Original Article

Role of Magnetic Resonance Imaging in Concomitant Periarticular Infections in Septic Arthritis of Large Joints in Children: A Systematic Review

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Abstract

Background: Septic arthritis associated with adjacent infections, presents a diagnostic challenge as the clinical presentation is similar to that of isolated septic arthritis, additional diagnostic tools are needed to detect these infections. The purpose of this study was to examine the effectiveness of magnetic resonance imaging (MRI) for diagnosis of concomitant infection in children with septic arthritis of large joints and its effect on patient outcome and treatment. **Materials and Methods:** Electronic literature research of PubMed, Cochrane and Scopus, was conducted in January 2022 using a combination of MeSH, search terms and keywords. The data extracted included the study details, demographic data, the proportion of patients having a concomitant periarticular infection, clinical presentation, blood parameters and culture findings and outcomes. **Results:** This review included seven studies with 499 patients. The mean age was 7.08 ± 2.38 years in the study. There was a male predominance, with 174 being males (62.36%). The most common joint involved was the hip joint (44.47%). 42.48% had concomitant periarticular infections detected by MRI. Osteomyelitis was the most common infection seen in 209 patients (41.84%). The mean duration of antibiotics given and hospital stay was significantly more in periarticular infections ($P > 0.05$). 32.5% of the patients with septic arthritis underwent a second surgical procedure whereas 61.11% of patients with periarticular infections underwent second procedure in this review ($P > 0.05$). **Conclusions:** The use of MRI to diagnose these complicated infections appears to be beneficial. Multi-centric randomised control trials are needed to investigate the efficacy of MRI and its impact on patient care and outcome.

Keywords: *Children, large joints, MRI, periarticular infection, septic arthritis*

Introduction

Septic arthritis is a term that refers to microbial invasion of the joint space. The incidence of septic arthritis is 2–10 cases per 100,000 population per year.[1] Early diagnosis and adequate treatment with systemic antibiotics and irrigation and debridement of the joint are critical to avoid complications.

Septic arthritis in children may occur in isolation but may be associated with periarticular infections in 17%–76% of patients.[2] The clinical findings in a patient having septic arthritis with adjacent infections are very similar to that of one with isolated septic arthritis. Laboratory tests serve only as a supporting evidence without confirming or refuting the presence of adjacent infections. This makes it difficult to identify these more complex infections. If an adjacent infection is present, surgical debridement of the septic joint alone is potentially insufficient. Failure to identify these distinct adjacent infections may result in inadequate initial treatment and worsening of the patient's clinical course.

Various studies have suggested that magnetic resonance imaging (MRI) has a higher sensitivity for diagnosing osteomyelitis and pyomyositis in comparison to bone scans and radiography. It is also beneficial in determining the amount and location of the collection. But, it is expensive, generally less accessible, and frequently involves sedation in young patients.[3] Further, it is unknown whether diagnosing these periarticular infections early leads to any decrease in in-hospital stay, duration of antibiotic duration, second surgical procedure and clinical and radiological sequelae. The purpose of this systematic review is to

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examine the effectiveness of MRI in diagnosing these complex infections and its impact on patient treatment and outcome.

Materials and Methods

Search strategy

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) format was used to conduct this review [Figure 1]. An electronic literature search was conducted up to January 2022, using a combination of MeSH, search terms, and keywords in the Cochrane Library, PubMed and Scopus databases [Table 1]. To optimise the search results, several combinations were employed, as well as the usage of Boolean operators. The search was supplemented by personally checking the bibliographies of the retrieved papers. Using the "similar articles" option, further articles were retrieved. To create a list of possibly relevant papers, two reviewers first reviewed the titles and abstracts and removed any duplicates (VG and AR). After screening the title and abstract, full-text articles were obtained.

Eligibility criteria

The studies included[1] original articles,[2] children with septic arthritis of large joints who have undergone an MRI,[3] describing the proportion of concomitant periarticular infection and[4] written in the English language. The exclusion criteria included[1] case reports,[2] case series of fewer than three patients,[3] letters to the editor,[4] narrative reviews,[5] animal studies,[6] biomechanical studies, and[7] diagnosis other than pyogenic septic arthritis. It was performed independently by two reviewers (VG and VS). In the presence of a disagreement about the inclusion or exclusion of a particular study, the opinion of the senior author was sought (RBK).

Data extraction

Two investigators (VG and VS) independently extracted data on an Excel spreadsheet (Microsoft) into a prearranged summary table based on study design, level of evidence, patient demographics, joint involved, the proportion of patients having a concomitant periarticular infection, clinical presentation, blood parameters, criteria for diagnosing septic arthritis and concomitant periarticular infection, culture findings and outcomes. A second reviewer independently verified the retrieved data by repeating the process (RBK). The Oxford Centre for Evidence-based Medicine criteria were used to assess the level of evidence.[4] In the event of a disagreement, the data extraction was

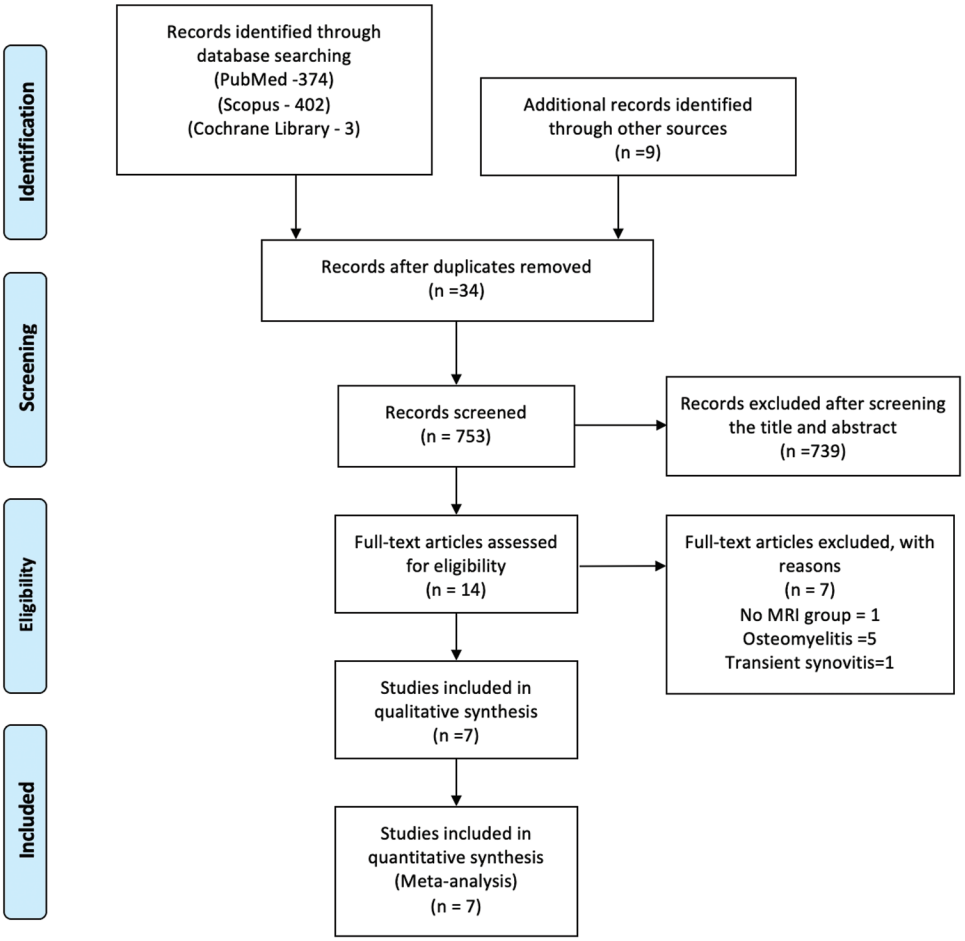

Figure 1: PRISMA flow chart

Table 1: Search terms used

Patient	Intervention	Outcome
"Septic arthritis"	"MRI"	"Periarticular arthritis"
"Infectious arthritis"	"Magnetic resonance imaging"	"Periarticular infection"
"Bacterial arthritis"	"Magnetic resonance image"	"Osteomyelitis"
"Bacterial arthritis"		"Pyomyositis"
"Suppurative arthritis"		
"Child"		
"Paediatric"		
"Paediatric"		
"Adolescent"		

resolved by the senior author (RBK). In studies providing data about individual patients included in the study, data was extracted from the tables provided.

Risk of bias assessment

Two investigators independently assessed the quality of research conclusions using the Methodological Index for Non-Randomised Studies (MINORS) (ideal maximum score of 16 for non-comparative studies and 24 for comparative studies) (VG and VS).[5] In the event of a disagreement, it was resolved by the senior author (RBK).

Statistical analysis

Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± SD and median. Quantitative variables were compared using an unpaired student *t* test/chi-square test. Spearman rank correlation coefficient was used to assess the association of various quantitative parameters. A value of $P < 0.05$ was considered statistically significant.

Results

Literature search

The initial literature search yielded 787 articles. 34 duplicate articles were removed. 753 articles were screened from their title and abstract. 14 articles were selected from among these after reading the abstracts and titles. Of these, seven articles were excluded because of inadequate data in the study. Finally, seven articles were considered for qualitative review[6-12] [Figure 1].

Study characteristics

One of the selected studies was of level II,[12] two of the studies were level III[10,11] evidence, and the rest were level IV[6-9] evidence. There were no comparative studies among all the studies involved. Four studies had a score of 14 out of 16 whereas 2 studies had a score of 13 out of 16 on MINORS score. Only one study had a score of 12 out of 16 [Table 2].

Demographic data

The total sample size of all the studies included in this review was 499 patients. The mean age for the patients included in the study was 7.08 ± 2.38 years. There was a male predominance (62.36%). The most common joint involved was the hip (44.47%) followed by the knee (29.72%). Either the positive gram stain or growth from blood or synovial fluid or cell count > 50,000 mm^3 in the synovial fluid was the most common criterion used to diagnose septic arthritis. One study by Lee *et al.* used cell count > 20,000 mm^3 as positive criteria for diagnosing septic arthritis.[7] In addition, Siddiqui *et al.* used Kocher's criteria[13] for diagnosing septic arthritis in presence of clinical features which were highly suggestive of septic arthritis.[11] Staphylococcus aureus was the most common organism isolated (52.75%) [Table 2].

Clinical features, blood and culture findings

The mean duration of symptoms before presentation was 5.44 ± 1.54 days. Only one study mentioned the average duration of symptoms in patients with septic arthritis and patients with concurrent periarticular infections separately.[11] The mean duration of symptoms in the septic arthritis group was 2 ± 2 (range 1–14) days and in the concomitant peri-articular group was 6 ± 4 (range 1–18) days in the study. This value was found to be statistically significant in their study ($P = 0.003$).

Two studies mentioned the mean blood parameters in patients with septic arthritis and patients with concomitant infections.[6,11] The mean value of WBC, ESR and CRP in patients with the concomitant periarticular group was $14.25 \pm 0.36 \times 10^3$ cells/ mL, 66.1 mm/h, and 67.1 ± 77.64 mg/L, respectively, whereas the mean values of WBC, ESR and CRP in patients with septic arthritis alone was $13.41 \pm 1.10 \times 10^3$ cells/mL, 58.08 ± 10.70 mm/h, and 29.68 ± 31.99 mg/L, respectively, in this study. However, no statistically significant association was found between both groups ($P > 0.05$) [Table 3].

Four studies mentioned the number of patients who were either blood or synovial fluid culture positive.[6,10-12] 24 (15.29%) and 134 (85.35%) patients with periarticular infection were positive on blood and synovial fluid culture, respectively, whereas 9 (7.96%) and 57 (50.44%) of patients with septic arthritis alone were blood and synovial culture positive. No significant relationship was found between patients with septic arthritis and periarticular infection

Table 2: summary of studies

Author	Year	Level Of Evidence	Study Design	MINORS score	Number	Sex	Joint involved	patients with CI	Duration of Symptoms (days)	SYMPTOM	WBC (X 10^3 cells/ mL)	CRP (mg/L)	ESR (mm/h)	Blood culture	Synovial culture	MRI findings
Hunter *et al.*[6]	2020	4	Retrospective	13	53	36 M 17 F	H-18,K-12,S-3,SI-10,A-8,E-1,W-1	29[a]	-	Fever (37)	12.5 –SA 14 - CI	77-SA 122-CI	-	22	4	Marrow oedema, osseus infiltration, Contrast enhancement
Lee *et al.*[7]	1999	4	Retrospective	12	9	6 M 3F	H-9	2	6	Pain[9]	13.85	-	73.3	-	-	Marrow oedema
Montgomery *et al.*[8]	2013	4	Retrospective	14	200	-	H-82,k-59,A-26,S-18,E-11,W-2,F-2	43	-	101.1 ^{o} F[b]	-	-	-	-	-	-
Refakis *et al.*[9]	2017	4	Retrospective	14	20	-	H-20	7	7.2	100^{0} F [b]	12.1	6.6	48.2	-	-	-
Rosenfeld *et al.*[10]	2015	3	Retrospective	13	87	55 M 32 F	K-34,H-28,A- 8,S- 8, E-8,W-1	51	5	-	14.8	16.1	55.5	0	87	-
Siddiqui *et al.*[11]	2021	3	Retrospective	14	73	43 M 30 F	H-36,k-24,E-5,A-3,S-2,P-1	43	2 days- SA 6 days-CI	Fever (50), Limited weight-bearing and pain (71)	13.8-SA 14.5- CI	19-SA 12.2-CI	55.3-SA 66.1-CI	11	43	osseus infiltration
Welling *et al.*[12]	2018	2	Retrospective	14	57	34 M 23 F	-	37	-	-	-	-	-	0	57	Marrow oedema, osseus infiltration, Contrast enhancement

M = male, F = female, H = hip, K = knee, S = shoulder, A = ankle, E = elbow, W = wrist, SI = Sacro-iliac joint, F = foot, P = polyarticular, SA = septic arthritis, CI = concomitant infection

[a]Three patients had concomitant pyomyositis

[b]Two studies mentioned the mean temperature of the patient included in their study

Table 3: Blood parameters

	SA	CI	*P* Value
WBC ($\times 10^3$ cells/ mL)	13.41 ± 1.10	14.25 ± 0.36	0.12
ESR (mg/L)	58.08 ± 10.70	–	0.18
CRP (mm/h)	29.68 ± 31.99	67.1 ± 77.64	0.39

SA = septic arthritis, CI = concomitant infection

Table 4: Blood and synovial culture positivity

	Number of patients	R(s)	*P* Value
SA (N)	113	–1	.74
Blood culture positive	9	0.2	.8
Synovial culture positive	57		
CI (N)	157	.59	.41
Blood culture positive	24	1	.2
Synovial culture positive	134		

SA = septic arthritis, CI = concomitant infection

Table 5: Number of patients undergoing repeat procedures

Study	Repeat procedure in SA	Repeat procedure in CI	*P* Value
Hunter *et al.*[6]	11(40.74%)	17(65.38%)	0.94
Refakis *et al.*[9]	2 (15.38%)	5(38.46%)	
Total	13/40 (32.5%)	22/36(61.11%)	

SA = septic arthritis, CI= concomitant infection

with either blood or synovial culture positivity ($P > 0.05$) [Table 4].

Magnetic resonance imaging and its impact on treatment and outcome

212 patients (42.48%) had concomitant periarticular infections detected by MRI in this study. Osteomyelitis was the most common infection seen in 209 patients (41.84%) followed by pyomyositis which was seen in three patients. Patients with septic arthritis of the Ankle and shoulder joint showed concomitant periarticular infection in 100% of the patients [Table 2]. However, a non-significant relationship was found between different joints involved and the development of concomitant infection in this review ($P = 0.78$).

Hunter *et al.* mentioned the total duration of antibiotics given and hospital stay.[6] The mean duration of antibiotics given, and hospital stay to patients with septic arthritis alone was 34.2 days and 11.6 days, respectively. However, patients with concomitant peri-articular infections were given antibiotics and hospitalised for a mean duration of 48 days and 19 days, respectively. There was a statistically significant increase in total antibiotic duration and hospital stay in patients with concomitant infections as compared to septic arthritis alone ($P < 0.05$) in their study.

Two studies mentioned the number of patients who underwent repeat surgical procedures in both the groups.[6,9] 32.5% of the patients with septic arthritis underwent a second surgical procedure whereas 61.11% of patients with periarticular infections underwent second procedure in this review. However, there was no significant increase in repeat procedures in patients with concomitant periarticular infections as compared to patients with septic arthritis ($P = 0.94$) [Table 5].

Only one study mentioned the radiological and clinical outcomes at the final follow-up. These authors found that one patient with septic arthritis had developed osteonecrosis of the femoral head at 22 months follow-up.[9]

Discussion

Septic arthritis associated with adjacent infections, such as subperiosteal abscesses, intramuscular abscesses, or osteomyelitis presents a diagnostic challenge as the clinical presentation is similar to that of isolated septic arthritis. additional diagnostic tools are needed to detect these infections. The use of MRI in the diagnosis of musculoskeletal infections is becoming more common. When compared to bone scans and plain radiographs, it has a higher sensitivity for diagnosing concomitant periarticular infections. The number of research papers examining the usefulness of MRI in diagnosing concomitant periarticular infections with septic arthritis is limited, that is why we conducted a systematic review of the available literature to examine the role of MRI in septic arthritis of large joints in children.

Jackson *et al.* treated 96 cases of septic arthritis and found that the majority of their patients with concomitant infections (44%) were under the age of six months.[2] The possible reason for this was given by Offiah AC that the cartilaginous epiphyses receive blood directly from the metaphysis, explaining the

reported higher incidence of concurrent infection in this age group.[14] Additionally, Frank *et al.* showed that the neonatal periosteum is thinner and more likely to perforate, spilling infection into the joint and adjacent soft tissues.[15] There is a significant positive relationship between septic arthritis and osteomyelitis when the metaphysis is intra-articular.[16] 42.84% of patients developed a concomitant periarticular infection in this review. However, no relationship was established between joint involved and development of concomitant infection in this review ($P < 0.05$).

The clinical presentation of individuals with concomitant infection is similar to that of patients with septic arthritis alone, making differentiation challenging. Furthermore, a child's incapacity to express his or her complaints, as well as the difficulties of examining an irritable kid, makes it difficult to localise concurrent infections. Low awareness of acute Septic Arthritis, clinicians with less orthopaedic training, and distance from specialised centres could all play a role in delayed presentation. Also, the geographical constrains, lack of knowledge, economical status, traditional bone setters, religion, poverty and cultural practices contributes to the late presentation.[17] Siddiqui *et al*. have shown that the chances of developing concomitant infection increases significantly with delay in presentation[11] ($P < 0.05$).

According to Unkilla *et al.*, patients with concomitant periarticular infections had a much higher and slower normalisation of C-reactive protein.[18] Rosenfeld *et al.* believed that children with CRP > 13.8 mg/L and ANC > 8.6 x 10^3 cells were more likely to have a concomitant periarticular infection.[10] Whereas, Montgomery *et al.* found no association between the blood parameters and chances of concomitant infections.[8] Similar results were seen by Siddiqui *et al.* in their study.[11] However, Hunter *et al.* showed that higher CRP level was seen in patients with concomitant infections.[6] No statistically significant association was found between the development of concomitant infection and blood parameters in this review.

Siddiqui *et al.* showed that patients with positive joint fluid bacterial cultures had a 72% (31/43) chance of getting concomitant osteomyelitis, whereas those with negative cultures had a 43% (12/28) chance ($P < 0.05$).[11] Hunter *et al.* found similar results but the value was not significant.[6] No significant association was found between blood or synovial culture positivity with septic arthritis or concomitant infection in this review. Montgomery *et al.* found a statistically significant association between infection by MSSA and MRSA and the development of concomitant infection.[8] However, the association between organism isolated and concomitant infection could not be calculated in this review.

Kirkhus *et al*. concluded that MRI is a useful supplementary tool in distinguishing among different types of arthritis and excluding or verifying important differential diagnoses such as osteomyelitis, tumours and fractures.[19] Manz *et al*. found that when MRI was used in septic arthritis, concurrent infections were more common than suspected osteomyelitis or septic arthritis alone.[20] In this review, overall periarticular infection was diagnosed with the help of MRI in 42.48% of patients. Merlini *et al.* recommended performing a contrast-enhanced MR in paediatric hip infection to diagnose osteomyelitis.[21] Lee *et al.* tried to distinguish between transient synovitis and septic arthritis based on MRI findings. The presence of low signal intensity changes in the bone marrow on fat-suppressed gadolinium-enhanced T1-weighted images and high signal intensity changes on fat-suppressed T2-weighted images indicates septic arthritis. According to these authors, the presence of extensive juxta-articular signal intensity changes was consistent with the presence of concomitant periarticular infections in the presence of septic arthritis.[7]

MRI may delay therapy initiation, but the relevance of this is difficult to assess. Laine *et al.* concluded that patients with septic arthritis of the hip who fail to clinically respond to an initial hip arthrotomy and appropriate antibiotics may benefit from an MRI for the identification of concomitant infections that may require further surgical intervention.[22] Refakis *et al*. also recommended that advanced imaging be used on an individual basis.[9]

In this review, there was a statistically significant increase in the in-hospital stay and antibiotic duration in patients with concomitant infections as compared to a patient with septic arthritis. 32.5% of the patients with septic arthritis underwent a second surgical procedure whereas 61.11% of patients with periarticular infections underwent second procedure in this review. But, this value was not significant ($P > 0.05$). In contrast, Montgomery *et al.* stated that advanced imaging may benefit children with septic arthritis by shortening hospital stays, reducing the number of operational procedures required, and possibly limiting infection-related sequelae by detecting concomitant infections earlier.[8] Livingston *et al.* believed that a second or additional procedure depended on clinical and laboratory parameters rather than the presence of periarticular infection. Repeat washout was related to a left shift in the CBC, positive blood or synovial fluid cultures, and a postoperative fever higher than 39°C.[23] We believe that the duration of antibiotics and hospitalisation is determined by the resolution of the patient's symptoms and acute signs of blood inflammation. We concur with Hunter *et al.* that children with concomitant infection have disseminated infection and are more likely to require antibiotics and hospitalisation for an extended period.[6] Furthermore, these children may be more immunocompromised. MRI, on the other hand, can aid to clear the infection more effectively by guiding the surgeon in identifying the extent and location of the disease before surgery and reduce the risk of infection-related sequelae in patients with concurrent periarticular infection.

The main limitation of this review is that the studies included are either of level III or level IV evidence. Heterogeneity of the diagnosis and management could have potentially created a bias in this review. Failure to report clinical and radiological outcomes at final follow-up is another limitation. Failure to confirm concomitant infection with either staining or culture as the fluid might be reactionary in nature is also one of the limitations.

Conclusion

The usefulness of MRI in diagnosing concomitant periarticular infections in patient with septic arthritis appears to be beneficial; however, there is limited evidence to suggest routine use of MRI. It is reasonable to infer that the risk of missing the extent of the infection, as in the case of concomitant osteomyelitis and periarticular abscess, justifies the use of MRI on individual basis. Further, Multicentric randomised control trials are needed to investigate the effectiveness of MRI for identifying concurrent infections and their impact on patient care and outcome.

Authors' contribution

VG: conceptualisation, data curation, and writing – original draft.
VS: data curation, methodology, writing – review and editing, and formal analysis.
RBK: data curation, methodology, writing – review and editing, and formal analysis.
AR: writing – review and editing and supervision.
RY: methodology and writing – review and editing.
SKS: writing – review and editing and supervision.

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Conflicts of interest

There are no conflicts of interest.

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