

Original Article

Frequency of Vitamin D Deficiency in Women with Polycystic Ovarian Syndrome

Rabia Jameel¹, Arooj Kamran², Samar Abbas Jaffri³, Sadia Sultan⁴

¹Department of Obstetrics & Gynaecology, Dow University of Health Sciences, Karachi,

²Dept of Obstetric & Gynecologist Dow University of Health Sciences, Karachi

³Assistant Professor of Medicine, Liaquat National Hospital and Medical College, Karachi

⁴Laboratory Services, Consultant Hematologist, National Medical Centre, Karachi

Correspondence: Dr. Sadia Sultan

Laboratory Services, Consultant Hematologist, National Medical Centre, Karachi

Email: sadiasultan96@yahoo.com

Abstract

Objective: To determine the frequency of vitamin D deficiency in women with the polycystic ovarian syndrome.

Methodology: This descriptive cross sectional study was conducted in Department of obstetrics and gynecology, civil hospital Karachi from July 18, 2014 to Jan 18, 2015. A total of 93 patients with PCOS were included in this study. Vitamin D deficiency was considered as 25-hydroxyvitamin D [25OHD] level < 20 ng/ml. Pregnant women with pre-existing medical conditions like hypertension, diabetes mellitus, acute pelvic inflammatory disease, liver or renal diseases, fibroid, and malignancies were excluded for this study.

Results: The mean age, duration of PCOS and BMI of the study population was 34.1 ± 4.6 years, 2.5 ± 1.2 years and 20 ± 3.0 kg/m² respectively. Out of the 93 patients, 35(37%) had no parity, 36(39%) had single parity, 15(16%) had two parity and 07 (08%) had more than two parity. A total of 61(65%) of women with PCOS had vitamin D deficiency.

Conclusion: As our study shows the prevalence of vitamin D deficiency among women with PCOS is substantial. Although our findings suggest that the role of vitamin D in the pathogenesis of PCOS is not yet clear, vitamin D deficiency is a common finding among PCOS patients. Finally, the potential relationship between vitamin D and PCOS requires further investigation.

Keywords: Polycystic ovary syndrome, Vitamin D deficiency.

Cite this article as: Jameel R, Kamran A, Jaffri SA, Sultan S. Frequency of Vitamin D Deficiency in Women with Polycystic Ovarian Syndrome. J Soc Obstet Gynaecol Pak. 2019; Vol 9(3):153-157.

Introduction

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age, characterized by the presence of polycystic ovaries, menstrual dysfunction, infertility and biochemical and clinical hyperandrogenism. The association of vitamin D with endocrine, metabolic, and genetic aspects in PCOS is largely unknown. Vitamin D is actually not really a vitamin after all.¹ It is actually a precursor hormone and is a key factor in maintaining hormone balance. It is the

building block of a powerful steroid hormone in your body called *calcitriol*.¹ There has been a lot of talk about Vitamin D lately probably because, upwards of 75% of the world's population is Vitamin D deficient and it can put one at risk of a myriad of health issues like rickets, tuberculosis, psoriasis, multiple sclerosis, inflammatory bowel disease, type-1 diabetes, high blood pressure, increased heart failure, insulin resistance, depression, obesity, breast and other cancers. It is estimated

Authorship Contribution: ¹ Concept and Idea, Data collection, Methodology, literature review, ³final approval and authored the study.^{2,4} Data collection, Data analysis, assisted in drafting the work,³ critically revising the important intellectual contents and reviewed the study.

Funding Source: none

Conflict of Interest: none

Received: Mar 14, 2019

Accepted: Oct 27, 2019

that many of these diseases could be reduced by 20% to 50% or more of vitamin D deficiency was corrected by increasing vitamin D intake through sun exposure, fortified foods or supplements.²

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age, presenting in up to 18% of this population. PCOS is characterized by the presence of polycystic ovaries, menstrual dysfunction, infertility, and biochemical (elevated androgens) and clinical (hirsutism and/or acne) hyperandrogenism.³ Women with polycystic ovary syndrome (PCOS) frequently suffer from metabolic disturbances, in particular from insulin resistance. Accumulating evidence suggests that vitamin D deficiency may contribute to the development of insulin resistance. The association of vitamin D with endocrine, metabolic, and genetic aspects in PCOS is largely unknown.⁴

Vitamin D has been well-known for its function in maintaining calcium and phosphorus homeostasis and promoting bone mineralization. There is some evidence that in addition to sex steroid hormones, the classic regulators of human reproduction, vitamin D also modulates reproductive processes in women and men. Vitamin D deficiency is common in women with polycystic ovary syndrome (PCOS), with 67-85% of women with PCOS having serum concentrations of 25-hydroxy vitamin D (25OHD) <20 ng/ml.⁵ There is accumulating evidence that vitamin D plays an important role in reproductive function.

Vitamin D and reproductive function have been found in the ovary, endometrium, and placenta. Vitamin D deficiency is associated with calcium deregulation, which contributes to the development of follicular arrest in women with PCOS and results in menstrual and fertility dysfunction.⁶ Studies have shown that women with PCOS have mostly insufficient vitamin D levels, and vitamin D replacement therapy may have a beneficial effect on insulin resistance (IR) in women with PCOS. People with higher levels of this vitamin are 40% less likely to develop diabetes. The vitamin helps the pancreas to secrete insulin. It also reduces

systemic inflammation, which influences insulin resistance.⁷

The aim of our study is to determine the frequency of vitamin D deficiency in women with polycystic ovary syndrome. Though the work has been done, but locally it is still minimum to provide significant baseline for further strategies and modification.

Methodology

It was a prospective cross-sectional study was conducted in the Department of Obstetrics and Gynecology, Civil Hospital Karachi., from July 18, 2014 to Jan 18, 2015. Taking the prevalence of vitamin D deficiency in women with polycystic syndrome patients i.e. 67%⁵, margin of error d=10% and 95% level of confidence. The sample size comes out to be n= 93. All women fulfilling the inclusion criteria were included after informed consent. Non probability sampling technique was used for the purpose of data collection. All the young women of age (18-45), any parity and polycystic ovary syndrome with duration more than equal to one year were included. PCOS women can be diagnosed by any two of them: 1) Oligo- and/or ovulation. Menstrual bleeding <2 day/cycle. 2) Clinical and/or biochemical signs of hyperandrogenism (hirsutism, weight gain, menstrual disorders). 3) Polycystic ovaries evident on ultrasound (>12 follicle of size 5-7mm). Vitamin D deficiency was defined as 25- hydroxyvitamin D [25OHD] level < 20 ng/ml.

Data was entered and analysed by using SPSS version 19.0. Mean and the standard deviation was calculated for age, duration of PCO and BMI. Frequency and percentage were calculated for outcome variable (vitamin D deficiency) and parity. Post-stratification was done by applying Chi-square test. P≤ 0.05 was taken as significant.

Results

The age range in our study was from 18 to 45 years with mean age of 34.5 ± 4.6 years, mean duration of PCO was 2.5±1.2 years and mean BMI was 20.1 ± 3.0. Out of these 93 patients, 35(37%) had no parity, 36 (39%) had single parity, 15(16%) had two

parity and 07(08%) had more than two parity. Overall 61(65%) of women with polycystic ovary syndrome had vitamin D deficiency. (Table I) When outcome variable was stratified with respect to age, duration of PCO, parity and BMI showed no significant difference as p-values are 0.584, 0.962, 0.445 and 0.752 respectively. (Table II)

Table I: Stratification with respect to Parity & Vitamin D deficiency

	n	%	Vitamin D deficiency		P-value	
			Yes	No		
Parity	0	35	37%	23	12	0.445
	1	36	39%	29	7	
	2	15	16%	6	9	
	>2	7	8%	3	4	

Table-II: Stratification of Outcome Variables with respect to Vitamin D deficiency

		Vitamin D deficiency		P-value
		Yes	No	
Age group	18-32	26	15	0.584
	33-45	35	17	
Duration of PCO	< 2 years	27	14	0.962
	≥ 2 years	34	18	
BMI	< 25 kg/m ²	42	21	0.752
	> 25 kg/m ²	19	11	

Discussion

In women with PCOS, low vitamin D levels are associated with obesity, metabolic and endocrine disturbances and vitamin D supplementation might improve menstrual frequency and metabolic disturbances in those women.⁸ Vitamin D deficiency is still considered a problem of the past by health care professionals and the public. Populations at risk include infants, children, pregnant and postmenopausal women. Furthermore, to our knowledge, this study is one of the rare describing associations of vitamin D deficiency with gonadotropins and sex hormone in PCOS women. The present study showed that in total 65% of women with PCOS had VD deficiency but without significant difference between groups according to BMI. Vitamin D deficiency is common in women with PCOS, with 67-85% of women with PCOS having serum concentrations of 25(OH)D <20 ng/mL.⁹

The prevalence of insufficient 25(OH)D levels (<30 ng/mL) was 72.8% in women with PCOS in one study.¹⁰ Low 25(OH)D < 50 nmol/L) was detected in 37% of the entire cohort of patients.¹¹ Vitamin D deficiency may exacerbate symptoms of PCOS, with observational studies showing lower 25(OH)D levels were associated with insulin resistance, ovulatory and menstrual irregularities, lower pregnancy success, hirsutism, hyperandrogenism, obesity and elevated cardiovascular disease risk factors.⁹ Multiple regression analysis of our data revealed that the presence of deficiency of vitamin D in PCOS women was associated with HOMA-IR and SHBG. Vitamin D has an important role in the pathogenesis of insulin resistance in PCOS.¹² The results in this study demonstrated that HOMA-IR was a better independent risk factor for the presence of vitamin D deficiency than SHBG in women with PCOS.¹² Low 25(OH)D level in PCOS women is associated with obesity and insulin resistance but not with PCOS per se.¹³ However in another study there were not any effect of vitamin D supplementation on insulin sensitivity and insulin resistance in women with PCOS, and vitamin D deficiency in their study.¹³ In our research obesity was significantly connected with vitamin D deficiency. Present data demonstrated that HOMA-IR and vitamin D deficiency significantly predicted the obesity risk, while SHBG was not significantly associated with obesity risk. In the PCOS cohort study of Hahn et al. 25(OH)D concentration was negatively correlated with body mass index, body fat, HOMA-IR, hyperinsulinemia and leptin level, and positively correlated with HDL cholesterol.¹⁴ One study demonstrated that in PCOS low 25(OH)D levels are significantly determined by the degree of adiposity.¹⁵ Women with PCOS and metabolic syndrome had lower 25(OH) D levels than PCOS women without these features.¹⁴ The investigators found significant negative correlations of 25(OH)D levels with BMI, waist circumference, waist-to-hip ratio, systolic and diastolic blood pressure, fasting and stimulated glucose, area under the glucose response curve, fasting insulin, HOMA-IR, HOMA-beta, triglycerides, and quotient total cholesterol/high-density lipoprotein (HDL) and

positive correlation of 25(OH)D levels with QUICKI and HDL.¹⁴

There was no association of vitamin D deficiency with gonadotropins and sex hormones except SHBG. Analysis of vitamin D and biochemical endocrine PCOS features revealed a significant correlation only between 25(OH)D and sex hormone binding globulin as well as the free androgen index.¹⁴ BMI resulted to be the best predicting factor of 25(OH)D levels, whereas SHBG, Free Androgen Index, glucose uptake, and fat-free mass were not.¹⁵ Another study observed a significant decrease in fasting glucose, stimulated glucose and C-peptide levels after vitamin D treatment.¹⁵ There were no changes in androgens. Their results suggest that vitamin D treatment might improve glucose metabolism and menstrual frequency in PCOS women.

It was reported that lower serum vitamin D levels in a large number of women with PCOS (n=545) compared to controls (n=145) (25.7 vs. 32.0 ng/mL, respectively), a substantial number of studies suggest that serum vitamin D levels are similar in women with and without PCOS.^{10,15,16} In fact, there has been one report that women with PCOS have significantly higher vitamin D levels compared to control women with similar age and BMI.¹³ Thus, there is inconsistency in the literature about whether vitamin D levels are similar between women with and without PCOS.

In previous studies, average serum vitamin D levels in women with PCOS were reported to be between 11 ng/mL and 31 ng/mL, with the majority having mean values <20 ng/mL.¹⁰⁻¹⁵ In our study, the mean 25-(OH)D₃ level in women with PCOS was also <20 ng/mL (12.1±6.6 ng/mL), and vitamin D deficiency (lower than 20 ng/mL) was observed in 65% of patients. However, vitamin D deficiency is also common in the general population, with 10% to 60% of adults having values lower than 20 ng/mL.^{17,18}

Thus, we can assume that although there is inconsistency in the literature about whether vitamin D levels are different between women with and without PCOS, vitamin D deficiency is equally

common in both groups. In fact, in our study, vitamin D insufficiency (<20 ng/mL) was observed in the majority of the subjects, which is supported by the findings that more than 90% of the pigmented population of the United States (Blacks, Hispanics, and Asians) suffer from vitamin D insufficiency.¹⁹

Many studies have investigated an association between vitamin D status and hormonal or metabolic features in PCOS. In women with PCOS, a low vitamin D level is thought to be related to metabolic risk factors such as insulin resistance, high total cholesterol, blood pressure, glucose, C-reactive protein, triglycerides, and low high-density lipoprotein (HDL) cholesterol.^{12,15} In addition, vitamin D replacement therapy may have a beneficial effect on insulin resistance or fasting and on stimulated glucose and triglycerides levels in women with PCOS.¹⁴ Furthermore, several studies have identified relationships between low vitamin D status and measures of hyperandrogenism such as SHBG, the degree of hirsutism, FAI, total T and dehydroepiandrosterone sulphate.^{11,12,15}

In the current study, a higher serum concentration of calcium was seen in women with PCOS. Although some reports found no differences, lower serum calcium concentrations in PCOS have also been reported.¹¹ Experimental studies show that an increase in intracellular free calcium is essential for meiotic resumption by mouse oocytes, and it has been suggested that disordered calcium regulation may in part be responsible for disorders of oocyte development such as PCOS.^{20,21} It is not clear from studies why women with PCOS showed higher calcium levels than controls, and this needs to be investigated in further studies.²²

Finally, we did not evaluate the presence of other potential confounding factors, such as outdoor times or dietary patterns which could affect the serum vitamin D levels.

Recommendations: High quality, large-scale RCTs are required to determine the optimal 25(OH) D₃ levels in the reproductive period and the amount of vitamin D supplementation required to achieve those levels for the numerous actions of vitamin D throughout a woman's life. Confirmation of experimental observations relating to

the risk of vitamin D deficiency would have important public health implications. In future early management and protocol will be recommended for proper diagnosis and intervention to control this deficiency.

Conclusion

The prevalence of vitamin D deficiency among women with PCOS is substantial. Although our findings suggest that the role of vitamin D in the pathogenesis of PCOS is not yet clear, vitamin D deficiency is a common finding among PCOS patients. Finally, the potential relationship between vitamin D and PCOS requires further investigation, since vitamin D deficiency has been continuously proposed to increase the risk of insulin resistance and T2DM, which is also core pathophysiology of PCOS. Further when results stratified with respect to age, parity, duration of PCO and BMI shows no significant difference.

References

- Muscogiuri G, Policolo C, Prioleta A, Sorice G, Mezza T, Lassandro A, et al. Low levels of 25(OH) and insulin resistance: 2 unrelated features or a cause-effect in PCOS? *Clin Nutr*. 2012;1(1):1-5.
- Wehr E, Pilz S, Schweighofer N, Guiliani A, Kopera D, Pieber TR, et al. Association of hypovitaminosis D with metabolic disturbance with polycystic ovary syndrome. *Eur J endocrinol*. 2009;161(2):575-582.
- Alpert PT, Shaikh U. The effect of vitamin D deficiency and insufficiency on the endocrine and paracrine systems. *Biol Res Nurs*. 2007;9(12):117-29.
- Rebecca L, Thomson, Spedding S, Jonathan D, Buckley. Vitamin D in the Aetiology and Management of Polycystic ovary syndrome. *Clin endocrinol*. 2012;77(3):343-350.
- Grundmann M, Versen-Hoyneck Fv. Vitamin D- roles in women's reproductive health? *Reprod Biol Endocrinol*. 2011;9(4): 177-116.
- Unfer V. Polycystic ovary syndrome: a vitamin deficiency? Floating a new pathogenesis hypothesis. *Eur Rev Med Pharmacol Sci*. 2011;9(4):177-116.
- Bostanci EI, Ozler S, Yilmaz NK, Yesilyurt H. Serum 25-Hydroxy Vitamin D Levels in Turkish Adolescent Girls with Polycystic Ovary Syndrome and the Correlation with Clinical/Biochemical Parameters. *J Pediatr Adolesc Gynecol*. 2018;31(3):270-273.
- 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;229:15-19.
- Santos BR, Lecke SB, Spritzer PM. Apa-I polymorphism in VDR gene is related to metabolic syndrome in polycystic ovary syndrome: a cross-sectional study. *Reprod Biol Endocrinol*. 2018;16(1):38.
- Kuhr DL, Sjaarda LA, Alkhalaf Z, Omosigho UR, Connell MT, Silver RM, et al. Vitamin D is associated with bioavailability of androgens in eumenorrheic women with prior pregnancy loss. *Am J Obstet Gynecol*. 2018;218(6):608.e1-608.e6.
- Cappy H, Giacobini P, Pigny P, Bruyneel A, Leroy-Billiard M, Dewailly D, Catteau-Jonard S. Low vitamin D3 and high anti-Müllerian hormone serum levels in the polycystic ovary syndrome (PCOS): Is there a link? *Ann Endocrinol (Paris)*. 2016 ;77(5):593-599.
- Figurová J, Dravecká I, Javorský M, Petříková J, Lazúrová I. Prevalence of vitamin D deficiency in Slovak women with polycystic ovary syndrome and its relation to metabolic and reproductive abnormalities. *Wien Klin Wochenschr*. 2016 ;128(17-18):641-648.
- Nutrition and bone health: with particular reference to calcium and vitamin D. Report of the Subgroup on Bone Health, Working Group on the Nutritional Status of the Population of the Committee on Medical Aspects of the Food Nutrition Policy Rep Health Soc Subj (Lond) 1998, 49:iii-xvii. 1-24.
- Bodnar LM, Simhan HN, Powers RW, Frank MP, Cooperstein E, Roberts JM. High prevalence of vitamin D insufficiency in black and white pregnant women residing in the northern United States and their neonates. *J Nutr*. 2007, 137(2):447-452.
- Holmes VA, Barnes MS, Alexander HD, McFaul P, Wallace JM. Vitamin D deficiency and insufficiency in pregnant women: a longitudinal study. *Br J Nutr*. 2009, 102(6):876-881.
- Heaney RP. Vitamin D in health and disease. *Clin J Am Soc Nephrol*. 2008, 3(5):1535-1541.
- Sun W, Xie H, Ji J, Zhou X, Goltzman D, Miao D. Defective female reproductive function in 1,25(OH)2D-deficient mice results from indirect effect mediated by extracellular calcium and/or phosphorus. *Am J Physiol Endocrinol Metab*. 2010, 299(6):E928-935.
- Johnson LE, DeLuca HF. Vitamin D receptor null mutant mice fed high levels of calcium are fertile. *J Nutr*. 2001, 131(6):1787-1791.
- Vigano P, Lattuada D, Mangioni S, Ermellino L, Vignali M, Caporizzo E, et al. Cycling and early pregnant endometrium as a site of regulated expression of the vitamin D system. *J Mol Endocrinol*. 2006, 36(3):415-424.
- Haldar D, Agrawal N, Patel S, Kambale PR, Arora K, Sharma A, et al. Association of VDBP and CYP2R1 gene polymorphisms with vitamin D status in women with polycystic ovarian syndrome: a north Indian study. *Eur J Nutr*. 2018 Mar;57(2):703-711.
- Halloran BP, DeLuca HF. Effect of vitamin D deficiency on fertility and reproductive capacity in the female rat. *J Nutr*. 1980, 110(8):1573-1580.
- Li HW, Brereton RE, Anderson RA, Wallace AM, Ho CK. Vitamin D deficiency is common and associated with metabolic risk factors in patients with polycystic ovary syndrome. *Metabolism*. 2011, 60(10):1475-1481.