International Journal of Clinical Obstetrics and Gynaecology

ISSN (P): 2522-6614
ISSN (E): 2522-6622

www.gynaecologyjournal.com
2023; 7(1): 82-87
Received: 21-11-2022
Accepted: 22-12-2022

Sherin Mohamed Rezk Shams Eldin
Department of Obstetrics and Gynaecology, Faculty of Medicine - Tanta University, Tanta, Egypt

Sherin Barakat El Bohoty
Department of Obstetrics and Gynaecology, Faculty of Medicine - Tanta University, Tanta, Egypt

Manal Fathy Mostafa Hamiesa
Department of Obstetrics and Gynaecology, Faculty of Medicine - Tanta University, Tanta, Egypt

Amal Elsayed Mahfouz
Department of Obstetrics and Gynaecology, Faculty of Medicine - Tanta University, Tanta, Egypt

Corresponding Author:
Sherin Mohamed Rezk Shams Eldin
Department of Obstetrics and Gynaecology, Faculty of Medicine - Tanta University, Tanta, Egypt

The effect of vitamin D3 supplementation in vitamin D3 deficient women with polycystic ovarian syndrome and it's relation to insulin resistance and visceral fat thickness

Sherin Mohamed Rezk Shams Eldin, Sherin Barakat El Bohoty, Manal Fathy Mostafa Hamiesa and Amal Elsayed Mahfouz

DOI: https://doi.org/10.33545/gynae.2023.v7.i1b.1256

Abstract
Background: Polycystic ovary syndrome (PCOS) is a multifactorial, heterogeneous, endocrine-metabolic disorder that commonly affects women at their reproductive age. PCOS is a complex syndrome characterized by chronic oligo-or anovulation, menstrual irregularities, hyperandrogenism, infertility, and polycystic ovarian morphologic features**.** The aim of the work WAS to evaluate the effect of vitamin D3 supplementation on insulin resistance, and visceral fat thickness in vitamin D3 deficient women with polycystic ovarian syndrome.
Methods: Patients were allocated randomly into 2 groups: Group I: 30 women received 50.000 Iu of oral vitamin D3 (Cholecalciferol) (Breva) once weekly for (12) weeks. Group II (placebo group): 30 women received placebo capsules once weekly for (12) weeks. Trans-abdominal US and transvaginal US examination were performed for detailed ovary imaging
Results: The difference in the glucose tolerance profile after treatment. There was a statistically significant difference between both groups regarding the mean fasting blood sugar levels (p =0.001), where the mean FBS in the intervention group was (79.60±9.464), while that of the placebo group was (89.67±9.181). Moreover, the HOMA-IR level varied significantly (p=0.017), where in the intervention group the mean level was (2.99±0.621), compared to a mean of (3.59±1.179) in the placebo group**.,** none of the mean hormonal levels varied significantly among the intervention group from before to after treatment, except for the mean 25- hydroxy-vitamin D level (p= <0.001), which increased from (13.26±7.203) before treatment, to (26.76±15.531) after treatment.
Conclusion: In conclusion, Vitamin D supplementation in an oral dose of 50.000 IU of vitamin D3 (Cholecalciferol) once weekly for (12) weeks among women with PCOS significantly increased serum 25OHD levels, and significantly decrease insulin resistance and visceral fat thickness no potential effect was detected on BMI, waist circumference (WC)and waist to hip Ratio.

Keywords: Vitamin D3 supplementation, polycystic ovarian syndrome, insulin resistance and visceral fat thickness

Introduction
Polycystic ovary syndrome (PCOS) is a common disorder in women of reproductive age, with a prevalence 5–16% under different diagnostic criteria and across several ethnic groups, with exact pathogenesis still unclear [2]. Polycystic ovary syndrome (PCOS) is a multifactorial, heterogeneous, endocrine-metabolic disorder that commonly affects women at their reproductive age. PCOS is a complex syndrome characterized by chronic oligo-or anovulation, menstrual irregularities, hyperandrogenism, infertility, and polycystic ovarian morphologic features [2].
The diagnosis of PCOS based on the Rotterdam criteria, Women with the two of the following criteria were considered as having PCOS: oligoovulation and anovulation, biochemical signs of hyperandrogenism, and polycystic ovaries on ultrasound examination (defined as the presence of 12 follicles measuring 2-9 mm in diameter and/or an ovarian volume >10 cm3) [3].
Excess luteinizing hormone (LH) and low follicle stimulating-hormone (FSH) are also common, and approximately 60%–80% of all PCOS cases are more vulnerable to develop insulin resistance (IR) and compensatory hyperinsulinemia, which exacerbates ovarian androgen production and ovulation dysfunction in PCOS patients [4].

The presence of hyperinsulinemia and insulin resistance is associated with an increased risk for impaired glucose tolerance, cardiovascular disease and type 2 diabetes mellitus. Many studies indicate that a defect in insulin action may be the primary cause of PCOS [5, 6].

Insulin resistance (IR) can be found in 60-80% and 95% of all women with PCOS and in 95% of obese women with PCOS respectively [7].

Another common property between PCOS women is increasing visceral fat. Women with PCOS have higher prevalence of central adiposity [8-9]. Adipose tissue plays a crucial role in the development and maintenance of PCOS [10]. Adipocytes seem to be prone to hypertrophy, as experienced by PCOS women, and both adipose tissue hypertrophy and hyperandrogenism (HA) are related to insulin resistance [11]. Insulin resistance and hyperandrogenism influence adipose cell function [12]. The aim of the work was to evaluate the effect of vitamin D3 supplementation on insulin resistance, and visceral fat thickness in vitamin D3 deficient women with polycystic ovarian syndrome.

Methods

This study is double - blind randomized controlled clinical trial, conducted on 60 patients with polycystic ovary syndrome recruited from Department of Obstetrics and Gynecology, Tanta University Hospital during a period from June 2020 to April 2021, The diagnosis of PCOS was be based on the Rotterdam criteria, Women with the two of the following criteria were considered as having PCOS: oligo ovulation or anovulation, clinical signs of hyperandrogenism, and polycystic ovaries on ultrasound examination.

1. PCOS women with vitamin D-deficiency (serum 25 hydroxy vitamin D (25 (OH) D) level less than 20 ng/mL)
2. Age between 20 - 38 years.
3. Body mass index ≥ 25kg/m^2& less than 30kg/ m^2

Exclusion criteria

1. Medical diseases such as thyroid dysfunction, liver, renal dysfunction lupus erythematous, cardio vascular disorders, hypertension or diabetes mellitus.
2. History of using any hormones and oral contraception within the last 6 months.
3. Women received Medication known to affect the metabolic parameters as anti-diabetic drugs, oral vitamin D3 and calcium supplementation

Allocation: Patients were allocated randomly into 2 groups:

Group I: 30 women received 50.000 Iu of oral vitamin D3 (Cholecalciferol) (Breva) once weekly for (12) weeks.

Group II (placebo group): 30 women received placebo capsules once weekly for (12) weeks.

All patients were be subjected to

1. Written informed consent which was proved by the medical ethical committee of faculty of medicine Tanta University.
2. Detailed history taking as regards:

- Demographic data as age, residence, occupation, and special habitt.

3. General examination that include pulse, BP, Temperature and Respiratory rate.
4. Gynecological examination that include abdominal exam (inspection, palpation, percussion and auscultation) and pelvic exam that include (external genital exam, the speculum exam, and the bimanual exam)
5. Trans- abdominal US and transvaginal US examination were performed for detailed ovary imaging
6. For biochemical and hormonal measurements, overnight fasting blood samples were taken from each participant at baseline and week 12 of the intervention on the 2nd or 3rd day of their spontaneous or progesterone-induced menstrual cycles.
7. Assessment of serum 25-hydroxyvitamin D (25(OH)D) concentration using a commercial ELISA kit.

Workup

1. The waist to hip ratio was calculated as waist circumference was measured by placed a tape measure around their middle at a point half way between the bottom of their ribs and the top of their hips (just above the belly button) Whereas hip circumference was the maximum extension of the buttocks as seen from the side.
2. Fasting plasma glucose was measured using enzymatic colorimetric method using glucose oxidase kit, Then fasting Serum insulin was assessed using ELISA kit. Insulin resistance was calculated by Homeostatic model assessment insulin resistant (HOMA-IR) formula.

$$\frac{\text{(Fasting plasma glucose in mg/dl X Fasting insulin in MU/L)}}{405}$$

3. Visceral fat thicknesses was assessed by trans-abdominal ultrasonography after overnight fasting before using a high-resolution B-mode Ultrasound system (Mindray DC-80A, US)by using a convex probe.

Statistical analysis

Statistical analysis was done by SPSS v25 (IBM Inc., Chicago, IL, USA). Quantitative variables were presented as mean, standard deviation (SD) and range and were compared between the two groups utilizing unpaired Student's t- test. Categorical variables were presented as frequency and percentage and were analysed utilizing the Chi-square test or Fisher's exact test when appropriate. Pearson or Spearman coefficient correlation (r) was used to estimate the degree of correlation between two variables. P value < 0.05 was considered statistically significant.

Results

1. The present study was a double - blind randomized controlled clinical trial, carried out to evaluate the effect of vitamin D3 supplementation on insulin resistance, and visceral fat thickness in vitamin D3 deficient women with polycystic ovarian syndrome.
2. The study was conducted on 60 patients with polycystic ovary syndrome who presented at the Department of Obstetrics and Gynecology, Tanta University Hospital.

Table 1: Age and baseline body measurements in the study & placebo group:

Before treatment	Study group (N= 30)	Control group (N= 30)	95% CI	P
Age (years)	24.80±4.180	25.07±3.600	-2.3, 1.7	0.792
Height (cm)	160.30 4.886	162.00±4.892	-4.2, 0.8	0.183
Weight (kg)	69.77±7.079	72.17±7.235	-6.1, 1.3	0.199
BMI (kg/m^2)	27.12 ± 2.079	27.46 ± 2.033	-1.4, 0.7	0.521
Waist Circumference (cm)	86.87 ± 10.673	81.93 ± 11.776	-0.9, 10.7	0.094
Hip Circumference (cm)	95.77 ± 8.795	96.93 ± 9.381	-5.9, 3.5	0.621

Waist/Hip Ratio	0.91 ± 0.130	0.85 ± 0.120	0.0, 0.1	0.056
Visceral fat layer thickness by ultrasound (mm)	79.68 ± 5.770	80.68 ± 5.020	-3.8, 1.8	0.477

Data is expressed as mean and standard deviation. 95% CI: 95% confidence interval of the mean difference between both groups. P is significant when < 0.05.

Table (1) shows that the mean age of the intervention group was (24.80±4.180), while that of the placebo group was (5.07±3.6). Prior to initiating the intervention, the mean BMI of the participants did not vary significantly between the intervention group and the placebo (27.12±2.079, 27.46±2.033 respectively), also there was no statistically significant difference was found when comparing the mean waist circumference, and the mean waist/hip ratio (86.87±10.673 versus 81.93±11.776,and 0.91±0.130 versus 0.85±0.120 respectively) among the intervention group and the placebo.

Moreover, there was no statistically significant difference was found when comparing the mean hip circumference and the mean visceral fat layer thickness among intervention group and the placebo group before treatment.

Table 2: Vital signs assessment before treatment in the study & placebo groups:

Before treatment	Study group (N= 30)	Control group (N= 30)	95% CI	P
Pulse	79.67±8.888	81.97±7.453	-6.5, 1.9	0.282
Temperature	37.04±0.152	37.10±0.175	-0.1, 0.0	0.213
SBP	119.17±10.346	122.33±8.683	-8.1, 1.8	0.204
DBP	84.50±10.533	89.17±11.225	-10.3, 1.0	0.102

Data is expressed as mean and standard deviation. 95% CI: 95% confidence interval of the mean difference between both groups. P is significant when < 0.05.

Table (2) demonstrates that the mean of the vital signs assessed before the beginning of the intervention did not vary significantly across both groups.

Table 3: Glucose tolerance profile before treatment in the study & placebo group:

Before treatment	Study group (N= 30)	Control group (N= 30)	95% CI	P
FBS (mg/dl)	90.97±8.092	89.87±8.492	-5.4, 3.2	0.610
PPBG (mg/dl)	122.73±25.046	125.10±15.415	-8.4,13.1	0.661
Fasting insulin (µLU/mL)	16.90±4.886	16.98±3.432	-2.1, 2.3	0.942
HOMA-IR	3.80±1.747	3.77±1.151	-0.8, 0.7	0.938

Data is expressed as mean and standard deviation. 95% CI: 95% confidence interval of the mean difference between both groups. P is significant when < 0.05.

Table (3) illustrates the glucose tolerance profile of the participants that was assessed before treatment There was no a statistically significance difference between the mean parameters of the two groups.

Table 4: Hormone level assessment before treatment in the study & placebo group:

Before treatment	Study group (N= 30)	Control group (N= 30)	95% CI	P
TSH (µU/mL)	3.66±1.697	3.51±1.803	-0.7, 1.1	0.732
25-hydroxy-vitamin D 25(OH)D (ng/dl)	13.26±7.203	11.24±7.289	-1.7, 5.8	0.285
FSH (mIU/mL)	5.40±2.896	6.20±3.084	-0.65, 2.5	0.248
LH (mIU/mL)	11.76±6.181	12.46±5.776	-2.4,3.8	0.652
Prolactin (ng/ml)	10.53±1.965	11.09±1.579	-1.5, 0.4	0.223
E2 (pg/mL)	49.50±3.173	50.79±3.569	-0.46,3.04	0.144
Testosterone (ng/dl)	56.53±17.075	49.86±16.208	-1.9, 15.3	0.126
DHEAS (µg/dL)	274.45±92.800	289.06±110.478	-67.3, 38.1	0.581

Data is expressed as mean and standard deviation. 95% CI: 95% confidence interval of the mean difference between both groups. P is significant when < 0.05.

Table (4) Regarding the mean hormone levels assessed before initiation of the treatment. There was no statistically significant found across both groups.

Table 5: Body measurements after treatment in the study & placebo group:

After treatment	Study group (n= 30)	Control group (n= 30)	95% CI	P
Weight (kg)	69.37±7.467	72.40±7.290	- 6.85, 0.78	0.117
BMI (kg/m2)	26.96±2.219	27.55±2.067	-1.7, 0.52	0.289
Waist Circumference (cm)	86.50±10.779	82.17±11.821	-1.5, 10.2	0.143
Hip Circumference (cm)	95.30±9.056	97.17±9.403	-6.64, 2.9	0.437
Waist/Hip Ratio	0.91±0.129	0.86±0.125	-0.01, 0.12	0.085
Visceral fat layer thickness by ultrasound (mm)	60.07±7.418	80.87±4.911	-24.1,-17.5	<0.001

Data is expressed as mean and standard deviation. 95% CI: 95% confidence interval of the mean difference between both groups. P is significant when < 0.05.

Table (5) illustrates the body measurements assessed after treatment. No statistically significant difference was observed regarding any of the parameters except for the visceral fat layer thickness that was assessed by ultrasound (p = <0.001), where the mean measure among the intervention group was (60.07±7.418), compared to (80.87± 4.911) across the placebo group.

Table 6: Glucose tolerance profile after treatment in the study & placebo group:

After treatment	Study group (n= 30)	Control group (n= 30)	95% CI	P
FBS (mg/dl)	79.60±9.464	89.67±9.181	5.3,14.9	0.001*
Fasting insulin (µLU/mL)	15.23±4.869	16.20±3.662	-1.3, 3.2	0.387
HOMA-IR	2.99±0.621	3.59±1.179	0.11,1.09	0.017*

Data is expressed as mean and standard deviation. 95% CI: 95% confidence interval of the mean difference between both groups. P is significant when < 0.05.

Table (6) demonstrates the difference in the glucose tolerance profile after treatment. There was a statistically significant difference between both groups regarding the mean fasting blood sugar levels (p =0.001), where the mean FBS in the intervention group was (79.60±9.464), while that of the placebo group was (89.67±9.181).

Moreover, the HOMA-IR level varied significantly (p=0.017), where in the intervention group the mean level was (2.99±0.621), compared to a mean of (3.59±1.179) in the placebo group.

Table 7: Hormone level comparison before and after treatment in the study group:

Study group (N= 30)	Before treatment	After treatment	95% CI	P
TSH (µU/mL)	3.66±1.697	3.66±1.687	0.0, 0.0	0.932
25- hydroxy- vitamin D 25(OH)D (ng/dl)	13.26±7.203	26.76±15.531	- 16.8, - 10.2	< 0.001
FSH (mIU/mL)	5.40±2.896	5.74±2.845	-1.14,1.8	0.648
LH (mIU/mL)	11.76±6.181	10.54±6.273	-4.39,1.99	0.451
Prolactin (ng/ml)	10.53±1.965	10.64±2.026	-0.26, 0.04	0.150
E2 (pg/mL)	49.50±3.173	48.99±3.698	-2.3, 1.3	0.569
Testosterone (ng/dl)	56.53±17.075	56.81±17.070	-0.93, 0.38	0.400
DHEAS (µg/dL)	274.45±92.800	273.86±93.302	-3.17, 4.33	0.753

Data is expressed as mean and standard deviation. 95% CI: 95% confidence interval of the mean difference between both groups. P is significant when < 0.05.

Table (7) shows that none of the mean hormonal levels varied significantly among the intervention group from before to after treatment, except for the mean 25- hydroxy-vitamin D level (p= <0.001), which increased from (13.26±7.203) before treatment, to (26.76±15.531) after treatment.

Discussion

Polycystic ovary syndrome (PCOS) is a most common cause of ovarian dysfunction in women of reproductive age, with a prevalence of 2.2–26% between countries, depending on the population studied and the diagnostic criteria applied [13].

A series of studies have demonstrated that vitamin D deficiency (VDD) is common in patients with PCOS and that VDD may be associated with metabolic and endocrine disorders in PCOS [14]. Compared with the general population, the prevalence of VDD is relatively higher in PCOS patients. Vitamin D is a steroid hormone that is involved in the balance of calcium phosphate and bone mineralization [15]. Vitamin D receptors are expressed at 2,776 genomic positions and modulate the expression of 229 genes in more than 30 different tissues, including the pancreas, liver, immune cells, brain and ovaries. As a result, vitamin D supplementation for PCOS therapy has attracted attention [16].

A number of studies have demonstrated associations between vitamin D levels and various PCOS symptoms, including insulin resistance, infertility and hirsutism. Vitamin D is thought to influence the development of PCOS through gene transcription, and hormonal modulation influences insulin metabolism and fertility regulation [17].

Evidence suggests that Vitamin D levels are similar in women with and without PCOS; however, there have been reports of lower levels and higher levels seen in women with PCOS. Several studies have reported low levels of vitamin D in women with PCOS, with average 25-hydroxy vitamin D (25OHD) levels between 11 and 31 ng/ml, with the majority having values 20 ng/ml (67–85%) [18].

The aim of this study was to evaluate the effect of vitamin D3 supplementation on insulin resistance, and visceral fat thickness in vitamin D3 deficient women with polycystic ovarian syndrome.

This was a double-blind randomized controlled clinical trial it was conducted at Department of Obstetrics and Gynecology, Tanta University Hospital on a 60 women with polycystic ovary syndrome; Patients were be allocated randomly into 2 groups: Group I: 30 women received 50.000 lu of oral vitamin D3 (Cholecalciferol) once weekly for (12) weeks and Group II (placebo group); 30 women received placebo capsules once weekly for (12) weeks.

Our finding showed that vitamin D supplementation for 12 weeks among PCOS women and vitamin D deficiency led to a significant reduction in fasting glucose level, Insulin resistance HOMA-IR-A significant decrease in visceral fat thickness by US and a significant increase serum vitamin D level. Although vitamin D supplementation compared to the placebo group no significant difference in waist circumference (WC), waist/Hip Ratio and BMI but the differences in change from baseline were not significant between two groups.

Regarding the intervention group, the mean age was 24.80 (± 4.180) and their mean baseline body measurements was 27.12 (± 2.079) for BMI, 0.91 (± 0.130) for Waist/Hip Ratio, and 79.68 (± 5.770) for the Visceral fat layer thickness assessed by ultrasound.

As for the placebo group, the mean age was 25.07 (± 3.600) and their mean baseline body measurements was 27.46 (± 2.033) for BMI, 0.85 (± 0.120) for Waist/Hip Ratio, and 80.68±5.020 for

the Visceral fat layer thickness assessed by ultrasound.

Our study highlighted that the intervention and the placebo groups did not differ from each other regarding the baseline body measurements, a finding that was consistent with what Rad *et al*. (2014) [19] and Asemi *et al*. (2015), [20] reported in their studies.

In the study of Gröber *et al*. [21] it is recommended vitamin D supplementation with daily doses of 400–2000 IU of vitamin D to maintain blood levels of 25(OH)D > 30 ng/mL according to the Endocrine Society guidelines in view of the common occurrence of vitamin D insufficiency. The dose of vitamin D in obese adults would be 2–3 times greater to assure blood levels of 25 (OH)D > 30 ng/mL due to vitamin D absorption from large body fat stores.

Another study of Rashidi *et al*. [22] which aimed to investigate the effects of vitamin D on metabolic disorders in women with PCOS and vitamin D deficiency, and reported that In vitamin D group, serum levels of 25 (OH) D increased.

Regarding the baseline hormonal level assessment, our study recruited females with serum 25 – hydroxy-vitamin D level less than 20 ng/ml, since Merzon *et al*. (2020) [23] mentioned that this is the cut off point for vitamin D deficiency. This was the cut-off point adapted by the previous studies as well Asemi *et al*. (2015) [24], Seyyed *et al*. (2018) [25].

In comparison with our study the study of Gupta *et al*. (26) reported that the majority of the subjects were vitamin D deficient at the baseline. In the study 92% of the enrolled PCOS patients were found to have vitamin D level less than 30 ng/ml. Thirty-four patients (68%) were vitamin D deficient (≤20 ng/ml) out of which 10 patients (29%) were severely deficient (<10 ng/ml). Twelve patients were vitamin D insufficient (24%) (20–30 ng/ml), showing high prevalence of vitamin D deficiency in the PCOS women.

Our study assessed the glucose tolerance profile prior to the initiation of the treatment and found that there was no statistically significant difference between the intervention and the placebo group.

These findings were similar to previous studies that reported minor difference between their intervention and placebo groups regarding the baseline measurements of the fasting glucose, insulin and HOMA-IR levels [27].

Regarding the glucose tolerance profile in our study after treatment, there was statistically significant difference between the intervention and placebo groups (p =0.001). where the mean FBS in the intervention group was (79.60±9.464), while that of the placebo group was (89.67±9.181)**.** As for the HOMA-IR level, the intervention group the mean level was (2.99±0.621), compared to a mean of (3.59±1.179) in the placebo group. On the other hand, the mean levels of the fasting insulin did not vary significantly across groups (p=0.387).

In comparison with our study a systematic review of, Wehr *et al*. [28] found that a significant increase in Vitamin D3 level of women in the Monthly group was 5.00±12.00 before treatment and 16.00±17.00 after treatment and a significant decrease in fasting glucose levels and no significant effects on insulin resistance factors after supplementation with 20,000 IU/w vitamin D for 24 weeks in PCOS women with obesity.

After treatment, our study found that there was statistically significant difference between the intervention and placebo group regarding the Visceral fat layer thickness (p= <0.001), where the mean measure among the intervention group was 60.07 (± 7.418), compared to 80.87 (± 4.911) across the placebo group and no change in the baseline body measures from before to after the treatment in the intervention group.

Moreover, Asemi *et al*. (2015) [29] highlighted in their study that the waist and Hip circumferences were significantly decreased after the end of the intervention. This contradiction could be due to subjective errors between both studies.

Conclusions

In conclusion, Vitamin D supplementation in an oral dose of 50.000 IU of vitamin D3 (Cholecalciferol) once weekly for (12) weeks among women with PCOS significantly increased serum 25OHD levels, and significantly decrease insulin resistance and visceral fat thickness no potential effect was detected on BMI, waist circumference (WC)and waist to hip Ratio.

Acknowledgements

Nil

Declarations Funding

There is no funding

Conflict of interest

Nil

Ethical approval

The study was approved from the ethics committee of Faculty of Medicine, Tanta University.

References

1. McCartney CR, Marshall JC. Clinical practice. Polycystic ovary syndrome. N Engl J Med. 2016;375:54-64.
2. Bachelot A. Polycystic ovarian syndrome: Clinical and biological diagnosis. Ann Biol Clin. 2016;74(6):661-667.
3. Sirmans SM, Pate KA. Epidemiology, diagnosis, and management of polycystic ovary syndrome. Clin Epidemiol. 2013;6:1-13.
4. Macut D, Bjekić-Macut J, Rahelić D, *et al*. Insulin and the polycystic ovary syndrome. Diabetes Res Clin Pract. 2017;130:163-170.
5. Dunaif A, Finegood DT. Beta-cell dysfunction independent of obesity and glucose intolerance in the polycystic ovary syndrome. J Clin Endocrinol Metab. 1996;81:942-947.
6. Barthelmess EK, Naz RK. Polycystic ovary syndrome: current status and future perspective. Front Biosci. 2014;6(1):104-119.
7. Carmina E, Oberfield SE, Lobo RA. The diagnosis of polycystic ovary syndrome in adolescents. Am J Obstet Gynecol. 2010;203:201e1.
8. Toscani M, Migliavacca R, de Castro JA, *et al*. Estimation of truncal adiposity using waist circumference or the sum of trunk skinfolds: a pilot study for insulin resistance screening in hirsute patients with or without poly cystic ovary syndrome. Metabolism. 2007;56:992-997.
9. Wiltgen D, Spritzer PM. Variation in metabolic and cardiovascular risk in women with different polycystic ovary syndrome phenotypes. Fertil Steril. 2010;94:2493-2496.
10. Pasquali R, Patton L, Gamblneri A. Obesity and infertility. Curr Opin Endocrinol Diabetes Obes. 2007;14:482-487.
11. Barber T, Franks S. Adipocyte biology in polycystic ovary syndrome. Mol Cell Endocrinol. 2013;373:68-76.
12. Corbould A. Chronic testosterone treatment induces selective insulin resistance in subcutaneous adipocytes of women. J Endocrinol. 2007;192:585-594.
13. Bacopoulou F, Kolias E, Efthymiou V, *et al*. Vitamin D predictors in polycystic ovary syndrome: a meta-analysis. Eur J Clin Invest. 2017;47(10):746-755.
14. Patra SK, Nasrat H, Goswami B, *et al*. Vitamin D as a predictor of insulin resistance in polycystic ovarian syndrome. Diabetes Metab Syndr. 2012;6:146-149.
15. He C, Lin Z, Robb SW, *et al*. Serum vitamin D levels and

polycystic ovary syndrome: a systematic review and meta-analysis. Nutrients. 2015;7:4555-4577.
16. Grundmann M, von Versen-Hoynck F. Vitamin D-roles in women's reproductive health? Reprod Biol Endocrinol. 2011;9:146.
17. Earthman CP, Beckman LM, Masodkar K, *et al*. The link between obesity and low circulating 25-hydroxyvitamin D concentrations: considerations and implications. Int J Obes. 2012;36(3):387-396.
18. Caron-Jobin M, Morisset AS, Tremblay A, *et al*. Elevated serum 25 (OH) D concentrations, vitamin D, and calcium intakes are associated with reduced adipocyte size in women. Obesity. 2011;19:1335-1341.
19. McGowan MP. Polycystic ovary syndrome: a common endocrine disorder and risk factor for vascular disease. Curr Treat Options Cardiovasc Med. 2011;13(4):289-301.
20. Ünlütürk U, Sezgin E, Yildiz BO. Evolutionary determinants of polycystic ovary syndrome: part 1. Fertil Steril. 2016;106(1):33-41.
21. Williams T, Mortada R, Porter S. Diagnosis and Treatment of Polycystic Ovary Syndrome. Am Fam Physician. 2016;94(2):106-113
22. Xavier LB, Sóter MO, Sales MF, *et al*. Evaluation of PCSK9 levels and its genetic polymorphisms in women with polycystic ovary syndrome. Gene. 2018;644:129-136.
23. Glintborg D, Andersen M. Management of Endocrine Disease: Morbidity in polycystic ovary syndrome. Eur J Endocrinol. 2017;176(2):R53-R65.
24. Chahal SK, Goyal P, Sodhi RK. Multiple Molecular Pathways Unfolding the Pathophysiology of Polycystic Ovary Syndrome. Ann Romanian Soc Cell Biol. 2021;25:3746-3765.
25. Carvalho LML, Ferreira CN, Sóter MO, *et al*. Microparticles: Inflammatory and haemostatic biomarkers in Polycystic Ovary Syndrome. Mol Cell Endocrinol. 2017;443:155-162.
26. Carvalho LML, Dos Reis FM, Candido AL, *et al*. Polycystic Ovary Syndrome as a systemic disease with multiple molecular pathways: a narrative review. Endocr Regul. 2018;52(4):208-221.
27. Azziz R, Carmina E, Chen Z, *et al*. Polycystic ovary syndrome. Nat Rev Dis Primers. 2016;2(1):18.
28. Morgante G, Cappelli V, Di Sabatino A, *et al*. Polycystic ovary syndrome (PCOS) and hyperandrogenism: the role of a new natural association. Minerva Ginecol. 2015;67(5):457-463.
29. Reddy TV, Govatati S, Deenadayal M, *et al*. Polymorphisms in the TFAM and PGC1-α genes and their association with polycystic ovary syndrome among South Indian women. Gene. 2018;641:129-136.

How to Cite This Article
Eldin SMRS, El Bohoty SB, Hamiesa MFM, Mahfouz AE. The effect of vitamin D3 supplementation in vitamin D3 deficient women with polycystic ovarian syndrome and it's relation to insulin resistance and visceral fat thickness. International Journal of Clinical Obstetrics and Gynaecology. 2023;7(1):82-87.