

Case Series

Familial juvenile idiopathic arthritis in three siblings including dichorionic diamniotic twins: a case series highlighting familial aggregation and genetic susceptibility

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Received: 09 June 2026

Accepted: 09 July 2026

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ABSTRACT

Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatologic disorder of childhood and is considered a multifactorial disease with genetic and environmental contributions. Familial occurrence of JIA remains relatively uncommon and clinically significant. We report a case series involving three siblings born out of a non-consanguineous marriage, including dichorionic diamniotic twin male siblings, presenting with inflammatory arthritis suggestive of oligoarticular juvenile idiopathic arthritis with recurrent episodes, separated by symptom-free intervals. The elder sibling, an eleven-year-old female, presented with recurrent fever and associated inflammatory arthritis involving the right wrist and elbow. The twin siblings presented with recurrent knee and wrist arthritis, elevated inflammatory markers and ultrasonographic evidence of synovitis. Both the twins had episodes previously diagnosed as reactive arthritis before evolving into a probable JIA phenotype. Extensive investigations excluded infectious, cardiac and other connective tissue etiologies. All siblings demonstrated favorable response to non-steroidal anti-inflammatory therapy. This case series highlights possible familial aggregation, genetic susceptibility and phenotypic variability in JIA.

Keywords: Juvenile idiopathic arthritis, Familial JIA, Pediatric rheumatology, Oligoarticular JIA, Twin siblings, Genetic susceptibility, Reactive arthritis

INTRODUCTION

Juvenile idiopathic arthritis (JIA) represents a heterogeneous group of chronic inflammatory arthritis occurring in children younger than 16 years with symptoms persisting for at least six weeks, after exclusion of other identifiable causes.¹⁻³ The disease is believed to arise from immune dysregulation in genetically susceptible individuals triggered by environmental factors.^{4,5} Although sporadic cases are more common, familial clustering has been reported and supports the role of hereditary predisposition in disease pathogenesis.^{6,7} Twin studies and sibling aggregation analyses have further strengthened evidence for genetic susceptibility.^{8,9} We report a familial case series involving three siblings including dichorionic diamniotic twins presenting with

probable oligoarticular JIA with variable clinical and serological manifestations.

CASE SERIES

Case 1

11-year-old female child, the elder sibling born to non-consanguineous parents, presented with a history of intermittent fever for 2 months, associated with episodic redness, swelling, and tenderness involving the right wrist and right elbow joints at the age of 4 years. The symptoms were also associated with decreased appetite. There was no history of morning stiffness, limping, rash, hepatosplenomegaly, uveitis, or developmental delay. The laboratory investigations revealed elevated inflammatory markers, and the rheumatoid factor (RF) was positive. The

child was treated with syrup ibuprofen for 7 days and showed significant clinical improvement. She was on sodium valproate therapy for seizure episodes and electroencephalography findings of epileptiform discharges, started at the age of 15 months and continued upto 3 years of age.

Anthropometry of the child was normal for age. Systemic examination including ophthalmological evaluation and cardiovascular examination was normal. ECG and 2D echocardiography were also normal.

Case 2

A 4-year-old male child, one of the dichorionic diamniotic twins born by LSCS. The child was admitted for the first time in November 2024 with complaints of fever for 15 days, along with pain and swelling of the left wrist joint for 7 days. The mother also reported a history of loose stools for 4 days. Blood investigations revealed elevated CRP levels. Based on the clinical presentation and laboratory findings, the child was diagnosed with reactive arthritis and treated with syrup ibuprofen for 5 days along with supportive symptomatic management. The child responded well to treatment, showed clinical improvement within 7 days, and was subsequently discharged in stable condition.

Five months later, in April 2025, the child was brought by the parents with complaints of fever for 10 days, associated with pain and swelling of the right wrist and right knee joints. On investigation, Salmonella IgM was found to be positive. The child was diagnosed with reactive arthritis and treated with injectable antibiotics along with syrup ibuprofen for 7 days. The child improved clinically with treatment and was discharged in stable condition.

Seven months later, in November 2025, the child presented with intermittent fever and recurrent swelling of the right knee joint with pain and decreased range of motion for the preceding 2 months, associated with an antalgic gait. There were additional complaints of decreased appetite and poor linear growth compared with age-matched peers. The anthropometric assessment revealed a height less than 3rd percentile and was diagnosed as constitutional short stature after bone age estimation following Greulich and Pyle method. Laboratory investigations demonstrated mild iron deficiency anemia and vitamin D deficiency. Inflammatory markers were elevated.

Ultrasonography of the right knee revealed joint effusion with synovial thickening and fluid collection in the suprapatellar recess. ANA was weakly reactive with a nucleolar pattern, while RF and HLA-B27 were negative. There was no history suggestive of psoriasis, tuberculosis, enthesitis, or ocular involvement. Based on the clinical history, physical examination, and laboratory findings, a diagnosis of oligoarticular juvenile idiopathic arthritis was made. The child responded favorably to naproxen therapy.

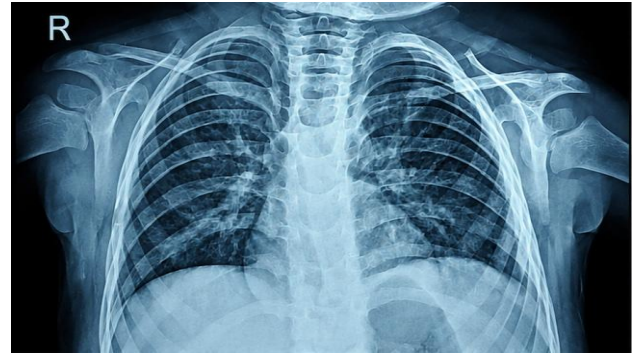


Figure 1: Case 2: X-ray of chest PA view of twin 1 dated 21 November 2025: normal study.



Figure 2: Case 2: X-ray of bilateral knee joints dated 21 November 2025 showing synovitis/effusion like changes.

Case 3

The second twin sibling, a 4-year-old male child, was admitted for the first time in April 2025 with complaints of fever for 20 days, associated with pain and swelling of both knee joints and decreased appetite. Anthropometric assessment and bone age estimation revealed constitutional short stature. On general physical examination, the child was noted to have pallor and right-sided scoliosis. Per abdominal examination revealed hepatosplenomegaly. The laboratory investigations demonstrated vitamin D deficiency, with an elevated ESR of 90 mm/hour by Westergren method. Serology for anti-hepatitis A virus antibodies was reactive, while liver enzyme levels were within normal limits. Based on the clinical and laboratory findings, a diagnosis of acute viral hepatitis A in the convalescent phase was made. In view of the associated joint symptoms, reactive arthritis was considered, and the child was treated with syrup ibuprofen for 7 days along with supportive symptomatic management. The child responded well to treatment and was discharged on vitamin D supplementation.

Seven months later, in November 2025 child was brought with complaints of fever for one and half month along with swelling and pain involving bilateral knee and wrist joints. Examination revealed bilateral knee and wrist swelling

with tenderness and restriction of movements. Right-sided scoliosis and a limb length discrepancy of 1 cm was noted. Ultrasonography demonstrated right knee joint effusion with fluid in suprapatellar and infrapatellar regions. ESR

and CRP were markedly elevated, and rheumatoid factor was mildly elevated. ANA and HLA-B27 were negative. The child improved with naproxen therapy and was diagnosed as oligoarticular juvenile idiopathic arthritis.

Table 1: Investigations.

Investigations	Cases		
	Case 1 (11-year female), date: 27 June 2019	Case 2 (4-year male twin 1), date: 20 November 2025	Case 3 (4-year male twin 2), date: 20 November 2025
Hemoglobin (g/dl)	9.7	10.4	9.4
TLC (/cu.mm)	12,430	9500	13,200
Platelets (/cu.mm)	413,000	256000	777,000
ESR (mm/hour)	95	60	125
CRP	Positive	8.32 mg%	8.84 mg/dl
Rheumatoid factor (IU/ml)	16.2	Negative	14.1
ANA	Negative	Weakly positive (nucleolar)	Negative
HLA-B27	Negative	Negative	Negative
Ferritin (ng/ml)	Normal	126.7	93.25
Vitamin D (ng/ml)	18.2	11.93	16.01
Ultrasonography of joints	USG of right wrist and right elbow normal	USG: effusion/synovitis in both the knee joints	USG: effusion/synovitis in the right knee and wrist joint

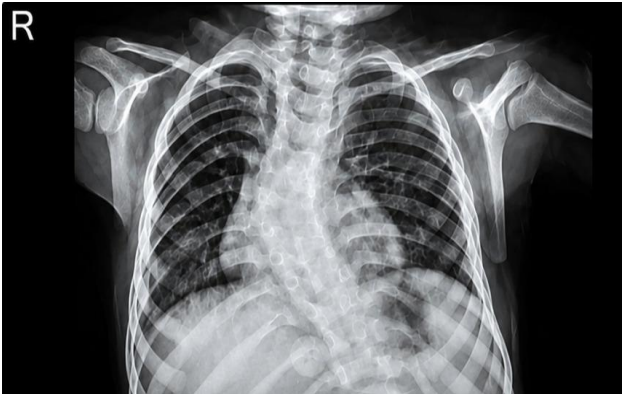


Figure 3: Case 3: X-ray of chest PA view of twin 2 showing scoliosis with convexity to right side.

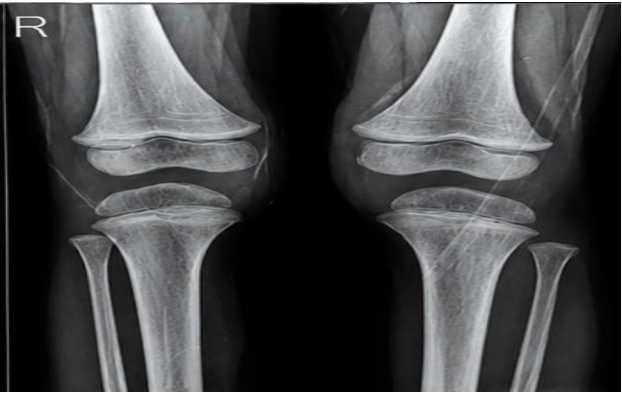


Figure 5: Case 3: X-ray of bilateral knee joints of twin 2 suggesting synovitis like changes.



Figure 4: Case 3: X-ray of bilateral wrist joints of twin 2 showing changes suggesting synovitis/effusion.

DISCUSSION

The present case series demonstrates probable familial aggregation of juvenile idiopathic arthritis in three siblings born out of non-consanguineous marriage, including dichorionic diamniotic twin siblings. Familial JIA is uncommon but increasingly recognized, supporting the contribution of genetic susceptibility to disease pathogenesis. Variability in clinical phenotype and serological markers among affected siblings has been documented in previous literature and is similarly observed in our cases. One sibling demonstrated ANA positivity, while others showed mild rheumatoid factor elevation. All the siblings exhibited elevated inflammatory markers and there was a favorable response to NSAIDs.

An important observation in this series is the repeated initial diagnosis of reactive arthritis in the twin siblings.

There was no family history suggestive of psoriasis, rheumatoid arthritis, ankylosing spondylitis, inflammatory bowel disease, thyroid disease, systemic lupus erythematosus except the elder female sibling diagnosed as oligoarticular juvenile idiopathic arthritis. The presence of synovitis on ultrasonography and recurrent episodes involving large joints supported inflammatory arthritis, rather than transient reactive disease in our cases.

Diagnosis of JIA in all the siblings including twins, further strengthens the possibility of hereditary predisposition despite the pedigree chart did not include any parents and grandparents having systemic arthritis. Previous studies have demonstrated increased concordance rates among twins and first-degree relatives.⁶⁻⁹ The occurrence of disease in siblings with varying clinical severity supports the concept of phenotypic variability in genetically susceptible individuals in our case series.

CONCLUSION

Although definitive genetic studies were not performed, this familial case series involving three siblings, including dichorionic diamniotic twins, highlights the importance of considering juvenile idiopathic arthritis in children presenting with recurrent inflammatory arthritis, particularly when they have previously been provisionally diagnosed with reactive arthritis. The familial clustering and phenotypic variability in our cases strongly suggest underlying genetic susceptibility. Regular follow-up of all children presenting with arthritis is essential for the early diagnosis of juvenile idiopathic arthritis and appropriate long-term management, which may help prevent long-term disability and growth impairment.

ACKNOWLEDGEMENTS

The authors would like to thank the medical director of the hospital. The authors are also thankful to the resident doctors and nursing staff of the department of pediatrics for the successful management of the children. The authors also thank the parents for their faith and patience and consent for the publication.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Cite this article as: Ranabijuli PK, Lodi N, Dasare PB, Reddy JR. Familial juvenile idiopathic arthritis in three siblings including dichorionic diamniotic twins: a case series highlighting familial aggregation and genetic susceptibility. Int J Contemp Pediatr 2026;13:1513-6.