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Comparison of Vitamin D Levels in Children with Musculoskeletal Pain with and without Hypermobility of Joints

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Abstract

Background

Vitamin D supplementation has been suggested as a part of an interdisciplinary approach for the management of chronic musculoskeletal pain in children and adolescents. This study aimed to compare vitamin D serum levels in Iranian children with chronic musculoskeletal pain with and without hypermobility.

Materials and Methods: This cross-sectional study was performed on otherwise healthy children aged 16 years or younger with chronic musculoskeletal pain, who were admitted to the rheumatology clinic of Bahrami Children Hospital, Tehran, Iran, from January 2018 to January 2019. Chronic musculoskeletal pain was defined as recurrent episodes of musculoskeletal pain within the past month to the past week. The subjects were categorized into two groups, with or without hypermobility. Hypermobility was diagnosed using Modified Criteria of Carter and Wilkinson. Serum 25-hydroxy vitamin D (25-(OH)D) level and baseline characteristics were compared, and 25-(OH)D <30 ng/mL was considered deficiency.

Results: A total of 72 children (41 girls and 31 boys, with the mean age of 7.36 ± 2.42 years) were included. Most participants (73.6%) were 3 to 7 years old. Sixty-four patients (88.8%) were diagnosed with vitamin D deficiency (25(OH)D <30 ng/mL). Children without joint hypermobility had a lower vitamin D level and a higher prevalence of vitamin D deficiency compared to those with hypermobility. However, the difference was not statistically significant.

Conclusion

Our study results suggested a high prevalence of vitamin D deficiency among children and adolescents with chronic musculoskeletal pain, but the difference in vitamin D deficiency between children with and without hypermobility was not statistically significant.

Key Words: Children, Chronic musculoskeletal pain, Joint hypermobility, Vitamin D.

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1- INTRODUCTION

Chronic musculoskeletal pain, described as pain in the muscles, ligaments, tendons, and/or bones lasting for longer than 3 months, is a commonly encountered condition in children and adolescents (1-3). According to a systematic review, 4 to 40% of children and adolescents have experienced musculoskeletal pain at some point during the previous 6 months. However, the studies vary widely due to the great heterogeneity between study populations, methodological features, and case definitions (3). Despite the considerable methodological diversity of the studies, it is generally known that chronic musculoskeletal pain is more frequent during adolescence compared to childhood (2, 3). Furthermore, chronic musculoskeletal pain is associated with several physical, biological, and psychosocial factors (4-7).

Joint hypermobility, defined as the ability of a joint (or a group of joints) to move passively and/or actively beyond the normal range of motion, may also be associated with chronic musculoskeletal pain. However, different studies have reported conflicting results (8, 9). Chronic musculoskeletal pain is known as a leading cause of disability in children and adolescents, lowering their quality of life and imposing a large economic burden on families and healthcare systems (2, 10).

As a result, an evidence-based, interdisciplinary strategy, that includes pharmacological, psychological, physical and complementary approaches, is needed for the management of chronic musculoskeletal pain and its associated factors (11). Few studies have investigated Vitamin D deficiency and the therapeutic effect of vitamin D supplementation in children with chronic musculoskeletal pain (12-14). It has been suggested that vitamin D can potentially influence cortical, immunological, hormonal, and neuronal changes associated with pain pathways, implicating its role in the pathophysiology of chronic musculoskeletal pain (15). In addition to the effect on bone mineralization and regulation of serum calcium level, vitamin D can also directly affect the skeletal muscles, act as a neuroactive steroid, and modulate inflammatory responses (16-18). Both chronic musculoskeletal pain and hypermobility are commonly encountered in the pediatric population of Iran, reported in 25.4% and 11.8% of children and adolescents, respectively (19, 20).

However, the serum level of vitamin D has not been previously assessed in Iranian children with chronic musculoskeletal pain with and without hypermobility. Moreover, there are no local guidelines on the measurement of serum vitamin D level in all or a subgroup of children with musculoskeletal pain. Our study, therefore, aims to evaluate the prevalence of vitamin D deficiency in Iranian children with chronic musculoskeletal pain. We also compared vitamin D level in children with and without joint hypermobility

2- MATERIALS AND METHODS

2-1. Study design and population

This cross-sectional study was conducted on 72 otherwise healthy children aged 16 years or younger, who were admitted at the rheumatology clinic of Bahrami Children Hospital, affiliated to Tehran University of Medical Sciences (TUMS), Tehran, Iran, from January 2018 to January 2019. The children were diagnosed with chronic musculoskeletal pain by the attending rheumatologist.

2-2. Method

The children underwent a thorough history and physical examination. Data, including age, sex, weight, height, body mass index (BMI), and hypermobility of joints were recorded. Weight and height were measured (without shoes) using a digital

scale and tape meter, respectively. BMI was calculated as weight in kilograms divided by height in squared meters. Diagnosis of joint hypermobility depended on the presence of at least 3 of 5 Modified Criteria of Carter and Wilkinson, including touching thumb to volar forearm, hyperextension of metacarpophalangeal joints so fingers parallel forearm, >10° hyperextension of elbows, >10° hyperextension of knees, and touching palms to floor with knees straight (21). A 5 ml sample of venous blood was taken from each patient, centrifuged for 15 minutes and stored at -18° c until analysis. After completion of patient selection, all samples were analyzed. Serum 25-hydroxy vitamin D (25-(OH)D) was measured by radioimmunoassay method. A 25-(OH)D level of <30 ng/mL was considered deficiency.

2-3. Ethical consideration

All parents were asked to fill informed consent forms and the study was approved by the Ethics Committee of Medical Faculty of TUMS.

2-4. Inclusion and exclusion criteria

We included otherwise healthy children aged ≤ 16 years with recurrent episodes of musculoskeletal pain within the past month to most recently one week before attending our outpatient clinic, who were diagnosed with chronic musculoskeletal pain and whose parents gave informed consent to their participation in the study. Those with a history of fracture, vitamin D administration, and corticosteroid administration, any underlying rheumatologic disease, Ehlers–Danlos syndrome, Marfan syndrome, and serum calcium or phosphorus imbalance were excluded from the study. Children who had any abnormal signs on physical examination such as swelling, erythema, tenderness or limited range of motion of joints were also excluded.

2-5. Data Analyses

SPSS software version 21.0 (SPSS Inc., Chicago, IL, USA) was used for data analysis. Data was shown by mean ±SD for continuous, and frequencies for categorical variables. Normal distribution was determined by Kolmogorov Smirnov test. The Pearson X2 test with Fisher's exact test were used for the assessment of categorical variables. Independent sample t-test (or Mann–Whitney U test) was used to compare continuous variables comparison. P-value < 0.05 was considered statistically significant.

3- RESULTS

A total of 72 children (41 girls (57 %), and 31 boys (43%)) with a mean age of 7.36 ± 2.42 years were included. Most participants (73.6%) were 3 to 7 years old. Based on Modified Criteria of Carter and Wilkinson, 36 children (50%) with musculoskeletal pain had joint hypermobility. Based on laboratory data, 64 (88.8%) children had vitamin D deficiency. Data was further compared across the two groups with and without hypermobility. Children with musculoskeletal pain and hypermobility were significantly younger and had significantly lower BMI compared to those without hypermobility. Children without hypermobility had a lower vitamin D level and higher prevalence of vitamin D deficiency compared to those with hypermobility. However, the difference was not statistically significant. The baseline, clinical and laboratory characteristics of participants are shown in **Table.1**.

Table-1: The baseline, clinical and laboratory characteristics of participants with and without hyperlaxity.

Variables	With hyper laxity, n=36	Without hyper laxity, n=36	P-value
Age group, number (%)<3 years 3-7 years >7 years	6(16.7%) 29(80.6%) 1(2.8%)	4(11.1%) 24(66.7%) 8(22.2%)	0.04
Gender, number (%) Male female	13(36.1%) 23(63.9%)	18(50%) 18(50%)	0.3
BMI (kg/m2), number (%) <15 15-19 >19	4(11.1%) 31(86.1%) 1(2.8%)	1(2.8%) 27(75%) 8(22.2%)	0.019
Serum vitamin D, ng/mL	18.8±11.2	16±9.7	0.2
Vitamin D deficiency (<30 ng/mL), number (%)	30 (83.3%)	34 (94.4%)	0.1

BMI: Body mass index.

4- DISCUSSION

Chronic musculoskeletal pain is one of the most common pediatric pain syndromes, and may occur together with joint hypermobility, which is another common condition in children and adolescents. The both conditions are associated with significant morbidity and healthcare costs (2, 9, 12). Vitamin D supplementation has been suggested to improve the outcome in children with chronic musculoskeletal pain (12-14). This study assessed the prevalence of vitamin D deficiency in children with chronic musculoskeletal pain, and compared vitamin D levels in children with and without joint hypermobility. Our study results showed a high prevalence of vitamin D deficiency among children and adolescents with chronic musculoskeletal pain. The prevalence of vitamin D insufficiency (25-(OH)D <30 ng/mL) among our patients was 88.8%, which is considerably higher than the prevalence of vitamin D insufficiency in healthy Iranian children and adolescents reported in a recent systematic review and meta-analysis (22). Our results are approximately similar to those of Park et al., who reported vitamin D levels of <30 ng/mL in 95% of Korean children and adolescents with nonspecific lower extremity pains (14), but higher than reports from UK and Canada (23, 24). Vitamin D deficiency is also highly prevalent in adults with musculoskeletal pain. According to Plotnikoff and Quigley, 93% of adult patients with persistent nonspecific musculoskeletal pain had 25-(OH)D levels <20 ng/mL (25). Heidari et al. also reported vitamin D deficiency in 63.4% of Iranian adults with chronic musculoskeletal pain (26). Some studies have shown that vitamin D therapy can improve musculoskeletal pain in pediatric population. According to a pilot study by Blagojevic et al., a 6-month prescription of vitamin D supplements reduces pain intensity and improves mobility and daily functioning in children with musculoskeletal conditions (12). The positive effect of vitamin D on chronic musculoskeletal pain in children has also been shown by Vehapoglu et al., who reported a significant reduction in pain intensity among children with growth pains after a single oral dose of vitamin D (27). While joint hypermobility is regarded as a major predisposing factor for musculoskeletal pain, our results showed that the difference regarding the prevalence of vitamin D deficiency was

not statistically significant, probably due to the high prevalence of 25-(OH)D deficiency in our patients. In a recent study on female university students with and without generalized joint hypermobility, Tuna et al. found a similar frequency of vitamin D deficiency in the two groups (28). Considering the high prevalence of vitamin D deficiency in our study population, this finding implies that 25-(OH)D serum level should be assessed in all children with chronic musculoskeletal pain, regardless of the existence of joint hypermobility.

Our study has a few limitations. Serum levels of 25-(OH)D could not be compared to those of a healthy cohort as our study didn't include healthy children without chronic musculoskeletal pain. Additionally, the causal association between vitamin D deficiency and musculoskeletal pain could not be determined as the study was cross-sectional. Since our main aim was to evaluate and compare the prevalence of vitamin D deficiency in pediatric chronic musculoskeletal pain with or without joint hypermobility, many parameters such as dietary vitamin D intake or exposure to sunlight were not measured. It should be emphasized that to have a better estimation of the epidemiology of vitamin D deficiency in Iranian children and adolescents with chronic musculoskeletal pain, larger, multi-centric studies are required.

5- CONCLUSION

In summary, our study reported a high prevalence of vitamin D deficiency in Iranian children diagnosed with chronic musculoskeletal pain. There was no significant difference regarding vitamin D deficiency between children with or without hypermobility. More attention should be paid to the role of vitamin D in the management of chronic musculoskeletal pain in pediatrics.

6- CONFLICT OF INTEREST: None.

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