Association between vitamin D levels and menstrual irregularities in reproductive age women

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Abstract

Background: Vitamin D was found to be linked with many derangements in the human body. Its association with menstrual irregularities has been significantly reported.

Objective: Evaluation of the association between vitamin D deficiency and menstrual irregularities.

Study design: This cross-sectional study was conducted from March 2023–August 2023 at the outpatient clinic
of a tertiary hospital. We recruited women presented with menstrual irregularities according to predetermined inclusion and exclusion criteria. A control group of women with regular cycles was included. Vitamin D level was evaluated in both groups.

Results: This study recruited 104 women (52 participants per group). Vitamin D deficiency was noted in 46/104 participants (44.2%). Women with menstrual irregularities were younger than those with regular cycles (p-value 0.0001). The menstrual cycle length differed significantly between both groups (p-value 0.0001). Vitamin D level was significantly lower in the study group than in the control group (20.0 ± 11.9 and 28.7 ± 16.6, respectively, p-value 0.003). Younger age was a significant predictor for irregular cycles (p-value 0.005).

Conclusion: Vitamin D deficiency was noted significantly among women with irregular cycles. Age was a significant predictor for irregular cycles rather than vitamin D levels.

Keywords: Irregular cycles; Reproductive age; Vitamin D.

Introduction

The menstrual cycle is a physiological sign of women's well-being (1). The cycle length differs from one woman to another, with a reported range from 18-35 days (2). At least one menstrual problem occurs in 64% of females. These problems might include menstrual irregularities, heavy menstrual bleeding, or oligomenorrhea (3). Evidence has shown that metabolic mechanisms may disrupt menstrual irregularity (4). Multiple metabolic mechanisms depend on vitamin D as an essential factor (5). Vitamin D affects reproductive hormone regularity and the menstrual cycle (6). It has been reported that vitamin D receptors were found in the reproductive organs (ovaries, endometrium, uterus, and placenta) (7). It was found that anti-mullerian hormone receptors included a domain for the vitamin D response element, which allows vitamin D to affect ovarian function (8). Accordingly, vitamin D deficiency was associated with a wide range of reproductive problems (9), particularly menstrual cycle irregularity and length (10). Other reported associations with vitamin D deficiency included endometriosis (11), polycystic ovary syndrome (12), uterine fibroids (13), and infertility (14). Another evidence reported an association between vitamin D deficiency and the severity of premenstrual symptoms (15). Also, it has been reported that estradiol levels are affected by fluctuations in vitamin D levels (1). Accordingly, this study evaluated the association between vitamin D levels and menstrual irregularities among Egyptian women.

Methods

This cross-sectional study was conducted at the outpatient clinics of obstetrics and gynecology at a tertiary hospital from March 2023 to August 2023. The study recruited women according to predetermined inclusion and exclusion criteria. The inclusion criteria were a) women aged 18-40 years, b) women presenting with any menstrual complaint as follows:

- Oligomenorrhea: defined as a menstrual cycle length > 45 days (16)
- Heavy menstrual bleeding is defined as excessive menstrual blood loss interfering with women's physical, social, emotional, and quality of life (17).
- A bleeding/spotting episode is defined as one or more consecutive days during which blood loss has been reported (18)
- Polymenorrhea: defined as intervals of up to 21 days (19).

The exclusion criteria included a) women taking vitamin D supplementation, b) women refusing to participate in the study, c) women taking hormonal contraceptive methods, d) women with a known cause of menstrual
irregularities such as thyroid disorders, hyperprolactinemia, polycystic ovary syndrome, or ovarian tumors. A control group of women presenting to the outpatient clinic without any menstrual-related complaints was recruited. They had to be non-pregnant and not take any hormonal contraceptive methods to be eligible for the study.

Eligible women were subjected to history taking and examination, including (age, weight, height, BMI, occupation, and education). They were asked to report the following:

- number of bleeding/spotting episodes
- cycle length in days
- number of menstrual bleeding days
- the presence or absence of dysmenorrhea.

Bleeding was evaluated using a bleeding diary that was given to each participant. Women were instructed to mark ○ for spotting and ● bleeding days. The usual menstrual bleeding was marked as /. Women were instructed to use standard disposable pads and to report the number of pads each day.

A blood sample was collected to measure serum Vitamin D after recruitment. Vitamin D was measured by ELISA (20). Results were interpreted as sufficiency (30–100 ng/mL), insufficiency (21–29 ng/mL), and deficiency (< 20 ng/mL) (21).

The sample size was calculated at a significance level of 99% and an error level of 10% using a difference in mean vitamin D level in women with irregular cycles (14.56 ng/ml) (22) and the mean vitamin D level in women with regular cycles (21.9 ng/ml) (22). The estimate of the pooled standard deviation of vitamin D was 8.76 ng/ml. So, by calculation, the minimum sample size required is 44 patients per group.

**Ethical approval:** This study was conducted after the approval of the research ethics committee on 21/3/2023 with a number of 5205#.

**Statistical Analysis**

Data was statistically described in terms of mean and standard deviation, frequencies (number of cases), and percentages when appropriate. P values less than 0.05 were considered statistically significant. All statistical calculations were done using the computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) release 22 for Microsoft Windows. The chi-square test was used for categorical variables, and the (t) test was used for continuous variables with normally distributed data. Non-normally distributed data were tested using Fisher's exact for categorical variables, and Mann-Whitney U tests for continuous variables. The strength of association was measured with odds ratio. Logistic regression was performed to determine the predictors for irregular menstrual cycle and confirm the association between it and vitamin D levels.

**Results**

This study recruited 52 women in each group. The study group included women with irregular cycles, while the control group included women with regular ones. Vitamin D deficiency was noted in 46/104 participants (44.2%).

Younger women had irregular cycles than (p-value 0.0001). There was no statistically significant difference in the other demographic data of the studied population (Table 1).

The menstrual cycle length differed significantly between both groups (p-value 0.0001). The number of pads/day was significantly increased among the control group than the study one (2.8 ± 1.1 versus 2.3 ± 0.5, p-value 0.001). The menstrual cycle pattern varied among the study group, with oligomenorrhea (65.4%) as the predominant pattern (Table 2).

Vitamin D level was significantly lower in the
study group than in the control group (20.0 ± 11.9 and 28.7 ± 16.6, respectively, p-value 0.003). Also, the study group included more women with deficient and insufficient vitamin D (51.9% and 32.7% respectively) level than the control group (36.5% and 26.9% respectively) (Table 3).

Among the factors associated with irregular cycles, younger age was a significant predictor (p-value 0.005) (Table 4).

**Discussion**

Vitamin D deficiency was present in 44.2% of the studied population. Higher results were reported previously, where 80% of the studied population was vitamin D deficient (23). Another study conducted among Egyptian mothers reported vitamin D deficiency to affect 40% of the studied population (24), which is similar to the current results. This discrepancy would be attributed to different races among studies, different cultural behaviors as women tend to wear clothes covering the entire body, and different territories with variable sun incidence (25).

Women with irregular cycles were younger than those with regular cycles. An earlier study contradicted this finding (26). However, this agreed with another one as women with irregular cycles had a mean age of 27.65 ± 0.36, while those with regular cycles aged 30.57 ± 0.17 (p-value < 0.001) (27). This was due to the effect of age on maturing and stabilizing sex hormones and the reproductive organs (27).

Vitamin D level was significantly lower in women with irregular cycles than those with regular ones. This agreed with previous results, as insufficient vitamin D was associated with increased cycle length, oligomenorrhea, and amenorrhea (28, 29). Another study reported improved cycle regularity among women after vitamin D supplementation. However, this study recruited women with polycystic ovary syndrome and added calcium supplantation (30).

The mechanism behind vitamin D's effect on menstrual cycle regularity is unexplained. It was assumed that it affects anti-mullerian hormone (AMH), which has an essential role in oocyte maturation and ovulation (30), as evidenced by decreased primordial follicle production, delayed follicle atresia, and decreased follicle development (31). This effect is mediated through vitamin D control of AMH production because of a domain for vitamin D signaling pathways on AMH receptors (31). Vitamin D receptors are present in the ovarian tissue, which correlates with steroidogenesis and follicle maturation (32). It affects estrogen and progesterone production (1). Another mechanism regulates calcium homeostasis, paramount in oocyte activation and maturation (8).

Among the factors associated with irregular cycles, younger age was a significant predictor. This agreed with previous results, as increasing age was associated with decreased odds of having irregular cycles (27). Another study reported that vitamin D insufficiency was associated with 13.3 times the odds of reporting irregular cycles (29), contradicting our results. Another reported a significant association between low vitamin D levels and irregular cycles, with no significant association with short or long cycles (7).

**Strength and limitations**

The study included a control group of women with regular cycles to get conclusive results; however, the small sample size is a limitation. Another limitation is the study design (cross-sectional study), as a randomized trial would be more powerful. Menstrual cycle evaluation was done using a diary to avoid recall bias. We did not evaluate possible risk factors contributing to irregular cycles.
Conclusion

Vitamin D deficiency was noted significantly among women with irregular cycles. Age was a significant predictor for irregular cycles rather than vitamin D levels.

Conflict of interest: None

References


### Table (1): Basic demographic data of the studied population

<table>
<thead>
<tr>
<th></th>
<th>Study group (N= 52)</th>
<th>Control group (N= 52)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years) (Mean ± SD)</strong></td>
<td>30.2 ± 7.3</td>
<td>35.1 ± 6.2</td>
<td>0.0001a</td>
</tr>
<tr>
<td><strong>Parity (Mean ± SD)</strong></td>
<td>2.5 ± 1.6</td>
<td>2.8 ± 1.5</td>
<td>0.324a</td>
</tr>
<tr>
<td><strong>BMI (Mean ± SD)</strong></td>
<td>27.2 ± 5.7</td>
<td>28.4 ± 5.2</td>
<td>0.275a</td>
</tr>
<tr>
<td><strong>Education N (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>6 (11.5%)</td>
<td>8 (15.4%)</td>
<td></td>
</tr>
<tr>
<td>Middle</td>
<td>26 (50%)</td>
<td>34 (65.4%)</td>
<td>0.096a</td>
</tr>
<tr>
<td>High</td>
<td>20 (38.5%)</td>
<td>10 (19.2%)</td>
<td></td>
</tr>
<tr>
<td><strong>Occupation N (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Housewife</td>
<td>40 (76.9%)</td>
<td>38 (73.1%)</td>
<td></td>
</tr>
<tr>
<td>Employee</td>
<td>12 (23.1%)</td>
<td>14 (26.9%)</td>
<td>0.494a</td>
</tr>
</tbody>
</table>

*a student t-test, b chi-square test*
Table 2: Menstrual cycle characteristics between both groups:

<table>
<thead>
<tr>
<th>Menstrual cycle pattern N (%)</th>
<th>Study group (N= 52)</th>
<th>Control group (N= 52)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intermenstrual bleeding</td>
<td>3 (5.8%)</td>
<td>0 (0.0%)</td>
<td>0.0001b</td>
</tr>
<tr>
<td>Oligomenorrhea</td>
<td>34 (65.4%)</td>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td>Amenorrhea</td>
<td>7 (13.5%)</td>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td>Polymenorrhea</td>
<td>7 (13.5%)</td>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td>HMB</td>
<td>1 (1.9%)</td>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td>Dysmenorrhea N (%)</td>
<td>Yes</td>
<td>3 (5.8%)</td>
<td>0.111b</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>49 (94.2%)</td>
<td></td>
</tr>
</tbody>
</table>

* a student t-test, b chi-square test

Table 3: Vitamin D levels among both groups

<table>
<thead>
<tr>
<th>Vitamin D level (ng/ml) (Mean ± SD)</th>
<th>Study group (N= 52)</th>
<th>Control group (N= 52)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D category N (%)</td>
<td>Sufficient</td>
<td>8 (15.4%)</td>
<td>0.046b</td>
</tr>
<tr>
<td></td>
<td>Insufficient</td>
<td>17 (32.7%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Deficient</td>
<td>27 (51.9%)</td>
<td></td>
</tr>
</tbody>
</table>

* a student t-test, b chi-square test

Table 4: Factors associated with irregular cycles

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.166</td>
<td>0.754- 0.951</td>
<td>0.005</td>
</tr>
<tr>
<td>Parity</td>
<td>0.488</td>
<td>0.991- 2.676</td>
<td>0.054</td>
</tr>
<tr>
<td>BMI</td>
<td>-0.034</td>
<td>0.885- 1.054</td>
<td>0.440</td>
</tr>
<tr>
<td>Education</td>
<td>0.219</td>
<td>0.615-2.521</td>
<td>0.543</td>
</tr>
<tr>
<td>Occupation</td>
<td>-0.134</td>
<td>0.875- 0.520</td>
<td>0.614</td>
</tr>
<tr>
<td>Vitamin D level</td>
<td>-0.059</td>
<td>0.861-1.032</td>
<td>0.202</td>
</tr>
</tbody>
</table>