CLINICAL PROFILE OF SERUM VITAMIN D LEVELS AND UTERINE FIBROIDS

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Abstract: -

Introduction: The most typical variety of benign uterine tumors are uterine fibroids, often known as leiomyomas or myomas. They originate from myometrium since they are uterine smooth muscle monoclonal cancers. Most of their makeup is made up of extracellular matrix (ECM), which is composed of proteoglycans, fibronectin, and collagen.

Methods: This cross-sectional study was carried out between January 1, 2021, and January 1, 2022, by the Department of Obstetrics and Gynaecology at Jawahar Lal Nehru Medical College in Ajmer in collaboration with the department of radiology and with permission from the institute's ethics council.

Results: According to the severity of vitamin d deficiency, it was found that the vitamin d levels in the study group were significantly lower than those in the control group: 39 percent of the study group had vitamin d levels below 19 ng/ml, compared to 14 percent and 13 percent in the control group for levels between 10 and 19 ng/dl, respectively. Vit. D levels averaged 15.13 ng/ml in the study group and 24.82 ng/ml in the control group. (Profoundly higher). Only 9% of women had fibroids greater than 5, while 53% had fibroids between 3 and 4. Vitamin D and the quantity of fibroids had an antagonistic relationship (P 0.001).

Conclusion: Our cross-sectional study makes vitamin D's impact in UF development difficult to identify. More comprehensive prospective cohort studies that monitor vitamin D levels and serial ultrasound imaging for uterine morphology at preset time intervals will help researchers understand how vitamin D affects UF formation, growth, or both. This hospital-based study may not fully depict the issue's regional demography.

Keyword: Uterine fibroids, Vitamin D, Tumor

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Introduction

Uterine fibroids, sometimes referred to as leiomyomas or myomas, are the most common type of benign uterine tumours.[1] Since they are uterine smooth muscle monoclonal tumours, their genesis is the myometrium.[2] Extracellular matrix (ECM), which includes proteoglycans, fibronectin, and collagen, makes up the majority of their composition. By the age of 50, the prevalence of leiomyomas increases to between 70 and 80 percent in women,[3] and abnormal uterine haemorrhage (heavy menstrual bleeding causing anaemia) and pelvic discomfort cause morbidity in 30% of cases (urinary symptoms, constipation and tenesmus).[4]

Uterine fibroid, often referred to as fibromyomas, leiomyomas, or myomas, is a significant gynaecological disorder that frequently affects women of reproductive age and is a noncancerous development of the uterus. The percentage of malignant uterine fibroids is under 0.1%. Regardless of their benign neoplastic nature, uterine fibroids are a significant cause of severe morbidity in a large section of the female population. The local mass impact that results in pressure on surrounding organs, excessive uterine bleeding, or pregnancy-related problems including infertility and recurrent miscarriages is what produces the clinical symptoms.[5] Due to these local pressure effects and bleeding, uterine fibroids rank as the leading cause of hysterectomy, accounting for roughly one-third of all hysterectomies, or over 2,00000 hysterectomies annually.[6] Fibroids are of unicellular origin and have a clear autonomy from the surrounding myometrium due to their outer covering of connective tissue. As a result, during surgery, leiomyomas can be easily "shelled out" of the uterus.[7] Localized nodular edoema or growth results from the localisation of pathological bodily humours in body tissue.

Methods

The department of obstetrics and gynaecology at Jawahar Lal Nehru Medical College in Ajmer conducted this cross-sectional study from January 1, 2021, to January 1, 2022 in partnership with the department of radiology and with approval from the institute's ethical council. Inclusion criteria included premenopausal women aged 20-50 years, single/ Multiple leiomyomas > 2cm3 irrespective of the number and symptoms, those women consented to participate in the study, age matched women without uterine leiomyoma were enrolled as controls, there were a few patients who were diagnosed with uterine fibroid elsewhere and had attended gynae OPD ultrasound scan report. Exclusion criteria included current pregnancy, or pregnancy within the preceding 6 months of study, currently lactating or lactating within preceding 6 months of study, subjects with a history of miscarriage within 6 months of the study, subjects currently or within preceding 6 months on vitamin D supplements or any hormonal treatment, women with hypertension, diabetes, autoimmune disorders, coronary, hepatic, or renal disease.

Methodology

Subjects fulfilling the inclusion criteria were included in the study after obtaining written, informed consent. After a patient was recruited for the study, history of presenting complaints, obstetrical, menstrual, personal, use of medications and family history was taken. A detailed general, physical, per abdomen, per speculum and per vaginal examination were done. History regarding factors which influence the levels of1,25-dihydroxy vitaminD3 was also taken. All women underwent ultrasound (TAS/TVS) examination using Philips affiniti 70G Ultrasound machine with a E8CS TVS probe and 4C TAS probe.

Statistical Analysis

Data was recorded into Microsoft® Excel workbook 2019 and exported into SPSS v21.0 (IBM, USA) for statistical analysis. Categorical data were expressed as frequency, percentage, and compared using Chi square test. Quantitative variables were expressed as mean, standard deviation, and compared using Student t-test. $P<0.05$ was considered statistically significant.

Results

Baseline Characteristics

Table 1 observed that most of the subjects aged between 41-50 years were among the study group (62%) and Control (60%). There was no significant difference between mean age between Study Group and Control (40.17±8.31 vs. 40.74±7.11; P=0.603). 56% of cases and 60% of controls were taking vegetarian diet. There was no significant difference between diet distribution among both groups (P=0.567). 8% of the study group and 6% of controls were nulliparous. There was no significant difference of parity distribution among both groups (P=0.579). Sunlight exposure for more than 1 hour was observed in 49% cases and amongst 64% of the control participant. P value being 0.032 i.e., non-significant observation. In this study, 65.5% of the cases were normal. There was no significant difference of mean BMI between both groups (22.25±3.92 vs. 21.46±3.96; P=0.157).

Presenting complaints

AUB was the most common complaint (34%) followed by dysmenorrhea (27%), infertility (22%), and pain abdomen (19%) (Table 2).

Vitamin D3 levels (ng/ml)

Table 3 shows that the vitamin d level in study group where significantly lower than control group comparing according to severity of vitamin d deficiency, it was found that 39% each of study group had vitamin d level below 19 ng/ml while that in control group it was 14% and 13% respectively for <10 ng/dl and 11-19 ng/dl. The mean value of vit d in study group was mean (ng/ml) 15.13±8.0 and that of control group was 24.82±9. (Significantly higher).

Number of fibroids

Table 4 shows that the only 9% women had fibroids >5 while 53% had fibroids 3-4.

Association between vitamin D and Number of fibroids in group 1

There was an inverse association between vitamin D and Number of fibroids (P<0.001).

Discussion

Uterine fibroids, which develop in the uterine muscle of premenopausal women, are the most prevalent benign pelvic tumours in women of reproductive age, with a frequency ranging from 5.4 percent to 77 percent.[8] Infertility, irregular bleeding, pelvic pressure symptoms, and growth or regress can all be caused by them. They may also be asymptomatic. Millions of women are affected by leiomyoma, and it is one of the main reasons for hysterectomy.[9] Depending on the patient's age, the condition being treated, whether fertility preservation is a concern, and personal preferences, treatment options may include medication therapy, surgical intervention, and uterine artery embolization or ablative procedures.[10]

The majority of the subjects aged between 41-50 years were among the study group (62%) and Control (60%). There was no significant difference between mean age between Study Group and Control (40.17±8.31 vs. 40.74±7.11; P=0.603). 56% of cases and 60% of controls were taking vegetarian diet. There was no significant difference between diet distribution among both groups (P=0.567). 8% of the study group and 6% of controls were nulliparous. There was no significant difference of parity distribution among both groups (P=0.579). Sunlight exposure for more than 1 hour was observed in 49% cases and amongst 64% of the control participant. P value being 0.032 i e non-significant observation. In this study, 65.5% of the cases were normal. There was no significant difference of mean BMI between both groups (22.25±3.92 vs. 21.46±3.96; P=0.157). In a study by **Sabry et al** (2013),[11] Cases and controls had median ages of 37.1±2.9, and 36.8±3.4 years, respectively. In the study by **Farzaneh et al (2020)**,[12] the mean age of the women with fibroids (42.71 ± 8.07 years) was slightly higher than the normal subjects, but not significantly different (39.75 ± 12.95 years; p = 0.10). 13 of 77 controls and 5 out of 71 cases both had significant levels of sun exposure. Although cases had less sun exposure than controls, there was no statistically significant difference (P=0.09) In a study by **Kumari et al**,[13] Nulliparous women made up just 4.9 percent of cases and 1.9 percent of controls. In comparison to controls, there were substantially more patients who were multiparous (P=0.041). Mean BMI for patients and controls, respectively, was 24.95± 3.01 and 24.36 ±3.01 (P=0.11). Mean BMI for patients and controls, respectively, was 24.95± 3.01 and 24.36 ±3.01 (P=0.11). In a study by **Alansari and El Megeed** (2021),[14] Only 28% of patients and 68% of controls had more than an hour of sun exposure. When compared to controls, cases had significantly less sun exposure (P=0.0001). In a study by **Singh et al**,[15] Mean BMI for patients was 27.18±3.68, whereas it was 25.92±3.51 for controls. In comparison to controls, cases' BMI was considerably higher (P=0.037).

AUB was the most common complaint (34%) followed by dysmenorrhea (27%), infertility (22%), and pain abdomen (19%). In the study by **Singh et al (2019),**[15] When we looked at Table 8 to examine the complaints, we discovered that abdominal discomfort (34%) was the most prevalent issue, with dysmenorrhea (27%) and infertility (22%) following (19 percent). In the study by **Suneja et al (2021)**,[16] The most prevalent condition was dysmenorrhea (77%) and was followed by pelvic discomfort (60%) and low back pain (47 percent).

Table 3, 4 and 5 shows that the vitamin d level in study group where significantly lower than control group comparing according to severity of vitamin d deficiency, it was found that 39% each of study group had vitamin d level below 19 ng/ml while that in control group it was 14% and 13% respectively for <10 ng/dl and 11-19 ng/dl. The mean value of vit d in study group was mean (ng/ml) 15.13±8.0 and that of control group was 24.82±9. (Significantly higher). Only 9% women had fibroids >5 while 53% had fibroids 3-4. There was an inverse association between vitamin D and Number of fibroids (P<0.001).In the study by **Alansary and El Megeed (2021**),[14] As shown by

the considerably lower mean vitamin D levels in the case group compared to the control study group (3.39±7.93 ng/ml vs. 21.71±8.95 ng/ml, respectively), low vitamin D levels may be a risk factor for the development of uterine fibroid. **Ajmani et al (2018)**,[17] did a similar case-control study and found that the mean vitamin D levels for patients and controls were, respectively, 12.58±4.09 ng/ml and 18.99±5.72 ng/ml (p=0.001). **Kaplan et al,**[18] also reported similar results in a case-control study. In comparison to the control group, the case group's mean vitamin D levels were considerably lower (6.54±4.66 ng/mL vs. 8.18±5.16 ng/mL, respectively; p=0.009). The reference range used to categorize the vitamin D level in all study groups was as follows: equal or >30 ng/mL=sufficient, 20-29.99 ng/mL=deficit. A study by **Paffoni et al (2013)**,[19] who submitted the same study in 126 fibroid-positive and 256 control women who visited two infertility clinics in Italy likewise discovered that the mean serum concentration of 25-hydroxyvitamin D3 was lower in fibroid-positive women than in controls (18.0 ± 7.7 vs. 20.8 ± 11.1 ng/mL, respectively, p = .010). Additionally, they noted that the crude odds ratio (OR) for the existence of fibroids in women with blood 25-hydroxyvitamin D3 levels < 10 ng/mL compared to those with 25-hydroxyvitamin D3 > 10 ng/mL was 2.2 (95 percent confidence interval [CI] 1.1-4.3) (p =.022).

Conclusion

Our study's cross-sectional design makes it difficult to pinpoint exactly how vitamin D contributes to the development of UFs. The role of vitamin D in the creation, growth, or both of UFs can be clarified by doing more thorough prospective cohort studies including monitoring of vitamin D levels and serial ultrasound imaging for uterine morphology at preset time intervals. Being a hospital-based study, it might not accurately reflect the full scope of the issue in terms of local demographics.

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Table 1: Baseline Characteristics

	Study Group (n=100)	**Control (n=100)**	**P value**
Age(years)			
20-30	17 (17.0%)	7 (7.0%)	0.032
31-40	21 (21.0%)	33 (33.0%)	
41-50	62 (62.0%)	60 (60.0%)	
Mean age (Years)	40.17±8.31	40.74±7.11	0.603
Diet			
Vegetarian	56 (56.0%)	60 (60.0%)	0.567
Mixed	44 (44.0%)	40 (40%)	
Parity			
Nulliparous	8 (6%)	6 (8%)	0.579
Multiparous	92 (94%)	94 (92%)	
Sun Exposure (hours)			
<1	51 (51.0%)	36 (36.0%)	0.032
≥1	49 (49.0%)	64 (64.0%)	
BMI (kg/m^2)			
Underweight	20 (20%)	22 (22%)	0.973
Normal	67 (67%)	64 (64%)	
Overweight	7(7%)	8 (8%)	
Obesity	6 (6%)	6 (6%)	
Mean BMI (kg/m^2)	22.25±3.92	21.46±3.96	0.157

Table 2: Presenting complaints

Presenting complaints	**Frequency**	**Percentage**
AUB	34	34%
Pain abdomen	19	19%
Dysmenorrhea	25	25%
Infertility	22	22%

Table 3: Vitamin D3 levels (ng/ml)

Vitamin D3 levels (ng/ml)	**Study Group (n=100)**	**Control (n=100)**	**P value**
≤10	39 (39.0%)	14 (14.0%)	<0.001
11-19	39 (39.0%)	13 (13.0%)	
20-29	12 (12.0%)	27 (27.0%)	
≥30	10 (10.0%)	46 (46.0%)	
Mean (ng/ml)	15.13±8.09	24.82±9.29	<0.001

Table 4: Number of fibroids (n=100)

Number of fibroids	**Frequency (n=100)**	**Percentage (%)**
1-2	38	38%
3-4	53	53%
≥5	9	9%

Table 5: Association between vitamin D and Number of fibroids in group-1 (n=100)

Vitamin D3 levels (ng/ml)	**1-2**	**3-4**	**≥5**	**Total**	**P value**
≤10	7	26	6	39	<0.001
11-19	14	22	3	39	
20-29	11	1	0	12	
≥30	6	4	0	10	
Total	38	53	9	100	