ISSN: 2320-9267

Indian Journal of Pharmaceutical and Biological Research (IJPBR)

Journal homepage: www.ijpbr.in

RESEARCH ARTICLE

The Association between Vitamin D Level and Uterine Fibroid in Premenopausal Women in a Tertiary Care Centre: A Hospital-Based Analytical Case-Control Study

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ABSTRACT

Background: Uterine fibroids are the most common benign smooth muscle tumors of the uterus and constitute a major cause of gynecological morbidity among women of reproductive age. Although their exact pathogenesis remains incompletely understood, increasing evidence suggests that vitamin D deficiency may contribute to fibroid development through its effects on cellular proliferation, apoptosis, extracellular matrix remodeling, and angiogenesis. Since vitamin D deficiency is highly prevalent among Indian women, understanding its relationship with uterine fibroids may provide opportunities for preventive and therapeutic interventions.

Objective: To evaluate the association between serum vitamin D levels and uterine fibroids among premenopausal women attending a tertiary care hospital and to assess the relationship between vitamin D status and fibroid characteristics.

Materials and Methods: A hospital-based analytical case-control study was conducted in the Department of Obstetrics and Gynaecology, MDM Hospital, Dr.Sampurnanand Medical College, Jodhpur, Rajasthan, over a period of six months. Fifty premenopausal women were enrolled, comprising 25 ultrasound-confirmed uterine fibroid cases and 25 age-matched controls without fibroids. Demographic, clinical, menstrual, and obstetric characteristics were recorded using a structured proforma. Serum 25-hydroxyvitamin D concentration was estimated by standard laboratory methods and categorized as deficient (<20 ng/mL), insufficient (20–29 ng/mL), and sufficient (≥30 ng/mL). Fibroid characteristics including type, number, and volume were assessed by ultrasonography. Statistical analysis was performed using SPSS software. Categorical variables were analyzed using the Chi-square test, while continuous variables were compared using the independent t-test. A p-value <0.05 was considered statistically significant.

Results: The mean age of cases and controls was 38.36 ± 3.67 years and 37.92 ± 4.79 years, respectively (p=0.452). Mean serum vitamin D levels were significantly lower among women with uterine fibroids than controls (12.43 ± 4.20 vs. 17.19 ± 5.65 ng/mL, p=0.001). Vitamin D deficiency was significantly more common in cases than controls (32.0% vs. 4.0%; p=0.028). Mean haemoglobin levels were also significantly lower among cases (10.08 ± 1.46 g/dL) than controls (11.18 ± 1.93 g/dL; p=0.029). Intramural fibroids constituted the commonest subtype (68%), while single fibroids were observed in 64% of cases. Significant associations were identified between vitamin D status and fibroid type (p=0.013) as well as fibroid number (p=0.031). However, no statistically significant association was observed between vitamin D status and fibroid volume (p=0.499).

Conclusion: Premenopausal women with uterine fibroids demonstrated significantly lower serum vitamin D levels than women without fibroids. Vitamin D deficiency was associated with the presence of uterine fibroids and showed significant relationships with fibroid type and multiplicity. These findings suggest that vitamin D deficiency may represent an important modifiable risk factor in uterine fibroid pathogenesis. Larger prospective multicentric studies are warranted to establish causality and evaluate the potential role of vitamin D supplementation in the prevention and management of uterine fibroids.

Keywords: Uterine fibroid; Leiomyoma; Vitamin D deficiency; Premenopausal women; Case-control study; 25-hydroxyvitamin D.

Indian J. Pharm. Biol. Res. (2026): https://doi.org/10.30750/ijpbr.14.3.38

Introduction

Uterine fibroids, also known as uterine leiomyomas, are the most common benign tumors of the female reproductive system, originating from the smooth muscle cells of the myometrium. They are estrogen- and progesterone-dependent monoclonal tumors characterized by excessive proliferation of smooth muscle cells and deposition of extracellular matrix. Although benign, uterine fibroids represent a significant cause of gynecological morbidity among women of reproductive age and are one of the leading indications for hysterectomy worldwide. Their presence can substantially impair reproductive health, menstrual function, and overall quality of life.[1]

The prevalence of uterine fibroids varies according to age, ethnicity, genetic predisposition, and diagnostic techniques. It is estimated that approximately 20–40% of women of reproductive age have clinically detectable fibroids, while imaging and histopathologicalstudies

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How to cite this article: Arora N, Deora RK, Chouhan B, Veeram PS, Kumawat K. The Association between Vitamin D Level and Uterine Fibroid in Premenopausal Women in a Tertiary Care Centre: A Hospital-Based Analytical Case-Control Study. Indian J. Pharm. Biol. Res. 2026;14(3):240-249.

Source of support: Nil

Conflict of interest: None.

Received: 13/06/2026 **Revised:** 29/06/2026 **Accepted:** 17/07/2026 **Published:** 03/08/2026

suggest that nearly 70% of women may develop fibroids by the age of 50 years. The incidence increases with advancing reproductive age and is highest among women between 35 and 50 years. In India, uterine fibroids constitute a common indication for gynecological outpatient visits and surgical intervention, imposing a considerable socioeconomic and healthcare burden.[2]

The exact etiology of uterine fibroids remains incompletely understood. Their development is considered multifactorial, involving complex interactions among genetic, hormonal, environmental, and growth regulatory factors. Estrogen and progesterone stimulate cellular proliferation and extracellular matrix production, while several molecular pathways—including transforming growth factor-beta (TGF-β), insulin-like growth factor (IGF), epidermal growth factor (EGF), and Wnt/β-catenin signaling—have been implicated in fibroid growth. Genetic alterations, particularly mutations in the MED12 gene, have also been identified in a substantial proportion of uterine fibroids, suggesting an important molecular basis for disease development.[3]

Clinically, uterine fibroids may remain asymptomatic or present with a wide spectrum of symptoms depending on their size, number, and anatomical location. Common manifestations include heavy menstrual bleeding, prolonged menstrual periods, dysmenorrhea, chronic pelvic pain, pressure symptoms involving adjacent pelvic organs, infertility, recurrent pregnancy loss, and obstetric complications. Excessive menstrual blood loss frequently leads to iron deficiency anemia, reduced work productivity, and impaired quality of life. Consequently, uterine fibroids continue to be a major contributor to healthcare utilization among women of reproductive age.[4]

Several epidemiological risk factors have been associated with uterine fibroid development, including increasing age, early menarche, nulliparity, obesity, hypertension, positive family history, and prolonged exposure to endogenous estrogens. Conversely, parity and menopause appear to reduce the risk of fibroid development. However, these established risk factors do not fully explain the occurrence or progression of uterine fibroids, leading researchers to investigate potentially modifiable biological factors that may influence disease pathogenesis.[5]

Vitamin D has recently emerged as a promising factor in the pathophysiology of uterine fibroids. Traditionally recognized for its role in calcium homeostasis and bone metabolism, vitamin D also exerts important extraskeletal effects through activation of the vitamin D receptor (VDR), which is expressed in reproductive tissues including the uterus, endometrium, ovaries, and myometrium. Activation of the VDR regulates genes involved in cellular proliferation, apoptosis, differentiation, angiogenesis, immune modulation, and extracellular matrix remodeling. These biological actions provide a plausible mechanism through which vitamin D may influence fibroid development and progression.[6]

Experimental studies have demonstrated that vitamin D suppresses proliferation of leiomyoma cells by inhibiting cell cycle progression, reducing expression of proliferative markers, and promoting apoptosis. Additionally, vitamin D inhibits TGF-β-mediated extracellular matrix accumulation, decreases collagen synthesis, suppresses angiogenesis, and attenuates fibrosis within fibroid tissue. Animal studies have similarly reported reduced fibroid growth following vitamin D supplementation, suggesting a potential therapeutic role for vitamin D in the management of uterine fibroids.[7]

Clinical evidence increasingly supports an inverse association between serum vitamin D levels and uterine fibroids. Several observational studies have reported significantly lower circulating concentrations of 25-hydroxyvitamin D among women with fibroids

compared with healthy controls. Furthermore, vitamin D deficiency has been associated with increased fibroid size, greater tumor multiplicity, and higher disease burden in some populations. Nevertheless, findings remain inconsistent across different ethnic groups and geographic regions, emphasizing the need for additional well-designed studies to clarify this relationship.[8]

Vitamin D deficiency is highly prevalent in India despite abundant sunlight throughout the year. Limited sun exposure, increased skin pigmentation, urban lifestyles, dietary inadequacy, obesity, and sociocultural practices contribute to widespread hypovitaminosis D among Indian women. Since vitamin D deficiency is both common and potentially correctable, establishing its association with uterine fibroids may have important implications for disease prevention, early detection, and non-surgical management.[9]

Evidence regarding the relationship between vitamin D status and uterine fibroids in Indian women, particularly from Western Rajasthan, remains limited. Regional variations in nutritional status, sunlight exposure, socioeconomic conditions, and lifestyle factors necessitate locally generated evidence. Therefore, the present hospital-based analytical case-control study was conducted in the Department of Obstetrics and Gynaecology, MDM Hospital, Dr.Sampurnanand Medical College, Jodhpur, to evaluate the association between serum vitamin D levels and uterine fibroids in premenopausal women. In addition, the study aimed to assess the relationship between vitamin D status and fibroid characteristics, including type, number, and volume, thereby contributing to the existing evidence regarding the role of vitamin D in uterine fibroid pathogenesis.[10-12]

Materials And Methods

Study Design

This was a hospital-based analytical case-control study conducted to evaluate the association between serum vitamin D levels and uterine fibroids in premenopausal women.

Study Setting

The study was conducted in the Department of Obstetrics and Gynaecology, MDM Hospital, Dr.Sampurnanand Medical College, Jodhpur, Rajasthan, India, a tertiary care teaching hospital catering to urban and rural populations of western Rajasthan.

Study Duration

The study was conducted over a period of six months.

Study Population

The study included premenopausal women attending the outpatient and inpatient services of the Department of Obstetrics and Gynaecology during the study period who fulfilled the eligibility criteria.

Sample Size

A total of 50 participants were enrolled in the study and divided into two groups:

- Cases (n = 25): Premenopausal women diagnosed with uterine fibroids on ultrasonography.
- Controls (n = 25): Age-matched premenopausal women without evidence of uterine fibroids on ultrasonography.

Sampling Technique

Consecutive eligible participants fulfilling the inclusion criteria were recruited until the desired sample size was achieved.

Inclusion Criteria

Cases

- Premenopausal women.
- Ultrasonographically confirmed diagnosis of uterine fibroid.
- Willingness to participate in the study and provide written informed consent.

Controls

- Premenopausal women.
- No evidence of uterine fibroids on ultrasonography.
- Willingness to participate in the study and provide written informed consent.

Exclusion Criteria

Women with any of the following conditions were excluded from the study:

- Pregnancy.
- Postmenopausal women.
- History of previous myomectomy or hysterectomy.
- Current vitamin D or calcium supplementation.
- Chronic kidney disease or chronic liver disease.
- Disorders affecting calcium or vitamin D metabolism.
- Malabsorption syndromes.
- Endocrine disorders such as hyperparathyroidism or thyroid disorders.
- Current use of corticosteroids, anticonvulsants, or other medications affecting vitamin D metabolism.
- Known gynecological malignancy.
- Refusal to provide informed consent.

Data Collection

After obtaining written informed consent, detailed demographic, socioeconomic, menstrual, obstetric, and clinical information was recorded using a predesigned and pretested case record proforma. Information regarding age, religion, locality, educational status, socioeconomic status, occupation, menstrual history, duration of symptoms, family history of uterine fibroids, parity, obstetric history, and presenting complaints was documented.

A detailed general physical examination, systemic examination, and gynecological examination were performed for all participants. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in metres (kg/m²). Pallor was assessed clinically, and haemoglobin estimation was performed using standard laboratory methods.

Ultrasonographic Evaluation

All participants underwent pelvic ultrasonography performed by experienced radiologists. In the case group, uterine fibroids were confirmed, and their characteristics including type (intramural, submucosal, or subserosal), number (single or multiple), and fibroid volume were documented. Controls underwent ultrasonographic examination to exclude the presence of uterine fibroids.

Estimation of Serum Vitamin D

Approximately 3–5 mL of venous blood was collected from each participant under aseptic precautions. Serum was separated by centrifugation and analysed for 25-hydroxyvitamin D [25(OH)D], the accepted indicator of vitamin D status, using the standard immunoassay available in the institutional central laboratory.

Vitamin D status was classified as:

- Deficient:<20 ng/mL
- Insufficient: 20–29 ng/mL
- Sufficient: ≥30 ng/mL

Outcome Measures

The primary outcome was the comparison of serum vitamins D levels between women with uterine fibroids and controls.

Secondary outcomes included:

- Association between vitamin D status and fibroid type.
- Association between vitamin D status and fibroid number.
- Association between vitamin D status and fibroid volume.
- Comparison of haemoglobin levels, BMI, menstrual characteristics, and other clinical variables between the study groups.

Statistical Analysis

The collected data were entered into Microsoft Excel and analysed using the Statistical Package for the Social Sciences (SPSS) software version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages.

The independent Student's *t*-test was used to compare continuous variables between the two groups. The Chi-square test or Fisher's exact test, wherever appropriate, was applied to compare categorical variables. A two-tailed *p*-value of less than 0.05 was considered statistically significant.

Ethical Considerations

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Approval was obtained from the Institutional Ethics Committee of Dr.Sampurnan and Medical College, Jodhpur, prior to commencement of the study. Written informed consent was obtained from all participants before enrolment, and confidentiality of patient information was strictly maintained throughout the study.

Results

A total of 50 premenopausal women were included in this hospital-based analytical case-control study, comprising 25 women with ultrasonographically confirmed uterine fibroids (cases) and 25 age-matched women without uterine fibroids (controls). The demographic profile, clinical characteristics, laboratory parameters, and serum vitamin D status were compared between the two groups. In addition, the relationship between vitamin D status and fibroid characteristics was evaluated.

Baseline Characteristics

The age distribution of the study participants was comparable between the two groups. The mean age was 38.36 ± 3.67 years among cases and 37.92 ± 4.79 years among controls, with no statistically significant difference (p = 0.452) (Table 1).

Women with uterine fibroids demonstrated a significantly different distribution of BMI categories compared with controls (p = 0.049). A significantly longer duration of symptoms was also observed among cases (p = 0.017) (Table 2).

Laboratory Parameters

The mean haemoglobin level was significantly lower among women with uterine fibroids than among controls

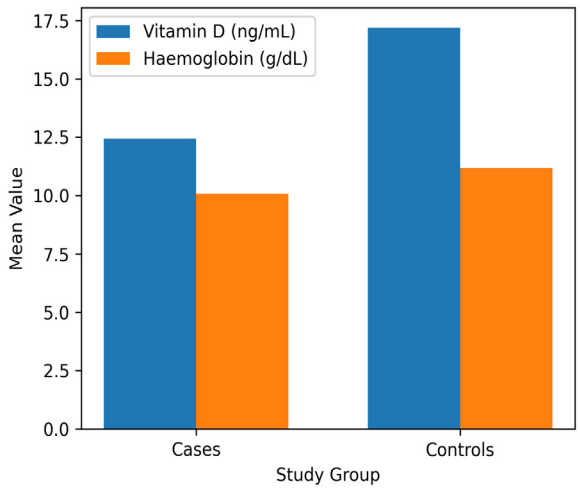

Figure 1: Comparison of serum vitamin D levels and haemoglobin between cases and controls

(10.08 ± 1.46 g/dL vs. 11.18 ± 1.93 g/dL; p = 0.029). Similarly, the mean serum vitamin D concentration was significantly lower in the case group (12.43 ± 4.20 ng/mL) compared with the control group (17.19 ± 5.65 ng/mL; p = 0.001) (Table 3, Figure 1).

Vitamin D Status

Vitamin D deficiency was significantly more prevalent among women with uterine fibroids. Deficient vitamin D levels were observed in 32.0% of cases compared with 4.0% of controls, whereas sufficient vitamin D levels were more frequently observed among controls (12.0% vs. 4.0%). The difference in vitamin D status between the two groups was statistically significant (χ^2 = 7.120, p = 0.028) (Table 4, Figure 2).

Characteristics of Uterine Fibroids

Among women with uterine fibroids, intramural fibroids were the most common subtype (68.0%), followed by

Table 1: Comparison of baseline characteristics between cases and controls

Variable	*Cases (n=25)*	*Controls (n=25)*	*p-value*
Age (years), mean ± SD	38.36 ± 3.67	37.92 ± 4.79	0.452
Rural residence	15 (60.0%)	11 (44.0%)	0.258
Illiterate	16 (64.0%)	13 (52.0%)	0.390
Multiparous	22 (88.0%)	20 (80.0%)	0.455
Irregular menstruation	17 (68.0%)	15 (60.0%)	0.768
Increased menstrual blood loss	14 (56.0%)	13 (52.0%)	0.550
Pain abdomen	10 (40.0%)	13 (52.0%)	0.395
Anaemia	18 (72.0%)	15 (60.0%)	0.370
Positive family history	15 (60.0%)	17 (68.0%)	0.556

Table 2: Comparison of BMI categories and duration of symptoms between study groups

Variable	*Cases (n=25)*	*Controls (n=25)*	*p-value*
Underweight (<18.5 kg/m²)	5 (20.0%)	1 (4.0%)	0.049*
Normal (18.5–24.9 kg/m²)	11 (44.0%)	7 (28.0%)	
Overweight (25–29.9 kg/m²)	7 (28.0%)	10 (40.0%)	
Obese (≥30 kg/m²)	2 (8.0%)	7 (28.0%)	
Duration of symptoms			0.017*
1–3 months	3 (12.0%)	12 (48.0%)	
4–6 months	9 (36.0%)	10 (40.0%)	
7–9 months	7 (28.0%)	2 (8.0%)	
10–12 months	5 (20.0%)	1 (4.0%)	
>12 months	1 (4.0%)	0 (0.0%)	

Table 3: Comparison of continuous laboratory variables between study groups

Variable	*Cases (Mean ± SD)*	*Controls (Mean ± SD)*	*p-value*
Haemoglobin (g/dL)	10.08 ± 1.46	11.18 ± 1.93	0.029
Vitamin D (ng/mL)	12.43 ± 4.20	17.19 ± 5.65	0.001

Table 4: Comparison of vitamin D status between study groups

Vitamin D status	*Cases n (%)*	*Controls n (%)*	*p-value*
Deficient (<20 ng/mL)	8 (32.0%)	1 (4.0%)	0.028
Insufficient (20–29 ng/mL)	16 (64.0%)	21 (84.0%)	
Sufficient (≥30 ng/mL)	1 (4.0%)	3 (12.0%)	

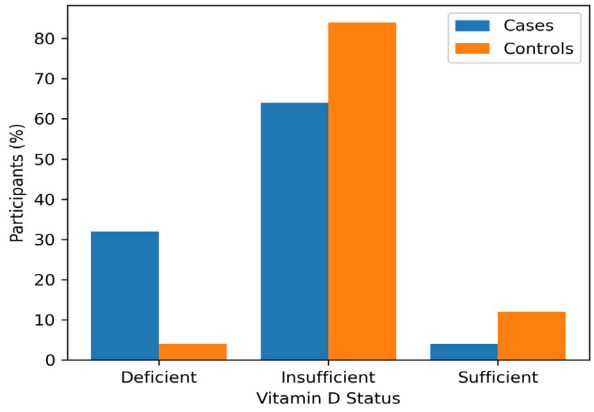

Figure 2: Comparison of vitamin D status between cases and controls.

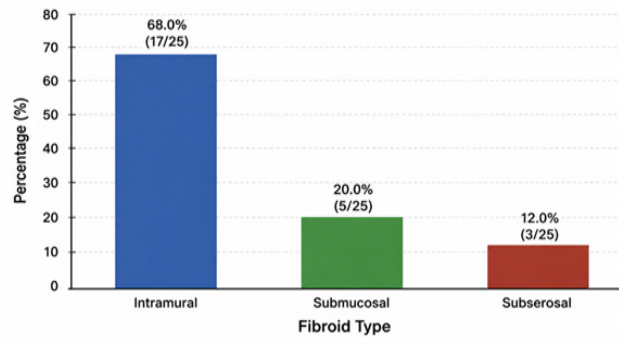

Figure 3: Distribution of Fibroid Types among Cases

submucosal fibroids (28.0%) and subserosal fibroids (4.0%). Single fibroids were observed in 64.0% of cases, while multiple fibroids were present in 36.0% (Table 5, Figure 3, Figure 4).

Association Between Vitamin D Status and Fibroid Characteristics

No statistically significant association was observed between vitamin D status and fibroid volume ($\chi^2 = 3.361$, $p = 0.499$) (Table 6).

Table 5: Distribution of fibroid characteristics among cases (n=25) Included

Characteristic	*n (%)*
Intramural	17 (68.0%)
Submucosal	7 (28.0%)
Subserosal	1 (4.0%)
Single fibroid	16 (64.0%)
Multiple fibroids	9 (36.0%)

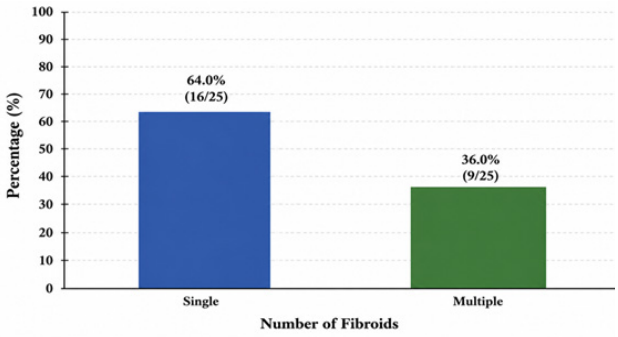

Figure 4: Distribution of Number of Fibroids among Cases

A statistically significant association was identified between vitamin D status and fibroid type ($\chi^2 = 12.72$, $p = 0.013$). Intramural fibroids predominated among women with deficient vitamin D levels (Table 7).

Vitamin D status also demonstrated a significant association with the number of fibroids ($\chi^2 = 6.70$, $p = 0.031$). Women with vitamin D deficiency were more likely to have multiple fibroids, whereas single fibroids predominated among women with insufficient or sufficient vitamin D levels (Table 8, Figure 5).

Summary of Principal Findings

The present study demonstrated that premenopausal women with uterine fibroids had significantly lower serum vitamin D concentrations and haemoglobin levels than women

Table 6: Association between vitamin D status and fibroid volume Included

Vitamin D status	*2–100 cc*	*100–200 cc*	*>200 cc*
Deficient	4	3	1
Insufficient	12	4	0
Sufficient	1	0	0

Chi-square = 3.361, p = 0.499

Table 7: Association between vitamin D status and fibroid type Included

Vitamin D status	*Intramural*	*Submucosal*	*Subserosal*
Deficient	7	2	0
Insufficient	9	5	0
Sufficient	1	0	1

Chi-square = 12.72, p = 0.013

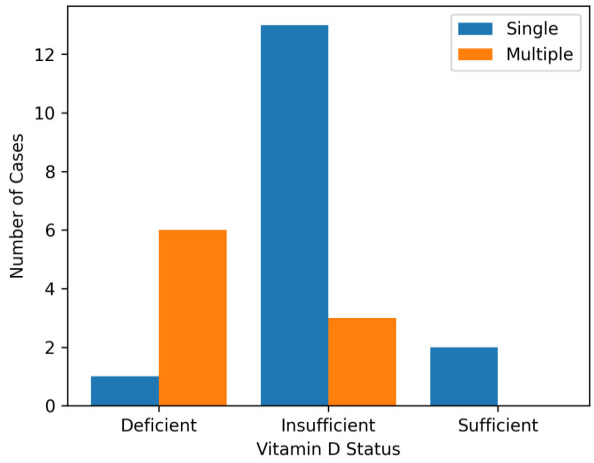

Figure 5: Association between vitamin D status and number of fibroids

Table 8: Association between vitamin D status and number of fibroids Included

Vitamin D status	*Single*	*Multiple*
Deficient	1	6
Insufficient	13	3
Sufficient	2	0

Chi-square = 6.70, p = 0.031

without fibroids. Vitamin D deficiency was significantly associated with the presence of uterine fibroids, fibroid type, and fibroid multiplicity, whereas no significant relationship was observed between vitamin D status and fibroid volume. Intramural fibroids and solitary fibroids constituted the predominant fibroid characteristics in the study population.

Discussion

The present hospital-based analytical case-control study was conducted to evaluate the association between serum vitamin D levels and uterine fibroids among premenopausal women attending a tertiary care centre in Western Rajasthan. Fifty participants, including 25 women with ultrasonographically confirmed uterine fibroids and 25 age-matched controls, were evaluated. The principal findings of the study demonstrated that women with uterine fibroids had significantly lower serum vitamin D concentrations than controls. In addition, vitamin D deficiency showed significant associations with the presence of uterine fibroids, fibroid type, and fibroid multiplicity, while no significant association was observed with fibroid volume.

The demographic characteristics of both groups were comparable with respect to age, locality, educational status, parity, menstrual regularity, family history, and most baseline clinical variables. The mean age of women with fibroids was 38.36 ± 3.67 years compared with 37.92 ± 4.79 years among controls, without a statistically significant difference. This similarity in age distribution minimized age-related confounding and strengthened the comparison between groups. Similar age distributions have been reported in previous studies evaluating vitamin D and uterine fibroids, where most affected women belonged to the late reproductive age group[13,14].

Body mass index demonstrated a statistically significant difference between cases and controls (p=0.049). Although obesity has been recognized as an established risk factor for uterine fibroids because of increased peripheral estrogen production and chronic inflammatory activity, the present study showed a heterogeneous BMI distribution. This finding suggests that factors other than obesity, including vitamin D deficiency, may independently contribute to fibroid development. Similar observations have been described by Sabry and Al-Hendy, who proposed that vitamin D may exert protective effects irrespective of body weight through regulation of cellular proliferation and extracellular matrix synthesis[15].

Women with uterine fibroids also had a significantly longer duration of symptoms than controls. This finding reflects the chronic nature of uterine fibroids and the gradual progression of symptoms before medical consultation. Although symptom duration itself may not directly

influence serum vitamin D concentration, prolonged disease may be associated with reduced physical activity, decreased outdoor exposure, and nutritional alterations that can contribute to lower vitamin D levels.

One of the important observations in the present study was the significantly lower haemoglobin concentration among women with uterine fibroids compared with controls (10.08 ± 1.46 g/dL vs. 11.18 ± 1.93 g/dL; p=0.029). Heavy menstrual bleeding is the commonest clinical manifestation of uterine fibroids and frequently results in chronic iron deficiency anaemia. The lower haemoglobin levels observed in the present study are therefore clinically expected and are consistent with previous reports demonstrating increased anaemia among women with symptomatic fibroids[16].

The principal finding of the present study was the significantly lower mean serum vitamin D level among women with uterine fibroids compared with healthy controls (12.43 ± 4.20 ng/mL vs. 17.19 ± 5.65 ng/mL; p=0.001). Furthermore, vitamin D deficiency was observed in 32% of women with fibroids compared with only 4% of controls, while sufficient vitamin D levels were more common among controls. These findings strongly support an inverse association between serum vitamin D concentration and uterine fibroid occurrence.

The results are in agreement with the landmark study by Baird et al., who demonstrated that women with sufficient vitamin D levels had a substantially lower likelihood of developing uterine fibroids than women with vitamin D deficiency[17]. Similarly, Paffoni et al. reported significantly reduced serum 25-hydroxyvitamin D concentrations among women with uterine fibroids, suggesting vitamin D deficiency as an independent risk factor for fibroid development[18]. Ciavattini *et al.* also observed that lower vitamin D concentrations were associated with both the presence and growth of uterine fibroids in reproductive-aged women[19].

The biological mechanisms supporting these observations are increasingly well understood. Vitamin D acts through the vitamin D receptor (VDR), which is expressed in normal myometrium and leiomyoma tissue. Activation of VDR inhibits smooth muscle cell proliferation, suppresses transforming growth factor-beta (TGF-β)-mediated extracellular matrix production, reduces collagen deposition, downregulatesfibronectin synthesis, promotes apoptosis, and inhibits angiogenesis. Collectively, these effects limit fibroid initiation and progression. Experimental studies have further demonstrated that vitamin D suppresses expression of proliferative genes and inhibits fibroid growth in both animal and human leiomyoma cell models[20,21].

The present study demonstrated that intramural fibroids constituted the commonest histological subtype, accounting for 68% of all fibroids, followed by submucosal (28%) and subserosal lesions (4%). This distribution is comparable to previous epidemiological studies reporting intramural fibroids as the predominant anatomical subtype because of their origin within the myometrium[22].

Interestingly, vitamin D status demonstrated a statistically significant association with fibroid type (p=0.013). Women with vitamin D deficiency showed a greater proportion of intramural fibroids, whereas sufficient vitamin D levels were observed in very few patients. Although limited published evidence has specifically examined the relationship between vitamin D status and fibroid subtype, these findings may indicate that vitamin D deficiency preferentially influences the development of intramural lesions through effects on myometrial cellular proliferation. Further multicentric studies with larger sample sizes are required to confirm this observation.

The study also identified a significant association between vitamin D status and fibroid multiplicity (p=0.031). Multiple fibroids were considerably more common among women with vitamin D deficiency, whereas women with higher vitamin D levels predominantly had solitary fibroids. These findings support previous reports suggesting that severe vitamin D deficiency may be associated with greater disease burden.[23] The anti-fibrotic and anti-proliferative properties of vitamin D may explain why lower serum concentrations predispose to the development of multiple leiomyomatous lesions rather than isolated tumors.

In contrast, no statistically significant association was observed between vitamin D status and fibroid volume (p=0.499). Although women with vitamin D deficiency tended to have larger fibroids numerically, the association failed to achieve statistical significance. Similar findings have been reported in certain observational studies where vitamin D deficiency was associated with fibroid presence but not with fibroid size after adjustment for confounding variables[24]. The absence of significance in the present study may largely be attributable to the relatively small sample size and limited number of women with large-volume fibroids.

The findings of the present study have important clinical implications. Vitamin D deficiency is highly prevalent among Indian women and represents a potentially modifiable risk factor. Screening women at risk for uterine fibroids, particularly those with heavy menstrual bleeding or multiple fibroids, may facilitate early identification of hypovitaminosis D. Although routine vitamin D

supplementation cannot yet be recommended solely for fibroid prevention, correction of vitamin D deficiency may provide additional health benefits and could potentially reduce fibroid progression. Randomized controlled trials evaluating vitamin D supplementation in women with uterine fibroids are warranted before definitive clinical recommendations can be made.

Conclusion

The present hospital-based analytical case-control study demonstrated a significant association between low serum vitamin D levels and uterine fibroids among premenopausal women. Women with uterine fibroids had significantly lower mean serum vitamin D concentrations and a higher prevalence of vitamin D deficiency than age-matched controls. Vitamin D deficiency was also significantly associated with fibroid type and fibroid multiplicity, whereas no significant relationship was observed with fibroid volume.

Intramural fibroids were the predominant subtype, and solitary fibroids were more common overall. Women with uterine fibroids also exhibited significantly lower haemoglobin levels, reflecting the clinical burden of abnormal uterine bleeding associated with the disease.

These findings support the growing evidence that vitamin D deficiency may represent an important, potentially modifiable risk factor in the pathogenesis of uterine fibroids. Assessment of vitamin D status may be considered as part of the comprehensive evaluation of premenopausal women with uterine fibroids, particularly those with symptomatic or multiple lesions. However, because of the limited sample size and observational nature of the study, a causal relationship cannot be established.

Future large-scale prospective multicentric studies and randomized controlled trials are needed to clarify the causal role of vitamin D in uterine fibroid development and to determine whether vitamin D supplementation can serve as an effective preventive or adjunctive therapeutic strategy in the management of uterine fibroids.

References

1. Stewart EA, Cookson CL, Gandolfo RA, Schulze-Rath R. Epidemiology of uterine fibroids: a systematic review. BJOG. 2017;124(10):1501-12.
2. Bulun SE. Uterine fibroids. N Engl J Med. 2013;369(14):1344-55.
3. Mehine M, Kaasinen E, Heinonen HR, Mäkinen N, Kämpjärvi K, Sarvilinna N, et al. Integrated data analysis reveals uterine leiomyoma subtypes with distinct driver pathways and biomarkers. Proc Natl Acad Sci U S A. 2016;113(5):1315-20.
4. Donnez J, Dolmans MM. Uterine fibroid management: from the present to the future. Hum Reprod Update. 2016;22(6):665-86.
5. Cramer SF, Patel A. The frequency of uterine leiomyomas. Am J Clin Pathol. 1990; 94(4):435-8.
6. Holick MF. Vitamin D deficiency. N Engl J Med. 2007;357(3):266-81.
7. Halder SK, Goodwin JS, Al-Hendy A. 1,25-Dihydroxyvitamin D3 reduces transforming growth factor-β3-induced fibrosis-related gene expression in human uterine leiomyoma cells. J Clin Endocrinol Metab. 2011;96(4):E754-62.
8. Sabry M, Al-Hendy A. Innovative oral treatments of uterine leiomyoma. ObstetGynecol Int. 2012;2012:943635.
9. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2011;96(7):1911-30.
10. Harinarayan CV, Joshi SR. Vitamin D status in India—its implications and remedial measures. J Assoc Physicians India. 2009;57:40-8.
11. Pal L, Hailpern SM, Santoro NF, Kallen AN, Carlson CA, Isaacs C, et al. Vitamin D insufficiency in reproductive-aged women: prevalence and predictors. Fertil Steril. 2008; 89(6):1745-51.
12. Baird DD, Dunson DB, Hill MC, Cousins D, Schectman JM. High cumulative incidence of uterine leiomyoma in Black and White women: ultrasound evidence. Am J Obstet Gynecol. 2003;188(1):100-7.
13. Paffoni A, Somigliana E, Vigano P, Benaglia L, Cardellicchio L, Pagliardini L, et al. Vitamin D status in women with uterine leiomyomas. J Clin Endocrinol Metab. 2013;98(8):E1374-78.
14. Ciavattini A, DelliCarpini G, Serri M, Vignini A, Sabbatinelli J, Tozzi A, et al. Hypovitaminosis D and uterine fibroids: opportunity for treatment? Endocrine. 2016;52(1):202-7.
15. Stewart EA. Uterine fibroids. Lancet. 2001;357(9252):293-8.
16. Khan AT, Shehmar M, Gupta JK. Uterine fibroids: current perspectives. Int J Womens Health. 2014;6:95-114.
17. Baird DD, Hill MC, Schectman JM, Hollis BW. Vitamin D and the risk of uterine fibroids. Epidemiology. 2013;24(3):447-53.
18. Paffoni A, Somigliana E, Vigano P, Benaglia L, Cardellicchio L, Pagliardini L, et al. Vitamin D deficiency and uterine fibroids: an observational study. Hum Reprod. 2013;28(4):1114-18.
19. Ciavattini A, DelliCarpini G, Serri M, Vignini A, Sabbatinelli J, Tozzi A, *et al*. The association between vitamin D and uterine fibroids. J Clin Endocrinol Metab. 2015; 100(2):E301-06.
20. Halder SK, Osteen KG, Al-Hendy A. 1,25-Dihydroxyvitamin D3 inhibits proliferation of human uterine leiomyoma cells. Fertil Steril. 2013;99(2):496-503.

21. Al-Hendy A, Diamond MP, Boyer TG, Halder SK. Vitamin D3 inhibits uterine fibroid growth through suppression of proliferation and extracellular matrix formation. Biol Reprod. 2015;92(6):142.
22. Laughlin-Tommaso SK. Non-surgical management of myomas. J Clin Med. 2019; 8(8) :1171.
23. Ali M, Al-Hendy A. Vitamin D and uterine fibroids: translating basic science into clinical practice. FertilSteril. 2017;107(5):1117-23.
24. Pavone D, Clemenza S, Sorbi F, Fambrini M, Petraglia F. Epidemiology and risk factors of uterine fibroids. Best Pract Res Clin Obstet Gynaecol. 2018;46:3–11.