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Original Research Article

"A Cross Sectional Study on Association between Serum Vitamin D Status and Insulin Resistance in Polycystic Ovarian Syndrome"

Dr. J Sreeja Shraddha[1*], Dr. Anupama Hari[2]

[1]Postgraduate, Mallareddy Medical College for Women, Hyderabad, Telangana, India
[2]Professor and HOD of Obstetrics and Gynecology, Mallareddy Medical College for Women, Hyderabad, Telangana, India

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***Corresponding author:** Dr. J Sreeja Shraddha
Postgraduate, Mallareddy Medical College for Women, Hyderabad, Telangana, India

Abstract

Polycystic ovarian syndrome is a common cause of ovarian dysfunction in women with anovulation world wide.50-70% of patients with PCOS exhibit metabolic abnormalities, including poor glucose tolerance and hyperinsulinemia. 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. It is suggested that there is an association between serum levels of vitamin D and metabolic parameters in women with PCOS, including fasting glucose levels, fasting insulin, insulin resistance, high blood pressure, lipid disorders, obesity, fertility and other clinical and laboratory- related parameters associated with PCOS. Given the high prevalence of vitamin D deficiency in the south Indian population, less number of studies, inconclusive studies, especially in the population of women with PCOS, as well as evidence from recent studies indicating a link between vitamin D levels with lab parameters, this study aimed to assess the relationship between vitamin D deficiency and insulin resistance in PCOS. Pearsons correlation showed 0.034 between HOMA IR and vitamin d levels indicating that vitamin d deficiency is associated with more HOMA IR values, the more insulin resistance. Pearsons correlation showed 0.05 between fasting insulin levels and vitamin d levels indicating the vitamin d deficiency is associated with more fasting insulin levels, the more insulin resistance. No significant relation is seen with fasting glucose insulin levels (Pearsons correlation value >0.05). In the study, it was found that a high percentage of PCOS women were vitamin D deficient. The study also showed a significant difference in the values of some clinical and metabolic parameters such as waist circumference, fasting insulin, HOMA-IR, BMI between PCOS women with and without vitamin D deficiency; however, no linear correlation was found between serum levels of vitamin D and baseline variables, except for HOMA IR values, fasting insulin levels, BMI, G120. In conclusion, our data confirm an association between vitamin D deficiency and Insulin resistance in patients with PCOS. Thus, vitamin D supplementation could be a beneficial treatment of PCOS women to abolish insulin resistance and regulate menstrual irregularities.

Keywords: Serum vitamin D levels, Fasting Insulin Levels, Insulin Resistance, BMI.

INTRODUCTION

Polycystic Ovarian Syndrome

Polycystic ovarian syndrome is a common cause of ovarian dysfunction in women with anovulation. It's the most common endocrine disorder in women worldwide with prevalence estimates between 4-8 %, approximately 6.5% women of reproductive age group have PCOS [1]. The main symptoms are characterized by chronic anovulation, hyperandrogenism, and/or the presence of polycystic ovary morphology from ultrasound examination [1]. Hyperandrogenism is the defining feature of women with PCOS. This syndrome is diagnosed according to the Rotterdam criteria [5]. In recent years, it was found that the syndrome is also associated with increased risk of cardiovascular disease, hypertension, high insulin resistance, impaired glucose tolerance, risk of type 2 diabetes, lipid abnormalities [metabolic syndrome] and gynaecological cancer, in particular endometrial cancer [2]. Genetics, intrauterine drug exposures, environment, life style, obesity play a role in the pathogenesis of this disease [3]. Long-term morbidity includes Subfertility, Miscarriage, Cardiovascular disease, T2DM, Malignancies, Psychiatric disorders [3].

Insulin Resistance in PCOS

50-70% of patients with PCOS exhibit metabolic abnormalities, including poor glucose tolerance and hyperinsulinemia [5]. This is not solely a consequence of increased visceral obesity; rather, obesity and hormonal abnormalities are thought to make additive contributions to insulin resistance: Patients with PCOS exhibit a greater degree of insulin resistance than patients with the same BMI and visceral adiposity who do not have PCOS [4]. The insulin resistance in at least 50% of PCOS women appears to be related to excessive serine phosphorylation of the insulin receptor [8].

Molecular causes of insulin resistance have been identified as an excessive phosphorylation of serine residues of the insulin receptor, mutations in insulin receptor gene or insulin receptor substrate-1 (IRS-1), a cellular adenosine depletion, a deficiency in peroxisome proliferator-activated receptor gamma (PPAR-gamma) and a defect at the glucose transport level [8]. A factor extrinsic to the insulin receptor, presumably a serine/ threonine kinase, causes this abnormality and is an example of an important new mechanism for human insulin resistance related to factors controlling insulin receptor signaling [8]. Serine phosphorylation appears to modulate the activity of the key regulatory enzyme of androgen biosynthesis, P450c17. It is thus possible that a single defect produces both the insulin resistance and the hyperandrogenism in some PCOS women [7]. Recent studies strongly suggest that insulin is acting through its own receptor (rather than the IGF-I receptor) in PCOS to augment not only ovarian and adrenal steroidogenesis but also pituitary LH release [7].

Vitamin D in PCOS

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/ml3.Vitamin D plays a physiologic role in reproduction including ovarian follicular development and luteinization via altering anti-müllerian hormone (AMH) signalling, follicle-stimulating hormone sensitivity and progesterone production in human granulosa cells .High prevalence of vitamin D deficiency has been found to be associated with metabolic syndrome which may have great impact on public health [18]. Low 25(OH) D levels may exacerbate the symptoms of PCOS, including insulin resistance, ovulatory, menstrual irregularities, infertility, hyperandrogenism, obesity and elevate the risk of cardiovascular diseases [13]. Vitamin D supplementation can lower the abnormally elevated serum AMH levels and increase serum anti-inflammatory soluble receptor for advanced glycation end-products in vitamin D-deficient women with PCOS. Low 25(OH) D levels are found to be significantly correlated with insulin resistance in women with PCOS [20]. Thus, genes involved in vitamin D metabolism have been suggested as candidate genes for the 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 [50].

Vitamin D in Insulin Resistance (PCOS)

The potential influences of vitamin D on glucose homeostasis include the presence of specific vitamin D receptor (VDR) in pancreatic β-cells and skeletal muscle, the expression of 1-α- hydroxylase enzyme which can catalyze the conversion of 25-hydroxy vitamin D [25(OH)D] to 1,25-dihydroxyvitamin D(25).Through its regulatory role of the calcium pool of β-cell intracellularly and extracellularly, vitamin D insufficiency appears to affect normal release of insulin particularly in reaction to a glucose intake since the secretion of insulin is mediated by a calcium dependent mechanism. There is also a presence of a vitamin D response element in the human insulin gene promoter [22]. Vitamin D–vitamin D receptor (VDR) complex regulates over 300 genes, including genes that are important for glucose and lipid metabolism as well as blood pressure regulation. Improvement in action of insulin may be mediated by vitamin D directly through the presence of VDRs in skeletal muscles, stimulation of expression of insulin receptors in bone marrow cells and through vitamin D activation of peroxisome proliferator activator receptor-δ, a transcription factor involved in the control of metabolism of fatty acids in adipose tissue and skeletal muscle [27]. Hence it is suggested that there is an association between serum levels of vitamin D and metabolic parameters in women with PCOS, including fasting glucose levels, fasting insulin, insulin resistance, high blood pressure, lipid disorders, obesity, fertility and other clinical and laboratory- related parameters associated with PCOS [26].

Given the high prevalence of vitamin D deficiency in the south Indian population, less number of studies, inconclusive studies, especially in the population of women with PCOS, as well as evidence from recent studies indicating a link between vitamin D levels with lab parameters, this study aimed to assess the relationship between vitamin D deficiency and insulin resistance in PCOS. As Vitamin D deficiency is associated with insulin resistance in PCOS patients. It's necessary to detect vitamin d deficiency (vitamin D levels) and insulin levels (for insulin resistance) in PCOS individuals, thereby helping in the treatment with vitamin d supplementation and use for further studies according to response in the patients after giving correction.

Aims and Objectives of the Study

1. To measure the Insulin resistance in the PCOS patients using fasting insulin levels, HOMA-IR values, ratio and the Vitamin D status and its deficiency in the body by measuring the 25 (OH) Vitamin D in blood.
2. To assess the relation between vitamin D levels, its deficiency and insulin resistance (HOMA IR

Scores).

3. To treat the patient to reduce insulin resistance and supplement vitamin D which in turn cures the PCOS to some extent.

MATERIALS AND METHODS

Study Design: Hospital based cross-sectional study.

Study Setting: OP based.

Study Population: Women with PCOS in the age group of 18-35 years.

Study Site: Malla Reddy Narayana Multispeciality Hospital, Tertiary care hospital attached to Malla Reddy medical college for women.

Period of Study: 20 Months JANUARY 2021-AUGUST 2022

Sample Size: 60

Inclusion Criteria

- Women diagnosed with PCOS according to Rotterdam criteria. ROTTERDAM CRITERIA - Two of the following three criteria are required:
- 1. Symptoms of anovulation - Infrequent menstrual bleeding (oligomenorrhea): One or two episodes in a 90-day period. Irregular menstrual bleeding (IrregMB) a range of varying lengths of bleeding-free intervals exceeding 17 days within one 90-day reference period.''Absent menstrual bleeding (amenorrhea): No bleeding in a 90-day period
  2. Hyperandrogenism- Clinically - hirsutism using Modified Ferriman-Gallwey scale for hirsutism. A score of 1 to 4 is given for nine areas of the body. A score of 8 or more is considered as diagnostic of hirsutism.

  (or) Less commonly male pattern alopecia.
  (or) biochemical (raised FAI free androgen index or free testosterone)
  3. Polycystic ovaries assessed by ultrasonography (figure no.05).
  Described as an ovarian volume of more than 10 mL and/or more than 12 follicles measuring between 2 and 9 mm in at least one ovary
  (or) increased stromal density in one or both ovaries.
  Other aetiologies must be excluded such as congenital adrenal hyperplasia, androgen secreting tumours, Cushing syndrome, thyroid dysfunction and hyperprolactinaemia criteria-
- Women Aged between 18-35 years (reproductive age group) - After 4 gynecological years after menarche.
- Weight of ≤250 pounds (113 kg)
- At least one menses in the past 6 months but no more than eight periods in the most recent 12 months without hormonal intervention.

Exclusion Criteria

- The use of metformin, other oral hypoglycemic agents, insulin, or any hormonal contraceptives in the 60 days before enrollment.
- currently pregnant or breastfeeding during the prior 30 days
- After medical termination of pregnancy, abortions in the prior 60days
- FBG level>125 mg/dL,
- Overt diabetics (Clinically or history based).
- history of chronic disorders such as liver or kidney diseases, diabetes mellitus, hypothyroidism,
- any hormonal intervention in the prior 60 days (OC Pills, Progesterone therapy) immune deficiency,
- congenital adrenal hypoplasia, Cushing's syndrome, hyperprolactinaemia, androgen-secreting tumours,
- use of any medication influencing endocrine parameters.
- Use of antiepileptics (like carbamazepine, valproate and lamotrigine) and antipsychotics(risperidone).
- Premature menopause and premature ovarian failure cases.
- History of using vitamin d supplements in 3 months ago.

METHODOLOGY

The study is started after approval by ethical committee. Informed consent is obtained for all patients who participate in the study and carried out according to the principles of the Declaration of Helsinki.

DATA COLLECTION

This cross-sectional study is performed at the Mallareddy medical college and hospital, Suraram, hyderabad in the department of Obstetrics and gyanecology from Jan 2021 to august 2022 in women of 18-35 years based on inclusion and exclusion criteria. Written informed consent is obtained from all the patients in the study and they were assured that all information would remain confidential. Counselling is done regarding the study and research purpose. After the patients approval, a detailed clinical history is taken and general examination is done according to the proforma. Standard procedures and grading systems used are mentioned in the annexures. After completing clinical examination, provisional diagnosis is made and patient is sent for Ultrasonography pelvis (transabdominal USG in unmarried, transvaginal in married). Diagnosis of PCOS is made on ROTTERDAM criteria.

After taking consent following lab investigations are done. A blood sample was taken from peripheral blood (after 8-12 hours of fasting). Complete blood picture assessed by Leishman stain., Thyroid profile assessed by chemoluminescent immune assay., Serum prolactin levels assessed by chemoluminescent immune assay., Serum testosterone assessed by radioimmunoassay assay if indicated. Fasting insulin levels assessed by chemoluminescent immune assay. Oral glucose tolerance test after 8 hrs fasting and 75gm glucose and levels checked after 1 hr and 2nd hr assessed by hexokinase method. 25 Hydroxy Vitamin D levels assessed by chemoluminescent immune assay. Patient is asked to get the reports following day and they are analysed.

All information obtained from history taking, physical examination, and also para-clinical measures is entered in a checklist and final diagnosis of PCOS is made. Vitamin D status and insulin resistance can be made out through this investigations.

CALCULATIONS

1) Insulin resistance was defined as an elevated fasting insulin levels (I0 > 20microIU/L), Homeostatic model assessment (HOMA-IR) = (I0* G0)/405 (from Matthews *et al.*,) I0 - fasting insulin levels, G0- fasting glucose levels. HOMA-IR: > 2.5, >2.9 - significant insulin resistance, based on the original HOMA research. Glucose/insulin ratio: fasting (G0/I0) <4.5 defined as insulin resistance.
2) Vitamin D Status is measuring the concentration of the 25-hydroxyvitamin D in the blood, which is the most accurate measure of stores of vitamin D in the body. Deficiency: <20 ng/mL = <50 nmol/L

Plan of Statistical Analysis

The collected data is stored in MS EXCEL and analysed. Statistical analysis is performed using EPI INFO, SPSS programs. The statistical methods used are chisquare test and pearson correlation coefficients. Independent sample's t test was used to find the difference between two continuous independent variables and the results were expressed in Mean and standard deviations. P value less than 0.05 was considered as statistically significant. ANOVA test was used to find the difference between more than two continuous independent variables and the results were expressed in Mean and standard deviations. P value less than 0.05 was considered as statistically significant. Chi Square test and Fisher's exact test was used to find the association between two categorical variables, results were expressed in frequencies and percentages and a P value less than 0.05 was considered as statistically significant. Correlation analysis was done to find the relation between two or more independent continuous variables, results were expressed in mean and standard deviations and a p value less than 0.05 was considered as a statistically significant. All data analysis was done using the Statistical software SPSS, Version 24.

RESULTS OF THE STUDY

1. 96.2 % of vitamin d deficient patients showed HOMA IR Values >2.9 as shown in table no.01.
2. 61.5 percent of vitamin d deficient patients showed fasting insulin levels > 20 ng/ml.
3. 59.6 percent of vitamin d deficient patients showed G0/I0 <4.5.
4. Pearsons correlation showed 0.034 between HOMA IR and vitamin d levels indicating that vitamin d deficiency is associated with more HOMA IR values, the more insulin resistance.
5. Pearsons correlation showed 0.05 between fasting insulin levels and vitamin d levels indicating the vitamin d deficiency is associated with more fasting insulin levels, the more insulin resistance. No significant relation is seen with fasting glucose insulin levels (Pearsons correlation value >0.05).
6. No significant relation is seen with BMI and vitamin d levels (pearsons correlation value >0.05).
7. Pearson correlation showed 0.018 between BMI>30 and HOMA IR, 0.014 with fasting insulin levels, 0.034 with fasting glucose insulin ratio, indicating insulin resistance increases with increase in BMI in obese patients. Values showed no significant relation with BMI<30 (Pearsons correlation value>0.05).
8. This study shows insulin resistance (with HOMA IR values and fasting insulin levels) is associated with vitamin d deficiency and the same either way., High BMI- obese patients is associated with more insulin resistance.

Table-1: Showing Insulin Resistance Categories

Fasting insulin levels_Cat	**Frequency**	**Percent**
<20	21	35.0
>20	39	65.0
Total	60	100.0
(Fasting glucose levels G0 MG/DL)/Fasting insulin levels	**Frequency**	**Percent**
<= 4.5	38	63.3
> 4.5	22	36.7
Total	60	100.0

HOMA IR	Frequency	Percent
<= 2.9	2	3.0
> 2.9	58	97.0
Total	60	100.0
Almost all patients showed insulin resistance. 97% showed significant insulin resistance with HOMA IR values.		

Table-2: showing vitamin d deficiency and prevalence the study population

Vitamin D Levels	Frequency	Percent
Vitamin D deficiency	52	86.7
Without Vitamin D deficiency	8	13.3
Total	60	100.0

Table-3: Showing Insulin Levels, Vitamin D Levels and Glucose Levels and Their Means

	N	Mean	Std. Deviation
Fasting insulin levels	60	23.7630	7.16946
Fasting glucose levels G0 MG/DL	60	93.6000	9.11917
(Fasting glucose levels G0 MG/DL)/Fasting insulin levels	60	4.3362	1.51281
HOMA IR	60	5.5063	1.78212
Vitamin d levels	60	15.0374	3.96354

Table-4: showing correlation of sociodemographic distribution with vitamin d levels of the population in the study

	SOCIODEMOG RAPHIC DISTRIBUTION OF STUDY POPULATION	Vitamin d levels		
		r	P	N
Correlations	Age	.043	.742	60
	Height	.244	.061	60
	Weight	.115	.382	60
	BMI	-.079	.547	60
	Waist	-.064	.625	60
	Hip	-.020	.881	60
	WH Ratio	-.072	.586	60
	Fasting insulin levels	-.246	.058	60
	Fasting glucose levels G0 MG/DL	-.137	.295	60
	G120	-.280*	.030	60

Table-5: showing the correlations between insulin resistance and vitamin d levels in the study population

		Fasting insulin levels	Fasting glucose levels G0 MG/DL	(Fasting glucose levels G0 MG/DL)/ Fasting insulin levels	HOMA IR	Vitamin d levels
Fasting insulin levels	Pearson Correlation	1	.092	-.886**	.954**	-.246
	P		.485	.000	.000	.058
	N	60	60	60	60	60
Fasting glucose levels G0 MG/DL	Pearson Correlation	.092	1	.155	.377**	-.137
	P	.485		.236	.003	.295
	N	60	60	60	60	60
(Fasting glucose levels G0 MG/DL)/ Fasting insulin levels	Pearson Correlation	-.886**	.155	1	-.772**	.072
	P	.000	.236		.000	.585
	N	60	60	60	60	60
HOMA IR	P	.954**	.377**	-.772**	1	-.275*
	P	.000	.003	.000		.034
	N	60	60	60	60	60
Vitamin d levels	Pearson Correlation	-.246	-.137	.072	-.275*	1
	P	.058	.295	.585	.034	
	N	60	60	60	60	60

Table-6: Showing Correlation of Insulin Resistance with BMI

		Fasting insulin levels	Fasting glucose levels G0 MG/ DL	(Fasting glucose levels G0 MG/DL)/ Fasting insulin levels	HOMA IR	Vitamin d levels	BMI
BMI	Pearson Correlation	.239	-.024	-.141	.213	-.079	1
	P	.065	.858	.284	.103	.547	
	N	60	60	60	60	60	60

		BMI(<30)	Fasting insulin levels	Fasting glucose levels G0 MG/DL	G0/i0	HOMA IR	Vitamin d levels
BMI(<30)	Pearson Correlation	1	-.002	.043	.082	.012	-.099
	P		.990	.781	.597	.939	.522
	N	44	44	44	44	44	44

		BMI	Fasting insulin levels	Fasting glucose levels G0 MG/DL	G0/i0	HOMA IR	Vitamin d levels
BMI(>30)	Pearson Correlation	1	.599*	.022	-.531*	.584*	-.108
	P		.014	.935	.034	.018	.689
	N	16	16	16	16	16	16

Table-7: Showing Vitamin D Deficiencies with BMI Variations-Vitamin D Deficiency

				HOMA IR_Cat		Total
				<= 2.9	> 2.9	
Vitamin D Deficiency	BMI	< 30	Count	1	38	39
			%	2.6%	97.4%	100.0%
		> 30	Count	1	12	13
			%	7.7%	92.3%	100.0%
	Total		Count	2	50	52
			%	3.8%	96.2%	100.0%
Insufficiency	BMI	< 30	Count		5	5
			%		100.0%	100.0%
		> 30	Count		3	3
			%		100.0%	100.0%
	Total		Count		8	8
			%		100.0%	100.0%
Total	BMI	< 30	Count	1	43	44
			%	2.3%	97.7%	100.0%
		> 30	Count	1	15	16
			%	6.3%	93.8%	100.0%
	Total		Count	2	58	60
			%	3.3%	96.7%	100.0%
Vitamin D Deficiency				**Fasting insulin levels_Cat**		
				<20	**>20**	**Total**
Vitamin D Deficiency	BMI	< 30	Count	15	24	39
			%	38.5%	61.5%	100.0%
		> 30	Count	5	8	13
			%	38.5%	61.5%	100.0%
	Total		Count	20	32	52
			%	38.5%	61.5%	100.0%
Insufficiency	BMI	< 30	Count	4	1	5
			%	80.0%	20.0%	100.0%
		> 30	Count	0	3	3
			%	0.0%	100.0%	100.0%
	Total		Count	4	4	8
			%	50.0%	50.0%	100.0%

Total	BMI	< 30	Count	19	25	44
			%	43.2%	56.8%	100.0%
		> 30	Count	5	11	16
			%	31.3%	68.8%	100.0%
	Total		Count	24	36	60
			%	40.0%	60.0%	100.0%
Vitamin D Deficiency				**g0/i0**		**Total**
				<4.5	**>4.5**	
Vitamin D Deficiency	BMI	< 30	Count	23	16	39
			%	59.0%	41.0%	100.0%
		> 30	Count	8	5	13
			%	61.5%	38.5%	100.0%
	Total		Count	31	21	52
			%	59.6%	40.4%	100.0%
Insufficiency	BMI	< 30	Count	2	3	5
			%	40.0%	60.0%	100.0%
		> 30	Count	3	0	3
			%	100.0%	0.0%	100.0%
	Total		Count	5	3	8
			%	62.5%	37.5%	100.0%
Total	BMI	< 30	Count	25	19	44
			%	56.8%	43.2%	100.0%
		> 30	Count	11	5	16
			%	68.8%	31.3%	100.0%
	Total		Count	36	24	60
			%	60.0%	40.0%	100.0%

CONCLUSIONS

Out of 60 patients studied, 97% showed significant insulin resistance, 86.7% showed vitamin d deficiency. 96.2% of vitamin d deficient patients are significantly Insulin resistant. Pearson correlation value showed 0.034 indicating correlation between serum vitamin d levels and HOMA IR (insulin resistance).

Most common group in the study is 26-30 years. I.e 41.7 %. This reflects that most of the Indian people have stress factors, sedentary lifestyle, rest in post natal period that might lead to PCOS.

Most of the patients of waist circumference is between 90-100cms I.e 46.7%., implies most of the PCOS patients have increased waist circumference leading to obesity. 90% patients have waist hip ratio > 0.8 indicating PCOS patients are more towards the obesity.

Most of the patients presented with irregular cycles (45%) followed by infertility 35%. Irregular cycles is the most common symptom with which the patient presents with. Most of the patients ignore irregular cycles and present with infertility. 86.7 %of the patients showed vitamin D deficiency. most of the patients are vitamin d deficient, not having proper exposure to sunlight and vitamin d rich food in India. 26.7 percent showed obesity BMI > 30kg/m2, 73.3% showed BMI >25kg/m2, indicating prevalence of obesity and over weight is more in India.

Mean vitamin d levels in BMI<30kg/m2 - 15.09kg/m2, BMI> 30- 14.8. Mean HOMA IR in BMI<30kg/m2- 5.32, where as it is 6.0044 in BMI>30 patients. Mean fasting insulin levels in BMI<30- 22.88, where as it is 26.17 in BMI>kg/m2. This indicates more insulin resistance, more vitamin d deficiency is associated with High BMI values.

Almost all patients showed insulin resistance. 97% showed significant insulin resistance with HOMA IR values, 39 patients showed fasting insulin levels more that >20 with insulin resistance (65%)., Fasting glucose levels G0/ Fasting insulin levels I0 with <= 4.5 showing insulin resistance were 63.3 percent, implying insulin resistance is the major pathogenetic factor in PCOS.

75% of vitamin d deficient patients have BMI> 25. 90.4% OF VITAMIN D deficient patients show W-H ratio>0.8. 38.5% of vitamin d deficient patients showed waist circumference between 81- 90 cms. 46.2% of vitamin d deficient patients have waist circumference between 90-100, total 92.3% showed waist circumference > 80 cms. Vitamin d deficiency s related to obesity in PCOS and in general. PCOS leading to overweight and obesity and vitamin d deficiency increases the effect of it.

Prevalence of vitamin d deficiency is more in 26-30yrs age group (40.4%) in my study. This shows improper exposure to sunlight and diet deficiency in those age group. Irregular cycles are more associated with vitamin d deficiency (38.5%), followed by

Infertility (34.6%), this means vitamin d effects at HPO axis and cellular level.

Mean value of HOMA IR is 5.5063., vitamin d-15.0374, fasting insulin levels is 23.7630. 96.2 % of vitamin d deficient patients showed HOMA IR Values >2.9., 61.5 percent of vitamin d deficient patients showed fasting insulin levels > 20 ng/ml., 59.6 percent of vitamin d deficient patients showed G0/I0 <4.5. Pearsons correlation showed 0.034 between HOMA IR and vitamin d levels indicating that vitamin d deficiency is associated with more HOMA IR values, the more insulin resistance.

Pearsons correlation showed 0.05 between fasting insulin levels and vitamin d levels, the trend towards the vitamin d deficiency association with more fasting insulin levels, the more insulin resistance. No significant relation is seen with fasting glucose insulin levels (Pearsons correlation value >0.05). No significant relation is seen with BMI and vitamin d levels (pearsons correlation value >0.05).

Pearson correlation showed 0.018 between BMI>30 and HOMA IR, 0.014 with fasting insulin levels, 0.034 with fasting glucose insulin ratio, indicating insulin resistance increases with increase in BMI in obese patients. Values showed no significant relation with BMI<30 (Pearsons correlation value>0.05). This study shows insulin resistance (with HOMA IR values and fasting insulin levels) is associated with vitamin d deficiency and the same either way., High BMI- obese patients is associated with more insulin resistance.

In the study, it was found that a high percentage of PCOS women were vitamin D deficient. The study also showed a significant difference in the values of some clinical and metabolic parameters such as waist circumference, fasting insulin, HOMA-IR, BMI between PCOS women with and without vitamin D deficiency; however, no linear correlation was found between serum levels of vitamin D and baseline variables, except for HOMA IR values, fasting insulin levels, BMI, G120.

In conclusion, our data confirm an association between vitamin D deficiency and Insulin resistance in patients with PCOS. Thus, vitamin D supplementation could be a beneficial treatment of PCOS women to abolish insulin resistance and regulate menstrual irregularities.

Our study also indicates that insulin resistance was an independent risk factor for the presence of vitamin D deficiency in women with PCOS. Further, we recommended long term follow up studies to identify the role vitamin D supplementation in patients with PCOS to confirm the beneficial role of vitamin D.

Further studies are needed to draw conclusive results about the role of vitamin D in the pathogenesis of PCOS, as most studies have not adjusted for confounding factors that may affect vitamin D status, such as dietary intake, intake of additional nutrients co-integrated with vitamin D, or factors that determine vitamin D deficiency (sun exposure, physical exercise, etc.). Also, due to the need for assessing the causality relation and to determine the effect of vitamin D on these all metabolic parameters, it is necessary to perform further randomised clinical trials in the patients in large population for detecting correlations.

Until then, it seems reasonable to screen women with PCOS at risk for vitamin D deficiency and prescribe vitamin D supplementation if they are deficient in vitamin D. Supplementation seems likely to improve different aspects of PCOS such as BMI, insulin resistance, lipid profile, cardiovascular risk, menstrual regularity, fertility, and bone health.

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