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Original Research Article

Investigating the relationship between Vitamin D level and Polycystic ovarian syndrome- A case control study

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ABSTRACT

Introduction: Polycystic ovary syndrome (PCOS) a heterogeneous disorder, characterized by hyperandrogenism, chronic anovulation, obesity, and insulin resistance (IR). Studies have demonstrated the beneficial effect of vitamin D supplementation on insulin resistance in PCOS.
Aim: To find the difference of vitamin D level between the PCOS and control groups. And to correlate serum 25(OH)D concentration and metabolic risk factors in PCOS women.
Materials and Methods: 49 women, diagnosed with PCOS were recruited as cases and another 49 women without PCOS served as controls. Demographic data like age, BMI, menstrual pattern, clinical features like hirsuitism, acne were recorded for both cases and control. The serum 25(OH)D and metabolic markers were measured. The primary outcome was the difference in vitamin D status between the cases and controls, the secondary outcomes were correlations between serum 25(OH)D concentration and metabolic risk factors in women with PCOS.
Results: Vitamin D level was significantly lower in cases than in controls ($P < 0.05$). The prevalence of IR was significantly greater in the Vitamin D deficiency group among cases ($P < 0.05$), but not so for BMI and fasting insulin. Also, prevalence of obesity and deranged lipid profile was not significantly increased in the vitamin D deficiency group of PCOS patients.
Conclusions: Vitamin D deficiency is prevalent in PCOS women in Eastern India, especially in those with IR and with metabolic risk factors like HDL – C. Larger sample sizes are needed to probe correlation with other metabolic risk factors in PCOS women.

1. Introduction

Polycystic ovary syndrome (PCOS) is a common endocrine disorder in women of reproductive age, the prevalence ranging from 9 to 18%.[1,2] Common features of PCOS are obesity, hyperandrogenemia, and insulin resistance (IR).[3] Studies have confirmed the relationship between PCOS and type 2 diabetes mellitus (T2DM), cardiovascular disease and metabolic syndrome.[4,5]

30–40% of PCOS women have IR and compensatory hyperinsulinaemia, of which ~10% develop T2DM.[6] Dyslipidaemia, comprising higher concentrations of triglycerides (TGs), low-density lipoprotein cholesterol (LDL-C), and lower concentrations of high-density lipoprotein cholesterol (HDLC), are more prevalent in PCOS than in healthy women.[7]

Vitamin D, a steroid hormone, is essential in skeletal growth and development, calcium/phosphorus metabolism, and bone mineralization.[8,9] Vitamin D receptors regulate the expression of 229 genes in ~ 30 different tissues, including the pancreas, liver, immune cells, brain and

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ovaries.[9] The difference of vitamin D levels between PCOS women and healthy women, and the relationship between vitamin D and metabolic factors in PCOS women has remained controversial.

Some studies have shown that PCOS women have vitamin D deficiency unlike age matched healthy women. Moreover, vitamin D deficiency is associated with homeostasis model assessment of insulin resistance (HOMA-IR), hyperinsulinaemia, dyslipidaemia, and metabolic risk factors in patients with PCOS.[10,11] However, other studies show different results.[12]

This case control study aims to investigate vitamin D status between PCOS and non-PCOS subjects and analyze the relationship between vitamin D deficiency and metabolic risk factors in women with PCOS.

2. Materials and Methods

2.1. Study design and participants

This survey was a case - control study. A total of 49 women, diagnosed with PCOS, were recruited from the gynecological clinic of JIMS Hospital, Kolkata from July 2020 to June 2021. 49 age-matched women without PCOS were selected as controls. The modified Rotterdam criteriawas usedfor diagnosing PCOS.[13] Women with hypothyroidism and hyperprolactinemia were excluded. The protocol was approved by the Institutional Review Board.

2.2. Outcome measures

Basic information, collected through questionnaire, included age, body mass index (BMI), and blood pressure. BMI >/= 28.0 kg/m2 was defined as obesity.[14] All biochemical indicators were tested in our hospital including serum 25-hydroxyvitamin D[25(OH)D], follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin (PRL), testosterone (T), fasting blood glucose, fasting insulin and lipid profile. HOMA-IR was calculated to evaluate insulin resistance (IR). HOMAIR = [fasting glucose(mmol/L) × fasting insulin(mIU/L)]/ 22.5. HOMA-IR > 2.5 was defined as IR.[15] Serum vitamin D levels <20 ng/mL, 20 - 30 ng/mL and >/= 30 ng/mL were defined as deficiency, insufficiency and normal respectively.[16]

The primary outcome was the difference in vitamin D level between the PCOS and control groups. The secondary outcome was the correlation between serum vitamin D concentration and metabolic risk factors in PCOS women.

2.3. Statistical analysis of data

Data was analyzed by SPSS (version 27.0). Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. One-way analysis of variance (one-way ANOVA) was used to compare means of three or more samples for numerical data.

3. Results

The differences in age, BMI, SBP, DBP, and PRL were found to be statistically significant (p value <.05). No statistically significant differences could be found in the other parameters between the two groups.

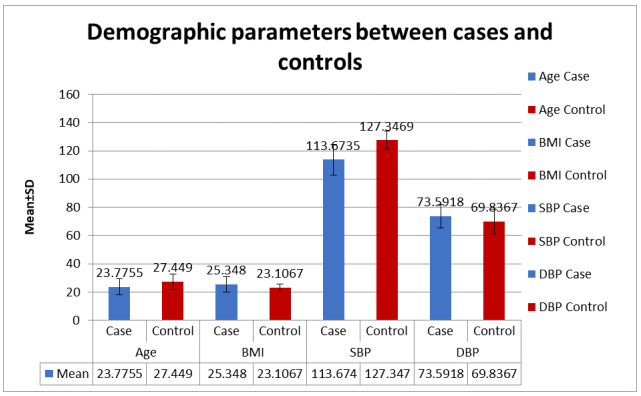

Fig. 1: Graphic representation of base line parameters between cases and controls

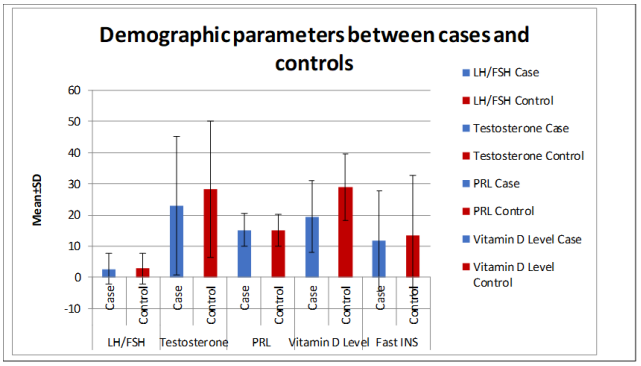

Fig. 2: Graphic representation of base line parameters between cases and controls

3.1. Vitamin D level status between PCOS women and controls

The serum 25(OH) D concentration was significantly lower in PCOS women than in controls (19.3967± 11.4876.vs. 28.8120± 10. 7247.p<0.0001) (Table 1, Figure 3). In addition, the prevalence rates of 25(OH)D deficiency and insufficiency were significantly higher in women with PCOS than in controls (65.3% vs. 18.4%, P <0.01; 26.5%) % vs. 22.4%, P < 0.0001). (Figure 4). Furthermore, the prevalence of normal 25(OH)D status in women with PCOS

Table 1: Comparing baseline characteristics of case and control groups

Characteristic	Case n=49	Control n=49	p-value
Age	23.78±5.67	27.45±5.45	0.001
BMI	25.35±5.44	23.11±2.81	0.013
SBP (systolic BP)	113.67±10.74	127.35±6.38	0.000
DBP (diastolic BP)	73.59±8.30	69.84±8.61	0.030
LH/FSH	2.61±4.91	2.80±4.89	0.846
Testosterone	22.98±22.37	28.31±21.92	0.236
PRL	15.24±5.18	15.05±5.04	0.854
Vit D Level	19.40±11.49	28.81±10.73	0.0001
Fast Insulin	11.63±16.01	13.47±19.30	0.609

was significantly lower than that in controls (8.2% vs. 59.2%, P < 0.01).

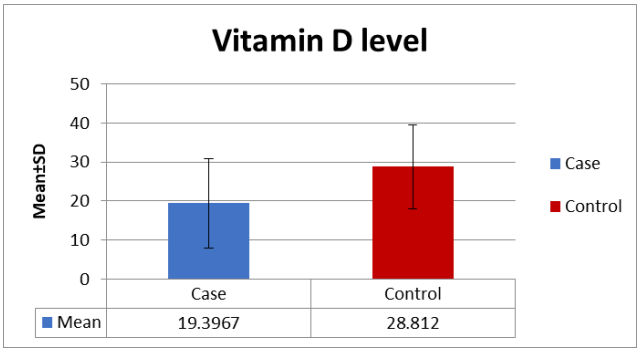

Fig. 3: Serum 25(OH)D concentration between women with PCOS and control group

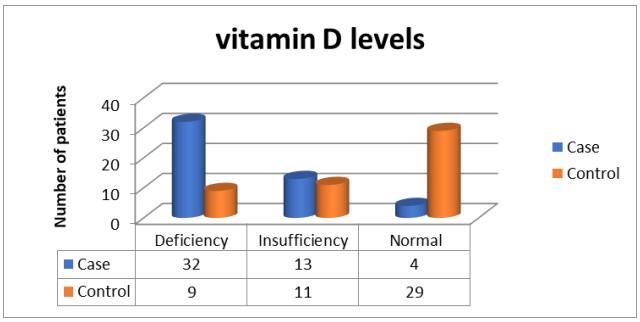

Fig. 4: Different Serum Vitamin D levels among cases and controls

Table 2 llustrates the difference in the metabolic factors(BMI, Fasting Insulin, and IR) between the 3 subgroups of deficiency, insufficiency and normal Vit D level among the PCOS patients. Only the difference in IR was found to be statistically significant. (P value <0.05).

Table 3 shows theprevalence of obesity, abnormal lipid profile and HOMA – IR among different vitamin D categories in women with PCOS. There was statistically significant difference in HOMA-IR, among the three groups (P < 0.05). No significant difference was found when comparing prevalence of obesity and deranged lipid profile among different groups (P > 0.05). The same is portrayed in the 3 figures below (Figures 5, 6 and 7).

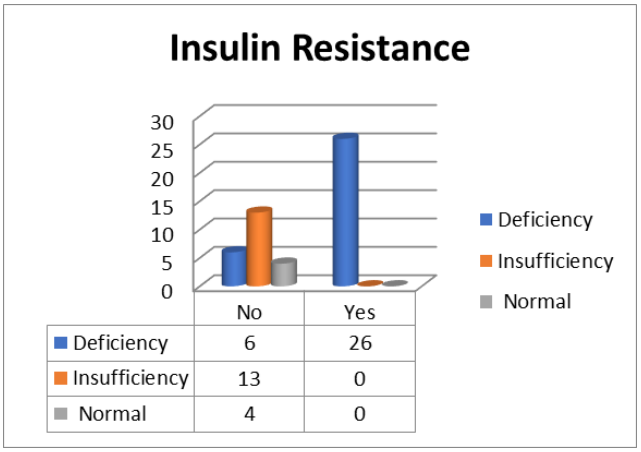

Fig. 5: Showing Insulin resistance among different levels of vitamin D in PCOS patients

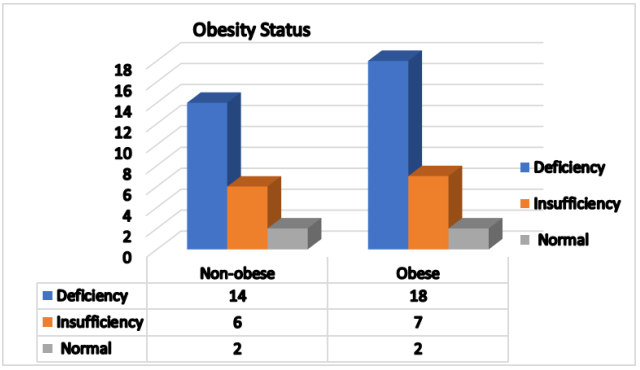

Fig. 6: Showing obesity status among different levels of vitamin D in PCOS patients

Table 4 shows that 62.5% of those PCOS women with hypercholesterolemia, 50% with increased HDL cholesterol, 85.7% with increased LDL, 100% with increased VLDL and 75% with increased triglycerides hadVit D deficiency. Also, excepting for 1 person with increased HDL, none of those PCOS women with normal

Table 2: Comparing metabolic factors with vitamin D deficiency, insufficiency, and normal sub-groups among PCOS women

Metabolic Factor	Deficiency (n=32)	Insufficiency (n=13)	Normal (n=4)	p-value
BMI	25.72±5.07	24.91±6.10	23.77±7.37	0.760
Fast Insulin	13.70±19.50	7.93±2.90	7.06±2.25	0.469
Insulin Resistance (IR)	4.09±3.80	1.42±0.42	1.52±0.49	0.026

Table 3: Comparing prevalence of obesity, lipid derangement and Insulin resistance between deficiency, insufficiency, and normal Vitamin D sub-groups of the cases

Metabolic parameters	Vit D Deficiency (n=32)	Vit D Insufficiency (n=13)	Normal Vit D (n=4)	p-value
Obese (BMI>28kg/M^2)	18 (66.67%)	7 (25.93%)	2 (0.54%)	0.967
Non-obese (BMI <28kg/M^2)	14 (63.6%)	6 (27.27%)	2 (9.1%)	
Lipid profile deranged	21 (75%)	6 (21.43%)	1 (4.55%)	0.195
Lipid profile normal	11(52.38%)	7 (33.33%)	3(14.28%)	
Insulin resistance present	26 (100%)	0	0	0.000
insulin resistance absent	6 (26.1%)	13 (56.5%)	4 (17.4%)	

Table 4: Shows the percentage of cases with a specific lipid derangement within different categories of Vit D level in PCOS patients

Lipid derangement type n=22	Deficiency (n=33)	Insufficiency (n=13)	Normal (n=4)	p-value
Cholesterol n=8	5 (62.5%)	3 (37.5%)	0 (0%)	0.191
HDL n=2	1 (50%)	0 (0%)	1 (50%)	0.028
LDL n=7	6 (85.7%)	1 (14.28%)	0 (0%)	0.160
VLDL n=1	1 (100%)	0 (0%)	0 (0%)	0.221
Triglyceride n=4	3 (75%)	1 (25%)	0 (0%)	0.241

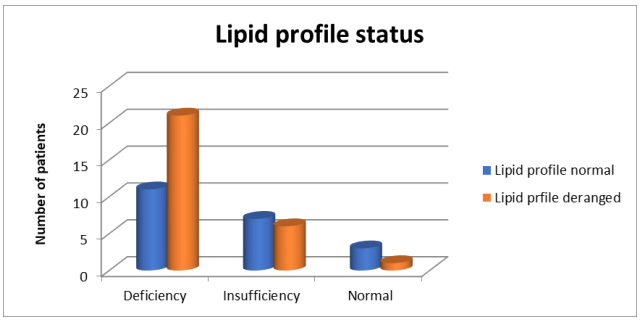

Fig. 7: Showing lipid profile status among different levels of vitamin D in PCOS patients

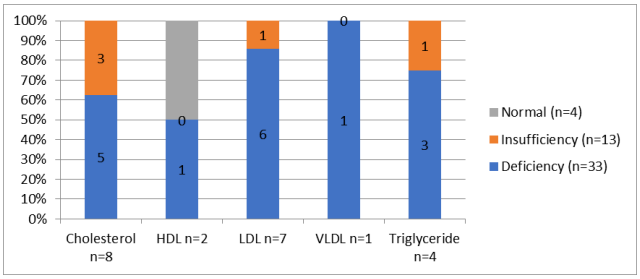

Fig. 8: Showing the relationship of individual types of lipid derangement with different categories of Vitamin D levels in PCOS patients

Vit D level had any lipid derangements. (Fig 3).

4. Discussion

More than one billion children and adults in the world have vitamin D deficiency.[17] Among PCOS women, there is a higher prevalence of vitamin D deficiency compared to non- PCOS women, and this deficiency is associated with ovulatory dysfunction, IR and hyperandrogenism[18]. Our study showed significantly lower levels of vitamin D among cases; moreover, the prevalence rates of 25(OH)D deficiency and insufficiency were significantly higher in women with PCOS than in controls, similar to a previous study.[19]

Multiple observational studies have shown that low vitamin D concentration is associated with increased BMI, IR, testosterone and dehydroepiandrosterone sulfate (DHEAS) levels in women with PCOS[22]. In our study, serum 25(OH)D concentration was found to be significantly lower in PCOS women with IR than in PCOS women without IR. In addition, the prevalence of 25(OH)D deficiency in PCOS women with IR was significantly higher than in women without IR. Epidemiological studies have confirmed that vitamin D status is negatively associated with diabetes, which may be multifactorial. Research confirmed that 25(OH)D increases the expression of insulin receptors, and inhibits the release of inflammatory cytokines that are proved to cause IRS.[20] Studies have reported that vitamin D indirectly improves function of insulin through regulation of

extracellular calcium.[21] However, other researchers like Ng et al. demonstrated that there was no statistically significant correlation between vitamin D level and BMI, WHR, and metabolic parameters among PCOS women.[12] In our study, lipid profile derangement regarding HDL – cholesterol was significantly more prevalent in vitamin D deficiency group among cases. This finding was concordant with the results of previous studies.[22]

Clinical manifestations of PCOS include obesity, metabolic syndrome and chronic inflammation, which are related to vitamin D deficiency.[23–26] Our findings revealed that serum 25(OH)D level in PCOS women was significantly negatively- correlated with HOMAIR, however, there was no significant correlation with obesity. This could be explained by small sample size and rural settings of the study with most of the population having generalized malnutrition.

Treatment with vitamin D was shown to improve the follicular development, menstrual cycle regulation, insulin resistance, and hyperandrogeni.[12] However, Xue et al. showed that vitamin D supplementation did not change the HOMA-IR, LDL, DHEAS, free testosterone, and total testosterone in women with PCOS.[27] Conflicting results may be related to sample size, vitamin D supplement dose, participant habits, and place of residence. Therefore, multi-center randomized controlled trials with large sample sizes are required to explore the metabolic role of vitamin D supplementation in women with PCOS.

5. Conclusion

PCOS women are more prone to vitamin D deficiency than normal subjects. Increased Insulin resistance and increased HDL- C are significantly more common in the Vitamin D deficiency group among PCOS women.

6. Limitations

The sample size of the participants was relatively small and it was wholly rural based single center study in the suburbs of Kolkata, eastern India. The result of this research needs to be proved through multi-center surveys with larger sample sizes in other areas in India.

7. Source of Funding

This study was not aided by any grants.

8. Conflict of Interest

None.

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