Original Article

Frequency of Vitamin D Deficiency in PCOS Patients Presenting at A Tertiary Care Hospital

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Abstract

Objective: To document the incidence of vitamin D deficiency among patients presenting with Polycystic ovarian Syndrome (PCOS) in a large tertiary care centre in Karachi.

Methodology: This descriptive cross-sectional study was conducted in the Department of Obstetrics & Gynecology, Jinnah Postgraduate Medical Centre, Karachi from 30th October 2018 to 29th April 2019. A total of 95 patients with polycystic ovarian syndrome, 18 to 45 years of age were included. Patients with hyperthyroidism, vitamin D therapy for > 3 months, heart failure, long term steroid treatment and acid peptic disease were excluded. Blood Samples were drawn and sent to the chemistry lab on the same day for determining Vitamin D levels.

Results: Mean age of our study participants was 32.60 ± 4.77 years (18 to 45 years). Majority of the patients i.e. 66 (69.47%) were between 31 to 45 years of age. Mean duration of symptoms was 6.34 ± 2.46 months (3 to 9 months). Mean BMI was 29.45 ± 3.13 kg/m^2 (26 to 32 kg/m$^{2)}$ (Table 1).Vitamin D deficiency was seen among 41 (43.16%) patients with a mean level of 16.67ng/ml ±3.12ng/ml (13.9ng/ml-18.5ng/ml). The lowest levels of serum vitamin D were found in women with a BMI of >30 kg/m^2. There were 26 unmarried participants and 69 married ones with vitamin D deficiency seen in 46.15% and 42%, respectively.

Conclusion: This study concluded that frequency of vitamin D deficiency in PCOS patients is quite high, especially among women with a BMI>30 kg/m^2

Keywords: Polycystic ovarian syndrome, Vitamin D deficiency, Insulin resistance, BMI

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Introduction

Among women aged between 15-49 years, the most frequent endocrine irregularity is polycystic ovarian syndrome (PCOS). In low-middle income countries, the prevalence of PCOS ranges from 6-20%.[1] However, the prevalence of PCOS is much higher in Pakistan, accounting for 52% compared to 20-25% in the United Kingdom (UK).[2]

PCOS adversely affects the health of women, ranging from physical, such as obesity and hirsutism,[3] psychological effects such as anxiety, depression, and sexual dysfunction[4] and nutritional deficiencies.[5] Overall, PCOS effect the quality of life of a woman.[6] Evidence suggests that PCOS is related to glucose intolerance, hypertension[7,8] and insulin resistance. Regardless of BMI, 60% of women with PCOS have insulin resistance[9], and 10% will develop type 2 diabetes mellitus by the age of 40.[10]

Vitamin D deficiency has been demonstrated as a cause for IR affecting its release from pancreatic Beta cells.[9] Additional irregularities like menstrual dysfunction, ovulation problems, and inability to conceive are significant clinical challenges encountered when there is a low level of Vitamin D.[11]]A recent study suggests that almost 44% of women with PCOS have low levels of Vitamin D.[5] According to a systematic review and meta-analysis, the level of 25(OH) vitamin D was less than 20ng/ml in 60–85% of women with PCOS.[12]

As studies have demonstrated a high prevalence of vitamin D deficiency, early recognition and treatment of this condition is necessary in order to reduce complications. The studies described above have been done in western population, which are different geographically from our population, so this study is conducted to document vitamin D insufficiency or deficiency among the local PCOS patients presenting at a

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tertiary care hospital in Karachi. The results gathered in this study will not only shed light on the extent of this problem in the local population but also add data to the existing literature on this important problem, further helping the local clinicians to approach the PCOS women for timely diagnosis and treatment so that the risk of future potential morbidities is reduced. The objective of this study was to determine the frequency of vitamin D deficiency in PCOS patients present at a tertiary care hospital in Karachi.

Methodology

This prospective cross-sectional study was conceived and carried out in the Department of Obstetrics & Gynecology, Jinnah Postgraduate Medical Centre, Karachi, from October 30th, 2018 to April 29th, 2019.

Our study participants were patients aged between 18 and 45 years. PCOS was diagnosed on ultrasound examination when > 12 follicles measuring 2-9 mm or an ovarian volume more than 10 cm3 was seen. Patients were selected through non probability consecutive sampling. Pregnant women (assessed on USG) or patients who had co-morbidities like heart failure determined by echo as EF<25%, renal disease determined by serum Creatinine> 3mg/dl) or endocrine disorders like hyperparathyroidism determined by blood parathormone (PTH) levels > 10 ng/dl or any patient on long term steroid treatment for > 3 months determined by physician prescription slip, patients already on vitamin D therapy for > 3 months, doctor's prescription as evidence or patients with acid peptic disease (diagnosed on history and medical record) were excluded from this study

The permission for data collection was sought from the Ethical review committee of the hospital. After taking informed written consent from the patients, diagnosed cases of PCOS were enrolled in the study after fulfilling inclusion/exclusion criteria. The researcher collected data on a prescribed questionnaire regarding demographic variables like name, age, gender and duration of disease. Blood samples were drawn on the same day and sent to the laboratory for vitamin D level determination in the pathological lab of JPMC. Serum Vitamin D levels in this study were measured by radioimmunoassay. The sample size was determined using Epi Info 7 application. The prevalence of Vitamin D deficiency was taken as 44% (an informed estimate from literature), and in the presence of a confidence interval of 95% with margin of error as 10% we calculated the sample size to be 95.

SPSS version 21 was used to analyze the obtained data. Continuous variable with mean and Standard deviation (SD) were calculated for age, duration of disease, BMI and Vitamin D levels. Frequency and percentages were calculated for marital status, residential area (rural/urban), sun exposure (low/medium/high), education level (illiterate / primary / middle / matric / graduate) monthly income (<20000/20001-40000/>40000) and vitamin D deficiency. Effect modifiers like age, marital status, BMI, duration of disease, education level (illiterate / primary / middle / matric / graduate), residential area (rural/urban), sun exposure (low/medium/high) and monthly income (<20000/20001-40000/>40000) were stratified to see the effects of these on outcome variable. Applying the chi-square test with p value ≤0.05 taken as significant.

Results

Mean age of our study participants was 32.60 ± 4.77 years (18 to 45 years). Majority of the patients i.e. 66 (69.47%) were between 31 to 45 years of age. Mean duration of symptoms was 6.34 ± 2.46 months (3 to 9 months). Mean BMI was 29.45 ± 3.13 kg/m^2 (26 - 32 kg/m$^{2)}$. Vitamin D deficiency was seen among 41 (43.16%) patients with a mean level of 16.67ng/ml ±3.12ng/ml (13.9ng/ml-18.5ng/ml). The lowest levels of serum vitamin D were found in women with a BMI of >30 kg/m^2. There were 26 unmarried participants and 69 married ones with vitamin D deficiency seen in 46.15% and 42%, respectively. Table I

Table I: Characteristics of enrolled participants (n-95)

	N	%
Age (in years)		
Mean age	32.6±4.77	
18-30	29	30.53
31-45	66	69.47
Duration of disease (in months)		
Mean duration of disease	**6.34±2.46**	
≤6 months	63	66.32
>6 months	32	33.68
Body mass index		
Mean (BMI)	**29.45±3.13**	
≤27 kg/m^2	34	35.79
>27 kg/m^2	61	64.21
Marital status		
Unmarried	26	27.37
Married	69	72.63
Place of living		
Rural	47	49.47
Urban	48	50.53
Monthly income		
<20000	23	24.21
20001-40000	39	41.05
>40000	33	34.74
Education		
Illiterate	15	15.79
Primary	15	17.79
Middle	20	21.05
Matric	23	24.21
Graduate	22	23.16
Sun exposure		
Low	44	46.32
Medium	20	21.05
High	31	32.63

Stratification of vitamin D deficiency with respect to age groups, duration of symptoms and BMI are shown in Table II

Discussion

Polycystic Ovarian Syndrome (PCOS) hallmarks are a clinical constellation manifested as anovulation due to hyperandrogens, with associated dysfunctional uterine

bleeding and a structural abnormal ovarian morphology.[13] Women affected are at a higher risk of obesity, infertility, type 2 diabetes mellitus, hypertension, dyslipidemia in addition to enhanced risk of cardiovascular events and cancer of endometrium when a diagnosis of PCO is made. [14] [15] Deficiency of vitamin D has been reported as a frequent finding in various clinical studies and no age group is exempt from this affliction.[16]Hypovitaminosis D predisposes to obesity among other risks and there is a well established connection observed with PCOS when vitamin D deficiency and obesity co exist.[17-20]

Table II: Stratification of Age, Duration of symptoms, BMI, socioeconomic status in PCOS patients with respect to Vitamin D deficiency

	Vitamin D deficiency		p-value
	Present (n-41)	Absent (n-64)	
Age (years)			
18-30 years	14 (34.1%)	25 (39.1%)	**0.611**
31-45 years	27 (65.9%)	39 (60.9%)	
Duration of disease			
≤6 months	27 (65.9%)	36 (56.3%)	**0.934**
>6 months	14 (34.1%)	18 (28.1%)	
Body mass index			
≤27 kg/m^2	17 (41.5%)	17 (26.6%)	**0.315**
>27 kg/m^2	24 (58.5%)	37 (57.8%)	
Marital status			
Unmarried	12 (29.3%)	14 (21.9%)	**0.717**
Married	29 (70.7%)	40 (62.5%)	
Place of living			
Rural	20 (48.8%)	27 (42.2%)	**0.906**
Urban	21 (51.2%)	27 (42.2%)	
Monthly income			
<20000	10 (24.4%)	13 (20.3%)	**0.133**
20001-40000	21 (51.2%)	18 (28.1%)	
>40000	10 (24.4%)	23 (35.9%)	
Education level			
Illiterate	4 (9.8%)	11 (17.2%)	**0.38**
Primary	9 (22.0%)	6 (9.4%)	
Middle	10 (24.4%)	10 (15.6%)	
Matric	10 (24.4%)	13 (20.3%)	
Graduate	8 (19.5%)	14 (21.9%)	
Sun exposure			
Low	18 (43.9%)	26 (40.6%)	**0.782**
Medium	10 (24.4%)	10 (15.6%)	
High	13 (31.7%)	18 (28.1%)	

It was postulated that Vitamin D is simple cost-effective and safe therapy for women with PCOS and vitamin D deficiency.[21] Vitamin D therapy may regulate insulin release, alter expression of insulin receptor thus improves IR as well as increase in the muscle mass.[22] PCOS patients in the presence of obesity are a group with a higher risk of metabolic abnormalities as compared to lean PCOS individuals.[23]

This study is planned and conducted to document the frequency of vitamin D deficiency in PCOS patients in the local population. The age range in this study was from 18 to 45 years, with a mean age of 32.60 ± 4.77 years. The majority of the patients, i.e. 66 (69.47%) were between 31 to 45 years of age. Frequency of vitamin D deficiency in PCOS patients was seen in 41 (43.16%) patients. Vitamin D deficiency is a frequently seen finding in PCOS women, and around 67–85% of PCOS patients have a serum 25(OH) D concentration of less than 25 ng/ml. Ovulation abnormalities, menstrual irregularities and difficulty in conceiving are the resultant challenges faced during the periods of low vitamin D status.[24] A recent study suggest that almost 44% of women with PCO have vitamin D deficiency.[5]

Low serum levels (20ng/ml) of the activated form of vitamin D (25(OH)D) were found to be fairly common among women with PCOS, with figures ranging from 67% to 85% frequently quoted.[25] It has been noted that a higher prevalence of deficiency in vitamin D is strongly associated with the metabolic syndrome, having a significant negative impact on health of affected people.[26]

Symptoms of PCOS are triggered in the presence of low serum vitamin D levels, in terms of a worsening blood sugar level due to insulin resistance, ovulatory and menstrual difficulties, infertility, hirsutism due to hyperandrogenism, obesity, and a significantly raised cardiovascular risk for the patient. Although the connection between a low level of vitamin D and its impact on health in terms of triggering PCOS symptoms is fairly well observed, it may still be too early to conclusively say that a definite connection in terms of causation exists between PCOS and vitamin D deficiency. This is due to inconsistent reports of both individual studies and meta-analyses of systemic review.[27]

The abnormally increased levels of serum AMH (Anti-Mullarian Hormone) can be lowered with judicious supplementation of Vitamin D in diet. It can also have a beneficial effect on lowering the serum anti inflammatory soluble receptors, further helping to stabilize serum glucose levels. In another study, vitamin D and calcium supplementation along with oral metformin resulted in normalizing menstrual and ovulation abnormalities in women diagnosed with PCOS.[28] On the contrary, Garg et al[11] recently refuted this observation, observing that they could not confirm a beneficial effect on Insulin resistance and cardiovascular risk factors after supplementing PCOS patients' diet with 4,000 IU/day of vitamin D for six months, even when treated with concurrent metformin.

Other authors have concluded that results of a causal relationship between PCOS and vitamin D deficiency remain inconclusive due to the various flaws in the studies, like a small sample size and short follow up duration.[27, 28] For this reason a randomized controlled trial with better study protocols is warranted to conclusively establish a causal relationship and impact of vitamin D supplementation in the management of PCOS.

It is known that low levels of activated Vitamin D are responsible for increased insulin resistance among women with PCOS. So, it is postulated that genes responsible for Vitamin D metabolism are infact the cause of susceptibility to

PCOS. A few polymorphisms in the VDR gene, such as Cdx2, Taq1, Bsm1, Apa1, and Fok1, were reported to play an influential role on insulin secretion and sensitivity in PCOS women.[29] Some mutations, such as the VDR Fok1 polymorphism, have been found to be protective against type 2 diabetes mellitus risk. Furthermore, the Apa1 polymorphism was also reported as conferring protection against vitamin D deficiency. [29]

A study by Figurová J et al, presented an interesting result. They found that the prevalence of Vitamin D deficiency was similar among the control group (46/66; 70%) and the study group with diagnosed PCOS (79/99; 80%; p = 0.138).[29] On the contrary, Li HW et al, in an observational study in 2011 found results which were in contrast to the study by Figurová J et al. They reported an increased incidence of Vitamin D deficiency in women diagnosed with PCOS. They reported a 72% incidence of Vitamin D deficiency among 25 women diagnosed with PCOS against a control group of 27 patients without PCOS.[5] An observational study by Wher et al having 206 subjects with PCOS also endorses the results obtained by Li HE et al where they reported significant deficiency of Vitamin D among 150 (72.8%) of the 206 subjects again giving substance to the claim that there does exist a causal relationship between Vitamin D deficiency and PCOS.[19]

Conclusion

This study concluded that the frequency of vitamin D deficiency in PCOS patients is quite high. So, we recommend that early recognition and management of vitamin D deficiency in polycystic ovarian syndrome patients should be done in order to reduce morbidity of these patients in terms of endocrine and cardiovascular risk reduction.

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