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FREQUENCY OF LEIOMYOMA IN FEMALES PRESENTING WITH INFERTILITY AND ITS ASSOCIATION WITH SERUM VITAMIN D3 LEVEL

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Abstract

Background: In women of reproductive age, uterine fibroid, a benign tumour of the uterine smooth muscle, is a common cause of menorrhagia and dysmenorrhea. Fibroid etiopathogenesis involves numerous factors. The aetiology of fibroids is influenced by hormonal variables, although other causes are still unknown. According to some theories, uterine fibroids form as a result of an inappropriate response to tissue repair that alters the formation of extracellular matrix. Vitamin D may be able to prevent this abnormal response by controlling it.

Objective: The study was conducted to determine the frequency of leiomyoma in patients presenting with infertility and to compare the mean serum vitamin D3 levels in females with and without leiomyoma.

Study design: A cross-sectional study

Place and Duration: This study was conducted in Jinnah Hospital, Lahore from July 2021 to January 2022

Methodology: Using a non-probability, consecutive sampling method 101 cases of 18 to 40 years presenting with infertility were included in the study. These patients were then divided into two groups on the bases of ultrasound findings. The group I included the patients with uterine fibrosis and group II included those without uterine fibrosis. Later, 5 ml of blood was drawn from each patient under an aseptic measure and was sent to the lab for measurement of serum vitamin-D3 levels. All the collected data was entered and analyzed into SPSS version 25

Results: The findings of this study revealed that the mean BMI was 27.99±5.95 kg/m2, mean serum vitamin-D3 levels was 31.67±4.179 ng/ml and mean age was calculated as 30.65±3.48 years. It was observed that 24.8 %(n=25) were in the age group of 18-28 years. There were 56.44%

(n=57) females from rural areas, and the Frequency of uterine leiomyoma was 15.8 % (n=16). The t-test of association revealed that patients with uterine leiomyoma had lesser mean Vit D3 levels compared to the patients without uterine leiomyoma with a significant p-value <0.05

Conclusion: We found that the frequency of uterine leiomyoma was 15.8 % (n=16). Both groups were compared for mean serum vitamin-D3 levels. P=0.000. It is concluded from the study results that the mean percentage of serum vitamin D3 level was significantly lower in uterine leiomyoma patients.

Keywords: Uterine leiomyoma, Infertility, Serum vitamin D3.

INTRODUCTION

Uterine fibroids (leiomyomas), which are the most common benign tumor of the uterus, are benign monoclonal tumors of smooth muscle that develop in the myometrium. They often take the form of many, rounded, well-circumscribed lumps ranging from a few centimeters to gigantic growths 20 cm in diameter and larger. They are estrogen- and progesterone-dependent cancers, although the cause is uncertain [1, 2].

Around 30% of patients with uterine fibroids present symptoms and seek medical attention before the age of 50, it is estimated that nearly two-thirds of the females may have at least or more uterine fibroids during their life. Women of all ethnicities are affected, but those of African descent are more likely to develop fibroids and do so earlier in life. The first-line imaging test for suspected fibroids is ultrasound (USG), which has a high sensitivity and specificity for identifying this condition [3, 4]. Transvaginal ultrasound scans (TVS) and transabdominal ultrasound scans (TAS) are two ways to do ultrasound exams; each has benefits and drawbacks [5]. A study reported that 63.4% of the Pakistani population is vitamin-D3 deficient and 7% of the females presenting with infertility have leiomyoma [6, 7].

Paffoni et al. (2014) conducted a study on the mean serum vitamin D3 levels among the females with and without uterine fibroid and found that to be 18.0 ± 7.7-vs 20.8-±11.1 ng/ml respectively, p = .010 [8]. Singh et al. conducted a similar study in 2019 and found that to be 10.81 ± 6.18 with uterine fibroid vs. 22.91 ± 16.18 without uterine fibroid, p< 0.0001 [9].

According to these investigations, the pathophysiology of uterine fibroids is linked to a reduction in serum vitamin D3. Since vitamin-D3 deficiency is relatively common in Pakistani society (63.4%) [6], and to the best of the candidates' knowledge, there are no local published statistics on this subject. This study must be carried out among the local population in order to determine the mean vitamin D3 levels in females with and without fibroids. If this finding is statistically significant, we will be able to prescribe additional vitamin D3 to female patients, which will help to reduce the number of patients who suffer from this condition.\

METHODOLOGY

Using non-probability, consecutive sampling method 101 cases were included in the study. We included patients aged between 18 to 40 years presenting with infertility as per the operational definition. However, we excluded the patients with an autoimmune disorder (positive RA factor or ANA), Patients with nodular liver on ultrasound, serum creatinine > 1.2mg/dl or serum bilirubin >1.5mg/dl as per clinical investigations, patients with hypertension (systolic blood pressure > 140mmHg on two or more occasions 12 hours apart), or have diabetes (fasting blood sugar level > 125mg/dl) as per investigations and patients who have taken serum vitamin D3 supplementation < 6 months as per history and clinical record.

Before collecting data from the study subjects, we obtained formal consent in writing and recorded the detailed history of the patient. These patients were then divided into two groups on the bases of ultrasound findings. The group I included the patients with uterine fibrosis and group II included those without uterine fibrosis. Later, 5 ml of blood was drawn from each patient under an aseptic measure and was sent to the lab for measurement of serum vitamin-D3 levels. The serum was separated for the quantitative assessment of 25 hydroxy vitamin D3 using a commercially available automated chemiluminescent micro particle immunoassay after the blood had been allowed to clot. The serum vitamin-D3 levels were presented as mean and standard deviation. We used SPSS version 25 for data analysis. The numerical variables i-e age, BMI and serum vitamin D3 was presented by mean + SD and range. On the other hand, the categorical Variable i.e. leiomyoma was presented as frequency and percentage. We used the Independent-sample-T-test for the comparison of mean serum-Vitamin-D3 levels between the two groups-taking p-values of <-0.05 as statistically significant.

RESULTS

In this study, 101 patients fulfilling inclusion and exclusion criteria were selected to compare the mean serum vitamin-D3 levels in females with and without leiomyoma.

The findings of this study revealed that the mean BMI was 27.99±5.95 kg/m2, mean serum vitamin-D3 levels was 31.67±4.179 ng/ml and mean age was calculated as 30.65±3.48 years. (As shown in Table I)

Table I Descriptive Statistic in the study

Variables	Mean	±SD
BMI (kg/m2)	27.99	±5.95
Serum vitamin-D3 (ng/ml)	31.67	±4.179
Age (years)	30.65	±3.48

It was observed that 24.8 % (n=25) were in the age group of 18-28 years and 75.2 % (n=76) were in the age group of 29-40 years. There were 56.44% (n=57) females from rural areas, and the Frequency of uterine leiomyoma was 15.8 % (n=16).

Table II Socio-demographic Factors of study subjects

Variable	n	%
Age group (Years)		
18-28	25	24.8
29-40	76	75.2
Place of Residence		
Rural	57	56.44
Urban	44	43.56
Uterine leiomyoma		
Yes	16	15.8
No	85	84.2

The t-test of association revealed that patients with uterine leiomyoma had lesser mean Vit D3 levels compared to the patients without uterine leiomyoma with a significant p-value <0.05. (As shown in Table III)

Table III: Association of variables with the mean serum vitamin-D3 levels using independent sample t-test

Variables		N	Serumvitamind3		p-value
			Mean	Std. Deviation	
Serum vitamin D3	with uterine leiomyoma	16	26.63	7.089	0
	without uterine leiomyoma	85	32.62	2.459	
Stratification according to variables					
Ages					
18-28 years	With uterine leiomyoma	2	26.5	7.778	0.043
	Without uterine leiomyoma	23	31.78	2.999	
29-40 years	With uterine leiomyoma	14	26.64	7.302	0
	without uterine leiomyoma	62	32.94	2.172	
BMI					
17-25 kg/m2	With uterine leiomyoma	5	26.4	8.385	
	without uterine leiomyoma	21	32.81	1.601	0.002
>25kg/m2	with uterine leiomyoma	11	26.73	6.872	0
	without uterine leiomyoma	64	32.56	2.69	

DISCUSSION

Menorrhagia and dysmenorrhea in women of reproductive age are frequently brought on by uterine fibroid, a benign tumour of uterine smooth muscle and Menorrhagia and dysmenorrhea in women of reproductive age are frequently brought on by uterine fibroid, a benign tumour of the uterine smooth muscle dysmenorrhea in women of reproductive age are frequently brought on by uterine fibroid, a benign tumour of the uterine smooth muscle [10]. Fibroid etiopathogenesis involves numerous factors. The aetiology of fibroids is influenced by hormonal variables, although other aspects are still unknown [11]. Numerous chronic illnesses, including cardiovascular disease, autoimmune disorders, and several malignancies, have been linked to vitamin D3 insufficiency [12]. Intriguingly, it has been linked in a few recent studies from Europe and Africa to the pathophysiology of uterine fibroid [9].

In the current study, out of 101 patients, 24.8 %(n=25) were in the age group of 18-28 years and 75.2 %(n=76) were in the age group of 29-40 years. The mean age was 30.65±3.48 years. The distribution of BMI was 27.99±5.95 kg/m2 and serum vitamin-D3 levels were 31.67±4.179 ng/ml. The frequency of uterine leiomyoma was 15.8 % (n=16). Both groups were compared for mean serum vitamin-D3 levels. P=0.000.

When comparing black and white women independently, both studies showed virtually similar conclusions. These 3 separate epidemiological research' consistency lends substantial credence to the validity of the association. [8]

According to Singh, et al. reported in their research conducted on analysis-of-vitamin-D-levels, -that, compared-to-26.9% of controls, severe deficiency (10 ng/dl) is associated with fibroid in 62.5% of affected women. In addition, only 6.94% of fibroid-afflicted women have vitamin-D -levels above 20 ng/dl, compared to 47.22% of controls. Similar research was carried out by-Paffoni-et al [8]. Their study showed that sufficient vitamin D levels were detected in 37% of cases as opposed to 45% in controls and that a significant deficit affected 15% of fibroid-afflicted women compared to 7% of controls. Because there is a higher proportion of women having fibroid have

severe vitamin D3 deficiency than controls, the link seems to be considerably stronger than in the study by-Paffoni-et al [8].

Andrea et al concluded that the mean (SD) serum level of-25-OH-D3 was 25.7- (10.7) ng/mL, and hypovitaminosis D was identified in 148 patients (71.1%). There was no discernible difference in the seasons of the determination (48.1%% autumn-winter vs.51.9-%% spring-summer-, -P = 0.42-).-The mean-25-OH-D3-serum levels of women with decreased Vit D levels (n = 148) and women with normal vitamin D blood levels (n = 60) were noticeably different (20.4 5.9 vs. 39.0 vs. 8.0 ng/mL; P 0.001). Every single woman with hypovitaminosis D had a typical vitamin D replacement therapy [13-16].

According to a recent assessment by Ciarmela et al, Women who are perimenopausal should be thought of as having an increased chance of getting fibroids., and it is also probable that any fibroids already present in these women may continue to grow. Women who have endured several months or years of estrogen-dominant menstruation additionally incur the chance of developing fibroids in a growth spurt due to their sensitivity to the hormone. [65]

According to Andrea et al.'s research, 25-OH-D3 is efficient at bringing vitamin D levels back to normal in females with fibroids. After receiving treatment for a year, the research group's average level of [25-OH-D3] was much greater than it was at the beginning- (30.7-10.5-vs. 19.9-7.0--ng/mL, P 0.00-). The effectiveness of supplementation also seems to be influenced by the serum levels of vitamin D during rest [18].

Vitamin D insufficiency is common in Pakistan and India, and women are most affected. The main cause appears to be dietary inadequacy [19]. In addition, a study in South India revealed that there is nearly 37% incidence of uterine fibroid in women of reproductive age [20]. There's a good chance that the actual number is higher because so many more go unreported. Therefore, the possibility of vitamin-D-insufficiency-in uterine-fibroid will introduce a completely new-therapeutic-component and have a significant influence on the outcome. [9]

CONCLUSION

In the current study, we compared the mean serum vitamin D3 levels in females with and without leiomyoma. We found that the frequency of uterine leiomyoma in patients presenting with infertility was 15.8 % (n=16). Both groups were compared for mean serum vitamin-D3 levels (P=0.000). It is concluded from the study results that the mean percentage of serum vitamin D3 level was significantly lower in uterine leiomyoma patients.

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