

Correlation Between Serum Uric Acid, Vitamin D and HbA1c and the Occurrence of Polycystic Ovarian Syndrome

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Abstract

Background: Polycystic ovary syndrome (PCOS) is a global hormonal disorder affect a considerable number of women annually. It is marked by hyperandrogenemia, which is an increase in the production of testosterone in the ovaries, and insulin resistance.

Objectives: The study aimed to determine the interaction between blood level of uric acid, vitamin D, and HbA1C in individuals with polycystic ovarian syndrome.

Materials and Methods: The study utilized patient data from a medical center in Karbala. The data (levels of uric acid, vitamin D, and HbA1C) were collected from medical records for 30 randomly selected female patients diagnosed with polycystic ovarian syndrome. These patients' ages ranged from 18 to 42 years. The data were collected and analyzed statistically by using GRAPH PAD PRISM software.

Results: findings of this study indicate that women diagnosed with polycystic ovarian syndrome had elevated levels of uric acid in their bloodstream (SUA) in comparison to women who do not have polycystic ovary syndrome. The incidence of hyperuricemia in female diagnosed with (PCOS) was significantly high (P value 0.01) compared to normal range. Vitamin D was also significantly more than normal (p value 0.01) while HbA1C was not significantly difference (p value 0.054)

Conclusion: Our findings indicate that women diagnosed with polycystic ovarian syndrome exhibit elevated amounts of vitamin D in their bloodstream, even in patient with normal or overweight. Elevated testosterone levels could potentially enhance vitamin D storage. The findings demonstrated slight non-significant rise in HbA1c levels in relation to body mass index. The findings revealed an increase in uric acid levels in relation to body mass index.

العلاقة بين حمض اليوريك في الدم وفيتامين دي والهيموغلوبين السكري وحدوث متلازمة المبيض المتعدد الكيسات

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الخلاصة

المقدمة: متلازمة المبيض المتعدد الكيسات هو اضطراب هرموني شائع لدى النساء. ويتميز بفرط الاندروجين بالدم وهو زيادة في انتاج هرمون التستوستيرون في المبايض، ومقاومة الانسولين.

الأهداف: هدفت الدراسة إلى تحديد العلاقة بين مستويات حمض اليوريك في الدم وفيتامين د ونسبة لدى الأفراد المصابين بمتلازمة المبيض المتعدد الكيسات.. الهيموغلوبين السكري

المواد والطرق: استخدمت الدراسة بيانات المرضى من أحد المراكز الطبية في كربلاء. تم جمع البيانات (مستويات حمض اليوريك وفيتامين د والهيموغلوبين السكري) من السجلات الطبية ل 30 مريضة تم اختيارها عشوائيا وتم تشخيص اصابتهم بمتلازمة المبيض المتعدد الكيسات. وتراوحت اعمار هؤلاء المرض بين 18 و 42 عاما. تم جمع العينات وتحليلها احصائيا باستخدام برنامج (GRAPH PAD PRISM)

النتائج: تشير نتائج هذه الدراسة إلى أن النساء المصابات بمتلازمة المبيض المتعدد الكيسات لديهن مستويات مرتفعة من حمض اليوريك في مجرى الدم مقارنة بالنساء اللاتي لا يعانين من متلازمة المبيض المتعدد الكيسات. كانت نسبة الإصابة بفرط حمض يوريك الدم لدى النساء المصابات أعلى مقارنة بالمعدل الطبيعي ($p=0.01$) فيتامين د ايضا كان اعلى من المعدل الطبيعي لدى النساء المصابات بالمبيض متعدد الكيسات ($p=0.01$) اما الهيموغلوبين التراكمي فلم يكن بمستويات اعلى او مهمة احصائيا ($p=0.054$).

الاستنتاج: تشير النتائج التي توصلنا إليها إلى أن النساء المصابات بمتلازمة المبيض المتعدد الكيسات يظهرن كميات مرتفعة من فيتامين د في مجرى الدم، حتى في المرضى ذوي الوزن الطبيعي أو الزائد. يمكن لمستويات هرمون التستوستيرون المرتفعة أن تعزز تخزين فيتامين د. أظهرت النتائج ارتفاعاً طفيفاً غير ملحوظ في مستويات HbA1c فيما يتعلق بمؤشر كتلة الجسم. وكشفت النتائج عن زيادة في مستويات حمض اليوريك فيما يتعلق بمؤشر كتلة الجسم.

1. Introduction

Polycystic ovarian syndrome (PCOS) was firstly described in 1935 by Stein and Leventhal (Motlagh Asghari et al., 2022). PCOS is a prevalent hormonal pathological condition in women who characterized by significant elevations in ovarian androgen production (hyperandrogenemia) and insulin resistance. While the exact cause of PCOS is still unknown, around 80% of affected women have insulin resistance and hyperinsulinemia. These conditions can lead to long-term effects such as an elevated risk for diabetes mellitus, dyslipidemia (abnormal blood lipid levels), and cardiovascular disease.

According to the National Institutes of Health's (NIH) diagnostic features, a comprehensive examination of women predicts 4–10% of women of reproductive age worldwide to have Polycystic Ovary Syndrome (PCOS). While PCOS can manifest at any age, the majority of cases typically occur between the ages of 20 and 30 or at beginning with the onset of menstruation (menarche) (Witchel, Oberfield and Peña, 2019). The causes of polycystic ovary syndrome remain unclear but genetic and environmental factors still play a vital role in developing this disease. However, elevated levels of androgen hormone disrupt ovarian function, resulting in dysregulation of reproductive hormones and impaired follicular development and ovulation (Motlagh Asghari et al., 2022).

PCOS appears with a range of clinical features that differ in type and severity in women. The most common symptoms include irregularity in the menstrual cycle and excessive bleeding, which occurs due to a persistent thickening of the uterine lining, excessive hair growth, or the appearance of hair in previously hairless parts of the body, such as the face, back, belly, and chest. Infertility or difficulties in achieving pregnancy, hormonal fluctuations, and weight variations can cause headaches (Sidra et al., 2019). The most efficient approach to managing PCOS symptoms is to closely monitor the patient's health state and adhere to a healthy lifestyle. This involves eating nutritious and well-rounded food, engaging in consistent physical exercise, and maintaining a healthy body weight, minimize or cease smoking and heavy alcohol consumption. Furthermore, in addition to complying with the prescribed treatment, a physician may also suggest alternative medications for PCOS management. For instance, one can use hormonal contraceptives to suppress the menstrual cycle and metformin to lower insulin resistance (Teede et al., 2018). Considerable number of studies showed that a number of markers could be fluctuated in the patient who suffer this syndrome such as uric acid, vitamin D, glucose metabolism disorder and other disturbances.

In humans, uric acid, specifically in the form of hydrogen urate ions, is the end result of the breakdown of purine metabolism. It is eliminated from the body via urine. However, in the majority of mammals, uric acid is converted to allantoin by the enzyme uricase through additional oxidation (Luo, Do and Liu, 2006). In male the concentration range of uric acid is about 25–80 mg/L and about 15–60 mg/L in women (Borghi et al., 2014).

Vitamin D is a collection of fat-soluble molecules that play a major role in enhancing the absorption of calcium, magnesium, and phosphate in the intestines. Additionally, vitamin D is essential for maintaining the balance of calcium in the body and regulating metabolism (Lehmann et al., 2015). Research identified vitamin D as the precise dietary deficit responsible for causing rickets, a disorder in children that is a sign of osteomalacia (Reid, Bolland and Grey, 2014).

Glycated hemoglobin (HbA1c) is a type of hemoglobin that is bonded to a sugar molecule chemically. The process of sugars binding to hemoglobin is known as glycation. The reference standard for measuring this is based on HbA1c, which is defined as beta-N-1-deoxy fructosyl hemoglobin (Shubrook Jr, 2010). We primarily measure HbA1c to ascertain the average blood sugar level over a three-month period. It could be ordered for diagnosis of diabetic patients and assessment of glycemic control.

The test is restricted to a three-month average because the average lifespan of a red blood cell is four months or 120 days (DM, 2008). Glycated hemoglobin causes a rise in highly reactive free radicals within blood cells, modifying their cellular membrane characteristics. As a result, clumps of blood cells form and the thickness of the blood increases, resulting in a reduction in blood circulation efficiency. Glycated hemoglobin can cause harm through inflammation, leading to the production of atherosclerotic plaque (atheroma) (Currie et al., 2010).

The present study attempts to examine the association between level of serum uric acid, vitamin D, and HbA1c levels and the occurrence of polycystic ovarian syndrome (PCOS) in women.

1. Patients and Methods

Data of this study were collected from patients record sheets in the Gynecology and Obstetrics Hospital in the Kerbala governed (from September 2023 to November 2023). thirty women were diagnosed with polycystic ovarian syndrome were selected in this research and their information were taken from their medical record sheets. The age of selected patient was range 18-48 years old. The levels of serum uric acid, vitamin D, and HbA1C were tested in the hospital laboratories and written in patients' sheets and used in this research in addition to the body mass index, marital status, residency, living standards, and family history of PCOS were recorded also.

1.1. Statistical Analysis

The collected data were analyzed statistically using the GRAPH PAD PRISM software, specifically version 5. Data mean value plus or minus the standard deviation was used. the dissimilarities across groups was tested using unpaired t-tests. Pearson's correlation coefficients to assess the correlation between the biochemical markers under study. A 'P' value less than 0.05 was considered to be statistically significant.

2. Results

The socio-demographic data of the selected patients were explained in Table 1 below, the percent of each group was found. The patients were divided into two age group (18-30year) and (31-42 year).

Table 1: Socio-Demographic Analysis of the Patients

Parameter	No	Percentage%
Age		
18-30	15	50
31-42	15	50
BMI		
Normal	12	40
Overweight	8	26.7
Obese	10	33.3
Marital status		
Single	9	30
Married	21	70
Residency		
City	27	90
Rural	3	10
Living standards		
Middle	16	53.3
Good	12	40
Very good	2	6.7
Family History		
No	19	63.3
Yes	11	36.7

In Table 2, minimum and maximum values of the variables were explained in addition to the Mean $\pm$ SD. One- sample t-test for the three markers is shown in Table 3.

Table 2: Demographic Statistics for Biochemical Parameters

Parameter	Minimum	Maximum	Mean $\pm$ SD
Age	18	42	29.93 $\pm$ 7.488
BMI	20.8	47.1	28.06 $\pm$ 6.225
Vitamin D	5.00	36.25	15.91 $\pm$ 7.056
HbA1c	4.4	9.7	6.13 $\pm$ 1.448
Uric acid	2.70	6.70	4.71 $\pm$ 1.106
BMI: Body Mass Index, HbA1C: Glycated hemoglobin, SD: Standard Deviation			

Table 3: Comparative Assessment of Vitamin D, Uric Acid, and HbA1c Levels with Statistical Evaluation

Parameter	Mean	SD	T- Value	P- Value
Vitamin D	15.91	7.056	18.693	0.001 S
Uric acid	4.71	1.106	3.559	0.001 S
HbA1c	6.13	1.448	2.005	0.054 NS
HbA1C: Glycated Hemoglobin, S: Significance differences, NS: Non-significant differences, P value $\geq$ 0.05				

Independent t-test and ANOVA test were also done for each age group to analyze the collected data and to interpret the correlation between the age factor and the markers levels. As shown in Table 4.

Table 4: Comparison of Vitamin D, HbA1c, and Uric Acid Levels Between Different Age Categories

Parameter	Age category	Mean $\pm$ SD	t-value	P-value
Vitamin D	18-30	16.3933 $\pm$ 6.42200	0.366	0.717 NS
	31-42	15.4367 $\pm$ 7.83751		
Hba1c	18-30	6.207 $\pm$ 1.5392	0.285	0.777 NS
	31-42	6.053 $\pm$ 1.4004		
Uric Acid	18-30	4.5600 $\pm$.84752	0.780	0.442 NS
	31-42	4.8773 $\pm$ 1.32747		
SD: Stander deviation, NS: Non-significant, P value $\geq$ 0.05				

ANOVA test was done to examine the effect of body weight (BMI) on the level of each variable (Uric acid, HbA1C, and Vitamin D) as it is clear in Table 5.

Table 5: Comparison of Vitamin D, HbA1c, and Uric Acid Levels Across BMI Categories

Parameter	Underweight	Normal	Overweight	Obese	P Value
Vitamin D	0	14.51 $\pm$ 7.96	16.40 $\pm$ 5.67	17.20 $\pm$ 7.29	0.671 NS
HbA1c	0	6.44 $\pm$ 1.488	5.75 $\pm$ 1.282	6.06 $\pm$ 1.582	0.585 NS
Uric acid	0	4.433 $\pm$ 1.186	4.64 $\pm$ 0.926	5.12 $\pm$ 1.122	0.351 NS
NS: non-significant, P value $\geq$ 0.05					

Pearson correlation test was done to examine the correlation between Glycated Hemoglobin level with the levels of Vitamin D and Uric acid.

Table 6: Pearson Correlation Analysis of HbA1c with Vitamin D and Uric Acid Levels

		Parameter	
		Vitamin D	Uric acid
Hba1c	Pearson Correlation	0.156	0.346
	P Value	0.411 NS	0.061 NS

3. Discussion

Polycystic ovary syndrome is considered now one of the most complicated and common disease that affect huge number of women around the world. It could be treated if diagnosed early and prescribed the correct medical treatment. Number of hormonal and biochemical changes could be occurred with this disorder. Examination of these changes could help physician to diagnose the case correctly. Uric acid, Vitamin D, and HbA1C are among these changes. Alteration in the levels of these markers could be examined in regular test for patient with PCOS. The total number of patients with polycystic ovary syndrome in this study was 30 with age between 18-42 years old (Table 1). Patients are divided into two groups based on their age, Ages 18-30 and Ages 31-42. The patients' weight was also recorded that 12 women were normal, 8 were overweight, and 10 obese according to the BMI calculation. The finding of this study shows that both women who are normal weight or obese are susceptible to polycystic ovary syndrome that mean overweight is not the only risk factor of this disease but still play a significant role. One other hand, the result also conducted that married women suffering from this disease more than that of single women by 70%, as the number of married women was 21 and this may relate to hormonal changes and activity of ovarian and reproductive system. There is no clear effect of genetic history on this disease, based on the results, where the percentage of women with a history of the disease was 36.7% and the percentage of women without a history of the disease was 63.3 that mean this pathological condition could occur without presence of genetic factor. The study found that women with polycystic ovarian syndrome (PCOS) have significantly elevated amounts of vitamin D in their blood (15.91) compared to normal levels, particularly among those who are overweight or normal BMI. Women diagnosed with Polycystic Ovary Syndrome (PCOS) may exhibit an enhanced capacity to retain and accumulate vitamin D within their bodies. Elevated testosterone levels may contribute to the accumulation of vitamin D. Several scientists have been demonstrated a notable increment in the occurrence of hyperuricemia in patients diagnosed with polycystic ovary syndrome (PCOS) compared to those without PCOS (4–7). Simultaneously, individuals with this disease usually develop obesity in their abdominal parts, a condition usually resulted in hyperinsulinemia and elevated testosterone levels. Considering that hyperuricemia might worsen insulin resistance and metabolic dysfunction (22), it is intriguing to investigate the correlation between uric acid levels and the distribution of body fat in patients with PCOS. This study is the first investigation into the connection between uric acid levels and body fat distribution in patients with PCOS, as far as we know. In our study, the incidence of hyperuricemia among patients with polycystic ovarian syndrome was 4.71%, which is higher than the usual ratio of 1.106. The data we collected indicated a favorable correlation between blood uric acid levels and increased total testosterone in women diagnosed with polycystic ovarian syndrome. The results of the study revealed that patients with polycystic ovary syndrome (PCOS) who had high levels of uric acid in their blood were more likely to be obese, with a ratio of 5.12 ± 1.122 . Polycystic ovarian syndrome (PCOS) is a prevalent endocrine condition in women that results in infertility. Most women with PCOS experience insulin resistance and elevated hemoglobin A1c levels. Thyroid dysfunction can have an impact on HbA1c levels and the outcomes of ovulation stimulation program. The result of this research doesn't show this result and this may relate to time of HbA1C

test or the number of the samples. The study found that women with polycystic ovarian syndrome display elevated amounts of vitamin D in their blood, specifically 15.91 units greater than the average levels. This effect is particularly pronounced in women who are overweight or obese. Women that were diagnosed with (PCOS) may exhibit an enhanced capacity to retain and accumulate vitamin D within their bodies. Elevated amounts of testosterone can facilitate the accumulation of vitamin D. This aligns with a 2014 study that the journal Nutrition and Metabolism published: The study revealed that women with PCOS exhibited elevated amounts of vitamin D in their bloodstream compared to women without the illness. The journal Clinical and Experimental Endocrinology published a study in 2016 that showed women with PCOS had higher blood levels of vitamin D than those without the illness, especially those who were overweight or obese. Velija Asmi et al. found that 68% (41 out of 60) of patients with polycystic ovary syndrome (PCOS) had vitamin D deficiency (VDD). Among these patients, 54% (22 individuals) were obese, while 46% (19 individuals) were non-obese (Velija-Asimi, 2014). Additionally, another study found that the prevalence of vitamin D deficiency (VDD) was higher in obese women with polycystic ovary syndrome (PCOS) compared to lean women with PCOS, with rates of 70% and 60%, respectively (Tsakova, Gateva and Kamenov, 2012). These studies suggest that the risk of VDD is the rational cause of deaths among patients with PCOS. Epidemiological studies indicate a correlation between low levels of vitamin D and impaired ability to clear glucose, reduced insulin production, and increased insulin resistance (Kotsa et al., 2009). Studies have found that vitamin D influences glucose metabolism, potentially leading to metabolic and endocrine abnormalities in women with PCOS. (Liu et al., 2009).

Multiple scientific studies have demonstrated that the occurrence of hyperuricemia is significantly greater in patients diagnosed with polycystic ovary syndrome (PCOS) compared to those without PCOS. Our study found that patients diagnosed with polycystic ovarian syndrome exhibited hyperuricemia (p value = 0.01). The elevation of serum uric acid may be related to high level of testosterone in women with PCOS. These findings are consistent with earlier research indicating that the occurrence of hyperuricemia in individuals with PCOS ranges from 25.48% to 26.29%, which is three times greater than the prevalence among women in the overall population (Dehlin, Jacobsson and Roddy, 2020) (Zhao et al., 2012). Published papers indicate that individuals with polycystic ovary syndrome (PCOS) who have high levels of uric acid in their blood are more likely to be obese. Furthermore, this association between hyperuricemia and obesity is statistically significant. When BMI was taken into account. Instead of no significant correlation between body mass index and occurrence of PCOS in this study may because of low volume of data, A previous study found a substantial positive correlation between the visceral obesity index and uric acid levels in patients with polycystic ovary syndrome (PCOS) (Zhao and Huang, 2015). The outcome data of the present study indicate that PCOS patients had a high average HbA1c level but not significantly differences. The incidence of increased HbA1c in patients with PCOS may occur because of chronic inflammation with PCOS. The slightly elevated HbA1C may revealed that patient have pre-diabetic state and may develop diabetes mellitus if not treated. According to a study conducted by Sebastião Medeiros (De Medeiros et al., 2014), 38% of patients with polycystic ovary syndrome (PCOS) had increased levels of HbA1c. 35% of the population had prediabetes, while 3% had diabetes. Jin-Joo Kim discovered that 31.2% of women with polycystic ovary syndrome (PCOS) had high levels of HbA1c (Kim et al., 2010). Table 6 shows that very low correlation between HbA1C and Vitamin D level ($r=0.156$) and low correlation between HbA1C and uric acid level ($r=0.346$) and this agree with other studies with same results.

4. Conclusion

PCOS is an endocrine disease can affect women with all ages. Affected women could be with normal, overweight or obese. Women with PCOS exhibit high levels of Uric acid and this may related to increased levels of certain hormones such as testosterone while HbA1C exhibit non-significant differences levels and this may require long time to be elevated. Vitamin D also show higher level than to be expected.

5. Ethical Approval

The research was approved by the scientific and ethical committee of pharmacy college, Kerbala university on 30 Nov. 2023.

6. Source of supply

Self-funded study

7. Conflict of interest:

The authors declare no conflict of interest

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