IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 17, Issue 8 Ver. 6 (August. 2018), PP 16-22
www.iosrjournals.org

Case Control Study of Serum Vitamin D Levels in PCOS Patients

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Date of Submission: 02-08-2018 Date of acceptance: 17-08-2018

I. Introduction

Polycystic ovarian syndrome (PCOS) is known as one of the most common endocrine disorders and affects 5-10% of women that is characterized by hyperandrogenism and chronic anovulation. PCOS as a multi-dimensional syndrome influences various systems as Infertility, irregular menses, acanthosis nigricans, insulin resistance, and hirsutism[1]. Also, it has some long-term consequences such as hypertension coronary artery diseases and type II diabetes.

Vitamin D plays a physiologic role in reproduction including ovarian follicular development and luteinization via altering Anti-Mullerian Hormone (AMH) signaling, follicle-stimulating hormone sensitivity and progesterone production in human granulosa cells[2]. It also affects glucose homeostasis..

The strong association between PCOS and insulin resistance indicates that insulin directly influences ovarian function while impaired glucose tolerance and insulin secretion have been shown to be associated with vitamin D deficiency[3]

The prevalence of vitamin D deficiency in women with PCOS is about 67-85 per cent, with serum concentrations of 25(OH)D <20 ng/ml[2] Although there is no significant difference in the 25(OH)D levels between PCOS and normal control

women, high prevalence of vitamin D deficiency has been found to be associated with metabolic syndrome which may have great impact on public health[4]. Low 25(OH)D levels may exacerbate the symptoms of PCOS,

II. Aims & Objectives

AIM OF THE STUDY:

In this study, we tried to investigate the association, between vitamin D levels and PCOS in our population. Also, we aimed to find a correlation between body mass index (BMI), hyperandrogenism and metabolic syndrome with serum level of 25(OH)D in PCOS patients.

III. Materials And Methods

PLACE OF STUDY:- Gandhi Hospital, Secunderabad
STUDY DESIGN:- case control study
SAMPLE SIZE:- 50 study group, 100 controls
STUDY DURATION:- 2016 september to 2017 December
SOURCE OF THE DATA:- All women in18-27age group (reproductive age) were recruited from our out-patient Gynaecology department, Gandhi hospital.
INCLUSION CRITERIA – CASES - women in18-27age based on the Rotterdam criteria diagnosed PCOS patients
CONTROLS- women in18-27 age (from the same socioeconomic population who were matched for their age with the cases) normal ovulating cycles no signs of hyperandrogenism.
EXCLUSION CRITERIA: any systemic disease use of any medication that might affect their reproductive physiology. Medications suspicious to affect vitamin D concentrations during 6 months prior to the study history of chronic disease or endocrinophaties history of smoking or drug abuse were excluded.

IV. Methodology

Measurements

Body weight was measured to the nearest 0.1 kg with a balanced-beam scale while wearing light clothing, and height was measured with a stadiometer to the nearest 0.5 cm. BMI was calculated based on the weight/(height)² formula. Waist circumferences between the lowest rib and the iliac crest, at the level of

umbilicus, were measured in duplicate to the nearest millimeter using flexible tape blood pressure was measured after PCOS women have been seated for at least 5 minutes.

Biochemical analysis

25(OH)D [normal range 30-60 ng/ml] was measured using a commercially available enzyme immunoassay (IDS, Boldon, UK) with intra- and interassay coefficients of variation (CV) of 5.6 and 6.4%, respectively.

TSH [0.1-4.0 μU/ml] (Bayer, Leverkusen, Germany) were measured by luminescence immunoassay.

Statistical Analysis

Data are presented as mean ± SD. Statistical analysis was conducted using SPSS version 11.5. Proportions were compared by using the Chi-square test. Group means were compared using the Student's -test and Mann-Whitney test. The Pearson correlation statistic was used to investigate correlations between variables. Bivariate correlation analysis (calculation of the Pearson coefficient) was used to assess the correlation of vitamin D levels to each parameter. Multiple logistic regression analyses were used to assess the independent effect of hypovitaminosis D on the odds for PCOS after adjustment for confounding factors. Statistical significance was set at <0.05.

V. Results

The anthropometric, hormonal and metabolic features of the women are studied, and their statistical significance are summarized in Table.

Table: 1

	CASES		CONTROLS		
	MEAN	STD	MEAN	STD	P VALUE
AGE	22.20	2.17	22.20	2.16	> 0.05
WT	61.28	17.20	50.65	9.77	< 0.001
HT	153.98	7.31	155.05	5.34	> 0.05
BMI	25.80	6.72	21.08	4.04	< 0.001
WAIST	84.10	11.36	76.47	9.62	< 0.001
HIP	96.67	14.07	89.95	10.59	< 0.001
WHR	0.87	0.07	0.85	0.07	> 0.05
HB (gms)	10.90	0.95	11.17	0.98	> 0.05
TSH	3.04	2.64	3.00	1.45	> 0.05
VIT D	11.96	6.94	16.04	7.19	< 0.001

GRAPH – 1

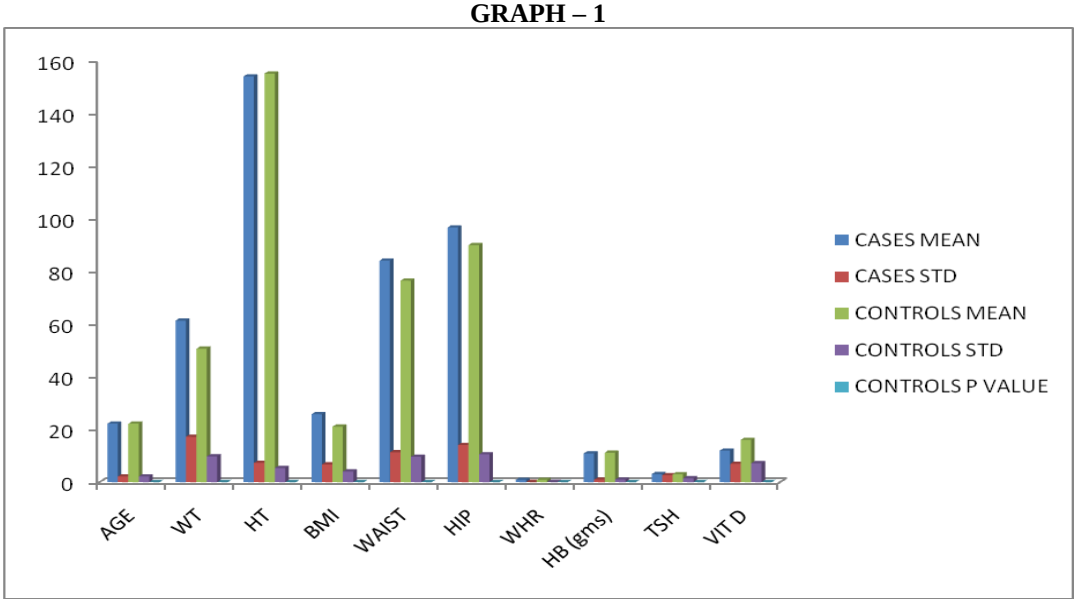
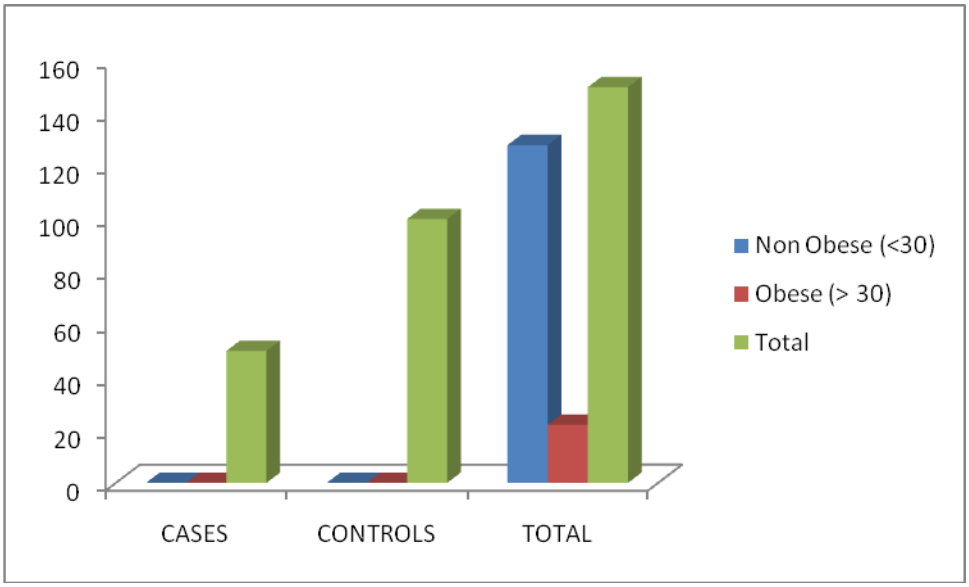


Table: 2 – BMI

BMI	CASES	CONTROLS	TOTAL
Non Obese (<30)	36 (28%)	92 (72%)	128
Obese (> 30)	14 (63%)	8 (37%)	22
Total	50	100	150

GRAPH – 2 – BMI



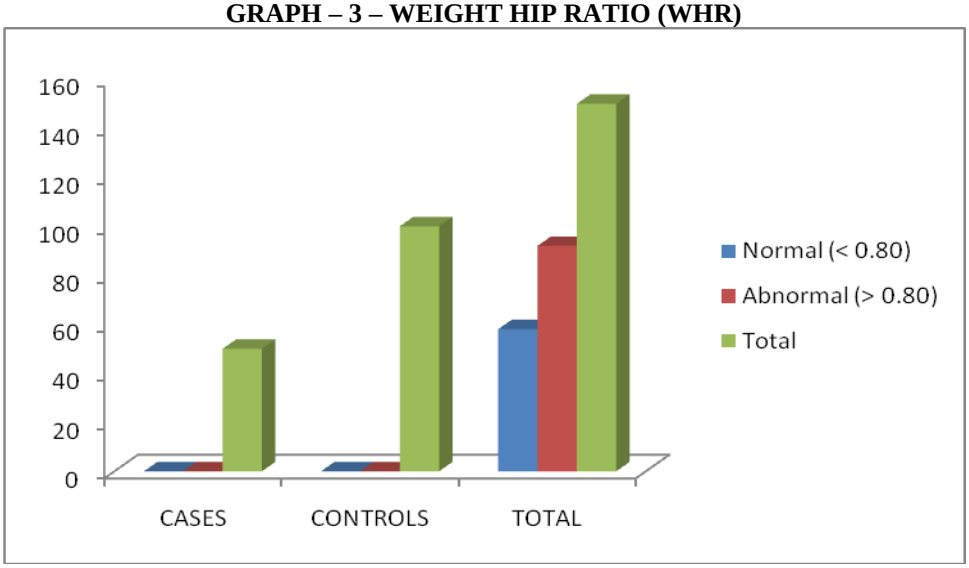
A Total of 128 subjects showed Non-Obesity (BMI <30) out of which 36 (28%) are cases and rest 92(72%) are controls. A Total of 22 subjects showed Obesity (BMI >30) out of which 14 (63%) are cases and the rest 8 (37%) are controls.

The difference is (P<0.001) statistically highly significant. Also, the ODDS Ratio(OR) 0.22 which is not strong risk factor.

TABLE – 3 – WEIGHT HIP RATIO (WHR)

WHR	CASES	CONTROLS	TOTAL
Normal (< 0.80)	12 (20%)	46 (80%)	58
Abnormal (> 0.80)	38 (41%)	54 (49%)	92
Total	50	100	150

GRAPH – 3 – WEIGHT HIP RATIO (WHR)

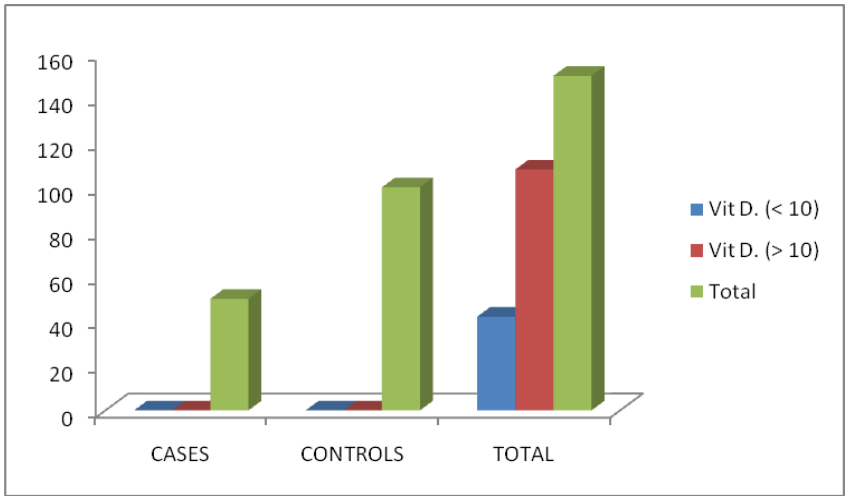


A Total of 58 subjects showed Normal WHR out of which 12 (20%) are cases and rest 46(80%) are controls. A Total of 92 subjects showed Abnormal WHR out of which 38 (41%) are cases and the rest 54(49%) are controls. The difference is (P<0.05) statistically significant. Also, the ODDS Ratio(OR) 0.37 which is not strong risk factor.

TABLE – 4 – SEVERE VITAMIN D DEFICIENCY

VIT D SEV. DEF	CASES	CONTROLS	TOTAL
Vit D. (< 10)	21 (50%)	21 (50%)	42
Vit D. (> 10)	29 (27%)	79 (73%)	108
Total	50	100	150

GRAPH – 4 – SEVERE VITAMIN D DEFICIENCY

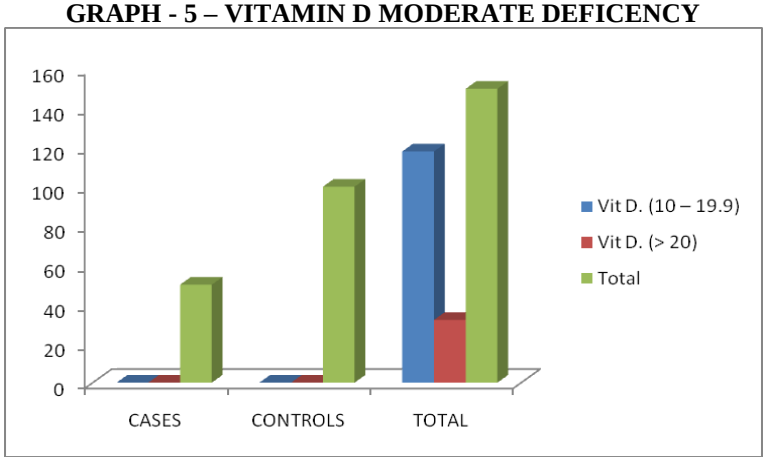


A Total of 42 subjects showed SEVERE VIT D DEF out of which 21 (50%) are cases and rest 21(50%) are controls.
A Total of 100 subjects showed NON-SEVERE VIT D DEF out of which 29 (27%) are cases and the rest 79 (73%) are controls.
The difference is (P<0.05) statistically significant. Also, the ODDS Ratio(OR) 2.72 which is in the concurrence with significance.

TABLE - 5 – VITAMIN D MODERATE DEFICENCY

VIT D SEV. DEF	CASES	CONTROLS	TOTAL
Vit D. (10 – 19.9)	43 (34%)	75 (66%)	118
Vit D. (> 20)	7 (22%)	25(78%)	32
Total	50	100	150

GRAPH - 5 – VITAMIN D MODERATE DEFICENCY

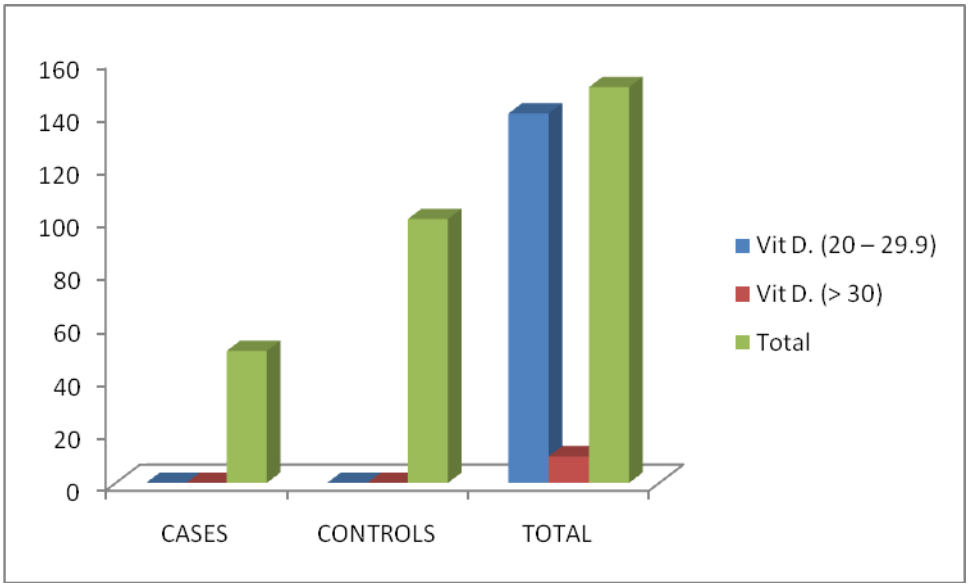


A Total of 118 subjects showed VIT D Insufficiency out of which 43 (34%) are cases and rest 75(66%) are controls.
A Total of 32 subjects showed NO VIT D Deficiency out of which 7(22%) are cases and the rest 25(78%) are controls.
The difference is (P>0.05) statistically not significant. Also, the ODDS Ratio(OR) 2.05 which is in the in coincidence with no significance.

TABLE – 6 – VITAMIN D INSUFFICIENCY

VIT D SEV. DEF	CASES	CONTROLS	TOTAL
Vit D. (20 – 29.9)	48 (34%)	92 (66%)	140
Vit D. (> 30)	2 (20%)	8 (80%)	10
Total	50	100	150

GRAPH – 6 – VITAMIN D INSUFFICIENCY



A Total of 140 subjects showed VIT D Insufficiency out of which 48 (34%) are cases and rest 92(66%) are controls.
A Total of 10 subjects showed NO VIT D Insufficiency out of which 2(20%) are cases and the rest 8(80%) are controls.
The difference is (P>0.05) statistically not significant. Also, the ODDS Ratio(OR) 2.09 which is in the in coincidence with no significance.

VI. Discussion

Age Distribution

Maximum number of patients in our study falls in the age group 18-27 years i.e., 22.20 ± 2.17 for the case group and 22.20 ± 2.16 for the control group. This is expected as this is the usual age of child bearing. Our result was compared with the findings of Harmandeep Gill, Pallavi Tiwari[7] 2012 and the age group of western studies was higher than Indian studies which reflects the socioeconomic and reproductive cultures of those countries others.

Height

Mean height of pcos 153.98±7.31 for the case group and155.20 ± 9.18 for the control group p value>0.05 which is insignificant. Our result was compared with the findings of Harmandeep Gill, Pallavi Tiwari 2012[7] and **others**, of mean heiht153.93±5.52 for the case group and 153.61 ± 4.98 for the control group pvalue(>0.05)

Weight

Mean weight of pcos 61.28±17.20 for the case group and 50.37 ± 9.18 for the control group p value <0.001 which is highly significant. Our result was compared with the findings of Harmandeep Gill, Pallavi Tiwari 2012[7] and others, of mean weigh51.42±13.6 for the case group and46 ± 7.33 for the control group P value (<0.01) which means significant.

BMI in present study Majority of our cases were had a BMI ≥ 26 Kg/m^2, BMI in PCOS, in controls ≥ 21 Kg/m^2,

Majority of our cases were lean as only 24% had a BMI ≥ 23 Kg/m^2, and none was morbidly obese. In contrast, 30-38% subjects are obese in other studies &Moreover, obesity is highly prevalent in women affected by PCOS, with the highest prevalence being reported in studies conducted in the USA and Australia, with 61–76% of women with PCOS being considered obese and 85% considered overweight or obese.

VIT D

In present study severe Vit D deficiency in PCOS were 42% and 21% were control, p value,0.05 and odds ratio 2.72 (CI: 1.35-5.71) which is statistically significant and severe Vit D deficiency is a strong risk factor which is comparable to Li HW, Brereton RE, Anderson RA, Wallace AM et. al. [11]

Serum 25-hydroxyvitamin D concentrations less than 25 nmol/L were classified as severe vitamin D deficiency and were found in 44.0% and 11.2% of subjects in the PCOS and control groups, respectively (P = .047). Among the PCOS subjects, 25-hydroxyvitamin D concentrations were negatively correlated with body mass index (P = .033), Vitamin D deficiency is highly prevalent in PCOS women in Scotland, and a larger proportion of PCOS patients than control women were found to be vitamin D deficient. which support the increasing evidence that vitamin D deficiency is associated with multiple metabolic risk factors in PCOS women.

Muscogiuri G, Policola C, Prioletta et.[8] noticed Low 25(OH)D (25(OH)D < 50 nmo/L) was detected in 37% of the entire cohort of patients. Body Mass Index (BMI), in particular total fat mass ($p < 0.001$), resulted to be the most predictor factor of 25(OH)D levels Our data demonstrated that in PCOS low 25(OH)D levels are significantly determined by the degree of adiposity

Thomson RL, Spedding S & Buckley JD described as Vitamin D deficiency is common in women with polycystic ovary syndrome (PCOS), with the 67–85% of women with PCOS having serum concentrations of 25-hydroxy vitamin D (25OHD)[9]

The serum 25-OH-VD mean levels were 56.31% lower in the obese PCOS patients Low serum 25-OH-VD concentrations result from the presence of obesity and insulin resistance. However, the dependency between PCOS and hypovitaminosis D is questionable. Hypovitaminosis D should be kept in mind while managing obese women with PCOS

When comparing women with PCOS (n = 85) to control women (n = 115) with similar age (30 year) and body mass index (BMI) (27 kg/m^2), Mahmoudi et al**.**[10] found the women with PCOS had a significantly higher vitamin D level (29·3 ng/ml in PCOS women vs 19·4 ng/ml in control women).

On the other hand, Li et al.[11] reported lower vitamin D levels, although not significant, in women with PCOS compared with women without PCOS (11 ng/ml in PCOS group vs 17 ng/ml in control group). However, the ovulatory control group (n = 27) was significantly older (35 year) and had a lower BMI (24 kg/m^2) compared with the PCOS group (n = 25, 28 year and 31 kg/m^2), which have both been shown to influence vitamin D levels.

Recently, Wehr et al.[12] also reported lower levels in women with PCOS (n = 545) compared to the control women (n = 145; 25·7 vs 32·0 ng/ml, respectively), and the PCOS women were significantly younger (27 vs 29 years, respectively).

VII. Conclusion

Polycystic Ovary Syndrome (PCOS), with the 70–85% of women with PCOS having serum concentrations of 25-hydroxy vitamin D (25OHD) <20 ng/ml. Vitamin D deficiency may exacerbate symptoms of PCOS. observational studies showing lower 25OHD levels were associated with insulin resistance, ovulatory and menstrual irregularities, lower pregnancy success, hirsutism, hyperandrogenism, obesity and elevated cardiovascular disease risk factors. There is some, but limited, evidence for beneficial effects of vitamin D supplementation on menstrual dysfunction and insulin resistance in women with PCOS. Vitamin D deficiency may play a role in exacerbating PCOS, and there may be a place for vitamin D supplementation in the management of this syndrome, but current evidence is limited and additional randomized controlled trials are required to confirm the potential benefits of vitamin D supplementation in this population. The first aim of the study was to find a relationship between vitamin D deficiency and PCOS, whereas the final result implicates to not only an association between vitamin D and metabolic syndrome, but also a real peril of pandemic of severe vitamin D deficiency which is considered as real threats for women of reproductive age. Although a direct association between PCOS and vitamin D was not found, it may need another study after the correction of vitamin D level.

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Dr. Sangeeta Shah." Case Control Study of Serum Vitamin D Levels in PCOS Patients."IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 17, no. 8, 2018, pp 16-22.