https://doi.org/10.48047/AFJBS.6.14.2024.8695-8701

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

The relationship between body mass index and vitamin d levels in women with polycystic ovary syndrome

Dr. Khushboo Shrimali[1] Dr. Manjinder Kaur[2] Dr. Ashish Sharma[3] Dr. Usha Rani[4] Soniya Pipliwal[5] Dr. Naren Kurmi[6] Dr. Bhavik singhvi[7]

Ph.D. Scholar, Department of Physiology, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India

Professor and HOD, Department of Physiology, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India

Professor and HOD, Department of Biochemistry, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India

Assistant Professor, Department of Physiology, Geetanjali Medical College and hospital, Udaipur, Rajasthan, India

Demonstrator, Department of Physiology, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India

Professor, Department of Physiology Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India

Demonstrator, Department of Physiology, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India

***Corresponding Author:** Dr. Naren Kurmi, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India

ArticleInfo

Volume6, Issue 14,2024

Received: 30July 2024

Accepted: 26 Aug2024

doi: 10.48047/AFJBS.6.14.2024.8695-8701

Abstract

Introduction: Polycystic ovary syndrome (PCOS) is a common hormonal and metabolic condition affecting women of reproductive age. It is characterized by persistent anovulation, increased androgen levels, insulin resistance, and mild inflammation. Women with PCOS are more susceptible to cardiovascular and metabolic complications. The present study was aim to investigate the correlation between body mass index and serum vitamin D levels in women with PCOS.

Methods: The present study was designed as cross sectional comparative study. The volunteers were recruited from the gynecology department of a tertiary care hospital and studied in the department of Physiology. The present study included 120 women between 18- 40 years. The study participants were divided into 2 groups. Group N included 52 volunteers with normal levels of vitamin D in women with PCOS and Group D includes 68 volunteers with hypovitaminosis D in women with PCOS.

Results: The study involved 120 patients with PCOS, categorized into two groups, N and D. In Group N, 15.38% (n = 8) were underweight, 61.53% (n = 32) had normal weight, 17.31% (n = 9) were overweight, and 5.77% (n = 3) were obese. In Group D, 10.29% (n = 7) were underweight, 27.94% (n = 19) had normal weight, 39.71% (n = 27) were overweight, and 22.06% (n = 15) were obese. The analysis of BMI showed significant differences in the rates of overweight and obesity between Groups N and D (p = 0.008 and 0.013, respectively). Furthermore, a negative correlation was observed between BMI and serum vitamin D levels across all participants.

Conclusions: The present study suggests that women with PCOS, who have hypovitaminosis D levels are generally more overweight or obese than those with normal vitamin D levels in women with PCOS. Consequently, it is advised that all PCOS patients undergo screening for vitamin D deficiency to prevent obesity and its related metabolic disorders.

Keywords: Ovary syndrome, polycystic, body mass index, vitamin d, obesity, abdominal reproductive health

1. Introduction

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age [1],with the prevalence of 15% [2].It is characterized by menstrual irregularities, ovarian dysfunction, clinical and biochemical evidence of hyperandrogenism and polycystic appearance of the ovaries [3].PCOS was diagnosed according to the Rotterdam Criteria 2003, in which at least two of three criteria are present i.e.; amenorrhea, hyperadrogenemia or their clinical manifestations, polycystic appearance of ovaries [2].Existing literature suggests that 30 to 40% of women with PCOS exhibit impaired glucose tolerance and insulin resistance (IR) with compensatory hyperinsulinemia, and 10% of this population develops type II diabetes mellitus by their 40s [4]. Additionally, many researchers have identified central obesity, cardiovascular disease, and endometrial cancer as common conditions among women with PCOS [5, 6].It has been found that IR is a primary contributing factor to ovulatory dysfunction and hyperandrogenic state in women with PCOS. Several cross-sectional and prospective studies have observed an inverse relationship between IR and Vitamin D, with a notable association between serum vitamin D levels and metabolic disturbances [7-9].Vitamin D is a lipid-soluble hormone which is involved in various physiological processes beyond bone health, including cell regulation and immune function. Research has shown that vitamin D receptors (VDRs) and the enzyme 1 alpha-hydroxylase are present in these tissues and affects their functions [9-11].

Though PCOS has been extensively studied for clinical manifestations and management but its association with Vitamin D has not been adequately explored. Hence, the present study was designed as cross-sectional comparative study with an aim to find out association between vitamin D and body mass index (BMI) in women with polycystic ovarian syndrome.

Methodology

The present study was designed as cross-sectional comparative study carried out from May 2023-June 2024. The volunteers were recruited from Gynecology department of a tertiary care hospital and evaluated in the Department of Physiology. The approval of the Human Research Ethics Committee was obtained prior to the commencement of the study, vide letter no. GU/HREC/EC/2022/2053A.

The study was conducted on 120 women with PCOS from the reproductive age group i.e., between 18-40 years The sample size was calculated from the pooled prevalence of PCOS (11.33%)[12]and prevalence of hypovitaminosis D in PCOS women of India-(80-90.6%) [13, 14].The confidence level of 95%, power of study 80% with the maximum allowable error of 10%. These participants were further sub-divided into 2 groups based on the levels of vitamin D:-

Group N (n=52): PCOS women between 18-40 years with serum Vitamin D levels >30ng/ml.

Group D (n=68): PCOS women between 18-40 years with serum Vitamin D levels <30ng/ml.

The participants with PCOS were diagnosed according to the Rotterdam criteria 2003 as mentioned earlier [2].

However, the participants with systemic diseases such as hypothyroidism, diabetes mellitus, hypertension, nephropathy, respiratory diseases, hyperandrogenic disorders (non-classical congenital adrenal hyperplasia, Cushing's syndrome, androgen secreting neoplasms), hyperprolactenemia, women already on any hormonal therapy, already on treatment for PCOS and vitamin D deficiency were excluded from study.

The participants were clearly informed about the nature and procedure of the study in local language. The study was conducted only after obtaining informed written consent from all the participants. A fasting sample for blood was taken on 2^{nd} or 3^{rd} day of menstrual cycle for biochemical assessment of serum vitamin D levels.

Demographic Data

Demographic characteristics included age, height and weight. Height was measured to the nearest millimeter by a wall mounted stadiometer. Weight was measured with weighing machine. Body mass index (BMI) was calculated as ratio of weight (in Kilograms) and height (in square meter).

Sample Collection

Fasting venous blood samples (10 ml) were collected from the participants on 2^{nd} or 3^{rd} day of menstrual cycle by vene puncture then transferred to plain vacuette (without anticoagulant). It was then allowed to clot for 30 minutes at room temperature. After the blood had clotted, it was placed in a centrifuge at 3000 revolution per minute to obtain the serum. The obtained serum were stored in deep freezer at (-20 ºC) until analyzed. For analysis frozen samples were thawed to equilibrate at room temperature for 30 minutes before processing.

The samples were analyzed for serum vitamin D levels by enzyme-linked immunosorbent assay (ELISA) kit method using ELISA Kit (Calbiotech, Inc. USA) [15, 16]. Test was run on the ELISA, BeneSphera^{TM} ELISA Microplate Reader E21 and Thermo scientific WELLWASHER which is based on competitive binding principle.

Procedure: All reagents and specimens were allowed to come to room temperature before use. All reagents were gently mixed without foaming. The procedure was then performed without interruption.

10µl of 25-OH Vitamin D, including standards, controls, and samples, was dispensed into each well. Next, 200µl of biotinylated 25 (OH) D working solution was added. The contents were mixed for 20 seconds using a plate shaker at 200-400 RPM. The plate was incubated at room temperature for 90 minutes, after which the contents were shaken out into a waste reservoir.

For washing, 300µl of 1X Wash Buffer was added to each well, shaken out, and the wells were struck on absorbent paper. This washing step was repeated two more times.

Next, 200µl of Streptavidin-HRP enzyme conjugate was added to each well, and the plate was incubated at room temperature for 30 minutes. The contents were shaken out again, and the washing steps were repeated.

Using a multi-channel pipette, 200µl of TMB Substrate was added to each well, followed by incubation at room temperature for 30 minutes, preferably in the dark. Then, 50µl of stop solution was added to stop the enzymatic reaction, and the plate contents were mixed for 20-30 seconds.

Finally, the optical density (OD) at 450nm was measured using an ELISA Reader within 10 minutes of adding the Stop Solution. The absorbance at 450nm was compared with the given 25(OH)D values in ng/ml and converted to nmol/L by multiplying the ng/ml values by 2.5.

The reference range was considered as deficient with vitamin D less than <10ng/ml deficient; insufficient with 10-30ng/ml; sufficient with 30-100ng/ml; and intoxication with vitamin D levels more than 100ng/ml. [16, 17]

Statistical Analysis

Statistical analysis was conducted using IBM SPSS Statistics version 20. Mean and standard deviation (SD) were calculated. Comparisons between normal levels of vitamin D and Hypovitaminosis D were performed using the unpaired Student's t-test for continuous variables and the Chi-square test for categorical variables. The correlation between BMI and serum vitamin D levels was assessed using Karl Pearson's correlation test. A p-value of less than 0.05 was considered statistically significant, while a p-value less than 0.001 was considered highly significant**.**

Result

TABLE 1: TABLE SHOWING MEAN SERUM VITAMIN D (ng/ml) IN GROUP N & D

	Group N (n= 52)		**Group D (n= 68)**		
Parameters	**Mean**	**SD**	**Mean**	**SD**	**P value**
Vitamin D (ng/ml)	42.79	±15.29	14.71	±1.47	<0.001**

** Highly significant. Result obtained by unpaired 't' test.

Table 2: TABLE SHOWING THE AGE-WISE DISTRIBUTION OF SUBJECTS AMONG GROUP N (NORMAL VITAMIN D LEVELS) AND GROUP D (HYPOVITAMINOSIS D LEVELS)

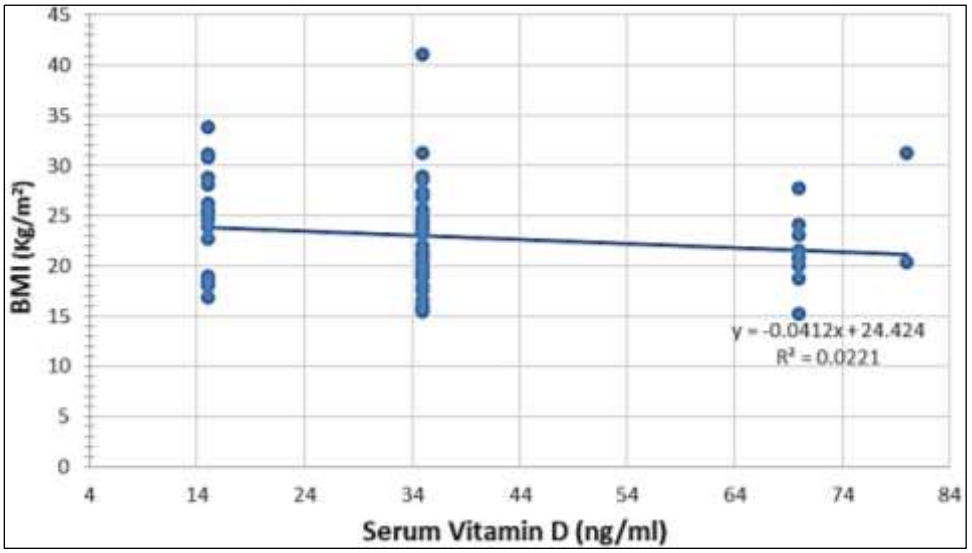
	Group N (n= 52)		**Group D (n= 68)**		
Age group (yrs)	**No.**	**%**	**No.**	**%**	**P value**
11-20	13	25%	16	23.53%	0.852 Φ
21-30	30	57.69%	44	64.71%	0.613 Φ
31-41	9	17.31%	8	11.76%	0.388 Φ
Total	**52**		**68**		
Mean	24.81		24.13		>0.05 Φ
SD	± 5.54		± 5.11		

Φ not significant.

Table 3: TABLE SHOWING THE DISTRIBUTION OF BODY MASS INDEX (Kg/m^2) OF PARTICIPANTS IN GROUP N & D

	Group N(n= 52)		Group D(n= 68)		
BMI (Kg/m^2)	**No.**	**%**	**No.**	**%**	**P value**
Underweight (<18.5)	8	15.38%	7	10.29%	0.40 $^{\Phi}$
Normal (18.5-24.9)	32	61.53%	19	27.94%	<0.001 **
Overweight (25-29.9)	9	17.31%	27	39.71%	0.008 *
Obese (≥30)	3	5.77%	15	22.06%	0.013*

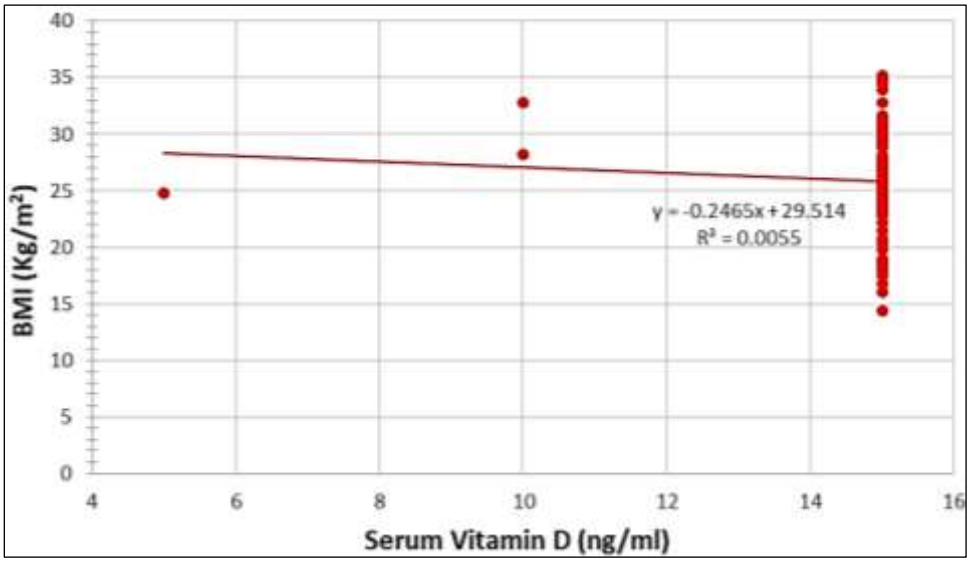
$^{\Phi}$ not significant,* Significant;**highly significant. Result obtained by Chi square test.



"r" = -0.148 (P >0.05$^{\Phi}$)Karl Pearson Correlation Test.

$^{\Phi}$ not significant.

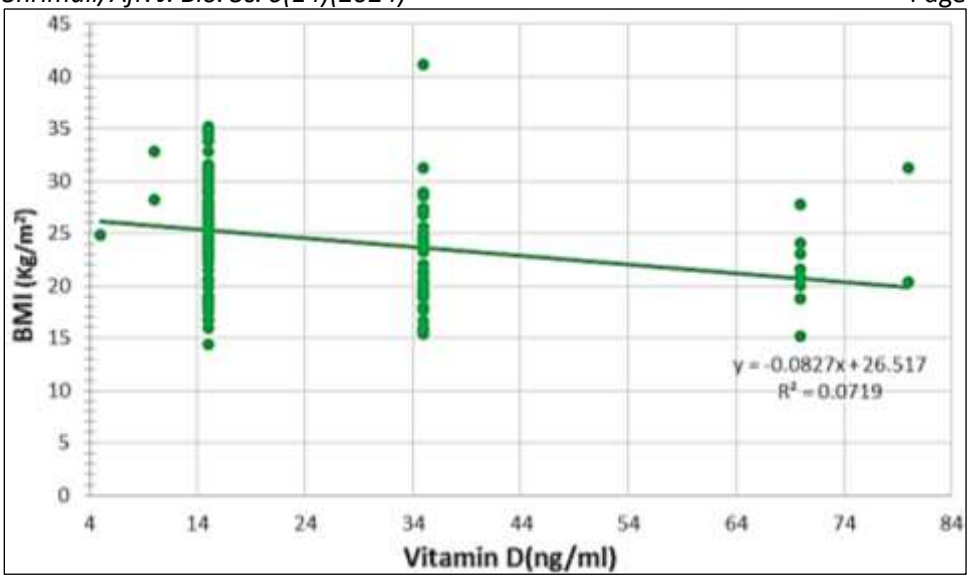
FIG 1: CORRELATION OF BMI AND SERUM LEVELS OF VITAMIN D OF GROUP N



"r" = -0.07 (P > 0.05$^{\Phi}$) Karl Pearson Correlation Test

Φ not-significant.

FIG 2: CORRELATION OF BMI AND SERUM LEVELS OF VITAMIN D OF GROUP D



r = -0.266 (P > 0.05$^{\Phi}$) Results obtained by Karl Pearson Correlation Test.
$^{\Phi}$ not significant.

FIG 3: CORRELATION OF BMI AND SERUM LEVELS OF VITAMIN D OF OVER ALL CASES

The present study was done on 120 participants with polycystic ovarian syndrome, who were sub-divided into 2 groups based on the vitamin D levels into two group N (vitamin D > 30ng/ml) and group D (vitamin D < 30ng/ml).

Table 1 clearly shows the mean Vitamin D levels to be significantly lower (P <0.001) in Group D (14.79 $\pm$ 1.47)as compared to Group N (42.79 $\pm$ 15.29).

Further, table 2 shows that the most of participants in both Group N and D were between the age groups of 21-30 years (57.67% and 64.71%, respectively). Also observed 25% & 23.53% of participants in group N and group D respectively were between age group of 11-20 years. The least number of participants were above 31 years.

Further, table 3 shows the 61.53% of participants with normal vitamin D levels in group N had a normal BMI, whereas 39.71% of participants with vitamin D deficiency were overweight and 22.06% were obese. This observation becomes more significant, if we pool the BMI over 25. 61.77%of participants had BMI over 25 in group D as compared to 13.08% in group N.

Fig. 1 shows the correlation of BMI & serum vitamin D levels of group N showing a non-significant (P>0.05) inverse correlation (r= -0.148).

Fig. 2 shows the correlation of BMI & serum vitamin D levels of group D showing a non-significant (P>0.05) inverse correlation (r= -0.07).

Fig.3 shows the correlation of BMI & serum vitamin D levels of both group N and D showing a non- significant (P>0.05) inverse correlation (r= -0.266).

Discussion

The present study was conducted on 120 women with PCOS in reproductive age group i.e., 18-40 years attending the Gynecology department of tertiary care Centre in the South Rajasthan. Majority of participants, 57.67% and 64.71% in group N and D respectively, were between the age group of 21-30 years indicating that most of the study population was in the peak of the reproductive age group. Since these patients were recruited from Gynecology OPD with PCOS, most of these patients had reported with infertility. However, it was reported by Gallagher JC (2013) that the decline in the vitamin D levels with age because of decreased synthesis of Vitamin D by the skin due to substrate deficiency and which is further accentuated due to Vitamin D receptor insufficiency [18].

The present study documents a non-significant (p>0.05) inverse correlation (r=-0.266) between vitamin D levels and BMI. This relationship is suggestive of low circulating levels of vitamin D in women with higher BMI. Though present study could not establish a significant correlation between these two parameters but Thomson RL *et al*., (2012) have proposed a strong association between vitamin D deficiency and obesity.[19] Additionally, Muscogiuri G *et al*., (2012), stated that the vitamin D deficiency could be strongly associated with degree of adiposity of the women with PCOS [20].The participants in our study from group D were mostly overweight and not overtly obese. Hence the degree of adiposity was not large enough to elicit a stronger association.

The effects of Vitamin D deficiency in women with PCOS, could be attributed to the development of insulin resistance

in obese individuals. The relationship of Vitamin D, PCOS and Insulin resistance sets up a vicious cycle, explained below:

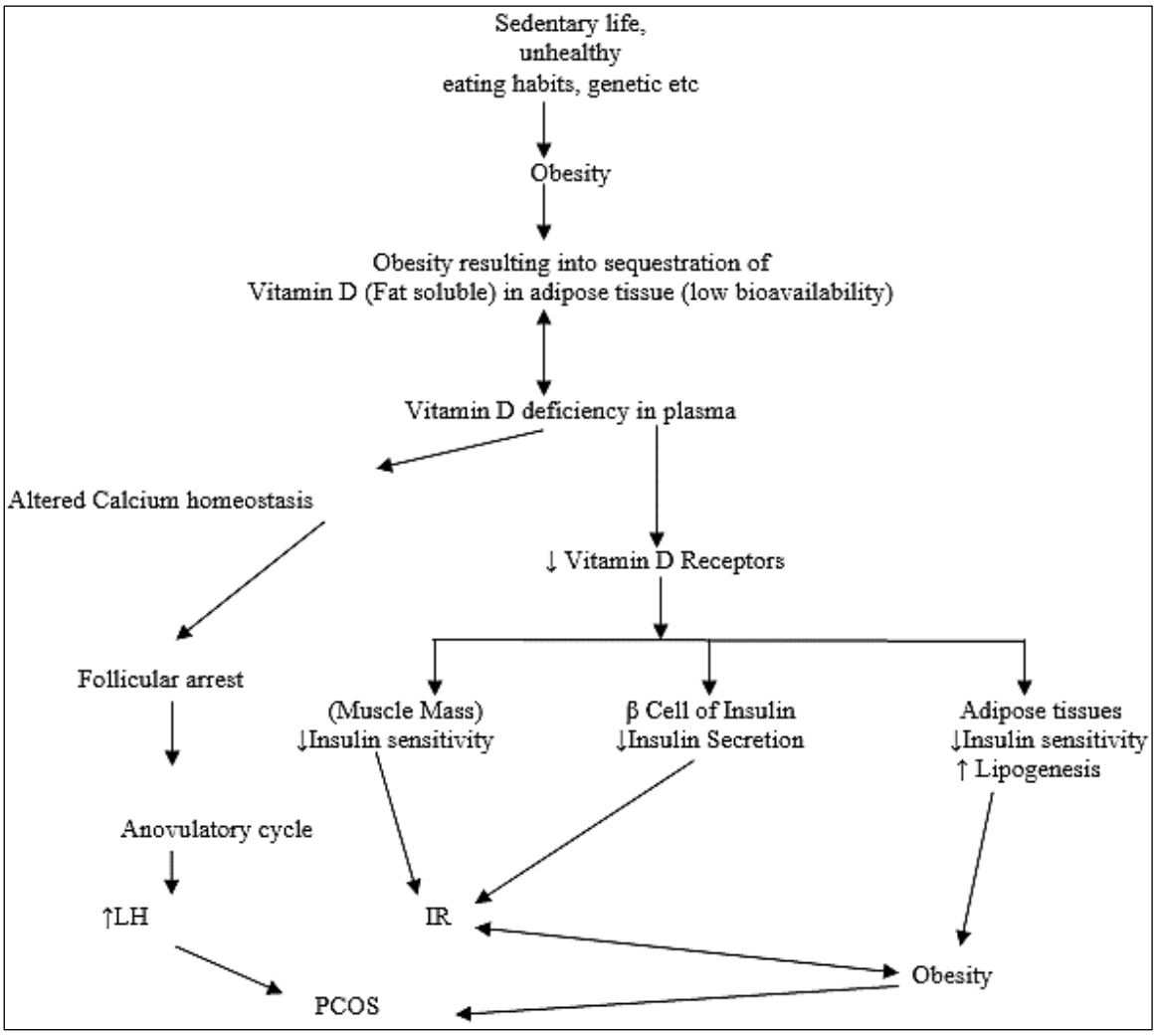


FIG 4:THE RELATIONSHIP BETWEEN VITAMIN D DEFICIENCY AND THE PATHOGENESIS OF INSULIN RESISTANCE AND METABOLIC SYNDROME IN PCOS

The relationship between BMI and vitamin D levels is complex and bidirectional. In obese individuals, several factors contribute to reduce vitamin D synthesis, including decreased outdoor activity, increased coverage by clothing, and dietary differences compared to non-obese individuals [21].Vitamin D, being fat-soluble is stored in adipose tissue, which sequesters and lowers its bioavailability in circulation. Consequently, women with PCOS who have higher BMI generally exhibit lower serum vitamin D levels as compared to their non-obese counterparts, as was similarly observed by Yildizhan R (2009); Sachdeva M (2024) [22, 23].

Research by Kumar A *et al*.,(2017) has shown that vitamin D deficiency has been found to worsen insulin resistance and other metabolic issues in PCOS, leading to further weight gain and fat accumulation [24].Vitamin D receptors (VDRs) are present in tissues crucial for energy metabolism, such as fat, muscle, and pancreatic β-cells. A deficiency in vitamin D may disrupt calcium homeostasis and decrease VDR expression resulting in impairment of insulin secretion and sensitivity as suggested by Morris (2005) [25].This disruption promotes fat storage and alters lipid metabolism. All these factors combined (reduced insulin secretion, decreased insulin sensitivity, and increased lipogenesis) aggravate insulin resistance, further exacerbating PCOS and its associated comorbidities as observed by Konradsen (2008); Teengarden D (2009) [26, 27].

Conclusion

In conclusion, the relationship between BMI and vitamin D levels in women with PCOS is complex, involving obesity, insulin resistance, and metabolic issues. Screening for vitamin D deficiency, especially in those with a high BMI, should be routine to improve health outcomes.

Limitations

This study has some limitations as firstly the sample size of the participants was relatively small and secondly the participants with PCOS were recruited from a single-center in the city of Udaipur, Rajasthan. Hence, the results of this research needs to be proved through multi-center surveys with large sample sizes in other areas.

Future Scope

In the future, it will be essential to investigate insulin levels and HOMA-IR in a larger sample of the obese women with PCOS. Additionally, an interventional study exploring the effects of vitamin D supplementation on these parameters could be conducted. Such research could provide valuable insights into the interplay between obesity, insulin resistance, and vitamin D, potentially informing new therapeutic strategies.

Acknowledgement

I am very thankful toDr. Jinni Gupta for providing the patients of PCOS. Dr. Anamika Vyas (HOD Department of microbiology) for giving permission to test serum Vitamin D levels on the Elisa machine andMr. Lalitlohar for assistance in testing the serum vitamin D levels.

References

[1] Fauser, B.C., Tarlatzis, B.C., Rebar, R.W., Legro, R.S., Balen, A.H. and Lobo, R., 2012. Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ASRM Sponsored 3rd PCOS Consensus Workshop Group. Fertility and Sterility, 97(1), pp.28-38.

[2] Group REA-SPCW, 2004. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertility and Sterility, 81, pp.19-25.

[3] Zacur, H.A., 2003. Epidemiology, clinical manifestations and pathophysiology of polycystic ovary syndrome. Advances in Stud Med, 3, pp.S733-S739.

[4] Teede, H., Deeks, A. and Moran, L., 2010. Polycystic ovary syndrome: a complex condition with psychological, reproductive and metabolic manifestations that impacts health across the lifespan. BMC Medicine, 8, p.41.

[5] Salley, K.E.S., Wickham, E.P., Cheang, K.I., Essah, P.A., Kargane, N.W. and Nestler, J.E., 2007. Glucose intolerance in polycystic ovary syndrome: a position statement of the Androgen Excess Society. Journal of Clinical Endocrinology & Metabolism, 92, pp.4546-4556.

[6] Ehrmann, D.A., Lilijenquist, D.R., Kasza, K., Azziz, R., Legro, R.S. and Ghazzi, M.N., 2006. Prevalence and predictors of the metabolic syndrome in women with polycystic ovary syndrome. Journal of Clinical Endocrinology & Metabolism, 91(1), pp.48-53.

[7] Lakshman, L.R., Pillai, B.P., Lakshman, R., Kumar, H., Sudha, S. and Jayakumar, R.V., 2013. Comparison of vitamin D levels in obese and non-obese patients with polycystic ovarian syndrome in a South Indian population. International Journal of Reproduction, Contraception, Obstetrics and Gynecology, 2(3), pp.336-343.

[8] Garg, R., Malhotra, J., Singh, S., Singh, R., Kokila, B.T. and Agrawal, P., 2017. Relationship between Vitamin D and Insulin Resistance in Polycystic Ovary Syndrome Women. Journal of South Asian Federation of Obstetrics and Gynaecology, 9(3), pp.211-215.

[9] Krul-Poel, Y.H.M., Koenders, P.P., Steegers-Theunissen, R.P., Ten Boekel, E., Wee, M.M.T., Louwers, Y., Lips, P., Laven, J.S.E. and Simsek, S., 2018. Vitamin D and metabolic disturbances in polycystic ovary syndrome (PCOS): A cross-sectional study. PLoSOne,13(12),p.e020-4748.

[10] Rahimi-Ardabili, H., PourghassemGargari, B. and Farzadi, L., 2013. Effects of vitamin D on cardiovascular disease risk factors in polycystic ovary syndrome women with vitamin D deficiency. Journal of Endocrinological Investigation, 36(1), pp.28-32.

[11] Aly, Y.E., Abdou, A.S., Rashad, M.M. and Nassef, M.M., 2016. Effect of exercise on serum vitamin D and tissue vitamin D receptors in experimentally induced type 2 Diabetes Mellitus. Journal of Advanced Research, 7(5), pp.671-679.

[12] Bharali, M.D., Rajendran, R., Goswami, J., Singal, K., Rajendran, V. and *et al*., 2022. Prevalence of Polycystic Ovarian Syndrome in India: A systematic Review and Meta-Analysis.Cureus,14(12).

[13] Mishra, S., Das, A.S., Das, S. and *et al*., 2016. Hypovitaminosis D and Associated Cardiometabolic Risk in Women with PCOS. Journal of Clinical and Diagnostic Research,10(5),pp.BC01-BC04.

[14] Selimoglu, H., Duran, C., Kiyici, S., Eroy, C., Guclu, M. and *et al*., 2010. The effect of vitamin D replacement therapy on insulin resistance and androgen levels in women with polycystic ovary syndrome. Journal of Endocrinological Investigation, 33, pp.234-238.

[15] Zerwekh, J.E., 2008. Blood biomarkers of vitamin D status. American Journal of Clinical Nutrition, 87, pp.1087S-1091S.

[16] Calbiotech, 2019. 25(OH) Vitamin D ELISA [Catalog No.: VD220B]. El Cajon, CA: Calbiotech.

[17] Morris, H.A., 2005. Vitamin D: A Hormone for All Seasons-How Much is enough? Clinical Biochemistry Reviews, 26, pp.21-23.

[18] Gallagher, J.C., 2013. Vitamin D and aging. Endocrinology and Metabolism Clinics of North America, 42(2), pp.319-332.

[19] Thomson, R.L., Spedding, S. and Buckley, J.D., 2012. Vitamin D in the aetiology and management of polycystic ovary syndrome. Clinical Endocrinology, 77(3), pp.343-350.

[20] Muscogiuri, G., Policola, C., Prioletta, A. and Sorice, G., 2012. Low levels of 25(OH)D and insulin-resistance: 2 unrelated features or a cause-effect in PCOS? Clinical Nutrition, 31, pp.476-480.

[21] Pereira-Santos, M., Costa, P.R., Assis, A.M., Santos, C.A. and Santos, D.B., 2015. Obesity and vitamin D deficiency: a systematic review and meta-analysis. Obesity Reviews, 16(4), pp.341-349.

[22] Yildizhan, R., Kurdoglu, M. and Adali, E., 2009. Serum 25-hydroxyvitamin D concentrations in obese and non-obese women with polycystic ovary syndrome. Archives of Gynecology and Obstetrics, 280, pp.559-563.

[23] Sachdeva, M., Goel, K., Rai, M. and Kukreja, S., 2024. Comparative study of vitamin D3 levels in polycystic ovarian syndrome vs non-polycystic ovarian females. International Journal of Reproduction, Contraception, Obstetrics and Gynecology, 13(1), pp.107-110.

[24] Kumar, A., Barki, S., Raghav, V., Chaturvedi, A. and Kumar, K.V.S.H., 2017. Correlation of Vitamin D with metabolic parameters in polycystic ovarian syndrome. Journal of Family Medicine and Primary Care, 6(1), pp.115-119.

[25] Morris, H.A., 2005. Vitamin D: A hormone for all seasons - How much is enough? Clinical Biochemistry Reviews, 26, pp.21-32.

[26] Konradsen, S., Ag, H., Lindberg, F., Hexeberg, S. and Jorde, R., 2008. Serum 1,25-dihydroxy vitamin D is inversely associated with body mass index. European Journal of Nutrition, 47(2), pp.87-91.

[27] Teegarden, D. and Donkin, S.S., 2009. Vitamin D: emerging new roles in insulin sensitivity. Nutrition Research Reviews, 22(1), pp.82-92.