ASSOCIATION OF VITAMIN D DEFICIENCY WITH POLYCYSTIC OVARIAN SYNDROME

Quratul Ain Hanif, Saima Qamar, Pakeeza Aslam, Hajra Omar, Nilofar Mustafa, Saima Masood

Combined Military Hospital Lahore/National University of Medical Sciences (NUMS) Pakistan

ABSTRACT

Objective: To determine the frequency of vitamin D deficiency in women with polycystic ovary syndrome.
Study Design: Cross sectional study.
Place and Duration of Study: Department of Obstetrics and Gynecology, Combined Military Hospital Lahore, from Apr 2018 to Sep 2018.
Material and Methods: This study involved 200 women aged between 18-45 years presenting with polycystic ovarian syndrome. Blood sample was analyzed for vitamin D level and serum levels of 25-hydroxy Vitamin D3<20ng/ml were labeled as vitamin D deficiency. A written informed consent was obtained from every patient. All the collected data was entered and analyzed through SPSS version 20.
Results: The age of the patients ranged from 18 years to 45 years with a mean of 26.82 ± 7.67 years. Majority (n=148, 74.0%) of the patients were aged between 18-31 years followed by 32-45 years (n=52, 26.0%). There were 92 (46.0%) obese patients in the study group. The frequency of vitamin D deficiency was found to be 58.0% in women suffering from PCOS. There was no significant difference in the frequency of vitamin D deficiency among age groups; 18-31 vs. 32-45 years (58.1% vs. 57.7%; *p*=0.958) and BMI groups; obese vs. non-obese (65.2% vs. 51.9%; *p*=0.056).
Conclusion: The frequency of vitamin D deficiency was found to be 58.0% in women suffering from PCOS. There was no significant difference in the frequency of vitamin D deficiency among age and BMI groups.

Keywords: Obesity, Polycystic ovarian syndrome, Vitamin D Deficiency.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age, presenting in up to 18% of this population[1]. PCOS is characterized by the presence of polycystic ovaries, menstrual dysfunction, infertility and biochemical (elevated androgens) and clinical (hirsutism and/or acne) hyperandrogenism. PCOS is also associated with an increased incidence of cardiovascular disease, type 2 diabetes, dyslipidemia and impaired glucose tolerance. Obesity and insulin resistance are closely linked to the development of PCOS and its clinical features[2] PCOS is the most common cause of anovulatory infertility in women[3].

A number of studies have demonstrated associations between vitamin D levels and various PCOS symptoms, including insulin resistance, infertility and hirsutim[2]. Vitamin D is thought to influence the development of PCOS through gene transcription, and hormonal modulation influences insulin metabolism and fertility regulation[4,5].

Vitamin D deficiency is common in general population in many parts of the world with 10-60% of adults having values lower than 20 ng/ml[6]. Vitamin D deficiency disrupts the function of all the systems of the body and increases the risk of chronic disease, including physical diseases such as cancer, cardiovascular, autoimmune and infectious diseases, and psychological disorders such as depression and chronic pain[7].

Vitamin D deficiency is also common in women with polycystic ovary syndrome (PCOS), with the 67-85% of women with PCOS having serum concentrations of 25-hydroxy vitamin D

Correspondence: Dr Saima Qamar, Department of Obs/Gynae, Combined Military Hospital Lahore Pakistan
Email: saimaomar@gmail.com
Received: 02 Jul 2018; revised received: 13 Nov 2018; accepted: 06 Dec 2018

(25OHD) <20ng/ml[8]. Studies suggest that lower 25OHD levels are associated with higher insulin resistance and vitamin D therapy may have a beneficial effect on insulin resistance and insulin secretion in obese women with PCOS. Vitamin D deficiency is also related with calcium dysregulation, which contributes to the development of follicular arrest in women with PCOS.

The current obesity epidemic suggests that the prevalence of PCOS will continue to rise. Vitamin D deficiency is already prevalent in our population, and determining its frequency among patients with PCOS can provide valuable input for a future management framework for both diseases.

MATERIAL AND METHODS

It was a cross sectional study, conducted at department of Obstetrics and Gynecology, Combined Military Hospital Lahore, from Apr 2018 to Sep 2018. Approval from the institutional ethical review committee was taken.

Sample size of 200 cases was calculated with 95% confidence level, 5% margin of error and taking expected percentage of vitamin D deficiency i.e. 25(OHD) <20 ng/ml i.e. 31.2% in women with PCOS. Patients were selected by non-probability, consecutive sampling.

Women between the ages of 18 to 45 years with the diagnosis of PCOS were included in the study. Polycystic ovary syndrome was defined as ultrasonographic detection of PCOS (12 or more follicles measuring 2-9 mm) with LH/FSH ratio >1 IU/L (normal value of LH/FSH ratio is ≤1 IU/L) in patients presenting with oligomenorrhea (cycles >35 days) or amenorrhea (fewer than 3 cycles in the past 6 months).

All pregnant or lactating women and patients on calcium and vitamin D supplementation were excluded from the study. Women with co-morbidities like hypertension, diabetes mellitus, deranged liver function tests, deranged renal function tests, gastrointestinal problems, and malnutrition were also excluded.

After taking informed consent, history, examination, hormonal profile and ultrasound were used to diagnose the PCOS. Blood sample in a sterilized disposable syringe was collected in lab for measurement of 25 hydroxy vitamin-D levels by Elecsys method on Roche Cobas e 411. All this information was recorded on a predesigned proforma.

All the collected data were entered and analyzed through SPSS version 20. Numerical variables i.e. age was presented by mean ± SD. Categorical variables i.e. vitamin D deficiency was presented as frequency and percentage. Data has been stratified for age and BMI (<30 & >30 Kg/m^2) to address effect modifiers. Post-stratification Chi-square test was applied taking $p \leq 0.05$ as significant.

RESULTS

The age of the patients ranged from 18 years to 45 years with a mean of 26.82±7.67 years. Majority (n=148, 74.0%) of the patients were aged between 18-31 years followed by 32-45 years (n=52, 26.0%). There were 92 (46.0%) obese patients in the study group. All these findings have been summarized in table-I.

The frequency of vitamin D deficiency was found to be 58.0%(116) in women suffering from PCOS. There was no significant difference in the frequency of vitamin D deficiency among age groups; 18-31 vs. 32-45 years (58.1% vs. 57.7%; p=0.958) and BMI groups; Obese vs. non-obese (65.2% vs. 51.9%; p=0.056) as shown in table-II.

DISCUSSION

According to American Society for Reproductive Medicine (ASRM) based consensus, PCOS should be defined by the presence of any two out of three criteria i.e. Oligo and/or anovulation, excess androgen activity and/or polycystic ovarian morphology on ultrasound.

A recent uncontrolled pilot study in 46 women with PCOS also observed improvements in reproductive function, with 50% (23/46) of oligo-or amenorrhoeaic women at baseline reporting improvements in menstrual frequency

after 24 weeks of weekly cholecalciferol (20000 IU), which significantly increased 25OHD levels (28.0-52.4ng/ml)[9]. Observational studies have found relationships between markers of hyperandrogenism and vitamin D status. Hirsute women with PCOS have lower 25OHD levels compared with women with PCOS without hirsutism (21.4 vs. 26.8 ng/ml) respectively[10].

In another study out of 60 cases 41 (68%) of women with PCOS had vitamin D deficiency (level <20 ng/ml) but without significant difference among the groups according to BMI (p=0.054) i.e. 22 (37%) were non-obese and 19 (31%) were obese[11].

The age of the patients ranged from 18 years to 45 years with a mean of 26.82 ± 7.67 years. A similar mean age has been reported previously by Akram *et al* in 2014 (26.23 ± 4.46 years)[12], Baqai *et al*[13] in 2010 (27.0 ± 8.0 years) and Rehman *et al*[14] in 2005 (26.47 ± 2.15) among women presenting with PCOS in local population.

Kim *et al*[15] observed relatively higher mean age of 34.1 ± 4.6 years in Korean population while Zandi *et al*[16] reported much lower mean age of 22.1 ± 4.2 years in Irani such patients. Kim *et al* have attempted to find the association between hypovitaminosis D and the development of PCOS and report that the prevalence of vitamin D deficiency is equally common among both patients and control[15].

There were 92 (46.0%) obese patients in the study group. A similar frequency of obesity (45.5%) has been observed previously by Anjum *et al*[17] in 2013 among patients of PCOS presenting at Dow University of Health Sciences, Karachi. Fouzia reported severe Vitamin D deficiency of 56% in polycystic ovary syndrome patient in study done in Railway hospital Rawalpindi in 2016[18].

The frequency of vitamin D deficiency was found to be 58.0% in women suffering from PCOS. Our observation is in line with that of Kim *et al* who observed vitamin D deficiency in 57.9% of women with PCOS in Korean population[15]. A comparatively lower frequency of 31.2% was observed by Wehr *et al* in Austria[19].

There was no significant difference in the frequency of vitamin D deficiency among age groups; 18-31 vs. 32-45 years (58.1% vs. 57.7%; p=0.958) and BMI groups; obese vs. non-obese (65.2% vs. 51.9%; p=0.056). Thus the frequency of vitamin D deficiency was unaffected by patients age and obesity. Similar insignificant difference with obesity was observed previously by Velija-Ašimi *et al*[11] (p=0.054) and Lakshman *et al*[20] (p>0.05)[20].

There is also need to see the effect of vitamin D replacement on disease symptoms in such patients. Such a study is therefore recommended in future practice.

Table-I: Baseline characteristics of study population.

Characteristics	Participants (n=200)
Age (years)	26.82 ± 7.67 (18-45)
18-31 years	148 (74.0%)
32-45 years	52 (26.0%)
Obese (BMI ≥30Kg/m^2)	92 (46.0%)
Non-Obese (BMI <30Kg/m^2)	108 (54.0%)

Table-II: Frequency of vitamin D deficiency in study population.

Characteristic		Vitamin D Deficiency n (%)	p-value
Age Groups	18-31 years	86/148 (58.1%)	0.958
	32-45 years	30/52 (57.7%)	
BMI Status	Obese (BMI ≥30Kg/m^2)	60/92 (65.2%)	0.056
	Non-Obese (BMI <30Kg/m^2)	56/108 (51.9%)	

Chi-square test, observed difference was statistically insignificant (p>0.05).

CONCLUSION

The frequency of vitamin D deficiency was found to be 58.0% in women suffering from PCOS. There was no significant difference in the frequency of vitamin D deficiency among age (p=0.958) and BMI (p=0.056) groups.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

REFERENCES

1. Sirmans SM, Pate KA. Epidemiology, diagnosis and management of Polycystic ovary syndrome. Clin Epidemiol 2014; 6: 1-13.
2. Lin MW, Wu MH. The role of vitamin D in polycystic ovary syndrome. Indian J Med Res 2015; 142(3): 238-40.
3. Dennet CC, Simon J. The role of polycystic ovary syndrome in reproductive and metabolic health: Overview and approaches for treatment. Diabetes spectr 2015; 28(2): 116-120.
4. Irani M, Merhi Z. Role of vitamin D in ovarian physiology and its implication in reproduction: A systematic review. Fertil Steril 2014; 102(2): 460–8.e3.
5. Kumar A, Bakri S. Vinod raghav correlation of vitamin D with metabolic parameters in polycystic ovarian syndrome. J Family Med Prim Care 2017; 6(11): 115-19.
6. Is Vitamin D deficiency a major global public health problem? J Steroid Biochem Mol Biol 2014; 144: 138-45.
7. KIA Dabhani, Kk Tsilidis. Prevalence of Vitamin D deficiency and Association with metabolic syndrome in a Qatari population. Nutr Diabetes 2017; 7(4): e263.
8. Guraya SS. Correlation of clinical, radiological and serum analysis of hypovitaminosis D with polycystic ovary syndrome: A systemic review and meta analysis. J Taibah Univ Sci 2017; 12(4): 277-83.
9. Rashidi H, Toolabi M, Najafian ME, Sadrian E, Safapoor N, Nazari P. The relationship of serum 25-hydroxy vitamin D3 concentrations with metabolic parameters in non obese women with polycystic ovarian syndrome. Middle East Fertil Soc J 2016; 21(4): 1-5.
10. Selimoglu H, Duran C, Kiyici S, Ersoy C. The effect of vitamin D Replacement therapy on insulin resistance and androgen levels in women with polycystic ovary syndrome. J Endocrinal Invest 2014, 101(6): 1740-46.
11. Asimi VZ. Evaluation of the association of vitamin D deficiency with gonadotrophins and sex hormones in obese and non-obese women with PCOS. Med Glas (Zerica) 2014; 11(1): 170-6.
12. Akram M, Roohi N. Endocrine correlates of polycystic ovary syndrome in pakistani women. J Coll Physicians Surg Pak 2015; 25(1): 22-6.
13. Baqai Z, Khanam M, Parveen S. Prevalence of PCOS in infertile patients. Med Chan 2010; 16(3): 437-40.
14. Rehman S, Salahuddin, Rehman MOU. Polycystic ovary syndrome treatment of subfertility with insulin lowering medications. Pak J Pharmacol 2005; 22(1): 35-9.
15. Kim JJ, Choi YM, Chae SJ, Hwang KR, Yoon SH, Kim MJ, et al. Vitamin D deficiency in women with polycystic ovary syndrome. Clin Exp Reprod Med 2014; 41(2): 80-5.
16. Zandi S, Farajzadeh S, Safari H. Prevalence of polycystic ovary syndrome in women with acne: hormone profiles and clinical findings. J Pak Derm Assoc 2010; 20: 194-8.
17. Anjum N, Zohra S, Arif A, Azhar A, Qureshi M. Prevalence of metabolic syndrome in Pakistani women with polycystic ovarian syndrome. Pak J Biochem Mol Biol 2013; 46(3): 97-100.
18. Hanif F, Naveed AK, Rahim A. Vitamin D level in unmarried females with Polycystic ovarian syndrome. JIIMC 2016; 11(2): 57-61.
19. Wehr E, Pieber TR, Obermayer-Pietsch B. Effect of vitamin D3 treatment on glucose metabolism and menstrual frequency in PCOS women-a pilot study. J Endocrinol Invest 2011; 34(10): 757-63.
20. Lakshman LR, Pillai BP, Lakshman R, Kumar H, Sudha S, Jayakumar RV. Comparison of vitamin D levels in obese and non obese patients with polycystic ovarian syndrome in a South Indian population. Int J Reprod Contracept Obstet Gynecol 2013; 2(3): 336-43.