to BMI. For adults, BMI is interpreted by using standard weight\status categories that are the same for all ages and for both men and women. The standard weight status categories associated with BMI ranges for adults are: BMI Weight Status Below 18.5 were considered underweight ,18.5 - 24.9 were considered normal, 25.0 - 29.9 were considered overweight, BMI ≥ 30 were considered obese. [26] Five ml of venous blood were withdrawn from PCOS patients, using a disposable syringe after 12-hour fasting.

Endocrine society clinical practice guidelines define Vitamin D deficiency as levels of 25OHD < 20 ng/mL, Vitamin D insufficiency as 25OHD between 21 and 29 ng/mL and normal as 25OHD level more than 30 ng/mL. [27]

The criteria of elevated HbA1c concentration (≥ 5.7%) with a threshold of ≥ 6.5% to diagnose T2DM were used as recommended by the American Diabetes Association. [28] Hyperuricemia was defined as an SUA level of at least 6 mg/dl in women.[29]

Data were checked and fed on computer system. The statistical analysis was made by the use of the Statistical Package for Social Sciences (SPSS) version 26. Standard statistical methods were used to determine the mean and standard deviation (SD), t-test for Equality of Means, Levene's Test for Equality of Variances were used. P-value ≤ 0.05 was considered to represent statistical significance.

The official permissions of the health directorate of Basra was done, informed consent was obtained from all participants. An assurance of anonymity was provided. The participants were told that the information is for scientific research only.

Results

The tables are comparison between the samples and the comparative sample through fixed factors, which are the age and variable factors, namely uric acid, vitamin D, HbA1c and BMI, all of which were clear statistical difference between the sample and the comparative sample except age.

Table1: demographical distributions of means and standard deviations between the study and control groups for modifiable and non-modifiable risk factors.

Variable	Case& Control	Mean	Std. Deviation
BMI	Case	25.8	4.06
	Control	24.64	2.28
Vit.D	Case	22.01	7.38
	Control	27.7	4.85
Uric Acid	Case	4.31	1.00
	Control	4.00	0.61
HBA1C	Case	5.55	1.08
	Control	5.10	0.48
Age	Case	24.30	6.01
	Control	23.27	5.90

Table 2: Equality of mean differences among variable (age, BMI, Vitamin D, Uric Acid, HBA1C) Between studied and Control group.

Levene's Test for Equality of Variances				t-test for Equality of Means				95% CI	
Variable	F	Sig.	t	df	Sig.	Mean Difference	Std. Error Difference	Lower	Upper
BMI	55.967	.000	3.550	398	0.000	1.16950	0.32943	0.52-	1.81
VIT.D	24.07	.00	-9.138-	398	0.00	-5.70 -	0.62	-6.93	-4.48
Uric Acid	39.737	.000	3.709	398	.000	.31000	0.08358	0.14	0.47
HBA1C	83.972	.000	5.342	398	.000	.44850	0.08395	0.28	0.61
Age	1.916	.167	1.720	398	.086	1.02500	0.59609	-0.14	2.19

Discussion

This study aimed to investigate the modifiable and non-modifiable factors associated with the occurrence of Polycystic Ovary Syndrome (PCOS) in a sample of women at reproductive age. Our findings demonstrate significant differences between women with PCOS and those without, in terms of BMI, Vitamin D levels, uric acid levels, and HbA1c, while age showed no significant difference.

BMI and PCOS: our results indicate that women with PCOS had significantly higher BMI compared to the control group. This finding aligns with previous studies, which suggest that obesity exacerbates insulin resistance (IR) and contributes to the pathophysiology of PCOS [9,10,18] . The relationship between obesity and PCOS is well-documented, highlighting the importance of weight management in the treatment and management of PCOS symptoms.

Vitamin D levels: the significant difference in Vitamin D levels between the PCOS and control groups underscores the potential role of Vitamin D in the development and exacerbation of PCOS. Vitamin D deficiency was prevalent among women with PCOS, which is consistent with prior research indicating that 67% to 85% of women with PCOS have Vitamin D levels below 20 ng/ml[12] . Vitamin D is crucial for various biological functions, including insulin sensitivity and hormonal regulation , which are often disrupted in PCOS patients [11]. Our findings suggest that addressing Vitamin D deficiency might be a beneficial strategy in the management of PCOS.

Uric Acid Levels: elevated uric acid levels were observed in women with PCOS compared to the control group, which supports the hypothesis that PCOS is associated with metabolic syndrome and related complications such as hyperuricemia [20]. High uric acid levels may reflect underlying metabolic disturbances, including insulin resistance and obesity, both of which are common in PCOS [9,10].

HbA1c and Insulin Resistance: our study found higher HbA1c levels in the PCOS group, indicating poorer glycemic control and higher insulin resistance compared to the control group. This finding is consistent with the well-established link between PCOS and increased risk of type 2 diabetes and metabolic syndrome. Insulin resistance is a key component of PCOS pathophysiology, contributing to hyperandrogenism and ovarian dysfunction [14-17]. These results highlight the importance of monitoring and managing blood glucose levels in women with PCOS to prevent long-term complications.

Age and PCOS: interestingly, there was no significant difference in age between the PCOS and control groups, suggesting that the other variables (BMI, Vitamin D, uric acid, HbA1c) play a more critical role in the development and manifestation of PCOS symptoms than age alone. This finding is important as it emphasizes that PCOS can affect women across a wide age range within the reproductive period, and age should not be considered a limiting factor in diagnosis and treatment.

Study Limitations

Several limitations of this study should be acknowledged. First, the study was conducted in a specific geographic region, which may limit the generalizability of the findings to other populations. Second, potential confounding factors such as lifestyle, diet, and physical activity were not controlled for, which could influence the results.

Conclusion

In conclusion, this study provides evidence that higher BMI, lower Vitamin D levels, elevated uric acid, and higher HbA1c are significantly associated with PCOS. These findings highlight the importance of comprehensive management strategies that address not only the reproductive aspects of PCOS but also metabolic and nutritional factors. Future research should aim to further elucidate the mechanisms linking these factors to PCOS and evaluate the effectiveness of targeted interventions in improving the health outcomes of women with PCOS.

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