Journal of Medical and Surgical Practice (JMSP)
ISSN: 2664-1704
Vol. 09, No. 04, 2023

The Relation Between PCOS and Level of Serum Vitamin D in Sample of Iraqi Women

Dr. Baydaa Hameed Hassan Al-Obaidi[1*], Dr. Nassrin Malik Aubead[2]

1. MBChB, Diploma in gynecology and Obstetrics

2. Assistant professor (Obstetrician and gynecologist), Department of Obstetrics and Gynecology-Hammurabi College of Medicine /University of Babylon

* *Corresponding Author* ***nissrenmalik@uobabylon.edu.iq.***

Original Article

Abstract

Background: *Polycystic Ovary Syndrome presents as a heterogeneous and complex pathology that is characterized by chronic anovulation with hyperandrogenemia, insulin resistance, and infertility.*

Objective: *To assess the effect of vit D on polycystic ovarian disease.*

Patients and method: *A case control study carried at our hospital for one year duration in the period from 2021-2022, in which 200 women were recruited and divided into two groups (100 women as case group, and another 100 as healthy control group). The diagnosis of PCOS were done according to Rotterdam criteria.*

Results: *The mean level of vit D in case group was (17.4±8.3) while in control group was (26.6±7.9) with significant difference (P<0.001). the mean age of patients group was (27.8±4.1) years, while for control was (28.1±5.6) years with no significant difference (P=0.6). Moreover the BMI was (29.3±3.3) kg/m2 in case group while it was (28.7±2.9) kg/m2 in control group with no difference (P=0.1).*

Conclusion: *Vitamin D were significantly decreased in PCOS women than that in healthy women.Insulin levels, Lipid profile and Hormonal profile of PCOS women were disturbed signifciantly compare to healthy women*

Keywords: *Vitamin D, Polycystic Ovary Syndrome, Iraqi women*

Received : July, 2023, **Published**: September, 2023

Citation: Al-Obaidi B.H.H, Aubead N.M The Relation Between PCOS and Level of Serum Vitamin D in Sample of Iraqi Women. JMSP 2023; 9(4): 65

1. INTRODUCTION

Polycystic Ovary Syndrome (PCOS) presents as a heterogeneous and complex pathology that is characterized by chronic anovulation with hyperandrogenemia, insulin resistance, and infertility (1). His etiology is still poorly understood, however, it is believed that its origin is multifactorial, and influenced by both genetic and environmental components (2, 3). PCOS affects 5-20% of the female population of reproductive age worldwide, being the most common endocrinological condition in this population group (1,4). This, in addition to the overall increase in its incidence makes it important to prepare health personnel on the subject (5,6). Getting a diagnosis can be a cumbersome process for both treating physicians and patients, because they can be found from asymptomatic cases, to cases with the manifestations typical with hyperandrogenism, hirsutism, acne, oligomenorrhea and amenorrhea (3,7). A timely diagnosis , a correct advice and an adequate start of treatment are vital to avoid or minimize conditionsacute and chronic conditions associated with this syndrome (2,8).

Etiology and pathogenesis:

Due to the heterogeneous nature of PCOS, various theories have been developed regarding its pathophysiology. Family addition suggests that there is an inherited genetic factor involving the presence of some genetic variants and mutations in various genes. The interaction between these genetic factors, combined with the presence of environmental factors such as diet and lifestyle, the chances of developing this syndrome (9). Studies agree that the pathogenesis of PCOS is based on the hypersecretion of androgens by thecal cells, which overexpress various enzymes such as CYP11A, CYP17 and 17bHSD2, responsible for of the synthesis of androgens. There are three prevalent factors that explain this hyperandrogenism: dysfunction way. In conclusion, the deliberated plans can be castoff alone or composed, and the status of adapting each patient's method with the highest the suitable substitutes obtainable are tinted.

Insulin resistance and hyperinsulinemia-induced thecal cell hypertrophy; and increased luteinizing hormone (LH) secretion due to dysfunction of the hypothalamic-pituitary axis (10).

Ovarian dysfunction is caused by an alteration in androgenic production that occurs at the ovarian level and adrenal. The activity of cytochrome P450c17 is increased, so the production of androgens. This leads to an alteration of ovulation and therefore of menstrual cycles. Histologically, an increased follicular recruitment was observed and the selection process

decreases. This an increase in the follicle pool also leads to the overproduction of androgens (11). Insulin resistance and hyperinsulinemia is of high prevalence in patients with PCOS, mainly when they are associated with obesity and metabolic syndrome (12). This condition is caused by the alteration to post-receptor level of peripheral tissues, which are unable to use glucose, producing a state of compensatory hyperglycemia and hyperinsulinemia. As a result, production increases androgenic activity of the ovary and adrenal glands, increases the secretion of LH in the the theca and there is a decrease in the levels of steroid hormone transporting globulin (SHBG) and insulin-like growth factor-binding protein-1 (IGF1-BP), which raises circulating levels of androgens and IGF1 (11). Neuroendocrine alteration also plays an important role in this pathology. LH is considered the the main factor of hyperandrogenism in PCOS. The increase in the frequency of hormone release gonadotropin-releasing hormone (GnRH) promotes the production of LH and decreases the release of FSH, which it promotes the production of androgens and interferes with follicular development. The hyperandrogenic state prevents the negative feedback that, under normal conditions, progesterone would provide on the GnRH pulsations (13).

Diagnosis

There is controversy about which criteria to use to make the diagnosis. However, globally it agrees to use the Rotterdam criteria, which stipulate that at least two of the criteria listed below: polycystic ovary morphology, oligo-anovulation and hyperandrogenism (14). To assess ovarian morphology, intravaginal ultrasound performed in the follicular phase is used by which an antral follicle count and ovarian volume measurements are made. We talk about morphology of polycystic ovaries when 12 or more follicles can be observed; or when a volume is documented ovarian of 10 ml or higher than this (14). Oligo-anovulation may present as oligomenorrhea or amenorrhea. Oligomenorrhea is referred to when patients report 8 or fewer menstrual periods per year or when these have a duration of more than 35 days. On the other hand, when patients deny bleeding for more than 90 days, and pregnancy has been ruled out, there is talk of amenorrhea (15). In a more unusual, this pathology may present as polymenorrhea, in this case patients report cycles short menstrual periods of up to 21 days or less; or menstrual cycles of normal duration in those documented serum progesterone less than 4 ng/ml while the patient is in the luteal phase (14).

Finally, the hyperandrogenism can be characterized by three main signs: hirsutism, acne and alopecia. The modified Ferriman-Gallway scale represents a useful tool for evaluating hirsutism put it takes into account epidemiological parameters for different population groups. Biochemically, to determine the presence of hyperandrogenism, the concentration of total testosterone and sex hormone-transporting globulin to calculate the concentration of free testosterone. Also, the measurement of dehydroepiandrosterone sulfate (DHEAS) can be performed, which corresponds to another androgenic molecule (16).

Vitamin D

Vitamin D (VD) is a fat-soluble vitamin obtained with the diet or via endogenous synthesis mediated by cutaneous exposure to solar radiation. It is metabolized in the liver and then in the kidney to obtain its active metabolite 1,25-dihydroxy-VD, also known as calcitriol, which interacts intra-cellularly with its receptor Vitamin D Receptor, regulating the transcription of numerous genes. Recently, the potential immunomodulatory role of VD has been positioned, evidenced through the presence of receptors for it in cells of the immune system (17). At the level of innate immunity, it decreases the secretion of pro-inflammatory cytokines, promotes the secretion of anti-inflammatory cytokines at the mast cell level and decreases the dendritic ability to mature and activate T cells. Regarding adaptive immunity, it would be associated with a change in the cytokine secretion profile of Th2 lymphocytes, suppression of the Th1 and Th17 response, decreased proliferation of B lymphocytes and antibody production, finally leading to an anti-inflammatory scene (18).

2. PATIENTS and METHODS

A case control study carried at our hospital for one year duration in the period from 2021-2022, in which 200 women were recruited and divided into two groups (100 women as case group, and another 100 as healthy control group). The diagnosis of PCOS were done according to Rotterdam criteria. Baseline criteria, menstrual history, clinical criteria of PCOS according to Rotterdam criteria were collected from both groups. We investigated the respondents for serum 25(OH) D and metabolic markers.

Ethical consent:

An informed written consent was obtained from the patient or relatives of the patients. The study was done after approval from the Ethical Committee of our hospital. The Declaration of Helsinki, the World Medical Association's code of ethics for studies involving humans, guided the conduct of this work.

Statistical analysis:

Data were transferred into computerized database using the Microsoft office , Excel Program , 2022 and the statistical package for social sciences version 28 (SPSS 28). All variables were tested for errors or inconsistency using the Case Summaries in SPSS and descriptive statistics. Descriptive statistics presented as mean, standard deviation, frequencies and proportions according to the variable type. Al statistical tests performed at a level of significance of 0.05 or less to be significant.

3. RESULTS

The mean age of patients group was (27.8±4.1) years, while for control was (28.1±5.6) years with no significant difference (P=0.6). Moreover the BMI was (29.3±3.3) kg/m2 in case group while it was (28.7±2.9) kg/m2 in control group with no difference (P=0.1) (**Table 1**). mean of Waist: hip ratio was (0.80±0.06) in case group and (0.79±0.02) in control group with no difference (p=0.1). mean of FBS was (85.20±12.33) mg/dl in case group and (84.8±11.79) mg/dl in control group with no difference (p=0.8). mean levels of fasting insulin was (15.12±3.63) mU/mL in case group and (10.6±3.29) mU/mL in control group with no difference (p=0.8). Significant differences were found between the studied groups among each of LH, progesterone, testosterone, Free Androgen index, SHBG, and DEHEA (P<0.05) (**Table 2**). There is significant differences between both groups in the study among HDL, and TG (P<0.05) (**Table 3**). The mean level of vit D in case group was (17.4±8.3) while in control group was (26.6±7.9) with significant difference (P<0.001) (**Table 4**).

Table 1. Baseline criteria in the studied groups

Variable	Case group (PCOS) (mean ± SD)	Control group (mean ± SD)	P. value
Age (years)	27.8±4.1	28.1±5.6	0.6 Ns
BMI (kg/m^2)	29.3±3.3	28.7±2.9	0.1 Ns
Waist: hip ratio	0.80±0.06	0.79±0.02	0.1 Ns
FBS (mg/dL)	85.20±12.33	84.8±11.79	0.8 Ns
Fasting insulin (mU/mL)	15.12±3.63	10.6±3.29	<0.001

S: significant, Ns: not significant

Table 2. Comparison between mean hormonal assay in the studied groups

Variables	PCOS (mean ± SD)	Control (mean ± SD)	P. value
FSH (IU/L),	9.08±4.11	9.30±3.58	0.6 Ns
LH (mIU/ml)	17.23±8.50	6.60±2.93	0.001 S
Progesterone (ng/ml)	1.04±0.06	1.07±0.08	0.002 S
Estradiol,(pg/dl)	53.72±5.61	52.77±4.82	0.2 Ns
Testosterone (nml/L)	2.06±0.45	1.77±0.38	<0.001 S
Free Androgen index	7.82 ± 1.81	2.37 ± 0.27	<0.001 S
SHBG nmol/l	34.0±12.23	55.42±17.05	<0.001 S
DEHEA µg/dl	159.27±54.13	141.87±31.64	0.006 S

S: significant, Ns: not significant

Table 3. Comparison between mean lipid profile in the studied groups

Group	PCOS (mean ± SD)	Control (mean ± SD)	P. value
LDL (mg/dL)	133.42±29.65	130.32±27.13	0.4 Ns
HDL (mg/dL)	44.16±8.43	54.12±11.09	<0.001 S
TG (mg/dL)	141.01±22.57	94.87±16.03	<0.001 S
Cholesterol (mg/dL)	162.70±15.13	161.20±13.23	0.4 Ns

S: significant, Ns: not significant

Table 4. Comparison between mean levels of vit D in the studied groups

Group	Case group (PCOS)	Control group	P. value
No.	100	100	-
Vit D (ng/mL) mean ± SD	17.4±8.3	26.6±7.9	<0.001 S

S: significant

4. DISCUSSION

In the present study lipid parameters (TG and HDL) were significantly difference in POCS, HDL was significantly lower in PCOS compared to control, these findings consistent with several studies such as González A et al., study in 2011 in which a total of 117 subjects were enrolled. Of these, 93 females with IR were compared against 24 females without IR. Raised TGL/HDL ratio was identified in (61.4%) women with insulin resistance and (38.6%) women without insulin resistance,. The raised up TGL/HDL ratio was significantly linked with insulin resistance (19). Decrease levels of serum vit. D may aggravate the appearance of PCOS clinical symptoms, including IR, ovulatory and menstrual irregularities, decrease the fertility, hyperandrogenism, fatness and raise the risk of CV diseases. Several observational researches submit a likely role of vit. D in an opposite relationship amongst vitamin D level and metabolic instabilities in patients with PCOS, but it is still hard to draw a certain supposition in the fundamental association due to unpredictable outcomes from several separate studies and from a new meta-analysis study of a systematic analysis (20). The most common finding in the current study was significant decrease of vit D in PCOS group than that in control group which is in agreement with Thomson RL et al., study revealed that prevalence of vitamin D deficiency in PCOS women is about 67%-85%, with serum levels of vit D <20 ng/ml (21). But it is not in agreement with Moini A et al., study that found there is no significant statistical difference regarding the level of vit. D concentration between both groups of the study (women with PCOS and those without PCOS), in addition to that they revealed that there is a strong relation between deficiency of vit D and metabolic disease which may have countless consequence on public health (22). In a recent study carried by Gokosmanoglu F and his colleague the study consisted of 231 patients, with 86% of them belonging to Group 1 and the remaining 14% belonging to Group 2., the research findings indicate a correlation between

reduced levels of 25(OH)D3 and elevated androgen levels in women diagnosed with polycystic ovary syndrome. The inclusion of vitamin D insufficiency as an additional risk factor in the pathogenesis of polycystic ovary syndrome (PCOS) warrants consideration. It is hypothesized that administering vitamin D supplementation to women residing in regions with documented shortage may potentially mitigate the likelihood of polycystic ovary syndrome (PCOS) onset (23).

5. CONCLUSIONS

Vitamin D was significantly lower in PCOS women than that in healthy women. Levels of insulin, hormonal assay and lipid profile were significantly disturbed in PCOS women

Ethical Clearance:

Ethical issues were taken from the research ethics committee. Informed consent was obtained from each participant. Data collection was in accordance with the World Medical Association (WMA) declaration of Helsinki for the Ethical Principles for Medical Research Involving Human Subjects, 2013 and all information and privacy of participants were kept confidentially.

Conflict of interest: Authors declared none

Funding: None, self-funded by the authors

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