ORIGINAL ARTICLE

Effect of Vitamin D Supplementation on Menstrual Cycle Regularization and Metabolic Parameters in Polycystic Ovary Syndrome Women- A Retrospective Study

Neelaveni Kudugunti[1], Srinivas Rao Paidipally[2], Kenchey Himaja[3], Rakesh Sahay[1]*

[1]Department of Endocrinology, Osmania Medical College and General Hospital, Hyderabad-500012 (Telangana) India, [2]Department of Endocrinology, Gandhi Medical College, Secunderabad-500003 (Telangana) India, [3]Institute of Diabetes, Endocrinology and Adiposity (IDEAS Clinics), Hyderabad-500072 (Telangana) India

Abstract:

Background: Polycystic Ovary Syndrome (PCOS) is the most common endocrine disorder in women of reproductive age, characterized by chronic anovulation, hyperandrogenism, with varying severity of reproductive and long-term metabolic consequences. *Aim and Objectives:* To study the effect of vitamin D supplementation on menstrual cycle dysfunction and metabolic parameters in PCOS women. *Material and Methods:* Seventy-five PCOS women who presented with oligomenorrhoea/ amenorrhea with varying severity of hypovitaminosis D were retrospectively analysed. Thirty eight women were compliant with vitamin D supplementation, whereas 37 were non-compliant. Baseline demographic, menstrual cycle dysfunction and metabolic parameters were compared with the data at 6 months follow up in both groups, and change in weight and vitamin D levels were compared in women with regularized vs non regularized menstruation. *Results:* Mean age was 23.87 ± 3.74 years, with mean BMI 28.9 ± 4.88kg/m^2. Vitamin D deficiency and insufficiency was seen in 85.3% and 14.7% subjects. Baseline characteristics among vitamin D deficient Vs insufficient were not significantly different except for vitamin D levels. Significant decrease in BMI and waist circumference was observed among both compliant and non-compliant groups. Menstrual cycles were regularized in 39.4% of compliant group and 43.2% of non-compliant women. *Conclusion:* Vitamin D supplementation was not associated with menstrual regularization, and may play a role in synergy with weight loss in improving metabolic parameters. Our study reemphasizes the beneficial role of lifestyle modifications aiming at weight loss in PCOS women.

Keywords: Body Mass Index, Polycystic Ovary Syndrome, Menstruation, Vitamin D

Introduction:

Polycystic Ovary Syndrome (PCOS) is the most common endocrine disorder in women of reproductive age, characterized by chronic anovulation, hyperandrogenism, with varying severity of reproductive and long-term metabolic consequences. In general, its prevalence varies between 5-10% and higher prevalence up to 22.5% has been reported from India, more so in adolescents [1-2].

Insulin resistance plays an important role in the pathogenesis of PCOS with clustering of metabolic and cardiovascular risk factors. Many studies have observed that vitamin D deficiency is associated with insulin resistance, type 2 diabetes, hypertension and increased risk for cardiovascular

events. Vitamin D deficiency is reported to be very common in India with a prevalence ranging from 75-95% in general population across all age groups, socioeconomic and geographic strata [3]. PCOS women have been found to have higher prevalence of vitamin D deficiency and correlation of vitamin D levels with various metabolic and endocrine parameters have also been demonstrated [4]. It has been suggested that vitamin D deficiency may play a role in the endocrine and metabolic dysregulation in PCOS women along with other causative factors [5-6]. Studies on the role of vitamin D receptor genes in glucose, lipid and blood pressure regulation further supports this [7-8]. Vitamin D receptors are present in almost all human tissues including ovary and endometrium, suggesting a role of vitamin D in reproductive dysfunction [9]. The management of PCOS is symptomatic and the treatment with available pharmacological agents is not satisfactory. There is a great need to develop other pharmacological interventions to manage PCOS effectively. In the recent years there has been a focus on the role of vitamin D as an adjuvant therapy in the management of PCOS women. Since vitamin D deficiency may have a role in exacerbating PCOS, it is logical to say, vitamin D supplementation may be of help in managing the syndrome. Studies on this aspect are limited. Hence, in this study, we retrospectively analysed the effect of vitamin D supplementation in PCOS women on regularization of menstrual cycle and metabolic parameters.

Material and Methods:

In this retrospective observational study, medical records of all the patients attending the endocrinology clinic from 1st January 2016 to 31st May 2019, who were diagnosed to have PCOS were retrieved. Rotterdam Criteria was used to diagnose PCOS after exclusion of hyperprolactinemia, hypothyroidism, Cushing's syndrome, congenital adrenal hyperplasia, androgen secreting tumours and drugs.

Total of 267 women were identified as having PCOS. Medical records of the 196 PCOS women who completed six months follow up were screened. Out of these, 123 PCOS women data was retrieved, who presented with oligomenorrhoea/ amenorrhea with documented vitamin D levels at the initial visit and at six months. Data of PCOS women, with normal vitamin D levels at initial visit and who were on oral contraceptive pills, metformin, D-chiroinositol and other nutraceuticals was excluded. Women who were on only progesterone for the withdrawal was included in the analysis. Total of 75 women were identified in the database fulfilling the inclusion and exclusion criteria. The medical records of these women including all the six months follow up, that is clinical, menstrual cycle regularization, anthropometric, hormonal and metabolic parameters were analysed. The process of inclusion and exclusion of PCOS women data has been shown in Fig. 1. Written Informed consent was taken from the women at the time of initial visit to use the data for clinical research purpose. Vitamin D levels >30 ng/ml was considered normal and 20-30 ng/ml and <20 ng/ml was considered insufficient and deficient respectively and collectively called hypovitaminosis D. BMI of 18.5 to 22.9 kg/m^2 was considered normal whereas 23 to 24.9 kg/m^2 and > 25 kg/m^2 was considered as overweight and obese respectively (Asian criteria).

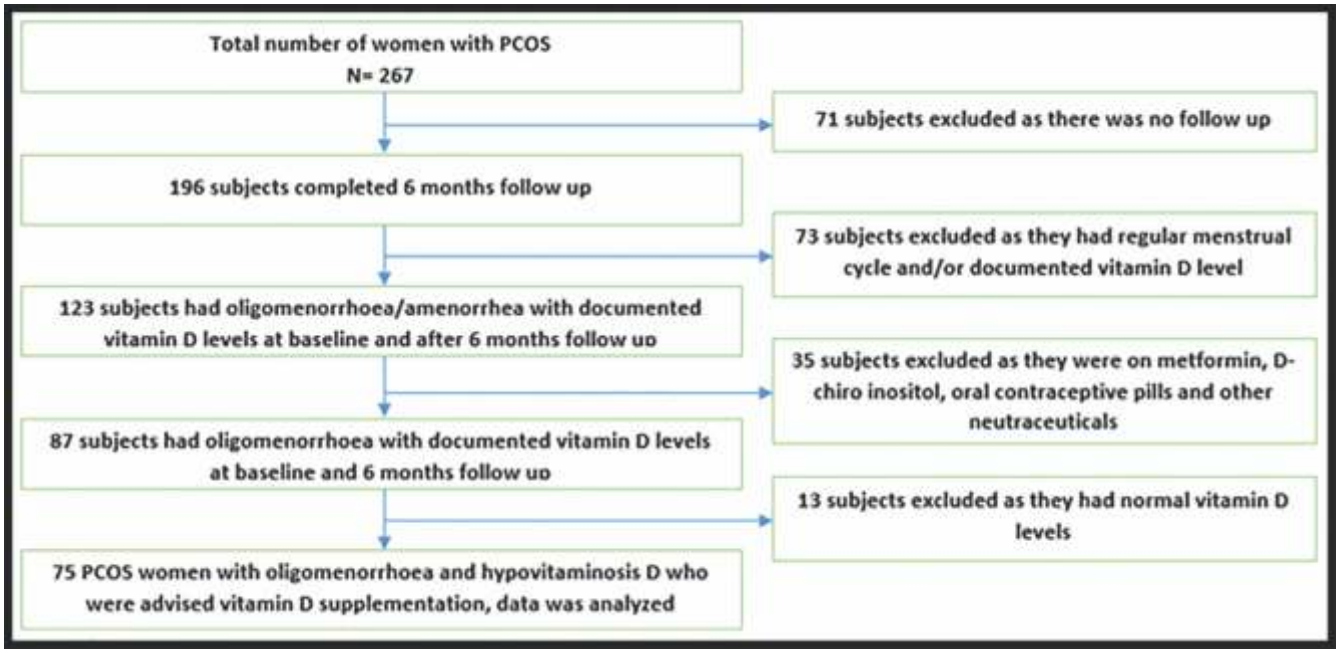

Fig. 1: Inclusion and Exclusion Criteria for Data Analysis in Women with PCOS

Assays:

At the study entry, venous blood samples were collected from all subjects for hormonal assay, lipid profile, Oral Glucose Tolerance Test (OGTT) with 75 g glucose and vitamin D levels. All blood samples were obtained in the morning between 0800 and 0900 hours after an overnight fast during early follicular phase (day 2 to 5) of a spontaneous or progesterone induced menstrual cycle. All subjects underwent transabdominal ultrasonography. Hormones were measured by chemiluminescent assay (ADVIA Centaur Siemens Healthcare Diagnostics). The ADVIA Centaur vitamin D assay measures 25(OH) vitamin D from concentrations of 4.2 to 150 ng/mL (10.5 to 375 nmol/L) [10]. The assay was standardized using internal standards which are traceable to the IDLC/MS/MS 25(OH) vitamin D RMP, which is further traceable to the National Institute of Standards and Technology Standard Reference Material 2972.

Plasma glucose levels were determined by the glucose oxidase method on a semi-auto analyzer. Total Cholesterol (TC) was determined using the cholesterol esterase method. High Density Lipoprotein (HDL) cholesterol was determined using cholesterol esterase method following selective precipitation of apolipoprotein B containing lipoprotein with a polyanion solution. Triglycerides (TG) were determined enzymatically as glycerol on a Hitachi semi-automated chemistry analyzer after hydrolysis with lipase. All lipid assays had intra and inter assay variation of less than 3%. Low Density Lipoprotein (LDL) cholesterol was calculated using Friedwald equation: LDL = TC – (HDL + TG/5). Insulin resistance was estimated using the Homeostatic

Model Assessment-Insulin Resistance 2 (HOMA-IR 2) using the oxford HOMA calculator [11]. Insulin resistance was defined for a HOMA index of >2.5.

Intervention:

All PCOS women with hypovitaminosis D were advised treatment with oral Vitamin D 60,000 IU weekly for 8 weeks then once monthly. Thirty-eight women complied with the treatment whereas 37 women did not comply with the treatment regimen of vitamin D supplementation as prescribed. Overweight and obese PCOS women were advised on nutrition and lifestyle modification to reduce their weight.

Data Analysis:

Baseline data (demographic, anthropometric, hormonal and metabolic parameters) of PCOS women with hypovitaminosis D were analysed. 6 months of follow up data on metabolic parameters and menstrual cycle regularization were analysed between vitamin D compliant and non-compliant group in comparison with the base-line data, to understand the effect of vitamin D. Regularization of menstrual cycle was considered when PCOS women had spontaneous menstruation cyclically, every 30 ± 5 days, and it was considered not regularized when they had menstruation after progesterone withdrawal.

Statistical Analysis:

Data was analysed using the statistical software package IBM SPSS version 22. Data was expressed as Mean ± Standard Deviation (SD) if normally distributed, and unpaired t-test and paired t test were used for statistical comparison. Categorical data expressed as percentages. P value < 0.05 was considered statistically significant.

Results:

Characteristics of PCOS Women at Initial Visit:

Data of 75 PCOS women with oligomenorrhoea/ amenorrhea and hypovitaminosis D were analyzed. Mean age of the PCOS women was 23.87 ± 3.74 years, with mean BMI of 28.9 ± 4.88kg/m^2. About 64/75 (85.3%) were vitamin D deficient and 11/75 (14.7%) were insufficient. 12% PCOS women were normal weight, 11% were overweight and 77% were obese as shown in fig. 2. About 12% (n=9) of PCOS women had prediabetes, 2.7% (n=2) had only Impaired Fasting Glucose (IFG), 5.3% (n=4), had Impaired Glucose Tolerance (IGT) only, whereas 4% (n=3) had both IFG and IGT.

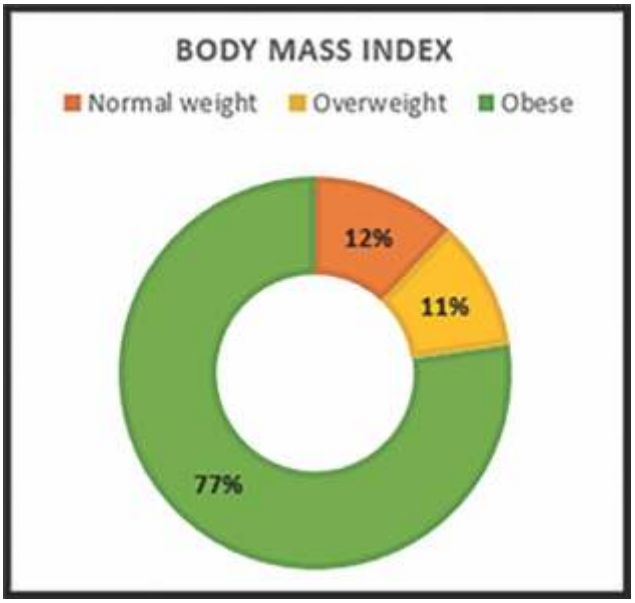

Fig. 2: Division of Subjects Based on BMI

Comparison of data between deficient and insufficient group has been shown in Table 1. Age, BMI, Waist Circumference (WC), Systolic Blood Pressure (SBP) and Diastolic Blood Pressure

(DBP) were not significantly different in deficient vs insufficient group. Similarly fasting and 2 hours post oral glucose tolerance blood glucose also were not different, including HOMA IR. Among lipid parameters except for TG, others were not significantly different.

Characteristics of PCOS Women at 6 Months Follow Up:

Based on the vitamin D levels at 6 months follow up visit, PCOS women were divided into compliant group with vitamin D levels > 30ng/ml and non-compliant group with vitamin D levels

Table 1: Baseline Characteristics of PCOS Women Based on Severity of Vitamin D

Parameters	Vitamin D Deficiency (< 20ng/ml) (n=64)	Vitamin D insufficiency (20-30 ng/ml) (n=11)	*P*
Age(years)	23.57 ± 3.81	25.54 ± 2.80	0.107
BMI (kg/m²)	28.73 ± 4.73	29.89 ± 5.81	0.468
WC (cm)	93.25 ± 6.81	93.72 ± 4.85	0.825
SBP (mm of Hg)	119.54 ± 7.85	121.63 ± 6.31	0.406
DBP (mm of Hg)	78.03 ± 5.77	78.36 ± 4.54	0.857
FBS (mg/dl)	87.32 ± 8.85	92.63 ± 8.93	0.071
Second hour blood glucose post OGTT (mg/dl)	115.2 ± 16.80	124.36 ± 20.65	0.111
TG (mg/dl)	131.48± 37.72	106.09 ± 21.25	0.034
TC (mg/dl)	169.05± 25.18	165.81 ± 17.25	0.684
HDL (mg/dl)	41.84 ± 5.9	42.00 ± 7.81	0.939
LDL (mg/dl)	97.08 ± 20.29	97.72 ± 14.41	0.920
TSH (mIU/L)	3.5 ± 1.68	2.54 ± 1.17	0.023
Serum testosterone(ng/ml)	45.12 ± 26.5	38.36 ± 23.93	0.431
Vitamin D(ng/ml)	9.03 ± 4.85	24.14 ± 3.29	0.0001*
HOMA IR	3.99 ± 2.57	3.93 ± 2.41	0.941

*BMI- Body mass index, WC- Waist circumference, SBP- Systolic blood pressure, DBP- Diastolic blood pressure, FBS- Fasting blood glucose, TG- Triglycerides, TC- Total cholesterol, HDL- High density lipoprotein, LDL- Low density lipoprotein, TSH- Thyroid stimulating hormone, HOMA IR- homeostatic model assessment-insulin resistance, *-(P<0.05) is considered significant*

<30 ng/ml. Effect of vitamin D supplementation on menstrual dysfunction and metabolic parameters was analyzed in compliant and non-compliant group in comparison with the baseline data, as shown in Table 2. There was significant decrease in BMI and WC in both groups. Menstrual cycles were regularized in 39.4% and 43.2% women in compliant and non-compliant group respectively. Fasting blood glucose significantly decreased at 6 months in compliant group, while 2 hours post OGTT blood glucose did not significantly change in both groups in

Table 2: Comparison of Baseline Data with 6 Months Follow up Data in Compliant and Non-compliant Groups PCOS Women

Parameter	Baseline	Compliant group (n = 38)	*P*	Baseline	Non-compliant group (n=37)	*P*
BMI (kg/m²)	27.88±4.26	26.70±5.84	0.051	30.51±4.90	29.03±5.34	0.028[b]
Menstrual cycle regularized (n) (%)	0/38	15(39.4%)		0/37	16(43.2%)	
WC (cm)	93.65±7.88	92.78±7.25	0.018[b]	93.27±5.34	92.77±4.98	0.044[b]
FBS (mg/dl)	87.47±7.42	84.55±7.08	0.003[b]	88.21 ± 9.45	87.83 ± 7.76	0.82
2nd hour blood glucose post OGTT (mg/dl)	114.89±14.67	112.28±12.00	0.1	118.37 ± 19.03	116.67 ± 12.42	0.35
SBP (mm of Hg)	118.94±7.60	119.81±7.76	0.42	119.24 ±6.24	120.27 ±6.33	0.031[b]
DBP (mm of Hg)	77.92±5.44	78.23±4.93	0.72	77.78 ±5.93	78.29 ±5.51	0.429
TC (mg/dl)	159.98±25.75	155.48±13.30	0.29	170.72 ±20.52	161.10 ±16.86	0.0001[b]
TG (mg/dl)	137.18±39.24	125.73±25.75	0.006[b]	113.43±28.29	106.63 ±18.53	0.094
HDL (mg/dl)	42.84±4.07	43.1±3.99	0.72	40.43 ±6.68	42.95 ±5.00	0.10
LDL (mg/dl)	92.38±15.89	86.66±10.32	0.027[b]	97.24 ±22.07	88.58 ±16.14	0.016[b]
Vitamin D (ng/ml)	10.99±8.76	34.93±4.85	0.0001[b]	13.95 ±8.53	16.82 ±7.86	0.206
Serum Testosterone(ng/ml)	44.00±18.88	41.09±20.40	0.221	40.87±17.88	21.47 ±15.68	0.0001[b]

*BMI- Body mass index, WC- Waist circumference, FBS- Fasting blood sugar, SBP- Systolic blood pressure, DBP- Diastolic blood pressure, FBS- Fasting blood glucose, TG- Triglycerides, TC- Total cholesterol, HDL- High density lipoprotein, LDL- Low density lipoprotein, *- (P<0.05) is considered Significant, b- denotes p<0.05 as compared to baseline which is considered significant*

Table 3: Change in the BMI and Vitamin D after 6 Months Follow up in PCOS Women with Regularized and Non-regularized Menstrual Cycles

Parameter	Baseline	6 months follow up (Menstruation regularized group)	*P*	Baseline	6 months follow up (Menstruation not regularized group)	*P*
BMI (Kg/m²)	29.58±4.66	27.18±4.26	0.0001[b]	28.87±4.82	28.89±4.87	0.964
Vitamin D (ng/ml)	13.56 ±7.09	24.76 ±11.71	0.0001[b]	10.91±7.8	26.86±10.83	0.0001[b]

*BMI- Body mass index, *- (P<0.05) is considered Significant, b- denotes p<0.05 as compared to baseline which is considered significant*

comparison to the baseline values. There was a significant decrease in TC and LDL-C and testosterone levels in non-compliant group.

The change in BMI and levels of vitamin D after 6 months follow up in comparison with baseline in women with regularized and non-regularized menstrual cycles was analyzed and shown in Table 3. There was significant increase in Vitamin D levels in both menstrual cycle regularized and non-regularized women in comparison to baseline levels but there was a significant decrease in BMI in women with regularized menstrual cycles.

Discussion:

Recently, several studies reported higher prevalence of vitamin D deficiency among PCOS women and observed its association with metabolic and endocrine dysfunction in them [12-13]. Current treatment options for PCOS are mainly lifestyle modification, hormonal therapy and insulin sensitizers. Considering the higher prevalence of hypovitaminosis D in PCOS, vitamin D supplementation could be an easy and low risk add-on therapy [14]. However, there is conflicting data regarding the effect of vitamin D supplementation on reproductive and metabolic dysfunction among PCOS women.

Many studies have shown that vitamin D levels are inversely associated with measures of obesity that overweight and obese individuals have lower levels of vitamin D than normal weight individuals [15]. The cause and consequent effect of this relationship is not clearly known. One proposed hypothesis is vitamin D deficiency may promote adipogenesis and cause obesity [16]. Low vitamin D is associated with increase in PTH that promotes calcium flux into adipocytes, which enhances lipogenesis and inhibits catecholamine induced lipolysis, leading to accumulation of fat and weight gain. Another hypothesis is, in obesity, adipose tissue sequesters the fat-soluble vitamin, and this leads to lower levels, and not only that obese individuals remain mostly indoors [17]. There has been inconsistent findings on effects of vitamin D supplementation on weight loss [18]. Khosravi *et al.* found that vitamin D supplementation for 6 weeks resulted in significant decrease in weight, BMI, waist and hip circumference in overweight and obese women

[19]. In our study, being retrospective in nature, it was difficult to assess the impact of lifestyle modification versus vitamin D supplementation on weight change. However, the significant decrease in BMI in both vitamin D compliant and non-compliant group suggesting on the role of lifestyle modification, rather than vitamin D supplementation.

Effect on Menstrual Regularization:

Menstrual dysfunction in PCOS is due to abnormal LH pulsatility, hyperandrogenemia, insulin resistance and other multiple intraovarian factors, which lead to poor follicular development, follicular arrest and anovulation. It has been found that presence of menstrual irregularity can be a predictor of underlying insulin resistance and is associated with unfavorable metabolic outcomes [20].

Overweight and obesity can further negatively impact the ovulatory performance, menstrual function and metabolic abnormalities. Evidence suggests that weight loss is associated with improved menstrual and metabolic functions. Ovulatory menstrual cycles can be obtained, even when the weight loss is relatively low, however, not all patients equally respond to these measures even if their weight loss is similar [21]. In our study, we found that 39.4% of the PCOS women had regularization of menstrual cycles who complied with vitamin D supplementation as has been recommended, with significant increase in vitamin D levels after 6 months, whereas 43.2% of PCOS women had regularization, who did not properly comply with the treatment as recommended, with no significant increase in vitamin D levels. The interesting observation is that women who had regularization of menstrual cycle had a significant decrease in their BMI at 6 months follow up in comparison with women with non-regularized menstrual cycles with no significant change in BMI, in spite of having significant improvement in vitamin D levels suggesting clearly that decrease in BMI resulted in regularization of menstrual function.

Trummer *et al.* in their study did not find a significant improvement in menstrual frequency in the vitamin D treated group which is consistent with our study [22]. Similarly, in another study by Tehrani *et al*., showed no significant effect of vitamin D and calcium alone treated group on menstrual cycle and other clinical and biochemical variables. However, they found greater improvement in menstrual function in metformin + vitamin D and metformin alone treated group [23]. Kadoura *et al*. also found vitamin D and calcium supplements can support metformin effect on regulation of menstrual cycle irregularity in vitamin D-deficient/insufficient PCOS patients, but this effect is not associated with any significant changes in gonadotropins or IGF-1 system [24]. Ornstein *et al*. [25] observed that dietary weight loss in adolescent PCOS women resulted in significant improvement in menstrual regularity, BMI, waist circumference and hirsutism score, which was in agreement with our study, weight loss is associated with menstrual cycle regularization.

Effect on Glucose, Lipid Metabolism and Androgen Levels:

There is conflicting data on the effect of vitamin D on glucose metabolism. In this study. Vitamin D supplementation resulted in significant decrease

in fasting plasma glucose in compliant group in comparison with non-compliant group, whereas, no significant change in 2 hour blood glucose post oral glucose tolerance test levels in both groups. Maktabi *et al*., observed a significant decrease in fasting plasma glucose, HOMA-IR, HOMA-estimated beta cell function (HOMA-β), CRP, and plasma malondialdehyde in 70 PCOS women receiving 50,000 IU of cholecalciferol every 14 days vs. placebo over 12 weeks [26].

Among lipid parameters, in the present study, the effect is heterogenous with significant decrease in TC in non-compliant group and TG in compliant group, whereas decrease in LDL cholesterol was in both the groups. It is well known that weight loss can cause significant improvement in insulin sensitivity resulting in decrease in blood glucose levels, TC, TG and LDL cholesterol, together with increase in HDL cholesterol [27]. In this study possibly weight loss together with vitamin D supplementation together working in synergy might have resulted in significant decrease in fasting plasma glucose levels, and TG levels in compliant group.

Pasquali *et al.* reported non uniform improvement of lipid parameters resulting from weight loss and lifestyle changes in PCOS women [21]. In another study, authors found the beneficial effect of vitamin D supplementation after 12 weeks of therapy on glucose metabolism and in menstrual regularization [28]. In a meta-analysis by Xin-Zhuan *et al.*, authors failed to detect any therapeutic effect of vitamin D on clinical and biochemical parameters in women with PCOS [29]. In our study, there was a significant decrease in serum testosterone concentrations in non-compliant group, whereas no significant change in compliant group, suggesting possibly no role of vitamin D and the reduction could possibly be due to weight loss. Significant improvement in androgen levels (testosterone and androstenedione) have been observed with lifestyle changes and weight loss [30].

Conclusion:

In our study, we found that vitamin D supplementation was not associated with menstrual regularization, but weight loss is associated with regularization of menstrual cycles and improvement in metabolic parameters and vitamin D supplementation may play a role in synergy with weight loss measures. Our study being retrospective in nature with inherent associated limitations together with smaller sample makes it difficult to draw generalizable conclusions. Properly designed randomized trials of adequate sample size are required.

Acknowledgements:

We would like to acknowledge the support of Dr. Sushil Kunder for providing assistance in statistical analysis and manuscript writing.

Clinical significance:

This study reemphasizes on the beneficial role of lifestyle modification aiming at weight loss in PCOS women at every stage apart from other modalities of treatment as and when required.

References

1. Gill H, Tiwari P, Dabadghao P. Prevalence of polycystic ovary syndrome in young women from North India: A Community-based study. *Indian J Endocrinol Metabol* 2012; 16(Suppl 2):S3-S9.
2. Malik S, Jain K, Talwar P, Prasad S, Dhorepatil B, Devi G, *et al*. Management of polycystic ovary syndrome in India. *Fertil Sci Res* 2014;1(1):23-43.
3. Ritu G, Gupta A. Vitamin D deficiency in India: prevalence, causalities and interventions. *Nutrients* 2014;6(2):729-75.
4. Krul-Poel YH, Koenders PP, Steegers-Theunissen RP, Ten Boekel E, Wee MT, Louwers Y, *et al*. Vitamin D and metabolic disturbances in polycystic ovary syndrome (PCOS): A cross-sectional study. *PloS one* 2018;13(12):e0204748.
5. He C, Lin Z, Robb SW, Ezeamama AE. Serum vitamin D levels and polycystic ovary syndrome: a systematic review and meta-analysis. *Nutrients* 2015;7(6):4555-4577.
6. Bacopoulou F, Kolias E, Efthymiou V, Antonopoulos CN, Charmandari E. Vitamin D predictors in polycystic ovary syndrome: a meta-analysis. *Eur J Clin Invest* 2017;47(10):746-755.
7. Holick MF. Vitamin D deficiency. *New Engl J Med* 2007; 357(3):266-281.
8. Pittas AG, Lau J, Hu FB, Dawson-Hughes B. The role of vitamin D and calcium in type 2 diabetes. A systematic review and meta-analysis. *J Clin Endocrinol Metabol* 2007;92(6):2017-2029.
9. Skowronska P, Pastuszek E, Kuczynski W, Jaszczol M, Kuc P, Jakiel G, *et al*. The role of vitamin D in reproductive dysfunction in women–a systematic review. *Ann Agric Environ Med* 2016;23(4):671-676.
10. Siemens Healthineers. ADVIA Centaur Vitamin D Total (VitD) Assay [directional insert 10699279_EN Rev. A, 2013–07]. Siemens Healthcare Diagnostics Inc.: Tarrytown, NY, USA, 2013. [cited on 2020 November 18]. Available from: https://www.healthcare.siemens.com/laboratory-diagnostics/assays-by-diseases-conditions/bone-metabolism-assays/advia-centaur-vitamin-d-total-assay.
11. HOMA2 Calculator [internet]. Ox.ac.uk [cited on 2020 November 21]. Available from: https://www.dtu.ox.ac.uk/homacalculator/.
12. Wang L, Lv S, Li F, Yu X, Bai E, Yang X. Vitamin D deficiency is associated with metabolic risk factors in women with polycystic ovary syndrome: a cross-sectional study in Shaanxi China. *Front Endocrinol (Lausanne)* 2020; 11:171.
13. Kumar A, Barki S, Raghav V, Chaturvedi A, Kumar KH. Correlation of Vitamin D with metabolic parameters in polycystic ovarian syndrome. *J Family Med Prim Care* 2017;6(1):115-119.
14. Foroozanfard F, Talebi M, Samimi M, Mehrabi S, Badehnoosh B, Jamilian M, *et al*. Effect of two different doses of vitamin D supplementation on metabolic profiles of insulin-resistant patients with polycystic ovary syndrome: a randomized, double-blind, placebo-controlled trial. *Horm Metabol Res* 2017;49(8):612-617.
15. González L, Ramos-Trautmann G, Díaz-Luquis GM, Pérez CM, Palacios C. Vitamin D status is inversely associated with obesity in a clinic-based sample in Puerto Rico. *Nutr Res* 2015;35(4):287-293.
16. Miao Z, Wang S, Wang Y, Guo L, Zhang J, Liu Y, *et al*. A potential linking between vitamin D and adipose metabolic disorders. *Canadian J Gastroenterol Hepatol* 2020;2020: 2656321.
17. Migliaccio S, Nisio AD, Mele C, Scappaticcio L, Savastano S, Colao A, *et al*. Obesity and hypovitaminosis D: causality or casualty? *Int J Obes Suppl* 2019;9(1):20-31.
18. Thomson RL. The impact of vitamin D on weight loss. *US Endocrinol* 2013;9(2):146–52.
19. Khosravi ZS, Kafeshani M, Tavasoli P, Zadeh AH, Entezari MH. Effect of vitamin D supplementation on weight loss, glycemic indices, and lipid profile in obese and overweight women: a clinical trial study. *Int J Prev Med* 2018;9: 63.
20. Brower M, Brennan K, Pall M, Azziz R. The severity of menstrual dysfunction as a predictor of insulin resistance in PCOS. *J Clin Endocrinol Metab* 2013;98(12):E1967-1971.
21. Pasquali R, Gambineri A, Cavazza C, Gasparini DI, Ciampaglia W, Cognigni GE, *et al*. Heterogeneity in the responsiveness to long-term lifestyle intervention and predictability in obese women with polycystic ovary syndrome. *Eur J Endocrinol* 2011;164(1):53-60.
22. Trummer C, Schwetz V, Kollmann M, Wölfler M, Münzker J, Pieber TR, *et al*. Effects of vitamin D supplementation on metabolic and endocrine parameters in PCOS: a randomized-controlled trial.

Eur J Nutri 2019;58(5): 2019-2028.
23. Tehrani HG, Mostajeran F, Shahsavari S. The effect of calcium and vitamin D supplementation on menstrual cycle, body mass index and hyperandrogenism state of women with poly cystic ovarian syndrome. *J Res Med Sci* 2014;19(9):875.
24. Kadoura S, Alhalabi M, Nattouf AH. Effect of calcium and vitamin D supplements as an adjuvant therapy to metformin on menstrual cycle abnormalities, hormonal profile, and IGF-1 system in polycystic ovary syndrome patients: a randomized, placebo-controlled clinical trial. *Adv Pharmacol Sci* 2019; 2019:9680390.
25. Ornstein RM, Copperman NM, Jacobson MS. Effect of weight loss on menstrual function in adolescents with polycystic ovary syndrome. *J Pediatr Adolesc Gynecol* 2011;24(3):161-165.
26. Maktabi M, Chamani M, Asemi Z. The effects of vitamin D supplementation on metabolic status of patients with polycystic ovary syndrome: a randomized, double-blind, placebo-controlled trial. *Horm Metab Res* 2017;49(7):493-8.
27. Rashidi H, Ghaderian SB, Moradi L. The effect of vitamin D3 on improving lipid profile, fasting glucose and insulin resistance in polycystic ovary syndrome women with vitamin D deficiency. *Middle East Fertil Soc J* 2018;23(3):178-183.
28. Waqar F, Shadab W, Sharif S, Riaz B. Effect of vitamin D supplementation on glucose metabolism in polycystic ovary syndrome. *J Soc Obstet Gynaecol Pak* 2018;8(3):148-153.
29. Jia XZ, Wang YM, Zhang N, Guo LN, Zhen XL*et al*. Effect of vitamin D on clinical and biochemical parameters in polycystic ovary syndrome women: A meta-analysis. *J Obstet Gynaecol Res* 2015;41(11):1791-1802.
30. Moran LJ, Hutchison SK, Norman RJ, Teede HJ. Lifestyle changes in women with polycystic ovary syndrome. *Cochrane Database Syst Rev* 2011; (7).

Author for Correspondence:
Dr. Srinivas Rao Paidipally, Department of Endocrinology, Gandhi Medical College, Secunderabad-500003 Telangana. Email: psrdr20@gmail.com. Cell: +91-9989050745.

How to cite this article:
Kudugunti N, Paidipally SR, Himaja K, Sahay R. Effect of Vitamin D Supplementation on Menstrual Cycle Regularization and Metabolic Parameters in Polycystic Ovary Syndrome Women-A Retrospective Study. *J Krishna Inst Med Sci Univ* 2021; 10(1):100-110

Submitted: *30-Oct-2020* ***Accepted:*** *14-Dec-2020* ***Published:*** *01-Jan-2021*