

A STUDY ON THE ROLE OF VITAMIN D3 ON UTERINE FIBROIDS

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Abstract

Introduction

Uterine fibroids are the most common benign tumors in women of reproductive age and are associated with abnormal uterine bleeding, pelvic pain and infertility. Vitamin D deficiency has been proposed as a potential contributor to fibroid development and growth. This study evaluated the association between serum vitamin D levels and uterine fibroids and examined the relationship between vitamin D status and fibroid volume.

Methodology

A hospital-based case-control study was conducted among 100 women, including 50 women with ultrasonographically confirmed uterine fibroids and 50 age-matched controls without fibroids. Sociodemographic, menstrual, obstetric, and family history data were recorded. Serum vitamin D levels were measured and classified as deficient, insufficient, or sufficient. Fibroid volume was assessed by ultrasonography. Statistical analysis was performed using SPSS version 26.0, and $p < 0.05$ was considered statistically significant.

Results

The mean serum vitamin D level was significantly lower in cases than controls (18.6 ± 6.2 vs. 27.4 ± 7.1 ng/mL; $p < 0.001$). Vitamin D deficiency was present in 64% of cases compared with 28% of controls ($p < 0.001$). Serum vitamin D levels showed a significant negative correlation with fibroid volume ($r = -0.46$; $p = 0.002$). Higher BMI, menstrual irregularities, prolonged menstrual bleeding, early menarche, and positive family history were significantly associated with uterine fibroids.

Conclusion

Vitamin D deficiency is significantly associated with the occurrence and larger volume of uterine fibroids. Assessment of vitamin D status may help identify women at increased risk and support preventive strategies. Larger prospective studies are needed to establish causality and evaluate the effectiveness of vitamin D supplementation.

KEYWORDS: Uterine fibroids, Vitamin D3, Leiomyoma, Fibroid volume, Vitamin D deficiency

INTRODUCTION

Uterine fibroids (leiomyomas) are the most common benign tumors of the female reproductive tract and arise from the smooth muscle cells of the myometrium. They affect a large proportion of women during the reproductive years, with cumulative prevalence estimates reaching 70–80% by the age of 50 years when assessed using imaging techniques (1,2). Although many fibroids remain asymptomatic, approximately one-third of affected women develop symptoms such as heavy menstrual bleeding, pelvic pain, pressure symptoms, and reproductive dysfunction, leading to significant impairment in quality of life and increased healthcare utilization (2,3).

The pathogenesis of uterine fibroids is multifactorial and involves genetic, hormonal, and environmental influences. Estrogen and progesterone play a central role in fibroid growth by promoting cellular proliferation and extracellular matrix deposition (4). Recent research has increasingly focused on non-hormonal factors that may contribute to fibroid development, among which vitamin D deficiency has emerged as a potential modifiable risk factor.

Vitamin D is a fat-soluble secosteroid hormone traditionally recognized for its role in calcium and bone metabolism. However, vitamin D receptors are expressed in several extra-skeletal tissues, including the uterus, suggesting broader biological functions (5). Experimental studies have demonstrated that the active form of vitamin D inhibits proliferation of leiomyoma cells, reduces collagen and fibronectin synthesis, and suppresses fibrotic signaling pathways involved in fibroid growth (6,7). These findings support a plausible biological link between vitamin D deficiency and uterine fibroid pathogenesis.

Several observational studies have reported lower serum 25-hydroxyvitamin D levels among women with fibroids compared with controls and have suggested an inverse relationship between vitamin D levels and fibroid size (8,9,10). Nevertheless, results across populations have been inconsistent, and data from Indian women remain relatively limited

despite the high prevalence of vitamin D deficiency in this region (11). Moreover, few studies have specifically evaluated the relationship between serum vitamin D3 levels and fibroid volume.

In view of these gaps, the present study was undertaken to assess serum vitamin D3 levels in women with uterine fibroids and to evaluate their association with fibroid occurrence and volume. Identification of vitamin D deficiency as a modifiable risk factor may offer a simple, safe, and cost-effective adjunct in the prevention and management of uterine fibroids.

METHODOLOGY

Study Design and Setting

This hospital-based observational case-control study was conducted in the Department of Obstetrics and Gynaecology at a tertiary care hospital in Chennai, over a period of 18 months (2024–2026). The study was approved by the Institutional Ethics Committee before commencement, and written informed consent was obtained from all participants prior to enrollment.

Study Population

The study included 100 women of reproductive age (20–45 years), comprising 50 women diagnosed with uterine fibroids (cases) and 50 age-matched women without uterine fibroids (controls). Participants were recruited from the gynecology outpatient department using purposive sampling after fulfilling the predefined eligibility criteria.

Women aged 20–45 years with ultrasonographically confirmed uterine fibroids measuring less than 5 cm in diameter were included in the case group, while women without fibroids served as controls. Pregnant, lactating, or postmenopausal women, those with large or symptomatic fibroids, previous myomectomy, adenomyosis, chronic systemic illnesses, recent hormonal therapy (within the previous three months), or vitamin D supplementation during the preceding six months were excluded from the study.

Sample Size

The sample size was calculated based on a previously reported moderate inverse correlation ($r = 0.40$) between serum vitamin D3 levels and uterine fibroid size by Singh et al. (12). Assuming a 90% confidence level and 90% statistical power, the minimum required sample size was estimated to be 100 participants.

Data Collection

After obtaining informed consent, detailed demographic and clinical information was collected using a structured proforma. Information regarding age, residence, educational status, body mass index (BMI), menstrual history, obstetric history, presenting complaints, family history, and relevant medical history was recorded. A comprehensive general, systemic, and gynecological examination was performed for all participants.

Ultrasonographic Evaluation

All participants underwent pelvic ultrasonography using transabdominal and/or transvaginal approaches according to clinical suitability. The presence or absence of uterine fibroids was confirmed, and in women with fibroids, the number, location (submucosal, intramural, or subserosal), and three perpendicular diameters were recorded. Fibroid volume was calculated using the standard ellipsoid formula:

Fibroid volume = $0.523 \times \text{length} \times \text{width} \times \text{depth}$

Measurement of Serum Vitamin D3

Approximately 3–5 mL of venous blood was collected under aseptic conditions from each participant. Serum was separated and analyzed for 25-hydroxyvitamin D3 [25(OH)D] concentration using a standardized chemiluminescence immunoassay (CLIA) method in the central laboratory. Vitamin D status was classified as deficient (<20 ng/mL), insufficient (20–29 ng/mL), or sufficient (≥ 30 ng/mL).

Outcome Measures

The primary outcome was the association between serum vitamin D3 levels and the presence of uterine fibroids. The secondary outcome was the correlation between serum vitamin D3 levels and fibroid volume among women with uterine fibroids.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean $\pm$ standard deviation, while categorical variables were presented as frequencies and percentages. Comparisons between groups were performed using the independent Student's *t*-test for continuous variables and the Chi-square test for categorical variables. Correlation between serum vitamin D3 levels and fibroid volume was assessed using Pearson's correlation coefficient. A *p* value of <0.05 was considered statistically significant.

RESULTS

The present study was conducted among 100 women of reproductive age group, 50 women diagnosed with uterine fibroids and 50 women without uterine fibroids attending the Department of Obstetrics and Gynaecology, at a tertiary care centre.

The majority of women with uterine fibroids belonged to the 31–35-year age group (28%), whereas controls were predominantly aged 26–30 years (28%), with no significant difference in age distribution ($p=0.621$). Most participants in both groups resided in urban areas (64% vs. 60%; $p=0.682$) and had secondary or higher education ($p=0.437$). However, overweight and obesity were more common among cases (44% and 24%, respectively) than controls (32% and 12%, respectively), while normal BMI was more frequent among controls (48% vs. 28%), demonstrating a significant association between higher BMI and uterine fibroids ($p=0.041$). (Table 1)

Table 1: Baseline sociodemographic and anthropometric characteristics of the study participants

Variable	Category	Cases (n=50)	Controls (n=50)	p-value
Age group (years)	20–25	6 (12%)	8 (16%)	0.621
	26–30	10 (20%)	14 (28%)	
	31–35	14 (28%)	12 (24%)	
	36–40	12 (24%)	10 (20%)	
	41–45	8 (16%)	6 (12%)	
Residence	Urban	32 (64%)	30 (60%)	0.682
	Rural	18 (36%)	20 (40%)	
Educational status	Illiterate	6 (12%)	4 (8%)	0.437
	Primary	10 (20%)	8 (16%)	
	Secondary	16 (32%)	14 (28%)	
	Graduate & above	18 (36%)	24 (48%)	
Body mass index (kg/m ²)	<18.5 (Underweight)	2 (4%)	4 (8%)	0.041*
	18.5–24.9 (Normal)	14 (28%)	24 (48%)	
	25.0–29.9 (Overweight)	22 (44%)	16 (32%)	
	≥30.0 (Obese)	12 (24%)	6 (12%)	

Women with uterine fibroids had a significantly higher prevalence of irregular menstrual cycles (32% vs. 16%; $p=0.048$), prolonged menstrual flow lasting more than five days (72% vs. 28%; $p<0.001$), menorrhagia (60% vs. 16%; $p<0.001$), and early menarche before 15 years of age (60% vs. 36%; $p=0.018$) compared with controls. A positive family history of fibroids was also significantly more common among cases (36% vs. 16%; $p=0.021$). In contrast, parity, history of abortion, and infertility did not differ significantly between the two groups ($p>0.05$). (Table 2)

Table 2. Menstrual and obstetric characteristics of the study participants

Variable	Category	Cases (n=50)	Controls (n=50)	p-value
Menstrual cycle	Regular	34 (68%)	42 (84%)	0.048*
	Irregular	16 (32%)	8 (16%)	
Duration of menstrual flow	≤5 days	14 (28%)	36 (72%)	<0.001*
	>5 days	36 (72%)	14 (28%)	
Menorrhagia	Present	30 (60%)	8 (16%)	<0.001*
	Absent	20 (40%)	42 (84%)	
Age at menarche (years)	<15	30 (60%)	18 (36%)	0.018*
	≥15	20 (40%)	32 (64%)	
Parity	Nulliparous	12 (24%)	8 (16%)	0.533
	Para 1	16 (32%)	14 (28%)	
	Para 2	14 (28%)	18 (36%)	
	≥Para 3	8 (16%)	10 (20%)	
History of abortion	Yes	10 (20%)	6 (12%)	0.275
	No	40 (80%)	44 (88%)	
History of infertility	Present	8 (16%)	4 (8%)	0.218
	Absent	42 (84%)	46 (92%)	
Family History of Fibroids	Present	18 (36%)	8 (16%)	0.021*
	Absent	32 (64%)	42 (84%)	

The mean serum vitamin D level was significantly lower among women with uterine fibroids (18.6 ± 6.2 ng/mL) than among controls (27.4 ± 7.1 ng/mL) ($p<0.001$). The mean fibroid volume in the case group was 68.5 ± 28.4 cm³, indicating predominantly moderate-sized fibroids. These findings suggest an association between lower serum vitamin D levels and the presence of uterine fibroids.

Vitamin D deficiency (<20 ng/mL) was observed in 64% of women with uterine fibroids compared with 28% of controls. Conversely, vitamin D sufficiency (≥30 ng/mL) was more common in controls (32%) than in cases (8%). The distribution of vitamin D status differed significantly between the two groups ($p<0.001$), indicating a strong association between vitamin D deficiency and uterine fibroids. (Table 3)

Table 3: Distribution of study subjects based on Serum Vitamin D3 Categories

Vitamin D Status	Cases (n=50)	Controls (n=50)	p-value
Deficient (<20 ng/ml)	32 (64%)	14 (28%)	<0.001*
Insufficient (20–29 ng/ml)	14 (28%)	20 (40%)	
Sufficient (≥30 ng/ml)	4 (8%)	16 (32%)	

Serum vitamin D levels decreased progressively with increasing fibroid volume. Women with small fibroids (<50 cm³) had the highest mean vitamin D level (22.8 ± 5.4 ng/mL), followed by those with moderate-sized fibroids (17.9 ± 4.8 ng/mL), whereas women with large fibroids (>100 cm³) had the lowest level (13.6 ± 3.9 ng/mL). This trend was statistically significant ($p=0.001$), suggesting an inverse relationship between vitamin D status and fibroid volume. (Table 4)

Table 4: Vitamin D Levels According to Fibroid Volume Categories

Fibroid Volume Category	Mean Vitamin D (ng/ml)	SD	p-value
Small Volume (<50 cm ³)	22.8	±5.4	0.001*
Moderate (50–100 cm ³)	17.9	±4.8	
Large (>100 cm ³)	13.6	±3.9	

A statistically significant moderate negative correlation was observed between serum vitamin D levels and fibroid volume ($r = -0.46$, $p=0.002$). This indicates that lower serum vitamin D concentrations were associated with larger fibroid volumes. (Table 5)

Table 5: Correlation Between Vitamin D and Fibroid Volume

Variable	Correlation Coefficient (r)	p-value
Vitamin D vs Fibroid Volume	-0.46	0.002*

Vitamin D deficiency was present in 32 (64%) women with uterine fibroids compared with only 14 (28%) controls, whereas vitamin D levels ≥20 ng/mL were more common among controls (72%) than cases (36%). The association between vitamin D deficiency and the presence of uterine fibroids was highly significant ($p<0.001$), suggesting that vitamin D deficiency may be an important risk factor for uterine fibroids. (Table 6)

Table 6: Association Between Vitamin D Deficiency and Fibroids

Vitamin D Status	Cases (n=50)	Controls (n=50)	p-value
Deficient (<20 ng/ml)	32 (64%)	14 (28%)	<0.001*
Not Deficient (≥20 ng/ml)	18 (36%)	36 (72%)	

DISCUSSION

The present case–control study evaluated the association between serum vitamin D levels and uterine fibroids among women of reproductive age while also assessing demographic, anthropometric, menstrual, obstetric, and familial factors. The findings demonstrated that women with uterine fibroids had significantly lower serum vitamin D levels than controls, a higher prevalence of vitamin D deficiency, and a significant inverse correlation between serum vitamin D levels and fibroid volume. In addition, higher body mass index (BMI), menstrual abnormalities, early menarche, and a positive family history were significantly associated with uterine fibroids, whereas age, residence, educational status, parity, abortion history, and infertility showed no significant association.

The demographic characteristics of the two groups were comparable with respect to age, residence, and educational status. Most women with uterine fibroids belonged to the 31–35-year age group, consistent with the well-established epidemiology of leiomyomas occurring predominantly during the late reproductive years. Stewart reported that uterine fibroids are uncommon before 25 years of age and become increasingly prevalent after 30 years (1). Similarly, Wise and Laughlin-Tommaso observed that fibroid incidence rises steadily after the third decade of life and peaks between 35 and 45 years (2). The lack of association between fibroids and residence or educational status in the present study is consistent with findings reported by Commandeur et al., who suggested that hormonal and genetic factors are more important determinants of fibroid development than socioeconomic characteristics (13).

A significant association was observed between BMI and uterine fibroids, with overweight and obese women accounting for 68% of cases compared with 44% of controls. Similar findings were reported by Baird et al., who demonstrated that obesity significantly increases the risk of uterine fibroids (3). Pavone et al. also identified obesity as an important modifiable risk factor because increased adipose tissue enhances peripheral estrogen production, thereby promoting leiomyoma growth (14). Bulun further emphasized the role of obesity in increasing estrogen bioavailability and stimulating smooth muscle proliferation within the uterus (15).

Women with uterine fibroids in the present study had significantly higher frequencies of irregular menstrual cycles, prolonged menstrual bleeding, menorrhagia, and early menarche. These observations are consistent with the FIGO PALM–COEIN classification, which recognizes leiomyoma as a major structural cause of abnormal uterine bleeding (4). Gupta et al. similarly reported heavy menstrual bleeding as the most common clinical manifestation of uterine fibroids (16). Wise and Laughlin-Tommaso also identified early menarche as an established risk factor because prolonged lifetime exposure to estrogen and progesterone increases the likelihood of fibroid development (2).

No significant association was observed between uterine fibroids and parity, history of abortion, or infertility. Comparable findings were reported by Pritts et al., who concluded that infertility is influenced primarily by fibroid size and location rather than the mere presence of fibroids (17). Coronado et al. also found that parity may have a modest protective effect, although the association becomes inconsistent after adjustment for confounding variables (18). These findings suggest that reproductive factors alone have limited influence compared with hormonal and metabolic determinants.

A positive family history was significantly more common among women with uterine fibroids, supporting the importance of genetic susceptibility. Commandeur et al. demonstrated that women with affected first-degree relatives have a two- to three-fold higher risk of developing fibroids (13). Molecular evidence further supports this relationship, with Mehine et al. identifying recurrent MED12 mutations in the majority of uterine leiomyomas (19).

The principal finding of the present study was the significantly lower serum vitamin D concentration among women with uterine fibroids. The mean serum vitamin D level was 18.6 ± 6.2 ng/mL in cases compared with 27.4 ± 7.1 ng/mL in controls, while vitamin D deficiency was present in 64% and 28% of participants, respectively. These findings closely agree with those of Paffoni et al., who reported significantly lower serum vitamin D concentrations among women with uterine leiomyomas (8). Singh et al. also demonstrated significantly lower vitamin D levels among Indian women with fibroids (12). Furthermore, Baird et al. observed that women with sufficient vitamin D levels had a substantially lower risk of fibroid development (9). A recent systematic review by Combs et al. further concluded that vitamin D deficiency is consistently associated with uterine fibroids and may represent a promising preventive and therapeutic target (10). Considering the high prevalence of vitamin D deficiency in India reported by Harinarayan and Joshi (11), these findings have important public health implications.

Another important observation was the significant inverse relationship between serum vitamin D levels and fibroid volume. Mean vitamin D concentrations progressively declined from women with small fibroids to those with large fibroids, with a significant negative correlation between vitamin D concentration and fibroid volume. Similar findings have been reported by Sharan et al., who demonstrated that vitamin D inhibits proliferation of uterine leiomyoma cells through regulation of catechol-O-methyltransferase (6). Ali et al. further showed that vitamin D3 reduces DNA damage and suppresses molecular pathways involved in fibroid progression (7). These biological mechanisms support the inverse association observed in the present study and suggest that vitamin D deficiency contributes not only to fibroid occurrence but also to tumor growth.

Although the present study was limited by its single-center design and relatively small sample size, it provides additional evidence supporting vitamin D deficiency as a significant and potentially modifiable risk factor for uterine fibroids. Larger multicenter prospective studies and randomized controlled trials are warranted to determine whether correction of vitamin D deficiency can prevent fibroid development or reduce disease progression. Overall, maintaining adequate vitamin D status may represent a simple, safe, and cost-effective adjunct strategy in the prevention and management of uterine fibroids.

CONCLUSION

The present study demonstrated a significant association between serum vitamin D deficiency and uterine fibroids among women of reproductive age. Women with fibroids had significantly lower mean serum vitamin D levels and a higher prevalence of vitamin D deficiency compared with healthy controls. Furthermore, serum vitamin D levels showed a significant inverse correlation with fibroid volume, indicating that lower vitamin D concentrations were associated with larger fibroid size. Higher body mass index, menstrual irregularities, prolonged menstrual bleeding, menorrhagia, early menarche, and a positive family history were also identified as significant factors associated with uterine fibroids, whereas demographic characteristics and obstetric factors showed no significant association. These findings support the hypothesis that vitamin D deficiency may contribute to both the development and progression of uterine fibroids. Routine assessment of vitamin D status in women at risk for fibroids may facilitate early identification and management. Further large-scale prospective studies are warranted to establish causality and evaluate the therapeutic potential of vitamin D supplementation.

Consent for Publication

Written informed consent for publication of anonymized clinical and research data was obtained from all study participants.

Availability of Data and Materials

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request and in accordance with institutional policies.

Funding

The authors received no external funding for this study.

Conflict of Interest

The authors declare that they have no competing interests.

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The authors sincerely thank all the participants who consented to take part in this study. We express our gratitude to the faculty and staff of the Department of Obstetrics and Gynaecology and the Department of Biochemistry for their support in patient recruitment, laboratory investigations, and data collection. We also acknowledge the administration of the study institution for providing the necessary facilities and infrastructure to conduct this research successfully. Finally, we thank everyone who contributed directly or indirectly to the completion of this study.

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