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Frequency of vitamin d deficiency in multiple sclerosis patients: a cross sectional study.

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FREQUENCY OF VITAMIN D DEFICIENCY IN MULTIPLE SCLEROSIS PATIENTS: A Cross sectional study

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INTRODUCTION: Vitamin D deficiency is linked to poor treatment response in patients with Multiple Sclerosis. The aim of this study is to define the frequency of Vitamin D deficiency for early detection and timely intervention leading to improved morbidity rates.

OBJECTIVE: To determine the frequency of vitamin D deficiency in Multiple sclerosis patients present at neurology ward of a tertiary care hospital in Larkana

DURATION OF STUDY: March 2016 to August 2016

STUDY DESIGN: Cross-sectional study

Setting: Neurology Ward Chandka Medical College Hospital, Larkana

SUBJECTS: Ages of 18 and 60 years, either gender, diagnosis of MS for more than 3 months, sun exposure for at least 30 minutes thrice per week for and give written informed consent were included in this study.

METHODS: This study was approved by an ethical review committee of the institute. Patients fulfilling inclusion criteria were enrolled in this study after taking written informed consent. The demographic variables like name, age, gender, duration of sun exposure & duration of disease were collected by the researcher. Blood Sample for a vitamin D level blood sample of these patients was drawn on the same day and sent to a laboratory for vitamin D level in the pathological lab of CMCH. Blood Vitamin D levels in this study were measured by radioimmunoassay. The data was analyzed using SPSS version 19.

RESULTS: Mean age of enrolled participants was 43.6 ± 11 years. Of 85 enrolled participants, 36 (42.4%) were male and 49 (57.6%) were female, the mean duration of disease was 6.2 ± 1.4 months, 70 (82.4%) participants were married and 15 (17.6%) were unmarried, 49 (57.6%) were employed, 43 (50.6%) were exposed to the sun for < 40 minutes a day. The frequency of vitamin D deficiency among patients with multiple sclerosis was 17 (20%) cases.

CONCLUSIONS: It is concluded from this study that the frequency of vitamin D deficiency among patients with multiple sclerosis was 20%.

KEYWORDS: Multiple sclerosis, vitamin D deficiency, sun exposure

INTRODUCTION:

Multiple sclerosis (MS) is an autoimmune, inflammatory, neurodegenerative, T-lymphocyte-mediated disease of uncertain etiology. Mostly it is because of genetic susceptibility; epidemiologic studies suggest environmental influence because the development of MS correlates most strongly with rising latitude in both the northern and southern hemispheres¹.

The diagnosis relies on recognition of the clinical patterns of the disease. Relapsing and remitting neurologic deficits is the hallmark of the disease in most patients. The pathologic hallmark of MS is focal demyelination within the brain and spinal cord. Although the lesions can occur at any site within the central nervous system, they have a predilection for involvement of the periventricular white matter, the corpus callosum, optic nerves, and the dorsal spinal cord. MS affects females two to three times more than male, risk increases from adolescence up to the age of 35 and then gradually declines and is rare after the age of 65. MS is rare in equatorial climates, and its prevalence increases with distance from the equator. Higher latitudes result in lower ultraviolet radiation exposure and lower vitamin D levels², from the relation with latitude; it appears that low solar UltraViolet B (UVB) doses during winter are an important risk factor³. However, low UVB exposure in summer also plays a role. This is an observation that MS patients consistently have lower levels of vitamin D. One recent study has shown prevalence of vitamin D as 17% in patients with MS.⁴ It is suggested that vitamin D may help to decrease the risk of MS and those patients with higher vitamin D levels are less likely to develop MS.⁵ It is observed that higher vitamin D levels may help to reduce MS activity and a slower the rate of progression of MS.⁶ Higher vitamin D levels also helps to prevent disability in MS patients.⁷ A case-control study compared the serum vitamin D levels of 103 MS patients with 110 controls and found that for every 10-nmol/L increase in serum 25(OH)D level the odds of MS was reduced by 19% in women, suggesting a "protective" effect of higher vitamin D levels.⁸ In addition, a negative correlation was found between Expanded Disability Status Scale scores among female MS patients and 25(OH)D levels. There are several other studies have supported the finding that lower levels of vitamin D in MS patients are associated with more severe disability.⁹ Lower levels during relapses have also been reported in patients with relapse-relapsing MS.¹⁰⁻¹² One small safety study of 12 patients taking 1000 µg per day (40,000 IU) of

vitamin D for 28 weeks showed a decline in the number of gadolinium-enhancing lesions on magnetic resonance imaging per patient; this led to a 25(OH)D serum concentration of 386 nmol/L (158 ng/mL) without causing hypercalcemia, hypercalciuria, or other complication.¹³

Ongoing, Randomized control trials are assessing vitamin D supplementation for the treatment and prevention of MS.¹⁴

RATIONALE:

The rationale of study is that the studies on the subject under consideration are scarce in Pakistan and secondly most of the studies done on retrospective data. Since VIT D deficiency is related to poor treatment results in patients with MS, this study by determining the frequency was lead to realization for early detection and timely intervention ultimately leading to improved morbidity rates.

OBJECTIVE

To determine the frequency of vitamin D deficiency in Multiple sclerosis patients present at neurology ward of a tertiary care hospital in Larkana.

OPERATIONAL DEFINITION

MULTIPLE SCLEROSIS:

Was defined as isolated limb weakness of power <2/5 on MRC score with the increased tone of > 2 scores determined by Modified Ashworth Scale on clinical examination > 3 months (Appendix I and II respectively) and according to the 2010 McDonald diagnostic criteria of MS (Appendix III)

VITAMIN D DEFICIENCY:

Patients were labeled Vitamin D deficient if less than 25 nmol/l at the time of presentation.

MATERIAL AND METHOD

Study Design: Cross-sectional study

Setting: This study was conducted at the Neurology Ward Chandka Medical College Hospital, Larkana.

Duration of Study: Six months March 2016 to August 2016

Sample Size: Taking the prevalence of VIT D deficiency as 17%⁴, confidence interval at 95% and margin of error at 8% and putting this information in Epi

Info 7, the sample size calculated is 85.

Sampling Technique: Non - Probability consecutive sampling

Inclusion Criteria:

1. Between the ages of 18 and 60 years,
2. Both genders
3. Diagnosis of MS as per operational definition for > 3 months
4. Give written informed consent prior to any testing under this protocol, including screening tests and evaluations that are not considered part of the subject's routine care.
5. Sun exposure for at least 30minutes thrice per week

Exclusion Criteria:

1. Patients that have other co-morbidities like heart failure determined by echo as EF>25 renal disease determined by serum Cr > 3mg/dl)
2. Endocrine disorders like hyperparathyroidism determined by blood PTH levels > 10 ng/dl
3. Any patient on long-term steroid treatment for less than 3 months. determined by physician prescription slip
4. Patients already on vitamin D therapy for more than 3 months. Doctor's prescription as evidence.

Data collection procedure:

The permission for the data collection was sought from the Ethical review committee of the hospital, the study was conducted in the department of Neurology, department, Chandka Medical College, Larkana. After taking the informed written consent from the patients. Diagnosed cases of Multiple sclerosis was enrolled in the study after fulfilling inclusion/exclusion criteria. The researcher was collect data on a prescribed questionnaire regarding demographic variables like name, age, gender, duration of sun exposure & duration of disease. Blood Sample for a vitamin D level blood sample of these patients was drawn on the same day and sent to a laboratory for vitamin D level in the pathological lab of CMCH. Blood Vitamin D levels in this study was measured by radioimmunoassay. The test was done free of cost at CMCH, Larkana lab and the results of these tests were collected on reporting date and was entered on the Performa by researcher herself.

Data analysis procedure:

Data was analyzed on a computer using SPSS software version 21. Mean and SD was calculated for age, duration of disease, duration of sun exposure and Vitamin D levels. Frequency and percentages were calculated for gender, age group, marital status, and employment status and outcome variable i-e vitamin D deficiency. Effect variable like age, gender, marital status, and employment status, duration of sun exposure and duration of disease were stratified to see the effects of these on the outcome variable. Applying chi-square test with p value <0.05 taken as significant.

Ethical consideration:

Permission for data collection was taken from the head of the department of the ward. Written informed consent was obtained from patients while ensuring that the data was kept confidential. Patients were thoroughly informed about the objectives and methods of the study.

RESULTS

A total of 85 patients were enrolled in this study during study period. The mean age of enrolled participants was 43.6±11 years. Majority of patients were less than 45 years accounting for 43 (50.6%) cases. Of 85 enrolled participants, 36 (42.4%) were male and 49 (57.6%) were female, the mean duration of disease was 6.2±1.4 months, 70 (82.4%) participants were married and 15 (17.6%) were unmarried , 49 (57.6%) were employed, 43 (50.6%) were exposed to the sun for < 40 minutes a day (Graph 1).

Outcome of study

The frequency of vitamin D deficiency among patients with multiple sclerosis was 17 (20%) cases (Graph 2)

Stratified analysis:

Stratified analysis of frequency of vitamin D deficiency among patients with multiple sclerosis by age, gender, duration of disease, duration of sun exposure, marital status and employment status is summarized in tables 1-6.

Stratified analysis by age:

Of patients <45 years of age, 9 (20.9%) had vitamin D deficiency compared to 8 (19%) cases among patients of age >= 45 years (p=0.522).

Stratified analysis by gender:

Of male patients, 3 (8.3%) had vitamin D deficiency compared to 14 (28.6%) cases among female patients (p=0.019).

Stratified analysis by duration of disease: Of patients with duration of disease of <6 months of age, 8 (14.8%) had vitamin D deficiency compared to 9 (29%) cases among patients of with duration of disease \geq 6 months (p=0.099).

Stratified analysis by duration of exposure to the sun: Of patients with duration of sun exposure <40 minutes, 11 (25.6%) had vitamin D deficiency compared to 6 (14.3%) cases among patients of with duration exposure to the sun \geq 40 minutes (p=0.151).

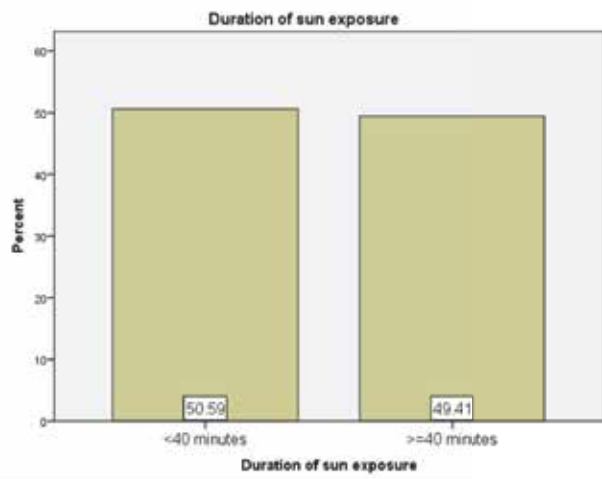
Stratified analysis by marital status:

Of married patients, 15 (21.4%) had vitamin D deficiency compared to 2 (13.3%) cases among unmarried patients (p=0.378).

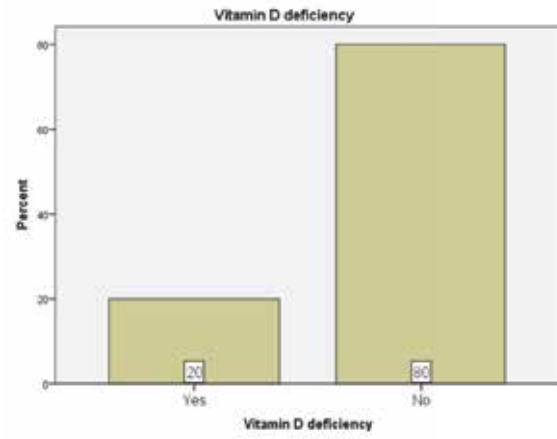
Stratified analysis by employment status:

Of employed patients, 14 (28.6%) had vitamin D deficiency compared to 3 (8.3%) cases among unemployed patients (p=0.019).

Graph 1:
DISTRIBUTION OF EXPOSURE TO SUN AMONG ENROLLED PARTICIPANTS (n=85)



Graph 2:
FREQUENCY OF VITAMIN D DEFICIENCY IN PATIENTS WITH MULTIPLE SCLEROSIS (n=143)



Mean vitamin D levels: 31.8 \pm 8 nmol/lit

Table 1: STRATIFIED ANALYSIS OF FREQUENCY OF VITAMIN D DEFICIENCY IN PATIENTS WITH MULTIPLE SCLEROSIS BY AGE

		Age		p-value
		<45 years (n=43)	\geq 45 years (n=42)	
Vitamin D deficiency	Yes	9 20.9%	8 19%	0.522
	No	34 79.1%	34 81%	

Table 2:
STRATIFIED ANALYSIS OF FREQUENCY OF VITAMIN D DEFICIENCY IN PATIENTS WITH MULTIPLE SCLEROSIS BY SEX

		SEX		p-value
		Male (n=36)	Female (n=49)	
Vitamin D deficiency	Yes	3 8.3%	14 28.6%	0.019
	No	33 91.7%	35 71.4%	

Table 3:
STRATIFIED ANALYSIS OF FREQUENCY OF VITAMIN D DEFICIENCY IN PATIENTS WITH MULTIPLE SCLEROSIS BY DURATION OF DISEASE

		Duration of disease		p-value
		<6 months (n=54)	>=6 months (n=31)	
Vitamin D deficiency	Yes	8 14.8%	9 29%	0.099
	No	46 85.2%	22 71%	

Table 4:
STRATIFIED ANALYSIS OF FREQUENCY OF VITAMIN D DEFICIENCY IN PATIENTS WITH MULTIPLE SCLEROSIS BY DURATION OF SUN EXPOSURE as

		Duration of sun exposure		p-value
		<40 minutes (n=43)	>=40 minutes (n=42)	
Vitamin D deficiency	Yes	11 25.6%	6 14.3%	0.151
	No	32 74.4%	36 85.7%	

Table 5:
STRATIFIED ANALYSIS OF FREQUENCY OF VITAMIN D DEFICIENCY IN PATIENTS WITH MULTIPLE SCLEROSIS BY MARITAL STATUS

		Marital status		p-value
		Married (n=70)	Unmarried (n=15)	
Vitamin D deficiency	Yes	15 21.4%	2 13.3%	0.378
	No	55 78.6%	13 86.7%	

Table 6:
STRATIFIED ANALYSIS OF FREQUENCY OF VITAMIN D DEFICIENCY IN PATIENTS WITH MULTIPLE SCLEROSIS BY EMPLOYMENT STATUS

		Employment status		p-value
		Employed (n=70)	Unemployed (n=36)	
Vitamin D deficiency	Yes	14 28.6%	3 8.3%	0.019
	No	35 71.4%	33 91.7%	

DISCUSSION

Hypovitaminosis D is currently one of the most studied environmental risk factors for multiple sclerosis (MS) and is potentially the most promising in terms of new clinical implications. The putative protective role of vitamin D in MS is based on a wide-ranging series of arguments. The first group of arguments exists outside of, or indeed before, the disease, including physiological, metabolic, experimental and immunological factors, in addition to which there are epidemiological data on the effects of latitude, past exposure to sunlight and serum vitamin D levels on the risk of MS in the general population. The second group of arguments stems from data on MS patients derived from biological and therapeutic studies.

Diseases that affect central nervous system myelin can be categorized as demyelinating (acquired, usually inflammatory) and dysmyelinating (abnormal formation of myelin, usually due to a genetic disease). The most common autoimmune inflammatory demyelinating disease of the central nervous system is multiple sclerosis (MS).

Several studies have shown that vitamin D levels are lower in MS patients than in controls.¹⁵⁻²⁰ In this study, the frequency of vitamin D deficiency among patients with multiple sclerosis was 17 (20%). A recent study²⁴ 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. 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. Additionally, low levels of

vitamin D appear to be associated with high levels of disability as measured by the Expanded Disability Status Scale (EDSS). The EDSS is a commonly used index of clinical disability in MS, with scores ranging from 0 (corresponding to a normal examination and function) to 10 (for death due to MS). Two recent studies conducted in 2014 support this association.^{21, 22} In the first study, 181 patients were prospectively followed, and EDSS scores were correlated with plasma vitamin D levels. Patients with vitamin D levels >50-nmol/L were 2.78 times more likely to have an EDSS <4 ($p=0.0011$).²⁵ The second study²⁶ was originally designed to evaluate the impact of early versus delayed interferon beta-1b treatment in patients with clinically isolated syndrome. Serum 25(OH)D concentrations were measured at baseline and at 6, 12, and 24 months. Patients were followed for 5 years with clinical assessments and MRI. A 50-nmol/L increase in average serum 25(OH)D levels within the first 12 months predicted a 57% lower rate of new active lesions ($p<0.001$), a 57% lower relapse rate ($p=0.03$), and a 25% lower yearly increase in T2 lesion volume ($p<0.001$) from months 12 to 60. Levels ≥ 50 nmol/L at following periods of up to 12 months predicted lower EDSS scores ($p=0.004$) during the subsequent 4 years.²⁶

Observational studies correlating vitamin D levels to MS severity cannot prove that increased sun exposure alleviates the symptoms of MS, especially given that severely disabled patients with MS receive less sun exposure, which can cause vitamin D deficiency. Even MS patients who are fully mobile are theoretically more susceptible to vitamin D deficiency because they avoid sun exposure, worsening their symptoms.²³

CONCLUSION

It is concluded from this study that the frequency of vitamin D deficiency among patients with multiple sclerosis was 20%. The frequency of vitamin D deficiency among male was 8.3% compared to female patients. Of employed patients, 14 (28.6%) had vitamin D deficiency compared to 3 (8.3%) cases among unemployed patients.

y ophthalmoplegia and areflexia while 4 patients (28%) presented with overlap syndrome having generalized weakness. In comparison to other study which showed that half of the patients with MFS eventually experienced profound weakness (overlap syndrome)^[15].

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Author's contribution:

Dr. Samar Iltaf Pechuho: data collection, data analysis, manuscript writing, manuscript review

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