

Original Article

Vitamin D Status in Patients with Proximal Muscle Weakness

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Abstract

Vitamin D deficiency has emerged as a concerning public health issue, and almost 25-50% of patients with proximal muscle weakness suffer for this deficiency. It has been documented that myopathy could be a presentation of hypovitaminosis D. Most often, it remains unnoticed or undiagnosed because muscle weakness develops gradually over the years. As fewer studies are available on this topic, the study was designed to assess the vitamin D status in patients presenting with proximal muscle weakness. This hospital-based descriptive cross-sectional study was conducted at the Inpatient and outpatient Department of Medicine of Dhaka Medical College Hospital for 6 months following approval of this protocol. The Ethical Review Committee approved the protocol, and informed written consent was obtained from all the patients. The patients were selected as per inclusion and exclusion criteria with the purposive sampling method. Data were collected by a preformed semi-structured questionnaire. Total 50 patients were included in the final analysis. Collected data were analyzed by the Statistical Package for the Social Sciences version-22 (SPSS). Among 50 patients, 70% were females and mean age was 58.92 ± 12.3 years with a frequent age group > 65 years (46%), where more than two third (68%) of the respondents were from urban area. Among the study subjects, the majority of them had involvement of the lower limb muscles (54%) and one-fifth of them (20%) had

both upper and lower limb involvement, whereas more than one-fourth (26%) had only upper limb involvement. The mean duration of illness was 8.6 ± 3.4 months. The study found more than three fourth, (78%) had hypovitaminosis D the and mean value of serum 25(OH) D was 22.3 ± 7.7 ng/ml. Among them 36% had mild insufficiency, 30% had a moderate deficiency, and 12% had severe deficiency. About two-thirds of proximal myopathy patients had hypovitaminosis D. Difficulties in walking, standing from sitting, climbing, raising hands above the head, bone and joint pain were significantly associated with the severity of vitamin D deficiency (P -value < 0.05). The severity of muscle weakness was strongly associated with the severity of vitamin D deficiency (P -value < 0.05). Females were comparatively more affected than males, it was not statistically significant. However, further large-scale analytical studies are needed to find the association of this hypovitaminosis with the disease process.

Key words: Hypovitaminosis D, Serum 25(OH)D, Vitamin D status, Proximal Myopathy, Muscle Weakness, MRC score

INTRODUCTION

Vitamin D is an essential part of calcium and phosphate homeostasis and thus to bone health. many other tissues including skeletal muscle are home to Vitamin D receptors.^{1,2} One of its metabolites, 25-hydroxycholecalciferol, influences the muscle's resting energy state and increases the protein turnover in muscle cells.³ Because vitamin D affects type 2 muscle fibers, it was tempting to speculate a protective effect of vitamin D on falls, via improvement in muscle function. A high number of Randomized control trials have investigated whether vitamin D supplementation affected muscle function and the incidence of falls.⁴

It is surprising that in South Asia, 80% of the healthy population is deficient in vitamin D (<20 ng/mL) and up to 40% of the population is severely deficient (<9 ng/mL).⁵ Those most at risk include older people in residential care⁶, darker-skinned women⁷(particularly if veiled), vegetarian diet⁸ and people with medical conditions that require sun avoidance or cause malabsorption.⁹ The salient features in vitamin D deficiency-related myopathy are the proximal distribution, the waddling gait, and pain and discomfort due to muscular effort.¹⁰ Myopathy or muscle weakness, worse in the legs than the arms and cutaneous hyperalgesia have been reported¹¹. New research suggests that leaked calcium is responsible for muscle cells to become fatigued and muscle lysis by a calcium driven

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enzyme¹² Muscle atrophy, particularly of type-2 fibres in vitamin D deficiency has been described histopathologically.^{13,14,15} Proximal myopathy has been seen in 70% of patients with severe osteomalacia. A serum 25-hydroxy vitamin D level below 30 ng/ml causes increased body sway, and below 10 ng/ml leads to symptoms like difficulties in standing from seat, inability to climb height, and muscle aches due to effort.¹⁶ An elevation in serum alkaline phosphatase with a low-normal plasma calcium concentration is clue to the diagnosis. Serum 25(OH)D level is the only way to confirm clinically present myopathy as biochemical signs like decreased Calcium and Increased Alkaline phosphatase levels are present late. The circulating Serum 25(OH)D level is the most appropriate pointer of vitamin D status because it is easily measurable, stable, and has a half-life of 3 weeks. Muscle biopsy is not directed and if done, shows nonspecific muscle fiber atrophy and no signs of inflammatory reaction.¹⁷ The ultimate evidence of the diagnosis rests on the response to therapy, as it is reversible and potentially treatable.^{18,19}

As this myopathy is potentially reversible with adequate vitamin D treatment, proper clinical evaluation and investigations should be conducted for appropriate treatment of the patient to reduce the morbidity. Keeping this in mind, this study aimed to assess the vitamin D status in patients with proximal muscle weakness and estimate the frequency of hypovitaminosis D in patients with proximal muscle weakness.

MATERIALS AND METHODS

This cross-sectional observational study was conducted in the department of medicine, DMCH. Fifty patients of either sex, age ≥18 years, with clinical features suggestive of proximal muscle weakness for at least three weeks were taken. Those diagnosed with thyroid disorders, pre-existing neurological or rheumatological conditions with lower limb weakness, patients taking corticosteroids, patients with alcoholism, pregnant women, and critically ill patients were excluded from the study.

- 1) Proximal muscle weakness, also known as proximal myopathy, is defined by the presence of one or more of the following features:²⁰
 - a. Difficulty in standing up from squatting or sitting position
 - b. Difficulty in walking
 - c. Difficulty in raising hands above shoulder
 - d. Difficulty in climbing up the stairs
- 2) Muscle power is graded according to the Medical Research Council scale:

GradeDescription	
0	No visible muscle contraction
1	Flickering contraction but no actual movement
2	Joint movement when effect of gravity removed
3	Movement against gravity but not against the resistance of the examiner
4	Movement against resistance but weaker than normal
5	Normal power ³⁾ Reference value of serum vitamin D ²¹ : Serum 25(OH)D in ng/ml unit is measured and it is categorized as following.

25 (OH)D level (ng/ml)	Interpretation
≥30	Normal
<30	Hypovitaminosis D
21-29	Insufficient/Mild hypovitaminosis D
10-20	Deficient/Moderate Hypovitaminosis D
<10	Severe deficient

History, clinical examination & necessary investigations for the study were done. Subjects or their relatives were briefed about the study's objectives, risk and benefits, freedom for participating in the study, and confidentiality. Informed written consent was obtained accordingly. Face-to-face interviews filled up the pre-structured Case Record Form (CRF)/data collection sheet.

RESULTS

Among 50 study participants, fifteen (30%) were males, and thirty-five (70%) were females, with an overall male-to-female ratio of 1:2.33. Among the 50 patients, the mean age was 58.92 ± 12.3 years. Most of the patients studied up to SSC (46%), and 10% were illiterate.

Among the 50 studied proximal myopathy patients, involvement of lower limb muscles was more frequent (54%), 20% had both upper and lower limb involvement, and 26% had only upper limb involvement. The mean duration of illness was 8.6 ± 3.4 months.

Serum 25(OH) D level was measured in all patients, and 78% showed hypovitaminosis D. Mean value of serum 25(OH) D was 22.3 ± 7.7 ng/ml. Among them, 36% had mild insufficiency, 30% had a moderate deficiency, and 12% severe.

In this study majority of the patients showed moderate muscle weakness (52%).

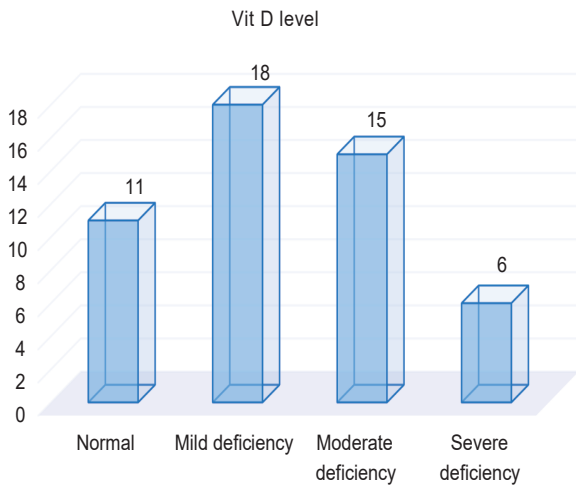


Fig.-1. Serum 25 (OH) D status in the patients (n=50)

Table I shows the MRC score of involved muscle in proximal myopathy patients.

Table 1. Muscle power assessment of the patients (n = 50)

Severity of myopathy	Score	Frequency
Severe (n=04)	00	00
	01	04
Moderate (n=26)	02	10
	03	16
Mild (n=20)	04	20

Table II shows socio-demographic profile of proximal myopathy patients showed hypovitaminosis D was significantly found among elderly patients (P-value < 0.05). Females were comparatively more affected than males, but it was not statistically significant. Females using veils outside of the home suffered from vitamin D deficiency (P-value < 0.05).

Table II. Socio-demographic characteristics and frequency of hypovitaminosis D in proximal myopathy patients (n= 50)

Variable	Normal Vit-D	Hypovitaminosis D	χ^2 value	P-value
Age groups				
18-35 years	02	02	16.88	0.001
36 - 50 years	02	06		
51 - 65 years	03	12		
> 65 years	04	19		
Sex				
Male	04	11	0.272	0.602
Female	07	28		
Residence				
Rural	02	14	1.237	0.262
Urban	09	25		
Monthly income (taka)				
< 15000	06	22	0.778	0.668
15000-40000	04	10		
> 40000	01	07		
Academic qualification				
Illiterate	01	04	1.679	0.642
Up to primary	03	11		
SSC	05	18		
HSC and above	02	06		
Use of veil (in female)				
Yes	03	21	14.258	0.004
No	04	07		

Table III shows presenting symptoms of proximal myopathy patients (n=50) were matched with the severity of vitamin D deficiency. Difficulties in walking, standing from sitting, climbing, raising hands above the head, and bone and joint pain were all significantly associated with the severity of vitamin D deficiency (P-value < 0.05).

Table III. Association of the presence of different symptoms with the severity of vitamin D deficiency in proximal myopathy patients (n= 50)

Symptom	Normal vit-D	Mild deficiency	Moderate deficiency	Severe deficiency	χ^2 value	P value
Difficulty in standing (n)						
Yes (27)	3	18	11	5	13.711	0.003
No (23)	8	10	4	1		
Difficulty in walking (n)						
Yes (22)	4	4	9	5	11.892	0.008
No (28)	7	14	6	1		
Difficulty in climbing (n)						
Yes (31)	8	7	11	5	8.434	0.038
No (19)	3	11	4	1		
Difficulty in raising the hand above the head (n)						
Yes (23)	5	9	7	2	0.507	0.917
No (27)	6	9	8	4		
Bone pain (n)						
Yes (21)	2	5	10	4	9.302	0.026
No (29)	9	13	5	2		
Joint pain (n)						
Yes (16)	3	2	7	4	12.384	0.007
No (34)	8	16	8	2		

Table IV shows the severity of vitamin D deficiency was not significantly associated with the duration of disease and involvement of the upper or lower limb of the proximal myopathy patients (n=50). The severity of muscle weakness was strongly associated with the severity of vitamin D deficiency (P-value < 0.05).

Table IV. Association of disease duration, limb involvement, and severity of muscle weakness with the severity of vitamin D deficiency in proximal myopathy patients (n= 50)

Variable	Normal vitamin-D	Mild deficiency	Moderate deficiency	Severe deficiency	χ^2 value	P-value
Duration of disease (n)						
< 6 months (12)	5	3	3	1		
6months–1year (22)	3	8	8	3	8.08	0.232
> 1 year (16)	3	7	4	2		
Limb involvement (n)						
Upper (13)	3	6	3	1		
Lower (27)	6	9	9	3	2.827	0.830
Both (10)	2	3	3	2		
The severity of muscle weakness (n)						
Mild (20)	7	10	3	0		
Moderate (26)	4	8	10	4	15.775	0.015
Severe (04)	0	0	2	2		

DISCUSSION

Among 50 study participants, fifteen (30%) were males, and thirty-five (70%) were females, with an overall male-to-female ratio of 1:2.33. Female predominance was observed in this study which is somewhat similar to other studies like Karthik A et al.²²

Most of the subjects were above 65 years (46%) with 22–86 years. Hossain et al.²³ reported that 80% of the study population belongs to the 31–50 years of age range. Another study by Mehta M et al.²⁴ reported majority 48% of cases was from 25 to 49 years of age

Among 50 patients majority were from urban areas (68%) than those from rural areas (32%). Mehta M et al.²⁴ reported majority of 92% of cases were from urban areas. Hossain et al.²³ found that 3/4th of the studied population with vitamin D deficiency were from urban areas. These findings support the findings of this study.

In this study majority of 56% of the patients were from a poor socio-economic background with a monthly income of fewer than 15,000 takas. The study by Micka et al.²⁵ Mehta M et al.²⁴ Jääskeläinen et al.²⁶ reported no such findings, whereas Hossain et al.²³ reported that among 212 patients, 85% (n=180) belonged to the middle class, which is different from this study. This could be due to the place and population of the study.

Out of 50 patients, most of the patients 46% studied up to SSC. This is analogous to the findings of Hossain et al., where those with higher education had lower levels of vitamin D. Contrary to the conclusions of this study, Jääskeläinen et al.²⁶ reported that those who had education >12 years had higher levels of vitamin D, than those with education 7–12 years and <7 years. Micka et al.²⁵ reported majority of 36% of the study population with lower levels of vitamin D had no formal education. Among the 50 studied proximal myopathy patients, involvement of lower limb muscles was more frequent (54%), 20% had both upper and lower limb involvement, and 26% had only upper limb involvement. The study by Al-said et al.²⁷ reported progressive proximal muscle weakness and Gait disturbances in 100% of cases, with diffuse musculo-skeletal pain (hips and lower limb) in 66% cases, back pain in 32% cases, carpopedal spasm in 13% cases and growth deficiency in 6% cases. Six patients (13%) had severe proximal muscle weakness with wheelchair-bound states. Twenty-two (42%) patients had a moderate weakness with a significant constraint of activities of daily living but with sustained independent mobility. As well, problems in rising

from a sitting position, inability to ascend height, and diffuse muscle pain were the main clinical symptoms in these patients. In a case study of 6 women by Hoigné et al.²⁸ reported that 100% of the cases clinical findings included mild proximal muscle weakness and gait abnormalities with difficulties running and climbing stairs. Another case study by Rawat et al.²⁹ reported patient had presented with quadriparesis. Another case study of an Indian man and a woman by Thabit et al.³⁰ reported that both had proximal myopathy and difficulty walking. These findings are supportive to the results of this study.

In this study of 50 patients Mean duration of illness was 8.6 ± 3.4 months. The majority, 44% were between 6–12 months. The severity of vitamin D deficiency was not significantly associated with the duration of disease and involvement of the upper or lower limb of the proximal myopathy patients. A study by Al-said et al.²⁷ reported that all the patients had symptoms of the disease duration ranging between 6–24 months with a mean of 14. In the case study of Rawat et al.,²⁹ patients had proximal muscle weakness for three years. Another case study by Thabit et al.³⁰ reported that a male patient had a one-year history of bilateral lower limb weakness, and a female patient had pain and aches in the pelvic region for 4 years with a referral to a rheumatologist for proximal development of muscle weakness. In another case study, Chandrashekara et al.³¹ presented a 42-year-old female with weakness in all four limbs, gradually deteriorating for one and half years.

Serum 25(OH) D level was measured in all patients, and out of 50 patients, 78% showed hypovitaminosis D. Mean value of serum 25(OH) D was 22.3 ± 7.7 ng/ml. Among them, 36% had mild insufficiency, 30% had a moderate deficiency, and 12% severe. In a study by Al-said et al., low Serum 25-hydroxy Vitamin D levels (<20 nmol/l) with a high level of parathyroid hormone were documented in 90% of patients. Which supports the findings of other studies.^{22,24,,27,28,32,33}

Out of 50 patients, the majority of the patients showed moderate muscle weakness (52%). Muscle power was graded according to the Medical Research Council scale. A study by Karthik A et al.²² reported that 36 of the patients who had a history of falls had motor weakness and MRC grading of 4 or less with severe Vitamin D deficiency. Also, a case study by Rawat et al.³⁴ reported that the patient had muscle power 3/5 in both upper limbs, while in lower limbs, it was 1/5 proximally and 3/5 distally. These findings are somewhat similar to the results of this study.

Among 50 patients Socio-demographic profile of proximal myopathy patients showed hypovitaminosis D was significantly found among elderly patients (P-value < 0.05). Females were comparatively more affected than males, but it was not statistically significant. Females using veils outside of the home suffered from vitamin D deficiency (P-value < 0.05). These findings are similar to the results of the study by Al-said et al.²⁷

Presenting symptoms of proximal myopathy patients (n=50) were matched with the severity of vitamin D deficiency. Difficulties in walking, standing from sitting, climbing, raising hands above the head, and bone and joint pain were all significantly associated with the severity of vitamin D deficiency (P-value < 0.05). The severity of muscle weakness was strongly related to the severity of vitamin D deficiency (P-value < 0.05). Karthik A et al. 22 found a correlation between the severity of vitamin D deficiency and loss of muscle power and frequency of falls, which supports the findings of this study.

CONCLUSIONS

A significant number of patients presenting with proximal myopathy to medical facilities have a low vitamin D level, which may remain undiagnosed. This morbidity increases with increasing age and female gender. This study is a picture of patients presenting to a tertiary level hospital. Further studies are required to support the findings and to understand the real scenario of the whole country.

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