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Migraine and vitamin D levels and the severity of headache in children

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Abstract

Introduction: A migraine is a condition where there is a headache that can cause severe throbbing paining or a pulsing sensation of pain on unilateral side of the head. It is a primary episodic headache disorder which is due to neurological, gastrointestinal, central nervous system and autonomic changes. The prime aim of the study was to determine the levels of vitamin D associated with the severity of headache in patients with migraine.

Methods: A total number of 108 children diagnosed with migraine were evaluated. Levels of vitamin D and 25-hydroxy vitamin D3 were measured by using ELISA method (enzyme-linked immunoassay). Serum vitamin D levels were defined as 30ng/ml. The severity of the headache was determined according to the MIDAS (Migraine Disability Assessment Score).,

Results: The mean serum 25-hydroxy vitamin D3 levels of migraine patients were 18.6±4.9 ng/ml. As the level of vitamin D decreased, so the severity of the headache increased, with a higher Migraine Disability Assessment score grade (p 0.05) which shows closer inverse proportional association of vitamin-D levels with migraine.

Conclusion: The high levels of headache are associated with reduced serum vitamin D levels in children with migraine.

***Keywords*:** migraine; vitamin D; headache; children.

Introduction

Headache is one of the common symptoms treated by a physician in a routine outpatient clinic and is seen in a wide variety of neurological disorders. World Health Organization categorizes headache disorders into the top 10 disabling conditions among two gender and into the five most disabling condition amongst women [1]. Migraine is defined as a common hereditary chronic neurovascular disorder, resulting from dysfunction of the autonomic nervous system. Few patients, it is associated with nausea or vomiting along with phonophobia and photophobia [2]. The incidence is 18% among women and 6% in men and maximum incidence is observed in ages between 25 and 55 [3].

The characteristic clinical features are (i) attacks lasts more than 4 hrs and less than 3 days without medication, (ii) the headache is felt unilaterally and throbbing, (iii) patients experiences severe discomfort from light and sounds. Attacks often accompanied by nausea or vomiting, (iv) pain may be moderate to severe [2-6]. Deficiency of vitamin D is a one among the global public health problems. The incidence of vitamin D deficiency is estimated to be 30-80% in children and adults worldwide [2, 3, 7]., Vitamin D deficiency may lead to many health problems including cardiovascular diseases, autoimmune diseases, infectious diseases, metabolic diseases, osteoarthritis, and inflammatory

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diseases, mental and different skin disorders [8-11]. In addition, deficiency of vitamin D has also been associated in pathogenesis of a number of neurological diseases especially like migraine [12, 13].

Material and methods

In this prospective cross-sectional study, 108 children who were diagnosed with migraine between the age group of 3 - 15 years were included in the study as per inclusion criteria from a tertiary referral paediatric neurology centre for a period of one year i.e., December 2018 and December 2019. The demographic data, symptoms and findings at the time of diagnosis, frequency and duration of the headache, and the diagnostic methods of cranial MRI and electroencephalography (EEG) were recorded. The diagnosis of migraine was done based on diagnostic criteria of the International Classification of Headache Disorders-III, (ICHD-III) published by the International Headache Society (IHS) in 2013 [14]., The severity of the headache was determined according to the MIDAS scale as; 0-5: Grade I, 6-10: Grade II, 11-20: Grade III, and ≥21: Grade IV [15]. The participants were categorised in to two groups. Group 1- with aura and Group 2 as without aura. , Subjects with any previous neurological diseases (mental retardation, seizure, epilepsy, etc)., any systemic or autoimmune diseases, any drug use (steroids, immunosuppressant's, vitamin D supplements, etc), chronic infection, or hospitalization within the previous 4 weeks were excluded as per the exclusion criteria of the study. Serum blood samples of all the study participants were collected on overnight fasting. The samples were processed immediately by centrifugation at 4000 rpm at room temperature. Clinical laboratory tests including complete blood count, serum total calcium, phosphorus, alkaline phosphates, serum albumin, vitamin B_{12} as well as liver, thyroid function tests, and kidney function tests and vitamin D [25-hydroxy vitamin D3, 25(OH)D3s were obtained and measured by specific routine methods. Studies groups were assigned according to serum vitamin D levels as deficiency (30ng/ml). The study was approved by the Ethics Committee and informed consent was obtained from all patients.

Statistical analysis

The statistical calculation was done by using the SPSS software version-24. In this study we observed that, SGOT and SGPT were found highly significant in sickle cell disease cases as compared to the controls and the Pearson's coefficient correlation shows us positive correlation with each other. The $P < 0.000$ was considered to be statistically highly significant. One-way analysis of variance (ANOVA) was used for the comparison of the parameters with normal distributions. Chi-square test was used for comparison of categorical variables.

Results

A total of 108 patients were recruited consisting of 70 female patients and 38 male patients with an age of 11.72±3.21 years (Range, 7-17 years). A family background history of migraine was determined in 42 (38.9%) patients include both male and females and there was a triggering factor for the pain in 86 (79.6%) patients. According to the family history and neurological examination, cranial imaging was applied to 78 (63%) patients both male and females (CT to 11 patients, MRI to 67 patients) and the results of those were determined as a normal without ant sysmpotes. Electroencephalogram was determined as normal in all patients. The frequency of headache was reported as every day in 2-6 times per week in 15 times,,once a week in 33, and 1-3 times in a month in 25 patients, respectively. According to the MIDAS grade evaluations, 31 (28.7%) patients were grouped as MIDAS grade 1, 41 (37.9%) were MIDAS grade 2, 21 (19.5%) were MIDAS grade 3, and 15 (13.9%) were MIDAS grade 4, respectively (Table 1).

Table 1: Comparison of vitamin D status among MIDAS grades.

	MIDAS Grade 1 (n=31) n (%)	*MIDAS Grade 2 (n=41) n (%)*	*MIDAS Grade 3 (n=21) n (%)*	*MIDAS Grade 4 (n=15) n (%)*	*p value*
Vitamin D deficiency (<12 ng/ml)	11(35.5)	14(34.1)	20(95.2)	15 (100)	<0.0001
Vitamin D insufficiency (12-30 ng/ml)	13(41.9)	24(58.5)	1(4.8)	0	<0.0001
Vitamin D sufficiency (>30 ng/ml)	7(22.6)	3(7.3)	0	0	<0.0001

The mean (±SD) level of vitamin D was 13.37±8.43 ng/ml (range, 1.34 ng/ml-35 ng/ml). The mean level of vitamin D in males was significantly higher than that of females (15.6±8.52 ng/ml vs. 12.1±8.18 ng/ ml) (p=0.042). According to vitamin D status, sixty (55.6%) patients were vitamin D deficient, 38 (35.2%) were insufficient, and 10 (9.3%) were sufficient. There was a significant difference among patients with MIDAS Grade 1 and Grade 2 and those with MIDAS Grade 3 and Grade 4 in terms of vitamin D levels ($p< 0.001$). Also, 95.2% of the subjects with MIDAS Grade 3 and in all subjects with MIDAS Grade 4 were vitamin D deficient (Table 2). Migraine with aura was determined in 19 patients and migraine without aura in 89 patients. There was

no difference between patients with aura and patients without aura in terms of the mean vitamin D levels (p=0.121) (Table 2). ,

Table 2: Comparison of vitamin D levels among study groups.

	Serum vitamin D level Mean ± SD	*p value*
MIDAS Grade 1	18.2±6.4	0.0001
MIDAS Grade 2	16.0±5.7	0.0001
MIDAS Grade 3	7.1±4.5	0.0001
MIDAS Grade 4	4.9±1.4	0.0001
Migraine with aura	16.0±11.0	0.121
Migraine without aura	12.8±7.7	0.121

The rate of vitamin D deficiency in subjects with aura was 47.4% and 57.3% in subjects without aura (Table 3). There was no correlation between the scores of MIDAS and serum levels of calcium, phosphorus, and alkaline phosphates (p=0.574, p=0.148, p=0.893, respectively).

Table 3: Comparison of vitamin D status in patients with or without aura.

	Migraine with aura n (%)	*Migraine without aura n (%)*	*p value*
Vitamin D deficiency (<12 ng/ml)	9(47.4)	51(57.3)	
Vitamin D insufficiency (12-30 ng/ml	6(31.6)	32(36)	0.48
Vitamin D sufficiency (>30 ng/ml)	4(21.1)	6(6.7)	

Discussion

In the present study, we found a significant negative relation between the serum levels of vitamin D and severity of migraine. The role of vitamin D in bone mineralization diseases is well defined; also low vitamin D levels may be related to non-specific pain and non-inflammatory skeletal myopathy [16-19]. Many of the studies were reported that low levels vitamin D levels may be associated with headache [20-22]. In a cross-sectional study of 12.615 subjects, Kjærgaard et al. demonstrated a significantly low level of serum 25(OH) D3 in non-migraine headaches patients [23]. In another Autor cross-sectional study, lower levels of serum 25(OH) D3 were measured in patients with musculoskeletal pain, fatigue, vomiting, and headache [24, 25]. Parkas, Rama et al. found that chronic tension headaches improved with vitamin D and calcium supplements in patients with vitamin D deficiency and osteomalacia and rickets [20]. Some several studies reported that vitamin D deficiency or insufficiency in migraine subjects, while many other studies showed normal levels of vitamin D [8, 26]. In a study, authors found a higher serum vitamin D level (50-100 ng/mL) was associated with a low odds ratio of migraine headaches than those with low serum vitamin D levels and some parameters of headache such as aura, severity, and duration [28]. In some few studies, the authors found an increase in migraine attacks in the autumn and winter months and a decrease in vitamin D levels in the same period time. The incidence of both migraine and vitamin D deficiency has been reported to increase at higher altitudes far from the equator [29-31]. The prevalence of childhood migraine in Turkey, height above sea level increases the frequency is higher than two times [32, 33]. The patients in the current study lived in a region of the lowest altitude in Turkey. Parkas et al. showed that there is a relationship between altitude and headache [34]. A similar study found an association between vit- D deficiency and headache [26]. In a study by Stewart et al, the relationship between severity and characteristics of headache and the MIDAS grade was examined in patients [15]. The MIDAS grades of patients aged<25 years were found to be significantly higher and the MIDAS scale was reported to be reliable. In the current study, it was determined that as the vitamin D level decreased, so there was a significant increase in the severity of the headache. Bıçakçı et al studied university students with migraine and determined severity of MIDAS grade 1 in 49%, MIDAS grade 2 in 19.3%, MIDAS grade 3 in 29.1% and MIDAS grade 4 in 9.7%. In the same study, the rate of migraine without aura was determined as 6%. The low rates were attributed to denial of headaches by university students [35]. In the current study, these rates were higher. On the contrary, when MIDAS grades were evaluated, there was no statistically significant difference between those with migraine with aura and those with migraine without aura.

Limitations

Majority of the patients in the study were from rural background that generally has an adequate exposure of sunlight. However, the vitamin D deficiency was observed in more than 50% of patients. The sample size of the study group was small as compared to the incidence of the migraine in the general population. This was due to the availability of limited resources as none of the patients of control or case groups were charged for the vitamin D levels. The study was an open study i.e. the investigator was not blinded. Thus we want to stress that vitamin D has been shown to exert multiple beneficial health effects beyond its proposed role in the prevention and treatment of migraine. Hence it could

be hypothesized that a widely introduced vitamin D treatment might be beneficial for many diseases beyond migraine. This should encourage a goal in public health care strategies to fight against vitamin D deficiency.

Conclusion

In the present study we showed that the severity of headache is associated with reduced serum vitamin D levels in children with migraine. The strongest connection reported to date is between serum vitamin D levels and migraine headaches; but our results need to be confirmed by large-scale population based studies. Fortunately, both migraine and vitamin D deficiency are controllable and treatable parameters, hence we suggest that effective healthcare programs should be organized countrywide for the monitoring and management of the serum levels of vitamin D and migraine.

Conflicts of interest

Authors declare no conflicts of interest.

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