Acta Medica Alanya

RESEARCH ARTICLE

ARAŞTIRMA

Acta Medica Alanya

2024;8(1): 65-71

DOI: 10.30565/medalanya.1452540

# The Assessment of Bone Metabolism Parameters in Paediatric patients with Genu varum and Genu valgus deformities

## Genu varum ve genu valgus deformitesi olan pediatrik hastalarda kemik metabolizmasi parametrelerinin değerlendirilmesi

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## ABSTRACT

**Aim:** There are a limited number of studies in the literature explaining the relationship between bone metabolism parameters such as vitamin D, calcium (Ca), parathormone (PTH), magnesium (Mg), and alkaline phosphatase (ALP) and pediatric lower extremity coronal plane deformities.This study aimed to examine the impact of bone metabolism parameters on the development of genu varum or genu valgus deformities.
**Methods:** 45 patients with genu varum and genu valgus whose vitamin D, Ca, PTH, Mg and ALP parameters were evaluated in our polyclinic were included in the study.
Results: 44 (97.8%) of the patients were bilateral and one (2.2%) was unilateral. The mean age of patients with genu varum (4.3±4.8) was significantly lower than that of patients with genu valgus (11.9±4.1) (p<0.001). Ca values were normal in 44 (97.8%), vitamin D in 23 (51.1%), PTH in 33 (73.3%), ALP in 2 (4.4%) and Mg in 43 (95.6%) patients. 3% (6.7) of the patients had comorbidities. 2 of these (66.7%) were rickets.
**Conclusion:** The study shows that ALP can be used as a screening test especially in the coming years. In addition, although there are no sufficient incidence and prevalence studies in the literature, we can say that genu varum is seen more frequently and mostly bilaterally than genu valgus.It is not uncommon for rickets to accompany lower extremity coronal deformities in children. In addition, McCune-Albright Syndrome (MAS) may be accompanied not only by fibrous dysplasia (FD) but also by bilateral genu valgum deformity.

Keywords: Genu varum; genu valgus; bone metabolism parameters.

## ÖZ

**Amaç:** Literatürde D vitamini, kalsiyum (Ca), parathormon (PTH), magnezyum (Mg) ve alkalen fosfataz (ALP) gibi kemik metabolizması parametreleri ile pediatrik alt ektremite koronal plan deformiteleri arasındaki ilişkiyi açıklayan sınırlı sayıda çalışma mevcuttur. Bu çalışmanın amacı, kemik metabolizması parametrelerinin genu varum veya genu valgus deformitelerinin oluşumundaki rolünü araştırmaktır.
**Yöntemler:** Polikliniğimizde D vitamini, Ca, PTH, Mg ve ALP parametreleri değerlendirilen 45 genu varum ve genu valguslu hasta retrospektif olarak çalışmaya dahil edildi.
**Bulgular:** Hastaların 44'ü (%97.8) bilateral, biri (%2.2) unilateral idi. Genu varumlu hastaların yaş ortalaması (4.3±4.8) genu valguslu hastalara (11.9±4.1) göre anlamlı derecede düşüktü (p<0.001). Ca değerleri 44 (%97,8), D vitamini 23 (%51,1), PTH 33 (%73,3), ALP 2 (%4,4) ve Mg 43 (%95,6) hastada normaldi. Hastaların 3'ünde (%6,7) ek patoloji vardı. Bunların 2'si (%66,7) raşitizmdi.
**Sonuç:** Çalışma, ALP'nin özellikle önümüzdeki yıllarda bir tarama testi olarak kullanılabileceğini göstermektedir. Ayrıca literatürde yeterli insidans ve prevalans çalışması olmamakla birlikte genu varumun genu valgusa göre daha sık ve çoğunlukla bilateral olarak görüldüğünü söyleyebiliriz. Riketsin çocuk alt ekstremite koronal deformitelerine eşlik etmesi nadir değildir. Ayrıca McCune-Albright Syndrome (MAS) sendorumuna sadece fibröz displazi (FD) değil bilateral genu valgum deformitesi eşlik edebilir.

Anahtar Kelimeler: Genu varum; genu valgus; kemik metabolizması parametreleri.

Received: 15/03/2024 Accepted: 23/04/2024 Published (Online): 30/04/2024

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To cited: Kürüm H, Demir Ş, Key S. The assessment of bone metabolism parameters in paediatric patients with genu varum and genu valgus deformities. Acta Med. Alanya 2024;8(1): 65-71 DOI: 10.30565/medalanya.1452540

## Introduction

Coronal plane angulations of the lower extremities are common in children and are usually physiological. Angular deformities of the lower extremity in the coronal plane have several causes, including abnormal physiological angulation, infection, trauma, skeletal dysplasia, and metabolic disease [1].

Genu varum is the presence of the tibiofemoral axis of the knee joint in the varus, which is normally in 0-6 degree valgus radiographically [2] (figure 1).

Figure 1. Bilateral genu varum

In common, children acquire an adult valgus alignment of 5-7° by the age of 6 years (figure 2). However, valgus may continue to progress in some [3].

Figure 2. Right genu valgum

The tibiofemoral angle (TFA), mechanical lateral distal femoral angle (mLDFA), and medial proximal tibial angle (mMPTA) are evaluated radiographically in genu varum or valgus. The lateral distal tibial angle (LDTA) should be measured. Mechanical axis deviation (MAD) can be determined by measuring the distance of the mechanical axis from the centre of the knee in millimetres. However, these measurements may not provide accurate results in young patients with deformities and additional evaluations may be required [4].

While evaluating children with genu varum or valgus, bone metabolism parameters should be questioned along with radiographic measurements. Especially vitamin D has an important place in bone metabolism. The enzyme that has a key role in vitamin D synthesis is 1-α-hydroxylase. PTH and Ca are effective in the regulation of this enzyme activity [5].

There are studies showing that insufficient Mg intake increases bone resorption and decreases bone mineral density [6].

In the age group where bone development continues and in cases requiring bone repair, there is an increase in bone ALP activity. Pathologically, primary and secondary hyperparathyroidism, hypo- and hyperthyroidism, primary bone sarcomas and bone metastases are the conditions that increase bone ALP activity the most [7].

Previous studies have established a correlation between vitamin D, Ca, PTH, Mg, and ALP levels and bone metabolism. The significance of these values in various bone disorders has been underscored. Nevertheless, there is a limited number of studies explaining the role of bone metabolism values in the development of lower extremity coronal deformity. In this study, the relationship between serum vitamin D, Ca, PTH, Mg and ALP parameters and deformity development was investigated in children with genu varum and genu valgus admitted to our hospital.

## Materials and Methods

A total of 45 patients aged between 18 months and 18 years with genu varum or genu valgus deformity, admitted to the hospital between 2010-2019, years were retrospectively analyzed. All imaging and medical records were extracted from electronic patient records (Picture Archiving and

Communication System—PACS software) in our hospital. Approval for the study was given by the local Ethics Committee (2021/01-04). Data collection and evaluation were done in accordance with the Declaration of Helsinki. All patients were informed about the treatment and their written consent was obtained.

**Inclusion criteria**

Eligible patients (those with a minimum follow-up of 6 months, under the age of 18, alive at the time of the study, and can be reached through the contact information in the patient file) with genu varum or genu valgus deformity admitted to our outpatient clinic were evaluated. For this purpose , we utilized files, PACS system X-rays, ortorontgenograms, as well as previously analysed serum Ca, vitamin D, PTH, ALP, and Mg values of persons who were admitted to our hospital from October 2010 to November 2019.

**Exclusion criteria**

Paediatric patients who were inability to stand, with or without support, were excluded from the study due to the incorrect results in X-ray measurements. Furthermore, paediatric patients aged 0-18 months with physiological genu varum and individuals who did not participate in the evaluations 6 months after the initial examination were also excluded from the study.

**Diagnosis**

Patient diagnoses were determined with the help of history, physical examination findings, laboratory parameters and radiological imaging. In the physical examination of the patients, whether there was gait disturbance, genu varum or genu valgus appearance was determined and recorded. In children older than 7 years of age, direct radiography and ortorontgenogram (figure 3) radiography techniques were used as radiologic imaging.

**Radiological evaluation**

A diagnosis of genu varum and young valgum was made on the ortorontgenogram. The development of coronal deformity of the lower extremity was evaluated by the average of the MDA values on both sides. Genu varum was defined as an MDA value of at least 11 degrees. Genu valgum was diagnosed as mTFA of 4 degrees or more and the mechanical axis falling lateral to the tibial spine (zones 2 and 3) [8] (figure 3)

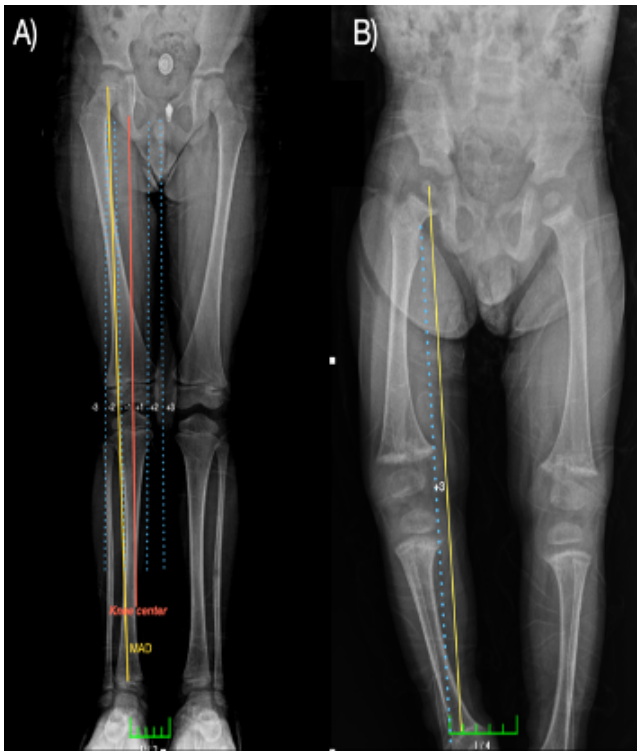


Figure 3. A) Ortorontgenogram image of the right knee of a patient with genu valgum where the mechanical axis deviation (MAD) passes from zone 2. B) Passing of MAD through zone 3 in the knee with genu varum.

**Laboratory Measurements**

Blood samples were collected from all patients by antecubital venous access using anticoagulant tubes containing EDTA (Ethylenediaminetetraacetic acid).The serum vitamin D, serum Ca, PTH, ALP, Mg values and other routine biochemical tests were performed using an automated analyser (Roche Diagnostic Modular Systems, Rotkreuz, Switzerland). The EDTA anticoagulated blood samples were collected after a 20-minute rest in the morning, stored at 4°C, and analyzed within 30 minutes after sample collection using the Sysmex K-1000 automated analyser (Sysmex, Caribbean, Latin America). The reference range for vitamin D is 25-70 ng/ml, for serum Ca it is 8.5-10.8 mg/dL, for PTH it is 15-65 pg × 109/L, for ALP it is 30-300 U/L and for Mg it is 1.7-2.7 mg/dL.

**Statistical Analysis**

While evaluating the findings obtained in the study, SPSS (Statistics Package for Social

Sciences) Windows 22.0 was used for statistical analysis. Chi-square analysis was used to compare categorical data. Data were presented as mean±standard deviation, number and percentage. Whether the measurement data are normally distributed was tested with the Shapiro-Wilk test. Student t-test was used to compare the normally distributed pairwise measurement data. Statistical significance was evaluated at the p<0.05 level.

## Results

A total of 45 patients, 20 (44.4%) females and 25 (55.6%) males, were included in the study. Genu varum was detected in 36 (80%) and genu valgus in 9 (20%) patients included in the study. There was bilateral involvement in 44 patients (97.8%) and left-sided involvement in 1 patient (2.2%) with genu valgum. Only 3 (6.7%) of these patients had an comorbidity. Of these, 2 (66.7%) had rickets and 1 (33.3%) had MAS (Table 1).

Table 1. Patients' demographic characteristics.

| | | | Total (n=45) |
|---|---|---|---|
| Gender | Female | n(%) | 20 (44.4%) |
| Age (year) | | | 5.8±5.2 |
| Deformity type | Genu Varum | n(%) | 36 (80%) |
| | Genu Valgus | | 9 (20.%) |
| Side | Bilateral | n(%) | 44 (97.8%) |
| | Left | | 1 (2.2%) |
| Comorbidity | Present | n(%) | 3 (6.7%) |
| | Comorbidity type | | 2 (66.7%) |
| | | | 1 (33.3%) |
| Ca(mg/dl) | | mean±SD | 9.6±0.7 |
| D vitamin(mcg/L) | | | 19.7±12.3 |
| PTH (pg/mL) | | | 99.8±141.6 |
| ALP(U/L) | | | 361.5±259.4 |
| Mg(mg/dl) | | | 2.1±0.3 |

Data are expressed as mean±standard deviation (SD) and number (n) (%)

The mean age of patients diagnosed with genu varum (4.3±4.8) was significantly lower than the mean age (11.9±4.1) of patients diagnosed with genu valgus (p<0.001). Bilaterality was observed in 35 (97.2%) of those diagnosed with genu varum and in 9 (100%) of those diagnosed with genu valgus, with no significant difference observed in terms of the side according to the diagnosis (p=0.999). Comorbidity was observed in 1 (2.8%) of those diagnosed with genu varum and in 2 (22.2%) of those diagnosed with genu valgus. There was no significant difference in terms of the presence of comorbidity according to the diagnosis (p=0.097) (Table 2).

Table 2. Comparison of the patients' age, side and comorbidity by diagnosis.

| | | | Genu Varum (n=36) | Genu Valgus (n=9) | p |
|---|---|---|---|---|---|
| Age (year) | | mean±SD | 4.3±4.8 | 11.9 ±4.1 | <0.001 |
| Side | Bilateral | n (%) | 35 (97.2%) | 9 (100%) | 0,999 |
| | Left | | 1 (2.8%) | - | |
| Comorbidity | Present | | 1 (2.8%) | 2 (22.2) | 0,097 |
| | Absent | | 35 (97.2) | 7 (77.8) | |
| Ca(mg/dl) | | mean±SD | 9.6±0.5 | 9.3 ±1.1 | 0.180 |
| D vitamin (mcg/L) | | | 20.7 ±13.3 | 15.9 ±6.5 | 0.300 |
| PTH(pg/mL) | | | 104.9 ±152.1 | 79.4 ±92.0 | 0.634 |
| ALP(U/L) | | | 352.4 ±238.1 | 397.8 ±346.6 | 0.644 |
| Mg(mg/dl) | | | 2.1 ±0.3 | 1.9 ±0.2 | 0.173 |

Data are expressed as mean±standard deviation (SD) and number (n) (%)

Vitamin D level was normal in 23 (51.1%) and low in 22 (48.9%) individuals. Vitamin D levels were found to be low in 15 (41.7%) individuals with genu varum and 7 (77.8%) individuals with genu valgum (p<0.071). ALP level was found to be elevated in 43 (95.6%) and normal in 2 (4.4%) individuals. ALP levels were elevated in all individuals with genu valgum deformity and in 34 (94.4%) of those with genu varum deformity (p<0.469). Ca, PTH and Mg levels between individuals are given in Table 3.

## Discussion

While bone metabolism aspects perform an important role in the development of juvenile lower extremity coronal plane deformities, paediatric individuals having genu varum and valgum deformity are only followed up in orthopaedics or treated by surgery in cases of deformity progression. However, coronal plane deformities have been associated with many conditions such as rickets [9], genetics, race [10], trauma

and metabolic disease [1] in previous studies. This study established a correlation between bone metabolism parameters and deformities of the lower extremity in the coronal plane. In the study, rickets and MAS were the most frequently observed diseases with coronal plane deformities. Furthermore, the study found that 22 (48.9%) of the patients had a low level of vitamin D. This low vitamin D level was identified as the most significant bone metabolism parameter linked to genu varum and genu valgum deformities.

Table 3. The category of the patient's blood values

| | | Total | Genu Varum | Genu Valgum | p |
|---|---|---|---|---|---|
| Ca | Low | 1 (2.2%) | - | 1 (11.1%) | 0.200 |
| | Normal | 44 (97.8%) | 36 (100%) | 8 (88.9%) | |
| D vitamin | Low | 22 (48.9%) | 15 (41.7%) | 7 (77.8%) | 0.071 |
| | Normal | 23 (51.1%) | 21 (58.3%) | 2 (22.2%) | |
| PTH | Low | 3 (6.7%) | 3 (8.3%) | - | 0.668 |
| | Normal | 33 (73.3%) | 26 (72.2%) | 7 (77.8%) | |
| | High | 9 (20%) | 7 (19.4%) | 2 (22.2%) | |
| ALP | Normal | 2 (4.4%) | 2 (5.6%) | - | 0.469 |
| | High | 43 (95.6%) | 34 (94.4%) | 9 (100%) | |
| Mg | Low | 1 (2.2%) | - | 1 (11.1%) | 0.364 |
| | Normal | 43 (95.6%) | 35 (97.2%) | 8 (88.9%) | |
| | High | 1 (2.2%) | 1 (2.8%) | - | |

Generally, from birth to 18 months of age, there is a normal physiological "varus" state in the knee, in which knee varus stays in normal ranges. After the age of two, children normally have increased valgus in their knees, often continuing into adolescence [11]. There are also studies reporting high rates of overweight children [12] and in some races [1]. In the study, it was found that the most of the patients diagnosed with genu varum had genu varum deformity secondary to physiological genu varum and the mean age of the patients diagnosed with genu varum (4.3±4.8) was significantly lower than the mean age of the patients diagnosed with genu valgus (11.9±4.1) ($p< 0.001$). Genu varum was detected in 36 (80%) and genu valgus in 9 (20%) patients included in the study. 44 (97.8%) of the patients had bilateral and 1 (2.2%) had left side involvement. In this study, we concluded that genu varum is more common than genu valgus and is usually bilateral.

Vitamin D has an important place in bone metabolism. Rickets is seen in vitamin D deficiency. Rickets occurs as a result of decreased cartilage and bone mineralization. Rickets is the most common disease among non-communicable conditions in children, and its incidence in our country has been reported in the range of 1.6-19% in different sources [13]. Rickets is an abnormality of the cartilage plates that affects mostly longer bones, causing poor bone development, deficient mineralization and osseous deformities such as knock knees and bow legs. A deficiency of phosphate (PO43-) or calcium ions (Ca2+) is usually a secondary finding as it is essential for normal bone regeneration and mineralization [14] Sakamoto et al. [15] reported that nutritional rickets was commonly observed in individuals with genu varum secondary to physiological genu varum. Ca value in 44 (97.8%) patients was found to be normal vitamin D value in 22 (48.9%) was found to be low in this study. İn this study, 3 (6.7%) of the patients had additional pathology. Only 2 patients had a diagnosis of rickets (66.7%) (Table 1). From the results of this study, it can be concluded that patients with low levels of vitamin D and high levels of ALP are likely to have nutritional rickets. Furthermore, it can be concluded that rickets are commonly associated with genu varum and valgus. As a result, relying on solely orthopaedic treatments is inadequate for the treatment of these deformities necessitating the inclusion of paediatric endocrinology.

Although serum bone ALP levels increase in infancy in both sexes, they tend to increase in proportion to growth rate until puberty [16]. Topak et al. [17] reported that there was no difference in ALP levels between individuals with developmental hip dysplasia and normal individuals. Although ALP is not specifically increased in toddlers solely because of an abnormality of bone metabolism, ALP is thought to be useful for screening for nutritional rickets [18]. Furthermore, recent research has shown a correlation between elevated ALP levels and the worsening of genu varum [19]. Similarly, the ALP level was found to be higher in all paediatric patients in this study. In addition, patients with

severe deformity and additional pathology had higher ALP values compared to others. Therefore, the study suggests that ALP may be used as a future screening test for paediatric lower extremity coronal plane curvatures.

Hyperparathyroidism caused by vitamin D insufficiency is frequently observed in MAS syndrome and can lead to the progression of bone abnormalities [20]. MAS is usually accompanied by fibrous dysplasia which may show monostotic and polyostotic course [21]. Initially, Gorgolini et al. [22] established an association between genu valgum deformity and MAS. In this study, the patient with MAS had bilateral genu valgum deformity.

Kobayashi et al. [23] reported that a low Mg diet reduces the elastic modulus of rat femurs and weakens the femur. Mg deficiency can affect bone directly (by reducing bone stiffness, increasing osteoclasts and reducing osteoblasts) and indirectly (by interacting with PTH and vit D, promoting inflammation/oxidative stress and subsequent bone loss) [24] Shinohara et al. [25] associated various bone metabolic biomarkers such as ALP and Mg with genu varum deformity. In our study, Mg value was normal in 43 (95.6%) of the patients and magnesium levels were not found to be effective in the formation of genu varum or genu valgus. However, studies with larger samples are needed to explain the effect of magnesium on these deformities.

The limitation of the study is that it is a retrospective review without comparing different methods and treatment strategies. Also, long-term follow-up of patients was not performed.

## Conclusion

We suggest that bone metabolism parameters should be investigated together with physical examination and radiological evaluation when evaluating paediatric patients with genu varum or genu valgus deformity in the orthopaedic outpatient clinic. The study shows that ALP can be used as a screening test especially in the coming years. In addition, although there are not enough incidence and prevalence studies in the literature, we can say that genu varum is observed more frequently than genu valgus and mostly bilaterally. Rickets frequently occur alongside coronal abnormalities of the lower extremities in children. Furthermore, MAS may be accompanied not only by FD but also by bilateral genu valgum deformity.

**Conflict of Interest:** The authors declare no conflict of interest related to this article.

**Ethics Committee Approval:** In this study, national and international ethical rules are observed. The study protocol was approved by the Fırat University Hospital Human Subject Research Ethics Committee (2021/01-04).

**Financial Disclosure:** The authors declared that this study has received no financial support.

**ORCID and Author contribution:** **H.K. (0000-0001-9352-2593):** Concept, Design, Supervision, Writing and Critical Review. **Ş.D. (0000-0002-1709-3851):** Literature Search, Resources, analysis and/or interpretation. **S.K. (0000-0003-3620-936X):** Materials, Data Collection and/or Processing, Writing Manuscript.

**Acknowledgments:** We would like to thank Murat Kürüm for his contribution to the conduct of the study. This study is based on the specialist thesis entitled "Evaluation of serum calcium, parathormone, vitamin D, alkaline phosphatase, growth hormone, magnesium parameters in pediatric patients with genu varum and valgus deformity" which was completed in 2021(Specialist thesis, Fırat University, Elazığ, Turkey, 2021).

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