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Comparison of vitamin D levels in children with motor development delay and asthma

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Abstract

Background & Objective: Vitamin D plays an important role in musculoskeletal health and is also potentially involved in the pathogenesis of chronic diseases. In this study, we aimed to determine the vitamin D status of children aged 2-6 years with motor developmental delay and compare them with asthmatic children. *Method:* Serum 25-Hydroxy cholecalciferol 25 (OH) D vitamin levels of children were measured between June 2020 and September 2020. Vitamin D deficiency was defined as a serum 25 (OH) vitamin D level less than 20 ng/mL and insufficiency as levels between 20 and 30 ng/mL. The deficiency and insufficiency rates and mean 25 (OH) vitamin D levels between the two groups were compared. *Results:* The study population included 818 children (192 children with asthma, 368 children with motor development delay and 258 healthy controls). There was no statistically significant difference between groups in terms of age and gender (p=0.130 and p= 0.082, respectively). Vitamin D deficiency and insufficiency were detected in one thirds of children with motor developmental delay (33.7%; 35.6% respectively). The rate of vitamin D deficiency of children with motor development delay between 24 - 47 months of age was found to be significantly higher than control and asthma group (p=0.001 and p=0.034).
Conclusions: Vitamin D deficiency and insufficiency were common between 2-6 years of age children with motor development delay. Acceleration of2 motor development between 24 - 47 months of age may be a cause of high incidence of D vitamin deficiency. Clinicians should check and optimize vitamin D status in children with motor development delay especially between 24 - 47 months of age.

Keywords: Vitamin D deficiency, vitamin D insufficiency, motor development delay, 2-6 years of age

INTRODUCTION

It is critical to identify the factors that play a role in delays in reaching developmental milestones in children. Vitamin D has long been recognised as a critical molecule due to its important role in musculoskeletal health. Since children have higher calcium demands than adults; they require a positive calcium balance to assure adequate calcium for the mineralization of growing bones.[1] Therefore, it is important to ensure adequate vitamin D status in order to achieve developmental milestones. It has been also shown that physiological function of 25 (OH) vitamin D with receptors found in the brain, skin, small intestine, T and B lymphocytes help in preventing type 1 diabetes, cardiovascular diseases, and respiratory infections.[2,3] Recent studies revealed that vitamin D deficiency has a number of biological effects that are potentially instrumental in the pathogenesis of asthma. A randomized controlled study revealed positive effects of vitamin D supplementation in pediatric asthma.[4] In this research we aimed to find out the vitamin D status in 2-6 years of age children in Mardin, Turkey due to the fact that it is a region where motor development delays are common. We also compared the status of vitamin D levels between children with asthma as one of the most common chronic diseases in childhood.

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METHODS

Study population and analysis

This was a cross-sectional study conducted in the largest training hospital in Mardin, Turkey. The study was approved by Diyarbakır Gazi Yaşargil Training and Research Hospital ethics committee (07.05.2021-760). The study population consisted of 818 children between 2-6 years age group; 368 children referred to the child neurology department because of motor developmental delay, 192 children with asthma without motor developmental delay and 258 healthy controls living in Mardin. Children with a history of preterm delivery, asphyxia, neuromuscular disease, epilepsy, metabolic diseases, genetic disease, and malnutrition were excluded. Also, children receiving vitamin D supplements and/or medications other than anti-asthmatics were not included in the study. Serum 25 (OH) vitamin D levels of children were measured by the ELISA method (using Bioactiva Diagnostica kits) in the same period (between June 2020-September 2020) to avoid seasonal variations. Vitamin D deficiency was defined as a serum 25 (OH) vitamin D level less than 20 ng/mL and insufficiency as levels between 20 and 30 ng/mL.[5] Children were divided into two groups according to age groups (24 - 47 months and 48 - 72 months of age). Vitamin D status was compared between groups and subgroups.

Motor development was assessed by two pediatric neurologists and a developmental specialist with the Denver Developmental Screening Test (DDST), which is a simple, user-friendly test and is widely used in our country for motor development assessment. In the gross motor area of the test, it is questioned whether the skills like head control, sitting, rolling, standing, walking, stair climbing, running, and jumping, which should be acquired in general, are acquired in accordance with the child's own age development profile. The test results in a "delay" if the child completely fails or refuses the items to the left of the age line. If there are two or more delays in the entire test, it is "abnormal" with or without a warning. Patients with DDST results which are interpreted as normal, suspect, and untestable were excluded. Conditions expressing only gross motor delay was defined as 'motor developmental delay.'

Statistical analysis

Descriptive statistics are given as mean ± standard deviation and median with minimum-maximum values for continuous variables depending on test distribution. Continuous variables are expressed as either the mean ± standard deviation (SD) or the median (interquartile range) and categorical variables are expressed as either frequency or percentage. Normal distribution of numerical variables was analyzed with the Shapiro-Wilk tests. Continuous variables were compared with One-way Anova test, and categorical variables were compared using Pearson's chi-square test. Conover-Inman test were performed for the binary comparisons among the groups.

For statistical analysis, Jamovi project (2020, Jamovi (Version 1.6.16.0) [Computer Software] Retrieved from https://www.jamovi.org) and JASP (Version 0.14.1.0, Retrieved from https://jasp-stats.org) were used. The significance level (p-value) was set at 0.05 for all statistical analyses.

RESULTS

A total of 818 participants, 343 (41.9%) female and 475 (58.1%) males were included in the study. There were three groups as follows: 192 children with asthma, 368 children with motor development delay, and 258 healthy controls. There was no statistically significant difference between the patient groups and the control group in terms of age and gender (p=0.130 and p= 0.082, respectively). It was determined that 32.3% (n=265) of subjects had vitamin D deficiency and 38.1 % (n=312) had vitamin D insufficiency. Mean of 25 (OH) vitamin D levels in both children with asthma and motor development delay were lower than control group (p<0.001). Vitamin D deficiency was most common in children with asthma (44.3%), followed by children with motor development delay (33.7%) and a statistically significant difference was found between groups (p<0.001). Demographic findings and vitamin D status in all groups are summarized on Table 1.

Significant differences between groups were represented as; a: I vs II, b: I vs III, c: II vs III. When the mean 25 (OH) vitamin D levels in the 24- 47 months of age group were compared, the mean values of children with motor development delay were found to be significantly lower than those in the control group (p=0.001). Although not significant, the mean 25 (OH) vitamin D levels of asthmatic children were also lower than in the control group (p=0.09). When children aged 48- 72 months were compared, the mean 25 (OH) vitamin D levels of asthmatic children were significantly lower than those of patients with motor development delay and the control group (p<0.001) (Table 2).

Table 1: Demographic findings and vitamin D status according to groups

	Children with asthma (N:192)[I]		Children with motor development delay (N:368)[II]		Control group (N:258)[III]		p
Age ($\overline{X}$ ±SD)	47.4±14.9		50.1±14.7		49.2±14.7		0.130
24- 47 months	104	(54.2%)	158	(42.9%)	120	(46.5%)	
48- 72 months	88	(45.8%)	210	(57.1%)	138	(53.5%)	
Female	69	(35.9%)	168	(45.7%)	106	(41.1%)	0.082
Male	123	(64.1%)	200	(54.3%)	152	(58.9%)	
Normal	33	(17.1%)	113	(30.7%)	95	(36.8%)	
Deficiency	85	(44.3%)	124	(33.7%)	56	(21.7%)	0.001[a,b,c]
Insufficiency	74	(38.5%)	131	(35.6%)	107	(41.5%)	

For the next evaluation, the percentage of children with vitamin deficiency and insufficiency were compared according to subgroups. Vitamin D deficiency was found in 33.8% (n=129) of children aged 24-47 months and 31.2% (n=136) of children aged 48-72 months. Vitamin D deficiency was found in approximately half (48.1%) of 24–47-month-old children with motor developmental delay and 32.7% of children with asthma. Among children aged 4-6 years, the frequency of insufficiency was higher in those with motor developmental delay (45.2%). There were statistically significant differences between groups in terms of D vitamin status (Table 3).

DISCUSSION

As a preventable disorder, vitamin D deficiency is widely observed in Turkey. Akman *et al*. demonstrated that vitamin D deficiency and insufficiency were 8% and 25.5%, respectively, in children between the ages of 1 and 16 years.[6] A recent study revealed that the prevalence of vitamin D deficiency (<12 ng/mL) was lowest in children at 1-3 years of age (5%).[7] Also, a study focusing on elementary school children found that vitamin D deficiency was observed in 5.62 % and insufficiency in 18.6 % of children.[8] Our study determined the frequency of vitamin D deficiency and insufficiency in a large group of children between **2**-6 years of age in Mardin. However, Mardin is located in a sun-drenched area and is under the influence of the desert climate coming from the south in summer. Since its scorching climate, it is not possible to go out at certain hours, so it is thought that the variability

Table 2: Mean of 25 (OH) vitamin D levels of children according to age groups

24- 47 months	Level of 25 (OH) vitamin D (±SD)	p	
Motor development delay [I] (N:158)	21.34±10.90		
Asthma [II] (N:104)	24.40±10.34	0.12[a]	0.001[b]
Control [III] (N:120)	27.97±10.04	0.09[c]	
48-72 months			
Motor development delay [I] (N:210)	23.93±7.92	0.001	
Asthma [II] (N:88)	19.92±9.88		0.001
Control [III] (N:138)	28.37±10.73	0.001	

Significant differences between groups were represented as; a: I vs II, b: I vs III, c: II vs III

Table 3: D vitamin status of children according to age groups

	D Vitamin status		p	
24- 47 months	**Deficiency**	**Insufficiency**		
Motor development delay [I] (N:158)	76 (48.1%)	36 (22.8%)	0.034[a]	0.017[c]
Asthma [II] (N:104)	34 (32.7%)	46 (44.2%)	0.001[b]	
Control[III] (N:120)	19 (15.8%)	53 (44.2%)		
48- 72 months				
Motor development delay [I] (N:210)	48 (22.9%)	95 (45.2%)	0.021[a]	0.045[c]
Asthma [II] (N:88)	51 (58%)	28 (31.8%)	0.69[b]	
Control [III] (N:138)	37 (26.9%)	54 (39.1%)		

Significant differences between groups were represented as; a: I vs II, b: I vs III, c: II vs III

between the patient groups' daylight utilisation hours does not show a significant difference. It is the twenty-sixth most populous city in Turkey with an urban population of 60% and a rural population of 43%. The importance of 25 (OH) vitamin D in childhood may have been underestimated in Mardin due to its economy based on agriculture, animal husbandry and trade, low income and one of the most diversified populations in Turkey.

In most of the studies in the literature, the effect of 25 (OH) vitamin D on cognitive and motor development has been described with conflicting results. A study from the UK involving 7,065 mother-child pairs demonstrated that babies with high maternal 25 (OH) vitamin D levels had higher gross and fine motor scores.[9] Similarly, a Spanish study with 1,820 pairs revealed higher circulating concentration of maternal 25 (OH) vitamin D levels in pregnancy was associated with improved mental and psychomotor development in infants.[10] However, two large studies from USA and Greece found no association between maternal or cord blood 25 (OH) vitamin D with cognitive development.[11,12] A randomized controlled trial revealed that neurodevelopment by the Ages and Stages Questionnaire-3 scores at 12 to 36 months of age, vitamin D deficiency was not associated with physical growth at baseline and at follow-up.[13] In contrary, in a recent study, a significant relationship was found between vitamin D status and gross motor development in 0-2-year-old children. This study revealed that a child with normal vitamin D levels was 35 times more likely to walk than a child with a deficiency.[14] Also, in another study 25 (OH) D levels >75 nmol/L were associated with higher gross motor ability compared to levels below 50 nmol/L.[15] To our knowledge, the relationship between 25 (OH) D levels and motor development in children aged 3-6 years has been evaluated only once in a study conducted in India and no relationship was found.[16] In our cohort, vitamin D deficiency was found most frequently in children aged 2-4 years with motor development delay. In addition, mean of 25 (OH) vitamin D levels in children with motor development delay was significantly lower than the control group. Although the importance of adequate vitamin D status for normal growth is well known, the role of 25 (OH) vitamin D in the brain is not clearly understood. However, there is evidence that vitamin D has neuro-protective functions and plays an important role in regulating the development, differentiation and branching of nerve cells by influencing neurotrophic factors. A meta-analysis on Magnetic Resonance Imaging (MRI) of the brain revealed that brain cell atrophy is associated with vitamin D deficiency.[17] In vivo and in vitro, studies suggest a possible role of vitamin D in neurodevelopment through Ca (2+) signalling, antioxidant function, metabolic regulation of neurotrophins and neurotoxins, and protection of the brain from inflammation.[18,19] Since motor development accelerates especially between 2-4 years of age, the need for vitamin D may be increased during this period. Although daily supplementation with 400 international units (IU) of vitamin D during the first years of life is recommended in Turkey, this prophylaxis may need to be extended in children with motor development delay.

Furthermore, the possible importance of vitamin D as a pleiotropic mediator contributing to lung health is increasingly recognised and children with asthma appear to be at increased risk

of vitamin D deficiency.[20] A review for vitamin D deficiency and acute lower respiratory infections in children stated that vitamin D supplementation is a low-cost, low-risk intervention that providers should consider for children, especially those at high risk for acute lower respiratory infection.[21] In a study investigating vitamin D deficiency as a risk factor for recurrent wheezing in Turkey, no significant association was found between vitamin D levels and hospitalisation, oxygen, or steroid treatment.[22] This study determined that vitamin D deficiency was detected more frequently in asthmatic children aged 48-72 months compared to 24-47 months of age. This may be due to the progression of the disease, so pediatricians should follow current recommendations when prescribing vitamin D supplementation for infants and children with chronic illness.

Our study has several limitations. Firstly, there is a lack of data regarding time spent in daylight and about calcium, alkaline phosphates, phosphorus, and parathormone levels. Additionally, this is a single-center study from Mardin; thus, it does not reflect the status of all Turkish children. Unfortunately, we could only report biometric data since we were not able to perform cognitive status. On the other hand, since our study group was similar in age and gender, etiological factors affecting motor development were excluded.

In conclusion, this is the first study to investigate vitamin D status in a specific subgroup such as motor development delay in early childhood. Vitamin D deficiency and insufficiency are common especially among 2 – 6 year of age children with motor development delay. Another notable finding was that vitamin D deficiency was more prevalent in children aged 24 - 47 months with motor development delay than in asthma, a chronic disease. Future research is needed to evaluate the association of vitamin D status in children referred to specialists for motor developmental delay.

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DISCLOSURE

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