Indian J Med Res 156, October & November 2022, pp 693-695
DOI: 10.4103/ijmr.ijmr_1345_21

Quick Response Code:

Correspondence

Effect of vitamin D deficiency on the metabolic profile of women with polycystic ovary syndrome

Polycystic ovarian syndrome (PCOS) is the most prevalent female endocrine disorder, which is achieving epidemic proportions in the Indian subcontinent with a reported prevalence ranging from 6.3 to 22.5 per cent[1,2]. Although PCOS has multifactorial aetiology, insulin resistance is one of the key drivers in the pathophysiology of PCOS, which can result in anovulation, menstrual irregularities, impaired glucose metabolism and metabolic syndrome[3]. The role of vitamin D in affecting the insulin sensitivity is chiefly attributed to the presence of 1,25(OH)2D3 receptors, through which it directly binds on pancreatic β-cells and improves production of insulin[4]. Another mechanism postulated is that 1,25-dihydroxy vitamin D improves insulin sensitivity of the liver, skeletal and adipose tissue by increasing the level of calcium inside these cells, which is essential for insulin-mediated intracellular processes, therefore reducing insulin resistance[5,6].

High prevalence of vitamin D deficiency (VDD) in women with PCOS (up to 70.3%) has been reported from India[7]. The VDD is postulated to affect the insulin resistance which, in turn, can affect various metabolic parameters; however, the results are varied and not well studied in Indian scenario[8]. Hence, the association of VDD on various metabolic parameters in women with PCOS was analyzed.

A retrospective analysis of database of 175 women in the age group of 16-49 yr attending the multidisciplinary PCOS clinic organised at ICMR-National Institute for Research in Reproductive and Child Health (NIRRCH), Mumbai, India, from 2016 to 2019 was used for this study. Diagnosis of adult PCOS was done using Rotterdam criteria, which included the presence of two out of three criteria of oligo/anovulation (OD), clinical or biochemical hyperandrogenism (HA), polycystic ovaries morphology on ultrasound (PCOM)[9]. For adolescent diagnosis of PCOS, criteria of HA along with persistent OD or HA along with OD and PCOM or both were used for diagnosis. PCOS phenotypes were classified as per the NIH consensus statement into four types[10]. The 25(OH)D levels were estimated by electro-chemiluminescence immunoassay method in a College of American Pathologists-accredited laboratory along with hormonal, biochemical, lipid and glycaemic profile[11]. VDD was categorized as per 25(OH)D levels of ≥20 ng/ml, 19.9-10 ng/ml and less than 10 ng/ml. These categorized 25(OH)D levels were associated with various metabolic parameters used to define metabolic syndrome as per the new International Diabetes Federation (IDF) consensus statement[12]. The 25(OH)D levels were also associated with other parameters that were used to measure the metabolic disturbances such as Homeostatic Model Assessment (HOMA) for Insulin Resistance index, fasting insulin and lipid ratio, which included total cholesterol/high-density lipoprotein (HDL) ratio and triglyceride/HDL ratio[13-15]. Association was sought between VDD and metabolic parameters using ANOVA in case of normal distribution and Kruskal-Wallis test in case of skewed distribution.

The mean age of these women was 26.92±4.5 yr, and the mean body mass index (BMI) was 26.3±5.2 kg/m^2. The most common phenotype was phenotype C having both HA and PCOM in 44.5 per cent (n=78) of women. This was followed by phenotype A having HA, OD and PCOM in 42.2 per cent (n=74) of women. The rest 13.14 per cent (n=23) of women constituted phenotypes B and D.

The mean 25(OH)D level was 12.9±8.1 ng/ml. Deficient levels corresponding to 10.0-19.9 ng/ml were seen in 46.2 per cent (n=81) and severe deficiency corresponding to less than 10.0 ng/dl was seen in 42.8 per cent (n=75) of PCOS women. Metabolic syndrome

Table. Association between metabolic parameters and 25-hydroxyvitamin D levels

Metabolic parameters	25(OH)D ≥20 ng/ml (normal and insufficient) (n=19)	25(OH)D 10-19.9 ng/dl (deficient) (n=81)	25(OH)D <10 ng/ml (severely deficient) (n=75)
BMI (kg/m^2)	26.4±5.9	26.3±5.6	26.2±4.6
Age (yr)	27.21±4.8	27.03±4.3	26.73±4.6
WC (cm)	85.84±15.9	85.88±14.5	85.23±11.7
TG (mg/dl)	88 (41-181)	87 (32-373)	95.6 (32-256)
HDL (mg/dl)*	49.3±11.15	42.7±10.09	44.6±8.8
FBS (mg/dl)	91±7.7	95±10.3	95.1±13.3
BP systolic (mmHg)	116.58±15.1	118±12.4	115±13.1
BP diastolic (mmHg)	72.16±9.7	75.33±10.55	73.99±9.6
Fasting insulin (Mu/l)	15.4 (1.97-28.6)	12.57 (3.81-104.8)	14.1 (3.09-109.7)
HOMA IR	3.3 (0.37-6.79)	2.85 (0.93-29.30)	3.2 (0.72-30.86)
Cholesterol/HDL ratio	3.4 (2.29-5.74)	4 (2.06-7.64)	3.9 (1-7.7)
TG/HDL ratio	1.7 (0.71-4)	2.1 (0.57-11.30)	2.1 (0.6-6.92)

P<0.05 (ANOVA). Data presented as mean±SD or median (minimum-maximum). 25(OH) D, 25-hydroxyvitamin D; BMI, body mass index; WC, waist circumference; TG, triglyceride; HDL, high-density lipoprotein; FBS, fasting blood sugar; HOMA-IR, Homeostatic Model Assessment for Insulin Resistance; BP, blood pressure; SD, standard deviation

was diagnosed in 32 per cent (n=56). The association between metabolic parameters and categorized VDD levels is shown in the Table. The mean level of BMI was not found significant across all three groups. A significant association was found between HDL and VDD (P=0.027). No other metabolic parameter was significantly associated with VDD.

In this study, a high prevalence of metabolic syndrome was seen among women with PCOS in our study group, which was similar to another study by Chandrasekaran and Sagili[16], who reported the prevalence of metabolic syndrome to be 33 per cent. Underlying insulin resistance, increased android obesity, atherogenic dyslipidaemia and hypertension are the potential contributors to develop this metabolic syndrome[16].

There is inconsistent evidence in literature regarding the effect of VDD on various metabolic parameters in women with PCOS[17,18]. Our study revealed that though BMI, which is a well-known confounding factor to affect vitamin D levels, was not variable across groups, still a significant association was found between HDL levels and VDD, though none of the other metabolic parameter showed significance. A systematic review protocol by Shi *et al*[19] elaborated the mechanism postulated by which 25(OH)D affects lipid profile. Further this 25(OH)D may affect the balance between the pro-inflammatory and anti-inflammatory cytokines[2,7]. The major limiting factor of this study was small sample size and lack of age-matched controls.

This study adds to the existing evidence of high prevalence of metabolic syndrome among women with PCOS. VDD affects the HDL levels, which is an important component of metabolic syndrome. However, more studies are required to evaluate the molecular mechanism of this association.

***Acknowledgment*:** The authors acknowledge the encouragement and guidance received from Director, ICMR-NIRRCH and Dr Sanjay Chauhan, Head of Operational and Clinical research at ICMR-NIRRCH, Mumbai. The authors also acknowledge staff for data collection and data entry.

***Financial support & sponsorship*:** The authors acknowledge the financial support from the ICMR-NIRRCH to run the multidisciplinary PCOS clinic.

***Conflicts of Interest*:** None.

Deepti Tandon[1], Beena Joshi[2], Shahina Begum[3], Suchitra Surve[1], Pratibha Kokate[1] & Anushree Devashish Patil[1]*
Departments of [1]Clinical Research, [2]Operational Research & [3]Biostastistics, ICMR-National Institute for Research in Reproductive & Child Health, Mumbai 400 012, Maharashtra, India
**For correspondence:*
rajshrinm@yahoo.co.in

Received May 7, 2021

References

1. Wolf WM, Wattick RA, Kinkade ON, Olfert MD. Geographical prevalence of polycystic ovary syndrome as determined by region and race/ethnicity. *Int J Environ Res Public Health* 2018; *15* : 2589.
2. Joshi B, Mukherjee S, Patil A, Purandare A, Chauhan S, Vaidya R. A cross-sectional study of polycystic ovarian syndrome among adolescent and young girls in Mumbai, India. *Indian J Endocrinol Metab* 2014; *18* : 317-24.
3. Rojas J, Chávez M, Olivar L, Rojas M, Morillo J, Mejías J, *et al*. Polycystic ovary syndrome, insulin resistance, and obesity: Navigating the pathophysiologic labyrinth. *Int J Reprod Med* 2014; *2014* : 719050.
4. Nandi A, Sinha N, Ong E, Sonmez H, Poretsky L. Is there a role for vitamin D in human reproduction? *Horm Mol Biol Clin Investig* 2016; *25* : 15-28.
5. Al-Shoumer KA, Al-Essa TM. Is there a relationship between vitamin D with insulin resistance and diabetes mellitus? *World J Diabetes* 2015; *6* : 1057-64.
6. Szymczak-Pajor I, Śliwińska A. Analysis of association between vitamin D deficiency and insulin resistance. *Nutrients* 2019; *11* : 794.
7. Mogili KD, Karuppusami R, Thomas S, Chandy A, Kamath MS, Tk A. Prevalence of vitamin D deficiency in infertile women with polycystic ovarian syndrome and its association with metabolic syndrome - A prospective observational study. *Eur J Obstet Gynecol Reprod Biol* 2018; *229* : 15-9.
8. Krul-Poel YHM, Koenders PP, SteegersTheunissen RP, Ten Boekel E, Wee MMT, Louwers Y, *et al*. Vitamin D and metabolic disturbances in polycystic ovary syndrome (PCOS): A cross-sectional study. *PLoS One* 2018; *13* : e0204748.
9. Azziz R, Diagnosis of polycystic ovarian syndrome: The Rotterdam criteria are premature. *J Clin Endocrinol Metab* 2006; *91* : 781-5.
10. Lizneva D, Suturina L, Walker W, Brakta S, Gavrilova-Jordan L, Azziz R. Criteria, prevalence, and phenotypes of polycystic ovary syndrome. *Fertil Steril* 2016; *106* : 6-15.
11. Han S, Qiu W, Zhang J, Bai Z, Tong X. Development of a chemiluminescence immunoassay for quantification of 25-hydroxyvitamin D in human serum. *J Anal Methods Chem* 2020; *2020* : 9039270.
12. The IDF Consensus Worldwide Definition of the Metabolic Syndrome. Available from: *https://file:///C:/Users/DELL/Downloads/IDF_Meta_def_final%20(2).pdf*, accessed on January 27, 2022.
13. Saxena P, Prakash A, Nigam A. Efficacy of 2-hour post glucose insulin levels in predicting insulin resistance in polycystic ovarian syndrome with infertility. *J Hum Reprod Sci* 2011; *4* : 20-2.
14. Kheirollahi A, Teimouri M, Karimi M, Vatannejad A, Moradi N, Borumandnia N, *et al*. Evaluation of lipid ratios and triglyceride-glucose index as risk markers of insulin resistance in Iranian polycystic ovary syndrome women. *Lipids Health Dis* 2020; *19* : 235.
15. Gutch M, Kumar S, Razi SM, Gupta KK, Gupta A. Assessment of insulin sensitivity/resistance. *Indian J Endocrinol Metab* 2015; *19* : 160-4.
16. Chandrasekaran S, Sagili H. Metabolic syndrome in women with polycystic ovarian syndrome. *Obstet Gynaecol* 2018; *20* : 245-52.
17. Kumar A, Barki S, Raghav V, Chaturvedi A, Kumar KVSH. Correlation of Vitamin D with metabolic parameters in polycystic ovarian syndrome. *J Family Med Prim Care* 2017; *6* : 115-9.
18. Saheb Sharif-Askari F, Saheb Sharif-Askari N, Halwani R, Abusnana S, Hamoudi R, Sulaiman N. Low vitamin D serum level is associated with HDL-C dyslipidemia and increased serum thrombomodulin levels of insulin-resistant individuals. *Diabetes Metab Syndr Obes* 2020; *13* : 1599-607.
19. Shi XY, Yao J, Fan SM, Hong PP, Xia YG, Chen Q. Effects of vitamin D supplementation on serum lipid profile in women with polycystic ovary syndrome: A protocol for a systematic review and meta-analysis. *Medicine (Baltimore)* 2020; *99* : e20621.