Subtype-specific profiles and predictive factors for early evaluation of vitamin D levels in newly diagnosed active juvenile idiopathic arthritis

Yanzhao He
Chongqing Medical University
Xiwen Luo
Children's Hospital of Chongqing Medical University
Mengwei Ding
Children's Hospital of Chongqing Medical University
Yuxiao Chen
Children's Hospital of Chongqing Medical University
Xuemei Tang
tangxuemei2008@163.com
Children's Hospital of Chongqing Medical University

Research Article

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Abstract

Background

Vitamin D deficiency is prevalent in children with juvenile idiopathic arthritis (JIA). Prevention and supplementation with vitamin D may help improve diseases. Understanding subtype-specific variations in vitamin D levels before initiating treatment could provide valuable insights for early monitoring.

Methods

This study included 236 newly diagnosed, untreated children with active JIA who were admitted to Chongqing Medical University Children's Hospital between May 2019 and April 2024. Demographic and clinical characteristics, inflammatory markers, vitamin D levels, bone metabolism, and bone mineral density were retrospectively reviewed. Univariable and multivariable analyses were performed to identify factors affecting vitamin D levels and assess intergroup differences among JIA subtypes.

Results

Univariable analysis showed positive correlations of calcium and phosphorus levels with vitamin D levels, while body weight, body mass index, normalized erythrocyte sedimentation rate (ESR), and IL-6 exhibited negative correlations ($p < 0.05$). Multivariable analysis identified reduced bone mineral density, normalized ESR, and normalized C-reactive protein (CRP) as significant variables associated with vitamin D levels. The stratified analysis revealed notable differences in gender, weight, and bone density across JIA subtypes.

Conclusion

Vitamin D deficiency is associated with inflammation in JIA. Findings from the multivariate generalized linear regression model emphasize the distinct patterns of vitamin D levels and their influencing factors across JIA subtypes, offering critical insights for early monitoring and informed clinical decision-making before treatment.

Trial registration

The study was registered on chictr.org.cn on June 12, 2022 (ID: ChiCTR2200060798).

Introduction

Juvenile idiopathic arthritis (JIA) is a chronic rheumatic disease in childhood starting before 16 years old. The prevalence of JIA varies between 16 and 150 per 100,000 people [1]. The main diagnostic criteria used are the 2001 International League Against Rheumatology (ILAR) classification and the 2018 Pediatric Rheumatology International Trials Organization (PRINTO) classification [2, 3]. The cause of JIA is not fully understood, and multiple factors such as genetics, environment, infection, and immunity are involved in the development of JIA. Treatment of JIA includes drug therapy such as non-steroidal anti-

inflammatory drugs (NSAIDs), disease-modifying anti-rheumatic drugs (DMARDs), glucocorticoids, and physical therapy, etc. Despite the effectiveness of the current treatment strategies, some patients with JIA may still develop a prolonged course and poor outcome, with symptoms persisting into adulthood, accompanied by different comorbidities, and with a high rate of disability [4].

Vitamin D is one of the regulators of the innate and adaptive immune system [5, 6]. Innate immune cells like neutrophils, macrophages, and monocytes can be activated and differentiated by vitamin D, which also has anti-inflammatory and immunomodulatory effects. Additionally, vitamin D plays a role in controlling T cell immunodeficiency and adaptive immunity. T cells that are persistently active in immune-mediated illnesses release inflammatory cytokines. When the vitamin D level decreases, it may reduce the ability to activate and shut down T cells, resulting in T-cell immune imbalance [7]. Many studies have suggested that vitamin D supplementation might be beneficial to reducing inflammation and immune cell proliferation and improving clinical symptoms in rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and ankylosing spondylitis (AS) [8, 9]. Low vitamin D concentration is associated with increased pro-inflammatory mediators and disease activity. Hence, the appropriate prevention and treatment of vitamin D deficiency is significant in rheumatic diseases [10].

In addition, vitamin D regulates calcium (Ca) and phosphorus (P) balance in bone by promoting intestinal absorption of Ca and P, increasing renal reabsorption of Ca, and regulating the activity of skeletal cells to maintain bone health [11]. It is related to the increase of bone mineral density (BMD) and the prevention of osteoporosis and fracture, which is also important for patients with rheumatic diseases who are receiving long-term glucocorticoid therapy [11, 12]. Therefore, maintaining vitamin D levels is of great significance for patients with chronic arthritis.

Vitamin D deficiency is common in children with JIA. Studies have reported that prolonged exposure to the inflammatory state and medication may affect vitamin D levels in JIA patients [10]. The existing research strategies for vitamin D and JIA are different. Two studies indicated that patients with JIA had significantly lower levels of vitamin D than healthy children [18, 19]. RA-related in-vitro experiments have confirmed that 1,25(OH)2D3 promotes the differentiation of T helper (Th) cells from Th1/Th17 to Th2, inhibits the production of B cells and autoantibodies, and reduces the release of pro-inflammatory cytokines by macrophages, such as IL-1β, IL-17, IL-6, and TNF-α, thereby suppressing synovial cell proliferation [21–23]. JIA encompasses both inherent and adaptive immune characteristics, suggesting a close relationship between vitamin D deficiency and immune regulation in JIA patients exhibiting more severe disease characteristics. However, due to the differences in population, geographical region, disease characteristics, disease status, etc., there are contradictions among these results [13]. Hence, we conducted this retrospective study by including untreated newly diagnosed JIA patients to explore the relationship between vitamin D levels and JIA subtypes at the early stages of the disease, and to provide a theoretical basis for clinical guidance on vitamin D monitoring and treatment supplementation.

Methods

Study design and populations

We conducted a retrospective study and enrolled 236 newly diagnosed and untreated patients with active JIA who were admitted to the Children's Hospital of Chongqing Medical University. These patients were diagnosed by more than two rheumatologists according to the ILAR or PRINTO classification criteria from May 2019 to April 2024. All included patients had complete clinical data. Twelve children who did not match the diagnostic criteria, had missing information, or were lost to visits were excluded (Fig. 1).

General and clinical information and assessment of vitamin D levels

General information included age, gender, and ethnicity. Clinical information consisted of height, body weight, body mass index (BMI), diagnosis, and the season of testing.

Vitamin D levels were measured using the Siemens AD-VIA Centaur XP fully automated electrochemiluminescence immunoassay analyzer. The levels of vitamin D were categorized as follows, (i) ≤ 10 ng/mL as severe Vitamin D deficiency, (ii) 10–20 ng/mL as Vitamin D deficiency, (iii) 20–30 ng/mL as Vitamin D insufficiency, and (iv) ≥ 30 ng/mL as normal Vitamin D [14].

To assess disease activity, we also measured pre-treatment ESR, CRP, cytokines (interleukin (IL)-10, TNF-α, IL-1β, IFN-γ, IL-6, IL-17A, IL-8, IL-4, IL-2), rheumatoid factor (RF), anti-cyclic citrullinated antibodies (anti-CCP), anti-nuclear antibodies (ANA), Ca, P, and alkaline phosphatase (ALP), and refined BMD examination to assess whether the patient present with reduced bone mass. Besides, the ESR or CRP was normalized to a 0 to 10 scale [15]. All the information gathered at the first diagnosis was considered baseline information. Furthermore, we confirmed the final JIA diagnosis by the recent follow-up.

Statistical analysis

The Shapiro-Wilk test was utilized to evaluate the normality of the data distribution. Normally distributed continuous variables were described with mean and standard deviation (SD), while non-normal continuous variables were depicted by median and inter-quartile range (IQR). Differences among the groups were analyzed by using one-way ANOVA to determine the factors that may affect vitamin D levels in children with JIA.

Multivariable generalized linear regression analysis was used to judge the correlation between vitamin D levels and JIA and to estimate the influence of different factors affecting whether vitamin D was deficient in JIA patients at the first diagnosis. Stepwise regression adopts the forward selection strategy to test JIA characteristic indicators, bone metabolism-related indicators, sociodemographic characteristics, and cytokines.

The multivariable regression model showed significant differences in vitamin D levels among subgroups of JIA in terms of gender, weight, and bone mass reduction. To evaluate the relationship between vitamin

D levels in each subtype of JIA and these variables, we conducted stratified analyses based on three variables. By interacting with gender, weight, and bone mass reduction, we further determined whether the interaction between different variables was statistically significant.

We used R language (version 4.3.3) for statistical analysis and data visualization. Coefficients and 95% confidence intervals (CI) were calculated to assess the associations. A two-sided *p*-value < 0.05 was set as statistically significant.

Results

General information of participants

We first searched and found 488 children diagnosed with JIA who had undergone vitamin D testing in the Database of the Department of Rheumatology and Immunology of Children's Hospital of Chongqing Medical University. After reviewing the electronic clinical records of 488 pediatric patients, 248 individuals were screened for simultaneous detection of CRP, ESR, RF, ANA, cytokines, and liver function indicators. 12 incomplete cases were excluded from verification by two rheumatologists. Finally, 236 patients with JIA were eligible, and the effective inclusion rate was around 96.15%.

Table 1 and Table 2 show the baseline characteristics of 236 pediatric patients. Male patients (56.36%) were more common, with Han patients being the majority (87.29%). The mean age was 108.87 ± 49.37 months. The mean body weight was 31.51 ± 15.93 kilograms (kg). According to the growth curve of children in China, the weight level of children at different ages was evaluated, with the highest proportion being normal weight (84.68%) [16, 17]. The average BMI of 138 children with JIA was 17.30 ± 3.87 (kg/m^2).

According to the ILAR classification criteria, the confirmed diagnosis at the last follow-up showed that the proportion of JIA diagnoses was oligoarticular JIA (oJIA) (11.02%), systemic JIA (sJIA) (10.17%), RF-positive polyarticular JIA (pJIA) (7.63%), RF-negative pJIA (17.37%), enthesitis-related arthritis (ERA) (27.54%), and undifferentiated JIA (26.27%), respectively (Table 2 and Supplementary Fig. 1). In patients with ANA positive (22.84%, 53/232), 26.42% (14/53) were undifferentiated JIA, and 20.75% (11/53) were oJIA. 8.09% (19/235) of JIA patients were anti-CCP positive, of which 89.47% (17/19) were RF-positive pJIA patients, and 10.53% (2/19) were undifferentiated JIA patients. The mean ESR of all patients was 36.57 ± 31.92 mm/1hr and the mean CRP was 23.91 ± 30.10 mg/L. Additionally, the mean level of IL-6, 69.07 ± 288.24 pg/ml, was higher (Table 2 and Supplementary Table 1).

Most patients in this cohort were initially diagnosed in the spring (33.47%), followed by the summer (30.08%). The mean vitamin D level of 236 patients was 21.23 ± 9.09 ng/ml. There were more children with vitamin D deficiency levels (41.53%) and vitamin D insufficiency levels (35.17%). We further evaluated the vitamin D levels in each JIA subgroup. The data demonstrated more vitamin D deficiency cases in ERA, RF-negative pJIA, and RF-positive pJIA groups, mainly located at the deficiency level. Ca, P, and ALP were mostly within the normal reference range, accounting for 97.41%, 99.57%, and 89.66%,

respectively. BMD examination revealed a decrease in bone mass in 69 (29.24%) children with JIA (Table 2 and Supplementary Table 1).

We further explored whether there were differences in vitamin D levels among children with different JIA subtypes (Supplementary Fig. 2). By consulting literature to understand the relevant factors that may affect vitamin D levels, combining relevant indicators in clinical diagnosis and treatment that may affect JIA diagnosis and reflect the inflammatory status of the disease, and considering the potential interaction between confounding factors, we conducted univariable analysis on JIA classification and related covariates that may affect vitamin D levels or JIA disease status. Figure 2 shows that the vitamin D levels in the sJIA group were lower than those in other groups, with significantly higher levels in the oJIA group ($p = 0.025$) and undifferentiated JIA group ($p = 0.005$) compared to the sJIA group. The estimated beta (95% CI) were 0.68 (0.10, 1.29) and 0.75 (0.24, 1.31), respectively. In addition, weight at the upper middle level, weight at the overweight level, BMI, normalized erythrocyte sedimentation rate, and elevated IL-6 hurt vitamin D levels. Instead, Ca and P levels have a positive impact on vitamin D levels ($p < 0.05$). Furthermore, the vitamin D levels of JIA patients measured during winter are significantly higher than those measured in other seasons. Gender, ethnicity, age, height, weight, tri-class weight, rheumatoid factor, anti-CCP, ANA, normalized CRP, IL-10 level, TNF-α Horizontal, IL-1 β There was no statistically significant difference ($p > 0.05$) in the effects of levels of vitamin D, IFN, IL-17A, IL-4, IL-2, ALP, and decreased bone density.

Multifactorial analysis revealed the differences in vitamin D levels among JIA subtypes

Model 1 (univariable analysis) compared the differences in vitamin D levels between JIA groups, and the results showed that the vitamin D levels in the ERA group, oJIA group, RF-negative pJIA group, and undifferentiated JIA group were higher than those in the sJIA group, with estimated coefficients (95% CI) of 0.14 (-0.39,0.71), 0.68 (0.10,1.29), 0.53 (-0.02,1.11), and 0.75 (0.24,1.31), respectively. Then in Model 2, age and gender were included. Model 3 incorporated three categories of body weight and surface area. Anti-CCP, ANA, normalized erythrocyte sedimentation rate, and CRP were added in Model 4. Finally, Model 5 included Ca, P, ALP, and bone density. The final estimated coefficients (95% CI) for the four groups were 0.66 (0.03, 1.31), 0.69 (0.02, 1.38), 0.70 (0.10, 1.32), and 0.77 (0.19, 1.39). The last model showed that the vitamin D levels in the patients with ERA, oJIA, RF-negative pJIA, and undifferentiated JIA were higher than those in the sJIA, and the differences were statistically significant ($p < 0.05$). On the contrary, although the vitamin D levels in the group of RF-positive pJIA were higher than those in the sJIA, the evaluation coefficients on Model 1 to 5 showed 0.08 (-0.55,0.73), 0.28 (-0.34,0.91), 0.23 (-0.39,0.87), 0.44 (-0.47,1.32), and 0.38 (-0.50,1.24), respectively, with no statistically significant difference ($p > 0.05$). It is worth noting that in Model 5, normalized ESR, normalized CRP, and decreased bone mineral density may be risk factors affecting vitamin D levels, and the differences were statistically significant ($p < 0.05$) (Table 3).

Stratified analysis showed the influence of multiple factors on vitamin D levels

Before conducting the stratified analysis, we assessed the interaction between JIA diagnosis and gender, weight, and bone mineral density and found a statistically significant interaction ($p < 0.05$ for all) (Supplementary Table 2). Following, we performed the stratified analysis in the fully adjusted model (Model 5) based on gender (male and female), weight (below, normal, above), and BMD (decreased and normal). The left side of Fig. 3 demonstrated that the impact of JIA diagnosis on vitamin D levels remained significant in women and individuals with normal weight. The data indicated that the vitamin D levels of female children with oJIA and undifferentiated JIA were notably higher than those with sJIA, and the effect of gender on vitamin D levels was more pronounced in women than in men. Additionally, children with normal body weight in ERA, oJIA, RF-negative pJIA, and undifferentiated JIA groups had significantly higher vitamin D levels than those in the sJIA group. There was no statistically significant difference in vitamin D levels between the RF-positive pJIA and sJIA groups. We also observed a negative correlation between overweight and vitamin D levels, while there was no statistically significant difference between the sJIA and non-sJIA groups. Therefore, JIA children with normal weight might be more conducive to stabilizing vitamin D levels.

Discussion

Juvenile idiopathic arthritis is a childhood-onset chronic rheumatic disease with complex etiology (genetic/environmental/immune factors) and variable outcomes, where current treatments often fail to prevent long-term disability. Vitamin D plays critical immunomodulatory roles by suppressing pro-inflammatory cytokines (e.g., IL-6, TNF α) and promoting immune balance while also maintaining bone health. In this retrospective study, we investigated the relationship between early active JIA in children and vitamin D levels and discovered that vitamin D deficiency or insufficiency was prevalent in JIA patients, consistent with previous research findings. These indicate that children with inflammatory arthritis have lower levels of circulating vitamin D concentration [18, 19, 13].

There were significant differences in vitamin D levels among different JIA subtypes. Our results showed that, in the early stages of active JIA, the vitamin D levels of sJIA are significantly lower than those of oJIA, RF-negative pJIA, ERA, and undifferentiated JIA, which is similar to the results reported by another study [18]. The vitamin D levels are higher in patients with RF-positive pJIA than those in sJIA without significant differences. A meta-analysis also indicated consistent results, but there was no significant difference in vitamin D levels between pJIA subgroups [20]. Therefore, we speculate that vitamin D might have a greater connection with sJIA and RF-positive pJIA patients [18].

There is no consensus on the relationship between vitamin D and disease activity. We observed a negative correlation between vitamin D levels and inflammatory markers IL-6 and ESR in children with JIA [24, 25, 13, 26]. Many previous studies have also found that vitamin D may negatively influence disease inflammation of SLE, AS, psoriatic arthritis, Sjogren's syndrome, and systemic sclerosis.

Therefore, improving vitamin D deficiency in JIA patients with appropriate vitamin D supplementation may be helpful [13, 27]. However, some studies have not found a correlation between insufficient vitamin D levels and active JIA or more severe disease characteristics [28, 29].

Although numerous JIA studies have reported poor levels of vitamin D in JIA patients, the relationship between vitamin D and JIA remains controversial. Thorsen et al.'s work and a Mendel randomized study also revealed that there was no causal relationship between vitamin D level and JIA. Specific polymorphisms in the vitamin D family genes were associated with uveitis in patients with JIA, AS, and Behcet's disease [30]. Unlike RA, there is no specific relationship between vitamin D receptor polymorphism and the development of SLE, and there may not be a causal relationship with AS [24, 27]. The above indicates that the mechanism of vitamin D regulating immune response has high heterogeneity in distinct diseases.

Through interactive-stratified analysis, we found that gender had a considerable impact on the vitamin D status of JIA patients. Specifically, the vitamin D levels of female patients with oJIA and undifferentiated JIA were significantly higher than those with sJIA, but one study from Norway did not indicate any differences in vitamin D levels between genders [29]. There are also differences in the correlation between gender and vitamin D deficiency in the population. The study by Song et al. demonstrated that in China, the average vitamin D level of women tends to be lower than that of men [23]. Studies from other countries have reported a significantly higher proportion of vitamin D deficiency in girls compared to boys [31], and lower levels of vitamin D in female patients with Sjogren's syndrome compared to the control group [10]. Some opposite findings have shown that the prevalence of vitamin D deficiency is higher in male participants than in females [32]. In addition, a study in Türkiye observed that at the end of summer, women had a higher proportion of vitamin D deficiency, while at the end of winter, there was no significant correlation between gender and vitamin D levels [33]. These may be due to limited outdoor activities for women, clothing, and the use of sunscreen products, resulting in less sunlight exposure for women [34]. The outcomes might stem from the intricate interplay of factors influencing vitamin D levels.

Moreover, our findings suggest that being overweight might be a risk factor for vitamin D deficiency in children with JIA. There was a significant correlation between obesity and increased involvement of lower limb joints in JIA patients at baseline, and obesity might have negative effects on the course and treatment of JIA [35], and the differences in dosage may lead to inadequate conventional administration in obese children [36]. The results of the meta-analysis indicated the inverse relationship between obesity indicators and vitamin D levels, but supplementing with vitamin D did not seem to reduce any obesity indicators, and more research is needed to elucidate the underlying pathophysiological mechanisms [37].

Interestingly, there were inconsistent results in our study regarding the relationship between decreased bone mineral density and vitamin D levels. Univariable analysis suggests a negative correlation between vitamin D levels and decreased BMD. Low bone mass is one of the complications of JIA, and serum

vitamin D levels are significantly positively correlated with the Z-score of BMD. In JIA, osteoporosis is more pronounced in the femoral neck and bone compared to the lumbar spine [38]. Supplementation of vitamin D improved serum vitamin D levels in children with persistent active pJIA, but bone mineral density remained unchanged. On the other hand, supplementation of vitamin D significantly increased bone mineral density in JIA patients receiving systemic corticosteroid treatment, but the average bone mineral density rapidly decreased after discontinuing vitamin D supplementation [27]. On the contrary, our multivariable analyses showed biases in the positive and negative relationships between vitamin D levels and decreased BMD across different groups. The meta-analysis of the vitamin D test demonstrated that when baseline vitamin D > 40 nmol/L, there was no effect on bone mineral density or fracture risk [11]. The meta-analysis of vitamin D supplementation (not taken simultaneously with calcium) also found no effect in preventing fractures [39]. It is worth noting that studies have exposed that the combination of vitamin K and D can significantly improve total bone mineral density [40]. The interaction of genetic, hormonal, nutritional, immune, or pharmacological stimuli influences bone metabolism and homeostasis. Skeletal cell function, Ca and vitamin D homeostasis, sex hormone metabolism, and puberty simultaneously affect bone health. Thus, these contradictory findings are not convincing enough to support the benefits of high-dose vitamin D supplementation for bone health, and more comprehensive assessments are urgent for children with high risk of vitamin D deficiency in prevention, treatment, and follow-up processes [12].

So far, vitamin D deficiency and bone damage are still important issues during the growth and development of JIA. Nonetheless, the effectiveness of vitamin D supplements in preventing and treating diseases remains to be confirmed [10, 18]. Marini F et al. found that the suboptimal status of vitamin D in JIA patients couldn't be improved by vitamin D supplementation [41]. There are also studies indicating that MTX treatment can further reduce the concentration of vitamin D [28]. Considering the high incidence of vitamin D deficiency in JIA patients and the use of steroids, guidelines recommend providing 2–3 times the dose of vitamin D to children with rheumatic diseases receiving systemic steroid treatment [42]. However, a prospective randomized trial involving 42 JIA patients illustrated that supplementing with cholecalciferol (2000 IU/day) for 24 weeks could increase serum vitamin D levels in JIA patients without reducing disease activity or improving BMD [43]. Patients with severe JIA may need more supplements to maintain normal vitamin D levels. Studies with long-term observation and a larger sample are required to investigate the relationship between vitamin D levels and disease activity among JIA and its subtypes [18, 44].

Our study fully considers the relationship between early JIA disease and vitamin D, the characteristics of JIA, and the relationship between inflammatory markers and vitamin D levels. However, serum vitamin D levels are subject to multiple confounding factors. Since vitamin D is primarily synthesized in the skin upon exposure to ultraviolet B (UVB) radiation [14, 18], its levels vary considerably by geography and season, particularly in high-latitude regions where winter UVB exposure is insufficient [31]. The use of sunscreen and increased indoor activities in modern lifestyles further limit skin synthesis [42]. Insufficient consumption of foods rich in vitamin D, such as fish and dairy products, can lead to a decrease in vitamin D levels [5, 14]. Given the research on the benefits of vitamin D supplementation

during the previous COVID-19 pandemic, doctors now more frequently recommend consuming vitamin D-rich foods or supplements during seasons with insufficient sunlight exposure [45, 46]. This may explain the univariable analysis finding that JIA patients tested in winter had higher serum vitamin D levels than those tested in other seasons, possibly due to non-iatrogenic interventions. Additionally, there are significant differences in dietary culture among different regions, which may partially explain the heterogeneity of vitamin D levels observed in various studies [9]. After strictly controlling for confounding factors, we found that the impact of JIA diagnostic features on vitamin D levels was insignificant. However, there was a significant negative correlation between inflammatory indicators and vitamin D levels, strongly suggesting the impact of inflammation on vitamin D. Moreover, individuals diagnosed with sJIA and RF-positive pJIA exhibited lower vitamin D levels compared to those with oJIA and undifferentiated JIA. This discrepancy could serve as a useful reference for rheumatologists in determining the necessity and timing of vitamin D supplementation for JIA patients.

There were some limitations in this study. As a retrospective investigation, it primarily focused on baseline data from patients without dynamic follow-up, treatment, or vitamin D supplementation, and did not account for potential confounding factors that may influence vitamin D levels, such as sunlight exposure and dietary intake. Secondly, although the diagnostic season showed correlation with vitamin D levels, this association might be influenced by unmeasured factors, including geographical variations, UVB exposure, and metabolic differences. Future prospective studies are needed to establish optimal vitamin D therapeutic strategies and maintenance levels to enhance clinical management of vitamin D supplementation in JIA patients.

Conclusion

Our findings demonstrated that there were notable variations in vitamin D levels between the various JIA subtypes. In the early period of disease, active sJIA patients had significantly lower vitamin D levels than oJIA, RF-negative pJIA, ERA, and undifferentiated JIA patients. Conversely, patients with RF-positive pJIA had higher vitamin D levels than those in sJIA patients without significant differences. The substantial negative connection between vitamin D levels and inflammatory indicators implies the connection between vitamin D insufficiency and inflammation in JIA. We built a multivariable generalized linear regression model and found markedly lower vitamin D levels in untreated and new-onset sJIA patients, which provides pediatric physicians with clinical support for individualized treatment strategies for vitamin D in JIA [12, 44].

Abbreviations

Juvenile idiopathic arthritis (JIA), Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), International League Against Rheumatology (ILAR), Pediatric Rheumatology International Trials Organization (PRINTO), Rheumatoid arthritis (RA), Systemic lupus erythematosus (SLE), Ankylosing spondylitis (AS), Calcium (Ca), Phosphorus (P), Bone mineral density (BMD), Body mass index (BMI), Interleukin (IL), Rheumatoid factor (RF), Anti-cyclic citrullinated antibodies (anti-CCP), Anti-nuclear

antibodies (ANA), Alkaline phosphatase (ALP), Standard deviation (SD), Inter-quartile range (IQR), Confidence intervals (CI), Kilograms (kg), Oligoarticular JIA (oJIA), Systemic JIA (sJIA), Polyarticular JIA (pJIA), Enthesitis-related arthritis (ERA), T helper (Th) cell.

Declarations

Ethical approval and consent to participant

The study adhered to according to the ethical guidelines of the Helsinki Declaration and was approved by the Human Research Ethics Committee of the Children's Hospital of Chongqing Medical University [the reference number of the ethical approval: 2022 (52)]. All data were captured through a retrospective review of the electronic medical records from the patient's regular visits. Our study has already obtained the necessary informed consent from the participants' parents or legal guardians of pediatric patients, including those younger than 16.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and analysed during this study are available from the corresponding author on reasonable request.

Competing interests

The authors declare no competing interests.

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Author contributions

XM.T and XW.L designed the study. YZ.H and XW.L collected the data, and drafted the manuscript. YX.C assisted in data filtering. XW.L, MW.D, and YZ.H conducted the statistical analysis. XM.T reviewed and revised the manuscript. All authors have reviewed the manuscript and approved the final submission.

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Tables

Tables 1 to 3 are available in the Supplementary Files section

Figures

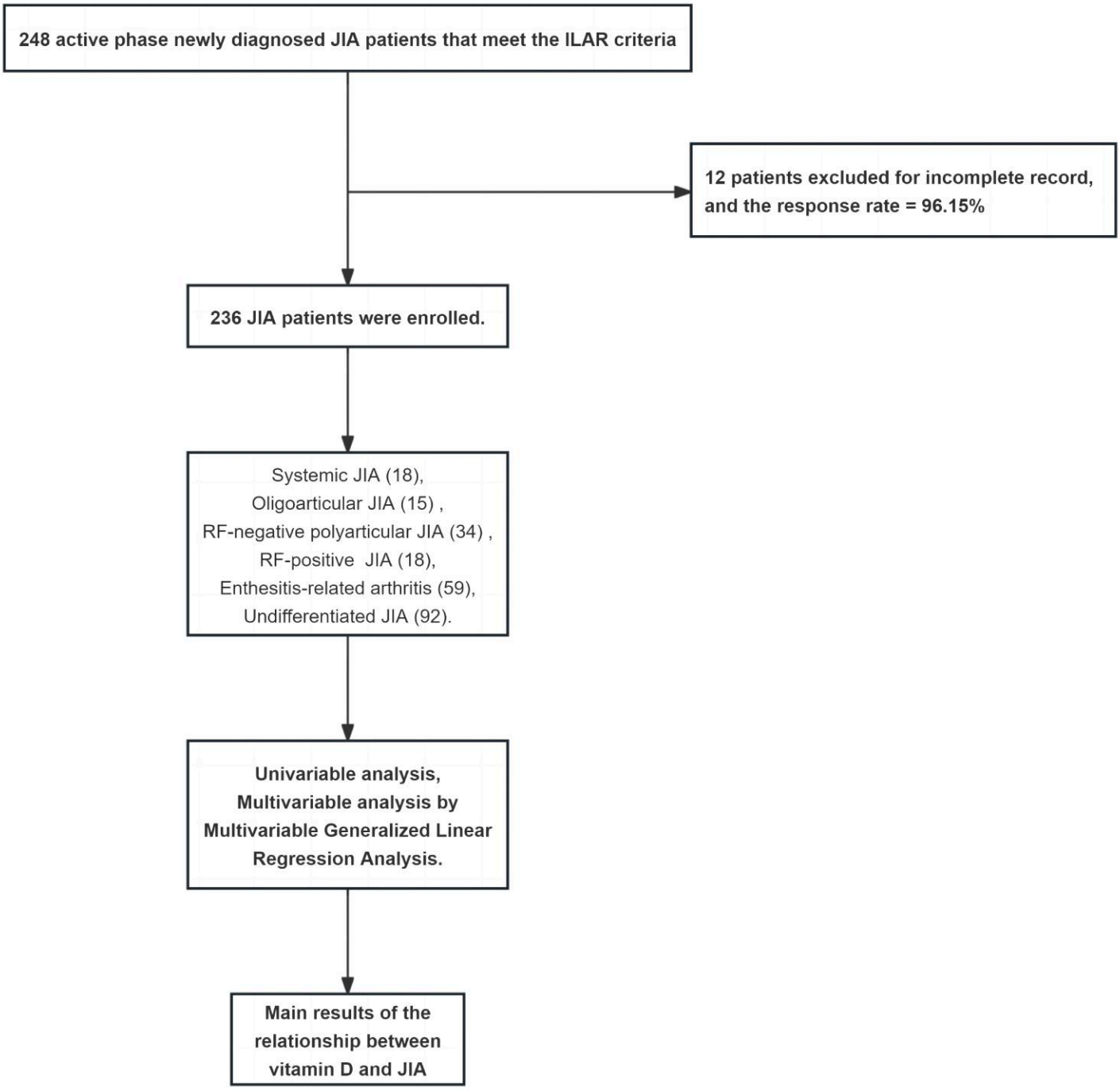

Figure 1

Flow chart of the study

JIA, juvenile idiopathic arthritis; ILAR, International League of Associations for Rheumatology; RF, rheumatoid factor.

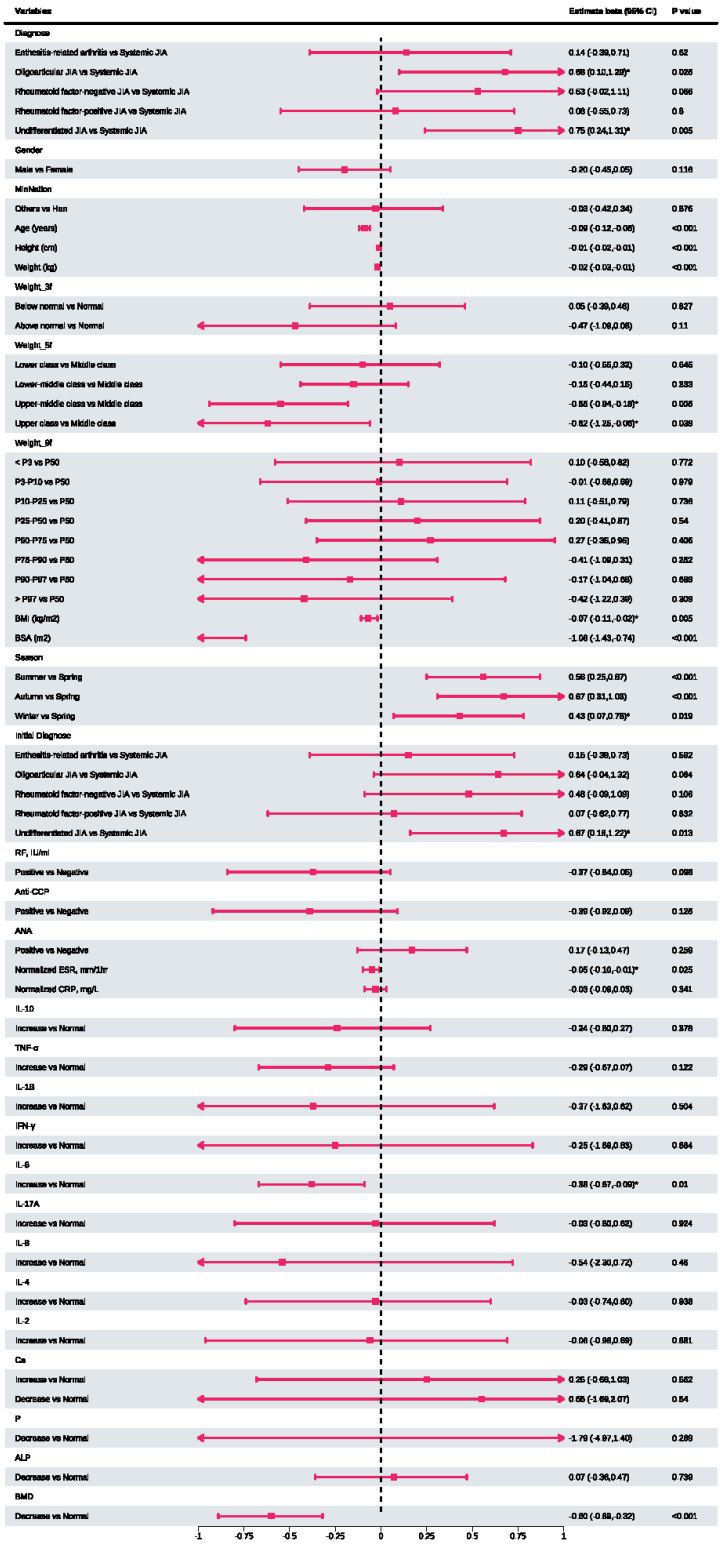

Figure 2

Univariable analysis of the association between vitamin D and JIA

JIA, juvenile idiopathic arthritis; 3f means three classifications of body weight; 5f means five classifications of body weight; 9f means nine classifications of body weight; BMI, body mass index; BSA, body surface area; BMD, bone mineral density; RF, rheumatoid factor; anti-CCP, anti-cyclic citrullinated

antibodies; ANA, anti-nuclear antibody; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; IL, interleukin; TNF, tumor necrosis factor; Ca, calcium; P, phosphorus; ALP, alkaline phosphatase.

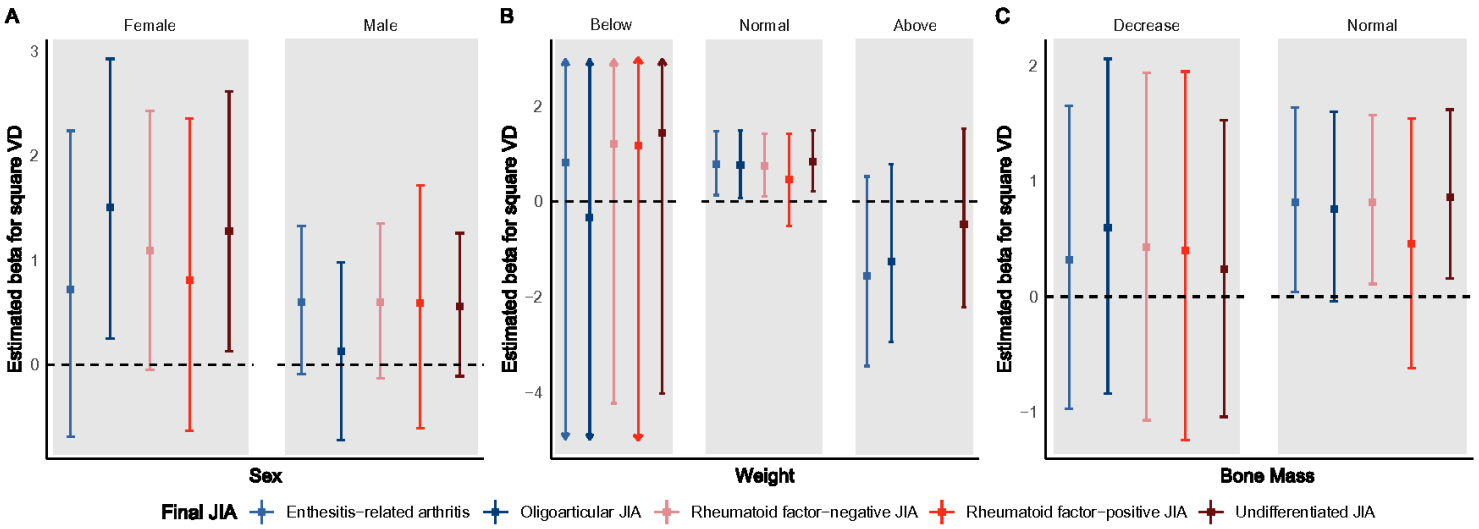

Figure 3

Stratified analysis of the association between gender, weight, BMD and JIA respectively

JIA, juvenile idiopathic arthritis.

Supplementary Files

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- Table1.xlsx
- Table2.xlsx
- Table3.xlsx
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- SupplementaryTable2.xlsx
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- SupplementaryFigure2.pdf