



EVALUATION OF VITAMIN D LEVELS IN WOM-EN WITH UTERINE LEIOMYOMA

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ABSTRACT **INTRODUCTION:-** Uterine fibroid is a benign tumour of uterine smooth muscle and a common etiology for menorrhagia and dysmenorrhoea in women of reproductive age group. The etiopathogenesis of fibroid is multifactorial. The main hormones which simulate uterine fibroid development and growth are estrogen and progesterone which induce its formation and growth, directly and indirectly through various growth factors. Vitamin D functions as a potent anti estrogenic and anti progesterogenic compound. There is an inverse correlation between the upregulated estrogen and progesterone receptor and VDR (Vitamin D receptor) expression in uterine fibroids. So, it is suggested that vitamin D implicated in the pathogenesis of uterine fibroid. This study was designed to Estimate serum Vitamin D level in women with uterine leiomyoma and to Compare Vitamin D levels in women with uterine leiomyoma with that of women without leiomyoma.

Material and Methods:- This prospective comparative monocentric observational study conducted on 100 non-pregnant women of age 20-50 year with symptomatic and asymptomatic leiomyoma and patients without leiomyoma. Patients were distributed in two groups, Group A and Group B

Group A :- this group consisted of non-pregnant women of age 20-50 year with symptomatic and asymptomatic leiomyoma.

Group B :- this group was control group consisting of patients without leiomyoma. Blood samples were collected by all patients and Serum 25-OH vitamin D levels was measured and compared for both the Vitamin D 3 Level in Uterine Fibroid (study group) and control group and data was analyzed by unpaired t test by using SPSS version 16.0.

Results:- Our study has shown that majority (70%) of patients in study group have deficient vitamin D3 levels i.e below 20ng/ml as compared to 44% of patients in control group whereas there are only 6% cases in study group having sufficient levels of vitamin D3 as compared to 28% patients in control group, this Data shows statistically significant difference of levels of vitamin D3 between study and control groups (Odds ratio (OR) : 0.13 with 95%(CI)(0.03-0.50) P=0.004).

We also observed that the mean of serum vitamin D3 in women with uterine fibroid volume < 50cm³ was (22.14±6.17) ng/ml while the mean of serum vitamin D3 in women with uterine fibroid volume => 200 cm³ was (8.80±2.05) ng/ml which shows lower serum vitamin D3 levels were significantly associated with increased total uterine fibroids volume (p-value<0.001).

Conclusion:-

- Mean serum vitamin D levels were significantly lower in patients with leiomyoma (17.06±7.24 ng/ml) than patients without leiomyoma (22.89±7.96 ng/ml) which signifies that vitamin D deficiency is a risk factor for uterine fibroid.
- Majority of patients with uterine leiomyoma (70%) were having more deficient levels of vitamin D (<20ng/ml) as compared to 44% in patients without leiomyoma and only 6% were having sufficient vitamin D levels (>30ng/ml) in study group as compared to 28% in patients without leiomyoma
- Lower serum levels of vitamin D3 were associated with the largest uterine fibroid burden and vice versa.

KEYWORDS :**INTRODUCTION**

Uterine fibroid is a benign tumour of uterine smooth muscle and a common etiology for menorrhagia and dysmenorrhoea in women of reproductive age group⁽¹⁾. An estimated incidence of leiomyoma is 20%-40% in women during their reproductive years including symptomatic and asymptomatic conditions. The etiopathogenesis of fibroid is multifactorial. The main hormones which simulate uterine fibroid development and growth are estrogen⁽²⁾ and progesterone⁽³⁾ which induce its formation and growth, directly and indirectly through various growth factors⁽⁴⁾. Vitamin D is believed to reduce the risk of chronic illnesses and neoplasms and its deficiency have been suggested to be risk factor in several gynaecological and obstetrical pathologies, such as infertility⁽⁵⁾ or polycystic ovary syndrome. Interestingly, it is also implicated in the pathogenesis of uterine fibroid in few recent conducted studies. Vitamin D3 exerts its effects via activation of its cellular receptor (VDR), which in turn alters transcription rate of target genes responsible for reduction in cell proliferation and regulation of biological processes including angiogenesis, extracellular matrix production and immune response^(6,7). Vitamin D3 receptor (VDR) is present in wide range of tissues including both myometrium and endometrium of human uterus and also expressed in uterine fibroid tissue.

It has been suggested that uterine fibroids develop because of aberrant response to tissue repair leading to altered extracellular matrix production and Vitamin D might suppress this abnormal response by regulating this response.

According to The Endocrine society practice guidelines, Vitamin D deficiency is defined as 25-OH Vitamin D below 20 ng/ml and Vitamin D insufficiency as a 25-OH Vitamin D of 21-29ng/ml and sufficiency as at least 30 ng/mL⁽⁸⁾. Preferred range is 40-60ng/ml when focusing on the pleiotropic effect of Vitamin D.

AIMS AND OBJECTIVE:

- To Estimate serum Vitamin D level in women with uterine leiomyoma.
- To Compare Vitamin D levels in women with uterine leiomyoma with that of women without leiomyoma.

MATERIAL AND METHODS:

We planned a monocentric prospective observational study over a period of one year to detect the difference in mean serum vitamin D3 in blood, if any exists. We kept equal number of subjects in both groups and on the basis of previous study (V. Singh et al., 2019)⁽⁹⁾, difference in the mean of Vitamin D3 level in women with uterine fibroid and normal control women ($\mu_1 - \mu_2$) was 12.1 and the maximum population variance (σ^2) was 16.18. The sample size calculated as $(n) = 2 (Z_{\alpha/2} + Z_{(1-\beta)})^2 \times \sigma^2 / (\mu_1 - \mu_2)^2$, assuming 0.05 level significance ($Z_{\alpha/2} = 1.96$), and 95% power ($Z_{(1-\beta)} = 1.64$) was 46. Further taking 10% of dropout rate and non-response rate total 50 subjects will be included in each groups (total 100).

In our study we included Women with single or multiple leiomyoma or presenting with symptoms menorrhagia, dysmenorrhoea, abdominal

- lump, dull aching lower abdominal pain, dyspareunia and excluded -
1. Women with history of pregnancy and miscarriage in last 6 months, currently lactating or lactating within 6 months prior to enrollment.
 2. Women currently on hormonal therapy or vitamin supplements.
 3. Women with history of myomectomy or hysterectomy.
 4. Women with liver and renal diseases.
 5. Women with metabolic and endocrinal disorders
 6. With Suspected adenomyosis.

Study procedure :

The present study was conducted on 100 non-pregnant women of age 20-50 year with symptomatic and asymptomatic leiomyoma and patients without leiomyoma attending the out patient department and admitted in the department of Obstetrics and gynaecology (i.e. Swaroop Rani Nehru Hospital, M.L.N. Medical College and Kamala Nehru Memorial Hospital, Prayagraj), in collaboration with department of Radiodiagnosis & Department of Pathology over a period of 1 year 2019-2020.

This study was undertaken to estimate and compare serum Vitamin D levels in women with uterine leiomyoma with that of women without leiomyoma.

STATISTICAL ANALYSIS:

t-test was applied. All statistical P value <0.05 was considered significant.

RESULTS AND OBSERVATION:

Table 1: Distribution of participants into study group and control group

| Group | Numbers | Percentage |
|---------------|---------|------------|
| Study group | 50 | 50% |
| Control group | 50 | 50% |
| Total | 100 | |

Total 100 cases were enrolled in this study. Out of 100, total 50 (50.0%) cases were leiomyoma (study group) and 50 (50.0%) were women without leiomyoma (control group).

Table 2: Comparison of serum Vitamin D (ng/ml) in between study group and control group patients

| Parameter | Mean | Median | Std. Deviation | Minimum | Maximum |
|--------------------------|-------|--------|----------------|---------|---------|
| Study Group | | | | | |
| serum Vitamin D (ng/ml) | 17.06 | 14.55 | 7.24 | 6.70 | 34.60 |
| Control Group | | | | | |
| serum Vitamin D (ng/ml) | 22.89 | 23.95 | 7.96 | 9.80 | 36.20 |
| p-Value=<0.001 | | | | | |

*=Significant (p<0.05), !=Unpaired t test

The mean value of serum vitamin D3 in women with uterine fibroid was (17.06±7.24) ng/ml while the mean value of serum vitamin D3 in the control group was (22.89±7.96) ng/ml. There was a statistically significant (p-value =<0.001) lower values of vitamin D among patients with leiomyoma as compared to controls. In our present study, the mean value of Vitamin D was significantly lower in study group (17.06±7.24)ng/ml as compared to control group (22.89±9.80)ng/ml.

Table 3: Level wise comparison of serum Vitamin D (ng/ml) in between study group and control group patients

| serum Vitamin D (ng/ml) | Study group (n=50) | Control group (n=50) | p-Value |
|-----------------------------|--------------------|----------------------|---------|
| Deficient (<20 ng/ml) | 35 (70.0%) | 22 (44.0%) | 0.006* |
| Insufficiency (20-30 ng/ml) | 12 (24.0%) | 14 (28.0%) | |
| Sufficiency (>30 ng/ml) | 3 (6.0%) | 14 (28.0%) | |

*=Significant (p<0.05), !=Chi square test

We found frequencies of deficient (<20 ng/ml), insufficiency (20-30 ng/ml) and sufficiency (>30 ng/ml) were 70%, 24%, and 6% in study group and 44%, 28.0% and 28.% in control group, respectively which showed frequencies of deficient levels (<20 ng/ml) were more in study

group whereas women with sufficiency levels (>30 ng/ml) were more in control group.

Table 4: The different means of serum vitamin D in the study group according to the total uterine fibroids volume (cm3)

| Total uterine fibroid volume(cm3) | | | | |
|-----------------------------------|----------|-------|--------|---------|
| | N | Mean | +/- SD | P-Value |
| <50 | 27 (54%) | 22.14 | 6.17 | <0.001 |
| 50-99 | 8 (16%) | 12.74 | 0.81 | |
| 100-149 | 9 (18%) | 10.46 | 0.82 | |
| 150-199 | 3 (6%) | 10.90 | 1.73 | |
| ≥200 | 3 (6%) | 8.80 | 2.05 | |

x=Significant (p<0.05)

We observed the frequencies of total uterine fibroids volume (cm³) according to various range <50, 50-99, 100-149, 150-199 and ≥200 were 54%, 16%, 18%, 6% and 6%, respectively. The means of serum vitamin D was 22.14±6.17, 12.74±0.81, 10.46±0.82, 10.90±1.73 and 8.80±2.05 in <50, 50-99, 100-149, 150-199 and ≥200 total uterine fibroids volume (cm³), respectively. The mean Vitamin D was significantly lower in patients with more value of total uterine fibroids volume (cm³) of study group and vice versa.

DISCUSSION:

Vitamin D functions as a potent anti estrogenic and anti progesterogenic compound. There is an inverse correlation between the upregulated estrogen and progesterone receptor and VDR (Vitamin D receptor) expression in uterine fibroids⁽¹⁰⁾. Vitamin D3 inhibits growth and induces apoptosis through suppression of BCL-2 –considered an important anti-apoptotic protein, suppression of catechol-o-methyltransferase (COMT) –which is involved in estrogen metabolism⁽¹¹⁾ and suppress the effect of transforming growth factor (TGF-BETA3)⁽¹²⁾. Vitamin D also significantly reduces protein expression of ECM associated collagen type, fibronectin, and plasminogen activator 1.

In our present study, the mean value of Vitamin D was significantly lower in study group (17.06±7.24)ng/ml as compared to control group (22.89±9.80)ng/ml. Similar results were seen with the study conducted by LW Sersam et al (2018)⁽¹³⁾ where mean value of serum vitamin D3 in women with uterine fibroid were lower (15.81±8.64) ng/ml as compared to mean value of serum vitamin D3 in the control group (34.25±8.07) ng/ml. Majority (70%) of patients in study group have deficient vitamin D3 levels i.e below 20ng/ml as compared to 44% of patients in control group whereas there are only 6% cases in study group having sufficient levels of vitamin D3 as compared to 28% patients in control group. Similar results were found in study conducted by Paffoni et al (2013)⁽¹⁴⁾ who found the frequency of leiomyomas was up to 2-fold higher in women with a condition of vitamin D deficiency, i.e, those with a serum concentration of 25-hydroxyvitamin D3 below 10 ng/mL.

Our result shows statistically significant lower values of serum vitamin D3 values were associated with more volume of uterine fibroid. Our results agree with those reported by LW Sersam et al (2018)⁽¹³⁾ where mean of serum vitamin D3 in women with uterine fibroid volume <50 cm³ was 21.61±/-6.22 ng/ml while the mean of serum vitamin D3 in women with uterine fibroid volume => 200 cm³ was (3.00±2.00) ng/ml.

CONCLUSION:

The conclusions drawn from the study were as follows.

- Mean serum vitamin D levels were significantly lower in patients with leiomyoma (17.06±7.24 ng/ml) than patients without leiomyoma (22.89±7.96 ng/ml) which signifies that vitamin D deficiency is a risk factor for uterine fibroid.
- Majority of patients with uterine leiomyoma (70%) were having more deficient levels of vitamin D (<20ng/ml) as compared to 44% in patients without leiomyoma and only 6% were having sufficient vitamin D levels (>30ng/ml) in study group as compared to 28% in patients without leiomyoma.
- The mean of serum vitamin D was 22.14±6.17, 12.74±0.81, 10.46±0.82, 10.90±1.73 and 8.80±2.05 in <50, 50-99, 100-149, 150-199 and ≥200 total uterine fibroids volume (cm³), respectively. Lower serum levels of vitamin D3 were associated with the largest uterine fibroid burden and vice versa.

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