Effects of Vitamin D Deficiency in Polycystic Ovarian Syndrome

Rand Jalal Abd Al-Ghanny¹, Mohanned Mohmmed Bakir Al-Moosawi²*, Baydaa Ahmed Abd³

¹Ministry of Higher Education and Scientific Research, Baghdad, Iraq
²Central Public Health Laboratory, Ministry of Health, Baghdad, Iraq
³The National Diabetes Center / Al Mustansiriya University, Baghdad, Iraq

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Abstract

Polycystic ovary syndrome is a very common cause of female infertility. This study aims to assess the prevalence of vitamin D deficiency and its association with clinical and anthropometric characteristics of Iraqi women with and without polycystic ovary syndrome. Fifty eightwomen with the disease and their matched control group were included. Their blood pressure was measured. Serum level of 25 hydroxy vitamin D of <20 ng/mL was graded as vitamin D deficiency. The polycystic ovary syndrome group had significantly lower levels of 25 hydroxy vitamin D, higher body mass index, and higher waist to hip ratio in contrast to the control group. The difference in body mass index was more significant in the obese category. Within subjects with the waist to hip ratio of ≥0.85, who were all vitamin D deficient, vitamin D was significantly lower and waist to hip ratio was significantly higher in patients than in controls. Vitamin D levels were significantly lower in patients than in controls in the non-hypertensive category. Further studies are needed to investigate the role of vitamin D in the pathogenesis of polycystic ovary syndrome.

Keywords: Polycystic Ovary Syndrome, Vitamin D, Body Mass Index, Waist-to-Hip-Ratio, Blood pressure.
Tetik al-mabiais, masa'dathia akhter ba'dikam man (28) il-jrgok di Vitamin (D), wa-jeex khawla jama'da al-ama, wa-nubbat amma khawla ma'muwa al-ama.

Himmalat Vitamin (D) akhter ba'dikam man (28) il-jrgok di Vitamin (D), wa-blhshkh la al-khawla jama'da al-ama.

Dhakhalu la ilal re'ah. Kanta masa'dathia Vitamin (D) akhter ba'dikam man (28) il-jrgok di Vitamin (D), Vitamin (D) akhter ba'dikam man (28) il-jrgok di Vitamin (D), la ilal re'ah. Kanta masa'dathia Vitamin (D) akhter ba'dikam man (28) il-jrgok di Vitamin (D), la al-khawla jama'da al-ama.

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1. Introduction

Polycystic ovary syndrome (PCOS) is one of the commonest causes of female infertility. Clinical features caused by high levels of androgens, oligomenorrhea, and polycystic ovarian morphology are necessary for diagnosis [1]. There is a dynamic relationship between activities of hypothalamic-pituitary-adrenal (adrenal/and or ovarian axis) and metabolic diseases such as obesity, with involvement of compensatory hyperinsulinaemia and insulin resistance [2, 3]. PCOS raises the risks of dyslipidaemia, hypertension, and hyperglycaemia [4], thus raising the risk of developing cardiovascular diseases [5]. Vitamin D deficiency is noticed in numerous countries [6]. In vitamin D deficiency, the emergence of many diseases can be caused by defect in the metabolism of calcium and the building up of pro-inflammatory cytokines. It has been reported to lead to the development of cancer, diabetes, atherosclerosis and hypertension [7, 8]. Despite this, there is no agreement on the differences in serum vitamin D levels among women having and not having PCOS. Many studies reported that vitamin D of patients with PCOS was inversely correlated with metabolic disturbances [9-22]. Increased risk of PCOS or its associated endocrine/metabolic disturbances were linked with polymorphism of vitamin D receptor gene, which presents the effect of vitamin D in PCOS pathogenesis [12, 13, 16].

The aim of this study is to assess the prevalence of vitamin D deficiency and its association with clinical and anthropometric characteristics of Iraqi women with and without polycystic ovary syndrome.

2. Materials and Methods

Across-sectionalcomparative analytical study design was applied on two unpaired groups. This study was conducted in the Central public health laboratory/Ministry of Health, Baghdad, Iraq, from July 2017 to October 2017. PCOS was diagnosed by using the 2003 Rotterdam criteria. According to these criteria, diagnosis requires the presence of at least two of the following three findings: hyperandrogenism, ovulatory dysfunction, and polycystic ovaries [23]. Fifty-eight female patients aged 18-45 years, single and married were included in this study. They had been diagnosed with PCOS at Al-Elwieya Educational Hospital and Kamal Al-Samarrai Hospital for fertility and infertility. They have never been diagnosed with any endocrine disorder (diabetes mellitus, hyperprolactinemia, Cushing syndrome), virilizing tumors, renal, or liver diseases, and never taken calcium or vitamin D supplements. Fifty-eight adult females without PCOS were enrolled as controls, matched with the patients based on age and BMI with the matching ratio between the two groups having the value of one. An oral consent has been taken from all participants.

Standard conditions were used for blood pressure measurement. It was found that the best method for evaluating vitamin D status is by measuring 25-hydroxy vitamin D level [24]. Serum concentration of 25-hydroxy vitamin D [25-(OH) D] was measured using mini VIDAS immunoassay analyzer by the Enzyme-Linked Fluorescent technique (ELFA) using VIDAS25 OH VITAMIN D TOTAL (VITD) kit (BIOMERIEUX, France). Vitamin D levels were considered sufficient when 25-(OH) D concentration was ≥ 30 ng/mL, insufficient when the concentration was 20-29 ng/mL, and deficient when the concentration was < 20 ng/mL [26, 27].
3. Results and Discussion

Table 1 illustrates that vitamin D deficiency was spotted in 93.1% of patients and 75.86% of controls, while 6.9% of patients and 24.14% of controls had insufficient vitamin D. No one of the subjects in both patients and controls had a sufficient level of vitamin D (≥30 ng/mL).

Table 1-General characteristics of PCOS patients and controls

| Characteristics          | Group     |
|--------------------------|-----------|
|                          | PCOS      | Control   |
|                          | N   | %     | N   | %     |
| Age                      |       |       |     |       |
| ≤ 20                     | 10  | 17.4% | 2   | 3.4%  |
| 21-30                    | 14  | 24.1% | 18  | 31%   |
| 31-40                    | 24  | 41.3% | 20  | 34.6% |
| ≥ 41                     | 10  | 17.2% | 18  | 31%   |
| Marital status           |       |       |
| Married                  | 38  | 65.5% | 40  | 68.9% |
| Unmarried                | 20  | 34.5% | 18  | 31.1% |
| BMI                      |       |       |
| Under weight             | 0   | 0%    | 2   | 3.4%  |
| Normal weight            | 10  | 17.2% | 20  | 34.5% |
| Over weight              | 14  | 24.2% | 16  | 27.6% |
| Obese                    | 34  | 58.6% | 20  | 34.5% |
| WHR                      |       |       |
| < 0.85                   | 16  | 27.5% | 26  | 44.8% |
| ≥ 0.85                   | 42  | 72.5% | 32  | 55.2% |
| Vitamin D levels         |       |       |
| Deficiency               | 54  | 93.1% | 44  | 75.86%|
| Insufficiency            | 4   | 6.9%  | 14  | 24.14%|
| Sufficiency              | 0   | 0%    | 0   | 0%    |
| Blood pressure status    |       |       |
| Hypertension             | 4   | 6.89% | 6   | 10.34%|
| Normal                   | 54  | 93.10%| 52  | 89.66%|

This study focused on vitamin D status in terms of the estimation of its deficiency in the two groups and its correlation with BMI, WHR, and HTN. We found a highly significant difference in vitamin D levels between PCOS women and controls (Tables 2 and 3). The same highly significant correlation between PCOS patients and controls was also found in BMI and
WHR. PCOS patients and controls did not show a significant difference in blood pressure (Table 2).

**Table 2-**Physical and biochemical parameters of PCOS patients and controls

| Parameters                          | Group                                | P-Value  |
|-------------------------------------|--------------------------------------|----------|
|                                     | PCOS (N= 58) Mean ± SD               | Control (N=58) Mean ± SD |
| BMI                                 | 31.5 ± 6.8                           | 27.4 ± 5.7   |
| WHR                                 | 0.87 ± 0.06                          | 0.84 ± 0.05  |
| Vitamin D levels (ng/mL)            | 10.2 ± 4.01                          | 13.3 ± 6.3   |
| Systolic blood pressure (mmHg)      | 117.6 ± 12.3                         | 116.5 ± 13.8 |
| Diastolic blood pressure (mmHg)     | 76.5 ± 10.01                         | 75.8 ± 11.4  |

*=N.S. - **=H.S.

We found a significant correlation in the BMI value between PCOS patients and controls of the normal weight group. The correlation becomes highly significant in the obese category, which indicates the potential relationship between obesity and PCOS (Table 3). The same highly significant correlation was noticed in WHR between PCOS patients and controls in the ≥0.85 category (Table 3).

**Table 3-**Distribution of vitamin D levels, BMI, and WHR in PCOS patients and controls.

| Characteristics | Group                  | PCOS | Control | P.Value  |
|-----------------|------------------------|------|---------|----------|
|                 | N | M ± SD | N | M ± SD |
| Vit. D levels (ng/mL) | | | | |
| Deficiency      | 54| 10.6 ± 3.9 | 44| 13.1 ± 6.3 | < 0.001*** |
| Insufficiency   | 4 | 22.1 ± 1.5 | 14| 22.8 ± 1.1 | > 0.05* |
| Sufficiency     | 0 | 0 | 0 | 0 | |
| BMI             | | | | |
| Under weight    | 0 | 0 | 2 | 27.13 ± 5.9 | 0 |
| Normal weight   | 10 | 21.1 ± 1.3 | 20 | 22.2 ± 1.5 | = 0.05** |
| Over weight     | 14 | 27.6 ± 1.9 | 16 | 26.8 ± 1.5 | > 0.05* |
| Obese           | 34 | 36.1 ± 3.9 | 20 | 34 ± 2.9 | < 0.001** |
| WHR             | | | | |
| < 0.85          | 16 | 0.79 ± 0.04 | 26 | 0.79 ± 0.02 | > 0.05* |
| ≥ 0.85          | 42 | 0.91 ± 0.04 | 32 | 0.88 ± 0.02 | < 0.001*** |

*=N.S. - **=S. - ***=H.S.
Previous researches reported that vitamin D in PCOS patients had a mean value of <20 ng/mL [26-27, 35]. In this study, vitamin D in PCOS group had a mean of lower than 20 ng/mL (10.2±4.4 ng/mL) (Table 2) and the deficiency state (<20 ng/mL) was observed in 93.1% of patients (Table 1). Previous studies recorded a prevalence of vitamin D deficiency in the general populations of 10% to 60% of adults [28, 29]. As illustrated in Table 1, the control group in our study also had a vitamin D deficiency of 75.86%, with a mean level of 13.3±6.3 ng/mL (Table 2). Wehr et al. reported that vitamin D level was lower in comparison with controls in a study of 545 women with PCOS [13].

Another study reported that PCOS women have significantly higher vitamin D concentrations in contrast to controls with similar BMI and age [10]. Thus, we can assume that vitamin D deficiency is predominant in both groups, regardless of the inconsistency in literatures concerning the fact that vitamin D levels were different between women with PCOS and control subjects.

The high prevalence of vitamin D in the current study can be caused by more than one factor. Vitamin D synthesis in the skin is one of the main sources of the vitamin. Women staying most of the day at indoor places, those putting sun-screen lotion on their skin to prevent the harmful effect of sunrays, especially during summer season, and those with certain wearing styles are susceptible to vitamin D deficiency [30-37]. Moreover, dietary habits of Iraqi people who consume poor vitamin D-containing food must be kept in mind as a further cause [36].

Actually, we observed the insufficiency in vitamin D in 6.89% of patients and 24.13% of controls (Table 1). These findings strengthen the above possibility of the presence of many factors other than PCOS that may play important roles in affecting vitamin D status in our studied group.

Several researches reported inverse correlations between many obesity measures (e.g. body fat, BMI, and waist circumference) and vitamin D levels in PCOS women and matched controls [11, 15, 21]. Li et al. showed an inverse correlation between BMI and the 25(OH)D levels, in which 72% of PCOS subjects had vitamin D deficiency and 44% had severe deficiency (<25 ng/mL) [18]. Wehr et al. observed the same association in a sample of 206 PCOS patients, among which 72% had vitamin D deficiency. An inverse relationship between 25(OH) D levels and BMI was also recorded in another study [19]. Sidabutar et al. recorded an inverse association of 25(OH) D with both BMI and WHR. In PCOS women group, they found that not all incidents of the deficiency of vitamin D are associated with PCOS because its levels were still normal in nine patients, but five patients had insufficiency and nine had deficiency [20].

This study presented a highly significant variation in serum vitamin D level within the WHR≥0.85 category between PCOS and matched controls (Table 4). Nonetheless, no significant correlation was found between normal, overweight, and obese groups with serum vitamin D level in patients and matched controls (Table 4).

The correlation between serum 25-OH vitamin D levels and the percent of body fat is stronger when compared to its correlation with body weight or BMI. Athletes and well-trained people may still have relatively high BMI and may be considered overweight or even obese despite the quite low total fat mass. This indicates that it is adiposity, not simply body mass that influences the serum level of 25-OH vitamin D [31]. These causes could contribute to the finding of our study. In addition to that, scientists found that, independent of BMI, women with PCOS have a higher prevalence of upper-body obesity, as demonstrated by increased waist circumference and waist-hip ratio, as compared to BMI-matched control women; a finding that strengthen the role of adiposity measured by WHR in PCOS [32].
Table 4-Distribution of the vitamin D levels in PCOS patients and controls based on BMI and WHR

| Characteristics | Vit. D levels (ng/mL) | Value |
|-----------------|-----------------------|-------|
|                 | PCOS | Control |       |
|                 | N | Mean ± SD | N | Mean ±SD |       |
| WHR             |     |           |     |           |       |
| < 0.85          | 16 | 11.6 ±6.3 | 26 | 16 ± 6.8 | <0.05 **|
| ≥ 0.85          | 42 | 9.7 ± 2.5 | 32 | 11.2 ± 5.0 | < 0.001 ***|
| BMI             |     |           |     |           |       |
| Under weight    | 0  | 0        | 2  | 21.2 ± 0.1 | -     |
| Normal weight   | 10 | 10.6 ± 5.3 | 20 | 15.4 ± 7.6 | > 0.05* |
| Over weight     | 14 | 10.6 ± 5.5 | 16 | 12.4 ± 5.9 | > 0.05* |
| Obese           | 34 | 10.06 ± 2.70 | 20 | 11.23 ± 4.24 | > 0.05* |
| Blood pressure status | |       |     |           |       |
| Hypertension(mmHg) | 4 | 11.1± 3.1 | 6  | 9.1± 1.4 | > 0.05* |
| Normal(mmHg)    | 54 | 10.16 ± 4.1 | 52 | 13.8 ± 6.5 | < 0.001 ***|

* = N.S.  ** = S.  *** = H.S.

At the time that PCOS patients within the WHR ≥ 0.85 category were found only in vitamin D deficient category, PCOS patients within the WHR < 0.85 category, along with controls in both WHR categories, were found in both insufficient and deficient vitamin D categories (Table 5). Similarly, the obese group in BMI classification lied also in the vitamin D deficient category only, unlike the other BMI categories (Table 5).

Higher WHR and BMI are associated with obesity. The above findings could be explained by the fact that obesity is associated with high prevalence of vitamin D deficiency. Causes may be attributed to volumetric dilution into the greater volumes of fat, serum, liver, and muscle, despite that the complete exclusion of other mechanisms is not possible, as they may contribute concurrently. On the other hand, low vitamin D could not yet be excluded as a cause of obesity [33].

Our results point out the role of vitamin D in the pathogenesis of PCOS. Vitamin D by itself can be a cause of PCOS. Evidences verify that vitamin D plays an essential role in reproductive activities and that the reproductive system, including ovaries, the endometrium, and the placenta, has receptors for vitamin D. Also, it has been found that calcium dysregulation, a condition related to vitamin D deficiency, is responsible for the increase in the follicular arrest and results in menstrual and fertility disorders in women with PCOS [22]. The PCOS group in our study had a significantly lower vitamin D concentration than the control group.

Only 6.89% of PCOS patients and 10.34% of controls in our study had HTN (Table 1) and they lied in the vitamin D deficient category only (Table 5).

Zhang and his colleagues suggested that the risk of hypertension increased substantially below 75 nmol/L as 25(OH) D decreased [34]. Kota et al. found that inadequacy of vitamin D causes an increase in systolic and diastolic blood pressure, proposing that vitamin D
deficiency is associated with renin-angiotensin-aldosterone system regulation [35]. This could explain why only the vitamin D deficient category has hypertension. Vitamin D concentrations were significantly lower in PCOS patients than in controls in the non-hypertensive blood pressure category, while this significant correlation was not present in the hypertensive category (Table 4).

The numbers of PCOS patients and controls in the non-hypertensive category (54 and 52, respectively) were remarkably higher than those numbers in the hypertensive category (4 and 6, respectively). This confers more statistical power in detecting significant differences and could explain the above finding.

**Table 5**-Vitamin D status in PCOS patients and controls ased on BMI, WHR and blood pressure

| Characteristics | PCOS | Control |
|-----------------|------|---------|
|                 | Vit. D levels (ng/mL) |           |
|                 | Insufficiency | Deficiency | Insufficiency | Deficiency |
|                 | N | M±SD | N | M±SD | N | M±SD | N | M±SD |
| BMI             |   |      |   |      |   |      |   |      |
| Under weight    | 0 | 0 | 0 | 0 | 2 | 21.2±0.1 | 0 | 0 |
| Normal weight   | 2 | 20.8±0.1 | 8 | 8.1±0.1 | 10 | 22.8±0.8 | 10 | 8±0.2 |
| Overweight      | 2 | 23.4±0.1 | 12 | 8.5±1.2 | 2 | 24.4±0.1 | 14 | 10.7±3.9 |
| Obese           | 0 | 0 | 34 | 9.9±2.7 | 0 | 0 | 20 | 11.2±4.2 |
| WHR             |   |      |   |      |   |      |   |      |
| < 0.85          | 4 | 22.10±1.50 | 12 | 8.25±0.2 | 12 | 22.58±1.00 | 14 | 10.4±4.05 |
| ≥ 0.85          | 0 | 0 | 42 | 9.70±2.5 | 2 | 24.42±0.02 | 30 | 10.29±3.70 |
| Blood Pressure  |   |      |   |      |   |      |   |      |
| (mmHg)          |   |      |   |      |   |      |   |      |
| Hypertensive    | 0 | 0 | 4 | 11.1±3.1 | 0 | 0 | 6 | 9.1±1.4 |
| Normal          | 4 | 22.1±1.5 | 50 | 9.2±2.3 | 14 | 22.8±1.1 | 38 | 10.5±3.9 |

This study records no significant difference in blood pressure between PCOS and control groups in all BMI, WHR, vitamin D, and blood pressure categories (Table 6). As we noticed earlier, our study showed variable findings in the studied groups regarding blood pressure status (Table 1). In addition, both systolic and diastolic blood pressure values did not differ significantly between PCOS and controls (Table 2). These findings make it unlikely to find significant differences in blood pressure between the two groups when studied based on other different parameters. Furthermore although we adjusted for BMI and WHR when we compared the blood pressure between the two groups (Table 6), scientists noted that even in the studies which did adjust the analyses for BMI, either statistically or by study design involving matching control women by BMI, the association between hypertension and PCOS was not always clear [30]. This could explain the variable findings regarding blood pressure in our study.
### Table 6: Association of systolic and diastolic blood pressure in patients and control group based on different parameters

| Characteristics          | Blood pressure (mmHg) | Systolic BP | Diastolic BP |
|--------------------------|-----------------------|-------------|--------------|
|                          | Patients      | Control    | P.value | Patients      | Control    | P.value |
|                          | N  | M ±SD | N  | M±SD | N  | M±SD | N  | M±SD |
| **BMI**                  |               |            |         |         |         |         |         |         |
| Under weight             | 0  | -    | 2  | 116.3±13.8 | -  | 0    | 0  | -    |
| Normal weight            | 12 | 117.9±12.4 | 2 | 116.4±14.2 | >0.05* | 1 | 67.3±22.6 | 2   | 66.3±21.3 | >0.05* |
| Over weight              | 16 | 118.5±12.7 | 1 | 118.3±12.3 | >0.05* | 1 | 66.3±23.8 | 1   | 67.5±20.5 | >0.05* |
| Obese                    | 30 | 117.7±12.4 | 2 | 116.6±13.9 | >0.05* | 3 | 67.5±22.5 | 2   | 66.5±21.5 | >0.05* |
| **WHR**                  |               |            |         |         |         |         |         |         |
| < 0.85                   | 16 | 118.5±12.5 | 2 | 116.5±12.9 | >0.05* | 1   | 66.2±22.3 | 2   | 71.5±6.6 | >0.05* |
| ≥ 0.85                   | 42 | 117.7±12.4 | 3 | 116.7±13.8 | >0.05* | 4   | 68.1±0.06 | 3   | 62.5±26.6 | >0.05* |
| **Vit. D levels (ng/mL)**|           |            |         |         |         |         |         |         |
| Deficiency               | 54 | 117.8±12.7 | 4 | 120.0±12.9 | >0.05* | 5 | 67.7±10.3 | 4   | 78.2±11.7 | >0.05* |
| Insufficiency            | 4  | 115.0±5.8  | 1 | 105.7±10.9 | >0.05* | 4   | 75.0±5.8  | 1   | 68.6±6.6 | >0.05* |
| Sufficiency              | 0  | 0      | 0  | 0      | -     | 0   | 0      | 0    | 0     | -     |
| **Blood Pressure (mmHg)**|               |            |         |         |         |         |         |         |
| Hypertensive             | 4  | 150.0±11.5 | 6 | 140.0±0.0 | >0.05* | 4 | 100.0±8.2 | 6   | 100.0±6.3 | >0.05* |
| Normal                   | 54 | 115.2±8.4  | 5 | 113.8±11.9 | >0.05* | 5 | 74.8±7.9  | 5   | 73.1±8.3 | >0.05* |

* N.S.

### 4. Conclusions

Vitamin D concentration was significantly lower in the PCOS group than in the control group. Further research is needed for studying the role of vitamin D in the pathogenesis of this disease.

### References

[1] Goodarzi MO, Dumesic DA, Chazenbalk G, Azziz R, "Polycystic ovary syndrome: etiology, pathogenesis and diagnosis,"Nat Rev Endocrinol, vol. 7, no. 4, pp.219-231, 2011. Available: [http://dx.doi.org/10.1038/nrendo.2010.217](http://dx.doi.org/10.1038/nrendo.2010.217).

[2] Sahin FK, Sahin SB, Balik G, Ural UM, Tekin YB, Cure MC, et al, "Does low pentraxin-3 levels associate with polycystic ovary syndrome and obesity?,"Int J ClinExp Med, vol. 7, no. 10, pp. 3512-3519, 2014.

[3] FigenKirSahin, et al, "Nesfatin-1 and Vitamin D levels may be associated with systolic and diastolic blood pressure values and hearth rate in polycystic ovary syndrome,"Bosnian Journal of Basic Medical Sciences, vol. 15, no. 3, pp. 57-63, 2015.
[4] Wild RA, Carmina E, Diamanti-Kandarakis E, Dokras A, Escobar-Morreale HF, et al, "Assessment of cardiovascular risk and prevention of cardiovascular disease in women with the polycystic ovary syndrome: a consensus statement by the Androgen Excess and Polycystic Ovary Syndrome (AE-PCOS) Society," J Clin Endocrinol Metab, vol. 95, no. 5, pp. 2038-2049, 2010. Available: http://dx.doi.org/10.1210/jc.2009-2724.

[5] Diamanti-Kandarakis E, Dunaif A, "Insulin resistance and the polycystic ovary syndrome revisited: an update on mechanisms and implications," Endocr Rev, vol. 33, no. 6, pp. 981-1030, 2012. Available: http://dx.doi.org/10.1210/er.2011-1034. http://dx.doi.org/10.1210/er.2011-1034.

[6] Kirbas A, Kirbas S, Anlar O, AK, Cure MC, Efe H, "Investigation of the relationship between vitamin D and bone mineral density in newly diagnosed multiple sclerosis," Acta Neurol Belg, vo. 113, no. 1, pp. 43-47, 2013. Available: http://dx.doi.org/10.1007/s13760-012-0123-0.

[7] Cumhur Cure M, Cure E, Yuce S, Yazici T, Karakoyun I, Efe H, "Mean platelet volume and vitamin D level," Ann Lab Med, vol. 34, no. 2, pp. 98-103, 2014. Available: http://dx.doi.org/10.3343/alm.2014.34.2.98.

[8] Luo C, Wong J, Brown M, Hooper M, Molyneaux L, Yue DK, "Hypovitaminosis D in Chinese type 2 diabetes: lack of impact on clinical metabolic status and biomarkers of cellular inflammation," Diab Vasc Dis Res, vol. 6, no. 3, pp. 194-199, 2009. Available: http://dx.doi.org/10.1177/1479164109337974.

[9] Kozakowski J, Kapucinska R, Zgliczynski W, "Associations of vitamin D concentration with metabolic and hormonal indices in women with polycystic ovary syndrome presenting abdominal and gynoidal type of obesity," Ginekol Pol, vol. 85, no. 10, pp. 765-770, 2014.

[10] Mahmoudi T, Gourabi H, Ashrafi M, Yazdi RS, Ezabadi Z, "Calcitropic hormones, insulin resistance, and the polycystic ovary syndrome," Fertil Steril, vol. 93, no. 4, pp. 1208-1214, 2010.

[11] Li HW, Brereton RE, Anderson RA, Wallace AM, Ho CK, "Vitamin D deficiency is common and associated with metabolic risk factors in patients with polycystic ovary syndrome," Metabolism, vol. 60, no. 10, pp. 1475-1481, 2011.

[12] Ranjzad F, Mahban A, Shemirani AI, Mahmoudi T, Vahedi M, Nikzamir A, et al. Influence of gene variants related to calcium homeostasis on biochemical parameters of women with polycystic ovary syndrome. J Assist Reprod Genet, vol. 28, no. 3, pp. 225-232, 2011.

[13] Wehr E, Trummer O, Giuliani A, Gruber HJ, Pieber TR, Obermayer-Pietsch B, "Vitamin D-associated polymorphisms are related to insulin resistance and vitamin D deficiency in polycystic ovary syndrome," Eur J Endocrinol, vol. 164, no. 5, pp. 741-749, 2011.

[14] Mazloomi S, Sharifi F, Hajhosseini R, Kalantari S, Mazloomzadeh S, "Association between Hypoadiponectinemia and Low Serum Concentrations of Calcium and Vitamin D in Women with Polycystic Ovary Syndrome," ISRN Endocrinol, vol. 2012, ID. 949427, 2012.

[15] Muscogiuri G, Policola C, Priorella A, Sorice G, Mezza T, Lassandro A, et al, "Low levels of 25(OH)D and insulin-resistance: 2 unrelated features or a cause-effect in PCOS?," Clin Nutr, vol. 31, no. 4, pp. 476-480, 2012.

[16] El-Shal AS, Shalaby SM, Aly NM, Rashad NM, Abdelaziz AM, "Genetic variation in the vitamin D receptor gene and vitamin D serum levels in Egyptian women with polycystic ovary syndrome," Mol Biol Rep, vol. 40, no. 11, pp. 6063-6073, 2013.

[17] Krul-Poel YH, Snackey C, Louwers Y, Lips P, Lambalk CB, Laven JS, et al, "The role of vitamin D in metabolic disturbances in polycystic ovary syndrome: a systematic review," Eur J Endocrinol, vol. 169, no. 6, 853-865, 2013.

[18] R. L. Thomson, S. Spedding, and J. D. Buckley, "Vitamin D in the aetiology and management of polycystic ovary syndrome," Clinical Endocrinology, 77, no. 3, 343–350, (2012).

[19] E. Wehr, S. Pilz, N. Schweighofer, A. Giuliani, D. Kopera, T. R. Pieber, and B. Obermayer-Pietsch, "Association of hypovitaminosis D with metabolic disturbances in polycystic ovary syndrome, European Journal of Endocrinology, vol. 161, no. 4, pp. 575–582, 2009.

[20] E. Sidjabutar, B. Halim, M. F. GanissiSiregar, D. Lutan, I. Adenin, and Y. Kaban, "Vitamin D Levels in Women with Polycystic Ovary Syndrome," in ASPIRE Conference Proceedings, The 6th Congress of the Asia Pacific Initiative on Reproduction, KnE Medicine, vol. 2016, pp. 125-132, 2016. DOI 10.18502/kme.v11i.547(2016)

[21] Rostand SG, "Vitamin D, blood pressure, and African Americans: toward a unifying hypothesis," Clin J Am Soc Nephrol, vol. 5, no. 9, pp. 1697–1703, 2010.
[22] Maryam Eftekhar, Elham Sadat Mirhashemi, Behnaz Molaei, Soheila Pourmasumi, "Is there any association between vitamin D levels and polycystic ovary syndrome (PCOS) phenotypes?, "Arch Endocrinol Metab, vol. 64, no 1., pp. 11-16, 2020.

[23] Tracy Williams, Rami Mortada, Samuel Porter, "Diagnosis and Treatment of Polycystic Ovary Syndrome," American Family Physician, vol. 49, no. 2, pp. 106-113, 2016.

[24] Israa Salim Musa, Entsar Jabbar Saheb, Rasha Hussain Kuba, "Toxoplasmosis and Its Potential Role to Change the Levels of C - reactive protein and Vitamin D3 in Atherosclerosis Patients" Iraqi Journal of Science, vol. 62, no. 6, pp. 1787-1792, 2021.

[25] Biomerieux SA, "VIDAS® 25 OH Vitamin D TOTAL (VITD) [package insert]," 376 Chemin de l'Orme 69280 Marcy-l'Etoile - France, part no. 9304004D, 2015.

[26] Thys-Jacobs S, Donovan D, Papadopoulos A, Sarrel P, Bilezikian JP, "Vitamin D and calcium dysregulation in the polycystic ovarian syndrome," Steroids, vol. 64, no. 6, pp. 430-435, 1999.

[27] Kotsa K, Yavropoulou MP, Anastasiou O, Yovos JG, "Role of vitamin D treatment in glucose metabolism in polycystic ovary syndrome," Fertil Steril, vol. 92, no. 3, pp. 1053-1058, 2009.

[28] Wehr E, Pieber TR, Obermayer-Pietsch B, "Effect of vitamin D3 treatment on glucose metabolism and menstrual frequency in polycystic ovary syndrome women: a pilot study," J Endocrinol Invest, vol. 34, no. 10, pp. 757-763, 2011.

[29] Jin Ju Kim, Young Min Choi, Soo Jin Chae, Kyyu Ri Hwang, Sang Ho Yoon, Min Jeong Kim, Sun Mie Kim, Seung Yup Ku, Seok Hyun Kim, Jung Gu Kim, "Vitamin D deficiency in women with polycystic ovary syndrome," Clin Exp Reprod Med, vol. 41, no. 2, pp. 80-85, 2014.

[30] Rhonda Bentley-Lewis, Ellen Seely, Andrea Dunaif, "Ovarian Hypertension: Polycystic ovary syndrome," Endocrinol Metabol Clin North Am, vol. 40, no. 2, pp. 433–x, 2011.

[31] Ode JJ, Pivarnik JM, Reeves MJ and Knous JL, "Body mass index as a predictor of percent fat in college athletes and non athletes, "Med Sci Sports Exer, vol. 39, no 3, , pp. 403-409, 2007.

[32] Susan Sam, MD, "Obesity and polycystic ovary syndrome, "Obes Manag, vol. 3, no 2, , pp. 69-73, 2007.

[33] Luka Vranic, Ivana Nikolasevic and Sandra Milic, "Vitamin D Deficiency: Consequence or Cause of obesity?," Medicina, vol. 55, no 9, , pp. 541, 2019.

[34] Dongdong Zhang, Cheng Cheng, Yan Wang, Hualei Sun, et al., "Effect of Vitamin D on Blood Pressure and Hypertension in the General Population: An Update Meta-Analysis of Cohort Studies and Randomized Controlled Trials, "Centers for Disease Control and Prevention, vol. 17, E03, 2020.

[35] Sunil Kumar Kota, Siva Krishna Kota, Sruti Jammula, Lalit Kumar Meher, et al., "Renin–angiotensin system activity in vitamin D deficient, obese individuals with hypertension: An urban Indian study, "Indian J Endocrinol Metab, vol. 15, no 4, pp. 395-401, 2011.

[36] Mohammed Mohammed B Al-Moosawi, Rana Faisal Hammadi, Iman Midhat Abbas, Bushra J A, A A Abdullah, "The proportion of vitamin D deficiency in reproductive age group women in Baghdad/Iraq, and its association with menstrual cycle characteristics and anthropometric measurements, "International Journal of Scientific & Engineering Research, vol. 10, no 1, pp. 406-414, 2019.

[37] Rosol J. Mohammed, Lina A. Salih "The Correlation between Maternal Vitamin D and Interleukin-17 Levels and Fetal Biophysical Profile, "Iraqi Journal of Science, vol. 62, no 6, pp. 1836-1842, 2021.