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ORIGINAL ARTICLE

Relationship of Vit D deficiency with Obesity, Metabolic abnormalities and Insulin resistance in patients with Polycystic Ovarian Syndrome

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ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is the leading endocrine disorder that affects women in their reproductive age with global prevalence of 6 to 26%. Many different studies have established a firm relationship between levels of vitamin D and various symptoms of PCOS that includes subfertility, cycle regulation, insulin resistance and hirsutism.
Aim: To validate the correlation of insulin resistance and obesity with vitamin D deficiency in women suffering with PCOS.
Methodology: A cross-sectional study was conducted including 110 PCOS patients. Anthropometric measures, demographics details, dietary and menstrual history were collected from the patients. Blood samples were also collected and analyzed for parameters of biochemical and hematological nature along with its hormone profile. All the data was analyzed statistically.
Results: Low Levels of vitamin D were observed to be greater in people considered overweight/obese as per their BMI. . The vitamin D deficient patients had significantly higher body weight (p = 0.05), BMI (0.01), testosterone (p = 0.03), LH (p=0.03) and serum calcium (p <0.0001). Univariate correlation analysis among all the important parameters and 25-hydroxyvitamin D revealed no significant correlation.
Conclusion: Vitamin D deficiency is quite commonly observed in patients dealing with PCOS and aggravates the abnormalities related to metabolism. For the prevention of adverse consequences, screening of PCOS patients for deficiency of 25-hydroxyvitamin D holds importance so that a suitable replacement therapy can be initiated.
Keywords: Vit. D deficiency, obesity, polycystic ovarian syndrome, insulin resistance

INTRODUCTION

Polycystic ovary syndrome (PCOS) is the leading endocrine disorders that affect women in their reproductive period, with being prevalent in 18% women of this age[1]. Characteristics of PCOS include infertility, elevated levels of androgen, existence of polycystic ovaries on ultrasound, hirsutism, menstrual dysfunction and hyperandrogenism.[2] An association between type 2 diabetes mellitus, risk factors of cardiovascular disease, compromised tolerance of glucose, dyslipidemia and PCOS has also been established.[3-4] Development of PCOS along with the clinical features are closely associated to insulin resistance .[2, 5-6] Prevalence of Insulin Resistance and obesity in women suffering from PCOS is 60%-80% and 95% respectively[2].

According to some recent studies, deficiency of vitamin D has been commonly observed in the patients of PCOS and that it is also linked with disorders of metabolism[7-9]. Upon comparison with the general population, vitamin D deficiency is found to be more prevalent in women with polycystic ovary syndrome[8,10]. Bone mineralization as well as the stabilization in the levels of calcium phosphate is carried out by vitamin D[11]. This steroidal hormone is either generated endogenously by a sunlight dependent reaction in the skin where cholesterol is converted into 7-dehydrocholesterol followed by hydroxylation in kidney and liver or is acquired through diet. D providing supplements of vitamin D for therapeutic purposes to treat PCOS is gaining attention in Pakistan and globally[12].

Many different studies have established a firm relationship between levels of vitamin D and various symptoms of PCOS that includes infertility, Insulin Resistance and hirsutism.[13-14] Concentration of serum 25-hydroxyvitamin D (25[OH]D) serves as the functional indicator about the status of vitamin D in the body and is widely accepted.[12] As per some studies, the average levels of 25OHD in women with PCOS were between 11 and 31ng/ml, which is lower than then the average female.[15-16,17] Furthermore, some observational studies determine relationships between the status of vitamin D in the body with markers associated with hyperandrogenism.

Thus, this study was conducted to validate the correlation of metabolic parameters, insulin resistance and hormonal parameters with vitamin D in the body in women suffering with PCOS.

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METHODOLOGY

Study setting, design and participants: The present study was cross-sectional research conducted from June 2021 to Dec 2021 over a six-month period at university of Lahore teaching hospital. The patients diagnosed with PCOS were recruited from the gynecology department of the hospital through non-probability consecutive sampling. The research study was initiated after the approval form the Ethical Review Board of the institute and written consents were taken from the participants.
Study participants: A total of 110 women were enrolled in the study. All the women included in the study were 18-40 years old, diagnosed with PCOS in accordance with Rotterdam criteria and had normal thyroid function. All the women who were pregnant or lactating and women consuming calcium and vitamin D supplements were excluded from the study. Women suffering from any other co-morbidities (such as hypertension, diabetes, kidney and liver diseases) and patients consuming any drugs which effect insulin sensitivity were also excluded from the study. The subject patients were classified into 2 groups based on the levels of 25-hydroxyvitamin D for comparison, where group A contained patients deficient in 25 hydroxyvitamin D while group B contained individual with normal levels of 25-hydroxyvitamin D.
Study measures: Clinical data along with details including age, BMI, drug history, dietary and menstrual history were collected from the patients. Samples of venous blood during fasting were also collected and analyzed for parameters of biochemical and hematological nature along with its hormone profile. The parameters included lipid profile, level of vitamin D, follicle stimulating hormone, luteinizing hormone (LH), prolactin, thyroid function tests, fasting insulin, calcium and testosterone.
Operational definitions: Rotterdam criteria was used to diagnose PCOS. Diagnosis of PCOS was determined to be successful if it at least fulfilled two of the following criteria: oligomenorrhea/ anovulation, hyperandrogenism that is either biochemical and/or clinical and detection of polycystic ovary by ultrasonography whereas in at least one ovary the small follicles are ≥ 12 and measure 2-9 mm and/or the ovarian volume > 10 cm^3[18].

Guidelines for clinical practice presented by endocrine society defines vitamin D deficiency when level of 25-hydroxyvitamin D becomes less than 20 ng/mL, vitamin D become insufficient with levels between 21 and 29 ng/mL and normal vitamin D to be more than 30 ng/mL[29]. During our study, all values including and exceeding 30 ng/mL were termed normal and any

value below 30 ng/mL was considered as a deficiency. Under weight, normal weight, overweight and obesity were considered as BMI ranging from 15 to 19.9, 20 to 24.9, 25 to 29.9 and 30 to 35 or greater.

Statistical analysis: All the data was processed and statistically analyzed using SPSS version 20. Data was depicted as standard deviation (SD) and mean and descriptive statistics were utilized to analyze the data. To compare the data among the groups we used Chi-square test and unpaired t-test. To perceive the relationship between 25-hydroxyvitamin D and other parameters of clinical nature, spearman's correlation was used. For all the tests performed, a two-tailed P<0.05 was deemed significant statistically. Permission was obtained from ethical committee to start this research.

RESULTS

Table 1: Comparison between both the groups with regard to demographic, body mass index and biochemical parameters

Variable	Group A 25[OH]D Deficient n = 99	Group B Normal 25[OH]D n = 11	p-value
Demographic and anthropometric characteristics			
Age (years)	29.7 ± 5.0	30.1 ± 7.1	0.53
Body wt. (kg)	73.9 ± 14.6	65.9 ± 12.7	0.05
BMI (kg/m^2)	30.8 ± 6.1	25.7 ± 5.9	0.01
Lipid profile			
Total Cholesterol (mg/dL)	183.6 ± 33.5	175.5 ± 31.2	0.37
Triglycerides (mg/dL)	138.9 ± 29.7	133.1 ± 29.9	0.65
LDL (mg/dL)	144 ± 21.1	143.1 ± 16.9	0.81
HDL (mg/dL)	41.8 ± 7.9	48.3 ± 7.2	0.007
Endocrine Parameters			
25(OH)D (ng/mL)	20.68 ± 0.26	30.63 ± 0.24	0.66
Testosterone (ng/dL)	74.6 ± 32	52.9 ± 40.1	0.03
T3 (pg/mL)	1.5 ± 0.3	1.4 ± 0.1	0.91
T4 (µg/dL)	10.1 ± 2.9	10 ± 3.1	0.09
TSH (µIU/L)	2.6 ± 1.4	2.4 ± 1.7	0.78
LH (IU/L)	36.7 ± 24.8	18.9 ± 5.3	0.03
FSH (IU/L)	6.7 ± 3.6	6.3 ± 3.8	0.72
Serum calcium (mg/dL)	7.8 ± 0.6	9.3 ± 0.6	<0.0001
Metabolic parameters			
Fasting glucose (mg/dL)	91.2 ± 10.5	87.4 ± 8.5	0.57
Fasting insulin (mIU/L)	16.5 ± 2.8	16.3 ± 2.4	0.89

BMI: Body Mass Index, LDL: Low Density Lipoprotein, HDL: High Density Lipoprotein, 25OHD: 25-Hydroxyvitamin D, TSH: Thyroid Stimulating hormone, LH: Luteinizing hormone, FSH: Follicle Stimulating hormone

Table 2: Association between 25[OH] Vit D and various parameters

Correlation of 25(OH)D with:	r	p - value
Anthropometric parameters		
BMI	– 0.016	0.78
Lipid parameters		
Total cholesterol	– 0.045	0.66
Triglycerides	0.105	0.29
LDL	– 0.059	0.61
HDL	– 0.125	0.23
Glycemic indices		
Fasting insulin	– 0.053	0.65
Hormonal characteristics		
FSH	– 0.16	0.23
LH	– 0.086	0.38
Testosterone	– 0.115	0.31

BMI: Body Mass Index, WHR: Waist to Hip Ratio, LDL: Low Density Lipoprotein, HDL: High Density Lipoprotein, HOMA-IR: Homeostatic Model Assessment Insulin Resistance, FSH: Follicle Stimulating Hormone, LH: Luteinizing Hormone

The mean age of the study participants is 29.8±5.1 years, mean body weight was 72.8±14.8 kg, mean BMI was 30.3±6.3 kg/m^2.Overall, 99 (90 %) of the women were deficient of Vit D3 levels. Low Levels of vitamin D3 were observed to be greater in people considered overweight/obese as per their BMI as presented in Figure 1. Demographical and biochemical differences among the two groups included in the study are presented in Table 1. The vitamin D deficient patients had significantly higher body weight (p=0.05), BMI (0.01), high density lipoprotein (HDL) (0.007) and significantly greater levels of testosterone (p = 0.03), LH (p = 0.03) and serum calcium (p < 0.0001). Univariate correlation analysis among all the important parameters and 25-hydroxyvitamin D is shown in Table 2. No significant correlation was observed between vitamin D and any parameters.

DISCUSSION

Our study is among those rare studies which associates deficiency of vitamin D with BMI, lipid parameters, glycemic and hormonal measures in women with PCOS in Pakistan. Our study reveals that the deficiency of vitamin D is very frequently observed in PCOS patients, occurring in 99/110 (90 %) women with PCOS. The rate of occurrence is similar with the previous studies conducted in developed countries which show the rate of vitamin D deficiency in about 85% of the women with PCOS [19]and also with another study conducted in Pakistan.[14] Our findings convey that the vitamin D replacement should be prescribed to all or any PCOS patient for the proper metabolic functioning.[2] In obese people, the sequestration of the fat-soluble vitamin D occurs in greater proportion in the adipose tissue and therefore, its bioavailability is decreased. On the other hand, obese individuals might tend to spend more time indoors and are less exposed to sunlight which leads to less biosynthesis of vitamin D in the skin. Dietary choice and metabolism of vitamin D might also be distinct among overweight and non-obese individuals.

Higher levels of LH in the PCOS patients with vitamin D deficiency are reported by our study which can be justified by the polymorphism of vitamin D receptors (VDR) and altered expression of aromatase gene in vitamin D deficiency which results in increased levels of LH, as described by previous studies.[20] Greater BMI of the vitamin D deficient patients might explain the related lower levels of HDL and is one of the characteristics of metabolic syndrome. Previously, the PCOS patients have been demonstrated to possess higher frequency of metabolic syndrome[20].

As per our data, insulin resistance was present in nearly all participants of the study. Association between symptoms of PCOS and the status of vitamin D has been demonstrated by many studies, but the studies were cross-sectional in nature thus establishment of causation cannot be done. However, it has been proposed that Action of insulin is enhanced by the biologically active state of vitamin D which enhances the synthesis of insulin and its release, expression of insulin receptors is also increased or proinflammatory cytokines are suppressed which are credited to mediate resistance to insulin[21].

According to our study, 25-hydroxyvitamin D was found to have no connection with parameters of clinical, hormonal and metabolic nature. Earlier studies inversely relate body weight, total cholesterol in the body, triglycerides and other disturbances related to metabolism found in the patients dealing with PCOS with 25-hydroxyvitamin D.[38] A small sample size might be the cause behind the disparity observed in our study.

Sample size being small along with cross-sectional study design proved to be the limitations of our study. Lastly, evaluation of presence of other possible confounding factors like dietary patterns or time spent outdoor was not done by us as these factors has the ability to affect levels of vitamin D in the serum.

CONCLUSION

Low levels of vitamin D is quite commonly observed in patients dealing with PCOS and aggravates the abnormalities related to metabolism. For the prevention of adverse consequences, screening of PCOS patients for deficiency of 25-hydroxyvitamin D holds importance so that a suitable replacement therapy can be institutionalized. Moreover, we did not find any correlation between serum vitamin D and hormonal or metabolic profiles in PCOS patients. Proper assessment of an association between polycystic

ovarian syndrome and vitamin D demands further investigations to be made as deficiency of vitamin D has been constantly suggested to promote the risk of developing resistance to insulin and type 2 diabetes mellitus.

Conflict of interest: Nil

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