

Hospital Based Assessment of Vitamin D Serum Levels in Indian Children with Chronic Musculoskeletal Pain with and Without Hypermobility: A Comparative Study

Mani Shankar¹, Babli Kumari², Rajnish Kumar³, Avinash Kumar Sahay⁴

¹Assistant Professor, Department of Pediatrics, NSMCH, Bihta, Patna, Bihar, India

²Senior Resident, Department of Dermatology, PMCH, Patna, Bihar, India

³Assistant Professor, Department of Pediatrics, NSMCH Bihta, Patna, Bihar, India

⁴Professor & Head, Department of Pediatrics, NSMCH, Bihta, Patna, Bihar, India

Received: 01-03-2023 Revised: 15-04-2023 / Accepted: 21-05-2023

Corresponding author: Babli Kumari

Conflict of interest: Nil

Abstract

Aim: The aim of the present study was to compare vitamin D serum levels in Indian children with chronic musculoskeletal pain with and without hypermobility.

Methods: A cross-sectional study was conducted in the Department of Paediatrics, for six months. Total 100 children were diagnosed with chronic musculoskeletal pain were included in this study. The subjects were divided into two groups, with or without hypermobility.

Results: There were a total of 100 kids, with a mean age of 7.43 2.48 years old (58 females and 42 boys). The most common age range was 3-7 years old (73.6%). 45 (or 90%) of the youngsters tested positive for vitamin D insufficiency in the lab. The data was also compared between the hypermobile and non-hypermobile groups. When compared to children without hypermobility, those that suffer from musculoskeletal discomfort are younger and have a lower body mass index. When compared to children with hypermobility, those without hypermobility had lower vitamin D levels and a greater rate of vitamin D insufficiency. There was a change, but it wasn't enough to warrant statistical significance.

Conclusion: There was no statistically significant difference in vitamin D deficit between children with and without hypermobility, despite the high frequency of vitamin D deficiency among children and adolescents with chronic musculoskeletal pain.

Keywords: Children, Chronic Musculoskeletal Pain, Joint Hypermobility, Vitamin D.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Muscle, ligament, tendon, and/or bone pain that lasts more than three months is called chronic musculoskeletal pain, and it is rather frequent in children and teenagers. [1-3] When a joint's range of motion is abnormally large compared to other joints in the body, it is said to be hypermobile or lax. One or more joints may be impacted. Eight percent to thirty-nine percent of children diagnosed with school age have joint hypermobility. [4-7] Age, sex, and ethnicity all have a role, and the prevalence declines with time. Girls, as well as youngsters of Asian descent, are more likely to be hypermobile than their Caucasian counterparts. [8]

Bone and mineral metabolism cannot function without vitamin D. It is necessary for appropriate growth plate calcification and bone mineralization, and it speeds up the absorption of calcium in the gut. It's essential for bone mineralization, skeletal development, and bone health because of the

function it plays in calcium and phosphorus homeostasis. Musculoskeletal problems (weakness, falls, fractures), infections, autoimmunity, heart disease, type 1 and type 2 diabetes, cancer, cognitive impairment, and mental illness all seem to be prevented by adequate vitamin D levels. [9,10]

Therefore, the therapy of chronic musculoskeletal pain and its accompanying causes requires an evidence-based, multidisciplinary strategy that incorporates pharmaceutical, psychological, physical, and complementary techniques. [11] Vitamin D insufficiency and the beneficial effects of supplementation have received little research in children with persistent musculoskeletal pain. [12] Indicating a role in the pathogenesis of persistent musculoskeletal pain, vitamin D has been hypothesized to affect cortical, immunological, hormonal, and neuronal alterations involved in pain

pathways. [13] Vitamin D not only influences bone mineralization and blood calcium level, but it also acts as a neuroactive steroid and modifies inflammatory responses. [14-16]

Accordingly, the current research set out to determine how common vitamin D insufficiency is among Indian children experiencing chronic musculoskeletal discomfort and to compare vitamin D levels across children with and without joint hypermobility.

Material & Methods

A cross-sectional study was conducted in the Department Of Pediatrics, NSMCH, Bihta, Patna, India for six months.

Inclusion criteria

- Healthy children aged ≤ 14 years with recurrent episodes of musculoskeletal pain within the past month to most recently 7 days before attending outpatient clinic, who were diagnosed with chronic musculoskeletal pain.

Exclusion criteria

- 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.
- Children who had any abnormal signs on physical examination such as swelling, erythema, tenderness or limited range of motion of joints.

Methodology

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

Variables	With hyper laxity, n=50	Without hyper laxity, n=50	P-value
Age group, number (%)			
<3 years	9 (18%)	5 (10%)	0.02
3-7 years	39 (78%)	32 (64%)	
>7 years	2 (4%)	13 (26%)	
Gender, number (%)	17 (34%)	25 (50%)	0.4
Male female	33 (66%)	25 (50%)	
BMI (kg/m ²), number (%)			
<15	5 (10%)	2 (4%)	0.017
15-19	42 (84%)	36 (72%)	
>19	3 (6%)	12 (24%)	
Serum vitamin D, ng/mL	18.2±11.5	17±9.5	0.3
Vitamin D deficiency (<30 ng/mL), number (%)	42 (84%)	48 (96%)	0.1

A total of 100 children (58 girls (58%), and 42 boys (42%) with a mean age of 7.43 ± 2.48 years were included. Most participants (73.6%) were 3 to 7 years old. Based on laboratory data, 45 (90%) children had vitamin D deficiency. Data was further compared across the two groups with and without hypermobility. Children with

Total 100 children were diagnosed with chronic musculoskeletal pain were include in this study. 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 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, $>10^\circ$ hyperextension of elbows, $>10^\circ$ hyperextension of knees, and touching palms to floor with knees straight.¹⁷ 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.

Statistical Analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2010) and then exported to data editor page of SPSS version 19(SPSS Inc., Chicago, Illinois, USA). Descriptive statistics included computation of percentages. Test applied for the analysis was chi-square test. The level of confidence interval and p-value were set at 95% and 5%.

Results

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.

Discussion

Joint hypermobility or laxity is having a range of motion beyond the limits of normal joint. It can affect one or more joints. Beighton scoring (BS), where in nine joints are evaluated, is used to define Joint hypermobility and BS 4-6/9 is reported as generalized joint hypermobility (GJH). [18,19] Hypermobility brings with it many problems as musculoskeletal or systemic manifestations. Musculoskeletal manifestations are traumas, degenerative joint and bone diseases, disturbed proprioception, muscle weakness and musculoskeletal traits. Systemic manifestations are cardiovascular involvements, skin, mucosae, fascia involvement, and nervous system involvement. [19] Joint hypermobility is common in childhood, occurring in 8–39% of school age children. [20,21]

A total of 100 children (58 girls (58%), and 42 boys (42%) with a mean age of 7.43 ± 2.48 years were included. Most participants (73.6%) were 3 to 7 years old. Based on laboratory data, 45 (90%) 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. 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. [22] Heidari et al. also reported vitamin D deficiency in 63.4% of Iranian adults with chronic musculoskeletal pain. [23] 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. [24]

The lack of association between 25(OH)D levels and musculoskeletal complaints was probably because of both groups having levels below normal limits. These results are uniform with other studies that also reported no association between these variables. In retrospective multicenter study on patients who applied to physical medicine and rehabilitation outpatient clinics with non-specific muscle pain, vitamin D deficiency was detected in 70.9% of patients (without information about whether patients are hypermobile or not). However,

vitamin D deficiency in this population was reported not associated with the severity and duration of pain. [25] Hypermobility, vitamin D deficiency, and female sex are risk factors for idiopathic musculoskeletal pain. [26] Of these, hypermobility and female sex are structural unchanging factors. However, it is possible to misdiagnosed musculoskeletal pain associated with vitamin D deficiency as a pain syndrome associated with joint laxity or vice versa. 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]

Conclusion

We found that a large percentage of Indian children who were diagnosed with persistent musculoskeletal pain also had vitamin D insufficiency. Vitamin D insufficiency was not significantly different between hypermobile and non-hypermobile children. Vitamin D's function in the treatment of children with persistent musculoskeletal pain needs further study.

References

1. Weiss JE, Stinson JN. Pediatric pain syndromes and noninflammatory musculoskeletal pain. *Pediatric Clinics*. 2018 Aug 1;65(4):801-26.
2. Kamper SJ, Henschke N, Hestbaek L, Dunn KM, Williams CM. Musculoskeletal pain in children and adolescents. *Brazilian journal of physical therapy*. 2016 Feb 16; 20:275-84.
3. King S, Chambers CT, Huguet A, MacNevin RC, McGrath PJ, Parker L, MacDonald AJ. The epidemiology of chronic pain in children and adolescents revisited: a systematic review. *Pain*. 2011 Dec 1;152(12):2729-38.
4. Larsson LG, Baum J, Mudholkar GS, Srivastava DK. Hypermobility: prevalence and features in a Swedish population. *Rheumatology*. 1993 Feb 1;32(2):116-9.
5. Decoster LC, Vailas JC, Lindsay RH, Williams GR. Prevalence and features of joint hypermobility among adolescent athletes. *Archives of pediatrics & adolescent medicine*. 1997 Oct 1;151(10):989-92.

6. Forleo LH, Hilario MO, Peixoto AL, Naspitz C, Goldenberg J. Articular hypermobility in school children in Sao Paulo, Brazil. *The Journal of rheumatology*. 1993 May 1;20(5):916-7.
7. Rikken-Bultman DG, Wellink L, van Dongen PW. Hypermobility in two Dutch school populations. *European Journal of Obstetrics & Gynecology and Reproductive Biology*. 1997 Jun 1;73(2):189-92.
8. Remvig L, Jensen DV, Ward RC. Epidemiology of general joint hypermobility and basis for the proposed criteria for benign joint hypermobility syndrome: review of the literature. *The Journal of rheumatology*. 2007 Apr 1;34(4):804-9.
9. Pludowski P, Holick MF, Pilz S, Wagner CL, Hollis BW, Grant WB, Shoenfeld Y, Lerchbaum E, Llewellyn DJ, Kienreich K, Soni M. Vitamin D effects on musculoskeletal health, immunity, autoimmunity, cardiovascular disease, cancer, fertility, pregnancy, dementia and mortality—a review of recent evidence. *Autoimmunity reviews*. 2013 Aug 1;12(10):976-89.
10. Vujosevic S, Borozan S, Radojevic N, Aligrudic S, Bozovic D. Relationship between 25-hydroxyvitamin D and newly diagnosed type 2 diabetes mellitus in postmenopausal women with osteoporosis. *Medical principles and practice*. 2014 Mar 18;23(3):229-33.
11. Caes L, Fisher E, Clinch J, Eccleston C. Current evidence-based interdisciplinary treatment options for pediatric musculoskeletal pain. *Current Treatment Options in Rheumatology*. 2018 Sep; 4:223-34.
12. Choroomb Kheirabadi M, Mousavi Torshizi M, Sadeghi P. Comparison of Vitamin D Levels in Children with Musculoskeletal Pain with and without Hypermobility of Joints. *International Journal of Pediatrics*. 2020 Sep 1;8(9):11967-72.
13. Shipton EA, Shipton EE. Vitamin D and pain: vitamin D and its role in the aetiology and maintenance of chronic pain states and associated comorbidities. *Pain research and treatment*. 2015;2015.
14. Ceglia L. Vitamin D and its role in skeletal muscle. *Current opinion in clinical nutrition and metabolic care*. 2009 Nov;12(6):628.
15. Groves NJ, McGrath JJ, Burne TH. Vitamin D as a neurosteroid affecting the developing and adult brain. *Annual review of nutrition*. 2014 Jul 17; 34:117-41.
16. Helde-Frankling M, Björkhem-Bergman L. Vitamin D in pain management. *International journal of molecular sciences*. 2017 Oct 18;18(10):2170.
17. Carter C, Wilkinson J. Persistent joint laxity and congenital dislocation of the hip. *The Journal of Bone & Joint Surgery British Volume*. 1964 Feb 1;46(1):40-5.
18. Beighton P, Paepe AD, Steinmann B, Tsipouras P, Wenstrup RJ. Ehlers-Danlos syndromes: revised nosology, Villefranche, 1997. *American journal of medical genetics*. 1998 Apr 28;77(1):31-7.
19. Castori M, Tinkle B, Levy H, Grahame R, Malfait F, Hakim A. A framework for the classification of joint hypermobility and related conditions. In *American Journal of Medical Genetics Part C: Seminars in Medical Genetics* 2017 Mar;175(1): 148-157.
20. Larsson LG, Baum J, Mudholkar GS, Srivastava DK. Hypermobility: prevalence and features in a Swedish population. *Rheumatology*. 1993 Feb 1;32(2):116-9.
21. Decoster LC, Vailas JC, Lindsay RH, Williams GR. Prevalence and features of joint hypermobility among adolescent athletes. *Archives of pediatrics & adolescent medicine*. 1997 Oct 1;151(10):989-92.
22. Plotnikoff GA, Quigley JM. Prevalence of severe hypovitaminosis D in patients with persistent, nonspecific musculoskeletal pain. In *Mayo clinic proceedings* 2003 Dec 1; 78(12):1463-1470. Elsevier.
23. Heidari B, Shirvani JS, Firouzjahi A, Heidari P, Hajian-Tilaki KO. Association between nonspecific skeletal pain and vitamin D deficiency. *International journal of rheumatic diseases*. 2010 Oct;13(4):340-6.
24. Blagojevic Z, Nikolic V, Kistic-Tepavcevic D, Terzic Supic Z, Kovacevic R, Zivkovic Z, Stevanovic D. Musculoskeletal pain and vitamin D deficiency in children: a pilot follow-up study of vitamin D therapy in musculoskeletal/orthopedic conditions. *Acta Chir Orthop Traumatol Cech*. 2016 Jan 1;83(1):21-6.
25. Karahan AY, Hüner B, Kuran B, Sezer N, Celik C, Salbaş E, Ordahan B, Gündüz B, Kulcu DG, Yalınman A, Atalay NŞ. Assessment of the relationship between vitamin D level and non-specific musculoskeletal system pain: a multicenter retrospective study (Stroke Study Group).
26. Juul-Kristensen B, Røgind H, Jensen DV, Remvig L. Inter-examiner reproducibility of tests and criteria for generalized joint hypermobility and benign joint hypermobility syndrome. *Rheumatology*. 2007 Dec 1;46(12): 1835-41.
27. Vehapoglu A, Turel O, Turkmen S, Inal BB, Aksoy T, Ozgurhan G, Ersoy M. Are growing pains related to vitamin D deficiency? efficacy of vitamin D therapy for resolution of symptoms. *Medical Principles and Practice*. 2015 Jun 1;24(4):332-8.

28. Filiz TU, Özdemir H, Kabayel DD, Doğanlar ZB. Is there a difference in 25-hydroxyvitamin D levels between female university students with and without joint hypermobility? The European Research Journal. 2019 Apr 7;5(4): 576-81.