Frequency of Vitamin D Deficiency Among Patients of Multiple Sclerosis in Pakistan

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ARTICLE INFORMATION	ABSTRACT

Multiple Sclerosis (MS) is a very common chronic demyelinating disorder of the central nervous system particularly among adults. In this study we aim to determine the frequency of vitamin D deficiency in patients of multiple sclerosis identifying such patients and providing proper treatment if needed, would help reducing the morbidity associated with MS. We conducted this study from August 2018 to February 2109 at Department of Neurology, Jinnah Postgraduate Medical Center Karachi. A total of 114 previously diagnosed patients of Multiple sclerosis were included in this study. Blood was drawn and sent for measurement of 25(OH)D levels. Patients was labeled as having vitamin D deficiency if the level of total 25(OH)D level was < 20ng/ml. The average age of the patients was 37.74±10.73 years. Frequency of vitamin D deficiency in patients of multiple sclerosis was 36.44% (42/114). Out of 42 deficient cases, 34(80.9%) were mildly deficient and 8(19.1%) were moderately deficient in Vitamin D. supplementation of vitamin D in healthy individuals is now being considered as a potent strategy for MS prevention. In utero and early-life exposure could also be important, but there is strong evidence that levels of vitamin D during end of adolescence and beginning of adulthood have a major effect in determining the risk of MS.

1. Introduction

Multiple Sclerosis (MS) is a chronic inflammatory demyelinating disorder affecting central nervous system (Awad & Stüve, 2010). It is one of the most common chronic neurological disorders among young adults, and the most common cause of non-traumatic neurologic disability in this age (Pugliatti et al, 2002; Benito- León et al 1998). The estimated number of individuals with MS has soared from 2.1 million in 2008 to a staggering 2.3 million in 2013 (Browne et al, 2014) with Iran having the highest number of cases in Asian Region (Nasr et al, 2016). The pathogenesis of MS is pretty complex, likely involving multitude of genes and their interactions with several other environmental factors. It has been linked to be mediated by autoimmune reaction among susceptible people (Ascherio & Munger, 2010 ; Benito-Leo'n et al, 2010) along with all these factors recent data on this subject strongly point towards the involvement of environmental and nutritional factors, especially vitamin D deficiency, as a causative agent of MS (Ho t al, 2014). Latitude is strongly correlated with ultraviolet radiation (UV) duration and intensity and skin sun exposure is the main source of vitamin D in most populations (Goldberg, 1974).

2. Literature Review

The link of vitamin D deficiency with risk of MS was suggested 30 years ago (Holick, 1995). Epidemiologic evidence strongly nominates vitamin D insufficiency in the etiology of MS (Ascherio et al, 2010). The most convincing evidence comes from a large perspective case-control study in US military personals which concluded that there was a 41% decrease in risk of MS for every 50-nmol/L increase in 25-hydroxyvitamin D (Munger et al, 2006). Also an study came to the conclusion that the higher

vitamin D levels are associated with less MS inflammatory activity providing evidence of a 57% decreased risk for new active MRI lesions for each 50 nmol/l increase in 25 (OH) vitamin D levels (Ascherio et al, 2014). One study has managed to show the link of vitamin D deficiency in Multiple Sclerosis patients as they found quite a sizeable number of patients with vitamin D deficiency and insufficiency 30% and 56% respectively (Shaygannejad et al ,2010). This is in conflict with a study done by Zaidi NR et al in Pakistan which found only 8% patients of multiple sclerosis to be vitamin D deficient. Owing to its varied but consistent prevalence vitamin D deficiency must be considered as an important factor in MS risk, prevention and treatment (Zaidi et al, 2016). Pakistan is a very populous country and suffers from wide spread vitamin D deficiency but unfortunately there is only a single research on the topic of MS related to vitamin D deficiency. In the current study we strive to elucidate the magnitude of the vitamin D deficiency in MS patients presenting to the one of the largest tertiary care hospitals of Pakistan, identifying such patients will result in focused treatment if needed, which would definitely help reducing the morbidity in MS.

3. Methodology

This cross-sectional study was conducted from August 2018 to February 2019 at the Department of Neurology, Jinnah Postgraduate Medical Center Karachi. Institutional clearance was obtained from the ethical committee of the Hospital. A total of 114 consenting patients who were between 18-60 years of age with previously diagnosed Multiple sclerosis with any score for > 6 months were included in the study. Patients were informed about the study purpose. Questionnaire regarding age, gender, duration of MS, duration of sun exposure, occupation and educational status was filled by the patient.

Patients taking vitamin D supplement and known cases of ischemic or hemorrhagic stroke, chronic diarrhea within 6 months which may have contributed to presumed vitamin D and nutrient deficiency and malignancy (ascertained through history and accompanied prescription) were excluded from the study.

Venous blood was drawn from the participants serum separator tube (SST). The labeled samples were transported to the laboratory within an hour. Tubes were immediately centrifuged at 4000g for 15 minutes to separate the serum which was stored at -70 °C until analysis. Total 25-OH vitamin D was measured on fully automated immunoassay analyzer Seimens ADVIA Centaur. Patients was labeled as having vitamin D deficiency if the level of total 25(OH) D level was < 20ng/ml. All values were catered in the pre-approved.

The Data was collected and analyzed on software SPSS version 18.0. Descriptive statistics will include mean ± standard deviation (SD) of continuous data, like age, duration of MS, sun exposure, monthly family income and 25(OH)D levels. Frequencies and percentages were calculated from the categorical data, like gender, educational status, occupation, and patients with Vitamin D deficiency. (25(OH)D level < 20ng/ml-Outcome Variable). The data was presented in the form of tables, pie charts (for categorical data) and histograms (for continuous data). Effect modifiers was controlled by stratification of age in groups, gender, duration of MS (6-12 months, 13-18 months, more than 18 months), duration of sun exposure, monthly income, occupation, educational status and Severity of deficiency of vitamin D (Mild- 25(OH) D level 20-10 ng/ml, Severe- 25(OH)D level < 10 ng/ml). Post stratification chi square test was applied with a p value of ≤ 0.05 was taken as significant.

4. Results and Discussion

A total of 114 previously diagnosed patients of Multiple Sclerosis were included in this study. The average age of the patients was 37.74±10.73 years. Similarly mean duration of MS, serum level of 25(OH) D, duration of sun exposure and family monthly income is reported in table 1. There were 76(66.67%) male and 38(33.33%) females, frequency of vitamin D deficiency in patients of multiple sclerosis was 36.44% (42/114), out of 42 patients with low levels of 25(OH) D deficiency and severe deficiency was found to be 80.9% and 19.1% respectively, education and employment status of the patients are also presented in table 2.

Variables	Mean	Std. Deviation	95% Confidence Interval for Mean	
			Lower Bound	Upper Bound
Age (Year)	37.74	10.73	35.74	39.73
Duration of Multiple Sclerosis (in months_	12.21	4.82	11.32	13.11
Serum Level of 25(OH) D	22.44	7.15	21.119	23.77

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Serum Level of 25(OH) D	22.44	7.15	21.119	23.77
Duration of sun exposure (minutes)	24.82	21.60	20.82	28.83
Family Monthly Income (Rs.)	34472	18337	31069	37874

TABLE 1: Descriptive statistics of the study patients

GENDER	
Males 76(66.67%)	76(66.67%)
Females 38(33.33%)	38(33.33%)
25 (OH) D LEVELS	
Normal levels	42(36.84%)
Decreased levels	72 (63.16%)
DEGREE OF DEFICIENCY	
Deficient levels	34(80.9%)
Severely Deficient Levels	8(19.1%)
LITERACY STATUS	
Illiterate	36(31.5%)
Secondary school	35(30.7%)
Matric/Intermediate	29 (25.4%)
Graduate	15(13.2%)
EMPLOYMENT STATUS	
Government job	27(23.6%)
Private job	73(64.1%)
Business	14(12.3%)

TABLE2: Frequencies of gender, vitamin D levels, degree of deficiency, literacy status, employment status of study population

Stratification analysis was performed and observed that frequency of vitamin D deficiency was significantly high in those cases who had below 10 minutes sun exposure (p-value 0.0005) whereas frequency of vitamin D deficiency in patients of multiple sclerosis was not significant with age, gender, education, occupation, socio economic status or duration of MS (p-value >0.05) as shown in table 3.

DURATION OF SUN EXPOSURE	VITAMIN D DEFICIENCY		Total	P-Value
	Yes	NO		
≤ 10 minutes	38(88.4%)	5(11.6%)	43	
11 to 30	4(8.7%)	42(91.3%)	46	0.0005
>30	0(0%)	25(100%)	25	
DURATION OF MS				
≤ 12 months	27(36.5%)	47(63.5%)	74	
13-18 months	12(40%)	18(60%)	30	0.846
>18 months	3(30%)	7(70%)	10	
AGE GROUPS (YEARS)				
≤30	14(43.8%)	18(56.3%)	32	
31-40	13(31.7%)	28(68.3%)	41	0.188
41-50	11(50%)	11(50%)	22	

51-60	4(21.1%)	15(78.9%)	19	
GENDER				
Male	25(32.9%)	51(67.1%)	76	0.217
Female	17(44.7%)	21(55.3%)	38	
EDUCATION				
Illiterate	12(34.3%)	23(65.7%)	35	
Secondary school	12(34.3%)	23(65.7%)	35	0.915
Matric or intermediate	12(41.4%)	17(58.6%)	29	
Graduate and above	6(40%)	9(60%)	15	
EMPLOYMENT STATUS				
Govt. Job	9(33.3%)	18(66.7%)	27	
Private Job	27(37%)	46(63%)	73	0.835
Business	6(42.9%)	8(57.1%)	14	
SOCIO ECONOMIC STATUS				
≤ 20,000	5(35.7%)	9(64.3%)	14	
20,001 to 40,000	28(35%)	52(65%)	80	0.706
>40,000	9(45%)	11(55%)	20	

TABLE 3: Correlation of duration of sun exposure, duration of MS, age, gender, education, employment status and socio economic with vitamin D deficiency.

Multiple sclerosis (MS) is the most common immune-mediated inflammatory demyelinating disease of the central nervous system. MS is characterized pathologically by multifocal areas of demyelination with loss of oligodendrocytes and astroglial scarring. Axonal injury is increasingly recognized as a core pathologic component of MS. It may have very typical presenting features but many atypical forms also exist. The possibility that vitamin D deficiency may be a risk factor for multiple sclerosis (MS) was proposed more than 30 years ago (Goldberg , 1974) primarily to explain the observation of a latitude gradient in MS prevalence. Latitude is strongly correlated with ultraviolet radiation (UV) duration and intensity and UVB is the main source of vitamin D in most populations (Swank et al, 1952). Strong observational evidence and experimental work further support a potential causal association (Ascherio et al, 2019). Although the exact mechanism of action of vitamin D is not known, given the available data and the safety profile of vitamin D, there is strong interest in conducting vitamin D treatment and prevention trials of MS. The underlying pathophysiology may have vital effects guiding timely intervention; thus consistent epidemiologic, immunologic, and genetic studies are important to fully comprehend how vitamin D mitigates MS risk and possibly helps to slow down disease progression. To determine the frequency of vitamin D deficiency in patients of multiple sclerosis, a total of 114 previously diagnosed patients of Multiple sclerosis of both genders, aged above 18 years to 60 years were included in this study. The average age of the patients was 37.74±10.73 year and there were 66.67% males and 33.33% females in our study. Based on multi- hospital-based study from India suggested that the prevalence of MS rose from 1.33/100,000 to 8.35 in last three decades (Pandit, & Kundapur. 2014 ; Singhal , 1999). Female to male ratio was 1.6:1 and the mean age at onset was 38.3 . There are no population-based studies concerning prevalence or incidence for MS from Pakistan.

Many patients with MS have low concentrations of vitamin D concentrations. In addition, MS relapses have further lowered concentrations than during remissions(Jelinek et al, 2015) and correlate inversely with disease severity (Correale et al, 2009).Frequency of vitamin D deficiency in our patients of multiple sclerosis was 36.44% (42/114) Out of 42 low levels of vitamin D, 34(80.9%) were deficient and 8(19.1%) were severely deficient. Other studies in Europe and America have found similar findings indicating lower dietary vitamin D intake and serum levels of 25 (OH) D in MS patients than healthy population (van der et al 2007; Dwyer et al, 2008). Studies in Isfahan have demonstrated that serum 25(OH) Deficiency (<30 nmol/L) were observed not only in MS patients but also in healthy individuals (Etemadifar et al 2006). A recent study showed that in clinically isolated syndrome patients (namely, those suffering a single demyelinating attack that is compatible with MS), vitamin D deficiency was a predictor of developing clinically definite MS (Martinelli et al, 2014). The association of disease activity with vitamin D levels in MS patients has been evaluated in multiple studies that demonstrated a lower MS relapse rate in patients with higher levels of vitamin D (Runia et al,2012). Additionally, low levels of vitamin D appear to be associated with high levels of disability as measured by the Expanded Disability Status Scale (EDSS) (Harandi et al 2012).

5. Conclusion

Vitamin D supplementation in healthy individuals is emerging as a dependable solution for prevention of MS. In utero and early-life exposure could even be important, but there is strong evidence that vitamin D concentrations during late adolescence and young adulthood have a serious effect in determining MS risk. Whereas future observational epidemiological studies, and genetic and molecular investigations, are warranted to strengthen and refine the hypothesis, evidence is approaching equipoise, at which the soundest decision might be to do a sizeable randomized trial to determine the safety and efficacy needed to promote large-scale vitamin D supplementation.

Evidence supporting a therapeutic effect of vitamin D in modifying the course of MS is less convincing than evidence of a preventive effect. However, given the safety of high doses of vitamin D, there is sufficient evidence to support the need for large randomized trials to determine whether vitamin D supplementation could delay the time to progress from a first demyelinating episode to MS or to MS treatment. Furthermore, screening of serum 25-hydroxyvitamin D concentrations is likely to spot a hefty proportion of patients who are vitamin D deficient or insufficient, who might benefit from vitamin D supplementation for prevention of osteoporosis and other complications.

Conflicts of Interest: All authors declare that there are no competing interests for the publications of this paper.

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