## Original Article

# Vitamin D Level in Patients with Juvenile Idiopathic Arthritis : A Study from a Tertiary Care Institute of Kolkata

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**Introduction :** Vitamin D insufficiency in children is a major public health concern Worldwide. Many studies have been published on Vitamin D deficiency and its affect in children and adolescents. Vitamin D has an impact on calcium metabolism as well as in bone mineralization. This vitamin serves as an immunomodulator as well. In certain studies, problems in Vitamin D metabolism have been linked to the release of proinflammatory cytokines, which restrict the development of regulatory T cells.

**General objective :** Vitamin D has been hypothesised to influence development, activity and therapy of autoimmune illnesses based on the findings of clinical and laboratory studies. We wanted to see how common vitamin D deficiency are prevalent in persons with JIA (Juvenile Idiopathic Arthritis) and the relation between Vitamin D and JIA disease activity.

**Methodology :** Study Design- Observational Cross-sectional study. Study Area- Patient suffering from JIA of any duration, attending Paediatric OPD (Out Patient Department) and IPD (In Patient Department) of College of Medicine and Sagore Dutta Hospital, Kolkata. Study population-50 patients of age 1 month - 12 years attended OPD or IPD in Pediatric department of College of Medicine and Sagore Dutta Hospital, Kolkata. Study Period- 1 year. Sample Size- 50 patients of Juvenile idiopathic arthritis.

**Analysis and Result :** We found in Less than 6 months, the mean Vit D was 22.5922, in 6 months to 3 years mean Vitamin D was 22.3863 and in More than 3 years, the mean Vitamin D was 24.1693. Difference of mean according to duration was found statistically significant (P 0.001).

**Summary and Conclusion :** Understanding the influence of genetic variations which increase the risk of development of disease and being able to identify precise goals for Vitamin D status as a potential adjunct therapy in the management of JIA will improve the quality of life of patients and family members in respect of JIA.

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***Key words* : Vitamin D, Juvenile, Idiopathic Arthritis.**

A major public health concern, Vitamin D deficiency affects millions of children and adolescents around the World. Several studies have reported Vitamin D deficiency and insufficiency during childhood. Vitamin D is known for its role in bone mineralization and calcium metabolism[1]. It also has an immuno-modulatory effect on immunity. Some studies observed that abnormalities in Vitamin D metabolism may lead to the release of proinflammatory cytokines that inhibit regulatory T cell production[2].

Childhood rheumatoid arthritis, most commonly known as Juvenile Idiopathic Arthritis (JIA), is characterized by chronic joint inflammation accompanied by swelling, pain, and movement limitations.3 There may be irreversible abnormalities in non-articular organs as well, including the eyes (as a result of iridocyclitis) or kidneys (as a result of amyloidosis), or they may result from drugs. JIA is managed with a goal to improve symptoms the quality of life (HRQL) of the patient and prevent irreversible damage[4].

Various studies have linked chronic inflammatory disorders with Vitamin D deficiency or insufficiency. Some studies have also found low levels of Vitamin D in JIA. It has been proposed that Vitamin D deficiency may play a role in JIA pathophysiology since it inactivates Th1 and Th17, both of which play a role in

***Editor's Comment :***

- Vitamin D deficiency is not uncommon in pediatric and adolescent age group. Its association with Juvenile Idiopathic Arthritis has be found.
- This article emphasised the relation and therapeutic benefits of Vitamin D in JIA children. However larger studies needed to evaluate its potential role.

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JIA pathophysiology[5]. The data on the association between serum vitamin D levels and disease activity is limited, however.

### Objective of research proposal :

***General objective —***

The possible role of Vitamin D in the pathogenesis, activity, and treatment of autoimmune disorders have been raised based on the results and observations of clinical and laboratorial studies. Our objective is to find the prevalence of Vitamin D deficiency and/or insufficiency and to investigate the relationship between Vitamin D and disease activity in patients suffering from JIA.

***Specific objective —***

We aim to accomplish the following through our study :

• To evaluate Vitamin D status in patients who have JIA and

• To correlate these findings with clinical and laboratory parameters of disease activity.

## Materials and Methods

***Study Design —*** Observational Cross-sectional study.

***Study Area —*** Patient suffering from JIA of any duration, attending Paediatric Outdoor or Indoor of College of Medicine and Sagore Dutta Hospital, Kolkata.

***Study Population —*** Approximately 50 patients of (age 1 month - 12 years) coming to Pediatric outdoor and indoor of College of Medicine and Sagore Dutta Hospital, Kolkata.

***Study Period —*** 1 year.

***Sample Size —*** 50 patient of Juvenile idiopathic arthritis

### Inclusion Criteria :

• Age between 1 month to 12-year suffering from JIA (meeting ILAR criteria) of any duration.

• Able to understand English/Bengali/Hindi.

• Absence of any other chronic diseases not related to the primary disease or its treatment.

• Absence of known hypovitaminosis D unrelated to primary disease.

### Exclusion Criteria :

• Age less than 1 month and more than 12 years.

• Known history of hypovitaminosis D unrelated to primary disease

• Not Able to understand English/Bengali/Hindi.

• Presence of other chronic comorbid medical condition.

### Study Tools :

• JADAS 27 score to assess disease activity status

• Electronic platform type weighing machine with calibration of 500 gm.

• Stadiometer with a calibration of 1 mm.

• Infantometer which has a fixed headboard and moveable footboard with a calibration of 1 mm.

• Phlebotomy equipment.

• 1ml of blood was sent for vitamin D assessment by Enzyme linked Fluorescent Assay(ELFA).

## Analysis and Results

Our study showed that the mean Vitamin D in male was 21.0690 and Mean Vitamin D in female was 25.3474. Difference of mean was statistically significant. Vitamin D levels of female patients did not follow a normal distribution. Mann-Whitney U test (U=136.5, W=367.5, p-value=0.088 two tailed) indicated that both samples did not have statistically significantly different distribution shapes as the p-value is above the critical value of 0.05. However, the observed different distribution shapes warrant further investigation, including further data collection. In Oligoarthritis, the mean Vitamin D was 21.9807 and in Polyarthritis mean Vitamin D was 23.7736. Mann-Whitney U test (U=145.0, W=265.0, p-value=0.235 two tailed) indicated that both samples did not have statistically significantly different distribution shapes as the p-value is above the critical value of 0.05. However, given the observed very different distribution shapes warrants further investigation, including further data collection.

We found in Less than 6 months, the mean Vitamin D was 22.5922, in 6 months to 3 years mean Vitamin D was 22.3863 and in More than 3 years, the mean Vitamin D was 24.1693. Difference of mean Vitamin D according to duration was statistically significant. Using Kruskal-Wallis analysis, it was examined if serum Vitamin D levels differed according to disease duration. No statistically significant differences were found between the three groups of patients (Chi square = 0.885, p =0.642, df = 2). The mean of JADAS27 (Mean±SD) of the patients was 12.0200 ± 11.30873. Vitamin D3 and JADAS correlated negatively, but this correlation statistically insignificant. According to the Spearman correlation, there was no statistically significant relationship between JADAS 27 and serum Vitamin D levels, (r = -0.012, p 0.941). No association between disease activity status of patients with JIA (Inactive, Low, Moderate and High) and Vitamin D status (Deficiency, Insufficiency and Sufficiency) was

observed, $\chi 2(6, N = 40) = 3.178$, $p = 0.786$ to patients living in urban areas (10.43).

Our study showed that the Mann-Whitney U test (U=45.0, W=73.0, p-value=0.012 two tailed) indicated that both samples have statistically significantly different distribution shapes as the p- value is below the critical value of 0.05 with mean rank in rural group much higher than urban group of patients. Kruskal-Wallis Test was conducted to examine the differences in serum Vitamin D levels according to duration of therapy. No significant differences (Chi square = 0.156, p =0.925, df = 2) were found among three group of patients. Patients receiving Vitamin D had a higher mean rank (23.28) for Serum Vitamin D levels compared to patients not receiving Vitamin D (16.74). However, Mann-Whitney U test (U=131.5, W=284.5, p-value=0.080 two tailed) indicated that both samples did not have statistically significantly different distribution shapes as the p-value is above the critical value of 0.05. However, given the observed very different distribution shapes warrants further investigation, including further data collection.

## Discussion

Soybilgic *et al* undertook a review of steroid-related osteoporosis, prevention, and treatment practises of paediatric rheumatologists in North America in 2014[6]. They discovered that the majority of paediatric rheumatologists advise kids on long-term corticosteroids to take vitamin D6. Vitamin D's significance in mediating bone health, particularly in relation to corticosteroids, has been proven. Even small dosages of corticosteroids have an effect on bone health in people with autoimmune illnesses, both short and long term. The significance of Vitamin D ininflammation and disease activity, as well as an optimal amount of Vitamin D consumption or 25(OH)D goal, has yet to be determined. The serum 25 (OH) Vitamin D level and serum phosphorus levels were shown to be considerably lower in patients compared to controls by Soumya *et al* (2014)[7]. The difference in mean serum calcium, alkaline phosphatase, and parathormone levels between the two groups was not significant. Vitamin D levels in the JIA group were 21.85 (7.29) higher than in the control group.

According to Finch *et al* (2018)[8], out of 38 studies looking at 25(OH)D levels in children with chronic arthritis, 32 (84.2%) revealed that a large number of children had inadequate (75 nmol/L) levels. The findings also suggest that children suffering from chronic arthritis have low Vitamin D levels.

When compared to patients who did not get Vitamin D, patients who received Vitamin D had a higher mean rank (23.28) for Serum Vitamin D levels (16.74). However, Mann-Whitney U test (U=131.5, W=284.5, p-value=0.080 two tailed) indicated that both samples did not have statistically significantly different distribution shapes as the p-value is above the critical value of 0.05. However, given the observed very different distribution shapes warrants further investigation, including further data collection. Peixoto D *et al*[9] (2013) have evaluated 31 females and 9 males, with a mean age of 22.3 (4-63 years) and disease duration of 14.6±12.1. In terms of vitamin D intake, they discovered that 32.5 percent had a high intake, 27.5 percent had normal readings, and 40 percent had insufficient intake. They discovered poor vitamin D levels in 75% of the patients, with insufficiency and deficiency rates of 47.5 percent and 27.5 percent, respectively. Vitamin D levels were considerably lower in JIA individuals with less sun exposure and a higher ESR. They also discovered that patients with more joint degeneration had lower vitamin D levels, however this was not statistically significant (p=0.07).

Table 1 — *Association between Disease Activity Status based on JADAS 27 score and Vitamin D status*

Disease Activity Status * Vit D status Crosstabulation

| | | Vit D status | | | Total |
|---|---|---|---|---|---|
| | | Deficiency | Insufficiency | Sufficiency | |
| Disease Activity Status : | | | | | |
| Inactive | Count | 4 | 3 | 2 | 9 |
| | % within Disease Activity Status | 44.4% | 33.3% | 22.2% | 100.0% |
| | % within Vit D status | 26.7% | 15.8% | 33.3% | 22.5% |
| | % of Total | 10.0% | 7.5% | 5.0% | 22.5% |
| Low | Count | 1 | 2 | 1 | 4 |
| | % within DiseaseA ctivity Status | 25.0% | 50.0% | 25.0% | 100.0% |
| | % within Vit D status | 6.7% | 10.5% | 16.7% | 10.0% |
| | % of Total | 2.5% | 5.0% | 2.5% | 10.0% |
| Moderate | Count | 3 | 2 | 0 | 5 |
| | % within Disease Activity Status | 60.0% | 40.0% | 0.0% | 100.0% |
| | % within Vit D status | 20.0% | 10.5% | 0.0% | 12.5% |
| | % of Total | 7.5% | 5.0% | 0.0% | 12.5% |
| High | Count | 7 | 12 | 3 | 22 |
| | % within Disease Activity Status | 31.8% | 54.5% | 13.6% | 100.0% |
| | % within Vit D status | 46.7% | 63.2% | 50.0% | 55.0% |
| | % of Total | 17.5% | 30.0% | 7.5% | 55.0% |
| Total | Count | 15 | 19 | 6 | 40 |
| | % within Disease Activity Status | 37.5% | 47.5% | 15.0% | 100.0% |
| | % within Vit D status | 100.0% | 100.0% | 100.0% | 100.0% |
| | % of Total | 37.5% | 47.5% | 15.0% | 100.0% |

A total of 154 patients (61 percent females, 88 percent non-Hispanic whites) were included in the study by Pelajo CF *et al* (2012)[10]. The average age of the participants was 10.6 years. The average 25(OH)D level in the blood was 29.2 ng/ml. Vitamin D deficiency was found in 13% of patients, whereas insufficiency was seen in 42%. The median value of JADAS-27 was 5.2. (range 0-30.7). 25(OH)D levels were not linked to JADAS-27 or its individual components in univariate or multivariate analysis. However, there was a non-significant negative connection between serum 25(OH)D levels and JADAS-27 (r=-0.29, p=0.14) in a subset analysis comprising all new onset (time from disease beginning 3 months) JIA patients (n=27). Nearly half of the patients had a deficient 25(OH)D level (20 ng/ml) in the first serum sample and a quarter had a deficient level in both tests, according to Sengler C *et al* (2018)[11]. Szymanska-Kaluza J *et al*[12] (2013) found that the concentration of 1,25(OH)2D in the serum of children with the disease was statistically significantly lower compared to the children in the control group (34.86 ±17.14 pg/ml *versus* 48.47 ±17.99 pg/ml, p = 0.0015 on average, respectively). However, 25(OH) D concentrations in both groups were similar (17.36 8.44 ng/ml on average *versus* 17.36 16.29 ng/ml on average), although lower than the recommended rate (ie, 30 ng/ml). When compared to the control group, Wang Y *et al* (2015)[13] observed that the JIA group had significantly lower serum 25(OH)D3 levels (median: 42.6 nmol/L *versus* 49.9 nmol/L; P 0.01). In the JIA group, the percentage of individuals with severe vitamin D deficiency was considerably higher than in the control group (17.0 percent vs 6.6 percent; P 0.05).

## Summary and Conclusion

In a study of 40 children with JIA, it was discovered that 15 (37.5 percent) had 25(OH)D deficiency and 19 (47.5 percent) had 25(OH)D insufficiency. The ideal Vitamin D status for children with JIA, whether reduced Vitamin D is caused by enhanced utilization or reduced Vitamin D status in children with JIA, the impact of Vitamin D on disease activity, or the involvement of VDR polymorphisms in JIA are all unknowns.

The long-term association between Vitamin D level and JIA in newly diagnosed people has yet to be studied. Investigating the genetic and environmental roles of Vitamin D in the prevention and control of JIA in children will aid in the discovery of Vitamin D's varied involvement in this disease understanding how genetic variations increase the risk of disease development and being able to identify precise goals for Vitamin D status as a potential adjunct therapy in the treatment of JIA will improve the quality of life of patients and their families.

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