Original Research Article

Correlation of vitamin-D with other metabolic parameters in women with PCOS

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Abstract

Background: PCOS is a common endocrine disorder among young women which results in metabolic and hormonal disturbances. Due to high risk of these patients to be associated with infertility, obesity, diabetes etc., it is considered as an important subject of study to correlate various biochemical and demographic parameters specifically.
Aim: The present study was aimed to accesses vitamin D levels in PCOS women to correlate with the metabolic parameters of PCOS.
Materials and methods: A total of 84 PCOS women following Rotterdam criteria were enrolled for the present study. Women who were on insulin sensitizers, hormone therapy and vitamin D were excluded. Various biochemical and demographic parameters such as weight, age, Fasting blood glucose, OGTT, Triglyceride, HDL, LDL, Vitamin D levels were measured. All the values were expressed as Mean ± SD. Unpaired *t*-test and Chi-square test were used for comparative study of the data between the groups.
Conclusion: Among the study population, obese women were high in number and were observed to be more prone to the metabolic disturbances due to PCOS. Hypovitaminosis- D was significantly observed among these women. Therefore, regular screening of Vitamin D levels would avoid many clinical complications among the women with PCOS and Obesity.

Key words

Vitamin D, PCOS, BMI, Obesity, Cholesterol.

Introduction

PCOS is a common endocrine disorder of women in reproductive age worldwide with clustering of metabolic disturbances like insulin resistance, hyperinsulinemia and dyslipidemia at a very young age. PCOS women are often associated with increased risk of infertility, endometrial carcinoma, obesity, insulin resistance, type 2 diabetes mellitus, dyslipidemia, hypertension, and cardiovascular disease (CVD) [1]. The cause for PCOS is unknown, however literature suggest the involvement of genes and environment (lifestyle) as strong causative factors [2]. It is also considered as a common health problem due to an imbalance of reproductive hormones like luteinizing, FSH, prolactin, testosterone or androgens. Vitamin D deficiency is reported to be very common in our country across all age groups and is linked with many metabolic disorders. Till date, in several studies vitamin D deficiency has been reported to be very common among all groups in India and is often linked with endocrine dysregulations in PCOS women along with the associated co-morbidities [3-5]. In this regard the present study was aimed to accesses vitamin D levels in PCOS women to correlate with the metabolic parameters of PCOS.

Materials and methods

Study population

A total of 84 PCOS women following Rotterdam criteria were enrolled for the present study. Informed consent was taken from all subjects prior sampling and institutional ethical clearance was obtained. Detailed information on clinical and anthropometric measures was collected through proforma. Obesity was measured by calculating body mass index (BMI) based on which the subjects were grouped into Normal, Overweight and obese (18-25, 25-30 and >30 kg/m^2 respectively).Women who were on insulin sensitizers, hormone therapy and vitamin D were excluded.

Biochemical assay

Three milliliter of fasting venous blood samples after an overnight fast for more than 12 hours were analyzed for biochemical parameters such as fasting blood sugar, OGTT 1^{st} hour, OGTT 2^{nd} hour, Total cholesterol (TC), Triglycerides (TG), High Density Lipoprotein (HDL) and Low Density Lipoprotein (LDL). Additionally, the serum vitamin D levels were measured for all the subjects using standard protocols. Vitamin D levels of <20 ng/mL was considered as deficiency, 20 and 30 ng/mL as insufficiency and more than 30 ng/mL as normal.

Statistical analysis

All the values were expressed as Mean ± SD. Unpaired *t*-test and Chi-square test were used for comparative study of the data between the groups. To find the association between Vitamin D and other clinical parameters Spearman's correlation was used. Appropriate statistical analysis was carried out using SPSS 19 version and a two tailed p-value of <0.05 was considered to be statistically significant.

Results

Study Characteristics

Data analysis of 84 individuals revealed on age range 16-45 years with a mean age of 25.63±5.3 of them 33% were non-obese, 32% overweight and 35% obese with a mean BMI of 22.8 ± 1.72, 27.7 ± 1.46 and 33.6 ± 2.89 respectively.

Biochemical Analysis

Impaired FBS, OGTT 1 hour and OGTT 2 hours, was seen in 8%, 17% 19.0% respectively. Abnormal lipid profile was observed in 76% of individuals with abnormal cholesterol (8.3%), TG (10.7%), HDL (69.0%) and LDL (33.3%) respectively (**Figure – 1**).

Abnormal levels of serum Vitamin D (Hypovitaminosis) was found in 80.9% of subjects which includes both insufficiency (61%)

and deficiency (20%). Further analysis of vitamin D with subject to BMI, FBS, OGTT, lipid profile and hormonal parameters was carried out which revealed low HDL levels among these individuals. The mean values of the overall biochemical parameters in total and in subgroups with respect to levels of vitamin D are given in **Table - 1** and **Table - 2**.

Figure – 1: Normal and abnormal demographic and biochemical parameters among study population.

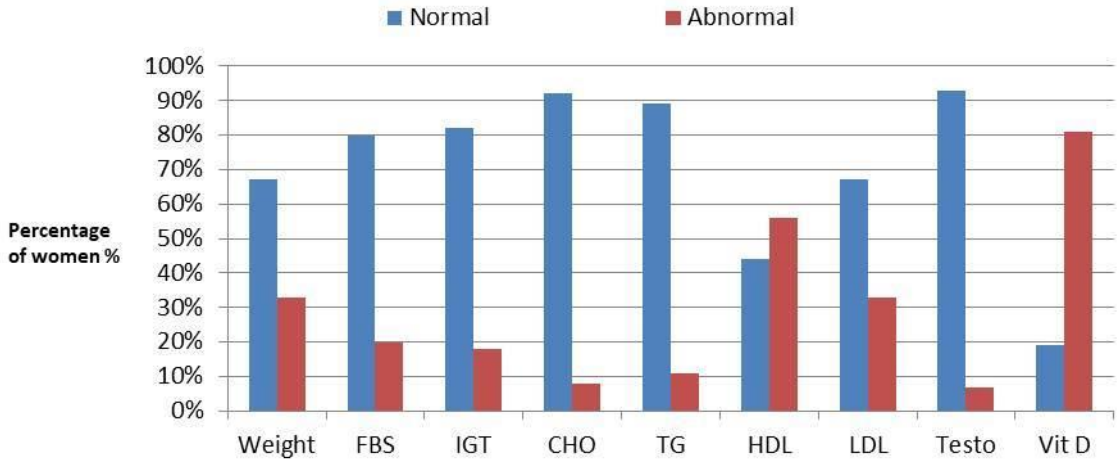


Table - 1: Means and SD of Demographic and Biochemical parameters.

Demographic And Biochemical Parameters	Mean ± SD
Age	25.63 ± 5.3
BMI	28.15 ± 4.9
Vitamin D	19.72 ± 9.8
OGTT- 2nd hour	121.71 ± 34.49
OGTT-1st hour	157.07 ± 45.57
FBS	93.42 ± 21.78
Total cholesterol	157.16 ± 26
Triglycerides	115.25 ± 56.07
HDL	40.34 ± 7.21
LDL	96.93 ± 24.4
TSH	3.14 ± 1.14
Testosterone	57.83 ± 10.91

Analysis of variance among the subgroups of vitamin D levels with reference to demographic and biochemical parameters revealed significant difference relating to BMI, HDL, LDL, Testosterone ($p<0.05$).

When univariate correlation analysis between Vitamin D and the considered biochemical and demographic parameters was carried out, only Testosterone showed a significant correlation with Vitamin D (**Table – 3**). The percentage of normal and abnormal within the subgroups of Vitamin D and the studied parameters are given in **Figure - 2**.

Discussion

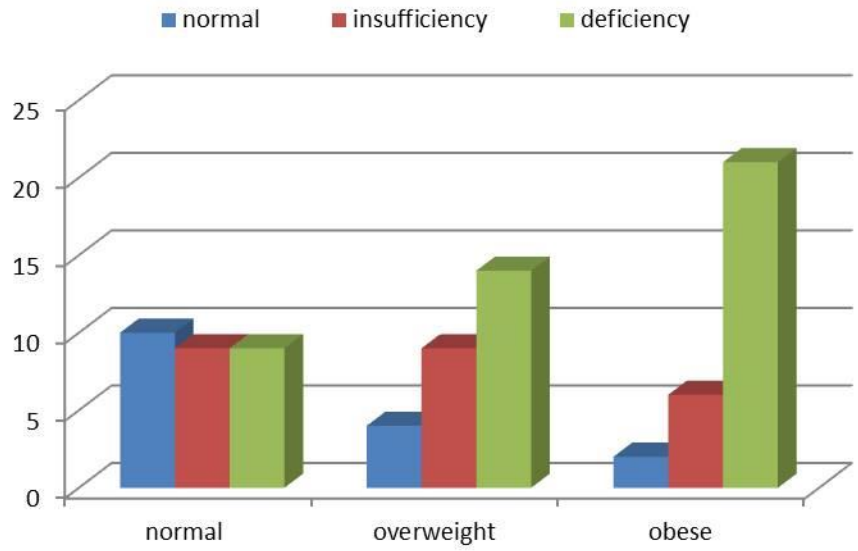
Vitamin D has a pleotropic effect on multiple regulatory pathways involved in intermediary metabolism. Till date, several clinical and epidemiological studies demonstrated the contribution of inadequate vitamin D levels in the causation of various diseases in humans [6-9]. Vitamin D deficiency is common in PCOS women; a common endocrine disorder and has

certain implications. In a cross-sectional study by Krul-Poel et al., serum 25(OH)D was significantly lower in PCOS women compared to fertile controls [10]. In agreement with an observational study by Thys-Jacobs, et al., our results demonstrated that majority of women with PCOS had vitamin D deficiency [11]. Our findings are in contrast with the results obtained by Lakshman LR, et al. in which both PCOS group and controls were vitamin D deficient and had similar levels of vitamin D [12]. In our study, nearly 81% of PCOS women had hypovitaminosis D, similar to the previous studies in developed countries that showed the prevalence to be 85% [13].

Table - 2: Correlation between Vitamin D levels and various metabolic and biochemical parameters.

Demographic and biochemical parameters	**Vitamin-D deficiency (<20) Mean ± SD**	**Vitamin-D insufficiency (20-30) Mean ± SD**	**Vitamin-D normal (>30) Mean ± SD**
Age	25.70 ± 5.31	26.33 ± 5.49	24.37 ± 4.92
BMI	29.49 ± 4.88	27.56 ± 5.29	25.37 ± 3.2
OGTT-2nd hour	123.38 ± 29.80	128 ± 42.42	107.68 ± 31.55
OGTT-1st hour	160.20 ± 46.41	159.54 ± 45.76	144.75 ± 43.58
FBS	96.77 ± 28.19	91.87 ± 10.87	86.56 ± 8.89
Total cholesterol	161.38 ± 27.13	155.81 ± 27.63	147.56 ± 17.46
triglycerides	125.25 ± 70.66	110.12 ± 38.26	95.46 ± 8.04
HDL	39.64 ± 6.64	38.03 ± 8.29	45.63 ± 4.01
LDL	102.19 ± 25.35	96.86 ± 23.9	82.55 ± 16.87
TSH	3.11 ± 1.15	3.22 ± 1.15	3.11 ± 1.15
testosterone	49.7 ± 6.24	62.72 ± 2.22	72.85 ± 8.15
Vitamin D	11.84 ± 5.24	25.07 ± 3.01	33.38 ± 3.34

Figure – 2: Vitamin D levels in Normal, over weight and obese PCOS women.



Studies on BMI and vitamin D levels have reported inverse associations. A study by Menon, et al. (2017) demonstrated lower vitamin D levels in obese PCOS compared to non-obese [14]. In our present work, hypovitaminosis D was observed in all the sub groups of BMI, indicating BMI as an independent component in the predisposition of PCOS.

Our findings revealed that, PCOS women with hypovitaminosis D had severe dyslipidemia with significant low levels of serum HDL being highly conspicuous regardless of other parameters. We observed the abnormally low levels of serum HDL in PCOS women with hypovitaminosis D which is in line with a pilot study that's how a development of HDL after treatment with vitamin D in a cohort of PCOS women [7]. In this study by Kotsa, et al., the mean HDL levels in the PCOS group before and after vitamin D treatment were 41.4 ± 2.14 mg/dl and 43.4 ± 1.59 mg/dl respectively [15].

According to National Cholesterol Education Program Adult Treatment Panel III guidelines, serum levels of LDL-C and non-HDL-C are the primary and secondary targets to prevent atherosclerosis, thereby, avoiding cardiovascular risk [16]. A meta-analysis revealed that dyslipidemia occurs more frequently in PCOS women and they had higher LDL levels, regardless of BMI [17]. PCOS women had higher concentrations (38.0 vs. 25.0 mg/l; P = 0.026) and proportions (12.8 vs. 8.2%; P = 0.006) of small dense LDL (LDL III), relative to controls according to Pirwany, et al. (2001) [18]. Our current study confirms these existing literatures giving a statistically significant value for LDL levels.

There are many evidences which suggest that high androgenic hormones, in particular, testosterone act as fundamental factors in the pathogenesis of PCOS [19, 20]. In our study, a fraction of PCOS women with normal vitamin D levels were showing abnormal testosterone levels. In fact, there seems to be an absence of inverse association between the levels of vitamin D and testosterone. The probable reason could be the effect of hyperplastic theca cells which are the source of ovarian androgens in PCOS [21]. An increase in BMI might explain the low HDL associated and is part of the metabolic syndrome. Many studies have shown a high prevalence of m etabolic syndrome in PCOS patients and their rel atives. Our data showed the presence of IR in almost all the study participants. The prevalence of IR is reported in 80% of PCOS patients from our country [22].

Coexisting hypovitaminosis D may exacerbate th e PCOS metabolic abnormalities, resulting in enh anced danger of CVD.The metabolic parameters did not show any change as per the increasing severity of the 25OHD deficiency. However, the heartening fact of our study is that the majority of the participants had mild forms of 25OHD deficiency and none of the participants had a severe deficiency. This could explain the lack of difference between the 25OHD deficiency and sufficient groups. Previous researchers have shown that a critical level of 25OHD is enough to carry out the metabolic functions without much disruption.

In our study, 25OHD did not show any relation with the clinical, metabolic, and hormonal parameters. Previous research has shown that the 25OHD is inversely correlated with the total cholesterol, triglycerides, body weight, and other metabolic disturbances in PCOS patients [23]. The observed discrepancy in our study could be due to the small sample size and presence of Vitamin D insufficiency in the majority of the patients. The strengths of our study include a detailed evaluation of all the patients and close follow-up in a single center. The limitations of our study include small sample size, cross-sectional design, and lack of evaluation of body fat and IR using robust methods.

Conclusion

Hypovitaminosis D is very prevalent in patients with PCOS and exacerbates defects in metabolism. It is vital that all PCOS patients be screened for vitamin D deficiency and that suitable replacement treatment be instituted to avoid negative effects. In order to confirm the results found in our research, further large scale trials with more patients are needed.

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