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Original Article

# Is there a relationship between serum vitamin D with dysmenorrhea pain in young women?

Mina zeynali[a,b], Hossein Khadem Haghighian[a,b,*]

[a] Student Research Committee, School of Health, Qazvin University of Medical Sciences, Qazvin, Iran
[b] Metabolic Diseases Research Center, Qazvin University of Medical Sciences, Qazvin, Iran

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ABSTRACT

Dysmenorrhea, also known as painful periods, or menstrual cramps, is pain during menstruation. This study was done in young women that assess the association of serum vitamin D concentration and severity of dysmenorrhea pain. This descriptive-analytic study conducted on young girls referred to Shahid fakuri clinic in Tehran. Eligible girls completed the visual analog scale (VAS) and 372 participants with mild, moderate and severe dysmenorrhea completed the study. In order To measure the serum concentration of 25-hydroxy vitamin D, 5 ml of blood was be taken from participants. Most of the participants (53.22%) described their menstrual pain as moderate, while 24.73% and 22.04% of participants reported severe and mild dysmenorrhea respectively. About 37% of women had Vit D insufficiency, 36.55% had moderate Vit D deficiency, and 26.34% had severe deficiency. There was a negative correlation between the serum levels of 25(OH) D and pain indices (PV: 0.044). Positive relationship between pain intensity and waist circumference, hip circumference, fat percentage, and fat mass was observed, but between pain intensity with BMI and WHR no significant relationship was observed. According to these results supplementation with Vit D may be useful to girls for decreasing of dysmenorrhea pain.



## Introduction

Dysmenorrhea is defined as pain associated with the menstrual cycle which affects millions of women of reproductive age. It is a common gynecological disorder that affects about 50% of women [1]. The prevalence of menstrual pain in the world ranges from 45 to 95% [2,3]. The prevalence of this disease in Iranian women at reproductive ages has been reported of 38.3%–100% in different regions of the country [4,5]. The difference in the rate of the dysmenorrheal outbreak in various studies is due to different criteria for the definition of this disease and possibly also due to the weather conditions in each region. Dysmenorrhea is divided into primary and secondary types. Primary type is a painful menstruation in the absence of a confirmed pelvic disease. It is a contraction pain in the lower abdomen that occurs before or during menstruation without any disease. Menstrual pain begins with the release of prostaglandins from endometrial cells and following that vascular contraction occurs that leads to pain [6]. Therefore, suppressing the synthesis or function of prostaglandins is the main goal in the treatment of this disease [7]. Various factors are associated with early dysmenorrhea such as family history, menarche's age, stress, and depression, too much caffeine consumption, body mass index, abortion history, smoking, and polyneuritis. This condition may be associated with systemic symptoms such as Headache, dizziness, nausea, vomiting, diarrhea, fever and fatigue. It has a negative effect on women's quality of life and in severe cases, their activities will be limited. Various therapeutic strategies, including Nonsteroidal anti-inflammatory drugs, oral contraceptives, herbal extracts, and supplements have been used to control menstrual pain, but there is still no definitive treatment strategy [7,8].

Vitamin D is a steroid hormone that is mainly produced in the skin or through exposure to sunlight (80–90%), and the rest is provided through diet and supplementation [9]. The decrease in serum 25-hydroxyvitamin D to less than 12 ng/ml is the sign of vitamin D deficiency. Levels of 12–30 ng/ml are considered as inadequate range, and values greater than 30 ng/ml indicates adequate ranges [10]. Vitamin D insufficiency and deficiency rate in Iranian adults is more than 80%, while the deficiency in pregnant women is 66.8% [11].

Some studies indicated a beneficial impact of cholecalciferol on such menstrual dysfunctions as oligomenorrhea and dysmenorrhea. Regarding numerous information on the function of vitamin D, both

* Corresponding author at: Department of Nutrition, Faculty of Health, Qazvin University of Medical Sciences, Qazvin, Iran.
*E-mail address:* khademnut@yahoo.com (H.K. Haghighian).

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traditional and lately published, there may be a sturdy correlation among vitamin D deficiency and different various factors, determining a huge range of polymorphic clinical manifestations where menstrual dysfunction is essential in girls at the age of puberty [12].

Because the vitamin D receptor is widespread and the mitochondrial cytochrome P450 enzyme 25-hydroxyvitamin D3-1α-hydroxylase (1α-OHase), which catalyzes the synthesis of D3 from its precursor 25(OH) D, is expressed in the human uterus and in immune system cells, and due to the fact vitamin D decreases the synthesis of PGs, a beneficial impact of vitamin D in the uterus pathophysiology is feasible [13–15].

The similar studies have focused on the issue that whether a high dose of vitamin D supplementation can improve menstrual problems or not? [16], while in this study we surveyed the serum concentration of vitamin D in women who suffer from dysmenorrhea.

The purpose of this study was to assess the association of serum vitamin D concentration and severity of dysmenorrhea pain in young women referred to Shahid fakuri clinic in Tehran.

## Methods

### *Participants*

This descriptive-analytic study was performed in single women referring to Shahid Fakouri health center in Tehran in 2017. More than thirty years of age, having metabolic disease, and being married were exclusion criteria. Patients completed the written consent form of the study. This investigation was approved by Ethics Committee of Qazvin University of Medical Sciences, Iran (the ethical codes of study was IR.QUMS.REC.1396.384).

### *Study design*

At the beginning of the survey, age, weight, height, waist circumference, body mass index, education level, medical history of diseases and the use or non-use of vitamin D supplementation was recorded. Dysmenorrhea was confirmed by questionnaire. Weight was measured on a scale with 100 g accuracy, wearing minimum clothing's, and height by a stadiometer with 1 mm accuracy with no shoes on. Obesity is evaluated by using the Body Mass Index (BMI). The BMI is calculated by dividing the weight in kilograms to the square of height in meter.

Waist circumference is measured by a tape measure at the natural waistline, which is located above the belly button and below the rib cage. Regardless of height or build, for most adults, a waist circumference measurement greater than 90 cm is an indicator of the level of internal fat deposits [17]. Body fat in percent and kilogram (with 0.01 accuracy) using the Omron 306 (Germany) was measured.

The severity of dysmenorrhea and menstrual period will be recorded for each patient. The dysmenorrhea severity is measured by Visual Analog Scale (VAS) (0= no pain, 10 =unbearable pain) [18].

In order To measure the serum concentration of 25-hydroxy vitamin D in the laboratory in sterile conditions, 5 ml of blood was be taken from participants and it will be placed in centrifuge at 3500 rpm for 5 min. Separated serum will freeze immediately, then it's measured by ELISA kit. A level of 25-hydroxy vitamin D more than 30 ng/milliliter demonstrates adequate for healthy people. A level less than 12 ng/mL indicates vitamin D deficiency. And concentration between 12-30 ng/mL shows insufficient level [19].

### *Sample size*

We used similar study Haidari et al. [20] to calculate the sample size. Based on the following formula and taking into account the following factors, the sample size is estimated at 311 people, of which 360 will be included in the study.

$N = Z^2 (P (P-1))/d^2$

p = Estimated proportion of the population that presents the characteristic (71.65%)

d = Tolerated margin of error (5%).

N = 311

**Table 1**
Anthropometric characteristics of the participants.

| Variables | Mean ± SD |
|---|---|
| Height (cm) | 158.17 ± 6.05 |
| Weight (Kg) | 60.13 ± 11.18 |
| BMI (kg/m2) | 24.03 ± 3.07 |
| Waist circumference (cm) | 78.64 ± 8.23 |
| Hip circumference(cm) | 106.19 ± 7.34 |
| Fat mass (%) | 15.17 ± 6.4 |
| Body fat percentage (%) | 27.66 ± 7.41 |
| WHR (cm) | 0.74 ± 0.044 |

## Statistical analyses

Statistical analyses were done using SPSS Software (version 17.0). The descriptive characteristics of the participants are expressed as Mean ± SD. The normal distribution of data was analyzed using the Smirnov-Kolmogorov statistical test. Pearson correlation coefficient was used to study the relationship between variables. $P < 0.05$ were considered statistically significant.

## Results

The mean age of participants was 22.4 ± 2.01 and the average of menarche age was 13.21 ± 1.44 years.

Anthropometric characteristics are summarized in Table 1. Most of the participants (53.22%) described their menstrual pain as moderate, while 24.73% and 22.04% of participants reported severe and mild dysmenorrhea respectively.

The average duration of menstruation cycle was 6.09 ± 1.11 days and the average duration of each menstrual dysmenorrhea was 2.18 ± 1.04 days.

Classification of participants based on dysmenorrhea intensity summarized in Table 2.

Table 3 shows the classification of participants according to the severity of pain based on the serum level of vitamin D.

There was a negative correlation between the serum levels of 25 (OH) D and pain indices. (PV: 0.044, Table 4).

Positive relationship between pain intensity and waist circumference, hip circumference, fat percentage, and fat mass was observed, but between pain intensity with BMI and WHR no significant relationship was observed. (Table 5)

## Discussion

Dysmenorrhoea is a common complaint experienced by many females in their reproductive years [21]. Painful menstruation without pelvic pathologic complications, is one of the most

**Table 2**
Classification of participants based on dysmenorrhea intensity.

| Dysmenorrhea intensity | number | percent |
|---|---|---|
| Without pain (0) | 0 | 0 |
| Mild (1-3) | 82 | 22.04 |
| Moderate (4-7) | 198 | 53.22 |
| Severe (8-10) | 92 | 24.73 |
| Total | 372 | 100 |

**Table 3**
Classification of participants according to the severity of pain based on the serum level of vitamin D.

| Dysmenorrhea | Severe deficiency of vitamin D | Deficiency of vitamin D | Insufficiency of vitamin D | Total |
|---|---|---|---|---|
| Mild (1-3) | 12 | 27 | 43 | 82 |
| Moderate (4-7) | 59 | 77 | 62 | 198 |
| Severe (8-10) | 27 | 32 | 33 | 92 |

**Table 4**
Correlation between the serum levels of 25(OH) D and pain indices[1].

| Variable | r | Pv |
|---|---|---|
| Pain duration | −0.432 | 0.061 |
| Pain intensity | −0.612 | 0.044 |

[1] Pearson correlation was used.

**Table 5**
Association of pain intensity with anthropometric indices[1].

| Dysmenorrhea | r | Pv |
|---|---|---|
| BMI | 0.107 | 0.061 |
| Waist circumference | 0.120 | 0.029 |
| Hip circumference | 0.139 | 0.025 |
| Fat mass (kg) | 0.164 | 0.01 |
| Fat percentage (%) | 0.161 | 0.012 |
| WHR | 0.082 | 0.101 |

[1] Pearson correlation was used. BMI: Body mass index; WHR: Waist-to-hip ratio.

common problems in women's gynecology and is one of the main causes for women referring to the clinic [22].

Serum concentration of vitamin D may play a role in the etiology of primary dysmenorrhea [23].

This study was conducted to evaluate the association between serum concentration of vitamin D and dysmenorrhea intensity in young girls. The results of this study showed a negative correlation between the serum levels of 25(OH) D and pain indices such as pain duration and pain intensity.

A prospective intervention study was performed to evaluate the effect of a single-loading oral dose of cholecalciferol (300 000 IU) on primary dysmenorrhea by Lasco et al. in 2012 [12]. In their study, 20 women received a single oral dose of Vit D3 (300 000 IU) just 5 d before the beginning of menstrual cycle and 20 women received placebo. They showed significant effect of Vit D in the treatment of primary dysmenorrhea. There was a negative correlation between the pain score at baseline and the levels of 25(OH) D, in this regard the results of that study are similar to ours.

The results of the Lasco's study demonstrated that patient's baseline serum 25(OH) D levels were in the lower quartile of the laboratory's normal range and in our study, 37.09% of women had vit D insufficiency, 36.55% had moderate Vit D deficiency, and 26.34% had severe deficiency. In that study, patients received a single high dose of Vit D3 but in our study, we just looked at serum levels of vitamin D and the participants did not receive any supplement.

Moini et al. conducted a randomized double-blind placebo-controlled clinical trial to investigate the effect of vitamin D supplementation in treatment of primary dysmenorrhea with Vit D deficiency [11]. It was conducted on 60 women with primary dysmenorrhea and Vit D deficiency. The study results showed that treatment of Vit D deficiency in patients with primary dysmenorrhea with Vit D deficiency improves dysmenorrheal pain.

Abdul Razzak et al. surveyed Vitamin D and parathyroid hormone (PTH) status among adolescent and young females with severe and very severe dysmenorrhea [13]. This study indicated that a high prevalence of vitamin D insufficiency and secondary hyperparathyroidism and/or low dietary calcium intake among adolescent and young adult females who experience severe and very severe dysmenorrhea may negatively affect bone metabolism during achievement of peak bone mass at a young age and adverse bone health at older age.

Also, a randomized double-blind trial carried out by Zarei et.al to determine the effect of combined calcium-vitamin D and calcium-alone on pain intensity and menstrual blood loss in women with primary dysmenorrhea [24]. The results of zarei's study showed that intake of the calcium-alone was effective in reducing menstrual pain intensity. The results could not reveal significant effects of calcium-vitamin D on the pain or any of the interventions on menstrual blood loss.

The steroid hormone vitamin D is historically recognized for its relevance to bone health and calcium homeostasis [9]. Recent years have witnessed a shift in focus to non-skeletal benefits of vitamin D; in this latter context, an accruing body of literature attests to a relevance of vitamin D to reproductive physiology. A large body of available literature suggests that vitamin D deficiency may be detrimental to reproductive biology [25]. The proposed mechanisms whereby vitamin D may participate in the regulation of reproductive physiology is vitamin D decreases the synthesis of PGs [26].

Prostaglandins are key regulators of reproductive processes, including ovulation, implantation and menstruation [27]. Prostaglandins have been identified to have a role in various pathological changes of the reproductive tract including menorrhagia, dysmenorrhea, endometriosis and cancer [28]. Although the mechanism by which prostaglandins modulate these changes remains unclear, much evidence suggests that prostaglandins and their receptors and downstream signaling pathways are involved in angiogenesis and in amelioration in cell adhesion, morphology, motility, invasion and metastases. The potential role of prostaglandin receptors in pathological changes of the endometrium has significance for the future development of therapeutic interventions [29].

The calcitriol receptor, more commonly known as the vitamin D receptor (VDR) and also known as NR1I1 (nuclear receptor subfamily 1, group I, member 1), presents in many tissues, it is expressed in the uterine endometrial cells as well as in the immune cells residing within the uterine endometrium, on the other hand the mitochondrial cytochrome P450 enzyme 25-hydroxyvitamin D3 (25[OH]D)-1α-hydroxylase (1α-OHase), which catalyzes the synthesis of 1α,25-dihydroxyvitamin D3 (1,25[OH]2D) from its precursor 25(OH)D, is expressed in the human uterus and in immune system cells, and due to the fact vitamin D abates the synthesis of PGs, so vitamin D can have salutary impact on the uterus pathophysiology [15].

In our study, we surveyed anthropometric characteristics such as height, weight, BMI, waist circumference, hip circumference, fat mass, body fat percentage, and WHR, Which is unique in this kind of studies. Participants of this study had mild, moderate and severe pain intensity while in most of the similar studies all of the participants had severe and very severe dysmenorrheal pain. This is one of the strengths of our study because our sample represents the population and our participants were not selected among those with severe pain.

To our knowledge, this is the first study in Iran investigating the relationship between serum vitamin D levels and severity of dysmenorrhea.

Our sample was very homogeneous with respect to education, race and socio-economic status, which limits cultural confounding factors, but also limits the external validity of our results. Other studies have found that socioeconomic status is inversely associated with dysmenorrhoea.

However, due to lack of funding in this study, we were not able to measure some inflammatory factors and oxidative stress in relation to dysmenorrhea pain. According to the importance of this issues on women's health, further research in this field in a new context, location, culture and some inflammatory factors is highly recommended.

## Conclusion

We found the negative correlation between the serum levels of 25(OH) D and pain indices, which is similar to some analogous studies, and the association of pain intensity with anthropometric indices were analyzed.

## Disclosures

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## Conflict of interest

The authors declare that they have no conflict of interest.

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