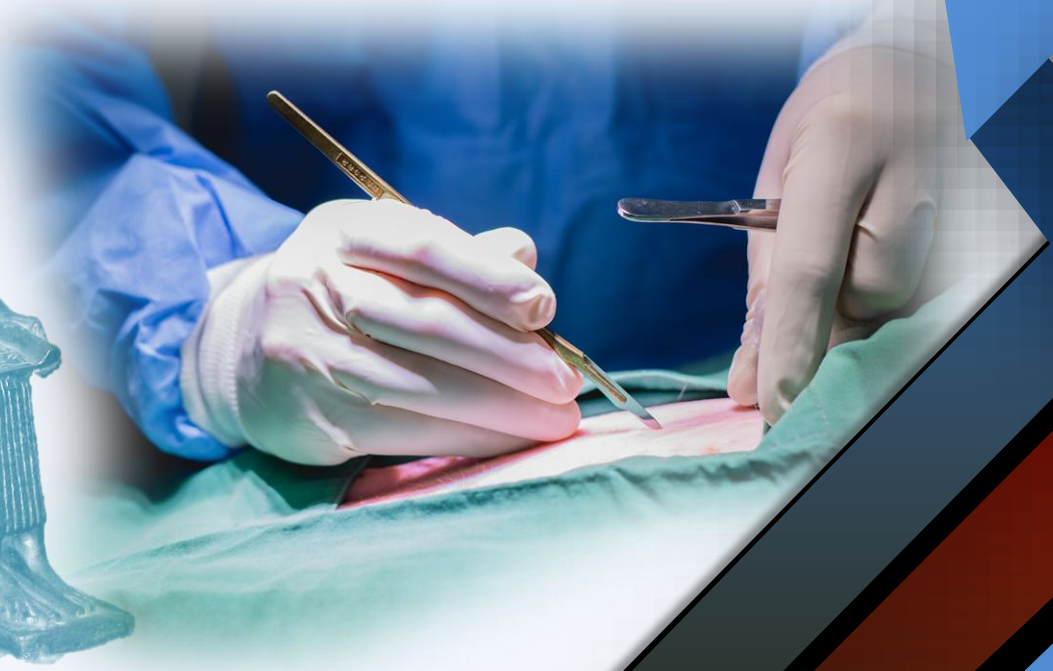
IJMA

International Journal of Medical Arts

Volume 7, Issue 1 (January 2025)



http://ijma.journals.ekb.eg/

P-ISSN: 2636-4174

E-ISSN: 2682-3780

Available online at Journal Website
https://ijma.journals.ekb.eg/
Main Subject [Rheumatology]

Original Article

Exploring the Potential Clinical Value of Vitamin D in Juvenile Idiopathic Arthritis

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Article information

Received: 20-10-2024

Accepted: 28-01-2025

DOI: 10.21608/ijma.2025.410183

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Citation: Kandeel SAS, Ali MA, Yossef BWA. Exploring the Potential Clinical Value of Vitamin D in Juvenile Idiopathic Arthritis. IJMA 2025 Jan; 7 [1]: 5256-5259. DOI: 10.21608/ijma. 2025.410183

Abstract

Background: Vitamin D deficiency has been linked to aggravated juvenile idiopathic arthritis [JIA] activity.

Aim: This study aimed to evaluate the levels of serum 25[OH] Vitamin D in children with JIA. In addition to investigate the correlation of Vitamin D with the disease activity and used medication.

Subjects and Methods: Thirty-Nine children with confirmed diagnosis of JIA and 28 apparently healthy children were included in the current study. The Juvenile Arthritis Disease Activity Score 71 [JADAS-71] was used to assess the disease activity. Serum 25[OH]D was evaluated using a direct, competitive electrochemiluminescence immunoassay.

Results: Patients with JIA exhibited a significantly lower levels of 25[OH]D than the controls [21.2 ± 7.4 vs 30.6 ± 10.9 ng/ml; $p < 0.001$]. Patients with active disease also had lower levels than those with non-active disease [16.9 ± 8.7 ng/ml, vs 25.6 ± 7.4 ng/ml; $p < 0.005$]. $VitD_3$ levels showed a significant negative correlation with daily systemic corticosteroid [SCS] [$r = -0.491$, $P = 0.005$].

Conclusion: Serum level of 25(OH) D were reduced in patients with juvenile idiopathic arthritis (JIA), and exhibited a negative association with disease activity and daily SCS dosages. These findings indicate that the disease outcome is influenced by vitamin D deficiency.

Keywords: Vitamin-D; Arthritis; Juvenile; Pediatric.

INTRODUCTION

The most prevalent type of chronic arthritis in children is juvenile idiopathic arthritis [JIA], which contributes significantly to both short-term and long-term disability. It affects 160/100,000 children and is characterized by chronic idiopathic synovitis with extra-articular manifestations [1, 2].

Although the etiology is unknown, the pathogenesis is believed to be influenced by numerous hormonal, genetic, viral and environmental variables [1, 3]. JIA is classified into subtypes based on the number of affected joints and extra-articular involvement in the first six months of the disease. Among the subtypes are systemic JIA, polyarticular JIA [≤5 joints], and oligoarticular JIA [<5 joints]. Arthritis with a fever that lasts longer than two weeks and at least one visible sign of systemic inflammation, such as a rash, lymphadenopathy, hepatosplenomegaly, or serositis, is known as systemic JIA [4,5]. There is some evidence that vitamin D deficiency increases the likelihood of autoimmune and other chronic diseases [6, 7].

Vitamin D deficiency is linked to the pathogenesis of many diseases including diabetes, rheumatoid arthritis, spondyloarthritis, glomerulonephritis, hyperuricemia. Furthermore, Vitamin D is recognized as an effective immune-modulator, modulating both innate and adaptive immune responses, in addition to maintaining calcium and phosphorus levels and regulating bone metabolism [8,9].

The metabolites of vitamin D have the potential to influence T-cell proliferation and dendritic cell function, enhance the synthesis of the anti-inflammatory cytokine interleukin 10 [IL-10], diminish the production of inflammatory cytokines including IL-17, IL-1, IL-6, and TNF-α and inhibit Th1 and Th17 cells, which are overproduced in juvenile idiopathic arthritis [JIA] [10-14].

AIM OF THE WORK

This study aimed to evaluate serum 25[OH] Vitamin-D levels in children with JIA and to investigate its correlation with disease activity and medication use.

PATIENTS AND METHODS

This prospective clinical trial included 39 children [8- 14 years of age] with JIA. In addition, 28 apparently healthy children were included as a control group. The study was conducted between May 2019 and October 2019. The follow up was done at the Rheumatology Clinics, Al-Azhar University Childhood Disabilities Center and Al-Azhar University Hospitals.

All patients and control guardians gave their informed consent in compliance with the local ethics committee's guidelines. The study protocol was approved by the same committee and completed in line with the Helsinki declaration codes and WHO guidelines for research conduction and reporting.

Diagnosis of patients with JIA was conducted in accordance with the classification criteria established by the International League of Associations for Rheumatology [15]. Patients with metabolic bone disease, chronic diseases, a history of acute infections within the month before blood collection, chronic diseases, and those taking vitamin D supplements or anticonvulsant medications before the study were excluded.

Disease subtypes, steroid dosages, drugs used, disease activity, and demographic characteristics were recorded and evaluated. The average daily systemic corticosteroid [SCS] dosage over the previous four weeks was calculated and represented as an equivalent prednisolone dose in mg/kg/day. Additionally, the use of other immunosuppressant [IS] drugs was recorded. The Juvenile Arthritis Disease Activity Score 71 [JADAS-71] was utilized to assess disease activity, with a score of ≤1 indicating inactive disease [16, 17]. Disease activity was assessed on the day when blood specimens were collected.

Levels of calcium, phosphorus, alkaline phosphatase, and 25-hydroxyvitamin D were assessed in both the patient and control groups. Serum 25 OH Vit-D was measured by direct, competitive electrochemiluminescence immunoassay by Cobas-e410 automated machine with normal reference range of 30-100 ng/ml. The insufficient levels ranged between 20-29 ng/ml and less than 20 ng/ml was set for deficient cases.

Data analysis: The SPSS 21.0 software was used for all of the analyses. For continuous variables, the results are shown as the mean and standard deviation [SD]. On the other side, categorical variables were displayed as frequencies and percentages. The "t" test and the Mann-Whitney test were used to compare data for continuous variables in order to assess how the study group and control group differed from one another. The Chi-square test or Fisher's exact test were used to evaluate differences for categorical variables. A significance criterion of 5% [$p<0.05$] was set as the margin of significance.

RESULTS

The study included 39 JIA patients, comprising 22 males [56.4%] and 17 females [43.5%]. At the time of enrollment, the mean age was 11.6±4.6 years, while the average duration of the disease was 22.9±3.11 months. The majority of the patients, 24 [66.6%] were prepubertal. JIA subtypes included the following: systemic JIA, 5 (12.8%); oligoarticular JIA, 23 (58.9%); and polyarticular JIA, 11 (28.2%), which comprised RF-positive polyarticular JIA, 5 (12.8%); and RF-negative polyarticular JIA, 6 (15.3%). The mean score of JADAS-71 was 3.9 [range 0.1 to 11.1]. Twenty patients (51.2%) had an active disease (JADAS-71>1). The pharmaceuticals used to treat JIA Methotrexate included, (28 patients, 71%), prednisolone (GCs) (24 patients, 61.5%), sulfasalazine (7 patients, 17.9%), hydroxychloroquine (2 patients, 5.1%), and nonsteroidal anti-inflammatory medicines (30 patients, 76.9%). Etanercept, a biologic medication, was administered to one patient (2.56%) and Intra-articular steroids Injections were administered to five individuals (12.8%). [Table 1]. Prednisolone therapy mean duration was of 11.9±6.8 months. A mean daily steroid dosage of 0.2 ± 0.1 mg/kg/d, patients exclusively treated with glucocorticoids had systemic onset JIA or were given them as a bridge medication

The mean level of vitamin D3 was [21.2±7.4 ng/mL] in the study group. JIA patients showed a significant reduction in levels of Vitamin-D3 than the controls [21.2±7.4 vs 30.6±10.9 ng/ml; $p < 0.001$]. Patients with oligoarticular onset had a 25[OH]D level of 23.6 ± 7.4 ng/ml, while those with polyarticular onset had a level of 20.6 ± 8.3 ng/ml and systemic onset patients showed a level of 15.4 ± 9.1 ng/ml. These results indicating notable variance between different types of JIA. However, there was no significant differences in the levels of Vitamin-D between males and females in the study group [21.1 ± 3.6 ng/ml vs 21.3 ± 4.4 ng/ml, $p > 0.05$]. The serum level of 25[OH] Vitamin-D in patients with juvenile idiopathic arthritis exhibiting active disease were significantly lower [16.9 ± 8.7 ng/ml] than those of non-active disease [25.6 ± 7.4 ng/ml; $p < 0.005$], also an inverse association between level of 25[OH] Vitamin-D and disease activity was noted $p < 0.005$. The serum calcium, phosphorus, and ALP values of patients and the control group showed a consistent pattern without any notable differences. In our comparison of patients utilizing glucocorticoids [GCs] versus those not using GCs, the latter exhibited significantly elevated levels of Vitamin D3 [27.8± 6.8 vs 16.2± 7.5 ng/mL, $P = 0.006$]. Additionally, we identified a significant inverse association [$r = -0.491$, $P = 0.005$] between daily SCS doses and VitD3 levels. The vitamin D levels in JIA patients showed no significant differences between those who received sulfasalazine or methotrexate and those who did not.

Table [1]: Characteristics of Participants Study Patients.

Variables		Study [n=39]	Control [n=28]	p
Male: Female		22: 17	15: 13	>0.05
Age [years]	mean±SD	11.6±4.0	12.6±2.5	>0.05
Mean BMI [kg/m^2]		16.8	17.4	>0.05
Pubertal stage [n,%]	Prepubertal	24 [61.5%]	19 [67.9%]	>0.05
	Pubertal	15 [38.5%]	9 [32.1%]	
Disease duration [month]		22.9±3.11	-	-
JIA subtype n,%	Systemic	5 [12.8%]	-	-
	RF-positive polyarticular	5[12.8%]	-	-
	RF-negative polyarticular	6 [15.4%]	-	-
	Oligoarticular	23[59.0%]	-	-
JADAS-71		3.9 [0.1-11.1]		
Disease activity	Active	20 [51.3%]		
	Inactive	19 [48.7%]		
Medications	NSAIDs	30 [76.9%]		
	Systemic steroids	24 [61.5%]		
	Methotrexate	28 [71.8%]		
	Sulfasalazine	6 [15.4%]		
	Hydroxychloroquine	2 [5.1%]		
	Etanercept	1 [2.6%]		
	Intra-articular steroid injection	5[12.8%]		

DISCUSSION

A number of researches have been conducted to investigate the connection between Vitamin-D insufficiency and autoimmune arthritis. The findings have shown that individuals with RA had lower levels of vitamin D compared to healthy controls [18-21]. In addition, evidence from a number of studies suggests that individuals with JIA have lower levels of vitamin D [22-26], which may be attributed to a variety of mechanisms that are connected with autoimmune and/or iatrogenic consequences [27-28]. Our results extend the previous observations, confirming significant reduced serum Vitamin-D levels among patients with JIA.

In a comparison between patients with active JIA and those with non-active disease, we observed that 25[OH] vitamin D levels were lower in the active disease group. Additionally, a negative correlation between vitamin D levels and disease activity score was identified. These findings support those of earlier researches noted an inverse relationship between vitamin D and disease activity. They also found that patients with active illness had lower 25[OH]D levels than individuals in remission [29–35]. These finding indicate that the outcome of the disease is significantly influenced by vitamin D deficiency.

Our results may be elucidated by previous studies that have shown that, Vitamin-D possesses immunomodulatory effects, which lead to a decrease in the production of inflammatory cytokines such as interleukins [IL-17, IL-1, IL-6], and TNF-α, while simultaneously enhancing the production of the anti-inflammatory cytokine interleukin 10 [IL-10]. Interleukin-6 plays a crucial role in the process of joint destruction [10, 11]. Reduced physical activity and limited outdoors time are prevalent among JIA patients, potentially explaining the lower vitamin D levels in this population. Patients with higher disease activity show reduced mobility, which may limit their outdoor time as well as a positive correlation exists between vitamin D levels and physical activity. Moreover, fatigue is a common and distressing symptom in children and adolescents with juvenile rheumatic diseases, significantly impacting their well-being and participation in daily activities [36–40].

The findings of our study indicated a notable difference in vitamin D levels among patients with JIA who underwent GCS therapy compared to those who did not; Additionally, we observed a negative correlation between vitamin D status and systemic GCS therapy. **Skversky et al.** [41] observed that patients undergoing glucocorticoid therapy are at double the risk of developing vitamin D deficiency compared to the general population. In addition, corticosteroids facilitate the degradation of both 25[OH]D and 1,25[OH]D, as well as mitigating the effects of vitamin D on bone formation [42, 43]. These factors may elucidate our findings.

Conclusion. Serum levels of 25[OH] D were reduced in patients with juvenile idiopathic arthritis [JIA], and serum vitamin D levels exhibited a negative association with disease activity and daily SCS dosages. Further studies are necessary to validate the relationship between vitamin D and JIA disease activity.

Financial and non-financial relationships and activities of Interest: None

REFERENCES

1. Helmick CG, Felson DT, Lawrence RC, Gabriel S, Hirsch R, Kwoh CK, et al; National Arthritis Data Workgroup. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part I. Arthritis Rheum. 2008 Jan;58[1]:15-25. doi: 10.1002/art.23177.

2. Bansal N, Pasricha C, Kumari P, Jangra S, Kaur R, Singh R. A comprehensive overview of juvenile idiopathic arthritis: From pathophysiology to management. Autoimmun Rev. 2023 Jul;22 [7]:103337. doi: 10.1016/j.autrev.2023.103337.

3. Rigante D, Bosco A, Esposito S. The Etiology of Juvenile Idiopathic Arthritis. Clin Rev Allergy Immunol. 2015 Oct;49[2]:253-61. doi: 10.1007/s12016-014-8460-9.

4. Borchers AT, Selmi C, Cheema G, Keen CL, Shoenfeld Y, Gershwin ME. Juvenile idiopathic arthritis. Autoimmun Rev. 2006 Apr;5[4]:279-98. doi: 10.1016/j.autrev.2005.09.011.

5. Petty RE, Southwood TR, Manners P, Baum J, Glass DN, Goldenberg J, et al.; International League of Associations for Rheumatology. International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. J Rheumatol. 2004 Feb;31[2]:390-2. PMID: 14760812.

6. Holick MF. Vitamin D deficiency. N Engl J Med. 2007 Jul 19;357[3]:266-81. doi: 10.1056/NEJMra070553.

7. Rovner AJ, O'Brien KO. Hypovitaminosis D among healthy children in the United States: a review of the current evidence. Arch Pediatr Adolesc Med. 2008 Jun;162[6]:513-9.

8. Adams JS, Hewison M. Unexpected actions of vitamin D: new perspectives on the regulation of innate and adaptive immunity. Nat Clin Pract Endocrinol Metab. 2008;4[2]:80-90. doi: 10.1038/ncpendmet0716.

9. Szymczak I, Pawliczak R. The Active Metabolite of Vitamin D3 as a Potential Immunomodulator. Scand J Immunol. 2016 Feb;83[2]:83-91. doi: 10.1111/sji.12403.

10. Jones G, Strugnell SA, DeLuca HF. Current understanding of the molecular actions of vitamin D. Physiol Rev. 1998;78[4]:1193-231. doi: 10.1152/physrev. 1998.78.4.1193.

11. Amson Y, Amital H, Shoenfeld Y. Vitamin D and autoimmunity: new aetiological and therapeutic considerations. Ann Rheum Dis. 2007 Sep;66[9]:1137-42. doi: 10.1136/ard.2007.069831.

12. Adorini L, Penna G. Control of autoimmune diseases by the vitamin D endocrine system. Nat Clin Pract Rheumatol. 2008 Aug;4[8]:404-12. doi: 10.1038/ncprheum0855.

13. Mesci N, Külcü DG. Relationship Between Serum 25-Hydroxy Vitamin D Level and Disease Activity in Patients with Rheumatoid Arthritis. Haydarpasa Numune Med J 2017;57[2]:78–82. doi: 10.14744/hnhj.2017.76376.

14. Szodoray P, Nakken B, Gaal J, Jonsson R, Szegedi A, Zold E, et al. The complex role of vitamin D in autoimmune diseases. Scand J Immunol. 2008 Sep; 68[3]:261-9. doi: 10.1111/j.1365-3083.2008. 02127.x.

15. Stabile A, Avallone L, Compagnone A, Ansuini V, Bertoni B, Rigante D. Focus on juvenile idiopathic arthritis according to the 2001 Edmonton revised classification from the International League of Associations for Rheumatology: an Italian experience. Eur Rev Med Pharmacol Sci. 2006 Sep-Oct;10[5]:229-34. PMID: 17121315.

16. Consolaro A, Giancane G, Schiappapietra B, Davì S, Calandra S, Lanni S, Ravelli A. Clinical outcome measures in juvenile idiopathic arthritis. Pediatr Rheumatol Online J. 2016 Apr 18;14[1]:23. doi: 10.1186/ s12969-016-0085-5.

17. Consolaro A, Ruperto N, Bazso A, Pistorio A, Magni-Manzoni S, Filocamo G, et al; Paediatric Rheumatology International Trials Organisation. Development and validation of a composite disease activity score for juvenile idiopathic arthritis. Arthritis Rheum. 2009 May 15;61[5]:658-66. doi: 10.1002/art.24516.

18. Hajjaj-Hassouni N, Mawani N, Allali F, Rkain H, Hassouni K, Hmamouchi I, Dougados M. Evaluation of Vitamin D Status in Rheumatoid Arthritis and Its Association with Disease Activity across 15 Countries: "The COMORA Study". Int J Rheumatol. 2017; 2017:5491676. doi: 10.1155/2017/5491676.

19. Lee YH, Bae SC. Vitamin D level in rheumatoid arthritis and its correlation with the disease activity: a meta-analysis. Clin Exp Rheumatol. 2016 Sep-Oct; 34[5]:827-833. PMID: 27049238.

20. Lin J, Liu J, Davies ML, Chen W. Serum Vitamin D Level and Rheumatoid Arthritis Disease Activity: Review and Meta-Analysis. PLoS One. 2016 Jan 11;11[1]: e0146351. doi: 10.1371/journal.pone. 0146351.

21. Mouyis M, Ostor AJ, Crisp AJ, Ginawi A, Halsall DJ, Poole KE. Hypovitaminosis D among rheumatology outpatients in clinical practice. Rheumatology [Oxford]. 2008 Sep;47[9]:1348-51. doi: 10.1093/rheumatology/ken203.

22. Dağdeviren-Çakır A, Arvas A, Barut K, Gür E, Kasapçopur Ö. Serum vitamin D levels during activation and remission periods of patients with juvenile idiopathic arthritis and familial Mediterranean fever. Turk J Pediatr. 2016;58[2]:125-131. doi: 10.24953/ turkjped.2016.02.001.

23. Finch SL, Rosenberg AM, Vatanparast H. Vitamin D and juvenile idiopathic arthritis. Pediatr Rheumatol Online J. 2018;16[1]:34. doi: 10.1186/s12969-018-0250-0.

24. Nisar MK, Masood F, Cookson P, Sansome A, Östör AJ. What do we know about juvenile idiopathic arthritis and vitamin D? A systematic literature review and meta-analysis of current evidence. Clin Rheumatol. 2013 Jun;32[6]:729-34. doi: 10.1007/s10067-012-2159-1.

25. Stagi S, Bertini F, Cavalli L, Matucci-Cerinic M, Brandi ML, Falcini F. Determinants of vitamin D levels in children, adolescents, and young adults with juvenile idiopathic arthritis. J Rheumatol. 2014 Sep;41[9]:1884-92. doi: 10.3899/jrheum.131421.

26. Marini F, Falcini F, Stagi S, Fabbri S, Ciuffi S, Rigante D, Cerinic MM, Brandi ML. Study of vitamin D status and vitamin D receptor polymorphisms in a cohort of Italian patients with juvenile idiopathic arthritis. Sci Rep. 2020 Oct 16;10[1]:17550. doi: 10.1038/s41598-020-74861-9.

27. Bardare M, Bianchi ML, Furia M, Gandolini GG, Cohen E, Montesano A. Bone mineral metabolism in juvenile chronic arthritis: the influence of steroids. Clin Exp Rheumatol. 1991 Jan-Feb;9 Suppl 6:29-31. PMID: 2060174.

28. Lin Z, Li W. The Roles of Vitamin D and Its Analogs in Inflammatory Diseases. Curr Top Med Chem. 2016;16[11]:1242-61. doi: 10.2174/1568026615666150915111557.

29. Stagi S, Bertini F, Cavalli L, Matucci-Cerinic M, Brandi ML, Falcini F. Determinants of vitamin D levels in children, adolescents, and young adults with juvenile idiopathic arthritis. J Rheumatol. 2014 Sep; 41[9]:1884-92. doi: 10.3899/jrheum.131421.

30. Tang X. Mingyue L. Association between vitamin D concentrations with disease activity and bone mineral density of juvenile idiopathic arthritis patients. International Journal of Rheumatic Diseases. Conference: 18th Asia Pacific League of Associations for Rheumatology Congress, APLAR. China. 2016. Conference Start 20160926. Conference End: 20160929. 2016; 19:158.

31. Peixoto D, Teixeira F, Lucas R, Costa J, Costa L, AD. Vitamin D status in patients with juvenile idiopathic arthritis. Ann. Rheum. Dis. Conf. Annu. Eur. Congr. Rheumatol. Eur. Leag. Against Rheum. EULAR. 2012; 2013:71.

32. Çomak E, Doğan ÇS, Uslu-Gökçeoğlu A, Akbaş H, Özdem S, Koyun M, Akman S. Association between vitamin D deficiency and disease activity in juvenile idiopathic arthritis. Turk J Pediatr. 2014 Nov-Dec; 56 [6]:626-31. PMID: 26388593.

33. Nisar M, Cookson P, Masood F, Sansome A, Ostor A. Is there a link between vitamin D and juvenile idiopathic arthritis? Ann Rheum Dis Conf Annu Eur Congr Rheumatol Eur Leag Against Rheum EULAR. Conference Start: 20130612. Conference End:20130615.2013:72.

34. Bianchi ML, Bardare M, Caraceni MP, Cohen E, Falvella S, Borzani M, DeGaspari MG. Bone metabolism in juvenile rheumatoid arthritis. Bone Miner. 1990 May;9[2]:153-62. doi: 10.1016/0169-6009[90]90081-p.

35. Tzoufi M, Siamopoulou-Mavridou A, Challa A, Lapatsanis PD. Changes of mineral metabolism in juvenile chronic arthritis. Acta Paediatr Suppl. 1994 Mar; 394: 52-7. doi: 10.1111/j.1651-2227. 1994.tb13215.x.

36. Fernandes MR, Barreto WDR Junior. Association between physical activity and vitamin D: A narrative literature review. Rev Assoc Med Bras [1992]. 2017 Jun;63[6]:550-556. doi: 10.1590/1806-9282.63.06.550. PMID: 28876433.

37. Nijhof LN, van de Putte EM, Wulffraat NM, Nijhof SL. Prevalence of Severe Fatigue Among Adolescents with Pediatric Rheumatic Diseases. Arthritis Care Res [Hoboken]. 2016 Jan;68[1]:108-14. doi: 10.1002/acr.22710.

38. Armbrust W, Lelieveld OH, Tuinstra J, Wulffraat NM, Bos GJ, Cappon J, et al. Fatigue in patients with Juvenile Idiopathic Arthritis: relationship to perceived health, physical health, self-efficacy, and participation. Pediatr Rheumatol Online J. 2016 Dec 6;14[1]:65. doi: 10.1186/s12969-016-0125-1.

39. Huang IC, Anderson M, Gandhi P, Tuli S, Krull K, Lai JS, Nackashi J, Shenkman E. The relationships between fatigue, quality of life, and family impact among children with special health care needs. J Pediatr Psychol. 2013 Aug;38[7]:722-31. doi: 10.1093/ jpepsy/jst016.

40. Kim J, Chung H, Amtmann D, Salem R, Park R, Askew RL. Symptoms and quality of life indicators among children with chronic medical conditions. Disabil Health J. 2014 Jan;7[1]:96-104. doi: 10.1016/j.dhjo.2013.08.007.

41. Skversky AL, Kumar J, Abramowitz MK, Kaskel FJ, Melamed ML. Association of glucocorticoid use and low 25-hydroxyvitamin D levels: results from the National Health and Nutrition Examination Survey [NHANES]: 2001-2006. J Clin Endocrinol Metab. 2011 Dec; 96 [12]:3838-45. doi: 10.1210/jc.2011-1600.

42. Gröber U, Kisters K. Influence of drugs on vitamin D and calcium metabolism. Dermatoendocrinol. 2012 Apr 1;4[2]:158-66. doi: 10.4161/derm.20731.

43. Soybilgic A, Tesher M, Wagner-Weiner L. A survey of steroid-related osteoporosis diagnosis, prevention and treatment practices of pediatric rheumatologists in North America. Pediatr Rheumatol Online J. 2014; 12:24. doi: 10.1186/1546-0096-12-24.

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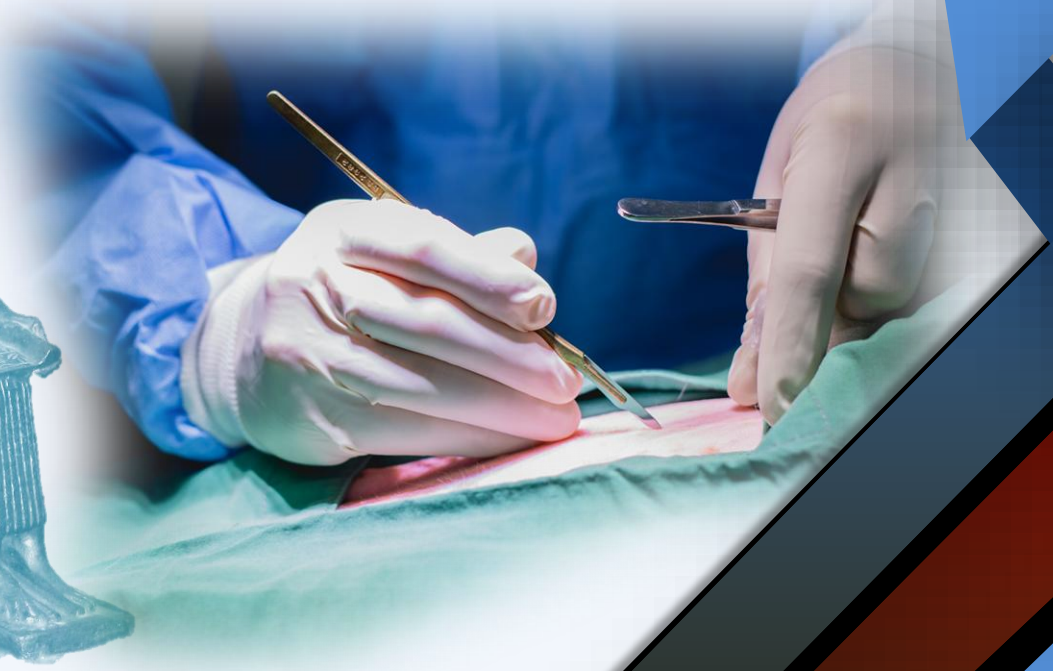
International Journal of Medical Arts

Volume 7, Issue 1 (January 2025)



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