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A cross-sectional study on the association of level of Vitamin D with severity of fibromyalgia syndrome in a tertiary care hospital, Kolkata

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ABSTRACT

Background: Fibromyalgia (FM) is a chronic disorder characterized by widespread pain associated with fatigue, stiffness, sleep disturbance, cognitive dysfunction, anxiety, and depression. The role of Vitamin D in the pathophysiology of FM is poorly known. Studies available to establish the association between Vitamin D and FM have inconsistent results. Some of the studies reported a positive association and others found no relation. It is not clear whether the pain is due to and/or associated with low levels of Vitamin D. **Aims and Objectives:** The objective of the current study is to estimate Vitamin D levels in FM patients and to find the association between Vitamin D levels and severity of FM. **Materials and Methods:** In this cross-sectional study, seventy patients who fulfilled the inclusion (American College of Rheumatology 2016 criteria) and exclusion criteria as has been considered for the study were enrolled and their serum 25 hydroxy-vitamin D level has been measured by enzyme-linked immunosorbent assay reader. Pre-designed questionnaires were prepared to measure FM severity. Pain intensity was measured by the Visual Analog Scale (VAS). **Results:** A total of 70 patients who were diagnosed with FM were included in our study. The majority of them (80%) were female and the rest (20%) were male. The mean age is 48.2 ± 9.2 years. Their mean body mass index (BMI) is 23.7 ± 3.82. The mean Vitamin D serum level was 22.4 ± 9.2 ng/dL. Vitamin D deficiency (VDD) was defined as patients with a serum level of 20 ng/mL and below. In our study, 62.8% (44) of the study population had VDD. According to VAS (0–10) pain scale, 15 (21.4%) subjects suffered from moderate pain and 55 (78.6%) subjects suffered from severe pain. The severity of FM was measured by the Fibromyalgia Severity Scale (FSS). The mean score of FSS was 22.7. To find the association between VDD and severity of FM, several covariates were identified and a multivariable logistic regression was done. **Conclusion:** VDD increases with an increase in age, BMI, VAS, and FSS, all of which are predicators of FM syndrome.

Key words: Fibromyalgia; Vitamin D; Fibromyalgia severity scale; Visual Analog scale

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INTRODUCTION

Fibromyalgia (FM) syndrome is a chronic disorder that presents with widespread musculoskeletal pain, stiffness, and easy fatigability. Patients often have multiple tender points distributed widely and symmetrically. It is also characterized by disturbed sleep, tiredness, cognitive dysfunction, anxiety, depression, and disturbances in bowel functions. FMS has been found in all ethnic groups. Women are more affected than men. Prevalence in the general population is 2% to almost 12%. Prevalence generally increases with age, with a peak prevalence occurring in the fifth-to-seventh decade of life.[1] Although the etiopathogenesis of FM remains unknown, it is thought that a combination of

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neuroendocrine, genetic, and environmental factors might play some role.[2,3] There is augmented pain and sensory processing due to abnormal pain perception.[4] Available data suggest sensitization of the peripheral and central nervous system plays a key factor in maintaining pain and other core symptoms of FM.[5] The American College of Rheumatology (ACR) Classification criteria for FM was first established in 1990 after a multicenter study based on a tender point examination.[6] Later on this classification was modified in 2010/2011 which includes widespread pain index (WPI) and symptom severity scale (SSS).[7] Widespread pain is defined as pain present in four out of five regions (four quadrant and axial). WPI is assessed as 0–19 scale over past week. SSS is the sum of severity scores, which includes symptoms such as fatigue, cognitive symptoms during the past 7 days, and somatic symptoms, such as headache, pain, or cramps in the lower abdomen, and depression during the past 6 months. SSS is assessed over a 0–12 scale. Further revisions of ACR 2010/2011 classification criteria were published in 2016.[8] In the 2016 revision along with WPI and SSS, the fibromyalgia severity scale (FSS) is developed which is the sum of WPI and SSS, ranging from 0 to 31 where 0 means no symptoms and 31 is the most severe symptoms. FSS is similar to the polysymptomatic distress scale (PSD). PSD scale measures the magnitude and severity of FM symptoms.[5,9] For diagnosis of FM, PSD scale should be at least 12.[10]

Vitamin D, a fat-soluble Vitamin, has a fundamental role in calcium homeostasis and bone metabolism. It also plays an important role as an immune system modulator.[2,11] Although low serum levels of 25 hydroxy-vitamin D (25[OH] Vitamin D) are common in chronic widespread pain syndrome, the role of Vitamin D in its pathophysiology is poorly known.[12] Many of the available studies reported a positive association and others found no association.[13,14] Theories were postulated to explain the role of 25(OH)-vitamin D deficiency (VDD) in the development and/or augmentation of pain intensity. Unfortunately, many of the studies to establish the association between VDD and FM have conflicting result.[15] It has been postulated that hypersensitivity of muscle and sensory hyper-innervations is responsible for the generation of musculoskeletal pain and this deep muscle pain developed during the early stage of VDD and that may precede into development of gross bone or muscle pathology.[16]

It is difficult to evaluate the severity of FM as there is no gold standard outcome measure to quantify the severity of FM. Multiple questionnaires and other instruments are being used to measure the severity of FM patients.[17] In this study, we were using FSS and Visual Analog Scale (VAS) to measure the severity of FM.

Aims and objectives

The objective of the current study is,

1. To estimate Vitamin D levels in FM patients
2. To find the association of Vitamin D level and severity of FM.

MATERIALS AND METHODS

An observational cross-sectional study was conducted jointly with the Department of Physical Medicine and Rehabilitation (PMR) and Department of Biochemistry at Calcutta National Medical College and Hospital (CNMCH), Kolkata, between April 2022 and September 2022 after getting ethical clearance from institutional ethical committee (EC-CNMC/2022/7 dated April 13, 2022).

Patients attending the PMR outpatients department (OPD) and pain clinic OPD under the PMR Department of CNMCH mostly presented with widespread pain and other symptoms and those who fulfill the inclusion and exclusion criteria have been considered for the study.

Inclusion criteria

The inclusion criterion was subject to fulfillment of FM diagnostic criteria as per ACR Criteria-2010/2011 with revision on 2016.[18]

Exclusion criteria

Patients other than FM diagnostic criteria are excluded.

RESULTS

A pre-structured pro forma is used to assess the severity of pain in FM patients. The demographic characteristics of all subjects, including age, sex, and body mass index (BMI), were recorded. The intensity of the widespread of the subjects was measured by the Visual Analog Scale. Blood samples are collected from FM patients and serum Vitamin D (25 OH D) is estimated using enzyme-linked immunosorbent assay reader.

Information obtained was recorded on the case record sheets and transferred to the master chart at the end of the study. Data so obtained are analyzed using standard statistical methods using the statistical calculator SPSS statistics version 2020.

This cross-sectional study consisting of seventy FM patients, of them 56 (80%) were females and the rest were males (14.20%). The mean age of the study participants was 48.2±9.2 years. The average BMI was 23.7±3.82. The mean Vitamin D serum level was 22.4±9.2 ng/mL. VDD was defined according to the Endocrine Society Clinical

Practice Guideline 2011[19] where patients with a serum level of 20 ng/mL and below were classified as having VDD. In our study, 62.8% (44) of the study population had suffered from VDD. The severity of FM was calculated using FSS, which is the sum total of WPI and SSS. The mean score of FSS was found to be 22.7.

VAS was used to delineate the subjective feeling of pain. Among the study subjects, all suffered from moderate-to-severe pain and the score thereby ranged from 4 to 10, with moderate pain being felt by 15 (21.4%) of them and severe pain by 55 (78.6%) of them.[20] To find the association between VDD and severity of FM, several covariates were identified and a multivariable logistic regression was done. It can be concluded that VDD was significantly associated with age, BMI, VAS, and FSS all of which are predicators of FM syndrome. Multivariable logistic regression showing the association of VDD with FM is shown in Table 1.

DISCUSSION

FM is a chronic painful condition associated with other non-painful symptoms. It has a significant effect on the quality of life of a person. In our study, 70 individuals participated of which 80% were female. Middle-aged female patients are commonly affected.[21,22] The mean age of our study participants was 48.2±9.2 years, which corresponds to the established literature. Obesity is a risk factor for FM. However, the average BMI of the study population was 23.7=3.82 which is within the normal range.

The aim of the study is to estimate Vitamin D levels in FM patients and its relation with the severity of FM. We have used Endocrine Society Clinical Practice Guideline 2011[19] where patients with a serum level of 20 ng/mL and below were classified as having VDD. In our study, 62.8% (44) of the study population had suffered from VDD. A number of studies are available to establish the association between Vitamin D level and FM but unfortunately the results are inconsistent. Many studies have reported a low or insufficient Vitamin D level in FM patients.[2,23,24]

Baygutalp[2] has analyzed the correlation of Vitamin D levels and clinical findings of FM patients and found a significantly lower level of serum 25OH Vitamin D level in FM patients as compared to the control group. Olama et al.,[23] and McBeth et al.,[24] also found significantly lower 25OH Vitamin D levels than controls. Both studies concluded that VDD is associated with FM. Abokrysha[11] published a study on VDD in women in Saudi Arabia and also concluded that VDD is often seen in FM patients. On the contrary Maafi et al.,[25] in their study have noticed that FM patients had significantly higher mean Vitamin D level than controls. Tandeter et al., and de Rezende Pena et al.,[26] found no association between VDD and FM. The association between pain and Vitamin D level in FM indicates that VDD may have an augmenting impact on pain intensity and functional status.[27] Wepner et al.,[28] included 30 female FM patients in their study and found significant improvement in pain scores after replacement with Vitamin D.

VAS was used to delineate the subjective feeling of widespread pain. Among the study subjects, all suffered from moderate-to-severe pain, and the score thereby ranged from 4 to 10, with moderate pain being felt by 15 (21.4%) of them and severe pain by 55 (78.6%) of them. Baygutalp[2] found significantly negative correlations between 25OH Vitamin D levels and widespread body pain (r=0.731, P<0.01) as measured by the VAS scale. In their study, Dogru et al.,[29] observed that although there was no correlation between Vitamin D level and VAS but significant changes occurred in VAS before and after replacement with Vitamin D.

Table 1: Multivariable logistic regression showing association of VDD with fibromyalgia (n=70)

Variables (No.)	VDD			
	<20 ng/dL	≥20 ng/dL	OR (CI)	P-value
	n (%)	n (%)		
Age (in years)			3.11 (1.03–10.0)	0.04
≤45 (36)	25 (69.4)	11 (30.6)		
>45 (34)	19 (55.9)	15 (44.1)		
BMI			2.44 (1.73–8.10)	0.03
≤24.9 (44)	28 (63.6)	16 (36.4)		
>25 (26)	16 (61.6)	10 (38.4)		
VAS*			0.22 (0.05–0.93)	0.04
2 (15)	7 (46.6)	8 (53.4)		
3 (55)	37 (67.2)	18 (32.7)		
FSS**			0.41 (0.11–0.53)	0.01
≤23 (38)	20 (52.6)	18 (47.4)		
>23 (32)	24 (75.0)	8 (25.0)		

*VAS: Visual Analog Scale, **FSS: Fibromyalgia symptom scale, VDD: Vitamin D deficiency, BMI: Body mass index, Hosmer Lemeshow: Chi-square 6.81 (df 7), P=0.63

In our study, disease activity was measured by FSS, which is the sum total of WPI and SSS. The mean score of FSS was found 22.7. D'Souza et al.,[30] in their study found that hypovitaminosis D may be a risk factor for worse symptom severity, anxiety, and depression in FM patients. The VDD is observed in FM in our study. A rise in FSS is associated with Vitamin D deficiency. An increase in age and BMI is also associated with increased VDD in our study. Vitamin D supplementation may reduce pain in FM through its anti-inflammatory, immunomodulation properties. In addition, Vitamin D by binding with Vitamin D response element inhibits the expression of epidermal growth factor receptor which is involved in pain sensing and processing.[31]

Limitations of the study

The small sample size is the limitation of our study. The other limitation is the lack of a control group.

CONCLUSION

In this study, the result shows that VDD increases with an increase in age, BMI, VAS, and FSS, all of which are predicators of FM syndrome. Hence, Vitamin D supplementation may relief the symptoms of FM syndrome.

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