

ASSESSMENT OF VITAMIN D AND CALCIUM LEVEL IN CHILDREN WITH GROWING PAIN**¹Mujammel Haque, ²Kamrul Laila, ³Mohammad Imnul Islam and ⁴Shahana Akhter Rahman**¹Assistant Professor, Dept. of Paediatrics, Bangabandhu Sheikh Mujib Medical University, Dhaka.²Assistant Professor, Dept. of Paediatrics, Bangabandhu Sheikh Mujib Medical University, Dhaka.^{3,4}Professor, Dept. of Paediatrics, Bangabandhu Sheikh Mujib Medical University, Dhaka.***Corresponding Author: Mujammel Haque**

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ABSTRACT

Background: Growing pain (GP), termed as benign nocturnal pains of childhood is the most common cause of recurrent musculoskeletal pain in children. GP has association with vitamin D (25OH-vit D) deficiency. **Objectives:** Estimation of vitamin D & calcium levels in children with GP to determine the relationship between vitamin D deficiency and GP. **Methods:** In this cross-sectional study fifty one children aged 4-12 years fulfilling the criteria of growing pain were enrolled. Age and sex matched 25 children were selected as control group who came with acute illness other than bone disease. Serum concentration of calcium (Ca) and vitamin D was measured. Comparison of serum concentration of vitamin D & calcium between children with GP and control group was done with student t test and chi-square test. **Results:** Mean age of the study population was 7.86 ± 2.71 years with the majority being males (60.78%). Vitamin D deficiency was found in 92.15 % of GP children and 48% of the control group children. Mean vitamin D level was 17.53 ± 5.48 ng/ml in vitamin D deficient group among GP children. Vitamin D deficiency was significantly higher among GP children. Most of the vitamin D deficient children had normal serum calcium level (93.61%), only 3 patient (6.38 %) had calcium deficiency with a mean calcium level 9.47 ± 0.78 mg/dl. **Conclusion:** Majority of children with Growing pain had vitamin D deficiency. Growing pain could be a manifestation of low vitamin D, so all children with growing pain or unexplained limb pain should be tested for serum vitamin D level.

KEYWORDS: Growing pain, Vitamin D, Limb pain.**INTRODUCTION**

In children, Growing pain (GP) is a well-known clinical entity and most common form of episodic childhood musculoskeletal pain, which occurs in about 25% to 40% of children without any organic pathology.^[1,2] Growing Pain was first described by French physician Marcel Duchamp.^[1] The prevalence of GP has been reported from 1928 and it ranges from as little as 2.6% to 49% of children.^[3] Oster found that as many as 15% of school-age children have occasional limb pain.^[4] Evans and Scutter in a very large community study in Australia reported a prevalence of 37% in children aged 4–6 years.^[5] Haque et al. found 19.3% of Bangladeshi school children aged 6-12years had growing pain.^[6]

Medical science is still unable to fully explain the exact causes of the discomfort and pain experienced by up to one third of all children at some time during early childhood.^[7] Description by Peterson seems easy to follow and was taken as the criteria for diagnosis of GP in the present study.^[8] GP has typical clinical features; it is usually non-articular, site is located in the shins, calves, thighs or popliteal fossa and GP is almost always

bilateral. The pain usually occurs in the evening or at night with pain intensity varying from mild to very severe. The duration ranges from minutes to hours. Children feel better when they're held, massaged. It almost always resolves by morning. There are no objective signs of inflammation on physical examination.^[3,9] Otherwise healthy children are most commonly affected by growing pain between the ages of 4 and 12 years, but they may also occur in younger age groups.^[1] Few studies have been done to elucidate the cause and pathogenesis of growing pain. The proposed causes of GP according to Yosef Uziel and Philip J Hashkes are : low pain tolerance, over use, low bone strength density, mechanical strains due to flat foot with mild outward turning of back of foot, blood perfusion change, family environment, stress and psychological disposition.^[7-10] Correct diagnosis of GP requires a thorough history and physical examination.

There is no sensitive or specific laboratory tests, when patients have typical clinical characteristics there is no need to do any unnecessary laboratory investigation or imaging tests.^[4] However, if the symptoms are atypical,

the diagnosis of GP should not be assumed without evaluating other causes.

It was postulated that GP has association with vitamin D (25OH-vit D) deficiency. A diet enriched in calcium, vitamin D might affect bone status and pain episodes.^[11] Main function of vitamin D is to maintain normal calcium homeostasis. Vitamin D increases the total intestinal absorption of calcium and phosphorus from 10-20% and 60% to 30-40% and 80%, respectively. In the setting of hypovitaminosis D, serum level of calcium is first to fall, but phosphorus level is maintained within the normal range. This hypocalcaemia then leads to secondary hyperparathyroidism, resulting in an increased serum level of 1, 25 dihydroxycholecalciferol, normalization of serum calcium and a fall in plasma phosphorus level. This homeostasis is achieved by PTH-induced bone re-sorption, which also increases the serum level of alkaline phosphatase. This condition, if left untreated, eventually leads to exhaustion of bone stores and recurrence of hypocalcaemia.^[12] In our country there are no studies available highlighting the association of vitamin D deficiency in the pathogenesis of growing pain. The aim of this study was diagnosis of growing pain in children with unexplained limb pain and estimation of serum level of vitamin D, calcium in children with GP to determine the relationship between vitamin D deficiency and GP.

MATERIALS AND METHODS

This cross sectional study was conducted at the OPD of Pediatric Department of Bangabandhu Sheikh Mujib Medical University (BSMMU), from June 2018 to June 2019. Fifty one children aged 4-12 years, presenting with limb pains and fulfilling the diagnostic criteria of growing pain were enrolled for the study. "Diagnostic criteria of GP given by Peterson (1986) includes: intermittent pains occurring once or twice per week, rarely daily, totally pain free in between the episodes; individual episodes lasting for 30 minutes to 2 hours. Sites are usually in the muscles of calf, sometimes anterior thigh muscles, shins and popliteal fossa and affect both limbs. Time of pain is in the evening or night, and physical examination is normal".^[4] Children with any systemic illness, organic cause of pain,

rheumatologic disorders, obvious signs of rickets and malnutrition were excluded. Written consent was obtained from parents. A pre-designed questionnaire was filled up by the investigator regarding demographic variables and characteristics of growing pain. Serum concentration of vitamin D and calcium was measured. In our country as there was no standard level of vitamin D in children, control had been taken in this study. Age and sex matched controls were selected not taking supplements containing vitamin D or calcium, who came with acute illness other than bone disease in paediatric OPD. Because of logistic constraints only 25 children were taken as control. In Bangladesh, most commonly used technique is direct enzyme-linked immunosorbent assay. That's why this study chose this technique to measure the serum 25 (OH)D levels. Serum concentration of Ca was measured by O-cresolphthaleine complexone (Roche/Hitachi 912). Laboratory reference ranges included Ca at 8.5 to 10.5 mg/dl. Depending on their vitamin D level, patients were classified into 3 categories: levels <20ng/ml as Vitamin D deficiency; levels 20-30ng/ml as Vitamin D Insufficiency; levels >30ng/ml as Vitamin D sufficiency.^[13] As the sample size was small, for the purpose of statistical analysis we included vitamin D insufficiency in the vitamin D deficient group. Serum levels falling out of the reference values were considered abnormal (high or low). Quantitative variables were reported as mean and SD while qualitative variables were described in proportions.

Statistical analysis was done manually. Comparison of the mean value of vitamin D and calcium between GP children and control group was done with unpaired student t test. Status of vitamin D deficient and sufficient level among GP and control group was compared by chi-square test. P value of <0.05 was considered to indicate statistical significance.

RESULTS

A total of 51 patients were studied in the present study. Table 1 shows that mean age of the study population and control was 7.86± 2.71 years and 8.63±3.06 years respectively (range 4-12 years). The study group comprised of 60.78 % boys and 39.21% girls.

Table 1: Age distribution of study population (n= 51+25).

Age (Years)	Case (n=51)		Mean ±SD	Control (n=25)		Mean ±SD
	Frequency	Percentage (%)		Frequency	Percentage (%)	
4-6+	19	37.25	7.86±2.71	10	40	8.63±3.06
7-9+	13	25.49		6	24	
10-12	19	37.25		9	36	

Table 2 depicts mean vitamin D and calcium level among study population and control group. The mean level of vitamin D in study population was 18.35±6.26 ng/ml and calcium was 9.47±0.78 mg/dl. Mean level of vitamin D was significantly low among cases than

control. Mean serum calcium level was not significantly different among the two groups.

Table 2: Comparison of mean level of serum 25(OH)D and calcium in GP children & control group (n=51+25).

Variable	GP (n=51) Mean±SD	Control (n=25) Mean±SD	*P value
S. 25(OH)D ngm/ml	18.35±6.26	29.21±6.95	<0.0001
S. Calcium	9.47±0.78	9.29±0.65	0.128

*unpaired student t test

Table 3 shows that vitamin D deficiency was found in 92.15 % of GP children, among whom 28 (59.57%) were boys and 19 (40.42%) were girls. Normal vitamin D level was found only in 7.84% children with GP. Among

control, vitamin D deficiency was found in 12 (48 %) children with a mean value of 23.88±3.86 ngm/ml. Vitamin D levels among cases and controls were significantly different.

Table 3: Status of serum 25(OH)D deficient and sufficient level among GP and control group (n= 51+25).

25(OH)D level	GP Group (n=47+4)		Control Group (n=12+13)		*P value
	Mean±SD	No (%)	Mean±SD	No (%)	
Vit D Deficient (≤30 ngm/ml)	17.53±5.48	47(92.15%)	23.88±3.86	12(48 %)	0.00005
Vit D Sufficient (>30-100 ngm/ml)	31.4±1.06	4(7.48%)	35.77±3.26	13 (52%)	

*Chi-square test

In vitamin D deficient group, most of the cases (93.61%) had normal serum calcium level, with a mean calcium level of 9.47±0.78 mg/dl.

Table 4: Serum calcium level among vitamin D deficient group (n=47).

Calcium level (mg/dl)	Frequency	Percentage (%)	Mean±SD	Range
Normal (8.5- 10.5)	44	93.61	9.47±0.78	7.5-11
Deficient (< 8.5)	3	6.38		

DISCUSSION

Non-specific musculoskeletal pain has been widely linked to hypovitaminosis D in otherwise healthy children.^[14,15] Most of the children with growing pain are vitamin D deficient and growing pains could be a specific manifestation of vitamin D deficiency in children. James Dowd, director of both the Arthritis Institute of Michigan and the Michigan Arthritis Research Center stated in a blog on vitamin D that growing pain is nothing else but a clinical expression of vitamin D deficiency.^[16]

Age distributions of growing pain children were between 4-12 years and highest numbers of cases were found in 4-6+ year age group in the present study. This finding is similar to a large community study by Evans and Scutter done in Australia where a prevalence of GP was found as 37% in children aged 4-6 years.^[17] Regarding gender distribution, more number of the cases in this study were boys. It could be the effect of the social background of our country, where boys get more care. This finding doesn't match with the study done by Vehapoglu et al. where most of the cases were girls.^[18]

In the present study it is found that among the children with growing pain aged between 4-12 years, 92.15% had vitamin D deficiency and the finding was significantly different from control group. A large number of control group children also had vitamin D deficiency (48%) but their mean level was significantly higher than GP children. Several studies done in our country reported that low vitamin D level is common among our children. But from this study it is apparent that significantly lower

level could be a risk factor for GP. Several studies reported similar results as our one.^[18-20] Vehapoglu et al. in a study done in Istanbul in 2015 found that 86.6% of children with growing pain had low vitamin D.^[18] Weng et al. reported that about 68% of children in Philadelphia, during the winter time were vitamin D insufficient (serum levels of 25-OH vitamin D3 < 30 ng/mL).^[19] Han et al. reported that 86% of school aged children in Seoul, had vitamin D deficiency.^[20]

In the present study mean serum vitamin D level among GP children was 18.35±6.26 ngm/ml, which was significantly lower than the mean value of control. Morandi et al. assessed 33 children with growing pain and found that mean vitamin D level of them was 15±6.9 ngm/ml which is similar to our study finding.^[21]

In our study, mean vitamin D level in the deficient group of GP children was 17.53±5.48 ng/ml, and the ratio of girls to boys in the deficient group was 1: 1.55 which showed that there were more boys in the deficient group. Han et al. in a study done in seoul reported that mean serum 25-OH vitamin D3 value in the insufficient group was 17.00±6.03 ng/ml, and the ratio of girls to boys in the insufficient group was 3:1.^[20] Mean 25-OH vitamin D3 level was similar to our findings but gender ratio didn't match. Haque et al. in their study also found slight male preponderance.^[6]

Mean serum calcium level both among the cases and control group were within normal range. A prospective study done by Vehapoglu et al. included one hundred

and twenty children with GP and found the mean calcium level of GP children as 9.7 ± 0.3 mg/dl which was within normal limit similar to our findings.^[18] In the current study normal serum calcium level was found in 93.61% cases of vitamin D deficient group, whereas only 3 (6.38%) cases had low calcium level. This is probably due to parathyroid hormone induced effect for maintaining normal calcium level.

All children with unexplained limb pain without identifiable organic pathology should be tested for vitamin D level and treated, if necessary.

CONCLUSION

From this study it can be concluded that there is a high prevalence of vitamin D deficiency among the children, it was further lower among children with growing pain. Growing pain could be a manifestation of vitamin D deficiency. However further studies at the community level including larger sample size should be carried out to draw definite conclusion.

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