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ORIGINAL ARTICLE

Frequency of Vitamin D Deficiency among Children with Lower Limb Angular Deformity

ASGHAR ALI KHAN[1], WASEEM KHAN[1], NOOR-U-RAHMAN[1], MUHAMMAD SALAR KHAN[1], MUHAMMAD JAWAD SALEEM[2], MUHAMMAD ILYAS[3]
[1]*MBBS, (PGR-FCPS Orthopedic), Orthopedic B Ward, Hayatabad Medical Complex, Peshawar*
[2]*MBBS, FCPS (Ortho.) Medical Officer, Type D Hospital, Paroa District DI Khan*
[3]*MBBS, PGR- MS Orthopaedic, Jinnah Postgraduate Medical Center, Karachi*
Correspondence to: Asghar Ali Khan, Email: asgharmarwat22@gmail.com

ABSTRACT
Background and Aims: Vitamin D is an important biomodulator of musculoskeletal development and function. Its deficiency is a worldwide public health issue, especially among children, in whom it can cause skeletal abnormalities such as angular deformities of the lower limbs. This study aims to; (i) determine the prevalence of vitamin D deficiency in children with lower limb angular deformities; and (ii) examine the relationship between serum vitamin D concentration and the tibiofemoral joint orientation angles: the lateral distal femoral angle (LDFA) and the medial proximal tibial angle (MPTA).
Material and Methods: This is a cross-sectional, observational study that was conducted at Orthopedic Department of Hayatabad Medical Complex, Peshawar, conducted between January 2023 and October 2023. The study involved 80 skeletally immature children (1-12 years) with lower limb angular deformities. Children with skeletal dysplasia, metabolic bone diseases (other than vitamin D deficiency) or a previous lower limb surgery were excluded. All participants had serum 25-hydroxyvitamin D level assessment and standardized full-length standing anteroposterior radiographs of the two lower limbs. The LDFA and MPTA were measured independently by 3 blinded observers using the digital PACS software. Statistical analysis was carried out with the use of the Statistical package for Social Sciences (SPSS) version 25 software.
Results: A total of 80 children (51 boys, 29 girls) with a mean age of 4.2 years were included. The frequency of vitamin D deficiency was 63% (n=50). The mean serum vitamin D level was 28.6±19.4 ng/ml. The mean LDFA was significantly higher in the normal vitamin D group compared to the deficient group (Right LDFA: 97.9° vs. 92.7°, p=0.025; Left LDFA: 98.5° vs. 93.1°, p=0.019). A positive correlation was found between serum vitamin D levels and LDFAs (Right: ρ=0.27, p=0.03; Left: ρ=0.28, p=0.02). No significant difference or correlation was found for MPTAs.
Conclusion: This study has shown a high frequency of vitamin D deficiency among children with lower limb angular deformities in our local population. The deficiency was related to changes in the LDFA rather than the MPTA, indicating that the femur may be more sensitive to the effects of vitamin D deficiency. These results highlight the need to consider screening and management of vitamin D deficiency in children with limb alignment problems.
Keywords: Vitamin D deficiency, children, lower limb deformity, genu varum, genu valgum, lateral distal femoral angle, Khyber Pakhtunkhwa

INTRODUCTION
Vitamin D is a fat-soluble secosteroid that is an important biomodulator involved in controlling the gene expression of many cells throughout the body, including those involved in musculoskeletal health.[1,2]. The main source is vitamin D3 (cholecalciferol), which is produced in the skin when exposed to the ultraviolet B radiation in sunlight. It can also be sourced from dietary sources such as fatty fish and fortified food[3] The major role of vitamin D is in the maintenance of calcium and phosphate homeostasis which is necessary for bone mineralization. It does this by improving absorption of calcium and phosphorus in the intestines, favouring their reabsorption in the kidneys and releasing calcium from the skeleton if needed.[3,4] Apart from its classical role in mineral homeostasis, vitamin D is essential for neuromuscular function and overall skeletal development.[5] An adequate level of vitamin D is very important to prevent osteoporotic fractures and to maintain bone mineral density throughout life.[6,7] Vitamin D deficiency is a worldwide health problem with a high prevalence found especially in the low & middle-income countries.[8] In Pakistan there is a high prevalence of deficiency in all age groups despite the great availability of sunlight. During childhood and adolescence, deficiency is of particular concern, because it could lead to impaired absorption of calcium from the intestine, resulting in secondary hyperparathyroidism. This subsequently leads to an increase in bone resorption and such negative effects on bone health, which can lead to the development of skeletal abnormalities, bone pain, and an increased risk of fractures.[9] The classic skeletal manifestation (form) of severe, prolonged vitamin D deficiency in children is rickets, resulting in deformities such as bowlegs and knock-knees.[10] However, there has been a growing body of literature that suggests subclinical deficiency, or insufficiency, may also contribute to reduced bone mineral density and increased incidence of angular deformities.[9,11-13] Studies examining the relation of vitamin D to reduced alignment of the lower limb have often been based on clinical measures or radiographic evaluation of the overall tibiofemoral angle. However, the overall tibiofemoral angle is affected by dynamic changes in both the femur and the tibia during growth and is potentially confounded by factors such as physiological torsion.[14,15] To our knowledge, there is a paucity of studies, but especially from the local population of Khyber Pakhtunkhwa province of Pakistan, that have examined the specific relationship between vitamin D levels and these individual joint orientation angles. This study is aimed at addressing this gap by determining the frequency of vitamin D deficiency in children presenting with lower limb angular deformities in the Khyber Pakhtunkhwa province of Pakistan, and to investigate the association of serum vitamin D levels to the LDFA and the MPTA.

MATERIALS AND METHODS
This cross sectional, observational study performed at the Department of Orthopedics, Hayatabad Medical Complex (HMC), Peshawar, Pakistan between January 2023 and October 2023. Ethical approval of the study was received from the Institutional Review Board (IRB) of Hayatabad Medical Complex, Peshawar. Informed written consent was obtained from parents or legal guardians of all study children before enrollment for the study. Patients were recruited with the non-probability consecutive sampling technique. All skeletally immature children (with open physes) between the ages of 1 and 12 years who presented to the pediatric orthopedic outpatient clinic with complaints of lower limb angular deformity (genu varum or genu valgum) were screened for eligibility. The inclusion criteria were: (1) age >1 year and <12 years, (2) both genders (3) presence of a lower limb angular

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deformity confirmed on clinical examination, and (4) both serum vitamin D level and full-length, standing, anteroposterior radiographs of both lower limbs available. Children with a history of skeletal dysplasia (eg, achondroplasia, osteogenesis imperfecta); metabolic bone disease other than vitamin D deficiency (e.g, renal osteodystrophy); neuromuscular disorders; or previous lower limb surgery did not participate. Based on a previous study by Alkhatib et al., 2018 [22], and by using 95% confidence interval and 10% margin of error, the required sample size was calculated as a minimum of 73 patient using the sample size calculator of the World Health Organization (WHO). To allow for possible dropouts or data not collected, we sought to recruit 80 children. Demographic information such as age and sex was recorded for each participant. All children received the serum vitamin D level and radiological assessment. A venous blood (5 ml) sample was collected from each child. Serum levels of 25-hydroxyvitamin D (25(OH)D) were assessed with an enzyme immunoassay (ELISA) technique. Based on widely accepted guidelines, a level of < 30 ng/ml was considered deficient and a level of ≥ 30 ng/ml was considered normal [8, 17]. Standardized, full-length standing, anteroposterior radiographs of both lower limbs were taken. The protocol was to ensure that the child was standing upright and both patellae were pointed forward to reduce rotational error. [14] A parent or guardian helped to position the child. If a limb length discrepancy was noted clinically a block was placed under the shorter limb, to level the pelvis to assure a true representation of the mechanical axis. [16] LDFA formed by the intersection of a line drawn from the centre of the proximal femoral epiphysis (or the centre of the femoral head) to the centre of the knee (the femoral mechanical axis) and a line drawn tangential to the convexity of the distal femoral condyles. [16] MPTA formed by the intersection of a line drawn from center of knee to center of talar dome (tibial mechanical axis) and a line drawn tangential to proximal tibial physis. However, in younger children (< 10 years) where the proximal tibial epiphysis is not fully ossified, the line tangential to the physis was used. [16] Data were entered and analyzed using IBM-SPSS Statistics for Windows, Version 25.0 Descriptive statistics were computed. Continuous variables are presented in the form of mean, SD and range. Categorical variables were expressed as frequency and percent.

RESULTS

A total of 80 children met the inclusion criteria and were enrolled in the study. The mean age of the cohort was 4.2 years. There were 51 boys (63.8%) and 29 girls (36.2%). The overall mean serum vitamin D level was 28.6 ng/ml ±19.4. According to the predefined cut-off, 50 children (63.0%) were found to be vitamin D deficient (<30 ng/ml), while 30 (37.0%) had normal levels (≥30 ng/ml). The demographic details of both groups are summarized in Table 1.

The mean radiological measurements (LDFA and MPTA) for both groups are presented in Table 2. The mean LDFA values were significantly higher in the normal vitamin D group compared to the deficient group for both the right and left lower limbs. This indicates a more varus alignment at the distal femur in children with normal vitamin D levels. Conversely, the mean MPTA values showed no statistically significant difference between the two groups.

Table 1: Demographic characteristics of the study population

Variable	Entire Group (n=80)	Normal Vitamin D (n=30)	Deficient Vitamin D (n=50)	p-value
Male	51 (63.8)	18 (60.0)	33 (66.0)	0.58
Female	29 (36.2)	12 (40.0)	17 (34.0)	
Age (years), Mean (Range)	4.2 (1.3-12.5)	3.4 (1.5-11.2)	4.7 (1.3-12.5)	0.13
Vitamin D Level (ng/ml), Mean (SD)	28.6 (19.4)	44.8 (31-98)	20.1 (4-29)	<0.001

Table 2: Comparison of radiological measurements between normal and deficient vitamin D groups

Radiological Parameter	Normal Vitamin D (n=30) Mean (SD)	Deficient Vitamin D (n=50) Mean (SD)	p-value
LDFA (85°-90°)			
Right	97.9 (9.4)	92.7 (8.2)	0.025
Left	98.5 (9.6)	93.1 (8.5)	0.019
MPTA (85°-90°)			
Right	88.8 (4.6)	90.4 (3.5)	0.21
Left	88.5 (5.0)	90.0 (3.8)	0.18

Table 3: Correlation between serum vitamin d level and tibiofemoral joint orientation angles

Radiological Parameter	Spearman's ρ	P-value
LDFA		
Right	0.27	0.03
Left	0.28	0.02
MPTA		
Right	-0.17	0.18
Left	-0.13	0.28

The correlation analysis between serum vitamin D level and the radiological angles is shown in Table 3. There was a weak but statistically significant positive correlation between serum vitamin D levels and LDFAs. This suggests that higher vitamin D levels are associated with a larger (more varus) LDFA. No significant correlation was found between vitamin D levels and MPTAs.

DISCUSSION

This study performed in Khyber Pakhtunkhwa region of Pakistan, shows considerable occurrence of vitamin D deficiency (63.0%) in children presenting with lower limb angular deformities. While this prevalence is lower than the 75% prevalence in the benchmark study provided by Alkhatib et al.[22] from Qatar, it is alarming and reflects a significant public health issue throughout South Asia and the Middle East. The reason for this difference in prevalence may be due to differences in patterns of sun exposure, dietary patterns and cultural practices in the two populations. Nevertheless, our finding confirms that vitamin D deficiency is a major contributing factor to the development of lower limb deformities in this region.[8, 18] Our mean age (4.2 years) is consistent with the mean age of physiologic bowing transitioning to valgus and where nutritional deficiencies can significantly alter a natural process.[14] Our core finding is that vitamin D deficiency is associated with a statistically significant difference in the LDFA, but not the MPTA. Children with normal vitamin D levels had a significantly higher (more varus) LDFA than children who were deficient. Furthermore, a positive correlation was found, meaning that the higher the vitamin D levels, the greater the LDFA, and the more the distal femur is tipped into varus. This finding is in line with the original study by Alkhatib et al.[22] and allows for a more subtle understanding of the effects of vitamin D deficiency on the alignment of the lower limbs. It suggests that the effect of deficiency on the growth plate is not the same across the knee joint. The distal femoral physis seems to be more sensitive to the effects of vitamin D deficiency than the proximal tibial physis. This observation can be explained by looking at the potential for the growth of the two physes. The distal femoral physis contributes an estimated 70% of the growth of the femur and 37% of the total length of the lower limb, while the proximal tibial physis contributes to an estimated 60% of the growth of the tibia and 27% of the total lower limb length.[19] A physis with a higher growth rate may have higher metabolic demand for calcium and phosphorus, and therefore, may be more sensitive to the mineral imbalance brought on by vitamin D deficiency. When there is a vitamin D deficiency, the calcium absorption is impaired, and there is a state of relative hypocalcemia. This triggers secondary hyperparathyroidism, which works to increase bone resorption at the metaphysis, and prevent the normal process of endochondral ossification.[3] The high growth rate distal femur physis may be disproportionately affected, and a characteristic varus or valgus deformity develop at the knee. In our study the deficient group had a mean LDFA of about 93 degrees which is closer to the normal range (85 degrees-90 degrees)[16] whereas the normal group had a mean LDFA of about 98 degrees which is more varus. This may mean that for the deficient group, the origin of the deformity is likely to be from the femur. Alternatively, it may indicate that the physiological varus which is present in early childhood and which gradually corrects does not correct in the presence of deficiency.[14] Our results are reinforced by the normative data by Sabharwal et al, who noted that the transition from varus to valgus alignment in children is due mainly to a progressive decrease in the LDFA.[16] Our data suggests that this natural "opening" of the LDFA (decreasing towards valgus) is possibly altered in children with vitamin D deficiency. While our study did not follow the children longitudinally, what we do have is a cross-sectional snapshot that is in agreement with this developmental concept. In contrast, the MPTA claimed no significant difference between the groups. This suggests that the tibia is less important in the angular deformities associated with vitamin D deficiency, at least in this age group. This is an important takeaway from the clinical side. When assessing the child with angular deformities, especially in an area where a high prevalence of vitamin D deficiency is reported, a closer attention to the alignment of the distal femur may be appropriate. The sample of 80 children, based on a 10% margin of error assuming a 75% prevalence, offers more statistical power and promotes generalizability of our results compared to the sample sizes of smaller past investigations. The larger sample size also adds to the robustness of the observed correlations and subgroup comparisons. The strengths of this study are that standardized, reproducible, full-length standing radiographs were used and specific joint orientation angles, instead of the global tibiofemoral angle, were measured. This way, the deformity is isolated to a particular anatomical site. Furthermore, the sample size calculation on the basis of suitable statistical parameters is the additional strength of the study design. However, this study has some limitations. The cross-section prevents us from establishing causality. We can only report an association, and not that vitamin D deficiency causes a change in LDFA. We didn't account for potential confounding factors such as BMI, which has a complicated and controversial relationship with vitamin D levels.[20, 21] Also, we didn't measure dietary intake of calcium and phosphorus, which may have independent effects on bone health and deformity. The study was carried out at one tertiary care centre and there may have been selection bias because the children presenting here may represent more severe cases. Finally, we did not follow up the children after vitamin D supplementation to evaluate the effect on their angle of joint orientation over time. Future research should be prospective and longitudinal and involve a larger and more diverse population. A randomized controlled trial looking at the effect of vitamin D supplementation on the progression or correction of LDFA in deficient children would provide the highest level of evidence.

CONCLUSION

Our study shows a high frequency (63.0%) of vitamin D deficiency in children with lower limb angular deformities from Khyber Pakhtunkhwa, Pakistan. The results indicate that this deficiency is not related to what happens to the proximal tibia, but rather is related to specific changes in the distal femur as measured by the LDFA. This supports the potential susceptibility of the distal femoral physis to the consequences of vitamin D deficiency. Clinicians in this part of the world and in similar circumstances must have a high index of suspicion for vitamin D deficiency among children with limb deformations and should consider screening and supplementation as part of their management protocol. Early diagnosis and treatment of deficiency may help reduce the risk for particular significant angular deformities requiring surgical intervention. Further research, including longitudinal interventional studies, is needed to confirm these findings and assess the impact of vitamin D supplementation on the natural history of alignment of the lower limbs in children.

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Conflicts of Interest: NIL

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