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Impact of Vitamin D Supplementation among the Women with Uterine Fibroid in Different Age Groups

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Abstract **Original Research Article**

Background: Uterine fibroid (UF) is a common tumor of the female reproductive system. Though most of the women with fibroids are asymptomatic, approximately 30% of them can mention about some severe symptoms like abnormal uterine bleeding, pelvic pain, anemia, back pain, urinary frequency and even infertility etc. *Generally, among the patients with uterine fibroids,* prevalence of vitamin D deficiency is found. But, the impact of vitamin D on reduction of the sizes the uterine fibroids are still unknown. ***Aim of the study:*** The aim of this study was to assess the impact of vitamin D supplementation among the women with uterine fibroid in different age groups. ***Methods:*** This prospective observational study was conducted in the department of Radiology & Imaging, BSMMU, Dhaka, Bangladesh during the period from January 2020 to December 2020. In total 75 women with uterine fibroid were enrolled in this study as study population. Before data collection proper written consents were taken from all the participants. Along with the data regarding fibroids and vitamin D status, all the demographic and clinical data were collected and analyzed. In data collection, a predesigned questioner was used. All data were processed, analyzed and disseminated by using MS Excel and SPSS version 23.0 program as per necessity. ***Results:*** In this study, in assessing the fibroid's sizes of several age group patients, between baseline and follow-up we found that, at baseline, in 20-30, 31-45 and >45 year's age groups, the mean ±SD sizes of fibroids were 3.32±0.46, 3.91±0.50 and 4.05±0.51 cm respectively. On the other hand, at follow-up stage in those groups the mean ±SD sizes of fibroids were found as 2.64 ±0.40, 3.66±0.48 and 3.5±0.47 cm respectively. Finally, in evaluating the impact of vitamin D supplementation among our participants, comparing the fibroid sizes between baseline and follow-up stages, we observed that, in >45 years' age group the fibroid size change was non-significant (P<0.05). But in 31-45 years' age group, the fibroid size was decreases significantly (P<0.008) and in 20-30 years' age group, that change was statistically extremely significant where the P value was less than 0.001. ***Conclusion:*** Vitamin D Supplementation have a significant role in decreasing the fibroid size in younger women with uterine fibroid. Specially, in 20 to 30 year's age group patients with uterine fibroid, vitamin D supplementations can ensure most excellent efficacy.

Keywords: Impact, Vitamin D, Women, Uterine fibroid, Pelvic pain.

INTRODUCTION

Uterine fibroid is the most common benign pelvic tumor in women of reproductive age which grows in the uterine muscle [1]. It may be complicated by a variety of symptoms including menstrual disturbance, bloated sensation, increased urinary frequency, or pelvic pain [2]. Uterine fibroids may also cause several reproductive problems like impaired fertility, miscarriage, pregnancy complications and adverse pregnancy outcomes [3, 4]. Many previous

studies revealed that, vitamin D deficiency increases the risk of uterine fibroids [5]. In a clinical study it was indicated that, vitamin D supplementation has a significant therapeutic effect among patients with small uterine fibroids [6]. But, another clinical trial advocated that, vitamin D levels have no significant effect on the occurrence of uterine fibroids [7]. Vitamin D which is a fat-soluble vitamin is a general term for a group of structurally similar sterol derivatives [8]. The target organs of vitamin D are widely scattered and different type of vitamin D binds with their specific receptors and play different roles in human body and the level of vitamin D3 in serum may represent the total contents of vitamin D in the body [9]. In some studies it was reported that, vitamin D has an anti-proliferative effect which can accelerate the release of tumor necrosis factors from macrophages, which has a broad killing effect on tumor cells [9, 10]. Besides human, animal experiments have also shown that, high doses of vitamin D can decrease the size of uterine fibroids [11, 12]. In a previous study [9] in was reported that, the relationship between the risk of uterine fibroids and vitamin D levels is still ambiguous and further researches are needed to be carried out.

METHODS & MATERIALS

This prospective observational study was conducted in the Department of Radiology & Imaging, Dhaka, Bangladesh during the period from January 2000 to December 2020. In total 75 women with uterine fibroids were enrolled in this study as study subjects. Before data collection, proper written consents were taken from all the participants. The whole intervention was conducted in accordance with the principles of human research specified in the Helsinki Declaration [13] and executed in compliance with currently applicable regulations and the provisions of the General Data Protection Regulation (GDPR) [14]. As per the inclusion criteria of this study, only diagnosed cases of fibroid, referred or admitted to the mentioned hospital were included as the study subjects. On the other hand, according to the exclusion criteria of this study, patients with massive vaginal bleeding, consuming hormonal drugs, sonographic evaluation of the features of the uterus is difficult or in the presence of suspected adenomyosis were excluded from this study. All the socio-demographic and family information was collected by face to face interview and disease-specific data were recorded. Besides these height, bodyweight, waist circumference was also recorded. Then vitamin D was supplemented to the participants as 40000 IU once weekly for 8 weeks followed by once monthly. Then repeat ultrasonography was done after 3 months, to assess the impact of vitamin D supplementation on the regression of the size of the fibroid. Serum vitamin level D was measured by high-performance liquid chromatography (HPLC) method. All data were processed, analyzed and disseminated by using MS Excel and SPSS version 23.0 program as per necessity.

RESULTS

In this study, the mean (±SD) age of total participants was 37.57±7.24 years. Among them 13, 55 and 7 cases were from 20-30, 31-45 and >45 year's age groups respectively and the mean (±SD) ages of those group's patients were 25.69±3.73, 39.00±4.15, 48.43±1.27 years respectively. In analyzing the parity of the participants, we found 20(26.7%), 14(18.7%) and 41 (54.6%) cases with '0', 1 and ≥2 parity among total patients respectively. Among total patients, 1.3% were underweight, 28% were with normal weight, 41% were with overweight status and 29% were obese. Besides; these 38.7%, 41.3% and 20% of our total study population were with mild, moderate and severe anemia respectively. In analyzing the vitamin D status of the participants, we found that, majority (n=45) of our total cases were with vitamin D insufficiency (20-29 IU). Then 23 cases were with vitamin D deficiency (<20 IU) and the rest 7 cases were with vitamin D sufficiency (≥30 IU). In this study, at baseline stage, in 20-30 year's age group 3, 6 and 4 cases were with small (<2.5cm), medium (2.5-4.9cm) and large (≥5cm) size fibroids respectively. Those size of fibroids were found in 5, 27 and 23 cases respectively in 31-45 year's age group and in 0, 4 and 3 cases respectively in >45 age group. On the other hand, at follow-up stage, in 20-30 year's age group 4, 7 and 2 cases were with small (<2.5cm), medium (2.5-4.9cm) and large (≥5cm) sized fibroids respectively. Those sized fibroids were found in 10, 24 and 21 cases respectively in 31-45 year's age group and in 0, 5 and 2 cases respectively in >45 age group. In this study, in assessing the fibroid's size of several age group patients, between baseline and follow-up we found that, at baseline, in 20-30, 31-45 and >45 year's age group, the mean ±SD sizes of fibroids were 3.32±0.46, 3.91±0.50 and 4.05 ±0.51 cm respectively. On the other hand, at follow-up stage in those group the mean ±SD sizes of fibroids were found as 2.64±0.40, 3.66±0.48 and 3.5±0.47 cm respectively. Finally, in evaluating the impact of vitamin D supplementation among our participants, comparing the fibroid sizes between baseline and follow-up stages, we observed that, in >45 year's age group the fibroid size change was non-significant ($P<0.05$). But in 31-45 year's age group, the fibroid size was decreases significantly ($P<0.008$) and in 20-30 year's age group, that change was statistically extremely significant where the P value was less than 0.001.

Table 1: Demographic status of participants (N=75)

Characteristics	Total	20-30 years	31-45 years	>45 years
	(N=75)	(n=13)	(n=55)	(n=7)
	N (%)	n (%)	n (%)	n (%)
Age Mean ±SD	37.57±7.24	25.69±3.73	39.00±4.15	48.43±1.27
Number of parities				
0	20(26.7)	5(38.5)	14(25.5)	1(14.3)
1	14(18.7)	3(23.0)	9(16.3)	2(28.6)
≥2	41(54.6)	5(38.5)	32(58.2)	4(57.1)
BMI distribution				
Under weight (<18.5)	1(1.3)	1(7.7)	0(0.0)	0(0.0)
Normal (18.5-24.9)	21(28.0)	5(38.5)	14(25.5)	2(28.6)
Over weight (25.0-29.9)	31(41.3)	1(7.7)	25(45.4)	5(71.4)
Obese (±30)	22(29.4)	6(46.1)	16(29.1)	0(0.0)
*Status of anemia among patients				
Mild	29(38.7)	3(23.1)	25(45.5)	1(14.3)
Moderate	31(41.3)	7(53.8)	19(34.4)	5(71.4)
Severe	15(20.0)	3(23.1)	11(20.1)	1(14.3)

*** Anemia was categorized clinically**

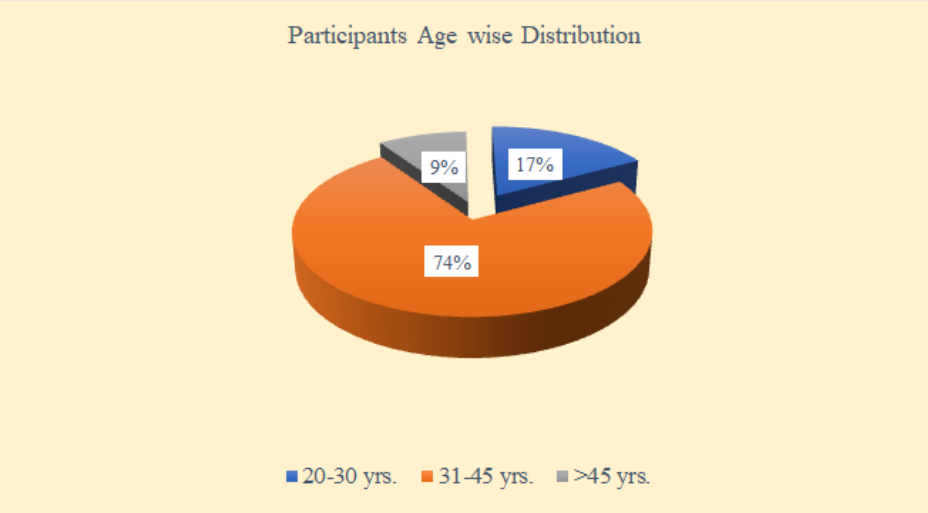

Figure 1: Pie chart showed, Age wise participant's distribution (N=75)

Table 2: Vitamin D status in different age groups of the participants (N=75)

Age Group	Vitamin D							
	Total		Deficiency (<20 IU)		Insufficiency (20-29 IU)		Sufficiency (≥30 IU)	
	(N=75)		(n=23)		(n=45)		(n=7)	
	n	%	n	%	n	%	n	%
20-30 yrs.	13	17.3	4	17.4	7	15.6	2	28.6
31-45 yrs.	55	73.3	15	65.2	35	77.8	5	71.4
>45 yrs.	7	9.3	4	17.4	3	6.7	0	0

Table 3: Fibroids size distribution as per ages of participants at baseline (N=75)

Fibroids size	Total		Age group					
			20-30 yrs.		31-45 yrs.		>45 yrs.	
	(N=75)		(n=13)		(n=55)		(n=7)	
	n	%	n	%	n	%	n	%
Small (<2.5cm)	9	12	3	30.8	5	9.1	0	0
Medium (2.5-4.9cm)	37	49.3	6	46.1	27	49.1	4	57.1
Large (≥5cm)	29	38.7	4	23.1	23	41.8	3	42.9

Table 4: Follow up fibroids size distribution as per ages of participants after Vitamin D supplementation (N=75)

Vitamin D Status	Total		Age group					
			20-30 yrs.		31-45 yrs.		>45 yrs.	
	(N=75)		(n=13)		(n=55)		(n=7)	
	n	%	n	%	n	%	n	%
Small(<2.5cm)	16	21.3	4	30.8	10	20	0	14.3
Medium (2.5-4.9cm)	34	45.3	7	38.4	24	43.6	5	71.4
Large (≥5cm)	25	33.4	2	30.8	21	36.4	2	14.3

Table 5: Age wise comparison of fibroids sizes (cm) between baseline and follow-up (After vitamin D supplementation) stages (N=75)

Age group	Baseline	Follow-up	P value
In Years	Mean ±SD	Mean ±SD	
20-30 yrs.	3.32±0.46	2.64±0.40	<0.001
31-45 yrs.	3.91±0.50	3.66±0.48	0.0086
>45 yrs.	4.05±0.51	3.5±0.47	0.0577

DISCUSSION

The aim of this study was to assess the impact of vitamin D supplementation among the women with uterine fibroid in different age group. In this study, at baseline stage, in 20-30 year's age group 3, 6 and 4 cases were with small (<2.5cm), medium (2.5-4.9cm) and large (≥5cm) size fibroids respectively. Those sized fibroids were found in 5, 27 and 23 cases respectively in 31-45 year's age group and in 0, 4 and 3 cases respectively in >45 age groups. On the other hand, at follow-up stage, in 20-30 year's age group 4, 7 and 2 cases were with small (<2.5cm), medium (2.5-4.9cm) and large (≥5cm) size fibroids respectively. Those size of fibroids were found in 10, 24 and 21 cases respectively in 31-45 year's age group and in 0, 5 and 2 cases respectively in >45 age groups. In a previous study [9], their results showed that, vitamin D supplementation has significant effect on the size of leiomyomas in premenopausal women with vitamin D deficiency (<20). Halder SK *et al*., in their study showed lower serum levels of either 25 hydroxyvitamin D3 or 1, 25-dihydroxyvitamin D3, related to increase the risk of symptomatic uterine fibroids [15]. Their another study suggested that, supplementation with the paricalcitol may be noninvasive medical treatment choice for uterine fibroids [16]. In this study, in assessing the fibroid's sizes of several age group patients, between baseline and follow-up we found that, at baseline, in 20-30, 31-45 and >45 year's age group, the mean ±SD sizes of fibroids were 3.32 ±0.46, 3.91 ±0.50 and 4.05 ±0.51 cm respectively. On the other hand, at follow-up stage in those group the mean ±SD sizes of fibroids were found as 2.64 ±0.40, 3.66 ±0.48 and 3.5 ±0.47 cm respectively. Recently, some other studies have also reported that, 25-dihydroxyvitamin D3 induced leiomyoma growth inhibition via catechol methyl transferase in vitro [17, 18]. The significant role of vitamin D deficiency (<20) in uterine fibroid development resulted from another study in which vitamin D3 administration is a safe, effective, nonsurgical medical treatment option for the uterine fibroids treatments (28) and the sufficient dose of vitamin D is associated with a reduced risk of uterine fibroids [16]. In our study, finally in evaluating the impact of vitamin D supplementation among our participants, comparing the fibroid sizes between baseline and follow-up stages, we observed that, in >45 year's age group the fibroid size change was non-significant (P<0.05). But in 31- 45 year's age group, the fibroid size was decreases significantly (P<0.008) and in 20-30 years' age group, that change was statistically extremely significant where the P value was less than 0.001. The results of another study are consistent with to other in-vivo and in-vitro studies in which vitamin D reduces the frequency as well as the size of leiomyomas [19, 20]. Besides these, the administration of vitamin D is a low cost and estimating a yearly cost of maintenance therapy in vitamin D deficiency (<20) context is approximately $32 [21, 22].

LIMITATION OF THE STUDY

This was a single centered study with small sample size. Moreover, the study was conducted at a very short period of time. So, the findings of this study may not reflect the exact scenario of the whole country.

CONCLUSION & RECOMMENDATION

As per the findings of this current study we can conclude that, vitamin D Supplementation have a significant role in decreasing the fibroid size in younger women with uterine fibroid. Specially, in 20 to 30 year's age group patients with uterine fibroid, vitamin D supplementations can ensure most excellent efficacy. For getting more specific findings, we would like to conduct similar more studied in several places.

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