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Original article

Cross-Sectional Assessment of the Association Between Circulating 25(OH)D Levels and Uterine Fibroid Occurrence Among Libyan Women of Reproductive Age

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Abstract
Benign tumors of the uterus, known as leiomyomas, constitute the most common non-cancerous growths occurring in the women's reproductive system and are often associated with substantial morbidity among women of reproductive age. Although many cases remain clinically silent, a significant proportion experience symptoms that impair daily functioning and reproductive health. The absence of well-established preventive strategies has directed attention toward modifiable biological factors, including vitamin D status. This comparative study included 122 women (71 diagnosed with fibroids and 51 healthy controls). Clinical data were obtained, and serum 25-hydroxyvitamin D concentrations were measured. Fibroid dimensions were assessed using ultrasonography. Statistical analysis employed independent t-tests for group comparisons and Pearson's correlation coefficient to examine relationships between variables. Comparative analysis revealed no meaningful variations in age or BMI between the study groups ($p > 0.05$). Both groups demonstrated vitamin D levels falling within the insufficient category, showing comparable measurements across groups ($p = 0.929$). Notably, an inverse relationship emerged between serum vitamin D concentrations and the largest fibroid measurements ($r = -0.58$, $p < 0.001$), indicating that lower vitamin D levels corresponded with larger tumor size. Furthermore, women diagnosed with fibroids exhibited a higher prevalence of metabolic conditions, especially elevated blood pressure and respiratory disorders. Although serum vitamin D levels did not differ significantly between groups, lower vitamin D concentrations were significantly associated with increased fibroid size, potentially reflecting its role in regulating cellular proliferation and extracellular matrix dynamics within the myometrium.
Keywords: *Uterine Leiomyoma, Vitamin D, 25-Hydroxyvitamin D, Fibroid Size, Ultrasonography, Hypovitaminosis D.*

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Introduction

Uterine smooth muscle tumors (fibroids) are widely encountered in gynecological practice and may lead to diverse symptomatic disturbances that affect overall well-being [1]. Uterine fibroids exhibit variability in terms of their location, size, and associated symptoms. Although many women remain asymptomatic, a considerable proportion experience significant acute and chronic symptoms [2]. Considering the diverse etiologies of fibroid tumors, a conclusive preventive treatment has yet to be identified, even though numerous initial attempts have been made [3]. The choice between conservative and operative interventions is determined by multiple clinical and demographic variables, including disease severity and fertility goals. Notably, available pharmacologic modalities remain largely palliative, with surgery continuing to represent the only definitive option [4,5].

Vitamin D is a steroid hormone; it exerts significant influence across various body systems, like the nervous, muscular, immune, and reproductive systems. Its functions encompass the control of cell division and specialization, suppression of angiogenesis, and promotion of programmed cell death [6]. Despite incomplete clarification of the mechanistic pathways, epidemiological and experimental data point toward a link between hypovitaminosis D [7]and enhanced myometrial proliferation, supporting its possible involvement in fibroid initiation and progression [8,9]. Evidence from both laboratory research and clinical investigations suggests that vitamin D can disrupt critical molecular mechanisms underlying fibroid development.

Through modulation of steroid hormone receptor pathways, control of genes guiding apoptosis and cell growth, and limitation of extracellular matrix synthesis, vitamin D seems to oppose fundamental processes driving uterine tumor expansion [10, 11, 12]. Multiple epidemiological studies have reported that elevated serum vitamin D levels correlate

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with decreased risk of developing uterine fibroids [13, 14]. Through its regulatory influence on steroid hormone pathways, 1,25(OH)2D3 may represent a promising adjunctive approach in the medical control of uterine leiomyomas [15]. This study was designed to examine the potential association linking vitamin D levels and the development of uterine fibroids in women during their reproductive years.

Materials and Methods

Study Design and Participants

This cross-sectional study included 122 women of reproductive age, divided into fibroid group (n = 71) and control group (n = 51). Participants were recruited from public and private outpatient gynecological clinics in Al-Bayda City from November 2023 to March 2026. Verbal consent was obtained from all participants prior to their inclusion. The purpose of the study was clearly explained to each participant, and their confidentiality was strictly maintained. Women with confirmed uterine fibroids by ultrasonography were included in the case group, while controls had no sonographic evidence of fibroids.

Exclusion Criteria

Participants were excluded from the study if they declined to provide informed consent or if they were currently receiving vitamin D supplementation for unrelated medical indications such as osteoporosis or osteomalacia. Individuals presenting with concurrent gynecological pathologies, including ovarian masses, endometrial hyperplasia, or polyps, were also excluded to avoid confounding effects. In addition, participants suffering from chronic kidney disease (stages 3–5) or disorders of calcium metabolism, such as primary or secondary hyperparathyroidism, were not eligible for inclusion.

Clinical and Anthropometric Assessment

Data collected included age, height, weight, and body mass index (BMI). Medical history (hypertension, diabetes mellitus, bronchial asthma) and surgical history (cesarean section, appendectomy, myomectomy) were documented.

Laboratory Analysis

Blood samples were collected to assess 25-hydroxyvitamin D concentrations using standardized laboratory methods. Vitamin D insufficiency was defined as levels below 30 ng/mL.

Ultrasonographic Evaluation

In the fibroid group, the maximum fibroid diameter (cm) was measured using transabdominal or transvaginal ultrasonography.

Statistical Analysis

Continuous variables were analyzed using independent samples t-tests. Categorical variables were summarized as frequencies and percentages. Pearson's correlation coefficient (r) was used to assess associations between serum vitamin D levels and fibroid size as well as age. Statistical analysis was performed using SPSS version 26.0. A p-value < 0.05 was considered statistically significant.

Results

Baseline Demographic and Anthropometric Characteristics, Medical, and Surgical History

The study groups were well-matched for age and BMI. Anthropometric data showed no statistically significant differences in age, BMI, or weight between the two groups, confirming they were well-matched for metabolic comparison (Table 1).

Table 1. Socio-demographic Profile

Variable	Control Group (n=51)	Fibroid Group (n=71)	p-value
Age (years)	34.24 ±7.28	34.80 ±5.71	0.705
Height (m)	1.61 ±0.05	1.62 ±0.04	0.231

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Weight (kg)	77.57 ±12.18	77.41 ±12.10	0.943
BMI (kg/m²)	30.11 ±5.11	29.39 ±4.68	0.425

Analysis of clinical histories revealed that most participants had no reported comorbidities. However, relatively higher frequencies of hypertension and bronchial asthma were observed in the fibroid group compared with healthy controls (Table 2). Surgical history was also more common among women with fibroids, suggesting a more complex clinical background in these patients (Table 3).

Table 2. Clinical Characteristics and Systemic Comorbidities

Medical Status	Healthy Controls (n=51)	Fibroid Group (n=71)
No Comorbidities	64.7%	53.5%
Hypertension	7.8%	12.7%
Diabetes Mellitus	11.8%	11.3%
Bronchial Asthma	3.9%	8.5%

Table 3. Surgical History Distribution

History	Control (%)	Fibroid (%)
No Prior Surgery	86.6%	78.6%
Cesarean Section	10.0%	11.4%
Appendectomy	1.7%	5.7%
Myomectomy	1.7%	4.3%

Comparison of Serum 25-Hydroxyvitamin D Levels

The principal variable evaluated in this study was the concentration of serum 25-hydroxyvitamin D. Analysis indicated that the average concentrations for both groups within the insufficient range (<30 ng/mL according to the study criteria). Statistical comparison revealed no meaningful variation between the control participants (mean: 22.92 ± 9.01 ng/mL) and those with fibroids (mean: 22.76 ± 9.57 ng/mL), yielding a non-significant p-value of 0.929 **(**Figure 1).

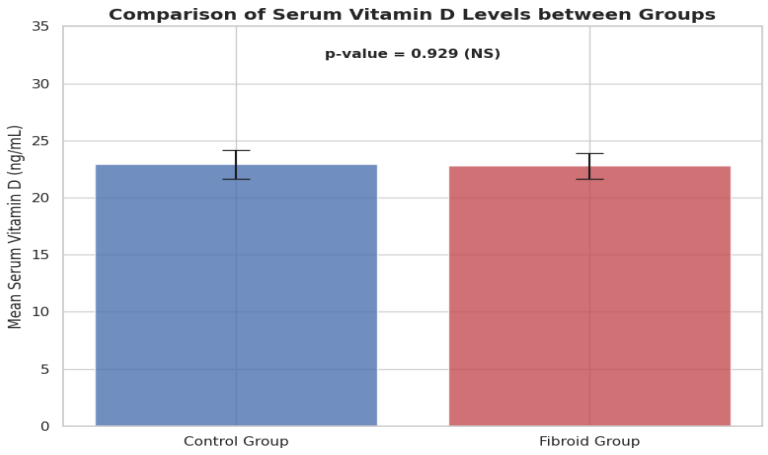

Figure 1. Comparison of Serum Vitamin D Levels of both groups

Correlation Analysis

Relationship of Vitamin D Status with Fibroid Tumor Size

One primary research goal involved assessing whether lower circulating vitamin D concentrations correlate with larger fibroid measurements.

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Table 4. Pearson Correlation Analysis of Vitamin D Status and Tumor Size Parameters

Correlation Pair	Pearson's r	Significance (p)
Vitamin D vs. Max Fibroid Size	–0.58	< 0.001*

Statistical significance at p < 0.01

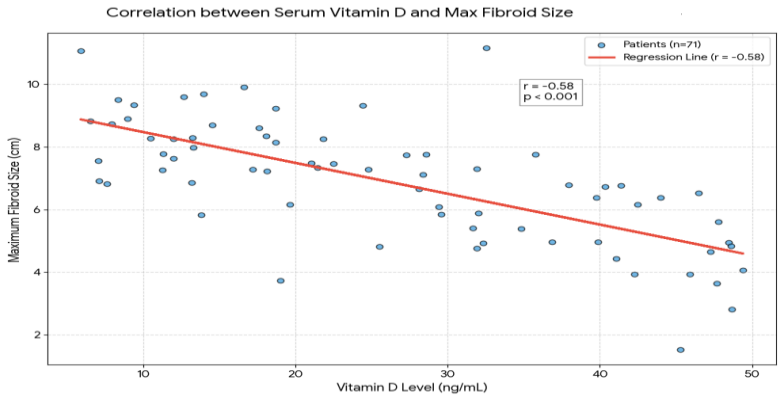

Figure2. Correlation of Vitamin D with Fibroid Dimension

Inverse relationship between serum Vitamin D levels (ng/mL) and the maximum dimension of uterine fibroids (cm) in the study group (n = 71). The red line represents the linear regression, indicating a significant negative correlation (r = -0.58, p < 0.001) (Table 4) - (Figure 2).

Analysis of Vitamin D Status in Relation to Age

To assess whether age-related changes in vitamin D status might confound the findings, we examined correlations between participant age and 25-hydroxyvitamin D levels. Statistical analysis revealed no meaningful association between circulating 25-hydroxyvitamin D concentrations and participant age (r = 0.09, p = 0.320). This finding indicates that vitamin D status in our study was not age-dependent. (Table 5).

Table 5. Correlation of Vitamin D Level and Age

Correlation Variables	Pearson's r	Significance (p)
Vitamin D vs. Age	0.09	0.320 (NS)

Discussion

A key microscopic diagnostic feature of uterine leiomyoma is the replacement of the normal myometrial architecture by tightly arranged, whorled bundles of myometrial smooth muscle cells, which are surrounded by an abundant extracellular matrix frequently exhibiting hyalinized changes [16]. Serum 25-hydroxyvitamin D may contribute to the progression and enlargement of uterine leiomyomas. A significant inverse correlation was found (r = –0.58, p < 0.001) between vitamin D levels and the maximum diameter of fibroids, suggesting that lower vitamin D status is associated with larger leiomyoma size and increased tumor growth. Research demonstrates that vitamin D can suppress the Transforming Growth Factor-beta 3 (TGF-β3) signaling cascade. As a central regulator of fibrosis, TGF-β3 promotes overproduction of extracellular matrix components—including types I and III collagen, fibronectin, and proteoglycans—that form the structural basis of leiomyomas [2]. Our findings are consistent with this molecular model; reduced vitamin D levels may diminish the regulatory control over extracellular matrix accumulation, resulting in enhanced matrix deposition and the consequent enlargement of fibroid masses observed in our case group.

Leiomyoma expansion occurs through combined mechanisms of smooth muscle cell multiplication and enlargement, hyperplasia, and hypertrophy. Vitamin D has been found to reduce expression of Proliferating Cell Nuclear Antigen (PCNA), a critical indicator of cellular proliferation and cell cycle progression in fibroid tissue [3]. The marked inverse association observed in our analysis suggests a potential relationship between lower vitamin D levels and increased

cellular proliferation and enhanced myofibroblast differentiation. This disruption of normal tissue architecture is further supported by our findings, which show that patients with the lowest 25(OH)D concentrations more frequently presented with larger fibroids. Our findings indicated elevated rates of high blood pressure (12.7%) and bronchial asthma (8.5%) among participants with uterine fibroids compared to controls. Chronic systemic inflammation and vascular stress are known to alter the tissue microenvironment.

In the absence of adequate Vitamin D—which also exerts protective effects on the vascular endothelium—the myometrium may be more susceptible to the hypoxia-inducible factors that promote angiogenesis and further fibroid growth [6]. No significant correlation was observed between serum vitamin D levels and age ($r = 0.09$) in this analysis. This finding suggests that vitamin D insufficiency is unlikely to be age-dependent and may instead reflect a more persistent metabolic state, which could consistently contribute to fibrotic processes over time [17]. These results emphasize vitamin D's dual role as both a dietary nutrient and a steroid hormone regulating cellular balance within the myometrium. Furthermore, clinical studies indicate that vitamin D supplementation could potentially retard or halt fibroid expansion [18].

Conclusion

In summary, these findings highlight the clinical importance of early screening for vitamin D insufficiency. Vitamin D supplementation may warrant further investigation as a potential adjunctive strategy for limiting fibroid progression and reducing disease burden, which may ultimately decrease the need for surgical intervention.

Conflict of Interest

There are no personal, financial, or professional interests to declare.

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