

Hypovitaminosis D Status in Newly Diagnosed Cases of MS versus Control Group

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Abstract

Background: Hypovitaminosis D is amongst those strongly suggested risk factors for multiple sclerosis (MS). Although the association of vitamin D deficiency with MS has been established in several studies in recent years, there are not many studies to assess and compare the degree of Hypovitaminosis D status of newly diagnosed patients with multiple sclerosis versus control group worldwide, especially in UAE.

Objective: To compare and observe the state of Hypovitaminosis D in newly diagnosed cases of multiple sclerosis versus control group and to determine presence of any significant association.

Methods: In this retrospective study, 30 cases of newly diagnosed multiple sclerosis were randomly selected and matched for age and sex with 30 controls. Demographics and serum vitamin D level for both groups were evaluated. Appropriate statistical analysis was performed to show any significant association.

Results: An independent-samples t-test was conducted. There was a significant difference in Vitamin D level for MS (Mean=37.08, SD=17.63) and control group (Mean=58.103, SD=21.5323); $p < 0.05$.

Conclusion: Findings of this study suggest:

1. There is significant association between vitamin D deficiency and Multiple Sclerosis
2. Hypovitaminosis D may be a contributing factor in lowering the mean age of MS diagnosis. We propose early evaluation for vitamin D insufficiency in cases of MS and emphasis on restoring serum vitamin D to satisfactory levels as part of clinical management of MS. It would be worthwhile doing a large randomized trial to establish the safety and efficacy needed to promote large-scale vitamin D supplementation.

Keywords: Neuropathy; Multiple sclerosis; Hypovitaminosis D; Vitamin D

Introduction

Although the role of Vitamin D in bone health through calcium and phosphorus homeostasis is known for a long time, several studies in last decade has revealed other important properties of vitamin D including the role in immunomodulation, growth and differentiation and neural development [1-3].

The immunomodulatory effects of vitamin D, in particular its ability to down regulate the T helper type 1 (Th1) cell activity through vitamin D receptors present on activated T lymphocytes, have made Hypovitaminosis D as one of those strongly suggested risk factors for multiple sclerosis (MS). This potentially has great impact with new clinical implications in the field [4,5].

Multiple sclerosis (MS) is an autoimmune inflammatory disorder of central nervous system which affects over 2.3 million people worldwide [6]. It is the most common cause of progressive neurological disability in young adults [7]. The prevailing thought is that MS is triggered by a combination of environmental factors and genetic susceptibility [8]. Observational studies on environmental links

have demonstrated that increased exposure to sunlight, [9-12] decreasing latitude [13] and high consumption of vitamin D-rich fish oils [14] are each associated with a reduced risk of developing MS.

It has been suggested that vitamin D affects the regulation of clinical disease activity as well as influencing the development of disease. It is observed that in MS patients, lower serum 25(OH)D levels are associated with an increased risk of relapse [15,16].

The strong correlation between UV index and vitamin D level has been shown in several studies [17-19]. Despite being located in high UV index area with sunny climate throughout the year, vitamin D insufficiency is known to be endemic in Gulf Region [20,21]. In studies done in Kuwait, Saudi Arabia and UAE the prevalence of hypovitaminosis D among adult population was reported to be 82.9% and 83.6% and 74%, respectively [22-24].

Recent studies also confirm the unexpected high incidence and prevalence of Multiple Sclerosis in Gulf region [25]. In a recent paper in 2016 Schiess et al. reported the prevalence of MS among Emiratis in Abu Dhabi (UAE) to be 57.09%, which is similar to another study from Dubai (UAE) in 2011 which determined the prevalence of 54.77% for the disease [26,27].

Although the association of vitamin D deficiency with MS has been established in several studies in recent years, there is no study to assess and compare the degree of hypovitaminosis D status of newly diagnosed cases of MS versus control group worldwide, especially in UAE.

Objective

To compare the vitamin D levels in newly diagnosed cases of multiple sclerosis versus control group of patients who visited neurology department for other minor neurological complaints and determine the presence of any significant association.

Methods

In this retrospective case-control study conducted in Neurology Department, Mafraq Hospital, Abu Dhabi, a total number of 30 cases of newly diagnosed multiple sclerosis who visited neurology clinic between 2010 to 2015 were randomly selected and were matched for age and sex with 30 patients who visited neurology department for other minor neurological complaints such as headache and backache. The diagnosis of MS was confirmed using McDonald 2010 criteria. For both patients and control group the exclusion criteria were those who were on Vitamin D supplementation for the past 6 months, those who use cyclosporine, lipid lowering agents and hormones and also the presence of chronic kidney disease, malabsorption and endocrine diseases. Demographics and serum vitamin D level for both groups

were evaluated by electrochemiluminescence method using commercial Kits. In order to eliminate the effect of season, patients and controls were matched for the time of assessment of vitamin D level as well. Subjects were categorized into three groups of normal (vitamin D levels >75 nmol/L), insufficiency (vitamin D levels 50–75 nmol/L) and deficiency (vitamin D levels <50 nmol/L).

Data of subjects hospitalized/seen in the neurology clinic at Mafraq hospital were incorporated into an existing database and compared with each other and the results were illustrated in the form of tables, charts and figures.

Statistical Package for the Social Sciences, Version 20.0 (SPSS Inc. Chicago, IL, USA) was used for statistical analysis. Results are expressed as mean ± Standard Deviation (SD). An independent-samples t-test was applied to compare means of two groups.

Results

A total number of 60 patients attending the Neurology department in Mafraq Hospital were enrolled in this study. The cohort comprised of 30 newly diagnosed cases of MS and 30 patients with minor neurological problems.

In this study, the mean age in case and control group was 30.1 and 30.9 years, respectively. 21 females and 9 males were included in each group (Table 1).

Characteristics	Cases (N=30)	Controls (N=30)
Gender		
Male	9 (30%)	9 (30%)
Female	21 (70%)	21 (70%)
Age (mean)	30.1 (SD=8.4)	30.9 (SD=9.4)
Serum Vitamin D (mean)*	37.21 (SD=17.9)	58.1 (SD=21.5)
Serum Vitamin D in Age Group <29	29.63 (SD=13.59)	54.67 (SD=25.06)
Serum Vitamin D in Age Group =>29	44.79 (SD=18.89)	61.54 (SD=17.51)
Serum Vitamin D in Males	38.62 (SD=20.41)	66.28 (SD=22.14)
Serum Vitamin D in Females	36.61 (SD=17.25)	54.6 (SD=20.81)
Vitamin D Status		
Deficient (vitamin D levels <50 nmol/L)	23 (73.3%)	13 (43.3%)
Insufficient (vitamin D levels 50–75 nmol/L)	6 (23.3%)	10 (33.3%)
Normal (vitamin D levels >75 nmol/L)	1 (3.3%)	7 (23.3%)
*P value<0.05		

Table 1: Demographics and clinical characteristics of cases and controls.

In MS group 96.6% of subjects were having low vitamin D (insufficiency 23.3% and deficiency 73.3%); while in the control group only 76.6% had low vitamin D level (insufficiency 33.3% and deficiency 43.3%).

The case group with median vitamin D level of 33.15 nmol/L and mean vitamin D level of 37.21 nmol/L (SD=17.9) showed a significant difference compared to controls with median of 55.15 and mean level of 58.1 nmol/L (SD=21.5) (Figures 1 and 2).

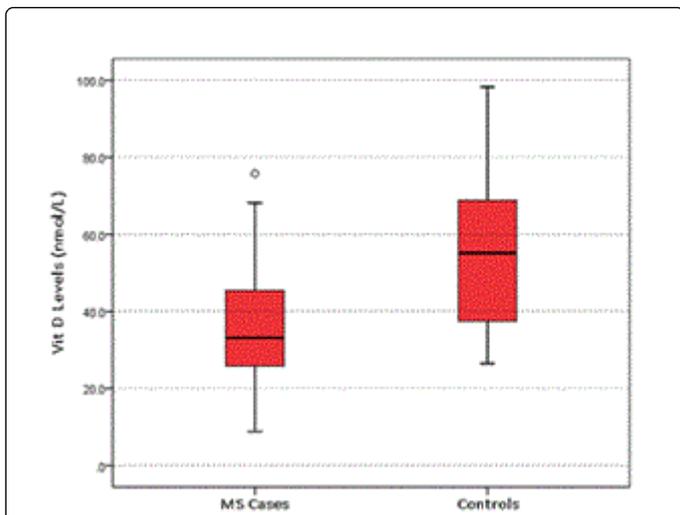


Figure 1: Vitamin D level in multiple sclerosis patients and controls. Box plot indicates median and interquartile range, small circles indicate outliers and asterisks represent mean.

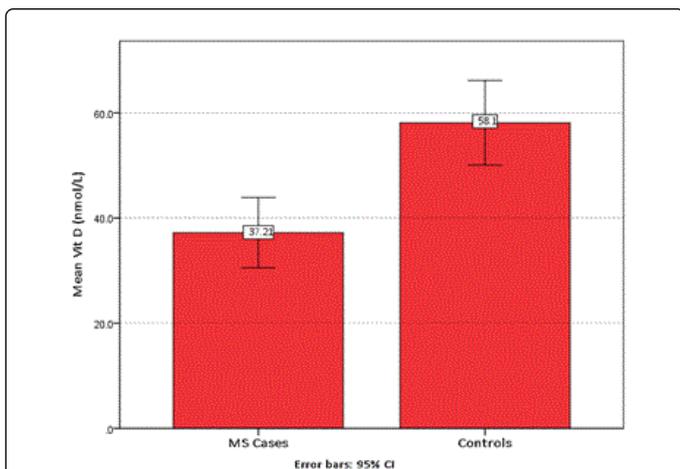


Figure 2: Mean level of Vit D in MS patients and controls. Error bars represent ± 1.96 , the 95% confidence interval.

There was no significant difference in vitamin D level between males and females in MS group or control group.

Serum levels of vitamin D between females of both groups was significant ($P=0.004$). There was also significant difference in vitamin D level between males of both groups as well ($P=0.011$) (Figure 3).

There was significant difference in vitamin D level between patients younger than 29 years of age (mean age of MS diagnoses based on literature) compared to those who are older than 29. ($P=0.01$)

This significant difference in vitamin D level was also observed in MS subjects below 29 years of age and controls in the same range of age ($P=0.01$) (Figure 4).

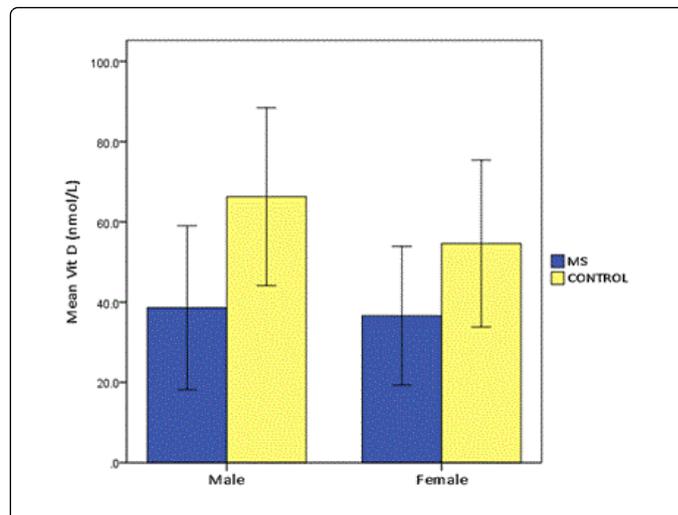


Figure 3: Vitamin D level in MS patients and controls based on gender.

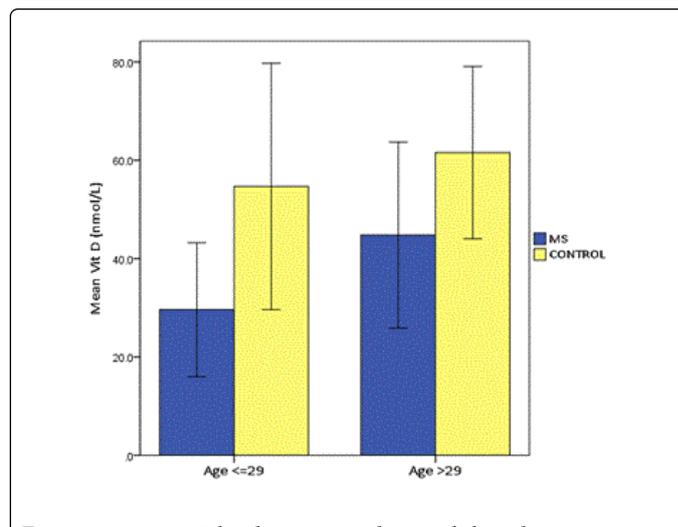


Figure 4: Vitamin D level in cases and controls based on age group.

Discussion

There have been many epidemiological data from clinical cross-sectional as well as prospective studies which support a potential relationship between vitamin D deficiency and an increased risk of developing MS [5,15,16,28].

Of the 60 subjects enrolled in this study The majority of the patients (even before the process of matching the subjects) were young females (70%) which is similar to other studies in this field [6,29]. 96.6% of newly diagnosed cases of MS were suffering from hypovitaminosis D, while the observed value for control was 76.6%. This was similar to a study in Hamadan, Iran, that reported 96% of newly diagnosed cases of MS were suffering from hypovitaminosis D [30].

There was no significant difference in vitamin D level between males and females; this is in contrast with some other studies [31]. The findings of this study suggest significantly lower levels of vitamin D for

females who were diagnosed with MS compared to females in control group. The results were also significantly different for males in both groups. These findings are consistent with recent studies which showed the same pattern [29,32]. There is an interesting finding in regard with sex difference and Vitamin D level which was observed in Experimental Autoimmune Encephalomyelitis (EAE), with dietary vitamin D delaying the onset and severity of the disease in female but not male mice [33].

Participants in this study were between 15-46 years of age with mean age of 30.1, which is consistent with proposed age distribution for MS patients [34-36] but interesting finding in this study was association between vitamin D level and age group. Based on our findings MS subjects below 29.2 years of age (which according to WHO report [37] is the mean age at onset of MS) had significantly lower levels of vitamin D compared to their counterparts in control group. Results of one study in Denmark highlighted that younger age at onset of MS was significantly associated with low exposure to summer sun [38]. There are other studies which support the presence of association between age at onset and severity of the disease [39].

Although it is likely that vitamin D becomes an integral part of MS treatment in near future; the knowledge of high rate of vitamin D insufficiency in gulf region [20,21] should encourage all neurologist across the region to evaluate serum vitamin D level for MS patients at earliest and begin Vitamin D supplementation if indicated.

Conclusion

Findings of this study suggest:

1. There is significant association between vitamin D deficiency and Multiple Sclerosis
2. Hypovitaminosis D may contribute in lowering the mean age of MS diagnosis.

This study proposes early evaluation for vitamin D insufficiency in cases of MS and emphasis on restoring serum vitamin D to satisfactory levels as part of clinical management of MS. It would be worthwhile doing a large randomized trial to establish the safety and efficacy needed to promote large-scale vitamin D supplementation.

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