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Evaluation of 25-hydroxy vitamin d3 levels in patients with small uterine myomas

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***Abstract*---**Background; Uterine fibroid are the most frequent benign pelvic tumors between women in reproductive period group that has multifactorial pathogenesis. Modern ideas of uterine fibroid pathogenesis have included vitamin D as a vital component. Aim and objectives; was to study the link between 25-hydroxy vitamin D3 levels in cases having small uterine myomas. Subjects and methods; This is a case-control study, was conducted at the Gynecology and Obstetrics department outpatient clinic at Al Zahraa University Hospitals, on 60 women divided into two groups: (Study group); included Thirty cases having fibroid uterus, (Control group); included Thirty women who had no fibroid uterus. Result; When compared to controls, vitamin D3 levels in cases were considerably lower. Conclusion; Vitamin D looks to be a promising and valuable anti-UF treatment. More large, well-designed randomized clinical trials are needed to look into the effectiveness of vitamin D in females with UFs of all ethnicities, especially those of color who are at higher risk of vitamin D deficiency. As a result, vitamin D may become a viable treatment choice for UF, with the added benefit of its pleiotropic impact.

Keywords---25-OH-D3, fibroids, myomas, supplementation, vitamin D

Introduction

In some recent report studies done in Europe and Africa, vitamin D insufficiency has been postulated as a risk factor in the etiology of uterine fibroid [1].
Vitamin D is thought to control cell proliferation and differentiation, as well as prevent angiogenesis and promote apoptosis [2].

Vit D deficiency is now thought to be a key risk factor for the progress of uterine fibroids. There are various theories concerning the use of vitamin D in the prevention or treatment of uterine fibroid tumors, however there are few active scientific research in this field. Vitamin D appears to be a viable, safe, and low-cost therapy for uterine fibroids prevention and treatment [3].

A uterine fibroid is a cluster of smooth muscle cells encased in a pseudo capsule of compressed muscle fibers. In the female vaginal tract, it is the most frequent benign tumour. Surgery, such as a myomectomy or hysterectomy, is the most common procedure for uterine fibroid [4].

Alternative solutions to surgical intervention are desperately needed, especially for women who want to keep their fertility. Selective progesterone receptor modulators (SPRMs), which have been shown to successfully treat fibroid symptoms, are now available. Gynecologists now have additional techniques allowing for creative solutions to uterine fibroids care [5].

Method

Patients and Methods

This was a case-control study which had been done at the Gynecology and Obstetrics department outpatient clinic at Al Zahraa University Hospitals. Ethical approval was gotten from Medical Research Ethics committee of obstetrics and Gynecology department at Al Zahraa University Hospital. The cases and controls were selected from attendace to gynacological clinic at booking. A verbal informed consent obtained from all Participants after explanation the purpose of the study.
Study populations were classified into two groups: Study group: Thirty cases having fibroid uterus. Control group: Thirty women who had no fibroid uterus
Inclusion Criteria for study group: Women aged from 20 years to less than 35 years, not pregnant, married and size of uterine myoma two cm or less.

Exclusion Criteria for study group: Women age less than 20 years or 35 years and more, pregnant females, unmarried females, size of uterine myoma more than two cm, those having a history of pre-existing malignancy or a prior myomectomy, as well as women using vitamin D supplements.

All cases were subjected to the followings:

A detailed medical history: Personal history: (Name, Age, residence, occupation, and special habits), menstrual history: 1st day of last menstrual period, obstetric history (gravida, parity, abortion, and congenital anomalies), contraceptive

history, past history: (medical and or surgical). Family history ((Diabetes mellitus (DM) and or Hypertension (HTN)) and complaint: Main complaint registered.

Examination: General physical examination included: Weight, height, blood pressure, pulse, lower limb edema, chest, heart and breast examination, Body Mass Index Abdominal examination: Abdominal examination was conducted for assessment of abdominal organs for each patient (liver, spleen, kidneys, and other abdominal organs). Pelvic examination included the following: Vulvar Examination: Examination of the vulvar area to detect any pathological lesions (congenital, inflammatory, traumatic, and neoplastic lesions). Vaginal Examination: Vaginal examination was conducted to detect pathological lesions (inflammatory congenital and neoplastic lesions). The cervix was examined to detect (erosion, discharge, lacerations, polyps, and neoplasia). Bimanual Examination: Bimanual examination was done to determine the size and position of the uterus, uterine mass, mobility and tenderness and the presence or absence of adnexal masses and to exclude pelvic or pelviabdominal mass which led to exclusion of the woman accordingly. Ultrasound Examination: All ultra sonographic examinations were performed at time of booking using a Sono Ace Medison X4 ultrasound machine (Company: Samsung Medison, Origin: Korea) 2D trans-abdominal 3.5 MHz probe and trans vaginal (5.0–7.0 mHz) ultrasound probes in the ultrasound unit at Al-Zahraa University Hospital All women were in a slightly tilted position with the head of the bed raised 30 degrees and with a small pillow under the pelvis. Regardless of whether the individual had a prior clinical diagnosis of fibroids or not, trans-vaginal ultrasound tests were conducted to check their condition, case or control selected accordingly. Ultrasound examination and reports were conducted by senior staff in USS unit. The report included measurement of the uterus position, dimensions, and endometrial thickness, comments on both adnexia and Douglas pouch.

Investigations: All women were subjected to extraction of venous blood sample at time of booking. Four cm venous blood sample was sent to the private well known Laboratory Services, to conduct the following: Complete blood count hemoglobin concentration (Hb %), red blood cells , white blood cells (WBCs), platelet count and measurement of 25-hydroxy vitamin D3. To separate the serum, the sample was centrifuged at 3000 rpm for eight–ten minutes after 15 minutes. After that, serum levels of 25-hydroxy vitamin D3, a metabolite of 1,25-dihydroxy vitamin

D3, were tested.

Data management and Statistical Analysis: The data collected during the history taking, basic medical assessment, lab tests, and outcome measurements were coded, inputted, and evaluated using Microsoft Excel software (Microsoft). The data was analysed with the help of the Statistical Package for the Social Sciences (SPSS version 20.0) (Statistical Package for the Social Sciences) software. A number and a percentage are used to describe qualitative data, whereas a mean and standard deviation are used to indicate quantitative data, depending on the sort of data being given. The following tests were used to assess the importance of differences: Pearson's correlation and Spearman's correlation were used to evaluate the correlation between two variables.

Results

In terms of age, the two groups are significantly different. Table (1)

Table 1
Age and BMI between the two studied groups

	Cases (n=30)		Controls (n=30)		x^2	p
	N	%	N	%		
Age ≤ 31 years	9	30	19	63.3	6.69	.010
Age > 31 years	21	70	11	36.7		
BMI						
BMI < 25 kg/m^2	2	6.7	6	20	2.62	.270
BMI = 25 - 30 kg/m^2	13	43.3	13	43.3		
BMI ≥ 30 kg/m^2	15	50	11	36.7		

This table shows that there is an important change between the two groups regarding hemoglobin. Table (2)

Table 2
Clinical characteristics of the two studied groups

	Cases (n=30)	Controls (n=30)	MU	p
Parity Mean ± SD	2.3 ± 1.49	1.97 ± 1.59	392	.381
Hemoglobin (g/dl) Mean ± SD	11.3 ± 1.84	12.37 ± 1.75	t 2.3	.025

This table shows that vitamin D3 level was significantly lower in cases compared to controls. Table (3)

Table 3
Vitamin D3 levels between the two studied groups

Variables	Cases (n=30)	Controls (n=30)	MU	p
Vitamin D3 (ng/ml) Mean ± SD	8.6 ± 2.51	10.97 ± 4.47	303	.028*

This table shows that there is a substantial negative association between vitamin D3 and age in cases group only. Table (4)

Table 4
Correlation between vitamin D3 levels and the different parameters in the two studied groups

	Vitamin D3			
	Case		Control	
	r	P	r	P
Age	-.367	.046	-.095	.616
Weight	-.169	.372	.172	.364
Height	-.284	.128	.096	.615
BMI	-.018	.924	.151	.424
Parity	-.189	.317	.068	.721
Hemoglobin	-.040	.832	-.091	.633

Discussion

In females of reproductive age, uterine fibroid (UF) is the most prevalent benign tumor. The term refers to the material's hard and fibrous nature, as well as its unique microscopic appearance [6].

In this study, In terms of age, there was a substantial disparity between the two groups (P = 0.010), Age ≤ 31 years were 9(30%) in cases group and 19(63.3%) in control group, Age > 31 years were 21(70%) in cases group and 11(36.7%) in control group. On the other hand there are no important change between the two studied groups according to BMI (P = 0.270), in cases group patients with BMI < 25 kg/m^2 were 2(6.7%), patients with BMI = 25 - 30 kg/m^2 were 13(43.3%) and patients with BMI ≥ 30 kg/m^2 were 15(50%) while in control group patients with BMI < 25 kg/m^2 were 6(20%), patients with BMI = 25 - 30 kg/m2 were 13(43.3%) and patients with BMI ≥ 30 kg/m2 were 11(36.7%).

This is similar to many previous studies showing that there is a important variance among cases and controls regarding age distribution [7]

Another similar study by Stewart et al., [8] observed that age and ethnicity were the most significant proven risk factors for the onset of UF.

In contrast to these findings, Munusamy et al. [9] indicated that the incidence of uterine fibroid in the reproductive stage range (Age ≤ 31 years) is around 37 percent, according to a research conducted in Southern India.

In current study in terms of hemoglobin, there is a statistically important change among the two groups. (P-value=0.025), hemoglobin mean was 11.3 ± 1.84 g/dl in case group and 12.37 ± 1.75 g/dl in control group. On the other hand, there were no notably variation differences between the two studied groups according to Parity (P-value=0.381), Parity mean was 2.3 ± 1.49 in cases group and 1.97 ± 1.59 in control group,

In the same line with the study results Singh et al., [1] showing that there were no statistically important variation between cases and control groups regarding Parity, P_0 was 6.94% in cases of fibroid and 6.94% in control group, P_1 was 19.44% in cases of fibroid and 13.89% in control group, P_2 was 38.89% in cases of fibroid and 43.06% in control group, ≥ P_3 was 34.72% in cases of fibroid and 36.11% in control group (P-value=0.93).

When compared to the control group, the vitamin D3 percent in the cases was considerably lower (P-value=0.028), vitamin D3 mean were 8.6 ± 2.51 ng/ml in cases group and 10.97 ± 4.47 ng/ml in control group.

According to Srivastava et al. [10], 25-hydroxyvitamin D3 insufficiency is substantially related with uterine fibroid, which is consistent with their findings. Lower 25-hydroxyvitamin D3 levels were observed to have an inverse association with the size of the fibroid uterus, according to the research. Estimation of the serum 25-hydroxyvitamin D3 concentration was carried out. When comparing cases and controls, the mean standard deviation (mean SD) concentration of 25-hydroxyvitamin D3 was considerably lower in the cases (15.10 ±6.09 vs 26.09 ±7.90, respectively, p =0.001). The size of the uterine fibroid grew in direct proportion to the decline in 25-hydroxyvitamin D3 levels (p = 0.014).

The findings of this study matched those of Paffoni et al., [11], who looked into a related study question in 126 females suffering fibroid and 256 controls who visited two infertility Italian hospitals. In comparison to controls, women with fibroid had lower mean blood concentrations of 25-hydroxyvitamin D3 (18.0± 7.7 vs. 20.8 ±11.1 ng/mL, respectively, p = 0.010). Furthermore, they found that the crude odds ratio (OR) for the existence of fibroids in women with blood levels of 25-hydroxyvitamin D3 < 10 ng/mL was 2.2 (95 percent confidence interval [CI] 1.1–4.3) (p = 0.022) when compared to those with 25-hydroxyvitamin D3>10 ng/mL.

On the other hand Srivastava et al., [10] found that the number of women with 25-hydroxy vitamin D3 shortage in cases (45 women who had as a minimum 1 uterine fibroid ≥10 mm identified on ultrasonography) was more than in controls (45 women those not having any uterine pathology), was 9(20%) and 3(6.67%) respectively (p < 0.001).

According to correlation between vitamin D3 levels and the different parameters in the two studied groups, there was a statistically important negative connection

between vitamin D3 and age in cases group only (P-value=0. 046) . While there were no important changeable correlation among vitamin D3 and Weight, Height, BMI, Parity and Hemoglobin in cases group P-values were 0.372, 0.128, 0.924, 0.317 and 0.832 respectively while P-values in control group were 0.364, 0.615, 0.424, 0.721 and 0.633 respectively (Fig.3 c,d,e,f, and g).

Mohammadi et al., [12], in a new systemic review, evaluated pooled data from trials with a total of 1730 subjects (835 patients with UFs and 895 controls). After analyzing the data, the researchers came to the conclusion that low vitamin D levels are linked to a greater risk of UFs diagnosis.

Identical outcomes were found. From 1996 to 1998, Baird et al., [13] in The National Institute of Environmental Health Sciences (NIEHS) Uterine Fibroid Study, included 1036 women in Washington, DC, who were 35–49 years old. According to a study of by Baird et al., women with sufficient vitamin D3 (>20 ng/mL) had a 32 percent reduced risk of fibroids than women with insufficient vitamin D (aOR 0.68, 95 percent confidence interval [CI] 0.48–0.96).

In consistent with the outcome of this study, Paffoni et al., [13] found a strong correlation among vitamin D3 levels and various variables, as more women with fibroid had serious vitamin D3 shortage relative to controls. Their study reported that 15percent of women with fibroid had severe deficiency compared to 7percent in controls, and adequate vitamin D levels were found in 37percent of instances compared to 45 percent in controls.

Conclusion

Vitamin D3 level was significantly lower in cases with small myomas compared to controls. There was a significant negative association among vitamin D3 and age in cases group only

Conflict of Interest: The Authors declare that there is no conflict of interest

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