ISSN: 0067-2904

Importance of Lactate Dehydrogenase, Cortisol, Dopamine, Zinc, and Vitamin D3 in Iraqi Patients with Polycystic Ovary Syndrome

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Received: 8/11/2023 Accepted: 2/2/2024 Published: 28/2/2025

Abstract

Polycystic ovary syndrome (PCOS) comprises a multiplex hormone-based disorder that is typically accompanied by several complications, including irregularity of menses, excessiveness of hair growth in face and body, acne, obesity, diminished fertility, and higher probability of developing diabetes. Many hormones and enzymes may undergo changes in PCOS patients. This study involved 138 women who were separated into two groups: PCOS women (n=90) with an age range of (22-45) years, and apparently healthy women (n=48) representing the control group with age being matched to the patient group. All patients attended to Al-Kadhimiya Teaching Hospital, Department of Obstetrical and Gynecology and diagnosed by a consultant physician. Following peripheral blood withdrawal (5 ml) from participants, serum was isolated and placed in an Eppendorf tube until used. ELISA kit was used to determine serum levels of some biochemical parameters (Lactate dehydrogenase, cortisol, dopamine, zinc, and vitamin D3). The results showed that LDH level was significantly elevated (P<0.0001) in PCOS patients (2.55±0.70) compared with the control (1.16±0.18). While, significantly lower levels of cortisol, dopamine, zinc and vit D3 (P<0.0001) were demonstrated in PCOS group (4.30±1.62, 48.45±26.27, 5.21±1.85 and 271.19±36.07, respectively), compared with the control (9.40±0.76, 252.52±47.47, 8.26±1.42, and 328.82±21.33, respectively). The study found an elevation in the serum level of LDH in PCOS patients compared to control, while cortisol, dopamine, zinc, and Vit D3 recorded a significant decrease in patients as compare to control.

Keywords: PCOS, LDH, Cortisol, Dopamine and Vitamin D3

أهمية نازعة هيدروجين اللاكتات والكورتيزول والدوبامين وفيتامين D3 في المرضى العراقيين المصابين بمتلازمة تكيس المبايض

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الخلاصة

متلازمة تكيس المبايض (PCOS) هي حالة هرمونية معقدة. يمكن أن تكون PCOS مرتبطة بمشاكل

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مثل الدورات الشهرية الغير منتظمة، ونمو الشعر الزائد على الوجه والجسم، وحب الشباب، والسمنة، وتقليل الخصوبة، وزيادة خطر الإصابة بالسكري. هناك العديد من الهرمونات والإنزيمات التي يمكن أن تتغير في مرضىPCOS . في هذه الدراسة، شملت 138 امرأة تم تقسيمهم إلى مجموعتين: نساء مصابات بمتلازمة تكيس المبايض وكان عددهم (90 امرأة) في الفترة العمرية من (22–45) عامًا، بالإضافة إلى نساء أخريات بصحة جيدة (48 امرأة) يمثلن مجموعة السيطرة وتم مطابقة أعمارهن مع مجموعة المرضى. تمت متابعة جميع المرضى في مستشفى الكاظمية التعليمي، قسم النساء والتوليد، وتم تشخيص مرض التكيس بواسطة طبيب استشاري. تم سحب 5 مل من الدم من كل مشاركة، وعزل المصل ووضعه في أنابيب eppendorf حتى الاستخدام. تم استخدام تقنية ELISA لتحديد مستوى بعض الجوانب الكيميائية (لاكتات ديهيدروجيناز، الكورتيزول، الدوبامين، الزنك وفيتامين D3) في المصل أظهرت النتائج زيادة كبيرة في مستويات إنزيم LDH (P<0.0001) في المرضى (0.70±2.55) مقارنة بمجموعة السيطرة (1.16±0.18). بينما كان هناك انخفاض ملحوظ في مستوى الكورتيزول، والزنك، وفيتامين D3، والدوبامين (P<0.0001) في مصل مرضى المرضى(1.62±4.30 ، 1.85±5.21، 36.07±271.19، و48.±26.2745) على التوالي، مقارنة بمجموعة السيطرة (0.40±9.76، 8.26±1.42، 328.82±21.33، و252.52±47.47) على التوالي. وجدت الدراسة ارتفاعا في مستوى LDH في مصل الدم لدى مرضى متلازمة تكيس المبايض مقارنة بالسيطرة، في حين سجل الكورتيزول والزنك وفيتامين د3 والدوبامين انخفاضا ملحوظا في المرضى مقارنة بالسيطرة.

1. Introduction

Polycystic ovary syndrome (PCOS) represents the most frequently encountered endocrine disease by women in their age of fertility. Increased serum concentrations of dehydroepiandrosterone-sulfate and testosterone, associated with ovulation-related complications, comprise the major features of PCOS. Along with additional hormonal defects, e.g. hyperprolactinemia, thyroid diseases, and adrenal hyperplasia, disturbances in the immune system are also common features for PCOS [1,2]. Cytomegalovirus (CMV) and Epstein-Barr virus (EBV) may contribute to hormonal and metabolic disorders involving the HPA axis, which contributes to the emergence of PCOS [3]. Lactate dehydrogenase LDH is one of the highly essential enzymes taking part in the anaerobic metabolic pathway and a member in the oxidoreductase class of enzymes. It exerts its action through catalyzing the reactions through which lactate is reversibly converted to pyruvate, through which NAD+ is also reduced to NADH in a reversible reaction [4]. Also, one of the main uses of LDH level is in inspecting tissue damage caused by infections [5]. The occurrence of LDH is ubiquitous in every type of tissue in various animals, plants, and other types of organisms. It is an essential factor in controlling the processes of DNA metabolism and gluconeogenesis. The enzyme was analyzed in a wide spectrum of organisms, revealing a high degree of structural preservation [6]. High serum LDH concentration could be the result of a multiplicity of factors, e.g. cardiovascular diseases, liver dysfunction, muscular trauma, anemia, malignancies, and hepatic disorders, along with several infectious diseases that include encephalitis, meningitis, encephalitis, and HIV. Furthermore, LDH serves as a non-specific indicator of tissue turnover, a metabolic process that occurs normally in the body [7, 8]. Serum LDH levels and its isoenzymes pattern are useful tumor markers for diagnosis and post-therapy surveillance in patients with ovarian dysgerminomas [9]. The glycolytic pathway is known to become more active in malignant tissue and, in these tissues, LDH passes to the circulation in great amounts because of the necrosis [10]. Cholesterol is the primary product in the process of cortisol synthesis, which takes place in the cortex layer of the adrenal gland. In earlier events, the pituitary gland releases the adrenocorticotropic hormone (ACTH) which stimulates higher numbers of LDL receptors and further activates cholesterol desmolase, leading to the conversion of cholesterol to pregnenolone and, thereby, cortisol. Different investigations reported higher incidence of stress in women with PCOS, which might be caused by the

activation of the feedback mechanism that involves the hypothalamus–pituitary–adrenal (HPA) axis [11]. It is well recognized that the activation of this axis is affected by different factors, including circadian rhythm, emotion, pain, anxiety, and particularly stress that apparently has a direct link to PCOS [12]. Such association might provide an explanation to the higher serum cortisol levels encountered in PCOS patients. Since cortisol is one hallmark of stress, elevated cortisol can affect ovulation and stress can suppress the surge of luteinizing hormone (LH) necessary for ovulation, leading to anovulatory cycles (cycles where ovulation doesn't occur) that contribute to pathogenic of PCOS [12]. The initial discovery of dopamine (DA) was reported by Arvid Carlsson, not only as an adrenaline precursor, but also as an independent neurotransmitter in the nervous system [13]. The hypothalamic-pituitary-gonadal (HPG) axis is the main actor in maintaining a properly functioning reproduction system. The hormones LH and FSH are released from the anterior pituitary under the induction of pulsating secretions of GnRH. The HPG axis also acts under regulation mechanisms exerted via different hormones, peptides, and neurotransmitters [14]. Deviations in any of the regulatory elements could lead to the induction of endocrinopathies, including PCOS. Previous reports suggested that thecal and stromal cell hyperplasia in the ovary, as well as hyperandrogenism, can result from excessive LH that is maintained via highly frequent GnRH pulses [15]. It is also noteworthy that dopamine is utilized as an antagonist to the release and pulsatility of GnRH release [16]. Zinc (Zn) is a highly important micro-element which occurs in the majority of tissues and fluids, mainly the intracellular compartments. In humans, the overall amount of zinc is approximately 2-3 g, of which a percentage of < 0.2% (15 µmol/L) exists in the plasma [17]. Zinc is vital for the reproductive system to function properly and for its cells to fulfill their extensive differentiation and proliferation requirements. This is true for both males and females, since zinc is vital for spermatozoans to develop, eggs to ovulate, zygote to be fertilized, pregnancy to take place, fetus to develop, and birth to occur [18]. Vitamin D is a steroid hormone with clear involvement in calcium metabolism and bone structure. Vitamin D is also highly important to prevent various complications, such as autoimmune conditions, high blood pressure, malignancies, diabetes, and obesity. Recent research indicated that deficient vitamin D is a common problem encountered in PCOS, with this vitamin status showing an association with the functioning of the reproduction system, changes in metabolism, and mental health. In addition, a negative association was found between the serum levels of Vitamin D and androgens [19]. Since the causes of polycystic ovary syndrome have not yet been understood and there is no clear explanation for its pathogenesis, the present study was designed to shed light on some factors such as LDH, cortisol, dopamine, zinc, and vitamin D3 that affect the functioning of the ovaries and may have a role in the pathogenesis of PCOS.

2.Methodology

A total of 90 female participants with PCOS were involved in this research. They were recruited from the Obstetrics and Gynecology department of Al-Kadhimiya Teaching Hospital, Baghdad, Iraq. The diagnosis of PCOS was confirmed by a consulting physician and was based on the Rotterdam criteria from 2003, as outlined in the Rotterdam ESHRE/ASRM Consensus of 2004 [20]. To be diagnosed with PCOS, patients needed to meet at least two out of the following three criteria: (i) Irregular or absent ovulation (ii) exhibiting either biochemical or clinical signs of hyperandrogenism, which includes hirsutism, alopecia, or acne, (iii) the presence of polycystic ovaries as observed through transvaginal ultrasound, indicating morphological changes in the ovaries [20]. The study was conducted between August 2022 and June 2023, and the age range of the participants was between 22 and 45 years. The control group, consisting of 48 fertile women, was matched in age to the PCOS patients. These women underwent ultrasound examinations to confirm

normal ovarian morphology and were tested for hormonal levels. The ethical approval was issued by the Ethics Committee (Iraqi Ministry of Health and Environment; Reference No. 360, Nov 31, 2022) and all participants provided written consent. To conduct various analyses, a 5 ml blood sample was taken from individual participants. After separation and storage in Eppendorf tubes, serum was maintained in a -20 ℃ until the time of analysis. Serum level of lactate dehydrogenase, cortisol, dopamine, zinc and vitamin D3 were determined for both patients and control group by using an enzyme linked immunosorbent assay (ELISA). The procedure was done according the following category numbers provided from commercial ELISA kits (My Bio source): lactase dehydrogenase (LDH; Cat No. MBS269509), cortisol (Cat No. MBS766080), dopamine (Cat No. MBS2700357), zinc (g #K387-100) and vitamin D3 (Cat No. MBS264661).

1.1. Measurement of BMI and waist circumference

According to the accepted classification by the World Health Organization (WHO), overweight and obesity in adults are based on body mass index (BMI), which is determined by dividing an individual's weight in kilograms by the square of height in meters. Based on this classification, individuals with a BMI greater than or equal to 25 kg/m^2 are considered overweight, while those with a BMI greater than or equal to 30 kg/m^2 are classified as obese. For a height less than 80-88 cm, women with weight higher than 88 kg are obese, although it may vary depending on race or ethnicity [21].

2.2. Statistical analysis

IBM Statistical Package for Social Sciences (version 29, Chicago, IL, USA) was employed to analyze the obtained data statistically. Expression of data was conducted in terms of frequency, percentage, mean, standard deviation, and range (minimum-maximum values). For quantitative data, Students-t-test was applied to examine possible significant differences between two independent means. Whereas ANOVA test was applied for those among more than two independent means. Pearson Chi-square test (χ^2-test), occasionally supported by Yate's correction or Fisher Exact test, was applied to examine possible significant differences among percentages. Differences were considered as statistically significant at $P \leq 0.05$.

3. Results and discussion

3.1 Anthropometric features of patients and control

Results in Table 1 revealed that the age mean values for the PCOS and control were 28.8 ± 5.9 vs. 28.0 ±5.6 years respectively, which ranged between 22-45 years for both groups. No statistically significant differences were obtained between the study groups according to age ($p = 0.064$); however, the mean values for age for both groups were almost identical, which is in a good accordance with groups matching. Along with increasing age, fertility declines especially in women [22]. Age is an important parameter that affects fertility. The impact of age in PCOS has captivated the attention of many researchers and served as the initial driving force behind several investigations into PCOS worldwide [23]. In this study, age range was fixed for the selected groups to be between 22-45 years (Table 1), which falls in the range of the female reproductive age which is between 15-49 years according to Letona and others [24]. It is important to mention that the postponement of childbearing poses a significant obstacle in the field of reproductive medicine due to the influential effect of advancing age on the likelihood of successful conception, whether through natural means or with the assistance of medical interventions [25]. Highly statistically significant differences were observed in the mean of the BMI (28.9 ±5.5 vs. 23.26 ±4.23 kg/m^2; $P \leq 0.001$) between PCOS and control groups, respectively. In addition, a high prevalence with percentage of 42.9 % was observed in obese subgroup in PCOS patients as compared with control (13.3 %). Obesity is strongly

linked to infertility through different ways, including molecular level; females with obesity face more challenges when trying to get fertility treatments and having a successful pregnancy. This can make their economic and social stressors even worse [26]. There is a strong association between BMI and getting the chance of pregnancy, specially in PCOS patient. However, among women diagnosed with PCOS, a greater initial BMI was linked to reduced chance of achieving pregnancy. Nevertheless, losing weight was associated with higher chance of achieving pregnancy as compared to maintaining a stable weight or gaining weight [27]. The results of waist circumference show a highly statistically significant difference ($P \leq 0.001$) when PCOS group was compared to the control group, with a higher mean in PCOS group (95.45 ±15.61 vs. 87.01 ±8.88 cm, respectively) . These results agreed with similar results obtained by Millan-deMeer and others [28]. The results in table 1 shows also a slightly lower waist circumference's mean value in comparison to that reported for a different non-Iraqi population of PCOS patients (90.9 ± 9.4 cm)in the research of Ishrat and co-workers [29]. Age, BMI and waist circumference are important clinical parameters, especially in the diagnosis and treatment of PCOS. Therefore, these measurements were collected, studied and detailed in Table 1 with full ranges and further specific calculations.

Table 1: Baseline characteristics in patients with PCOS and control.

		PCOS		Controls		P value
		No	%	No	%	
Age (years)	<20years	2	2.2	2	4.0	0.265
	20---24	22	24.4	20	40.0	
	25---29	30	33.3	11	22.0	
	30---34	15	16.7	9	18.0	
	=>35years	21	23.3	8	16.0	
	Mean±SD (Range)	28.8±5.9 (18-39)		28.0±5.6 (19-35)		0.064
BMI (Kg/m2)	Underweight (<18.5)	1	2.9	2	13.3	0.074
	Normal (18.5-24.9)	6	17.1	6	40.0	
	Overweight (25-29.9)	13	37.1	5	33.3	
	Obese (=>30)	15	42.9	2	13.3	
	BMI: Mean±SD (Range)	28.90±5.50 (15.57-38.22)		23.26±4.23 (17.80-30.33)		0.001*
	Weight (Kg) Mean±SD (Range)	72.64±14.05 (45-115)		60.54±8.03 (45-76)		0.0001*
	Height (cm) Mean±SD (Range)	1.59±0.07 (1.50-1.73)		1.62±0.05 (1.53-1.70)		0.152
Waist circumference (cm)	Underweight	13	14.4	3	6.0	0.066
	Normal (80-88)	27	30.0	24	48.0	
	Obese	50	55.6	23	26.0	
	Mean±SD (Range)	95.45±15.61 (60-124)		87.01±8.88 (58.42-96.52)		0.001*

3.1.1 Demographic and baseline characteristics in PCOS patients and control group

The demographic characteristics of the study groups are presented in Table 2. These include maternal status, menstrual cycle, past medical history, use of contraceptive pills, family history in PCOS, duration of disease (years), and history of abortion. In the control group, participates were separated into married (79%) and not married (20.8), with regular menstrual cycle. It is evident that the two groups are approximately well matched and the obtained results could be considered creditable.

Table 2: Baseline and clinical characteristics in patients with PCOS and control.

Characteristics		PCOS		Control	
		No	%	No	%
Married	Yes	69	76.7	38	79
	No	21	23.3	10	20.8
Menstrual cycle	Irregular	87	96.7	-	-
	Regular	3	3.3	48	100
Use of contraceptive pills	Yes	5	5.6	-	-
	No	85	94.4	48	100
Past medical Family history	Yes	9	10.0	-	-
	No	81	90.0	48	100
Duration (years)	<1year	35	38.9	-	-
	1---4	37	41.1	-	-
	5---9years	18	20.0	-	-
	Mean±SD (Range)	2.42±2.34 (1M-9Y)		-	-
History of abortion	Yes	32	35.6	-	-
	No	58	64.4	-	-

Long and irregular menstrual cycles, a hallmark of PCOS, have been associated with higher androgen and lower sex hormone binding globulin levels [30]. In this study, only 5 of the women with PCOS were in use of contraceptive pills (metformin) to treat infertility, regulate menstrual disturbances, alleviate symptoms of hyperandrogenism, reduce weight and manage the metabolic disorder. A previous study found that PCOS patients with a positive paternal history of both diabetes mellitus (DM) and hypertension (HT) have an adverse endocrine and metabolic profile. A paternal history of DM and HT poses a risk to PCOS [31]. The long duration of polycystic ovary disease may lead to complications such as increased risk of cardiometabolic disease, diabetes and cancer [32,33]. In this study, 35% of women with polycystic ovary syndrome had a history of miscarriage. A previous study revealed that PCOS has a greater impact on the risk of spontaneous abortion in pregnant women than previously thought. This could be attributed to the high prevalence of obesity in their population. Women

having PCOS are more likely to have an unfavorable pregnancy and birth outcome, and may require more monitoring throughout pregnancy and parturition [34].

3.2. Serum levels of biochemical parameters of patients and control group

The mean values of biochemical parameters in PCOS and control are revealed in Table 3 and Figures 1, 2, 3, 4 and 5. The study showed that LDH levels were significantly elevated ($P \leq 0.0001$) in PCOS (2.55±0.70) compared with the control (1.16±0.18). While, significantly lower levels of cortisol, dopamine, zinc and Vit D3 ($P \leq 0.0001$) were recorded in PCOS (4.30±1.62, 48.45±26.27, 5.21±1.85 and 271.19±36.07, respectively) compared with the control (9.40±0.76, 252.52±47.47, 8.26±1.42 and 328.82±21.33, respectively).

3.2.1. LDH Serum level in PCOS patients and control

Figure 1 shows a significant rise in the serum LDH level of PCOS patients ($P \leq 0.001$) in comparison to control. Previous research recorded an elevation in LDH in PCOS compared to the control [35, 36]. High serum levels of LDH might be caused by faster release, resulting from more vicinal location inside the cell and/or stronger blood or lymph flow, in addition to the genetic influence [37]. Earlier research demonstrated that LDH located within the granulosa cells is expressed in higher rates as compared to the enzyme in oocytes [38]. Also, a remarkable increase in LDH expression was observed in PCOS patients in the late stage of follicular development [39]. Other studies suggested that diet rich in trans and saturated fatty acids results in higher content of unhealthy LDH cholesterol in the circulation. Such type of diet was reported to have association with inflammatory responses and insulin resistance, a condition known to fundamentally result in Type 2 Diabetes. As patients with PCOS are at higher risk to be insulin sensitive, reduction in the consumption of trans and saturated fats is essential [40]. The present study disagrees with an earlier report that suggested the LDH expression was reduced in PCOS patients. Surplus levels of the nerve growth factor in the follicular fluid of PCOS patients could cause a significant reduction in the expression of LDH, impairment in the granulosa cells/oocytes communication, and reduction in oocyte developmental capacity. Others suggested that the low level of LDH may be affected by glycolysis in ovarian tissues and found a significant reduction in LDH expression in ovarian tissues of rats suffering from PCOS [41, 42].

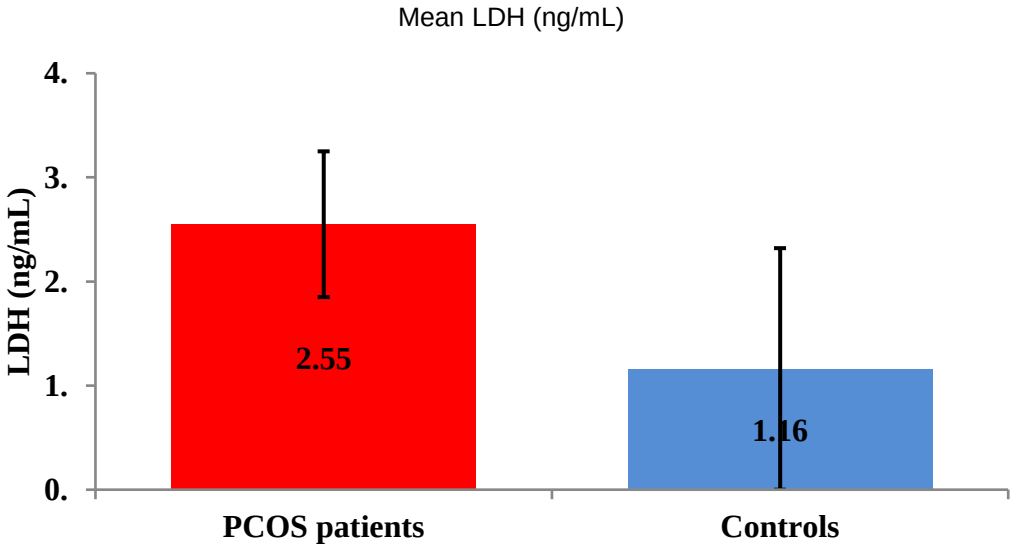

Figure 1: The mean serum levels of LDH in PCOS and control subjects.

3.2.2. Cortisol serum level in PCOS patients and control

The results demonstrated in Figure 2 reveal a significant decrease in mean cortisol level in the sera of PCOS patients ($P \leq 0.001$) in comparison to that in the control group. Nevertheless, this observation does not agree with several previous studies which stated that cortisol is relatively higher in PCOS patients [43, 44]. This could be explained by the effect of the metformin treatment that PCOS patients may follow, which may lead to lower cortisol levels. Thus, there is a need to more extensive research to explain the effect of metformin and its interaction with cortisol, particularly in the case of PCOS. Earlier investigation also suggested that PCOS patients did not show elevated levels of cortisol [45]. This may due to several reasons such as the treatment, psychological state of patients and even the time of sample collection (before the menopause cycle or after).

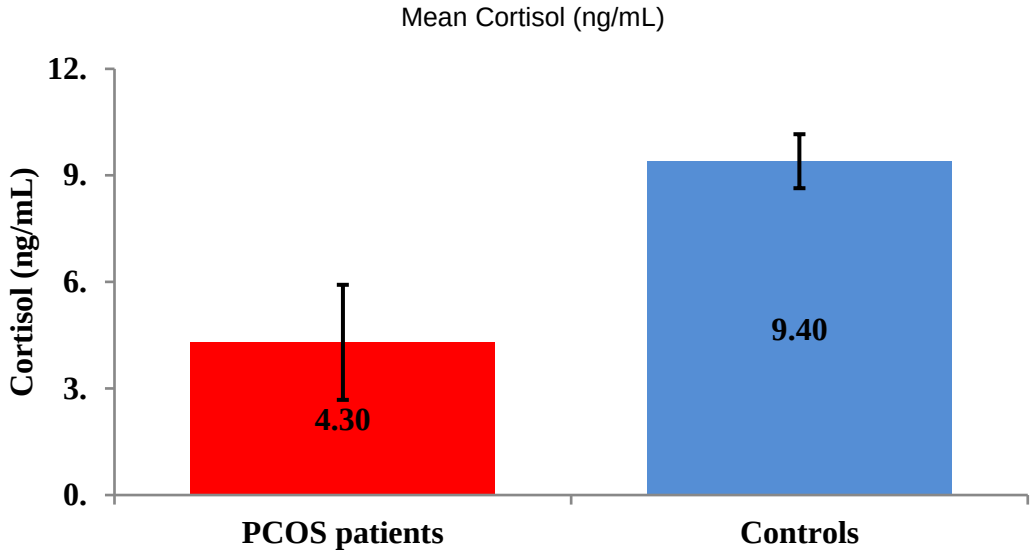

Figure 2: The mean serum levels of cortisol in PCOS and control subjects.

3.2.3. Dopamine serum level in PCOS patients and control

The results shown in Figure 3 and Table 3 reveal a significant decrease in mean dopamine level in the sera of PCOS patients ($P \leq 0.001$) in comparison to the control. These results are in agreement with those reported earlier [46,47]. PCOS patients were also reported with reduced serum levels of norepinephrine, dopamine and serotonin [48]. However, it is difficult to measure the levels of these transmitters within the brain's GnRH regulatory regions because such tissues are very difficult to obtain. It will be very helpful to understand these transmitters within tissues for better understanding of the pathogenesis of PCOS [49]. For this specific purpose, tissues from the hypothalamus, pituitary gland, hippocampus and frontal cortex were previously examined. There are relatively rare reports covering the role of transmitters in PCOS. Dopamine is relatively deficient in patients with PCOS, which was suggested to have association with the raise in GnRH secretion, along with being an indication of changes in catecholamine metabolism and brain opioid activity which were also reported in PCOS [50]. Some evidence exists on reduced levels of DA in PCOS patients. DA acts in lowering GnRH levels and therefore decreased DA levels result in elevated LH levels in patients with PCOS [51]. The reduction in the dopaminergic tone, along with the downregulation in Drd2 signaling, could provide an explanation for the elevated VEGF and vascularization, which result in a raise in the tendency to develop ovarian hyper-stimulation syndrome in women with PCOS [52]. The results of this study did not agree with those of previous studies that

reported significantly higher levels of DA in PCOS patients and suggested this rise to be triggering the role of catecholamines in the pathogenesis of PCOS [53, 54]. Another study suggested that the elevated levels of dopamine in depressed women who had chronic infection of toxoplasmosis may reflect the effect of chronic infection that may alter the expression of dopamine, which skews the immune response towered Th 17 that affects the expression level of proinflammatory cytokines and neutrophils response [55].

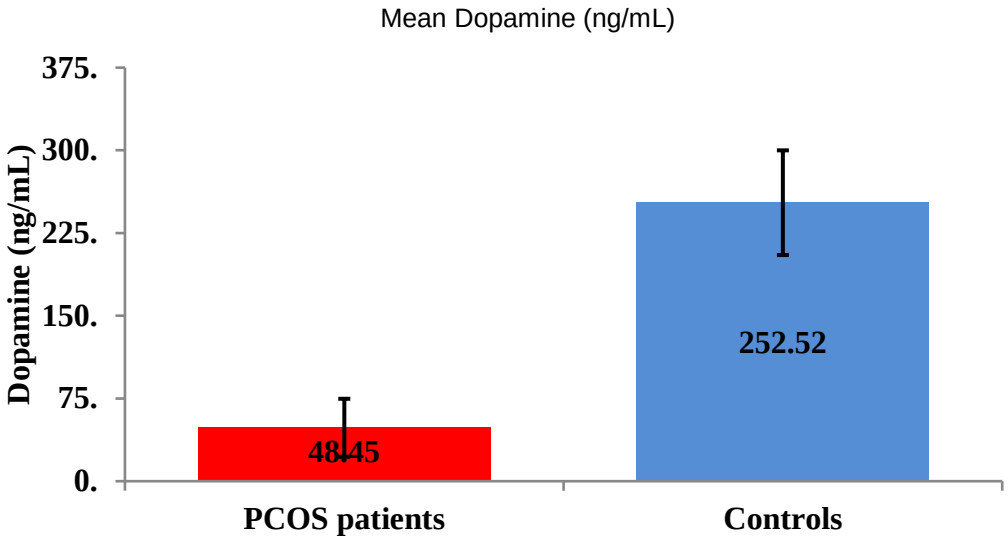

Figure 3: The mean serum level of dopamine in PCOS and control subjects.

3.2.4 Zinc serum level in PCOS patients and control

The results demonstrated in Figure 4 and Table 3 show a significant decrease in the mean zinc level in the sera of PCOS patients ($P \leq 0.001$) in comparison to the control. Also, 82 (91%) of PCOS patients, as compared to 32 (64%) of the control group, had lower values than the control. Our results agree with those reported earlier [56, 57]. Zinc deficiency shows higher incidence in PCOS patients, which is particularly obvious in PCOS patients with insulin-resistance. In fact, one study revealed that zinc concentration is the most accurate predictor of PCOS, being better than the BMI and cholesterol level [58]. Insufficient zinc could lead to higher risks of diabetes, obesity, and glucose intolerance; all considered as essential factors contributing to worse development of PCOS [59]. Furthermore, several indicators of insulin resistance (e.g., low insulin level) and of low lipid levels (e.g., total cholesterol and triglycerides) were previously reported. The levels of testosterone and dehydroepiandrosterone were reported to be lower. Zinc has an essential contribution in the protection of this system via its antioxidative properties. Also, zinc supplements appear to cause improvement in PCOS symptoms, especially within women developing dysregulated insulin resistance and lipid balance [60]. Moreover, lower zinc concentrations in PCOS patients were associated with impairment in the metabolic processes of hormones, fat, and glucose, along with elevated expression of oxidative stress biomarkers [61]. A study performed by [62] noticed that it is also worth noting the positive relationship between the concentration of zinc in follicular fluid and the quality, as well as maturation status, of oocytes retrieved from the ovaries of individuals with a history of infertility associated with PCOS.

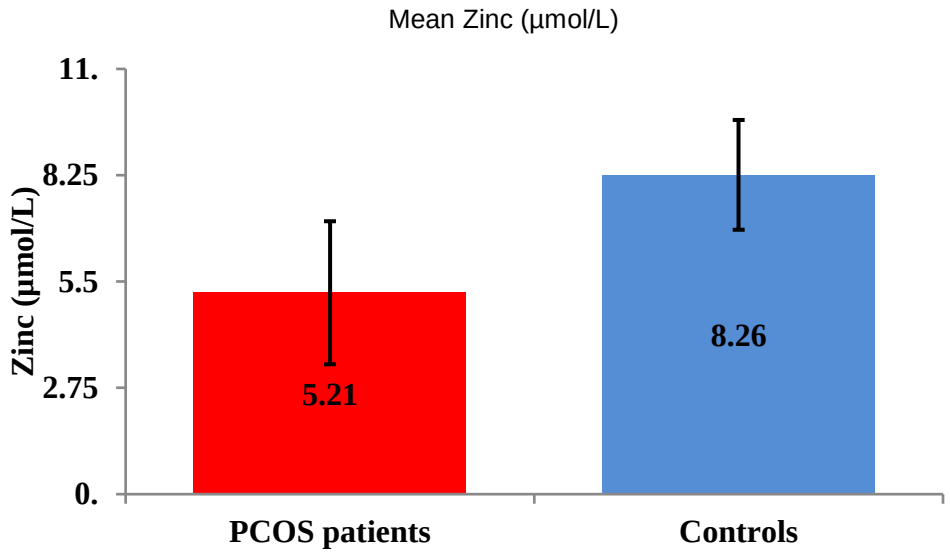

Figure 4: The mean serum level of zinc in PCOS and control subjects.

3.2.5 Vitamin D_3 serum level in PCOS patients and control

Figure 5 and Table 3 show a significant decrease in mean vit D_3 level in the sera of PCOS subjects $P \leq 0.001$ in comparison to the control. Deficient vitamin D might lead to higher tendency to develop PCOS [63]. A previous study suggested that the decreased levels of VD3 lead to increase the incidence of *Toxoplasma gondii* infection in atherosclerosis patients [64]. Another research demonstrated that vitamin D supplementation could cause improvement of blood pressure profiles and reduction of insulin resistance, as well as reduction in the concentrations of total testosterone and androstenedione in PCOS [65]. Decreased vitamin D concentration was shown to occur in obese women who have PCOS in comparison with non-obese PCOS women [66]. Impairment in glucose tolerance and higher risk of type 2 diabetes are observed, along with increased insulin resistance, in PCOS patients. Also, higher risk of type 2 diabetes was demonstrated to have association with deficient vitamin D [67]. A meta-analysis study revealed that patients deficient in vitamin D develop higher risk of PCOS, which also results in disorders in the metabolism and endocrine system [68]. The current study not only investigated the biochemical parameters in PCOS but also acknowledges the significance of previous studies on Iraqi women, exploring infertility and its correlation with inflammation and various epidemiological conditions [69, 70].

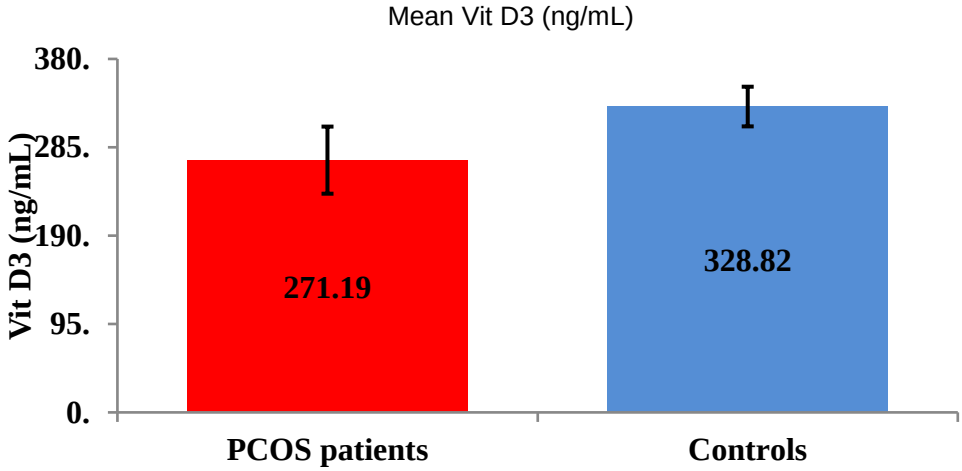

Figure 5: The mean serum level of vit D3 in PCOS and control

Table 3: Biochemical parameters in PCOS and control subjects.

Parameters	PCOS Patients (mean± SD)	Average	Controls (mean± SD)	Average	P value
LDH (ng/mL)	2.55±0.70	1.360-4.488	1.16±0.18	0.787-1.505	0.0001*
Cortisol (ng/mL)	4.30±1.62	0.502-7.100	9.40±0.76	7.889-10.598	0.0001*
Dopamine (ng/mL)	48.45±26.27	22.5-200.2	252.52±47.47	152.6-352.1	0.0001*
Zinc (µmol/L)	5.21±1.85	2.778-10.0	8.26±1.42	4.241-10.0	0.0001*
Vit D3 (ng/mL)	271.19±36.07	90.2-316.9	328.82±21.33	283.1-449.1	0.0001*
*Significant difference between two independent means using Students-t-test at 0.0001 level					

4. Conclusions

Since the results of the current study showed a significant increase in LDH, and a significant decrease in cortisol, dopamine, vitamin D3, and zinc levels, this may indicate a strong relationship of these factors with the pathogenicity of PCOS. Hence, these factors must be taken into consideration when following up patients.

However, the study encountered an important limitation, namely, the sample size of PCOS. Although PCOS has been a well-known disease for a long time, its causes and treatment are still unknown. Therefore, some biochemical and immunological factors were selected and statistically linked to some human characteristics of the patients in an attempt to reveal some aspects of the pathology of PCOS. We also aimed to uncover therapeutic targets that might be possible to be used to reduce the effects of this syndrome, which can affect and cause other diseases such as diabetes and cardiovascular disease.

Conflicts of interest

There are no conflicts of interest.

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