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

Mehdi Saeedan, Yasamin Ghazvini Ko, Sudhir Kumar Palat Chirakkara, Shobhit Sinha and Ahmed Shatila
Neurology Department, Mafraq Hospital, Abu Dhabi, UAE
*Corresponding author: Saeedan M, Neurology Department, Mafraq Hospital, Abu Dhabi, UAE, Tel: 00971558117437; E-mail: mesaeedan@hotmail.com
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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=17.83) 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).

![Table 1: Demographics and clinical characteristics of cases and controls.](image-url)

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).
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).

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 Ancephalomyelitis (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 between 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.

**References**

1. Eyles DW, Brown J, Mackay-Sim A, McGrath J, Feron F (2002) Vitamin D3 and brain development. Neuroscience, pp. 1–44.
2. Bouillon R, Okamura WH, Norman AW (1995) Structure-function relationships in the vitamin D endocrine system. Endocrine Rev 16: 200–257.
3. Studzinski GP, Moore DC (1995) Sunlight can it prevent as well as cause cancer? Cancer Res 55: 4014–4022.
4. Lemire JM (1992) Immunomodulatory role of 1,25-dihydroxyvitamin D3. J Cell Biochem 49: 26–31.
5. Dudani SJ, Kalhan S, Sharma SP (2011) Vitamin D and multiple sclerosis: Potential pathophysiological role and clinical implications. Int J App Basic Med Res 1: 71–74.
6. Browne P, Chandraratna D, Angood C, Tremlett H, Baker C, et al. (2014) Atlas of Multiple Sclerosis 2013: A growing global problem with widespread inequity. Neurology 83: 1022-1024.
7. Compston A (1998) Genetic susceptibility to multiple sclerosis. McAlpine's Multiple Sclerosis, London, pp: 104-144.
8. Compston A, Coles A (2008) Multiple sclerosis. Lancet 372: 1502-1517.
9. Bäarnhielm M, Hedström AK, Kockum I (2012) Sunlight is associated with decreased multiple sclerosis risk: No interaction with human leukocyte antigen-DRB1*15. Eur J Neurol 19: 955–962.
10. Freedman DM, Dosemeci M, Alavanja MC (2000) Mortality from multiple sclerosis and exposure to residential and occupational solar radiation: A case-control study based on death certificates. Occup Environ Med 57: 418–421.
11. Kampman, MT, Wilsgaard, T, Møllgren, SI (2007) Outdoor activities and diet in childhood and adolescence relate to MS risk above the Arctic Circle. J Neurol 254: 471–477.
12. Beretich BD, Beretich TM (2009) Explaining multiple sclerosis prevalence by ultraviolet exposure: A geospatial analysis. Mult Scler 15: 891–898.
13. Simpson S, Blizzard L, Otahal P (2011) Latitude is significantly associated with the prevalence of multiple sclerosis: A meta-analysis. J Neurol Neurosurg Psychiatry 82: 1132–1141.
14. Kampman MT, Wilsgaard T, Møllgren SI (2007) Outdoor activities and diet in childhood and adolescence relate to MS risk above the Arctic Circle. J Neurol 254: 471–477.
15. Runia TE, Hop WC, De Rijke YB (2012) Lower serum vitamin D levels are associated with a higher relapse risk in multiple sclerosis. Neurology 79: 261–266.
16. Mowry EM, Krupp LB, Milazzo M (2010) Vitamin D status is associated with relapse rate in pediatric-onset multiple sclerosis. Ann Neurol 67: 618–624.
17. Holick MF (2002) Vitamin D: the underappreciated D-lightful hormone that is important for skeletal and cellular health. Curr Opin Endocrinol Diabetes Obes 9: 87–98.
18. Hayes CE, Nashold FE, Spach KM, Pedersen LB (2003) The immunological functions of the vitamin D endocrine system. Cell Mol Biol 49: 277–300.
19. Holick MF (2002) Sunlight and vitamin D: Both good for cardiovascular health. J Gen Intern Med 17: 733–735.
20. Muhairi, Shamma J (2015) Vitamin D Deficiency among Healthy Adolescents in Al Ain, United Arab Emirates. BMC Public Health 13: 33.
21. Naeem Z (2010) Vitamin D deficiency - An ignored epidemic. Int J Health Sci (Qassim) 4: V-VI.
22. Zhang F, Al Hooti S, Al Zenki S (2016) Vitamin D deficiency is associated with high prevalence of diabetes in Kuwaiti adults: Results from a national survey. BMC Public Health 16.
23. Hussain AN, Alkhazaniz AH, Al Shaker M, Raha E, Gabr A (2014) Increasing trends and significance of hypovitaminosis D: A population-based study in the Kingdom of Saudi Arabia. Arch Osteoporos 9: 190.
24. Bani-issa, Wegdan (2017) Vitamin D deficiency and its determinants in adults: A sample from community-based settings in the United Arab Emirates. Int J Endocrinol 2017: 3906306.
25. Bohlega S, Inshasi J, Al Tahan AR, Madani AB, Qahtani H, et al. (2013) Multiple sclerosis in the Arabian Gulf countries: A consensus statement. J Neurol 260: 2959-2963.
26. Schiess N (2016) How global MS prevalence is changing: A retrospective chart review in the United Arab Emirates. Mult Scler Relat Disord 9: 73–79.
27. Inshasi JI, Thakre M (2011) Prevalence of multiple sclerosis in Dubai, United Arab Emirates. Int J Neurosci 121: 393–398.
28. Smolders J (2010) Vitamin D and multiple sclerosis: Correlation, causality and controversy. Autoimmun Dis 2011: 629538.
29. Kingwell E, Marriott JJ, Jette N, Pringsheim T, Makhani N, et al. (2013) Incidence and prevalence of multiple sclerosis in Europe: A systematic review. BMC Neurolog 13: 128.
30. Mazdeh M, Seifirad S, Kazemi N, Seifrabie M, Dehghan A, et al. (2013) Comparison of vitamin D3 serum levels in new diagnosed patients with multiple sclerosis versus their healthy relatives. Acta Medica Iranica 51: 289-292.
31. Barnes, MS, Bonham, MP, Robson, P (2007) Assessment of 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D3 concentrations in male
and female multiple sclerosis patients and control volunteers. Mult Scler 13: 670–672.

32. Kragt JJ, BM van Amerongen, Killestein J, Dijkstra CD, Uitdehaag CH (2009) Higher levels of 25-hydroxyvitamin D are associated with a lower incidence of multiple sclerosis only in women. Mult Scler January 2009 15: 9-15.

33. Spach KM, Hayes CE (2005) Vitamin D3 confers protection from autoimmune encephalomyelitis only in female mice. J Immunol 175: 4119-4126.

34. Richards RG, Sampson FC, Beard SM, Tappenden P (2002) A review of the natural history and epidemiology of multiple sclerosis: Implications for resource allocation and health economic models. Health Technol Assess 6: 1.

35. Soilu-Hanninen M, Laksonen M, Laitinen I, Erlinna J, Lilius E, et al. (2008) A longitudinal study of serum 25-hydroxyvitamin D and intact parathyroid hormone levels indicate the important of vitamin D and Calcium homeostasis regulation in Multiple sclerosis. J Neurol Neurosurg Psychiatr 79: 152-157.

36. Weinshenker BG, Bass B, Rice GPA, Noseworthy J, Carriere W, et al. (1989) The natural history of multiple sclerosis: A geographically based study. Brain 112: 133-146.

37. World Health Organization (2008) Atlas: Multiple sclerosis resources in the world. World Health Organization, Geneva.

38. Laursen JH, Søndergaard HB, Sørensen PS, Sellebjerg F, Oturai AB (2016) Association between age at onset of multiple sclerosis and vitamin D level-related factors. Neurology 86: 88-93.

39. Trojano M, Liguori M, Bosco Zimatore G, Bugarini R, Avolio C, et al. (2002) Age-related disability in multiple sclerosis. Ann Neurol 51: 475-480.