

Vit D3 (25 hydroxylated vitamin D) deficiency in cases of polycystic ovary syndrome in high school girls

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Abstract: Background: polycystic ovary syndrome (pcos) is a common endocrine disorder in women of reproductive age. Patients and methods. The present study is a prospective interventional study including one hundred and fifty women (90) of them complaining of some symptoms of PCO (irregular menstruation, acne, hirsutism (in the department of Obstetrics and Gynecology of EL-Mahalla General Hospital and in the period between June 2017 and December 2017. Results: This show that there were highly significance difference between included groups as regard menstrual cycle before and after ttt in group 2 with p value (0.000) and significant difference in group 3 with p value (0.016) and non significant difference in group 1 with p value (0.063). This table show highly significant difference between studied groups before and after ttt in group 1,2 with p value (0.001), (0.000) respectively and non significant difference in group 3 with p value (0.80) as regard FSH hormonal assay. This table show that there was a highly significant difference between included group as regard LH hormonal assay before and after ttt in group 2 with p value (0.000) and non significant difference in group 1,3 with p value (0.23), (0.34) respectively. This table show change in serum calcium before and after ttt which was highly significant difference between studied girls in group 2,3 with p value (0.000). This table show show change in serum vit d before and after ttt which was highly significant in group 2,3 with p value (0.000) and non significant in group 1 with p value (0.15). Discussion: There was change in hormonal profile due to drug intervention such as: FSH after ttt with p value (0.001, 0.000, 0.80) in group 1,2,3 respectively. it was highly significant in group 1,2 and non significant in group 3; LH highly significant in group 2 with p value (0.000) and non significant in group 1,3 with p value (0.23, 0.34) respectively. Conclusion This study showed the positive effects of calcium & vitamin D supplementation on (pco morphology in u/s), menstrual regularity (hormonal study), and improvement of acne and hirsutism in girls with PCOS (in group 2). Improvement of ca serum level and vit d (in group 2,3). Vitamin D deficiency was recompensed in 67% (group 2, 3) of the PCOS patients who had taken calcium & vitamin D supplementation. Most of patients diagnosed by PCO had vitamin d deficiency. [Asmaa Fath Elbab Abdel Halim, Hanaa Farouk Ahmed and Mai Ali Abdelaziz Elgheity. **Vit D3 (25 hydroxylated vitamin D) deficiency in cases of polycystic ovary syndrome in high school girls.** *Nat Sci* 2018;16(11):197-202]. ISSN 1545-0740 (print); ISSN 2375-7167 (online). <http://www.sciencepub.net/nature>. 26. doi:[10.7537/marsnj161118.26](https://doi.org/10.7537/marsnj161118.26).

Keywords: Vit D3; hydroxylated vitamin D; deficiency; case; polycystic ovary syndrome; high school; girl**1. Introduction**

Polycystic ovary syndrome (PCOS) is a common endocrine disorder in women of reproductive age, The prevalence of PCOS varies according to diagnostic criteria which include:

Rotterdam criteria:

- Clinical and/or biochemical hyperandrogenism.
- Oligo/amenorrhea.
- Anovulation.
- Polycystic ovaries appearance on ultrasound.

(March et al., 2010).

PCOS is multifactorial disease, and the individual susceptibility is probably determined by multiple genetic and environmental risk factors. It is primarily characterized by ovulatory dysfunction and hyperandrogenism, but the clinical presentation is heterogeneous and patients may present some of various signs and symptoms which presented by:

- Hirsutism, acne, alopecia.

- Irregular menstrual cycles, oligomenorrhea, amenorrhea.
- Ovulatory dysfunction and infertility.
- Increased risk of T2 diabetes, dyslipidemia, hypertension.

Exclusion of other androgen excess disorders: Cushing syndrome, androgen secreting tumors, hyperprolactinemia, thyroid disease, drug-induced androgen excess and other causes of anovulation.

The normal level of vit D is (20-50) ng/ml. Vit D deficiency in women with pcos having serum concentration <20 ng/ml (*Jin Ju Kim, 2010*).

There is increasing evidence that vitamin D affects insulin and glucose metabolism, and a low vitamin D status is suspected to be a risk factor for impaired glucose tolerance, insulin resistance and T2DM.

It has been suggested that the combination of vit D deficiency and dietary calcium insufficiency (because serum calcium regulates PTH release) may

be largely responsible for the menstrual abnormalities associated with PCOS.

Aim of the work

1- To find the Relation between vitamin D deficiency in high school girls with polycystic ovary syndrome (PCOS).

2- To evaluate the role of vitamin D supplementation in improving some of clinical manifestation of PCOS (irregular menstruation, acne, hirsutism).

3- To compare the role of metformin and vit D3 in improving some symptoms of PCO.

2. Patients and Methods

The present study is a prospective interventional study including one hundred and fifty women (90) of them complaining of some symptoms of PCO (irregular menstruation, acne, hirsutism (in the department of Obstetrics and Gynecology of EL-Mahalla General Hospital and in the period between June 2017 and December 2017.

The Inclusion criteria were

1. High school girls (16 – 20) years old.
2. Patients diagnosed as PCOS (lab & u/s).
3. Patients presented with irregular menstruation.
4. Patients presented with other PCOS symptoms (hirsutism, cane).

The exclusion criteria were:

1. No history liver or kidney disease.
2. No history vit D supplementation in last 3 months.

3. No compined oral contraceptives supplementation.

4. No lipid lowering agents supplementation.

5. No insulin sensitizing agents supplementation.

The patients will be classified into 3 groups:

After counselling every patients about the nature of study and the regimen of ttt:

- Written and verbal consent were obtained from the patient before starting the study.

- The ethical committee clearance was obtained from Al-Azher University.

TTT of patients subdivided into 3 groups:

- Group 1 (metformin 1500 mg/day).
- Group 2 (vit d 400 iu/day +ca 1000 mg/day).
- Group 3 (vit d 400 iu/day +ca 1000 mg/day +metformin 1500 mg/day).

- In clinical trial investigating the effects of Vit D, Calcium and Metformin (vit d 400 iu/ day +ca 1000 mg/day +metformin 1500 mg/day) in regulating menstrual cycles, treatment of acne and hirsutism were evaluated for 3 months and follow up for another 3 months.

- Patients also received laser ttt for hirsutism and acne.

- 1ry outcome (improving serum level of vit d and ca).

- 2ry outcome (regular menstruation, ttt of acne and hirsutism).

- Outcome depends on type of ttt.

3. Results

Table (1): Change in menstrual cycle due to drug intervention:

Groups Before	Group I N=29		group II N=34		group III N=27	
	regular	irregular	regular	irregular	regular	irregular
regular	23	1	11	21	20	7
irregular	0	5	0	2	0	0
Test of significance	McNemar test= 0.063		McNemar test=0.000*		McNemar test=0.016*	

N.B: * < 0.05 was significant

This table shows that there were highly significance difference between included groups as regard menstrual cycle before and after ttt in group 2

with p value (0.000) and significant difference in group 3 with p value (0.016) and non significant difference in group 1 with p value (0.063).

Table (2): Skin manifestation of the studied groups before drug intervention:

Medical history	Group I N=29 No. (%)	Group II N=34 No. (%)	Group III N=27 No. (%)	Test of significance	p- value
Skin manifestation:					
No symptoms	12 (41.4)	5 (14.7)	5 (18.5)	X ² = 21	0.02*
Acne only	11 (37.9)	6 (17.6)	12 (44.4)		
Acne +hirsutism	0 (0.0)	4 (11.7)	0 (0.0)		
Hirsutism only	7 (24.13)	18 (52.9)	10 (37.03)		

N.B: * P value < 0.05 was significant

All skin manifestation were improved after drug intervention and laser among the studied groups.

This table show highly significance between the studied groups as regard skin manifestation before and after ttt with p value (0.02).

Table (3): Ultrasound picture of the studied groups before drug intervention:

Groups	Group I N=29 No (%)	group II N=34 No (%)	group III N=27 No (%)	Test of significance	p- value
U/S:					
• Typical PCO criteria	11 (37.9)	5 (14.7)	16 (59.3)	X ² =13.1	0.001*
• PCO criteria	18 (62.1)	29 (85.3)	11 (40.7)		

N.B: * P value < 0.05 was significant

This table show highly significant difference between studied groups wit p value (0.001).

Table (4): Change in FSH assay due to drug intervention:

Groups	Group I N=29	group II N=34	group III N=27	Test of significance	P value
FSH: (Mean ± SD)					
Before	18.04 ± 11.2	30.1 ± 8.3	12.8 ± 7.4	F=29.4	0.000*
After	11.9 ± 6.2	8.9 ± 2.7	10.8 ± 6.03	F=2.72	0.068
FSH:	t**=3.65	t=14.5	t=1.82		
Before-After	P value= 0.001*	P value= 0.000*	P value=0.80		

N.B: * P value < 0.05 was significant

This table show highly significant difference between studied groups before and after ttt in group 1,2 with p value (0.001), (0.000) respectively and non

significant difference in group 3 with p value (0.80) as regard FSH hormonal assay.

Table (5): Change in LH due to drug intervention:

Groups	Group I N=29	group II N=34	group III N=27	Test of significance	P value
LH: (Mean ± SD)					
Before	12.2 ± 9.3	30.02 ± 8.7	9.5 ± 6.2	F=57.5	0.000*
After	8.2 ± 4.5	7.8 ± 2.9	7.6 ± 3.9	F=0.15	0.86
LH:	t=2.41	t=15.85	t=2.24		
Before-After	P value=0.23	P value= 0.000*	P value=0.34		

N.B: * P value < 0.05 was significant

This table show that there was a highly significant difference between included group as regard LH hormonal assay before and after ttt in group 2 with p value (0.000) and non significant difference in group 1,3 with p value (0.23), (0.34) respectively.

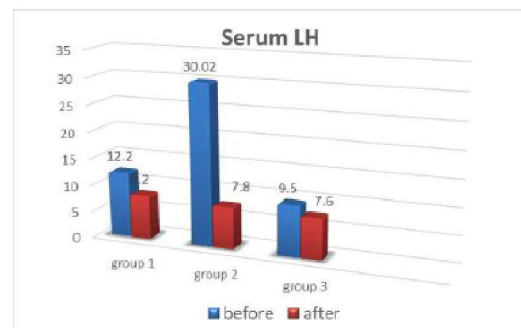


Figure (1): Difference in mean of serum LH assay among the studied groups.

Table (6): Change in prolactin assay before and after drug intervention:

Groups	Group I N=29	Group II N=34	Group III N=27	Test of significance	P value
Hormonal profile					
Prolactin: (Mean ± SD)					
Before	17.2±9.5	20.01±12.9	17.8±8.5	F=0.61	0.55
After	17.7±9.1	19.3±12.4	17.8±8.5	F=0.39	0.67
Prolactin:	t=0.38	t=1.69	t=1.0		
Before- After	P value=0.71	P value=0.100	P value=0.33		

N.B: * P value < 0.05 was significant

This table show change in hormonal assay prolactin with no significant difference between all studied girls with p value (0.71), (0.100), (0.33) in group 1,2,3 respectively.

Table (7): Change in Calcium due to drug intervention:

Groups	Group I N=29	Group II N=34	Group III N=27	Test of Significance	P value
Lab. profile					
Calcium: (Mean ± SD)					
Before	7.9 ±2.03	6.9 ± 2.4	7.6 ±2.8	F=1.6	0.212
After	8.3±1.7	10.8 ± 1.2	11.9 ± 1.9	F=36.1	0.000*
Calcium:	t=1.53	t=9.6	t=11.12		
Before-After	P value=0.14	P value= 0.000*	P value= 0.000*		

N.B: * P value < 0.05 was significant

This table show change in serum calcium before and after ttt which was highly significant difference between studied girls in group 2,3 with p value (0.000).

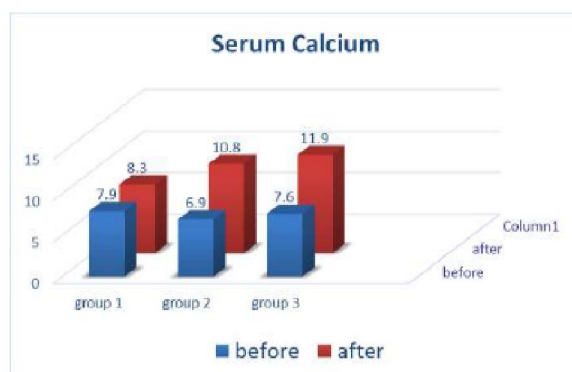


Fig (2): Difference in mean of serum calcium assay among the studied groups.

Table (8): Change in vitamin D due to drug intervention:

Groups	Group I N=29	Group II N=34	Group III N=27	Test of significance	P value
Lab. Profile					
Vitamin D: (Mean ± SD)					
Before	18.3±6.9	6.2±5.7	16.9 ± 8.5	F=0.71	0.49
After	19.8 ±6.4	34 ±5.1	35.9 ±6.6	F=63.8	0.000*
Vitamin D:	t=1.49	t=20.11	t=12.87		
Before- After	P value=0.15	P value= 0.000*	P value= 0.000*		

N.B: * P value < 0.05 was significant

This table show show change in serum vit d before and after ttt which was highly significant in group 2,3 with p value (0.000) and non significant in group 1 with p value (0.15).

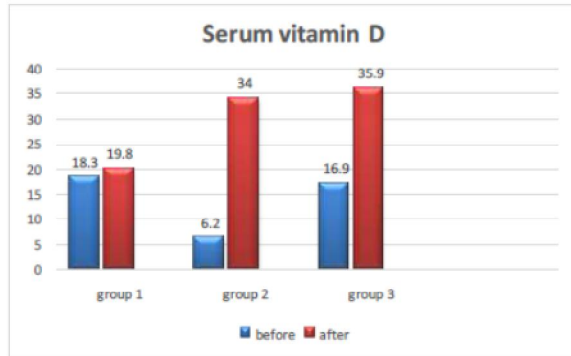


Fig. (3): Difference in mean of serum vitamin D assay among the studied groups

4. Discussion

Regarding to distribution of treatment in our study screening for pco was done in 150 girls, 90 of them (60%) diagnosed as pco group1 (32.2%) received ttt in the form of (metformin) only, group 2 (37.8%) received ttt in the form of (metformin +calcium +vit d), group 3 (30%) received ttt in the form of (calcium and vit d).

In our study the three groups were similar for demographic and biometric parameters as height with P value (0.44), weight with P value (0.65) and BMI with P value (0.44) which not statistically significant among all groups in our study as shown in table (3).

Also the mean maternal age and age of menarche in our study were (18.2±1.5 yr), (13.1± 1.3yr) respectively with no significant difference between studied groups with P value (0.17), (0.41) respectively as shown in (table 1,3).

In the present study there is no significant difference between studied groups as regard age, age of menarche, weight, height, BMI with p value (0.17, 0.41, 0.65, 0.44, 0.44) respectively (table 3).

In current study we reported a highly significance between studied groups as regard HB (gm/dl) and urea (mg/dl) with p value (0.001) for both and significant difference regarding RBCs count (million cell/cmm) with p value (0.02) on the other hand there is no significant difference regarding creatinine (mg/dl), SGPT (u/l), urine analysis with p value (0.37, 0.44, 0.27) respectively (table 4).

Regarding the menstrual cycle changes before and after drug intervention we found that there was a highly significance difference in group 2 (the number of girls who had irregular cycle decreased from 23 to 2 with p value (0.000) (67.64%) in group 3 (the number of girls who had an irregular cycle decreased

from 7 to 0) there was significance difference with p value (0.016) and (25,9%), there were non significance difference of studied girls in group 1 with p value (0.063) (20.7%) Table 5.

This is in agreement with the study of *Raziah deghani Firouzabadia, Abbas Aflatooniana et al. (2012)* results who demonstrated that A better improvement was gained in regulating menstrual abnormalities 70%, in group 2 (metformin 1500+ca 1000+vit d 100000 iu/month for 6 months), also Vitamin D deficiency was recompensed in 74% of the PCOS patients who had taken calcium & vitamin D supplementation.

While in the study had been done by *Wehr, Pieber & Obermayer-Pietsche (2011)* Interventional studies have furthered this link. In one such intervention, women with PCOS were treated with a dose corresponding to just under 3, 000 IU of vitamin D per day for 6 months. By the 3-month mark, 30% of the women who had previously reported irregular cycles, noted improvements in menstrual frequency, and this agree with our study but differ in dose of vit d and by the 6-month mark, 50% of the women had reported such improvements (*Lips, 2010*).

In addition, triglyceride levels and fasting and post-challenge glucose levels were found to significantly improve by the end of the study (*Lips, 2010*), offering a potential mechanism for the improvement in menstrual regularity.

Another interventional study was conducted with overweight and obese women with vitamin D deficiency and PCOS (*Mazloomi et al., 2012*).

Also the study of *FangFang a nKeNi b, et al. (2016)* Vitamin D supplementation had significant effect on the improvement of menstrual cycles were also observed when metformin plus vitamin D was compared with metformin alone (95%).

In our study as regard to skin manifestation of PCO (acne, hirsutism) there is asignificant difference before and after drug intervention with p value (0.02) this not agree with study performed by (*Parviz Toossi, Zahra Azizian et al., 2015*).

Furthermore, there were no significant differences in serum concentrations of 25 (OH) D among patients with mild, moderate and severe/very severe acne (P value=0.29).

But coincided with The study demonstrated that supplementation with 4000 IU/day of vitamin D for 12 weeks to PCOS women resulted in significant decreases serum total testosterone levels, hirsutism (, *Fatemeh Foroozanfard, et al. 2017*).

Patients in our study had been treated by laser intervention beside drugs. Metformin 2 treatment of women with PCOS results in a decline of free bioavailable Testosterone, leading to significant improvement of clinical manifestations of

hyperandrogenism (acne and hirsutism) metformin used in ttt of group 1 & 2.

In the current study we found that there was highly significance in U/S (PCO morphology) between studied groups before and after treatment with p vaue (0.001) this coincided with the study of **Fang Fang a nKeNi b, et al. (2016)** Vitamin D supplementation had significant effect on the improvement of PCO morphology, (U/S) **(95%)**.

Additional high-quality RCTs are required to confirm the effectiveness of vitamin D on PCOS.

There was change in hormonal profile due to drug intervention such as:

1. **FSH** after ttt with p value (0.001, 0.000, 0.80) in group 1,2,3 respectively. it was highly significant in group 1,2 and non significant in group 3.

2. **LH** highly significant in group 2 with p value (0.000) and non significant in group 1,3 with p value (0.23, 0.34) respectively.

3. **Prolactin** was non significant in all studied groups with p value (0.71, 0.100, 0.33) respectively.

These results dis agree with the results of study concluded that as all PCOs subjects had hypovitaminosis D, Serum samples were used for determination of 25 (OH) D, calcium, follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin (PRL), There was no relationship with the severity of hypovitaminosis D and the presence of acne, hirsutism, polycystic ovaries and central obesity. Based on Pearson's test, no significant correlations were found between 25 (OH) free testosterone, FSH, LH, TSH and prolactin.

In European Journal of Endocrinology (Krul-Poel, Snackey et al. 2013)

A systemic search of electronic database was carried out up to January 2013 for observational studies and clinical trials in women suffering from pcos with outcome measures that were related to vitamin d status. this study suggest an inverse association between vit d status and metabolic disturbances of pco:

- **Calcium** in the current study was highly significant in group 2,3 with p value (0.000, 0.000) and non-significant in group 1 with p value (0.14).

- **Vitamin D** also in our study showed that was highly significane in group 2,3 with p value (0.000, 0.000) respectively and non-significant in group 1 with p value (0.15).

Vitamin d and calcium supplementation improve serum level of vit d and calcium.

Conclusion

This study showed the positive effects of calcium & vitamin D supplementation on (pco morphology in u/s), menstrual regularity (hormonal study), and impeovement of acne and hirsutism in girls with PCOS (in group 2). Improvement of ca serum level and vit d (in group 2,3).

Vitamin D deficiency was recompensed in 67% (group 2,3) of the PCOS patients who had taken calcium & vitamin D supplementation.

Most of patients diagnosed by PCO had vitamin d deficiency.

Recommendation

Routine screening of all aldoscents for serum vitamin d especially in girls who diagnosed as PCO and give vit d supplementation by drugs and sun exposure.

Further researches should be done.

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