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Vitamin D deficiency and uterine fibroids in Kashmiri women: A retrospective case-control study

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Abstract
Uterine fibroids are the most common benign tumors of the female genital tract and, although often asymptomatic, can cause menorrhagia, pelvic pain, infertility, and reduced quality of life; emerging evidence suggests that vitamin D, which has antiproliferative effects on myometrial and fibroid cells, may play a role in their pathogenesis, with deficiency being linked to an increased risk of fibroid development.
Objective: To determine the association between low vitamin D levels and the occurrence of uterine fibroids.
Material & methods: This hospital-based case-control study was conducted at the Department of Obstetrics and Gynaecology, LD Hospital, Srinagar, enrolling 80 women (40 cases and 40 matched controls) using convenience sampling. Participants provided informed consent, underwent face-to-face interviews to collect socio-demographic and clinical data, and had blood samples collected for biochemical analysis in accordance with standard procedures.
Results: A total of 80 women (40 cases & 40 controls) were included, with comparable age, residence, BMI, parity, and comorbidities, though infertility was more common among cases. Cases had significantly lower mean serum vitamin D levels than controls (21.54 ± 15.12 vs 31.42 ± 18.68 ng/mL; p = 0.011), with deficiency (<20 ng/mL) linked to higher odds of fibroids (OR 4.33; 95% CI 1.67-11.23; p = 0.002).
Conclusion: The study found that women with uterine fibroids had significantly lower vitamin D levels, with deficiency and infertility identified as independent risk factors.

Keywords: Case control, uterine fibroids, vitamin D, Kashmiri, Infertility

Introduction
The most frequent benign neoplastic threat that occurs in women of reproductive age is uterine fibroids. These are monoclonal, benign tumors that arise from the smooth muscle cells of the uterus and are predominantly located in the pelvis. They constitute one of the most common pathologies of the female genital tract [1, 2]. UFs occur in 5-70% of all women [3-5]. UFs are more prevalent among reproductive-aged women and are not observed in pre-pubescent girls, indicating that tumor origin depends on hormonal changes [3, 6, 7]. By the age of 50 years, 77% of women get these monoclonal tumours, whereas they manifest clinically in only 25%-50% of women [1]. UF tumors vary greatly in size, location, and symptoms. Most tumors are largely asymptomatic, but they may also cause a wide range of severe and chronic symptoms in approximately one-quarter to one-third of the affected women [2]. The most common symptoms include menorrhagia, prolonged menstrual bleeding, pelvic pressure, pelvic pain, secondary iron deficiency anemia, abdominal and pelvic pain, gastric disorders like bloating and constipation, voiding symptoms, infertility, and obstetric pathologies (Including miscarriage and premature labor) and infertility [8, 2]. UFs are also a massive financial burden [1]. In addition to the direct health care expenses, indirect costs due to lost income from time off work and disability due to uterine fibroids are estimated to be 1.6 to 17.2 billion dollars annually and globally [9, 10]. All these factors adversely affect a woman's quality of life.
The exact cause of uterine fibroids remains unclear. However, considering the immunomodulatory effects of vitamin D on cell growth and cell differentiation, several studies have cited vitamin D deficiency as a potential cause of uterine fibroids [13]. For humans, vitamin D is considered to be one of the essential nutrients. Vitamin D is a name for a group of steroid compounds, soluble in fats, which exert powerful effects on the human body, and whose receptors are found in various organs the myometrium and UF tumor tissue [2]. Studies have reported that t both leiomyoma and primary myometrial cells showed an inhibited growth

pattern corresponding to the concentration of vitamin D (14).
The effect of Uterine Fibroid causes morbidities that can be seen in all ethnicities, but are common in African and Asian women. This disparity is thought to be associated with serum levels of vitamin D, as the risk of vitamin D deficiency is ten times higher in developing countries such as India and Africa (1). With the changing lifestyle, the deficiency of vitamin D is increasing. There is a lack of studies regarding the relationship between uterine fibroids and vitamin D, especially in the Kashmiri population. Owing to this background, the present study was conducted with the aim of studying the association between vitamin D levels and fibroids among Kashmiri women.

Material and Methods

- **Study Design:** Hospital-based case-control study.
- **Study Setting:** Department of Obstetrics and Gynaecology, Lalla Ded (LD) Hospital. It is an associated hospital of the Government Medical College Srinagar.
- **Study Period:** The Study was conducted over a period of 6 months from June 2025 to November 2025.
- **Study Participants:** A total of 80 women were enrolled and divided into two equal groups (1:1 ratio):
- **Cases (n = 40):** Women diagnosed with uterine fibroids confirmed by transabdominal ultrasonography.
- **Controls (n = 40):** Women without any evidence of uterine fibroids.

Inclusion criteria

1. Aged 18 years and above
2. Those willing to participate

Exclusion criteria

1. Using vitamin D or calcium supplements within 6 months before study enrolment.
2. Pregnancy
3. Lactation
4. Women with parathyroid dysfunction.
5. Women with chronic medical conditions such as hypertension, diabetes, CKD, or any cardiac ailment.

Each case was matched with one control (1:1).

Sampling technique and sample size: A convenience sampling method was used. The final sample comprised 40 cases and 40 controls.

Study procedure

Participants were thoroughly informed about the study, and written informed consent was obtained. Face-to-face interviews were conducted using a semi-structured, pretested questionnaire. The questionnaire included information on socio-demographic characteristics such as age and residence, along with clinical and obstetric details including comorbidities, obstetric history, presence of heavy menstrual bleeding, dysmenorrhea and infertility status if present (primary or secondary). In women diagnosed with fibroids, additional data regarding the number, location, and type of fibroids (intramural, subserosal, or submucosal) as well as the maximum fibroid diameter (in millimetres) were recorded. All participants were assured of confidentiality throughout the study. Following interview and clinical evaluation, approximately 5 ml of venous blood was collected from each participant in the sitting position using standard aseptic precautions. A tourniquet was applied briefly to minimize stasis, and the sample was drawn from the antecubital vein into lithium heparin vacutainer tubes. The samples were promptly transported to the laboratory for biochemical analysis. Serum 25-hydroxyvitamin D [25(OH)D] levels, considered the most reliable indicator of vitamin D status as it reflects cutaneous synthesis, dietary intake, and hepatic conversion, were measured using the electrochemiluminescence immunoassay (ECLIA) technique with commercially available ELISA kits. Based on the serum concentrations, vitamin D status was categorized as:

Vitamin D levels	Interpretation
<10 ng/ml	Vitamin D Deficiency
10 to 19.9	Vitamin D insufficiency
>=20	No deficiency

Statistical analysis

Data was entered in Microsoft Excel software and analysed using an appropriate statistical software. Categorical variables were expressed as frequencies and percentages. The crude measure of association between Vitamin D levels and fibroid was expressed as the Odds Ratio (OR), and its 95% confidence interval (CI). To control for confounding variables, the data were analyzed by calculating the adjusted Odds Ratio by means of multivariable logistic regression to evaluate the extent of risk association. A p-value less than 0.05 was considered statistically significant.

Results

A total of 80 women were included in the study, comprising 40 cases with uterine fibroids and 40 age-matched (± 5 years) controls without fibroids. The age distribution, residence, body mass index, parity, and comorbidity profile were comparable between the two groups; however, infertility was more frequent among cases (Table 1). Among cases, most fibroids were ≥3 cm in size, and intramural fibroids were the predominant type (Table 2).
Mean serum vitamin D levels were significantly lower in cases than controls (21.54 ± 15.12 ng/mL vs 31.42 ± 18.68 ng/mL; p = 0.011). Vitamin D deficiency (<20 ng/mL) was present in 65% of cases compared with 30% of controls and was associated with a significantly higher odds of uterine fibroids (OR 4.33; 95% CI 1.67-11.23; p = 0.002) (Table 3). On multivariable logistic regression analysis, serum vitamin D levels remained independently associated with uterine fibroids, with a reduction in odds for each 1 ng/mL increase in vitamin D (OR 0.96; 95% CI 0.93-0.99; p = 0.019). Infertility was also independently associated with fibroids, while age, BMI, and parity were not significant after adjustment (Table 4).

Table 1: Baseline characteristics of study participants.

Variable	Cases (n=40)		Controls (n=40)	
	Frequency	Percentage (%)	Frequency	Percentage (%)
Age (years)				
≤30	7	17.5	9	22.5
31-40	18	45.0	16	40.0
>40	15	37.5	15	37.5
Residence				
Urban	28	70.0	30	75.0
Rural	12	30.0	10	25.0
Body Mass Index (kg/m^2)				
Normal (<25)	32	80.0	34	85.0
Overweight (25-29.9)	8	20.0	6	15.0
Obese (≥30)	0	0	0	0
Parity				
Nulliparous	9	22.5	8	20.0
Primiparous	7	17.5	6	15.0
Multiparous (≥2)	24	60.0	26	65.0
Infertility status				
Present	14	35.0	6	15.0
Absent	26	65.0	34	85.0
Comorbidity				
Present	7	17.5	5	12.5
Absent	33	82.5	35	87.5

Table 2: Distribution of cases according to the largest fibroid size and type of uterine fibroid

Variable	Cases (n=40)	
	Frequency (n)	Percentage (%)
Largest fibroid size		
<3 cm	6	15.0
3-5 cm	17	42.5
>5 cm	17	42.5
Type of fibroid		
Intramural	24	60.0
Subserosal	14	35.0
Submucosal	2	5.0

Table 3: Association between Serum Vitamin D Levels and Uterine Fibroids among Cases and Controls.

Vitamin D levels (ng/mL)	Cases (n=40)	Controls (n=40)	Odds Ratio (95% CI)	P value
Deficient (<20)	26	12	4.33 (1.67 - 11.23)	0.002
Non Deficient (≥20)	14	28		
Mean± SD	21.54±15.12	31.42±18.68		0.011

Table 4: Multivariable Logistic Regression Analysis for Factors Associated with Uterine Fibroids.

Variable	Adjusted Odds Ratio (aOR)	95% Confidence Interval	P value
Serum Vitamin D (per 1 ng/mL increase)	0.96	0.93 - 0.99	0.019
Age (per year increase)	1.02	0.95 - 1.10	0.51
BMI (Overweight vs Normal)	1.31	0.42 - 4.08	0.64
Parity (Nulliparous vs Multiparous)	1.58	0.61 - 4.09	0.35
Infertility (Present vs Absent)	2.87	1.01 - 8.12	0.047

* adjusted for age, BMI, parity, and infertility.

Discussion

In recent years, vitamin D has been recognized for its roles beyond bone health, with evidence suggesting protective effects against various adverse health outcomes, including cardiovascular disease, malignancies, autoimmune disorders, infections, and pregnancy-related complications. Data from the NIEHS Uterine Fibroid Study suggest an inverse association between vitamin D levels and uterine fibroid development [15]. However, studies examining this relationship are limited, particularly in the Kashmiri population. Therefore, the present study was conducted to assess the association between serum vitamin D levels and uterine fibroids among Kashmiri women.

In our study, we found a statistically significant association between low serum vitamin D levels and the presence of uterine fibroids among Kashmiri women with an Odds ratio of 4.33 (Table 3). The risk of developing uterine fibroids was found to increase progressively with decreasing vitamin D levels. Importantly, this association persisted even after adjustment for potential confounders such as age, body mass index, parity, and infertility, highlighting an independent relationship between vitamin D status and uterine fibroid development (Table 4). Our findings are consistent with existing literature demonstrating an inverse relationship between serum vitamin D levels and uterine fibroids. Baird DD *et al*. reported lower odds of fibroids among women with sufficient vitamin D compared to those with insufficiency [15]. Similar associations have been observed by

Paffoni A *et al*. [16], Kapoor S *et al*. [1], and Cetin F *et al*, who noted lower vitamin D levels in women with a higher number of fibroids [13]. The biological plausibility of this association is supported by many studies. Vitamin D has been shown to exert anti-proliferative, anti-fibrotic, and pro-apoptotic effects on leiomyoma cells. It also inhibits leiomyoma cell proliferation, reduces extracellular matrix production, and suppresses profibrotic mediators such as transforming growth factor-β3. These mechanisms suggest that deficiency of vitamin D may therefore remove an important regulatory control on myometrial smooth muscle cell growth, facilitating fibroid development [14, 17].

Given the central role of vitamin D in regulating cellular proliferation and fibrosis, widespread vitamin D deficiency may contribute meaningfully to uterine fibroid development. In Kashmiri women, particularly those with darker skin pigmentation, reduced cutaneous synthesis of vitamin D due to limited sunlight exposure significantly lowers circulating vitamin D levels. This deficiency may diminish the local vitamin D-D-mediated inhibitory effects on myometrial smooth muscle cells, thereby promoting leiomyoma initiation and growth. The high prevalence of vitamin D deficiency among Kashmiri women is attributable to prolonged winters with limited sunlight exposure, traditional clothing practices, and dietary inadequacies. This offers a biologically plausible explanation for the increased susceptibility to uterine fibroids in this population, thereby reinforcing the findings of the present study [18].

Another important finding in this study was the independent association between infertility and uterine fibroids. Fibroids (especially intramural and submucosal) are known to affect fertility adversely by causing uterine cavity distortion, disrupting endometrial receptivity, and altering uterine contractility. Our findings are supported by various studies in the literature supporting higher rates of infertility among women with fibroids [20]. However, age, BMI, and parity were not independently associated with fibroids even after adjustment (Table 4).

In our study, heavy menstrual bleeding (HMB) was the most common presenting symptom among cases, reported by 52.5% of women. Infertility was the next most frequent complaint (12.5%), followed by dysmenorrhea and abdominal pain (7.5% each). Other symptoms, including polymenorrhagia, postmenopausal bleeding, increasing abdominal size, and combined presentations, were less common. Overall, menstrual disturbances constituted the predominant clinical presentation among cases. Our results are supported by the literature [21]. With regard to fibroid characteristics, intramural fibroids were the most common type, and the majority were ≥3 cm in size, which is consistent with prior literature [22].

Limitations: The study had a few limitations. First, the sample size was relatively small, which may limit the generalizability of the findings. Second, it was conducted at a single hospital rather than across multiple centers, restricting the applicability of the results to broader populations. Additionally, the level of sun exposure, which could influence outcomes, was not assessed.

Conclusion

This study demonstrated that women with uterine fibroids had significantly lower vitamin D levels compared to those without fibroids. Low vitamin D emerged as an independent and significant risk factor for the development of uterine fibroids, suggesting it may be a potentially modifiable factor. Infertility also appeared as an independent risk factor. Given the high prevalence of vitamin D deficiency in the Kashmiri population, these findings have important clinical and public health implications, reinforcing the role of vitamin D in the pathophysiology of uterine fibroids and underscoring the need for further prospective and interventional studies.

Conflict of Interest

Not available

Financial Support

Not available

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