

Role of Vitamin D supplementation on the size of Uterine Leiomyomas in Women with Vitamin D Deficiency

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Abstract

Objective: To determine the role of vitamin D supplementation on size of uterine leiomyomas in vitamin D deficient woman.

Methods: The study was conducted in the Department of Obstetrics and Gynaecology, Rawalpindi, from July 2019 to January 2020. This was a quasi-experimental study. A probability consecutive sampling method was used. Sixty-five women with a diagnosis of 1 to 2 uterine leiomyomas measuring 4– 8 cm in diameter, vitamin D insufficiency and experiencing heavy vaginal bleeding were included. The 25-hydroxyvitamin D levels in the blood were checked. Vitamin D was then administered in five dosages over a period of ten weeks, with each patient receiving a total dose of 50,000 IU of vitamin D after every fourteen days. After 6 months, an ultrasound was done to determine the size of the fibroid. The mean size of leiomyomas was compared before and after vitamin D for six months using a paired t-test.

Results: Mean age of the patients was 35.85±6.140 year. Mean age at menarche of the patients was 11.62±1.206 year. Mean marital life of the patients was 9.47±6.046 year. Mean Hb levels of the patients were 11.406±1.1875 mg/dl. Mean size of leiomyoma before treatment was 54.170±4.5493 mm, while mean size of leiomyoma after treatment was 44.991±2.7046 mm, with a p-value of 0.001.

Conclusion: Vitamin D supplementation has been demonstrated to considerably reduce the growth of uterine fibroids. It would seem that females with vitamin D insufficiency can effectively treat their uterine fibroids by taking vitamin D supplements.

Keywords: Vitamin D Deficiency, Uterine Fibroids, Leiomyoma Size.

Introduction

The leiomyomas are the most frequent solid benign gynaecological uterine tumours. They developed from the clonal growth of a single myometrium cell ¹. It is the most frequent benign pelvic tumour in women of childbearing age, with incidences ranging from 5.4% to 77% globally ².

Particularly when they are located in the submucosa, UFs are frequently linked to severe morbidity. Anaemia, severe and protracted menstrual bleeding, pelvic pain, and infertility are all possible symptoms for women with UFs ³.

Uterine fibroid is a multifactorial disease. Uterine fibroids are largely fueled by ovarian hormones, including estrogen and progesterone, growth factors, cytokines, and chemokines. Smooth muscle cells that have a large amount of the extracellular matrix (ECM), which is made up of proteoglycans, fibronectin, and collagen, are what make up fibroids. The chance of developing uterine fibroids is influenced by genetic and epigenetic variables, even though the origin of uterine fibroids is unclear. Other risk factors have also been found like age, race and ethnicity, family history, body mass index, early exposure to pollutants from the environment, vitamin D insufficiency, and other factors are some of these ^{4,5}.

Depending on the location and size of the fibroids, UFs can present with a variety of symptoms and degrees of severity. Since UFs are thought to affect up to 70% of women at some point in their lives, physicians must pay close attention to how they affect society and women's quality of life ⁶. Depending on the symptoms, age, general health, concern for fertility preservation, and individual patient's preferences, management options for uterine fibroids include medicinal therapy, radiologically guided procedures, and surgical interventions. To treat UFs, non-surgical procedures and therapies should be taken into consideration ⁷.

Approximately 70% of women of reproductive age have leiomyomas, which are more common in young age ⁸.

Contributions:

SA, SY - Conception, Design
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There are no minimally invasive procedures which can successfully shrink leiomyoma size without side effects. The pathophysiology of uterine leiomyomas is unclear. Vitamin D deficiency has a higher chance for development of developing uterine fibroids. Since the majority of women with uterine leiomyoma have low vitamin D levels (≤ 20 ng/mL), normal vitamin D levels may be linked to a lower risk of uterine fibroids⁹.

Additionally, the serum level of 25-hydroxyvitamin D3 is significantly lower in affected women than in control women, indicating an inverse relationship between total leiomyoma volume and vitamin D serum levels¹⁰. These findings suggest that vitamin D may be important for the growth of leiomyomas. The vitamin D, or more specifically, its active metabolite 1,25[OH]2D₃, is important for calcium and phosphate regulation in the body.

Since vitamin D has been shown to have antiproliferative properties and antitumorigenic agent in cancer cells. It affects proliferation, cell cycle progression, the Wnt/-catenin pathway, and apoptosis has therefore been shown to be a key mechanism by which vitamin D exerts its anticancer effects^{11,12}.

According to a cross-sectional study done in Iran, women with uterine leiomyomas had mean blood levels of 25-hydroxyvitamin D3 that were lower (21.37 ± 7.4 ng/mL) than women without uterine leiomyomas (24.62 ± 9.2 ng/mL)¹³. Another cross-sectional observational study found an inverse correlation between serum 25-hydroxyvitamin D levels and the volume of uterine leiomyomas ($p=0.000$) and concluded that participants with big fibroid masses had significantly lower blood 25-hydroxyvitamin D levels than those with smaller fibroid masses¹⁴.

The size of the leiomyoma was significantly reduced in females treated with vitamin D compared to placebo (52.58 versus 61.11 mm, respectively) in a double-blinded, prospective randomised trial in which females diagnosed with uterine leiomyoma and vitamin D deficiency were treated with vitamin D or placebo every two weeks for 10 weeks. These findings suggested that vitamin D3 supplementation can be a useful medical therapy for the management of uterine leiomyoma by reducing the mass of the tumour¹⁵.

The goal of this study was to determine how vitamin D supplementation affected the size of uterine leiomyomas in women who were vitamin D deficient. By reducing the size of the uterine leiomyoma and subsequently its symptoms without necessitating any significant surgical procedures, this study will contribute to lowering the burden of disease on healthcare providers and enhancing the wellness of women.

Materials And Methods

The study was conducted in the Department of Obstetrics and Gynaecology from July 2019 to January 2020. It was a quasi-experimental study, and non-probability consecutive sampling technique was used for collection of samples. With a 95% confidence interval and 80% power of the study, a sample size of 65 women was estimated.

The women of reproductive age with a diagnosis of 1 to 2 uterine leiomyomas measuring 4–8 cm in diameter, vitamin D insufficiency and experiencing heavy vaginal bleeding were included.

The women with co-morbid disorders such as hypertension (BP140/90mmHg), diabetes (BSR>200mg/dl), heart disease (abnormal ECG and medical record), hepatic (ALT or AST>40IU, hepatitis B or C), or renal diseases (creatinine>1.5mg/dl), those who are pregnant, going through menopause, and already taking vitamin D supplements, were excluded.

The informed consent was taken from women included in the study after approval from the hospital's Ethical Board of RMU. A thorough history of demographic information was gathered, such as heavy monthly flow, anaemia, dysmenorrhea, pelvic pressure, backache, bloating, frequent urination, and dyspareunia. The levels of serum 25-hydroxyvitamin D were determined and recorded on a Performa with particular design features. The Vit D was then administered in five doses over ten weeks, with each patient receiving a total dose of 50,000 IU of vitamin D after every fourteen days. The size of the uterine leiomyoma was recorded six months after the start of the treatment by trans-abdominal ultrasound by gynecologist. The level of vitamin D was also measured after 6 months.

The data was entered using SPSS version 25, and the outcomes were assessed. While qualitative factors like the presence of heavy menstrual bleeding, anemia, dysmenorrhea, pelvic pressure, backache, bloating, frequent urination, and dyspareunia were expressed as the frequency of occurrence and the percentage of women who experienced these symptoms, quantitative factors like age, the size of the uterine leiomyoma, and serum levels of 25-hydroxyvitamin D3 were expressed as the mean value along with the standard deviation. The mean size of the leiomyoma before and after receiving vitamin D treatment for six months was compared using a paired t-test. P-values of 0.05 or lower were considered to represent statistically significant relationships.

Results

For this study, a total of 65 women with uterine fibroids and vitamin D insufficiency were chosen. The patients' mean age was 35.85 ± 6.14 years. The patients' mean age at menarche was 11.62 ± 1.206 years. In the age range of 31 to 45, the patients' average length of marriage was 9.47 ± 6.046 years. The patients' mean haemoglobin levels were 11.406 ± 1.1875 mg/dl.

Table 1: Change in size of leiomyoma before and after the treatment with vitamin D

	n	Mean	Std. Deviation	p-value
Size of leiomyoma (mm) before treatment		54.170	4.5493	
Size of leiomyoma (mm) after treatment	65	44.991	2.7046	0.001

According to the patients' age distribution, 42 patients (64.4%) were above 30 years, and 23 patients (35.3%) were between the ages of 18 and 30. Six patients (9.2%) suffered dysmenorrhea, while 11 patients (16.9%) had anaemia. 3 individuals (4.6%) had pelvic pressure. Back pain affected 22 (33.8%) people. 12.4% of the patients had bloating. 5.6% of the patients experienced frequent urination. Six (9.2%) of the patients suffered dyspareunia.

Table 2: Change in levels of vitamin D before and after the treatment with vitamin D

	n	Mean	Std. Deviation	p-value
Level of vit. D (ng/ml) before treatment		16.613	1.3728	
Level of vit. D (ng/ml) after treatment	65	36.050	1.5268	0.001

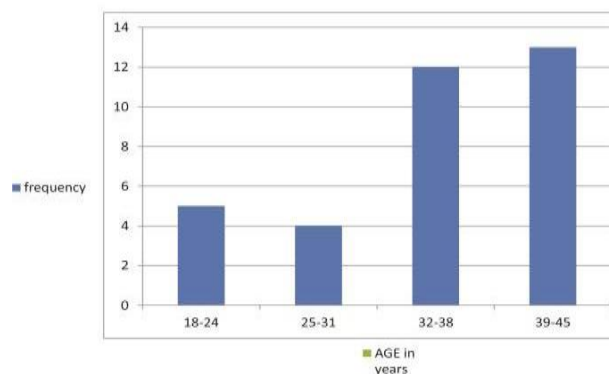


Figure 1: Graphical representation of the frequency distribution of the age group

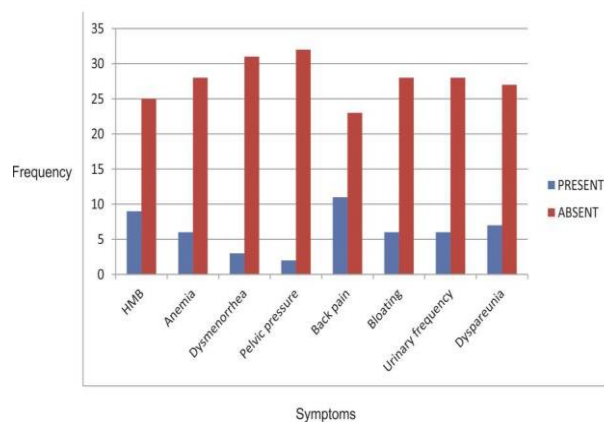


Figure 2: Graphical representation of the frequency distribution of symptoms

According to location of leiomyoma distribution, 14(21.9%) had intramural myomas, 40(61.5%) had subserosal myomas, 9(13.8%) had pedunculated myomas and 3(4.3%) had submucosal myomas (**Figure 3**). According to parity distribution, 10(15.3%) were nulliparous, 19(29.2%) were primiparous and 36(55.3%) were multiparous (**Figure 4**). Mean size of leiomyoma before treatment was 54.170 ± 4.5493 mm, while mean size of leiomyoma after treatment was 44.991 ± 2.7046 mm with p-value of 0.001 (**Table 1**), which is statistically significant. A paired t-test was applied. The mean level of vitamin D before treatment was 16.613 ± 1.3728 ng/ml, while the mean level of vitamin D after treatment was 36.050 ± 1.5268 ng/ml, with a p-value of 0.001 (**Table 2**), which is statistically significant. A paired t-test was applied.

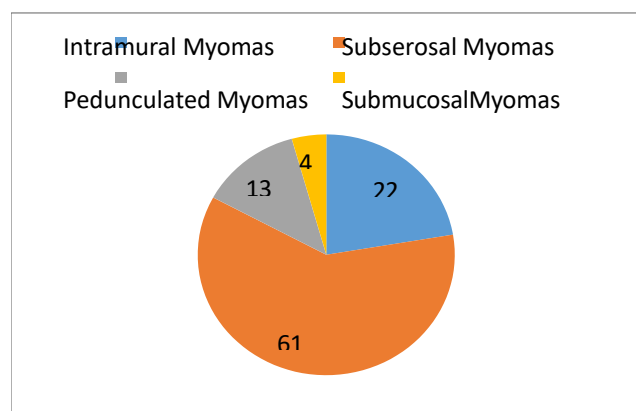


Figure 3: Percentage distribution of the location of Leiomyoma

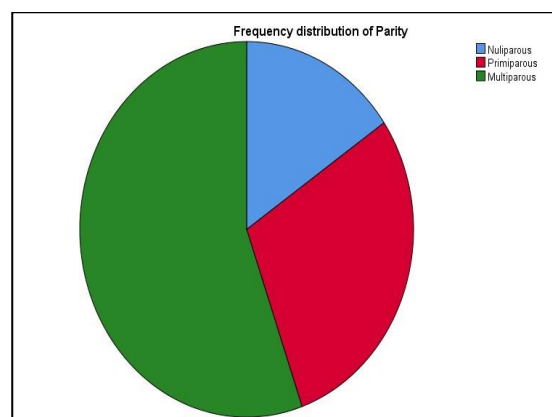


Figure 4: Frequency distribution of parity

Discussion

The aim of this study was to investigate the effect of vitamin D supplementation on the development of uterine leiomyomas. Our study showed that women with vitamin D deficiency develop leiomyomas that are considerably smaller when they take a vitamin D supplement. Additionally, following the administration of vitamin D, the levels of 25-hydroxyvitamin D₃ increased significantly.

A class of steroid substances known as vitamin D has a profound effect on a variety of bodily functions, including the neurological, immunological, and genitourinary systems. There are different types of vitamin D, including vitamin D₁ (calciferol), which is most frequently found in fish oils, vitamin D₂ (ergocalciferol), which is found in plants, and vitamin D₃ (cholecalciferol),

which is made by the skin. The liver's 25-hydroxylase enzyme transforms vitamin D into 25-hydroxyvitamin D [25(OH)D], which is then hydroxylated in the kidneys to form 1,25-dihydroxyvitamin D [1,25(OH)D]. 1,25(OH)D, the most active form of this vitamin, has activity in nearly all human body tissues¹⁶.

UFs are exceedingly frequent benign uterine tumours that can seriously harm a patient's physical and mental health. Fibroids with symptoms are often handled and treated. However, there is currently no evidence to recommend routine therapy for the majority of asymptomatic UFs. Therefore, it is crucial to estimate the risk of new fibroid formation and give effective therapy. It is well accepted that age and vitamin D status have a substantial impact on UFs. It is yet uncertain, though, what clinical level of vitamin D is necessary for new fibroid development. In the current investigation, we discovered that vitamin D levels may help assess the likelihood that asymptomatic UFs will develop⁵.

Meta-analysis by Alsharif et al. concluded that vitamin D supplementation is a cost-effective and non-invasive therapeutic alternative to surgery⁹. Low 25-hydroxyvitamin D levels have been associated with symptoms of uterine fibroids, according to Ciebia et al. In a study, Ciebia M and associates concluded that paricalcitol supplementation would be a possibility for a noninvasive medical treatment for uterine fibroids¹⁷.

Our conclusion that treatment with 1,25-dihydroxyvitamin D₃ reduces the growth of uterine leiomyoma tumours, matched with the results of a study by El Sabeh M¹¹. Dalla-Valasa & associates concluded that 1,25-dihydroxyvitamin D affects apoptosis, alters several genes linked to cell development, promotes cell proliferation, and stimulates protein synthesis. These characteristics form the basis for 1, 25-dihydroxyvitamin D₃'s ability to combat leiomyoma tumours¹².

Furthermore, meta-analysis by Mohammadi et al. Confirmed an inverse relationship between serum vitamin D levels and the presence of uterine fibroids among different populations, particularly in Asian cohorts, where the effect was most pronounced (SMD = -1.20; p < 0.001)¹⁸. Similarly, Okoro et al. Found significantly lower vitamin D levels in women with uterine fibroids compared to healthy controls, emphasising that vitamin D deficiency is a modifiable risk factor¹⁰.

Suneja et al. highlighted the effect of vitamin D₃ supplementation in improving the associated symptoms of fibroids, including menorrhagia, pelvic pain, and dysmenorrhea. While the leiomyoma volume reduction was modest, the symptomatic relief and serum vitamin D elevation were consistent with our outcomes¹⁹.

Conclusions

To conclude, we demonstrated that vitamin D deficiency was independently related to the presence of asymptomatic UFs, suggesting that vitamin D level might be considered in a UF risk measure. In addition, it was discovered that the frequency and volume of UF were considerably greater in these women as compared to the control participants; this finding is in keeping with previous publications and indicates a negative link between blood Vitamin D levels and the prevalence and volume of UF. In addition, there was a dose-dependent relationship between the amount of vitamin D in the serum and the size of the fibroid tumour. Vitamin D is well recognised as the primary regulator of calcium homeostasis. Numerous studies have shown that 1, 25-dihydroxyvitamin D is an effective anticancer drug that suppresses the growth of uterine cancer. These observations and results provide additional evidence in favour of the possible use of 1, 25(OH)₂D₃ or its powerful analogues for nonsurgical uterine leiomyoma therapy. It has been demonstrated that vitamin D Supplementation can shrink uterine fibroids. It would seem that using vitamin D supplements could be an efficient medical care for uterine fibroids.

References

1. Alkutbi SH, Nassir ES, Ibrahim AI. Uterine leiomyomas (Uterine fibroids). *Annals of the Romanian Society for Cell Biology*. 2021;25(4):6662-86.
2. Ahmad A, Kumar M, Bhoi NR, Akhtar J, Khan MI, Ajmal M, Ahmad M. Diagnosis and management of uterine fibroids: current trends and future strategies. *Journal of basic and clinical physiology and pharmacology*. 2023 May 1;34(3):291-310. <https://doi.org/10.1515/jbcpp-2022-0219>
3. Vahdat M, Allahqoli L, Mirzaei H, Giovannucci E, Salehiniya H, Mansouri G, Alkatout I. The effect of vitamin D on recurrence of uterine fibroids: a randomized, double-blind, placebo-controlled pilot study. *Complementary Therapies in Clinical Practice*. 2022 Feb 1;46:101536. <https://doi.org/10.1016/j.ctcp.2022.101536>

4. Islam MS, Akhtar MM, Segars JH. Vitamin D deficiency and uterine fibroids: an opportunity for treatment or prevention?. *Fertility and sterility*. 2021 May 1;115(5):1175-6. <https://doi.org/10.1016/j.fertnstert.2021.02.040>
5. Xu F, Li F, Li L, Lin D, Hu H, Shi Q. Vitamin D as a risk factor for the presence of asymptomatic uterine fibroids in premenopausal Han Chinese women. *Fertility and sterility*. 2021 May 1;115(5):1288-93. <https://doi.org/10.1016/j.fertnstert.2020.12.001>
6. Micić J, Macura M, Andjić M, Ivanović K, Dotlić J, Micić DD, Arsenijević V, Stojnić J, Bila J, Babić S, Šljivančanin U. Currently available treatment modalities for uterine fibroids. *Medicina*. 2024 May 26;60(6):868. <https://doi.org/10.3390/medicina60060868>
7. Fortin CN, Jiang C, Caldwell MT, As-Sanie S, Dalton V, Marsh EE. Trends in emergency department utilization among women with leiomyomas in the United States. *Obstetrics & Gynecology*. 2021 May 1;137(5):897-905. <https://doi.org/10.1097/AOG.0000000000004333>
8. Alsharif SA, Baradwan S, Alshahrani MS, Khadawardi K, AlSghan R, Badghish E, Bukhari IA, Alyousef A, Khuraybah AM, Alomar O, Abu-Zaid A. Effect of Oral Consumption of Vitamin D on Uterine Fibroids: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. *Nutrition and Cancer*. 2024 Mar 15;76(3):226-35. <https://doi.org/10.1080/01635581.2023.2288716>
9. Okoro CC, Ikpeze OC, Eleje GU, Udigwe GO, Ezeama CO, Ugboaja JO, Enechukwu CI, Umeononihu OS, Ogbado CA, Oguejiofor CB, Njoku TK. Association between serum vitamin D status and uterine leiomyomas: a case-control study. *Obstetrics & Gynecology Science*. 2023 Oct 17;67(1):101-11. <https://doi.org/10.5468/ogs.23143>
10. El Sabeh M, Saha SK, Afrin S, Islam MS, Borahay MA. Wnt/ β -catenin signaling pathway in uterine leiomyoma: role in tumor biology and targeting opportunities. *Mol Cell Biochem*. 2021 Sep;476(9):3513-3536. <https://doi.org/10.1007/s11010-021-04174-6>
11. Dallavalasa S, Tulimilli SV, Bettada VG, Karnik M, Uthaiiah CA, Anantharaju PG, et al. Vitamin D in Cancer Prevention and Treatment: A Review of Epidemiological, Preclinical, and Cellular Studies. *Cancers*. 2024 Sep 20;16(18):3211. <https://doi.org/10.3390/cancers16183211>
12. Farzaneh F, Sadeghi K, Chehrazhi M. Vitamin D status in women with uterine fibroids: a cross-sectional study. *Open Access Macedonian Journal of Medical Sciences*. 2020 Apr 5;8(B):109-13.
13. Kumari R, Nath B, Gaikwad HS, Sharma M. Association between serum vitamin D level and uterine fibroid in premenopausal women in Indian population. *Drug Discoveries & Therapeutics*. 2022 Feb 28;16(1):8-13. <https://doi.org/10.5582/ddt.2021.01019>
14. Hajhashemi M, Ansari M, Haghollahi F, Eslami B. The effect of vitamin D supplementation on the size of uterine leiomyoma in women with vitamin D deficiency. *Caspian journal of internal medicine*. 2019;10(2):125. <https://doi.org/10.22088/cjim.10.2.125>
15. Magagnoli L, Cassia M, Galassi A, Ciceri P, Massó E, Gelpi R, et al. Vitamin D: are all compounds equal?. *Clinical Kidney Journal*. 2025 Mar 13;18(Suppl 1):i61-i96. <https://doi.org/10.1093/ckj/sfae417>
16. Taha AA, Elsayed FA, Al-Fakharany RS, Khamis Y. Possible Impacts of Vitamin-D Supplements on Uterine Fibroid. *Egyptian Journal of Medical Research*. 2024 Jul 1;5(3):50-62. <https://doi.org/10.21608/ejmr.2024.235405.1459>
17. Ciebiera M, Kociuba J, Ali M, Madueke-Laveaux OS, Yang Q, Bączkowska M, et al. Uterine fibroids: current research on novel drug targets and innovative therapeutic strategies. *Expert Opinion on Therapeutic Targets*. 2024 Aug 2;28(8):669-87. <https://doi.org/10.1080/14728222.2024.2390094>
18. Mohammadi R, Tabrizi R, Hessami K, Ashari H, Nowrouzi-Sohrabi P, Hosseini-Bensenjan M, Asadi N. Correlation of low serum vitamin-D with uterine leiomyoma: a systematic review and meta-analysis. *Reproductive Biology and Endocrinology*. 2020 Dec; 18:1-8. <https://doi.org/10.1186/s12958-020-00644-6>
19. Suneja A, Faridi F, Bhatt S, Guleria K, Mehndiratta M, Sharma R. Effect of Vitamin D3 Supplementation on Symptomatic Uterine Leiomyoma in Women with Hypovitaminosis D. *Journal of Mid-life Health*. 2021 Jan;12(1):53-60. https://doi.org/10.4103/jmh.JMH90_19