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Original Research Article

# Vitamin D Status and Biochemical Markers in Children with Rickets and their Correlation with Growth Parameters

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**Abstract:**

**Introduction:** Vitamin D deficiency is a leading cause of nutritional rickets in children, resulting in impaired bone mineralization. Diagnosis typically relies on clinical, biochemical, and radiological findings, but their prognostic and treatment-evaluation value remain limited. This study explores the relationship between vitamin D status, biochemical markers, and clinical/radiological outcomes in children with rickets following supplementation therapy**.**

**Objectives**: To assess the effectiveness of vitamin D and calcium supplementation on the clinical, biochemical, and radiological parameters in children diagnosed with nutritional rickets.

**Materials and Methods:** A total of 216 pediatric patients (ages 6 months–18 years) with primary rickets were enrolled from a tertiary care hospital. Age-specific vitamin D and calcium regimens were administered. Clinical signs, serum levels of calcium, phosphate, alkaline phosphatase (ALP), and vitamin D, along with radiological changes, were assessed at baseline and at 6, 12, 18, and 24 weeks. Data were analyzed using Chi-square and ANOVA tests ($p < 0.05$ considered significant).

**Results:** Most participants were male (117), from rural (68%) and low socioeconomic (58.3%) backgrounds. Common findings included bowed legs (70), widened wrists (62), and difficulty walking (63). Radiological signs like cupping and fraying were seen in 156 cases. Significant biochemical improvements were observed by 18 weeks. ALP levels declined from a mean of 653 IU/L to 115.3 IU/L by week 24. Clinical, radiological, and biochemical recovery was observed in 93.3%, 85.6%, and 98.3% of cases, respectively.

**Conclusion:** Vitamin D and calcium supplementation significantly improved clinical, biochemical, and radiological outcomes. ALP levels strongly correlated with disease severity, underscoring the importance of a multifactorial diagnostic and evaluative approach.

**Keywords-** Rickets, Vitamin D, Biochemical Markers, Radiological Markers.

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## Introduction

Vitamin D deficiency is the leading cause of rickets. Rickets develops in children when mineralization of the bone matrix becomes inefficient. Diagnosis requires evaluating clinical features, conducting biochemical tests, and examining radiological findings [1,2]. The clinical response to treatment further confirms these test results. Anticipated factors associated with rickets include exclusive breastfeeding without vitamin D supplementation, limited sunlight exposure, and poor lifestyle factors such as inadequate diet and inadequate housing [3,4,5].

As per the osteology the visible symptoms associated with rickets are widening of the wrist bone, bossing of the skull, bowed-shaped legs, widening of the ankles, and less than optimum growth of the child [6]. The rickets that is associated with nutritional deficiency has the biochemical characteristics of hyperparathyroidism, decreased level of serum Calcium and phosphate, along with elevated levels of the alkaline phosphatase and decreased level of serum 25 OHD [7]. The rickets is evident in the radiographic images along the growth plate of long bones. In the region of the growth plate, the cartilaginous expansion of the bones occurs without the mineralization of the bone. The thickness of the longitudinal junction of mineralizing metaphysis increases. This results in an increase in the gap between epiphysis and metaphysis due to a partial or completely invisible shadow region where provisional calcification occurs [8,9].

Although the radiological and clinical parameters of rickets are evident, they are not regular and distinct in terms of the prognosis of the rickets. Grading the severity of the disease solely on the basis of the radiographic and clinical parameters is not possible. Similarly, the treatment response of the rickets cannot be assessed [10]. The study of Vitamin D status and biochemical markers in children with rickets and its correlation with growth parameters aims to understand the severity of rickets while correlating it with biochemical markers and vitamin D deficiency.

## Materials and Methods

**Participants:** The pediatric patients between the ages of 6 months and 18 years presenting at the outpatient department at ABC tertiary care hospital with the symptoms of delayed milestones, diarrhea, respiratory tract infection, and increased incidence of bone fractures were considered for this study. The patients with primary rickets were only included in the study. Those with secondary rickets or any other congenital disorder or comorbidities associated with rickets were not included in the study. In total, 216 patients participated in this study.

**Intervention:** Children participating in this study primarily had vitamin D deficiency. They were treated with a calcium and vitamin D supplement regimen according to their age group. Patients in the age group of 6 months to 12 months were given a single dose of 50000 IU of vitamin D A daily dose was given for 12 weeks of 2000 IU of vitamin D, and a maintenance dose of 400 IU of vitamin D was given for 24 weeks. Along with it, they were given 300 to 400 mg daily.

Patients between the age group of 1 year to 12 years were given a single dose of 150000 IU of vitamin D. A Daily dose of 3000 to 6000 IU of vitamin D for 12 weeks, 600 IU of vitamin D dose for 24 weeks as a maintenance dose, along with 600-1200 mg of calcium daily. Patients who were above 12 years were given 300000 IU of vitamin D as a single dose. Followed by a daily dose of 6000 IU for 12 weeks. Then maintenance dose of 600 IU of vitamin D for 24 weeks, along with 1300-1500 mg of calcium daily. Table no. 1 illustrates the intervention for the treatment of vitamin D and calcium.

**Table 1: Supplements given to the patients**

| Sr. No. | Age-group | Single dose | Daily dose | Maintenance dose | Calcium daily doe |
|---|---|---|---|---|---|
| 1 | 6 months to 12 months | 50000 IU of vitamin D | 12 weeks of 2000 IU of vitamin D | 24 weeks of maintenance dose of 400 IU of vitamin D | 300 to 400 mg |
| 2 | 1 year to 12 years | 150000 IU of vitamin D | 12 weeks of 3000-6000 IU of vitamin D | 24 weeks of maintenance dose of 600 IU of vitamin D | 600-1200 mg |
| 3 | Above 12 years | 300000 IU of vitamin D | 12 weeks of 6000 IU of vitamin D | 24 weeks of maintenance dose of 600 IU | 1300-1500 mg |

During the follow-ups, their serum levels of biochemical markers of rickets, radiological parameters, and growth parameters were assessed. The clinical parameters included craniotabes in the skull, Harrison's sulcus, that is, the indentation of the rib cage, widened wrist and knee bones, rachitic rosary in the thorax region, swelling and tenderness of the joints, bow-shaped legs, pectus carinatum of the sternum, and difficulty in walking.

The following radiological parameters were assessed: the enlargement of the epiphyseal region, occurrence of splaying, cupping, and fraying of the metaphysis region, rachitic rosary, the calcification zone of the bone is lost, occurrence of pathological fractures, thickening of the periosteal region, and the abnormal hip bone angle of the femur. The biochemical factors included the serum levels of calcium, vitamin D, phosphate, and Alkaline phosphatase. The patients were followed up at 6 weeks, 12 weeks, 18 weeks, and 24 weeks from the diagnosis of the disease.

**Statistical analysis:** The data obtained from each factor of the parameters were statistically compared using the Chi-square and ANOVA tests. The observations reported during each follow-up were tabulated and statistically compared using Pie charts. If the p-value was found to be less than 0.05, then the correlation was considered to be significant.

## Results

Among the total of 216 pediatric patients, 117 were male and 99 were female. From the total population, 28.05% belonged to the age group of 6 months to 12 months. 34.23% were among the age group of 1 to 6 years. 26.95% were from the age group of 6 to 12 years, and 10.77% were from the age group of 12 to

18 years. Patients belonging to rural areas were 68%, while those from urban areas were 42%. While considering the socioeconomic status of the patients, it was found that 126 cases belonged to patients with low socioeconomic status, whereas patients with high socioeconomic status were 15, and those with middle-class socioeconomic status were 55. Comparing the demographics of the population with the gender, it was found that male patients from rural areas were more prone to rickets compared to females.

The following were the clinical parameters found in the patients. It was found that 10 cases had craniotabes in the skull,14 had Harrison sulci of the rib cage, and the widened wrist and knees were observed in 62 and 36 patients, respectively. The lower limb was bowed in 70 patients, there were 62 patients who had knock knee, deformity such as pigeon chest was found in 4 patients. 63 patients reported difficulty in walking and tenderness as well as swelling of the joints. Other than the deformation of the bones, symptoms of rickets, that is malnutrition, potbelly, defects in the dentition, and weak muscles were also reported in the patients. Table no. 2 gives the details of the osseous deformity and clinical parameters along with the response to the treatment in 6 weeks, 12 weeks, 18 weeks, and 24 weeks.

**Table 2: Clinical parameters associated with rickets**

| Sr. No. | Clinical parameters | Cases during diagnosis | At 6th week | At 12th week | At 18th week | At 24th week |
|---|---|---|---|---|---|---|
| 1 | Craniobates | 10 | 7 | 3 | 3 | 1 |
| 2 | Harrison sulcus | 14 | 12 | 13 | 10 | 5 |
| 3 | Widened wrist | 62 | 63 | 70 | 78 | 79 |
| 4 | Widened ankles | 36 | 38 | 40 | 42 | 42 |
| 5 | Bowed lower limb | 70 | 65 | 66 | 55 | 50 |
| 6 | Knock knee | 62 | 61 | 52 | 41 | 36 |
| 7 | Pigeon chest | 4 | 2 | 1 | 0 | 0 |
| 8 | Difficulty in walking | 63 | 54 | 43 | 31 | 20 |

The first response of the treatment observed in the patients was pain and tenderness of the bone, while the last response of the treatment was correction of lower limb deformity. It was observed that the normal range of the parameters was achieved within 4-6 weeks, but some people did not respond at all, even though they received 3 lac to 6 lac IU of vitamin D. The patients for whom lower limb deformity was not corrected underwent corrective osteotomy.

The radiological parameters found in the study population were as follows: 68 cases of enlargement in the epiphyseal region, 156 cases had cupping, fraying, and splaying of the bones. 44 cases of the rachitic rosary in the thorax region, 114 cases of loss of provisional zone of calcification, 82 cases of periostal thickening, and 5 cases of pathological fractures. In the majority of cases, 85.5% of the cases demonstrated the symptoms of healing in radiological parameters, while the rest of the patients did not show improvement after the treatment. Table no. 3 demonstrated the radiological symptoms presented and the improvement associated with it after every 6 weeks.

**Table 3: Radiological findings of the patients**

| Sr. No. | Radiological markers | Cases during diagnosis | At 6th week | At 12th week | At 18th week | At 24th week |
|---|---|---|---|---|---|---|
| 1 | Enlargement in the epiphyseal region | 68 | 54 | 35 | 21 | 10 |
| 2 | Splaying, fraying & cupping | 156 | 123 | 95 | 75 | 50 |
| 3 | Rosary due to rickets | 44 | 33 | 51 | 22 | 15 |
| 4 | Loss in the zone of calcification | 114 | 105 | 88 | 63 | 41 |
| 5 | Thickening of the periosteal region | 82 | 56 | 23 | 12 | 1 |
| 6 | Pathological fractures | 5 | 3 | 1 | 0 | 0 |
| 7 | Coxa vara/coxa valga | 0 | 0 | 0 | 0 | 0 |

The findings of this study supported the fact that the level of vitamin D was correlated with the severity of rickets. The 44 cases of rickets with extremely low levels of vitamin D, that is, below 30nmol/l, had more radiological markers that started healing with treatment. Elevated levels of ALP were correlated with the severity of rickets. In all, 4 biochemical parameters were tested in this study: the level of serum calcium, serum phosphate levels, serum ALP levels, and serum levels of vitamin D. It was

observed that at presentation, the mean of the serum calcium levels of the population was 6.09 mg/dl, whereas the serum phosphate level mean was 3.98mg/dl. These values improved significantly after 6 weeks of treatment. It increased to the level of normal values, within the 18th week, it was in the normal range, that is, 8mg/dl for calcium and 5.05 mg/dl for phosphate.

Similarly, the mean values of the levels of ALP during the presentation were significantly higher than that of 653 IU/L. It started improving after weeks of treatment, and it was observed that the fall in the levels of ALP was gradual. By the 24th week of treatment, the levels of ALP reached their normal value, that is, 115.3 IU/dl. Table no. 4 illustrates the biochemical at presentation and during the follow-ups of 6 weeks, 12 weeks, 18 weeks, and 24th weeks.

**Table 4: Findings of the biochemical parameters**

| Sr No. | Biochemical parameters | Cases during diagnosis | At $6^{th}$ week | At $12^{th}$ week | At $18^{th}$ week | At $24^{th}$ week |
|---|---|---|---|---|---|---|
| 1 | Alkaline phosphatase level (IU/l) | 652±242 | 584±202 | 447±98 | 361±102 | 115.3±46 |
| 2 | Calcium mg/dl | 6.09±0.1 | 6.5±0.3 | 7.1±0.6 | 8±0.5 | 8.5±0.3 |
| 3 | Vitamin $D_3$ (mmol /l) | 23.0±0.5 | 39.5±7.4 | 78.13±16.23 | 82.01±12.3 | 96.3±8.3 |
| 4 | Phosphate mg/dl | 3.98±0.3 | 4.0±0.2 | 4.2±0.3 | 4.8±0.5 | 5.05±0.2 |

As per the observations of the clinical parameters, 93.3% of them were resolved during the course of 24 weeks, 85.6 % of radiological parameters were resolved, and 98.3% of the biochemical parameters were resolved in 24 weeks. Figure no.2, 3 and 4 illustrates the cases resolved. Statistically, it was found that the difference in the treatment on radiological, biochemical, and clinical outcomes was significant

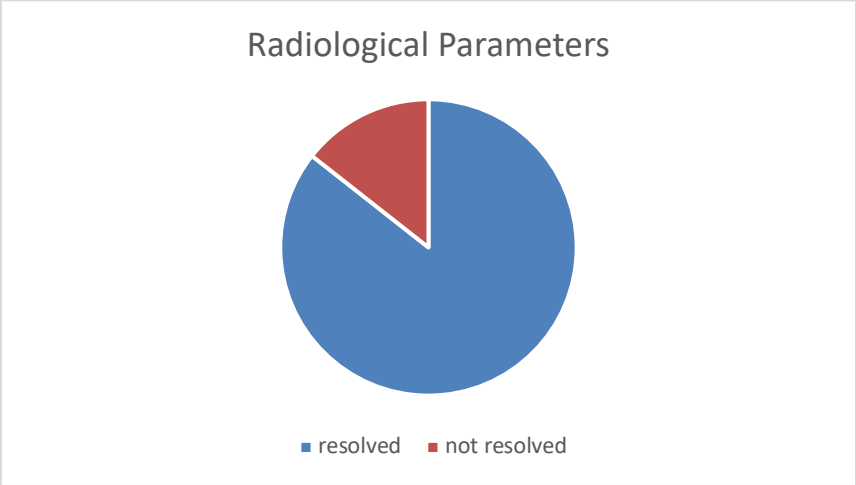


**Figure 1: Radiological parameters**

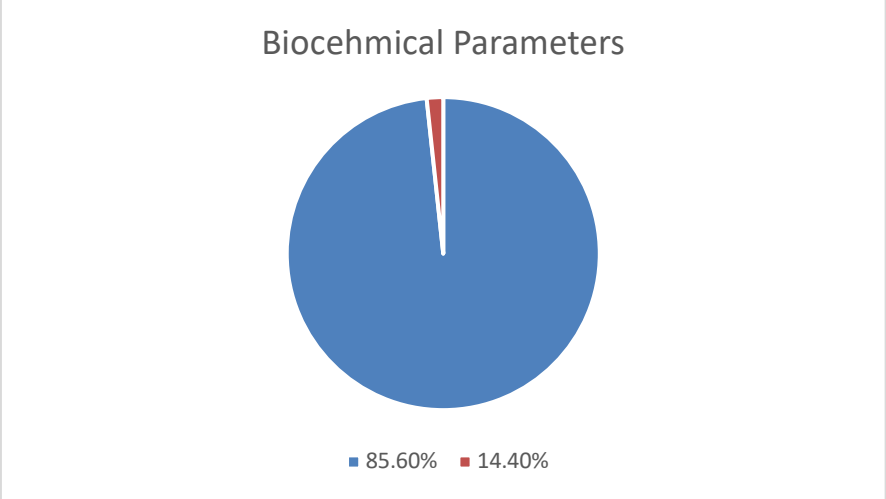


**Figure 2: Biochemical parameters**

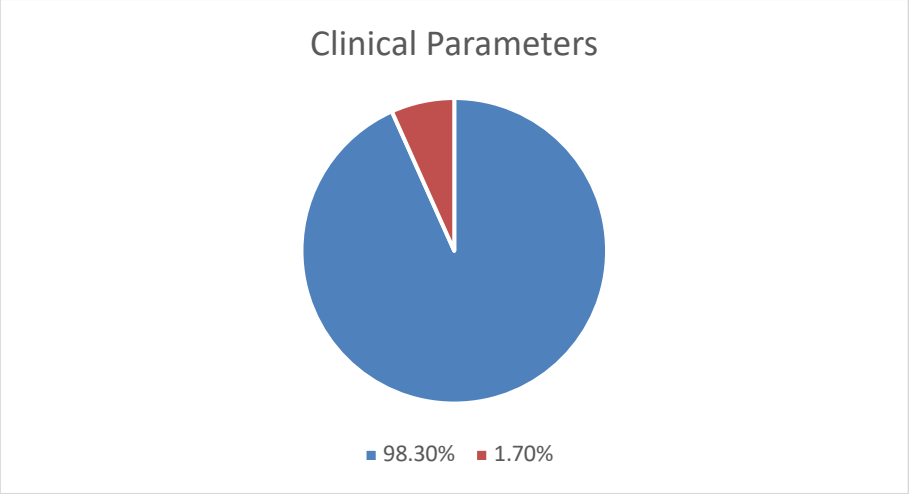


**Figure 3: Clinical parameters**

## Discussion

All around the world in the developing countries, rickets is a major health concern. The nutritional conditions of the mother and child during the newborn stage contribute significantly to rickets, including causes such as lack of supplementation of vitamin D, Lack of food rich in vitamin D, prolonged breastfeeding, and lack of exposure to sunlight. Apart from the nutritional factors, a study conducted considered the type of housing, clothing, type of food the mother was given, parity of the mother, age of complementary feeding, and duration of complementary feeding [10, 11]. It was found that these factors contributed significantly to the occurrence of rickets.

The most common clinical parameters observed in this study were Harrison sulcus, craniotabes, and tenderness in the wrist and knee. A similar study encountered a significant number of these parameters were present, and it correlated the occurrence of these parameters with the lesser availability of sunlight [12]. Yet another study found that with the increase in exposure to sunlight, the levels of vitamin D improved significantly, which contributed to a lesser occurrence of rickets [13]. Mothers who took advice from the pediatricians beforehand had fewer cases of rickets [14].

Along with the radiological parameters, it was found that biochemical parameters were significantly altered; the levels of calcium, phosphate, and vitamin D were significantly lowered. On the other hand, the levels of ALP were significantly high, indicating the severity of the rickets. The results of the biochemical parameters were consistent with the findings of the other study.

Radiological parameters showed the appearance of the healing lines in the region of the epiphysis, and mineralization of that region improved significantly. A study conducted with a similar objective also found that with treatment, the healing lines were visible in the epiphysis region. 46.3% of the radiological parameters improved within 12 weeks, and around 88.24% improved at the 24th week of the treatment [15, 16]. The majority of the radiological parameters, that is, 88.24% of them, resolved within the mean time period of 5 months.

The severity of the rickets also had a significant influence on healing. The severe cases required more time to show radiological healing. The majority of the patient population responded positively to the treatment. Supplementation with vitamin D and calcium not only improved the serum calcium levels and vitamin D levels but also significantly improved the levels of ALP. The results were consistent with the studies conducted with a similar aim, which reported consistent findings [17].

**Limitation:** The sample size of the population included in this study is limited to confirm the findings of the study; further investigation is required on a larger sample size of the population.

## Conclusion

The study found that the radiological, clinical, and biochemical parameters improved significantly with the supplementation of vitamin D and calcium. The severity of the rickets in the study population was indicated by the levels of ALP. The three parameters are required to diagnose, assess the prognosis, and evaluate the outcomes of the treatment of rickets.

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