

Vitamin D₃ and Risk of Uterine Fibroid-Effect of Vitamin D₃ as A Medical Management of Uterine Fibroid

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Abstract: Objective: To evaluate possible relation between serum vitamin D₃ deficiency and the uterine fibroid disease and to assess the effect of vitamin D₃ administration as a medical management on growth of uterine fibroid. **Patient and methods:** This study was prospective case-control study done from October 2015 to October 2017 in Al Galaa Maternity Teaching Hospital. It Included 55 women their age between 20: 45 years divided into 2 groups: Group A: (control group): 25 women without fibroid or other medical disease, and Group B: (study group): 30 women with fibroid then group B divided in to two subgroups: Subgroup B1: 15 women of study group who had vitamin D deficiency received medical treatment with Vitamin D for 3 months. And Subgroup B2: The other 15 women of study group did not receive vitamin D. We measured serum vitamin D in all women (group A and group B) at start of the study. Both subgroups B1 and B2 were followed by transvaginal 2 D ultrasound for assessment of fibroid size by measurement the mean fibroid size which is the sum of two largest perpendicular diameters then divided by two. This assessment of fibroid done for both subgroups B1 and B2 at start of the study and after 6 months from the start of study to know the average change in fibroid size within 6 months with and without treatment by vitamin D. **Results:** The women of control group their mean serum vitamin D was 10.90 ± 0.48 ng/mL, While the women of the study group their mean serum vitamin D was 5.79 ± 2.60 ng/mL, Where P value was less than 0.05 so was considered statistically significant. While the difference in the mean fibroid size at start of study and after 6 months in both subgroup B1 and subgroup B2 both were statistically not significant (P value > 0.05). **Conclusion:** There was a significant association between sever serum vitamin D deficiency and existence of fibroids. But there was no association between size of fibroid and vitamin D administration. [Wael Ahmed Ezzat Kamel Ammar, Emad Abd El Rahman EL Tamami, Fahd Abd El Aal Mohammed El Omda, Mohammed Ibrahim Mostafa El Mohandes and Ahmed Abd El Fatah Taha. **Vitamin D₃ and Risk of Uterine Fibroid-Effect of Vitamin D₃ as A Medical Management of Uterine Fibroid.** *Nat Sci* 2018;16(3):1-5]. ISSN 1545-0740 (print); ISSN 2375-7167 (online). <http://www.sciencepub.net/nature>. 1. doi:[10.7537/marsnsj160318.01](https://doi.org/10.7537/marsnsj160318.01).

Key words: vitamin D₃ deficiency, uterine fibroid.

1. Introduction:

The fibroids are the commonest gynaecological tumors. Fibroids are benign smooth muscle neoplasms that typically originate from the myometrium. Their incidence among women is generally cited as 20 to 25 percent, but has been shown to be as high as 70 to 80 percent in studies using histological or sonographic examination. Uterine fibroids are currently the most common indication for hysterectomy worldwide⁽¹⁻⁴⁾.

Most women with fibroids are asymptomatic. It is estimated that only 20% to 50% of women with one fibroid or more experience symptoms that can be directly attributed to the tumor itself. However, symptomatic patients typically complain of bleeding, pain, pressure sensation, or infertility. In general, the larger the fibroid, the greater the likelihood of symptoms^(1,5).

Treatment of women with uterine fibroids must be individualized, based on symptomatology, the size

and location of fibroids, age, the needs and desires of the patient for preservation of fertility or the uterus, the availability of therapy, and the experience of the therapist. Symptomatic uterine fibroids may be treated medically, surgically, or with a combination of both^(3,6).

Vitamin D status has recently been related to the development of uterine fibroids, with observations showing that lower vitamin D levels correlate with a higher risk and greater volume of uterine fibroids, both in black and white ethnicities⁽⁷⁾. These findings were also confirmed in the study conducted in infertile women⁽⁸⁾. A potential therapeutic benefit of vitamin D supplementation in the inhibition of development and/or growth of uterine fibroids has been consistently established both in vitro⁹ and in animal studies⁽¹⁰⁾. However, no evidence is currently available addressing the benefits of treatment with vitamin D for

women with fibroids, neither in the context of IVF studies or in the general gynecological population ⁽¹¹⁾.

The aim of this study is to evaluate possible relation between serum vitamin D₃ deficiency and the uterine fibroid disease and to assess the effect of vitamin D₃ administration as a medical management on growth of uterine fibroid.

2. Patient and methods:

This study was prospective case-control study done from October 2015 to October 2017 in Al Galaa Maternity Teaching Hospital. It Included 55 women their age between 20: 45 years divided into 2 groups: Group A: (control group): 25 women without fibroid or other medical disease. And Group B: (study group): 30 women with fibroid then group B divided in to two subgroups: Subgroup B1: 15 women of study group who had vitamin D deficiency received medical treatment with Vitamin D for 3 months. And Subgroup B2: The other 15 women of study group did not receive vitamin D. We measured serum vitamin D in all women (group A and group B) at start of the study. Both subgroups B1 and B2 were followed by transvaginal 2 D ultrasound for assessment of fibroid size by measurement the mean fibroid size which is the sum of two largest perpendicular diameters then divided by two. This assessment of fibroid done for both subgroups B1 and B2 at start of the study and after 6 months from the start of study to know the average change in fibroid size within 6 months with and without treatment by vitamin D. We measured serum vitamin D in group B1 after 3 months (the period of treatment by vitamin D) and all were sufficient (above 30 ng/mL).

Study group was with the following inclusion and exclusion criteria: Inclusion criteria: Age between 25: 45 years old, single fibroid and mean fibroid size less than or equal 5 cm. Exclusion criteria: s Severe vaginal bleeding (as menorrhagia or metrorrhagia), urgent myomectomy should be done, suspicion of malignancy by rapid growth, hypercalcaemia (because vitamin D supplementation is contraindicated in

patients with hypercalcaemia) and other medical diseases.

Informed consent: The fundamental principle is respect for the individual. Their right to self-determination and the right to know, understand to make informed decisions, right to privacy, confidentiality.

Methodology: All included women were subjected to the following: History taking, general and abdominal examination, vaginal examination and assessment was performed to identify abnormalities of the reproductive tract, pelvic (transvaginal) 2D ultrasound and laboratory investigations including: Serum vitamin D, serum calcium (ca), kidney function (urea and creatinine), liver function test (SGOT and SGPT), complete blood picture (CBC).

Serum vitamin D samples was collected where ORG 570 25-OH vitamin D (ORGENTEC Diagnostika GmbH Carl-Zeiss-Stra Be 49-51 -55129 Mainz – Germany) is an ELISA based test system intended for the quantitative measurement of total concentration of 25- (OH)- vitamin D in human serum or plasma samples (EDTA plasma, heparin plasma, citrate plasma) used in the assessment of vitamin D sufficiency.

Data were statistically described in terms of mean standard deviation (SD), median and range when appropriate. Comparison between the study groups was done using Student t test for independent samples. p values less than 0.05 was considered statistically significant. All statistical calculations were done using computer program IBM SPSS (Statistical Package for the Social Science; IBM Corp, Armonk, NY, USA) release 22 for Microsoft Windows.

3. Results:

This table (1) showed that age, number of deliveries, number of abortions and BMI were no significant difference between the control group and the study group (P > 0.05).

Table (1): Demographic data of control group (without fibroid) and study group (with fibroid):

Demographic data	Control group	Study group	P value
Age (years) Mean ± SD	33.20 ± 3.35	33.63 ± 3.41	> 0.05
Number of deliveries Mean ± SD	2.16 ± 1.10	2.13 ± 1.10	> 0.05
Number of abortions Mean ± SD	0.20 ± 0.57	0.20 ± 0.55	> 0.05
BMI (Kg / m ²) Mean ± SD	28.92 ± 3.69	28.43 ± 3.66	> 0.05

Table (2): Comparison between control group (without fibroid) and study group (with fibroid) in ca, urea, creatinine, SGOT, SGPT, Hb and RBS:

Items \ Group	Control group	Study group	P value
Ca mean \pm SD	9.18 \pm 0.46	9.17 \pm 0.48	> 0.05
Urea mean \pm SD	20.65 \pm 6.57	20.51 \pm 6.57	> 0.05
Creatinine mean \pm SD	0.75 \pm 0.14	0.75 \pm 0.15	> 0.05
SGOT mean \pm SD	14.92 \pm 4.58	13.60 \pm 4.90	> 0.05
SGPT mean \pm SD	16.96 \pm 4.77	16.23 \pm 4.72	> 0.05
Hb mean \pm SD	12.98 \pm 1.21	12.57 \pm 1.29	> 0.05
RBS mean \pm SD	85.48 \pm 6.75	84.67 \pm 7.26	> 0.05

This table (2) showed that ca, urea, creatinine, SGOT, SGPT, Hb and RBS were no significant difference between the control group and the study group ($P > 0.05$).

Table (3): Comparison between control group (without fibroid) and study group (with fibroid) in vitamin D₃:

Item \ Group	Control group	Study group	P value
Vitamin D ₃ mean \pm SD by ng/mL	10.90 \pm 0.48	5.79 \pm 2.60	< 0.05

Table (3) showed that vitamin D₃ was deficient in study group (with fibroid) while vitamin D₃ was insufficient in control group (without fibroid) P value less than 0.05 so was considered statistically significant.

Table (4): showing that change in fibroid size in untreated cases after 6 months was statistically not significant because P value was > 0.05.

Table (4): Comparison between size of fibroid at start of study and after 6 months in untreated cases (group B2):

Item \ Group	At start of study	After 6 months	P value
Fibroid size in cm mean \pm SD	3.22 \pm 0.77	3.24 \pm 0.81	> 0.05

Table (5): Comparison between size of fibroid at start of study and after 6 months in treated cases with vitamin D₃ (group B1):

Item \ Group	At start of study	After 6 months of treatment	P value
Fibroid size in cm mean \pm SD	3.49 \pm 0.64	3.48 \pm 0.64	> 0.05

Table (5): showing that change in fibroid size in treated cases with vitamin D₃ after 6 months was statistically not significant because P value was > 0.05.

We measured serum vitamin D in group B1 after 3 months (the period of treatment by vitamin D) and all were sufficient (above 30 ng/mL).

4. Discussion:

This study showed that there was no statistically significant difference between the control group and

the study group as regards age, number of deliveries, number of abortions, BMI, calcium, kidney function tests (urea and creatinine), liver function tests (SGOT and SGPT), Hb and random blood sugar ($P > 0.05$). So both control and study groups were with the same demographic data and without other medical diseases.

This study showed that the women of control group who were without fibroid and without other medical disease their mean serum vitamin D was 10.90 \pm 0.48 ng/mL, while the women of the study group who were with fibroid and without other

medical disease their mean serum vitamin D was 5.79 ± 2.60 ng/mL where P value was less than 0.05 so was considered statistically significant.

So this study showed that there was relation between vitamin D deficiency and fibroid.

This study showed that the mean of fibroid mean size in women who did not received medical treatment by vitamin D (Subgroup B2) at start of study was 3.22 ± 0.77 cm and after 6 months was 3.24 ± 0.81 cm, P value was > 0.05 so was statistically not significant.

This study showed that the mean of fibroid mean size in women who received medical treatment by vitamin D (Subgroup B1) at start of study was 3.49 ± 0.64 cm and after 6 months was 3.48 ± 0.64 cm, P value was > 0.05 so was statistically not significant.

So this study showed that the difference in the mean fibroid size at start of study and after 6 months in both subgroup B1 (women with fibroid treated by vitamin D) and subgroup B2 (women with fibroid did not treated with vitamin D) both were statistically not significant (P value > 0.05).

The results of this study as regarding deficiency of vitamin D with fibroid are agreed with the study of **Sabry, et al, 2013**⁽⁷⁾ who concluded that lower serum vitamin D levels are inversely correlated with uterine fibroid burden in different ethnic groups. Vitamin D deficiency is a possible risk factor for the occurrence of uterine fibroid.

The results of this study as regarding deficiency of vitamin D with fibroid are also agreed with the study of **Baird, et al, 2013**⁽¹²⁾ who conclusions were: there was an evidence that sufficient vitamin D is associated with a reduced risk of fibroids.

The results of this study as regarding deficiency of vitamin D with fibroid are also agreed with the study of **Nicholas Bakalar, 2013**⁽¹³⁾ which said that inadequate levels of vitamin D may increase the risk for uterine fibroids. They found that having a vitamin D level above 20 decreased the risk for fibroids by 32 percent, and that each increase of 10 nanograms per milliliter in vitamin D was associated with a 20 percent lower risk of having a fibroid tumor.

In agreement to the results of the current study as regarding deficiency of vitamin D with fibroid **Paffoni, et al, 2013**⁽¹⁴⁾ where their conclusions was: Vitamin D is an emerging regulator of uterine leiomyoma development. Cohort and interventional studies are needed to confirm a causal relationship and to investigate the potential therapeutic benefits of vitamin D supplementation.

Similarly, in agreement with us **Chakradhari et al, 2011**⁽¹⁵⁾ concluded that vitamin D inhibits growth of human uterine leiomyoma cells through the down-regulation of PCNA, CDK1 and BCL-2, and suppresses COMT expression and activity in Hu LM

cells. Thus, hypovitaminosis D appears to be a risk factor for uterine fibroids.

The present study showed that there is no correlation between vitamin D levels and BMI. Because BMI was not statistically significant difference between the control group and the study group (P value > 0.05). This was agreed with the study of **Sabry et al, 2013**⁽⁷⁾ which concluded also that there is no correlation between vitamin D levels and BMI.

5. Conclusion and Recommendation:

The current study showed a significant association between sever serum vitamin D deficiency and existence of fibroids. But there was no association between size of fibroid and vitamin D administration.

Clinical trials with prolonged duration of follow up will be needed to address whether vitamin D would be a potential, effective and safe non-surgical treatment option for human uterine fibroids as line of medical treatment.

Role of vitamin D supplementation in post myomectomy cases to study rate of recurrence of fibroid.

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