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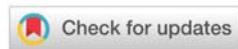
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Research Article

Neurological manifestations of Vitamin D deficiency among medical students

Abstract

Background and Objective: Vitamin D status and neurological manifestation of Vitamin D deficiency in medical students is seldom investigated. Design and settings: Cross sectional Survey conducted at King Khalid University Hospital Riyadh Saudi Arabia.

Methods: 650 medical students filled questionnaire. Serum 25-hydroxyl vitamin D (25(OH) D) levels were measured for Vitamin D status, PTH and Calcium were also estimated. Vitamin D deficiency is defined as 25(OH) D < 20 ng/ml (50 nmol/liter), insufficiency ;21–29 ng/ml (52. 5– 72. 5 nmol/liter). 25(OH) D levels was assayed in serum by electro-chemi-luminescence immunoassay) ECLIA (by Cobas machine).

Results: 650 students; age 21.43±1.7yrs, mean 25 (OH) D; 43.3 ± 31.7 nmol/liter which is subnormal. 25 (OH) D Deficiency in 34(5.23%), Higher prevalence of neurological symptoms found with lowest quartile of 25 (OH) D than highest quartile. Low levels of 25 (OH) D were associated with body pains, cognitive decline, muscle weakness and visual symptoms. Inverse association was found between 25 (OH) D and Multiple sclerosis. B= - 0.072, S.E.=0.33, p=0.029, exp (B) =0.931.

Conclusion: Vitamin D deficiency is common. Neurological symptoms are associated with lower levels of 25 (OH) D. Prevalence of MS was high. Periodic assessment and supplementation of Vitamin D may reduce future disability.

Introduction

Interest in Vitamin D is surging worldwide due to its immense emerging, proven and possible benefits [1,2], in a wide range of diseases like CVD [3,4] diabetes mellitus (DM) [5,6].

Cancer [7–10], multiple sclerosis [11] and autoimmune diseases [12], part from its traditional role in the bone health and reduction of bone fractures [13,14].

Recent researches have in sighted revolutionary knowledge on diverse non-classical actions of recent researches have in sighted revolutionary knowledge on diverse non-classical actions of vitamin D which were unknown till recently. Vitamin D is emerging as neuroprotectant [15,16] and protects against Multiple Sclerosis, Epilepsy, Parkinson's disease, Autism and Schizophrenia [17]. It has great implication in function of nervous system. Vitamin D receptors are mapped in the

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Epilepsy, Parkinson's disease, Autism and Schizophrenia [17]. It has great implication in function of nervous system. Vitamin D receptors are mapped in the brain [16]. Current studies have shown that vitamin D is neurotrophic and repairs nerve damage and promote its growth [17–19]. It combats neurotoxicity and protects against cognitive decline [20,21]. A recent study in 2014 have shown that vitamin D is implicated in metabolic and contractile functi

Methods

Present study was a cross sectional study conducted on randomly selected 650 medical students from all the study years, both males and females, in King Saud University, Riyadh Saudi Arabia. From January to December 2018. This research study was reviewed by the Institutional Review board (IRB) ethical committee of KKHU. The research followed the tenets of the Declaration of Helsinki. All subjects signed written consent documents after being informed of the purpose of the study including its risks and benefits and that information will be confidential.

Sample size

The presumed prevalence of Vitamin D deficiency was

taken as 55% the sample size and it came to be 380 the degree of precision 0.05 and the $Z_{\alpha} = 1.96$ to compensate on participate and uncompleted files. We took the sample size 650 students. Participants were asked to fill a questionnaire for the information regarding demographics, comorbidities, detailed sun exposure information how often how long how many days a week, which part of the day. Dietary habits and nutritional intake, detailed information about any atypical neurological symptoms, muscle weakness thinning of muscle, leg pain spasm of the muscle, stiffness, numbness, visual disturbances were noted down.

25-OH Vitamin D levels was assayed in serum by electro-chemi-luminescence immunoassay (ECLIA) By Cobas machine in central lab of King Khalid University Hospital. Vitamin D deficiency is defined as 25(OH)D level of <20 ng per milliliter 50 nmol per liter which we used in our study [22–26].

Lab investigations included serum calcium, creatinine, albumin, alkaline phosphatase, PTH, 25 (OH) D levels were investigated and kept in record. Standard definitions of vitamin D deficiency, insufficiency and normal levels were used for evaluation. Lab test were performed in central lab of King Khalid University Hospital King Saud University Riyadh Saudi Arabia.

25 (OH) D and PTH were estimated by COBAS e 602, Roche Germany. The range of PTH is 1.65 to 6.9 pmol/L in our Lab. And that of 25 (OH) D is from 50–250 nmol/L. The diagnosis of multiple sclerosis was made by clinical diagnosis supported by MRI findings.

Statistical Analysis: data is represented as mean+ SD. Pearson's correlation and binary logistic regression analysis was performed to determine the association of Vitamin D with various neurological symptoms. A p value of <0.05 was considered significant. SPSS for windows 17 (Chicago, Illinois USA) was used for statistical analysis.

Results

Total 650 students participated, 265(40.7%) males with mean age 21.43±1.7 yrs, BMI was 23.66±5.4 kg/m². Total 9(1.5%) were diabetic, 4 (0.6%) were hypertensive. PTH was 4.02±1.6 pmol/L, serum creatinine was 70.4±16.9mmols/l, calcium was 2.3±2.2 mmols/l, Alkaline phosphatase was 95.5±25.9, albumin level was 41.9±5.1mmols/l Mean 25(OH) D level was 43.3±31.7 nmol/L, Vitamin D deficiency 25(OH)D below 20 ng/ml (50 nmol/liter) ⁽²⁶⁾ was present in 34(5.23%), Vitamin D Insufficiency vitamin D insufficiency as a 25(OH) D of 21–29 ng/ml (52. 5–72. 5 nmol/liter) ⁽²⁶⁾ was present in 422(64.9%)students.

Table 1 shows the atypical neurological and muscular symptoms in medical students pertaining to the highest and lowest quartile of 25(OH) D. A protective role of Vitamin D is pretty obvious. And medical students with higher levels of 25(OH) D were having less prevalence of neurological symptoms than medical students with lowest quartile of Vitamin D (Table 1).

The most common neurological and muscular manifestation was intense fatigue followed by Myalgia and Arthralgia. Other

Table 1: Showing the baseline characteristics of the study population pertaining to vitamin D levels.

Variables	Lowest quartile of vitamin. D	Highest quartile of vitamin. D
	<25 N=133	>60 N=136
Age (yrs)	21.2±1.8	21.3±1.7
Weight	67.2±19	64.6±19.05
BMI	22.9±7.2	23.96±5.9
HTN	0.75%	0%
DM	1.5%	0%
VIT. D Level	15.8±5.8	83.8±33.8
Numbness	60 (32.3%)	4(2.9%)
weakness	80(60.1%)	6(4.4%)
Visual disturb.	(11.2%)	0%
Generalized Pain	78(58.6%)	16(11.7%)
Lower body pain	56(42.1%)	21(15.4%)
Diagnosis of Multiple Sclerosis	7(5.2%)	1(0.73%)

presentations included numbness of leg and face, progressive muscular weakness difficulty in getting up from squatting position, stiffness of all body muscles. Inconvenience in swallowing solid food, pain on full contraction and spasm of leg muscles. In coordination, cognitive decline difficulty in memorizing lessons, difficulty in concentration, dim vision, unexplained pain in the eye, problem in peripheral vision, dizziness and depression. 7(5.2%) of the 133 students with low 25(OH) D, were diagnosed with Multiple Sclerosis.

On of cardiac and skeletal muscle [22] and its deficiency is associated with reduced muscle mass, impaired physical performance and muscle pain [23,24]. Vitamin D deficiency is associated with incidence and progression of Multiple sclerosis [25]. Medical students are a special subset of population on which there is future responsibility of best health care provision to the community. Thus their wellbeing is of great importance. In view of prevalent Vitamin D deficiency in the region frequent Vitamin D screening and surveillance for deficiency associated neurological manifestations of Vitamin D is crucial in medical students in order to postpone and prevent neurological and muscular deficits.

Table 2 shows the bi-variate correlation of neurological symptoms with 25(OH) D level, a significant and negative correlation was found between numbness $r=-0.230$, $p=0.012$; Diagnosis of Multiple Sclerosis $r=-0.123$, $p=0.049$; PTH, $r=-0.204$, $p=0.002$; Peripheral vision defect $r=-0.265$, $p=0.006$ an inverse correlation was found between PTH levels and 25(OH)D further. A significantly positive correlation was found between 25(OH) D, and albumin $r=0.138$ $p=0.030$ (Table 2).

Table 3 shows the exact 25(OH) D level in medical students pertaining to the presence of a neurological symptom. Significantly lower levels of 25(OH) D were seen in patients with neurological symptoms. Medical students with muscular weakness had 25(OH) D level 26.7±23.4 vs 47.42±29.7 in medical students without muscular weakness.

Table 2: Correlation of vitamin D levels with salient variables in medical students.

Variables	r-value	P-value
Weakness and fatigue	-0.356	0.000*
Numbness	-0.385	0.000*
Peripheral vision problem	-0.333	0.001*
Multiple sclerosis	-0.378	0.000*
Leg pain	-0.359	0.000*
PTH	0.204	0.002*
Albumin	0.138	0.030*
Gender	0.018	0.77
HTN	0.02	0.745
BMI	0.212	0.220
Calcium Level	0.142	0.028*
ALT	0.116	0.069

Table 3: Showing Vitamin D level in the presence or absence of a symptom.

Variables	Vitamin D levels in medical students pertaining to Neurological Symptoms.
Multiple Sclerosis	
Yes	21.57± 28.4
No	46.66± 30.76
Numbness	
Yes	28.9±27.3
No	41.29±23.3
Weakness	
Yes	26.7± 23.4
NO	47.42±29.7
Peripheral vision problem	
Yes	21.2±17.7
No	46.5± 28.5
Circular shapes	
Yes	27.6 ±28.8
No	44.6±28.3
Leg pain	
Yes	35.6±22.8
No	48±31.8

Medical students who were previously diagnosed with multiple sclerosis had 25(OH) D levels 21.5±28.4 Vs. 46.66±30.76 in students without multiple sclerosis. Medical students who were having visual disturbances or cognitive decline had suboptimal 25(OH) D levels. Logistic regression analysis revealed that 25(OH) D deficiency contributed greater odds for having the disease. A significant negative association was found between 25(OH) D and MS. In binary logistic regression analysis Taking MS as dependent variable 25(OH) D level had a significant negative effect with B=-0.072; SE=0.033; Significance 0.029; Exp (B)=0.931.

Discussion

Vitamin D deficiency is often under diagnosed and undertreated. In spite that vitamin D is an easily available safe, and affordable, inexpensive product. And vitamin D supplementation is an attractive promising intervention to alleviate several disease burdens, and to achieve better

health outcome. Deficiency in vitamin D interferes with the absorption of calcium from the gastro intestinal tract, resulting in weakness and pain in the muscles and bones [27]. A recent study on Vitamin D deficiency conducted in 2009 on Saudi Arabs showed increased prevalence of Vitamin D deficiency among Saudi Arabs (both males and females) [28].

The Third National Health and Nutrition Examination Survey (2010) found that low vitamin D status is a widespread problem in the US and that serum vitamin D concentrations are related to depression in young adult in the US population [29]. Depression is one of the leading causes of disability among young adults in the US [30]. Vitamin D deficiencies can initially present as musculoskeletal pain, the populations that are most at risk are those that have decreased sun exposure.

The present study shows that 25(OH) D is a significant predictor or a risk factor for several neurological symptoms in medical students. Higher levels of 25(OH) D seem to be protective. Most but not all the neurological symptoms have a significant association with 25(OH) D status. The most common complaint was body aches, like leg pain, backache or generalized muscle pain and extreme fatigue. There is now clear evidence supporting a significant role for vitamin D in the biology and function of skeletal and cardiac muscle, including intracellular calcium handling, differentiation and contractile protein composition [31].

A better characterization of the role of Vitamin D Receptors in the context of inflammation- mediated muscle wasting and weakness may also potentially translate into significant clinical applications by using vitamin D supplementation as a potential strategy for reversing muscle wasting [32].

The prevalence of MS among the medical students was astonishing high being 1.2% of the total study population. The 25(OH) D levels in medical students with MS were lower than those without Multiple Sclerosis. There is evidence in the literature that nurses and doctors are at increased risk of developing Multiple Sclerosis. Geoffry and Richard in their article have reported a high prevalence of Multiple Sclerosis in KEY West Florida USA [33]. The precise pathogenesis remains obscure.

Vitamin D deficiency seems to be an environmental risk factor for MS [34-37].

Recent studies have shown that Vitamin D deficiency is a risk factor for MS ¹¹ Vitamin D deficiency is associated with onset progression and severity of Multiple Sclerosis.¹⁴ Further vitamin D is a prognostic factor for Multiple Sclerosis. ¹⁵

The present study supports a protective effect of vitamin D intake on risk of developing MS.

Limitations

Although sample size was appropriate yet it is confined to a particular group of people the medical students and cannot be generalized to common public or population as a whole as it was not population-based. Therefore, the findings might

not reflect the actual prevalence of vitamin D deficiency in the general population as a whole, but it is of significance for a group of people.

Although the 25(OH) D was estimated many times in a day but it was evaluated only once during the season. It would have been more useful if patients were evaluated at different season times of the year to determine the effects elicited by seasonal changes on vitamin D levels.

Conclusion

Vitamin D deficiency is common among medical students. Neurological symptoms are associated with lower levels of 25(OH) D. Prevalence of MS was high among medical students. Present study supports a protective effect of vitamin D intake on risk of developing MS. Periodic assessment and supplementation of Vitamin D may reduce future disability in this special group of population.

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