

Original Research Article

Vitamin D levels in persons with traumatic spinal cord injury: a multicentre observational study

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ABSTRACT

Background: According to the published literature, Vitamin D deficiency is prevalent in spinal cord injury (SCI). Many studies were done earlier to find out different factors which predispose the SCI population to the risk of vitamin deficiency, but correlation with any such factor is still uncertain. Studies from India are scarce. The present study was conducted in view of this lacuna in existing knowledge in India and in the developing countries, to observe the levels of Vitamin D in traumatic SCI patients admitted for rehabilitation.

Methods: In this prospective, observational, multicentre study, all patients admitted consecutively in the three study centres, satisfying the selection criteria were included. The level of 25-OH Vitamin D was assessed by Chemiluminescence procedure. Vitamin D level <20 ng/ml was taken as deficient, 20-29ng/ml as insufficient, ≥30 ng/ml was the optimum and ≥150 ng/ml was taken as toxic level.

Results: Among 56 patients of traumatic spinal cord injury who were included in the study, having mean age of 32.32±11.82 years, only 14 (25%) were having optimum Vitamin D level. 25 (45%) subjects were deficient in Vitamin D, whereas 16 (28%) were having insufficient levels. One subject was found to have toxic level of Vitamin D (156 ng/ml). No differences of Vitamin D levels were observed between demographic and clinical groups.

Conclusions: Although a high rate of Vitamin D deficiency was encountered in SCI individuals, the role of different factors causing Vitamin D deficiency remains unproven. Also the amount of Vitamin D required to forestall insufficiency is still unknown, indicating a necessity for more studies with well-defined outcome measures.

Keywords: ASIA impairment scale, Spinal cord injury, Vitamin D

INTRODUCTION

Global incidence of spinal cord injury (SCI) is 3.6 to 95.4 patients per million and in India the average annual incidence of SCI is 15,000 with a prevalence of 0.15 million.^{1,2} Spinal Cord Injury (SCI) is truly a devastating injury with profound consequences to the individual, his family and society. SCI is predominantly caused by

automobile accidents, falls, practice of various sports, and acts of violence.³ Spinal trauma has been determined as an important factor to bone loss immediately after injury due to changes generated by immobility and reduced impact activity.^{4,5} These changes include increased bone resorption, hypercalciuria and suppression of parathyroid hormone (PTH).⁶ It is estimated that 21 to 81% of individuals with SCI will be diagnosed with osteoporosis

and have a 5 to 23% greater chance to present fractures when compared to individuals without physical limitations.⁴ Beside fractures post spinal trauma patients also present with additional complications, such as pain, pressure ulcers, and spasticity etc.⁷ Although in SCI, immobilization is the main triggering factor for bone loss, neural lesions, reduced sun exposure, obesity, circulatory problems and hormonal changes are also implicated in the pathogenesis of osteoporosis.⁸ Additionally individuals with SCI have higher prevalence of chronic urinary infections, neurogenic bladder dysfunction and nephrolithiasis and more likely to develop Chronic Kidney Disease (CKD), which has impact on a wide range of biological functions including the synthesis of the bioactive form of Vitamin D and the consequences of Vitamin D insufficiency. Vitamin D has an important role in calcium homeostasis and when in low concentration, results mainly in decreased bone mineral density, increased risk of fractures, and secondary hyperparathyroidism, which play an important role in the development of post SCI osteoporosis.⁹

Longer time since the injury, complete lesions, low body mass index (BMI), age, history of previous fracture, alcohol use, and paraplegia are considered risk factors for developing osteoporosis in individuals with SCI.¹ Furthermore, individuals with spinal cord injury (SCI) experience neuro-inflammation, impaired lung function, muscle dysfunction and accelerated cardio-metabolic disease, all of which may benefit from the optimization of Vitamin D nutrition. The prevention and treatment of post injury bone loss also has a major impact on rehabilitation, prognosis and quality of life of these patients.

A better knowledge of the importance of Vitamin D for SCI individuals may lead to improvements in nutritional management, emphasize the development of clinical practice guidelines and encourage more research in this area.

The purpose of this study was to observe the serum levels of Vitamin D in individuals with SCI and their relationships with duration of the injury, level of injury, ambulation status and many other factors. To our knowledge, there are very few studies in India, which have evaluated the Vitamin D level of traumatic SCI patients.

METHODS

It was a prospective, observational study done in the Department of Physical Medicine and Rehabilitation/Neurorehabilitation of three tertiary care hospitals. The study was approved by the Institutional Ethical Committee. The study has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experimentation with human subjects. All patients of traumatic spinal cord injury, admitted in the Rehabilitation wards of the three study centres during the period January 2017 to June 2019 satisfying the inclusion and exclusion criteria were

included in the study after taking informed consent. Our inclusion criteria were, all adult (age >18 years) Indian patients of traumatic spinal cord injury, both genders, willing to participate in the study. Exclusion criteria were, non-traumatic spinal cord injury, spinal cord injury patients with polytrauma or traumatic brain injury, those who have taken Calcium and Vitamin D supplementations (other than fortified food items) in last 3 months, persons with any other skeletal injury or deformity, known cases of chronic liver or kidney disease or nephrolithiasis, previous diagnosis of any metabolic bone disorder. Neurological examination and American Spinal Injury Association Impairment Scoring (AIS) were done according to the International Standards for Neurological Classification of Spinal Cord Injury, on the day of admission. The skeletal level of injury of the subjects was determined by plain X-ray. Vitamin D3 levels were measured on the day of admission through the use of Chemiluminescence procedure in all the three centres. Although there is no consensus on serum 25(OH)D levels yet, values of Vitamin D3 level <20 ng/ml was taken as deficient, 20-29 ng/ml as insufficient, ≥ 30 ng/ml was the optimum and ≥ 150 ng/ml was taken as toxic level, as per the standard laboratory values of the three centres. All patients having deficient or insufficient Vitamin D3 level were given Tablet Calcium carbonate 500mg once daily and Capsule Cholecalciferol supplementation 60000 units per week for 8 weeks.

Statistical analysis

Data analyses were performed by the use of Statistical package for social sciences (SPSS) version 21. Descriptive statistics were reported as mean \pm SD. A p value of <0.05 was considered statistically significant. The normality of the data was tested using the Shapiro-Wilk test; this indicated that non-parametric statistical tests should be used. The Kruskal-Wallis test was used to compare the variation in Vitamin D levels with the various ambulatory status parameters.

The post hoc Dunn's test was used for pair wise comparison. For comparison of categorical variables between groups having post injury duration <3 months and >3 months, we applied Fisher's exact test. Fisher's test was also applied for comparing the categorical variables between Vitamin D deficient and optimum Vitamin D groups. Spearman's correlation coefficient was used to test the potential relationships between Vitamin D level and age and between Vitamin D level and duration since injury.

RESULTS

Total 56 patients from the three study centres, who satisfied the inclusion and exclusion criteria, were enrolled in the study. Their age (mean \pm SD) was found to be 32 \pm 11.8 years and mean duration of hospital stay for rehabilitation was 2 \pm 1.4 months. The most common cause of traumatic spinal cord injury as found in our study was

fall from height. Others had road traffic accidents, some sustained gunshot injury, and some of them experienced a railway accident. A few people gave history of fall of heavy objects on their back, which is a very common etiology of SCI in developing countries, as people carry weight on their back and head for various reasons in developing countries.

Table 1: Demographic and clinical profiles of patients (n=56).

	Number (%)
Gender	
Male	43 (76.78)
Female	13 (23.21)
Residence	
Rural	32 (57.14)
Urban	24 (42.86)
Duration since injury	
<3 months	15 (26.79)
>3 months	41 (73.21)
Mode of injury	
Fall from height	47 (83.92)
Road traffic accident	5 (8.92)
Gunshot injury	2 (3.57)
Misc.	2 (3.57)
Surgery	
Yes	42 (75)
No	14 (25)
Pressure ulcer	
Yes	23 (41.8)
No	33 (58.2)
Skeletal level	
Cervical	7 (12.55)
Dorsal	36 (64.29)
Lumbar	13 (23.21)
AIS	
A	36 (64.28)
B	10 (17.86)
C	8 (14.28)
D	2 (3.57)
Ambulation status	
Non-ambulatory	7 (12.50)
Therapeutic standing	19 (33.93)
Walking with aids	30 (56.57)

AIS: American Spinal Injury Association (ASIA) Impairment Scale

The entire study population was divided into 2 groups according to their Vitamin D levels. One group was having subjects with either deficient or insufficient level of Vitamin D, another group having optimal level. One patient with toxic level of Vitamin D (156 ng/ml) was excluded from this analysis. As a reason of having toxic level, over-the-counter use of Cholecalciferol granules with milk for prolonged time, was elicited from the history of the subject.

Table 2: Vitamin D profile (n=55).

Variables	Vitamin D deficiency (Insufficient + Deficient) Number (%) (n ₁ =41)	Optimum Vitamin D Number (%) (n ₂ =14)	P value
Gender			
Male	32 (74.4)	11 (25.6)	0.508
Female	9 (75)	3 (25)	
Pressure ulcer			
Present	17 (73.9)	6 (26.1)	0.838
Absent	24 (75)	8 (25)	
Duration since injury			
<3months	11 (78.6)	3 (21.42)	0.636
>3 months	30 (73.2)	11 (26.8)	
Ambulation status			
Non ambulatory	4 (57.1)	3 (42.9)	0.714
Therapeutic standing	16 (84.2)	3 (15.8)	
Walking with aids	21 (72.4)	8 (27.6)	
ASIA impairment scale			
AIS A	29 (80.6)	7 (19.4)	0.300
AIS B	6 (60)	4 (40)	
AIS C	5 (62.5)	3 (37.5)	
AIS D	1 (100)	0 (0)	

ASIA: American Spinal Injury Association, AIS: ASIA Impairment Scale

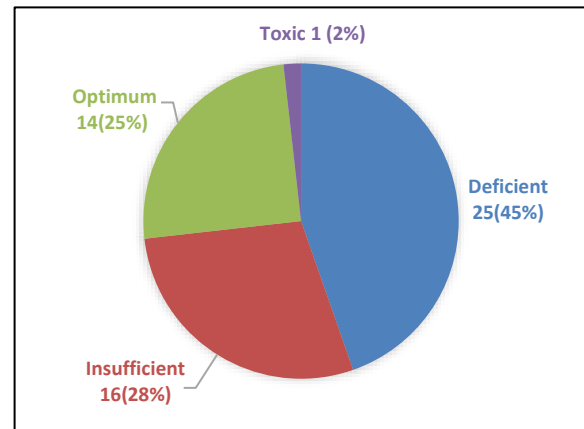


Figure 1: Levels of Vitamin D in traumatic spinal cord injury patients (n=56).

The Vitamin D profiles of 55 study subjects show 58.2% males and 16.4% females were suffering from hypovitaminosis D. Low levels of Vitamin D was observed in 73.9% patients with pressure ulcer, whereas only 26.1% had optimal levels of Vitamin D in spite of having a pressure ulcer. Among 41 subjects having post-injury duration of more than 3months 73.2% had Vitamin D deficiency or insufficiency.

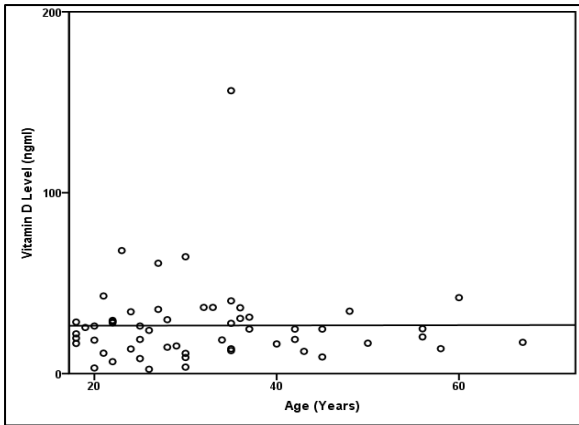


Figure 2: Vitamin D level versus age ($p=0.832$ and $\rho=0.029$).

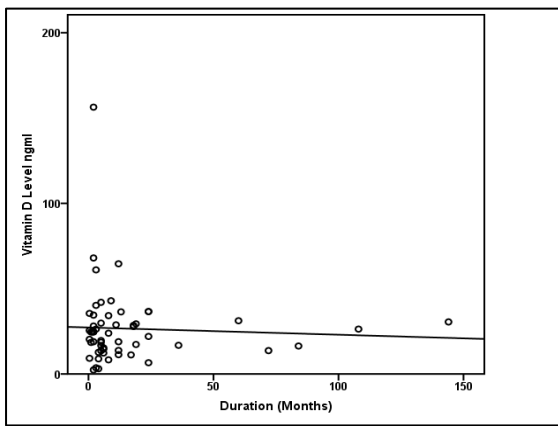


Figure 3: Vitamin D level versus duration in months ($p=0.707$ and $\rho=0.051$).

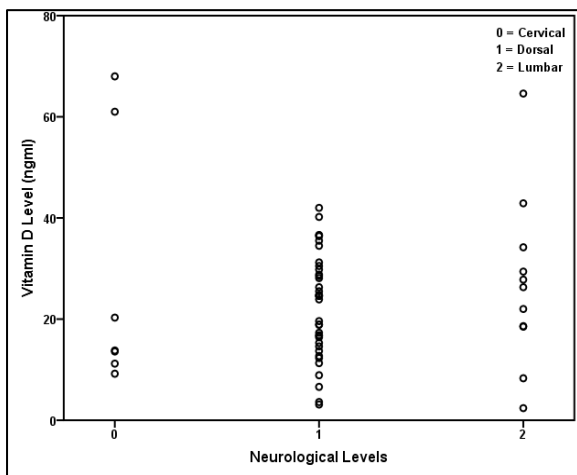


Figure 4: Vitamin D level versus neurological levels ($p<0.533$).

According to AIS classification, 80.6% subjects with AIS A, 60% subjects with AIS B, 62.5% subjects with AIS C and 100% with AIS D showed low levels of Vitamin D in their blood.

We compared different factors between the two groups, like- gender, duration since injury, presence or absence of pressure ulcer, ambulatory status and ASIA Impairment Score (AIS), although, no significant difference was found between these two groups.

There was no relationship between Vitamin D level and age ($p=0.832$ and $\rho=0.029$), also no correlation was observed between Vitamin D level and duration since injury ($p=0.707$ & $\rho=0.051$), as shown in Figure 2 and 3 respectively. No difference in Vitamin D level was observed for different neurological levels of injury ($p<0.533$) as depicted in Figure 4.

DISCUSSION

Vitamin D deficiency has been extremely prevalent within the SCI population, as well as in those with other disabilities because of multiple etiologies.¹⁰⁻¹² In current study 73% (45% deficient+28% insufficient) SCI patients have Vitamin D level below the optimum level. Similarly Gifre et al, also found 60% of individuals with SCI having hypo-vitaminosis D.⁴

Persons with SCI often have a lower calcium intake in comparison to the general population, including fortified milk (Vitamin D), which is the major dietary source of Vitamin D, other than the supplements.¹³ There are several biological plausible mechanisms by which Vitamin D may act upon cardio-metabolic and musculoskeletal health. Along with negative effect on bone tissue, Vitamin D deficiency may impair other aspects such as muscle strength, and cause complications related to different organs.¹⁴ The impact of insufficiency on such systems remains ill-defined in SCI.

A large proportion of people suffering from SCI are young adults according to published literature, which was confirmed in this study sample, whose mean age was 32 ± 11.8 years. A study conducted by Nogueira et al.¹⁵ with 59 subjects showed an average age of 37 years. Opperman et al also observed similar results in relation to the mean age of individuals with SCI.¹⁶

In the current study, most of the SCI patients having duration since injury greater than 3 months had Vitamin D deficiency (73.2%). An important expected result was that the time elapsed since injury was inversely proportional to the Vitamin D levels, but we have found that 78.6% of patients with duration since injury <3 months also have Vitamin D deficiency. This finding is probably related to the shorter time of sun exposure due to limited mobility in both acute and chronic spinal cord injury.

SCI is a complex condition that leads to lifestyle and biopsychosocial changes.^{15,17} Prolonged immobilization may lead to suppression of the PTH-Vitamin D axis, when an accelerated bone demineralization occurs, there is calcemia and consequently decrease secretion of PTH and conversion of the bioactive portion of Vitamin D.¹⁷ So it is

well recognized that significantly increased ionized calcium in the early stage of a SCI, whereas serum calcium concentration remains normal. In patients with a chronic SCI, concentration of serum calcium significantly decreases.¹⁸

As highlighted by Karapolat et al, there is suppression of the PTH-Vitamin D axis in the acute period after the injury, while a reverse activity of PTH during the chronic phase can be observed. PTH values gradually increased from the first days until 36 months after the SCI.^{8,19} As showed in study by Oleson et al a higher amount of deficient or suboptimal Vitamin D status in individuals with a chronic SCI compared with an acute SCI.¹¹

Synthesis and metabolism of Vitamin D mainly depends on exposure to short wave ultraviolet B (UVB) rays, which will initiate the entire process of activation of 25-OH-Vitamin D in 1,25(OH)₂-Vitamin D, also known as calcitriol, via its substrate 7-dehydrocholesterol, into the epidermis.²⁰ Low solar exposure in patients with SCI might be related with immobilization, longstanding hospitalization, as well as delayed patient's ambulation due to poor financial conditions, for hiring a professional who could assist in that, in order to increase the time of sun exposure.²¹

The study by Zhou et al showed a higher prevalence of low Vitamin D level in patients with pressure ulcer compared with patients without a pressure ulcer.²² However, presence of pressure ulcer and low Vitamin D may reflect a common cause, which is lack of mobility. In current study, 73.9% subjects with pressure ulcer were found to be having either deficient or insufficient serum Vitamin D levels, which denotes a quite high percentage. Significantly lower Vitamin D level in patients with an incomplete injury compared with that in patients with a complete injury (14.6 versus 18.2 ng/ ml) was found by Nemunaitis et al.¹² In contrast to this, out of 36 complete SCI injury patients in our study, 29 have low Vitamin D levels, while 12 out of 19 subjects with incomplete injury have Vitamin D levels lower than normal.

Twenty one out of 29 subjects who were ambulatory with aids, 4 out of 7 non ambulatory subjects and 16 out of 19 subjects doing therapeutic standing only had hypovitaminosis D. Poorer physical activity as well as lower functional independence have been correlated to a poor Vitamin D status in individuals with a SCI.²³ Similarly Benlidayi et al found that in non-functionally ambulatory individuals with a SCI had higher amount of Vitamin D insufficiency compared with functionally ambulatory patients.²⁴

There was no significant difference in Vitamin D status between individuals with tetraplegia and paraplegia, in a study with no difference in Vitamin D status comparing individuals with able-bodied controls to paraplegia and tetraplegia.¹² In contrast a significantly lower Vitamin D status in individuals with a tetraplegia compared with

individuals with paraplegia as reported by another study.²² These results clearly showed that having a SCI may produce a high variability in mobility, independence as well as functionality. Therefore, it is not obvious whether having tetraplegia or paraplegia might be a better predictor for lower Vitamin D level. The level of functionality seems to have a higher impact on Vitamin D deficiency in this population, as patients in constant need of assistance or restrained to bed, will not spend enough time under the sun.

Because of the complications of their impairment per se, individuals with a SCI are already at a higher risk of cardiovascular disease or osteoporosis that are identified with a Vitamin D deficiency and might lead to serious health problems.²⁵ The chance for osteoporosis, falls, and fractures already increases independent of the Vitamin D status in patients with SCI and may rise much more in case of Vitamin D deficiency, which might worsen osteoporotic conditions.²⁶⁻²⁹ However, implementation of an adequate supplementation strategy in clinics and hospitals prevents patients from such further health risks. Muscle weakness and pain, depression which are critical for rehabilitation are also related to Vitamin D deficiency, making diagnosis and treatment of Vitamin D deficiency more important in SCI patients.³⁰

Limitations

The sample size was small. There was no control group. Influence of season, race, ethnicity (other than Indian) and BMI was not taken into consideration. Serum iPTH was not measured, as the facility was not available in the lead centre. Long term follow-up data is not available. Further studies are needed, to grant accurate recommendations or guidelines to stop deficiency in individuals with an acute and chronic SCI.

CONCLUSION

From the above study, it can be concluded that majority of the individual with SCI have Vitamin D deficiency and the deficiency is more common in chronic patients. This might ensue to prolonged limitation of mobility which ends up in insufficient sun exposure, and these factors may aggravate bone loss related to low impact activity and decreased mobility resulting from SCI. We recommend to test Vitamin D status regularly in SCI population and to supplement deficient individuals with a dose of 50000 IU / weekly for eight week which is based on Endocrine Society recommendation and an active, healthy lifestyle with regular outdoor activities to forestall patients from a Vitamin D deficiency. Treatment of suboptimal status should be instituted in both acute and chronic stages of the SCI. When supplementing SCI individuals, close interactions between Vitamin D and related bone minerals should be kept in mind, and practices should be individualized with clinical conditions. Information, education and communication should be carried out about the advantages of sun exposure and the way sun exposure

should be practiced, as a preventive measure for Vitamin D deficiency with no cost involved, which is very important for developing countries. Normal levels of Vitamin D can prevent many musculo-skeletal complications and improve the quality of life.

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