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RESEARCH ARTICLE
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AN INTERVENTIONAL STUDY FOR DECREASED VITAMIN-D LEVELS AS A RISK FACTOR FOR DEVELOPING UTERINE FIBROID

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Abstract
Uterine fibroids or leiomyomas are the most common tumors of females in their reproductive life, they usually represent heavy mensural bleeding, dragging abdominal pain, and pressure symptoms, there are numerous uterine fibroid risk factors, and vitamin D deficiency has a significant effect on reproductive women. In general, black women are more likely to suffer from uterine fibroid than other ethnic groups, with estimates of incidence ranging from 5.4% to 77% globally. Uterine fibroid frequency in Pakistan is believed to be around 54%. The treatment options depend upon the size, quantity, and location of the uterine fibroid. Agonists for gonadotropin-releasing hormone, selective progesterone receptor modulators, tranexamic acid, and dydrogesterone, while surgical treatment shrinks the fibroid, medical treatment only reduces the symptoms temporarily. The **o**bjectiv**e** of this study was to assess the decreased Vitamin -D level as a risk factor for developing uterine fibroid. In this study, 5000 IU of vitamin D was given orally as an adjuvant therapy together with 500 mg of tranexamic acid and 10 mg of dydrogesterone. Vitamin D a, steroid hormone with a significant impact on other body areas is vitamin D, Deficiency of vitamin D may strongly correlate with the growth of leiomyomas. Our study concluded that there was evidence of a strong association between the administration of vitamin D and the reduction of the size of uterine fibroid

Key Words: Uterine Fibroid, Leiomyoma, Vitamin-D, Size, Heavy bleeding, dragging pain

INTRODUCTION:

In the second century AD, uterine fibroids—then known as Scleromas were referred to as uterine stones. The term "fibroid" was first used in the 1860s, and they are the most common benign growth of the pelvis throughout the period of childbearing. Estrogen supports and promotes growth. Uterine fibroids develop during the reproductive cycle, increase during labor, and then decline after menopause; however, they might occasionally still cause problems after menopause. In premenopausal years, an irregular ovulatory cycle with high estrogen might result in sudden growth.

Estrogen causes the uterus to maintain and develop in size since fibroids are susceptible to it (Banerjee et al., 2022). The most frequent benign condition of the female genital tract is uterine fibroids, which most frequently affects premenopausal women. The primary cause of hysterectomy is uterine fibroid; conservative treatment may lessen bleeding, but for those women who wish to regain their uterus or fertility, a few cutting-edge techniques may be advised. Uterine fibroids' true cause and pathophysiology remain unknown. According to Ciebiera, M. et al. (2017), the uterine fibroid is linked to heavy monthly bleeding, dragging bladder pressure sensations, abdominal pain, and numerous unfavorable perinatal outcomes. Uterine fibroid incidence ranges between 54% and 77% globally (Navarro, A. et al., 2021). Uterine fibroids are thought to occur frequently—about 54% of the time—in Pakistan (Ibrar et al., 2010). Heavy menstrual flow is caused by uterine fibroid. Tumors can result in a wide variety of clinical signs and symptoms, including heavy menstrual cycles, pressure symptoms affecting the nearby organs, and fertility problems. Many women with uterine fibroid are unintentionally diagnosed on a normal gynecological exam or pelvic ultrasound/MRI (Munusamy et al., 2017). Tumors cause a broad range of clinical signs and symptoms such as heavy menstrual periods, pressure symptoms related to the surrounding organs and fertility issues. Many women with uterine fibroid are accidentally diagnosed on their routine gynecological examination or pelvic ultrasound / MRI (Munusamy et al., 2017).

The primary cause of hysterectomy is uterine fibroid; conservative treatment may lessen bleeding, but for those women who wish to regain their uterus or fertility, a few techniques may be advised. The actual causes of uterine fibroids are unknown. Further study is needed to determine whether vitamin D' have anti-tumor properties that can help uterine fibroid symptoms subside. Recent studies and research have revealed that vitamin D plays a significant role in improving and managing uterine fibroid. Leiomyomas can range in size from tiny seeds to large masses that can deform the uterus. According to their location, uterine fibroids can be single or many (Viva et al., 2021). Ultrasound (TVS) displays the size and location of the uterus in the pelvic cavity based on radiographic measurements of the uterus' size. According to a CT scan, the uterus appears as a single mass of tissue on the bladder's posterior side. The uterus' anatomy can be seen on an MRI in the shape of a zone (Woźniak, A., & Woźniak 2017). Imaging techniques (such as an MRI or CT scan) or ultrasonography are used to diagnose uterine fibroids. In accordance with fibroid location, size, and scoring method, it also offers a standard classification system. Imaging does not reveal any mutations or symptom presentation; In addition to transvaginal ultrasonography, a pelvic examination can also be used for diagnosis. (Aninye and Laitner, 2021). Regarding the management of the uterine fibroid the use of contraceptives, gonadotropin hormone analogs (GnRHa), and selective progesterone receptor modulators. (Dolmans and others, 2021) Myomectomy surgery, hysterectomy, uterine artery embolization, and magnetic resonance-guided focused ultrasound are surgical options available. Numerous studies have established a strong link between vitamin D deficiency and the development of fibroid tumors (De La et al., 2017).

Methodology: It was a randomized controlled interventional trial study. Patients were selected from the outpatient Department of Gynecology and Obstetrics JPMC Karachi, it took 10 months to complete. A total of 113 patients were interviewed from the outpatient Department of Gynecology and Obstetrics Patients were taken by using stratified random sampling. Out of 111 this patient who were allowed to participate in the study, the remaining patients were excluded due to the aggressiveness of their pressure symptoms which could have led to surgery, on the other hand, selected patients getting samples of serum vitamin-D cases of uterine fibroid that had been detected through radiographic investigation were also collected and after getting sample of serum vitamin D also, in this study we gave 50,000 IU of vitamin D /orally were prescribed as an adjuvant therapy along with Tranexamic acid 500mg and Dydrogesterone 10 mg orally. Inclusion criteria include females between the ages of 30 and 50 years, Menorrhagia, premenopausal women, and, dominant myomas of 3 to 13 cm in size, Exclusion criteria include, Pregnancy, women under 30, malignancy and, myomas nor less than 3cm and not more than 13 cm.

Sample size:
Taking the frequency of the templet reference studies, the sample size was calculated by using online software through PASS 2020. Group sample sizes of 30 sufficient vitamin D (>20 ng/ml) and 83 insufficient vitamin D (≤20 ng/ml) produce an odds ratio with a width that is equal to 1.723 when the estimated sample proportion 1 is 0.24 a two-sided 95% confidence interval for the population, the estimated sample proportion 2 is 0.32, and the sample odds ratio is 0.68 (Baird et al., 2013).

Data collection tool:
We employed quantitative chemiluminescent immunoassay (CLIA) (Snellman et al., 2010) as one of the immunoassay methods to estimate the results

Statistical Analysis:
To conduct statistical analysis. The mean and standard deviation for continuous data were calculated using NCSS 2020 Statistical Software (2020), and counts and percentages were used for categorical variables. The two-sample T-test was used to compare the means of the two groups, and the paired t-test was used to compare the groups' means before and after the intervention. At a p-value of 0.05 or lower, the findings were deemed significant (Baird et al., 2013).

Ethical consideration:
Permission for the study was taken by the Institutional Board Review (IBR) of Basic Medical Institute, JPMC, and Karachi, for research was conducted with (Reference No F.2-81/2021-GENL/61531/JPMC.

Results:

Table 1: Mean Change in Vitamin-D Level (ng/ml) Before and After Intervention

Vitamin-D level (ng/ml)	n	SD	SEM
Before intervention (ng/ml)	111	8.04	0.76
After intervention (ng/ml)	111	7.31	0.69
Mean difference from before to after intervention (ng/ml)	17.90		
SD of mean difference	± 8.94		
95 % Lower Class Limit	16.23		
95 % Upper Class Limit	19.58		
t-value	21.09		
p-value	0.001*		

Table 1 revealed that in 111 patients, the mean level of vitamin-D before intervention was 22.08 8.04 ng/dl, and after intervention, it was 39.98 7.31 ng/dl. The average rise in vitamin-D concentration following mediation was found to be 17.90 8.94 ng/dl. With p=0.001, it was determined that the difference between the vitamin-D level before and after the intervention was statistically significant.

Table 2: Mean Change in Size of Fibroid Uterus (cm) Before and After Intervention

Size of fibroid uterus (cm)	N	SD	SEM
Before intervention (cm)	111	1.99	0.19
After intervention (cm)	111	1.31	0.12
Mean difference from before to after intervention (cm)	4.84		
SD of mean difference	± 1.55		
95 % Lower Class Limit	4.55		
95 % Upper Class Limit	5.13		
t-value	32.79		
p-value	0.001 *		

Table 2 demonstrated a mean difference in the size of the fibroid uterus between the 111 patients before and after the intervention. The mean fibroid uterine size was 8.49 ± 1.99 cm prior to intervention, and 8.49 ±199 cm following intervention. With a statistical significance level of P=0.01, the mean uterine fibroid size decreased by 4.84 ±1.55 cm on average following the intervention.

Figure1: Change in Vitamin D level (ng/ml) before and after intervention

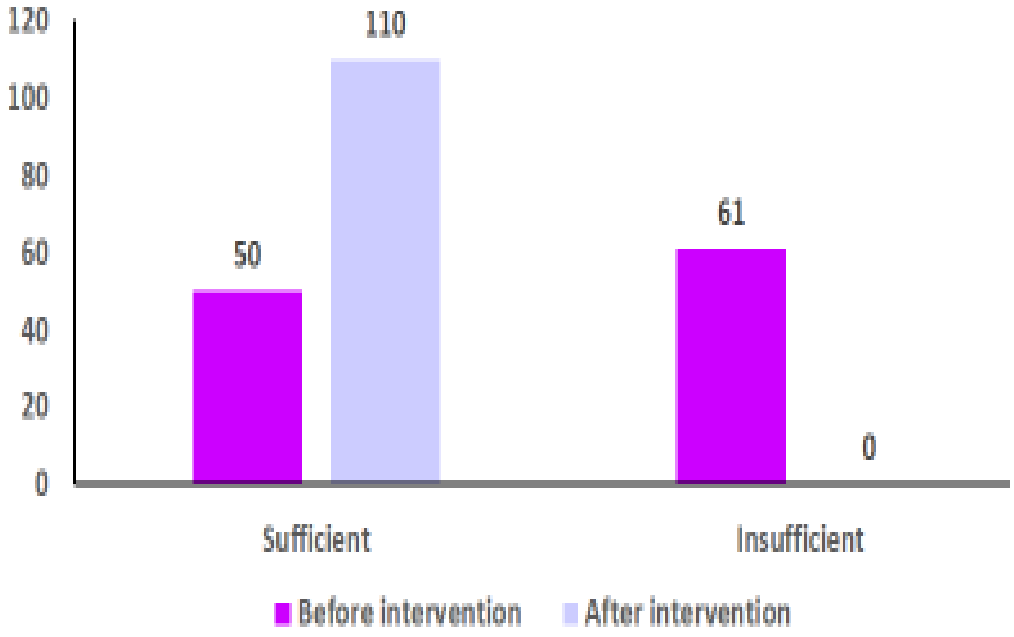


Figure 2: Change in size of fibroid uterus (cm) before and after intervention

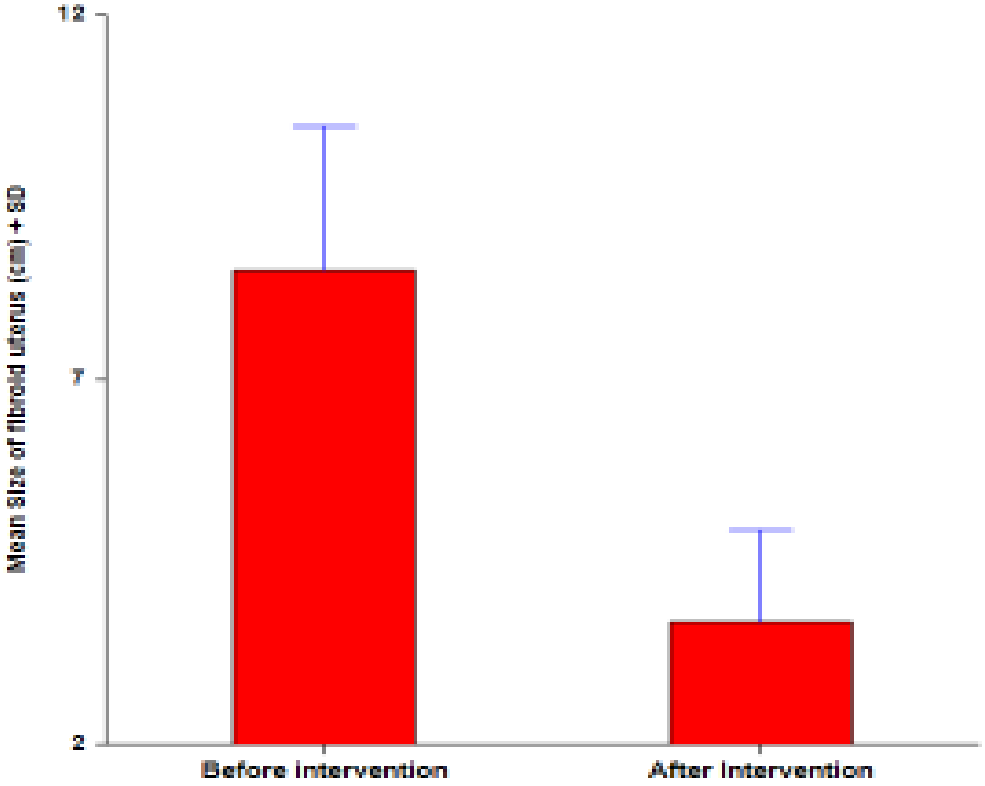
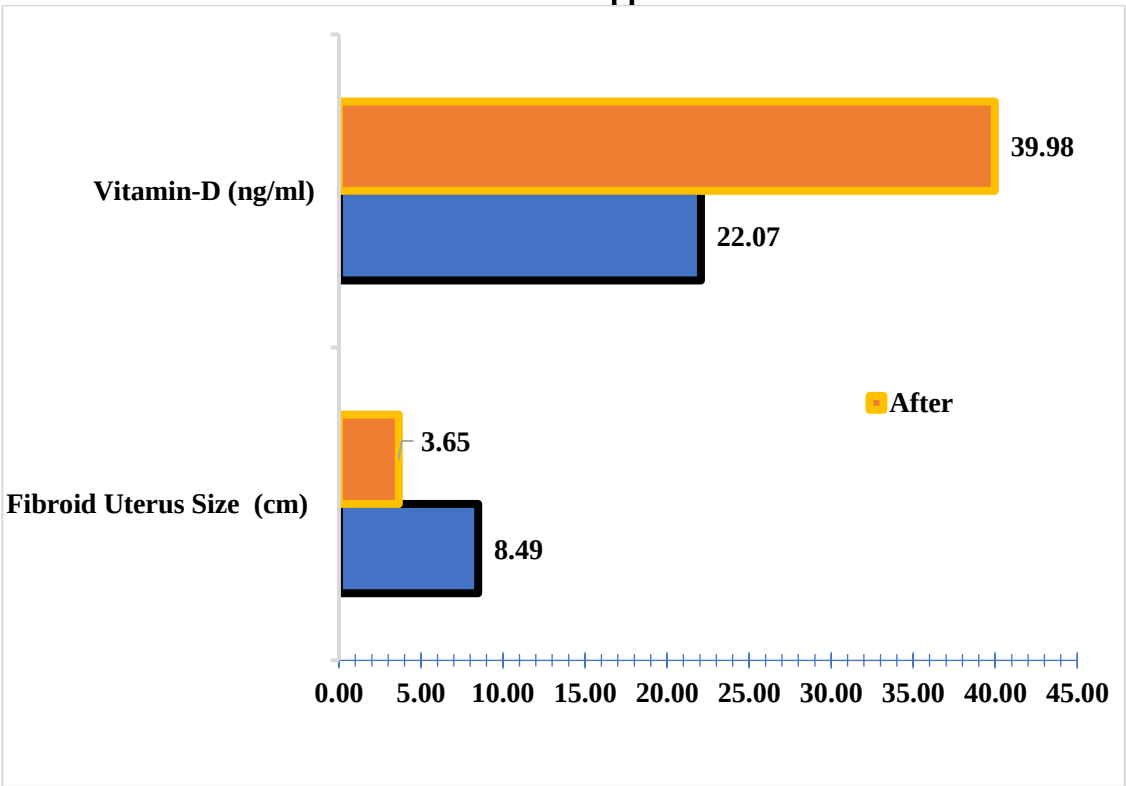


Figure3: Comparison of size of fibroid uterus (cm) and vitamin D level (ng/ml) before and after oral vitamin D supplementations.



Discussion:

This study was conducted in the Obstetrics & Gynecology Department, of Jinnah Postgraduate medical center, Karachi, which is a tertiary care hospital. In our study, we gave vitamin D 50,000 IU orally per week for ten months to the uterine fibroid patients, drastically improving the symptoms and the patient's quality of life. Another study conducted open-label clinical research on uterine fibroid and vitamin-D-deficient women, who were given 50,000 IU orally per week for 12 months which also improved the symptoms of the patient (Ciavattini et al., 2016).

A cohort study showed that low serum vitamin-D levels were remarkably concerned with the development of uterine fibroid and inverse co-relation is seen between the vitamin-D levels and uterine fibroid size (Sabry et al., 2013).Our results proved that Vitamin-D supplements along with conventional treatment have a marked effect on vitamin-D deficient women on the size of uterine fibroids in premenopausal women. Current medical treatments are prescribed to avoid risks that belong to long-term treatment. Recent novel discoveries such as oral GnRH antagonists, SERM, Vitamin D, and green tea extract etc, had beneficial effects with few side effects (Brakta,S,et al., 2015). Our study proved that patients who were treated with Tranexamic acid 500 mg and Dydrogestrone10mg orally along with 50,000 IU of vitamin-D supplements not only decrease in the size of uterine fibroid from 8.49 to 3.65 cm but also reduces the symptoms of the patient efficiently. Another study suggested that the mean fibroid size changed after taking intervention in 8 weeks before it was 47.98cm and then 41.81 cm respectively (Davari et al., 2021.

Conclusion:

Our study concludes and supports that there was evidence of a powerful relationship between the reduction in the size of a fibroid tumor and vitamin D.

In our study, 50,000 IU of vitamin D along with Tranexamic acid 500 mg and Dydrogesterone 10mg orally, supports the reduction of the size of uterine fibroid among mild to moderate symptoms caring women This study concluded that uterine fibroid was more common among multiparous women. This study strongly recommended that vitamin D supplements reduce the size of the uterine fibroid. It was a safe acceptable mode of novel treatment and it is a noninvasive agent.

Limitation Of Study:
The results obtained by this interventional study may not be applied to the huge population.
Women with leiomyoma with sizes around 12 and 13 are preferred to be treated with surgical intervention. My study was conducted on a small sample size.

Financial Support and Sponsorship:
There is no relevant affiliation or financial involvement with any organization or with financial interest or conflict with the subject or material.

Patient Education:
Patients need to understand that the majority of women with fibroids are benign in nature, the word such as a tumor creates a potential harmful effect on wellbeing of the patient. Fibroid can carry a heavy burden of disease which must impact on future fertility and the quality of life. Discuss with the patient regarding the risk factors (Kyle et al., 2022).

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