International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Moshika et al. Int J Reprod Contracept Obstet Gynecol. 2024 Aug;13(8):2082-2085
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20242075

Original Research Article

A study on role of vitamin D3 in uterine fibroids

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Received: 07 June 2024
Revised: 05 July 2024
Accepted: 06 July 2024

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ABSTRACT

Background: Fibroids are one of the significant non-cancerous growths prevalent in females. Vitamin D is found to have a significant influence in the development of fibroid by suppressing the formation of an impaired extracellular matrix (ECM) due to the abnormal reaction to tissue damage response by regulating it. The study is done to find out the mean vitamin D3 levels among women with fibroids and without fibroids, respectively.
Methods: This study was a hospital based analytical study done in the department of obstetrics and gynaecology, Chettinad Hospital and Research Institute, Chennai, India for a period of 18 months. Two groups of 60 each, one group with fibroids and the other without fibroids were recruited. Venous blood was drawn from both groups using venipuncture technique and the serum vitamin D3 levels were estimated and compared.
Results: The mean vitamin D3 level was 12.98±7.79 ng/ml for those with fibroids and 44.50±9.60 ng/ml for normal group. The mean value was significantly lesser among those with fibroids than those normal with p value of less than 0.05. The mean vitamin D3 levels were similar between various sizes of fibroids.
Conclusions: In this study, the level of vitamin D3 was significantly lower among those with fibroids than those women who did not had any fibroids which shows that normal vitamin D3 levels might be protective against uterine fibroids and vitamin D deficiency can lead to the development of fibroids.

Keywords: Fibroid, Vitamin D, Myometrium, Extracellular matrix, Leiomyoma

INTRODUCTION

Fibroids, also referred to as uterine leiomyomas, are distinct, non-malignant growths originating within the smooth muscle layer of the uterus, known as the myometrium. They are the most frequent non-cancerous tumours occurring in the female genital system. These benign tumours stem from connective or mesenchymal tissues and represent one of the most common mesenchymal neoplasms of the uterus. Fibroids most frequently affect women in their 30s to 40s. Ethnicity is found to be significantly associated with development of fibroid with Black race is found to have a two to threefold increase in the risk of incidence of fibroid.[1] The overall incidence of uterine fibroid is between 20% to 77%.[1] It has been estimated that the prevalence of fibroids in India is 24% in urban areas and 37.65% in rural areas.[2] The development of fibroid is found to be multifactorial with the significant role of genetic , hormonal and inflammatory mechanisms. ESR1, CYP17A1, COL1A1. COL3A1, MED 12 is some of the genetic loci which has been found to have a significant role in the development of fibroid. Steroid hormones like Progesterone and Oestrogen are significantly found to be associated with the development of fibroid, Multiple molecular pathways are found to have a role in the pathogenesis of uterine fibroids, including the transforming growth factor-β (TGF-β) pathway, mitogen-activated protein kinase (MAPK) pathway, phosphatidylinositol 3-kinase (PI3K)/Akt pathway, and hedgehog signalling pathway. A diet high in fruits, vegetables, and fibre may be protective against fibroid growth, while dietary factors such the consumption of red

meat, processed foods, and alcohol have been linked to the formation of fibroid tumours.[3,4] Vitamin D though being the principal hormone of calcium and phosphorus haemostasis, found to have a significant association with reproductive physiology. Reduced serum vitamin D levels have already been linked to a number of obstetrical and gynaecological diseases, including polycystic ovarian syndrome and infertility. Vitamin D is found to have a significant role in the development of fibroids.[5] Ciebiera et al in his review stated that vitamin D alters the expression of PCNA, CDK1, M-phase promoting factor, Bcl-2 and COMT genes and also alters the TGF-β pathway which are directly involved in the development of fibroid.[5] According to Brakta et al 25-dihydroxyvitamin D3 is an anti-fibrotic agent that prevents the immortalized human uterine fibroid HuLM cells from proliferating. Moreover, it has been observed that vitamin D3 dramatically decreases MMP-2 and MMP-9 activity levels and raises VDR and TIMP-2 levels in a concentration-dependent manner.[6] Researches have shown the therapeutic supplementation of vitamin D in the women with fibroid have reduced the size of the fibroid and also helps in prevention of complications associated with fibroid.[7] Thus, the study is carried out with an objective of correlating the vitamin D3 levels in women with uterine fibroids and supplementation of vitamin D3 to reduce the incidences of uterine fibroids and management in women.

METHODS

The present study was a hospital based analytical study done at Chettinad Hospital and Research Institute, Chennai, India for 18 months between June 2022 to January 2024. The study was carried out among patients with fibroid and normal women attending to the department of obstetrics and gynecology during the study period. The study included 120 women with 60 of them having fibroid and other 60 without fibroid. Convenient sampling technique was adopted. The inclusion criteria include women in age group of 20-50 years, women with at least one uterine fibroid (for participants with fibroids), minimal volume of uterine fibroid to be 2 cm^3 (for participant with fibroids) and transvaginal ultrasonography (USG) showing no fibroids (for participants without fibroids). Women with history of pregnancy or abortion in the last 6 months, on hormonal therapy or vitamin supplementation and those with other preexisting illness like hypertension, diabetes, autoimmune disorders, coronary, hepatic and renal diseases were excluded from the study.

The data was collected using a semi structured interview schedule. All the women attending to in-patient and outpatient department were screened for the symptoms of fibroids. Those who presented with symptoms were examined using transvaginal ultrasonogram and if fibroids were present. After getting informed consent they were included into the group with fibroids. Normal woman those without any symptoms were also examined using transvaginal USG and after the conformation of absence any fibroid tissue was included into the group without fibroids. For all the participants after explaining the procedure of drawing venous blood. Following aseptic precautions, 5 ml of blood was drawn and then sent to the laboratory for serum vitamin D and hemoglobin estimation. Ethical approval for the study was obtained from institutional ethics committee. All the participants enrolled in the study were duly informed about the study procedure and consent was obtained from all. The collected data was entered into Microsoft excel 2019 and the master chart was created. The master chart was then loaded onto statistical package for the social sciences (SPSS) version 26 for statistical analysis. The quantitative variables were expressed in terms of mean and standard deviation and the qualitative variables using frequency and percentage. To compare the mean between the group's independent samples t-test was used. To compare the distribution of qualitative variables between the groups, Chi square test was used.

RESULTS

Both the groups were found to be similar with regard to the age of the participants. The body mass index was found to be more among the women who were normal (37.58±11.05) than those with uterine fibroids which is 31.27±1.95. With regard to parity, the proportion of nullipara was more among those with fibroids than those without any fibroids. The age at menarche was also found to be similar between those with fibroids and those who did not (Table 1).

Table 1: Baseline characteristics of the study participants.

Variables	Fibroid (n=60)	Normal (n=60)	T value	P value
Age (in years)	42.23±7.95	41.88±6.91	0.25	0.797
BMI (Kg/m^2)	31.27±1.95	37.58±11.05	4.36	0.001
Multiparity	54 (90%)	60 (100%)	6.31	0.012
Age at menarche (in years)	11.57±1.26	11.57±0.90	0.001	1.00

Among those with fibroids, 68.3% had complained of abdominal pain followed by 25% with IRMC. The other complaints recorded were abdominal distension, amenorrhea, bleeding PV and HMB (Figure 1) 65% had one fibroid followed by 28.3% with two.38.3% fibroids were in LUS followed by anterior wall (28.3%), posterior wall (25%) and right adnexa (20%). In 61.6% the fibroid was less than 5 cm and in 30% it was between 5 to 8 cm (Table 2). The mean haemoglobin level among those with fibroid was 11.01±1.07 gm% and for those without fibroid was 12.39±0.81 gm%. The mean value was significantly lesser among those with fibroids than those normal. The mean vitamin D3 level was 12.98±7.79 ng/ml for those

with fibroids and for those normal the mean value was 44.50±9.60 ng/ml. The mean value was significantly lesser among those with fibroids than those normal with P value of less than 0.05 (Table 3).

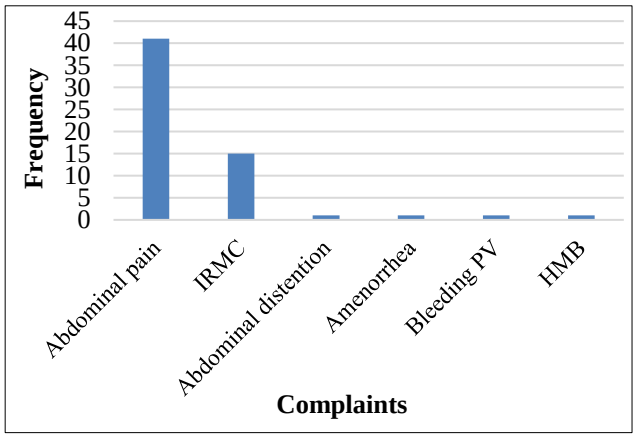

Figure 1: Distribution of complaints among those with fibroids.

Table 2: Distribution of fibroid characters among the study participants.

Character of fibroids	Frequency (n=60)	Percentage (%)
Number		
1	39	65
2	17	28.3
3	4	6.7
Location		
LUS	23	38.3
Anterior wall	17	28.3
Posterior wall	15	25
Right adnexa	12	20
Left adnexa	11	18.3
Left lateral	3	5
Fundus	3	5
Right lateral	2	3.3
Size of fibroids (in cm)		
<5	37	61.6
5-8	18	30
>8	5	8.3

Table 3: Vitamin D status and mean haemoglobin concentration in study participants.

Variables	Fibroid (n=60)	Normal (n=60)	T value	P value
Haemoglobin (gm%)	11.01±1.07	12.39±0.81	7.98	0.001
Mean vitamin D3 (in ng/ml)	12.98±7.79	44.50±9.60	19.73	0.001

The mean vitamin D3 levels among those with fibroid of less than 5 cm was 11.41±3.05 ng/ml, for those with 5 to 8 cm size fibroids, the mean was 14.58±12.10 ng/ml and for those with more than 8 cm, the mean was 18.78±10.66 ng/ml. The mean vitamin D3 levels were similar between various sizes of fibroids The difference is statistically not significant with p value greater than 0.05 (Table 4).

Table 4: Association of vitamin D3 levels with size of the fibroid.

Size of fibroids (in cm)	Vitamin D3 (in ng/ml)		F value	P value
	Mean	SD		
<5	11.41	3.05		
5-8	14.58	12.10	2.64	0.079
>8	18.78	10.66		

DISCUSSION

The present study was hospital based analytical study with the objective of comparing the mean vitamin D3 levels between women with fibroids and without fibroids. The study was carried out in Chettinad Hospital and Research Institute, Kelambakkam, Tamil Nadu for a period of 18 months. Two groups of 60 each one group with fibroids and the other without fibroids were recruited. Venous blood was drawn from both groups using venipuncture technique and the serum vitamin D3 levels were estimated. Both the groups were found to be similar with regard to the age of the participants. Choudhary et al also did a study with similar age group across both the groups.[8] The age at menarche was also found to be similar between those with fibroids and those who did not.

In the present study, the mean vitamin D3 level was significantly lesser among those with fibroids than those normal with p value of less than 0.05. This suggests that lower vitamin D levels have a higher risk of developing fibroid. This finding was similar to the study by Guo et al that assessed the causal association between vitamin D and fibroids by genomic analysis through SMPs and observed that even one SD decrease in serum vitamin D levels has a significant risk in the development of fibroids.[9] In their study in Egypt, Sabry et al discovered that reduced serum vitamin D levels are negatively connected to UF burden across ethnic groups. The study found that vitamin D insufficiency may be a risk factor for the development of uterine fibroids.[10]

In our study, the mean vitamin D3 levels were similar between various sizes of fibroids This finding was contrast to the observation made by Hajhashemi et al in their study in Iran among the patients with vitamin D deficiency and demonstrated that the size of leiomyomas decreased significantly in the group of participants who received vitamin D as intervention compared to placebo.[11]

Similarly, Xess et al in their study in India among the fibroid patients illustrated that vitamin D therapy halts the

progression of the size of fibroid whereas the placebo group showed an increase in size of the fibroid.[7] The study by Singh et al among Indian women too, observed that serum vitamin D concentrations were lower in women with fibroids than their normal counterparts and concluded that there is a strong association between fibroid size and serum vitamin D levels.[12]

The contrasting difference in our study can be due to the fact that the studies were of intervention type that assessed the impact of size of fibroid with the vitamin D therapy through follow up. Our study being an observational study could not elicit the long-term effect of vitamin D.

CONCLUSION

In this study, the level of vitamin D3 was significantly lower among those with fibroids than those women who did not had any fibroids. The probability of occurrence of fibroids might be more among those with lower serum levels of vitamin D3. The above leads to the idea that normal vitamin D3 levels might be essential for the non-development of uterine fibroids or the lower levels might bring in some pathological factors leading to the development of fibroids The limitations of the study is as the study is retrospective, temporal association between cause and effect could not be established. The present study was a single centre study so the population could be homogenous.

ACKNOWLEDGEMENTS

The authors would like to acknowledge the help rendered by Professor Dr. Vijayalakshmi K department of obstetrics and gynaecology for guiding the study and improving the methodology.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Moshika, Sailatha. A study on role of vitamin D3 in uterine fibroids. Int J Reprod Contracept Obstet Gynecol 2024;13:2082-5.