

## To determine the association of serum VIT D level and uterine fibroid in premenopausal women

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### Abstract

**Background:** Uterine Fibroid are monoclonal, benign tumors originating from the smooth muscle cell of uterus and predominantly located in the pelvis. Main hormones for uterine fibroid are estrogen and progesterone. Fibroids mainly consist of extracellular matrix that contain collagen, fibronectin and proteoglycans. vitamin D deficiency has been proven to be a major risk factor in the development of fibroid. Mean 25(OH)D serum levels are significantly low in uterine fibroid women as compared to healthy women. **Aims & objectives:** To estimate serum vitamin D level in the premenopausal women under age group of 30 to 45 years diagnosed with uterine fibroid and healthy women of same age, weight, locality and ethnicity and to compare serum vitamin D level among both groups. **Materials and methods:** An observational case control study done in the dept of Obstetrics & Gynaecology of MGM Medical College & M.Y Hospital, Indore Madhya Pradesh from 1<sup>st</sup> April 2020 to 31<sup>st</sup> march 2021 in the women attending outpatient dept, in the age group of 30-45 year. After obtaining informed consent, 3 ml of blood sample was collected from all the participants and vit D level measured in the serum by ELISA. **Result:** total 200 women (100 cases, 100 control) underwent the study. Most study participants among case and control are of age 30-35 years. None of them had BMI below normal and most of control and cases were overweight. Most common parity among them was 2. 91% of cases had vit D deficiency while 32% of control had vit D deficiency and 68% of control were having normal vit D levels. **Conclusion:** The present study shows there is positive correlation between vit D level and uterine fibroid (OR=21.48), which is suggestive of some contribution of hypovitaminosis of vit D in etiology of uterine fibroid.

**Keywords:** uterine fibroid, vit D

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### Introduction

The term, uterine fibroids (UF) also called uterine leiomyoma, represents the most common benign gynaecological tumor affecting the uterus[1]. Although the exact origins of this risk discrepancy are unknown, research suggest that vitamin D insufficiency is a crucial factor. Several causes, including vitamin D deficiency through DNA damage, could cause genomic instability and hence transform normal myometrium stem cells to fibroid cells. When compared to Caucasian women, African American women had a tenfold higher risk of vitamin D insufficiency[2]. In comparison to Caucasian women, these women have a threefold greater incidence rate and relative risk of UFs. Total Six percent of women in the age group 30–49 years have gone for hysterectomy in our country. The UF-caused morbidities affect women of all ethnicities, but disproportionately affect African American women more.

Vitamin D3 is produced in the skin during the summer months or received from dietary sources. Uterine Fibroids Uterine fibroids are noncancerous uterine growths. Risk factors There are few known risk factors for uterine fibroids, other than being a woman of reproductive age. The enzyme 1- $\alpha$ -hydroxylase in the kidneys converts both 25-OH-D2 and 25-OH-D3 to the most active form of vitamin D (1,25 dihydroxyvitamin D). Vitamin D3 (cholecalciferol) is converted to 25-hydroxyvitamin D3 (25(OH)D) in the liver and then to 1,25-dihydroxyvitamin D3 (1,25(OH)2D) in the kidney. Types of uterine fibroids Complications Although uterine fibroids are rarely hazardous, they can cause pain and consequences such as a decline in red blood cells (anaemia), which causes exhaustion, as a result of excessive blood loss. This active 1,25 dihydroxyvitamin D enhances calcium absorption and bone resorption in the intestine while

lowering calcium and phosphate excretion in the kidneys. Staging[3] Mild deficiency: 25-hydroxyvitamin D less than 20 ng/mL Moderate deficiency: 25-hydroxyvitamin D less than 10 ng/mL Severe deficiency: 25-hydroxyvitamin D less than 5 ng/mL. • Intramural fibroids: These fibroids develop in the muscular wall of the uterus. The most common signs and symptoms of uterine fibroids include: • Heavy menstrual bleeding • Menstrual periods lasting more than a week • Pelvic pressure or pain • Frequent urination • Difficulty emptying the bladder • Constipation • Backache or leg pains • Rarely, a fibroid can cause acute pain when it outgrows its blood supply, and begins to die. Early menstruation, obesity, vitamin D deficiency, a diet high in red meat and low in green vegetables, fruit, and dairy, as well as alcohol intake, including beer, all contribute to the development of fibroids. • Submucosal fibroids: These fibroids are uncommon.

### Material & methods

#### Study Design

Observational case control study.

#### Study Period

18 months from the date of approval.

#### Study Population

100 clinically diagnosed women with uterine fibroid and 100 healthy women in the age group of 30 to 45 year irrespective of their parity attending opd of obstetric and gynaecology department satisfying the inclusion and exclusion criteria will be enrolled in the study

#### Study Sites

M. G. M. Medical College and MYH indore.

#### Sampling Frame

All the women attending obs and gyne OPD in MYH.

#### Inclusion Criteria

1. Premenopausal women within the age group of 30 to 45 years.

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2. Women diagnosed with uterine fibroid in the age group of 30 to 45 year.

2. Women with associated liver and kidney disease, cardiovascular disease, autoimmune disease, known diabetic or hypertensive, inflammatory bowel disease.
3. Women who will not give consent

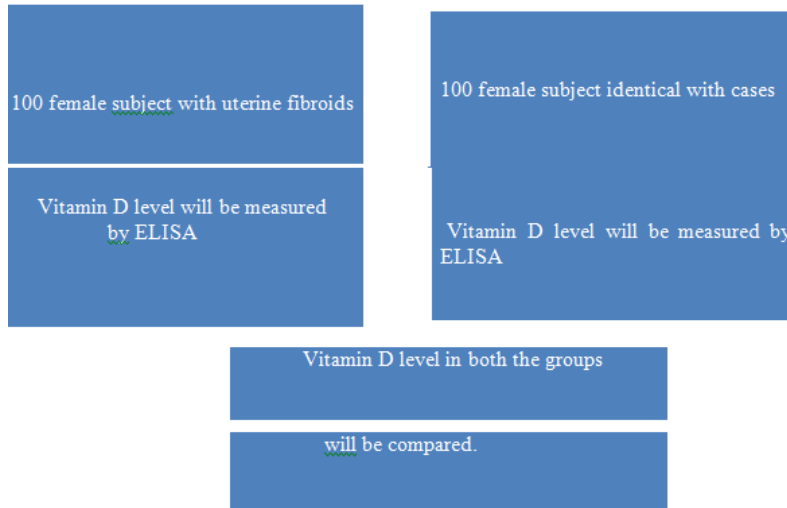
**Exclusion Criteria**

1. Postmenopausal women and women below 30 year of age

**Sampling Methods**

purposive sampling has been done.

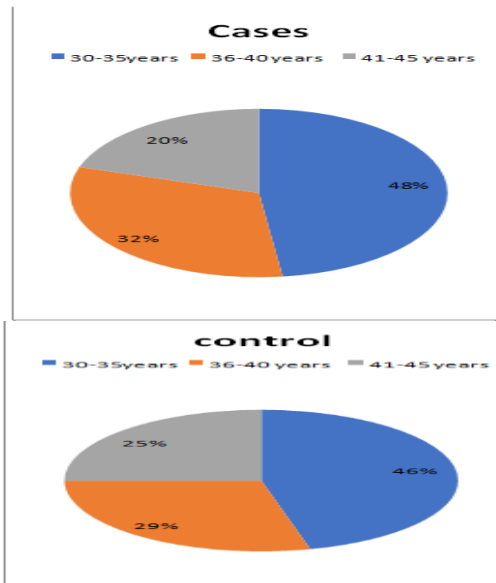
**Study Process**



**Result**

**Table-1: Age Distribution among cases and control.**

| Age group   | Cases | control |
|-------------|-------|---------|
| 30-35years  | 48    | 46      |
| 36-40 years | 32    | 29      |
| 41-45 years | 20    | 25      |

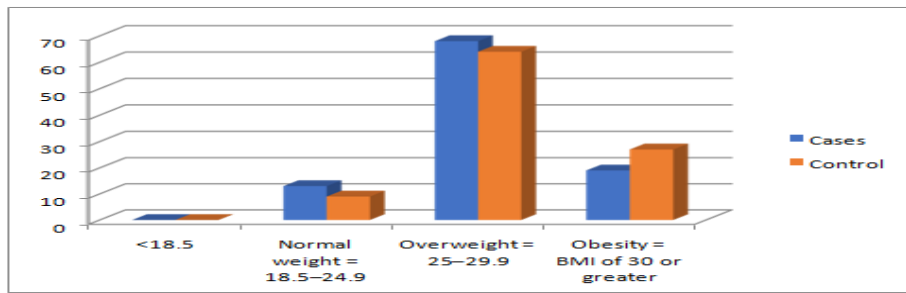


The table 1 shows the most of study participant among cases and control group are of age 30-35 years 48% and 46% respectively followed by 36-40 years 32% and 29% respectively and 36-40 years 20% and 25 % respectively.

**Table-2 BMI among cases and control**

| BMI | Cases | Control |
|-----|-------|---------|
|-----|-------|---------|

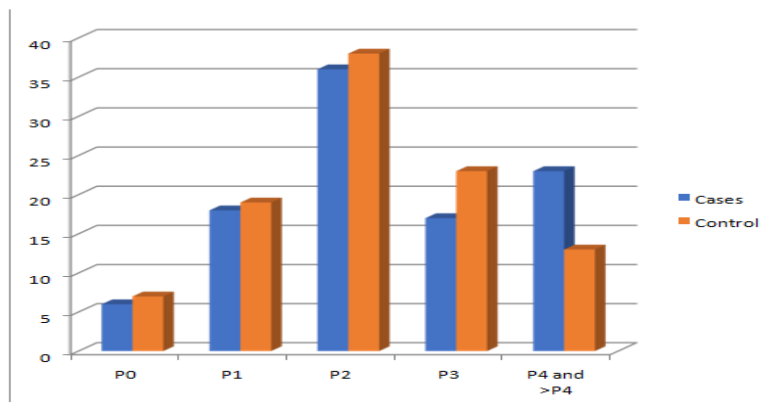
|                                |    |    |
|--------------------------------|----|----|
| <18.5                          | 0  | 0  |
| Normal weight = 18.5–24.9      | 13 | 9  |
| Overweight = 25–29.9           | 68 | 64 |
| Obesity = BMI of 30 or greater | 19 | 27 |



The table 2 shows none of the control or cases have BMI below normal while most of control (64%) n cases (68%) were overweight and 19% of cases and 27% control were obese.

**Table-3 Parity among cases and control**

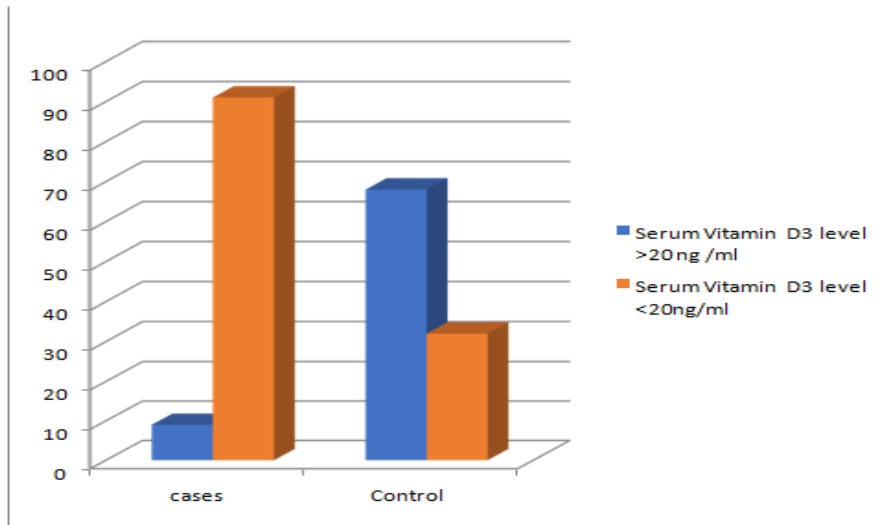
| Parity     | Cases | Control |
|------------|-------|---------|
| P0         | 6     | 7       |
| P1         | 18    | 19      |
| P2         | 36    | 38      |
| P3         | 17    | 23      |
| P4 and >P4 | 23    | 13      |



The table 3 shows most of the case and controls have parity of 2 i.e. 36% and 38% respectively.

**Table-4 Serum Vitamin D3 level among cases and control**

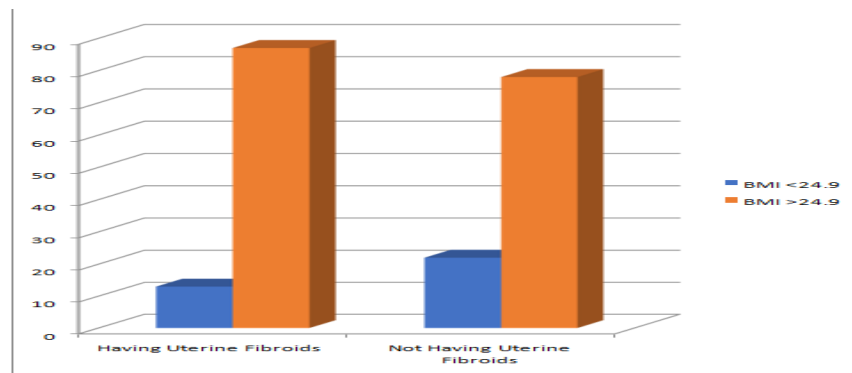
|                                  | Cases (with Fibroid) | Control (without Fibroid) |
|----------------------------------|----------------------|---------------------------|
| Serum Vitamin D3 level <20 ng/ml | 91(a)                | 32(b)                     |
| Serum Vitamin D3 level >20ng/ml  | 9(c)                 | 68(d)                     |



The table 4 shows the 91 % of cases have deficiency of vitamin D and while among control 68% are having normal vitamin D level , 32% shows deficiency vitamin D. and a statically significant difference were observed in vitamin D deficiency and uterine fibroid cases.

**Table-5 BMI and fibroids**

|           | Cases (with Fibroid) | Control (without Fibroid) |
|-----------|----------------------|---------------------------|
| BMI >24.9 | 87(a)                | 78(b)                     |
| BMI <24.9 | 13(c)                | 22                        |



**Calculation of exposure rates**

a. Among BMI and Uterine Fibroid.

Exposure rate among cases =  $\frac{a}{a+c} = \frac{87}{100} = 87$  per cent

$$\frac{a}{a+c} = \frac{87}{100}$$

Exposure rate among controls =  $\frac{b}{b+d} = \frac{78}{100} = 78$  per cent

$$\frac{b}{b+d} = \frac{78}{100}$$

It shows the exposure of higher BMI among the cases 87%.

b. Among vitamin D level and uterine fibroids.

Exposure rate among cases =  $\frac{a}{a+b} = \frac{91}{100} = 91$  per cent

Exposure rate among controls =  $\frac{c}{c+d} = \frac{32}{100} = 32$  per cent

$$\frac{c}{c+d} = \frac{32}{100}$$

P < 0.001

It shows that the exposure of serum vitamin D deficiency among the cases is 91 % while the exposure of serum vitamin D deficiency among control group is 32 % only.

**Estimation of risk**

$$\text{Relative risk} = \frac{\text{incidence among exposed}}{\text{incidence among nonexposed}} = \frac{\frac{a}{a+b}}{\frac{c}{c+d}} = \frac{\frac{91}{100}}{\frac{32}{100}} = 2.84$$

Though relative risk cannot be precisely calculated in cases control study in present study those who are having higher BMI are 1.4 times

more vulnerable to develop uterine fibroids as compare to those who have normal or less BMI

b. Among vitamin D level and uterine fibroids

$$\text{Relative risk} = \frac{\text{incidence among exposed}}{\text{incidence among nonexposed}} = \frac{\frac{a}{a+b}}{\frac{c}{c+d}} = \frac{\frac{91}{100}}{\frac{32}{100}} = 2.84$$

Though relative risk cannot be precisely calculated in cases control study in present study those who are having vitamin D deficiency are 6.7 times more vulnerable to develop uterine fibroids as compare to those who have normal vitamin d level.

**Calculation of odds ratio**

a. BMI and Uterine fibroids

$$\text{Odds Ratio} = \frac{ad}{bc} = \frac{87 \times 22}{78 \times 13} = 1.89$$

b. Among vitamin D level and uterine fibroids.

$$\text{Odds Ratio} = \frac{ad}{bc} = \frac{91 \times 68}{32 \times 9} = 21.48$$

Odds Ratio is key parameter in the case control study in our study we obtained odds ratio 21.48 which is interpreted as follows – The Risk of developing Uterine fibroid among female of age 30-45 yrs who are having Vitamin D deficiency is 21.48 times more than those who have normal serum vitamin D levels.

### Discussion

The present study is to determine the association of serum vitamin D level and uterine fibroid in premenopausal women (age 30-45 years) here our findings. In the present study most of study participant among cases and control group are of age 30-35 years 48% and 46% respectively. In a study done by Munusamy MM and et al the prevalence of uterine fibroid is highest in age group 35-45 years i.e. 77%[4]. In another study by Wong JY and et al the most women were of premenopausal age[5]. None of the control or cases have BMI below normal while most of control (64%) n cases (68%) were overweight and 19% of cases and 27% control were obese. In a study by Sun and et al in China includes the 100% study subject are either overweight or the obese[6]. The present study shows there are 6% cases and 7% control were nulliparous. 18% cases 19% controls were primiparous while 76% cases were multiparous and 74% controls were multiparous. Vitamin D deficiency and BMI is also compared 178 participant were having BMI >24.9 among them 139 were deficient in Vitamin D while 39 were having normal Vitamin D levels, those who were having BMI <24.9 were only 22 among them 16 were deficient in vitamin D and 6 were efficient in Vitamin D serum level. Co-relation between BMI and uterine fibroids incidence is also observed in present study among all participant 35 participant were having BMI <24.9 and among them 13 participants were suffer from Uterine Fibroids and 22 were not having. BMI >24.9 observed in 165 Participant, 87 were suffering from Uterine Fibroid while 78 were not. The exposure rates among the people with higher BMI is 87% as compared with BMI <24.9 is 78 percent, Relative risk also calculated though relative risk is not so accurate for case control study which is observed RR= 1.4, Odds Ratio = 1.89 was observed. This finding is compared with the study Sun and et al in China where OR observed was 2.716[6]. Another study Wong JY and et al states that Increased BMI was associated with an increased risk of fibroid recurrence (OR, 1.59; 95% CI, 0.99–2.54;  $P < .05$ )[5]. Co-relation between Vitamin D deficiency and uterine fibroids incidence is mainly Observed in the present study and the findings were 91 % of cases have deficiency of vitamin D and while among control 68% are having normal vitamin D level, 32% shows deficiency of vitamin D. and a statically significant difference were observed in vitamin D deficiency and uterine fibroid cases. The exposure rates among the cases is 91% as compared with control 32%, Relative risk also calculated though relative risk is not so accurate for case control study which is observed RR= 6.7, Odds Ratio = 21.48 was observed. Which is highly significant and suggestive that Vitamin D plays important role in etiology of Uterine Fibroids. Similar observation are seen in In a cohort of black and white females from North Africa, Sabry M and et al found a link between lower serum vitamin D levels and an increased risk of uterine leiomyoma in 2013[7]. Two more investigations, by Baird et al. and Paffoni et al[8,9], found a substantial inverse association between vitamin D blood levels and the severity of fibroids in African-American females, implying that the lower the vitamin D level, the more severe the leiomyoma burden. Women with vitamin D insufficiency were more likely to develop leiomyomas, according to Paffoni et al[9], with an adjusted odds ratio of 2.4. With an adjusted odds ratio of 0.68, Baird et al[8]. discovered that women with adequate vitamin D levels were less likely to have uterine fibroids.

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