

## Review Paper

## Investing Neonatal Septic Arthritis: A Systematic Review



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**Citation** Harsha N, Kotha R, Madireddy A. Investing Neonatal Septic Arthritis: A Systematic Review. *Journal of Pediatrics Review*. 2024; 12(1):53-64. <http://dx.doi.org/10.32598/jpr.12.1.1104.3>

**doi** <http://dx.doi.org/10.32598/jpr.12.1.1104.3>

## Article info:

Received: 23 Oct 2023  
First Revision: 18 Nov 2023  
Accepted: 13 Dec 2023  
Published: 01 Jan 2024

## ABSTRACT

**Background:** Septic arthritis is an uncommon condition in neonates. It is a serious disorder, especially because of the possibility of sequelae, if not identified and treated early. In addition, due to the rarity of this condition in neonates and the paucity of signs and symptoms, the diagnosis of septic arthritis is more difficult in older children. The published literature is limited to case series, which is why the purpose of this systematic review is to provide a comprehensive summary of neonatal septic arthritis based on the existing literature.

**Objectives:** The published literature is limited to case series, which is why the purpose of this systematic review is to provide a comprehensive summary of neonatal septic arthritis based on the existing literature. This study identifies the changing trends over time, specifically focusing on intravenous cannulation as a major risk factor that led to the undertaking of the study.

**Methods:** The preferred reporting items for systematic reviews and meta-analyses protocol guidelines were used in this study. Three search engines were used for 239 articles. A total of 26 studies were screened in full text, of which 16 articles underwent quantitative analysis. Due to limited data and heterogeneous reporting, the data were summarized descriptively.

**Results:** The total number of babies and joints studied was 307 and 313, respectively, of which the proportion of male babies was mentioned in 12 case series, accounting for 136(228) (60% [42%-71%]) subjects. The most common presenting symptoms were swelling at the involved joint, erythema, and decreased range of motion in variable order. The most common site of involvement was the hip joint (42%), followed by the knee joint (27%). *Staphylococcus aureus* (40%) was the most commonly cultured pathogen, followed by *Klebsiella* (18%). Antibiotics were reported in only 12% (38 babies) of the cases. Open surgery was performed on 16% of the 49 babies. The rest of the babies responded to joint aspiration and irrigation, with or without immobilization. Prompt laboratory and radiographic evaluations could help reduce delays in diagnosis and improve outcomes. Blood and tissue cultures were positive in most of the cases. Previous culture reports for the same unit guide the addition of empirical antibiotics.

**Conclusions:** In our case series, the majority of the babies were premature. The most common joint involved is the hip joint. The most common underlying cause is sepsis and catheterization. Intravenous cannulation is also a major risk factor because of the continuity of metaphysis and

## Key Words:

Neonate, Sepsis, Septic arthritis, Knee joint

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## Introduction

Septic arthritis is the inflammation of the joints, secondary to an infectious aetiology that most commonly includes bacterial but can also be fungal, viral, or have other pathogens [1]. It is an uncommon and critical condition in neonates mainly because babies can become permanent handicaps if not diagnosed and treated early [2]. The important reason for the delayed diagnosis is the paucity of symptoms and signs in neonates [3]. Osteoarticular infections in newborns are usually blood-borne infections [4, 5]. Neonates requiring neonatal intensive care unit admission for prematurity, ventilator therapy, and invasive procedures are known to be predisposing actors, which are related to the risk of bacteremia [6].

The incidence of septic arthritis varies in different regions, such as 0.12/1000 live births in Singapore [5] and 1 in 1500 in India [7]. Such a low rate of incidence indicates the difficulty of earlier diagnosis. Also, attention has been paid to neonatal septic arthritis of the lower limbs, especially the hip [8–13], but there are reports of involvement of the shoulder joint [14].

*Staphylococcus aureus* is the most prevalent organism involved in osteoarticular infections as the risk of this bacteremia rises with invasive procedures. However, there is an increasing trend of cases due to *Klebsiella* that have been reported [9–11, 15], a possible reason being contaminated equipment, which should alert the physicians for further cases. Other reported bacterial pathogens include *Candida* [16], *Pseudomonas*, *Staphylococcus epidermidis*, *Streptococcus spp.*, *Haemophilus influenza*, *Proteus*, and so on.

Neonatal septic arthritis is an uncommon condition and less reported; accordingly, this systematic review summarizes the epidemiology, presenting symptoms, laboratory values, radiological inputs, microbiology, and treatment results of neonatal septic arthritis and demonstrates the changing trends.

## Methods

### Search strategy

The literature was screened by the authors using the following searches: Medical subject heading (MeSH) term=population, search fields=neonate; MeSH term=diagnosis, search fields=septic arthritis. PubMed, Scopus, Embase, and Ovid/Medical Literature Analysis and Retrieval System Online (MEDLINE) databases were

used. Search fields were alternated until no new articles were revealed. At that point, the search was considered complete.

During neonatal periods and infancy, there is an anastomosis between joints and bone arteries that facilitates the transmission of bacterial infections from bone to joint and vice versa. Therefore, during neonatal periods and early infancy, in most cases, these infections are associated with osteoarthritis. Therefore, we included these two diseases.

### Study screening and selection

The search yielded a total of 253 studies (Figure 1). After the removal of duplicate articles, 239 studies remained. Based on the title and abstract review performed by all four authors, a total of 26 articles were included in the qualitative review. The bibliographies of all the reviewed articles were thoroughly evaluated to determine if any other relevant articles had been unintentionally overlooked. The independent full-text screenings of the articles were performed by all four authors. Of the 26 screened articles, 10 studies did not meet our inclusion/exclusion criteria (Table 1). The resulting 16 articles underwent quantitative analysis. We incorporated all studies, regardless of their timeframe. We specifically included articles that were in the English language.

### Data collection

The categories for data gathering included population demographics, gestational age, age of presentation, average birth weight, presence of risk factors, such as prematurity, presenting features, number of joints involved, probable causative factors, laboratory values, imaging modalities, microbiologic diagnosis, medical management, surgical management, and complications. The variables under demographic features were gestational age, emphasizing prematurity, age of presentation, and gender, with a mainly male predominance. The presenting features were recorded as binary variables. The C-reactive protein (CRP), leukocyte count, and initial temperature were recorded. The use and positive results of ultrasound, computed tomography, and magnetic resonance imaging were recorded. Joint involvement, aspirate, surgical, and blood cultures as well as the disease course and hospitalization details were all documented. The duration of treatment, including intravenous or oral antibiotics was noted. Meanwhile, open versus ultrasound/computed tomography-guided percutaneous drainage operations performed along with type/num-

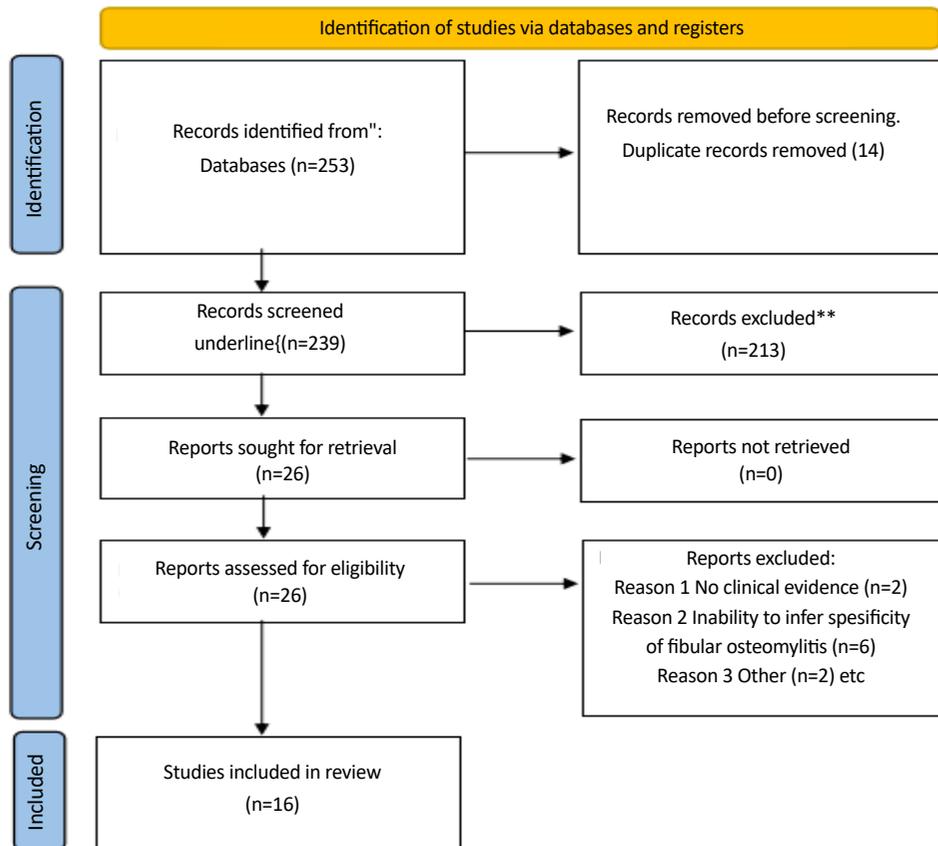


Figure 1. The preferred reporting items for systematic reviews and meta-analyses protocol flow diagram *Journal of Pediatrics Review*

ber are also included in records. After follow-up completion, any secondary sequelae detected were accounted for accordingly.

**Quality assessment**

To assess the included studies, which were predominantly case series, the guidelines from the National Institutes of Health (NIH) were used [17]. Since all the published literature is limited to a level of clinical evidence of IV, a quality assessment tool for case series under NIH was used. This tool has been modified to appropriately evaluate the methodologic quality of case series in light of their most common pitfalls. It includes nine questions. According to the NIH quality assessment

tool for case series studies, as described by Uthraraj et al. (2022) and Rubin et al [8, 13]. (2020), it was determined that these two studies are in the poor-quality category (6/9). On the other hand, Salamon [19], Li et al. [20], Khriesat et al. [10] were classified as good-quality studies (9/9). The remaining studies were classified as of fair quality (8/9) [19, 20].

**Data abstraction and statistical analysis**

Due to heterogeneous data and a smaller sample size, we also included an extended time frame, which is why a meta-analysis could not be performed.

Table 1. Inclusion and exclusion criteria

Inclusion Criteria	Exclusion Criteria
The onset of symptoms in neonatal period (<28 days)	Level V evidence
The diagnosis of septic arthritis of a joint	The absence of at least one data table beyond the demographics
Level IV evidence or higher	Minimum follow-up of 3 months

**Table 2.** Demography of case series

No.	Authors (y)	Country	Journal	Number of Patients	Number of Joints
1	Utharaj et al. 2022 [8]	India	Cureus	14	16
2	Rubin et al. 2020 [13]	United States	The Journal of Paediatrics	45	23
3	Salamon et al. 2020 [19]	Slovenia	Signa Vitae	15	7
4	Sreenivas et al. 2016 [9]	India	European Journal of Orthopaedic Surgery & Traumatology	29	34
5	Li et al. 2016 [20]	China	Medicine	52	56
6	Khriesat et al. 2011 [10]	Jordan	Journal of Paediatric Infectious Disease	27	37
7	Kabak et al. 2002 [2]	Turkey	Paediatrics International	14	14
8	Bos et al. 1998 [14]	The Netherlands	The Journal of Bone and Joint Surgery	8	10
9	Merchant et al. 1997 [16]	India	Journal of Tropical Paediatrics	8	8
10	Halder et al. 1996 [6]	Malaysia	Southeast Asian Journal of Tropical Medicine	10	14
11	Abuekteish et al. 1996 [11]	Jordan	European Journal of Pediatrics	17	20
12	Vidigal et al. 1994 [12]	Brazil	International Orthopaedics	14	14
13	Adeyemo et al. 1993 [15]	Nigeria	Annals of Tropical Paediatrics	12	23
14	Frederiksen et al. 1993 [21]	Denmark	European Journal of Paediatrics	22	7
15	Ho et al. 1989 [5]	Singapore	Singapore Medicine Journal	11	21
16	Pittard et al. 1976 [22]	America	The Journal of Paediatrics	9	9

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All data were summarized descriptively according to the recommendations of Dhawan et al. [18]. Frequencies and proportions were calculated for categorical variables. Mean±SD were calculated for continuous variables. Data abstraction and figure creation were performed via Microsoft Excel software, version 16.42.

## Results

### Demographic characteristics

This review included 16 articles for a total of 307 neonates with involvement in 313 joints (Table 2). This review included neonates worldwide from 1976 to 2022.

This study included neonates with a prematurity (<37 weeks) proportion of 66% (7%-100%). A total of 12 case series mentioned the gender proportion, of which males comprised 136/228 cases (60%), and females comprised 92/228 cases (40%; Table 3) The age of onset of symptoms was predominantly in the third week, at an average of 20 days (8–40 days).

### Involved joints

The most common site of involvement was the hip joint (42%), followed by the knee joint (27%).

### Presenting symptoms

The paucity of signs and symptoms is one of the important reasons for the delayed diagnosis of septic arthritis. Similarly, the presence of initial symptoms was vague and less reported, which included fever and irritability. However, most of the neonates presented with joint swelling, tenderness, erythema, and a reduced range of movements of the affected joint, with or without pseudo-paralysis, in variable order (Table 4).

### Underlying causes

The most important cause documented is neonatal intensive care unit admission, with the reasons being respiratory distress syndrome, sepsis, and birth asphyxia (Table 4). Umbilical catheterization has been a documented risk factor in 36 cases in 4 case series.

Table 3. Patient details

No.	Authors (y)	DOL of Symptoms	Birthweight (Average)	No. (%)		Most Common Joint
				Prematurity	Male	
1	Uthraraj et al. 2022 [8]	8	1800 g	8(57)	6(43)	Hip [14]
2	Rubin et al. 2020 [13]	30	1040 g	39(87)	No record	Knee [14]>hip [9]
3	Salamon et al. 2020 [19]	19	3670 g	None	9(60)	Shoulder [3]>hip [2]
4	Sreenivas et al. 2016 [9]	23+4	No record	20(69)	12(42)	Hip [14]>knee [2]
5	Li et al. 2016 [20]	17+6	3010 g	7(13.5)	37(71)	Knee [22]>hip [13]
6	Khriesat et al. 2011 [10]	12-33	2915+935 g	13(48)	15(56)	Hip [19]
7	Kabak et al. 2002 [2]	34	2450 g	4(29)	9(64)	Hip [6]>knee [5]
8	Bos et al. 1998 [14]	NR	No record	2(25)	No record	Shoulder [8]
9	Merchant et al. 1997 [16]	26+11	1310 g	8(100)	No record	Knee [15]
10	Halder et al. 1996 [6]	15.6	1430 g	9(90)	6(60)	Knee [9]
11	Abuekteish et al. 1996 [11]	19	2500 g	9(53)	11(67)	Hip [17]
12	Vidigal et al. 1994 [12]	17	2500 g	1(7)	No record	Hip [14]
13	Adeyemo et al. 1993 [15]	17	2200 g	3(25)	5(42)	Hip [12]
14	Frederiksen et al. 1993 [21]	<40 days	1765 g	13(59)	14(64)	Hip [7]
15	Ho et al. 1989 [5]	20-40	2270 g	6(55)	6(55)	Knee [10]>hip [6]
16	Pittard et al. 1976 [22]	22	2106 g	6(67)	6(67)	Knee [9]

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### Microbiology

*S. aureus* (40%) was the most commonly cultured pathogen, followed by *Klebsiella* (18%). One case series included eight exclusively reported cases of *Candida*. Other microorganisms reported were *Pseudomonas*, *Streptococcus*, *H. influenzae*, *Staphylococcus haemolyticus*, *Escherichia coli*, *Proteus*, and so on.

### Laboratory assessment

The blood parameters usually assessed in cases of osteoarticular infections are white blood cell count, erythrocyte sedimentation rate, and CRP (Table 5). In the reported case series, CRP and erythrocyte sedimentation are elevated. The white blood cell counts also showed variability, with five case series showing a normal range and seven case series showing elevated levels. As the literature says, elevated inflammatory markers are not always necessary in cases of septic arthritis.

### Imaging

Earlier case series studies in this review mainly used radiographs as the modality of imaging (Table 5). The important findings were radiological changes in epiphysis and metaphysis, soft tissue swelling, bone lesions, periosteal bone formation, joint dislocation, or subluxation, in variable order and depending on the day of diagnosis. Subsequently, ultrasonography has become the imaging modality, where findings include joint effusion, thickened periosteum, thickened synovium, elevated synovium, and subperiosteal abscess. Magnetic resonance imaging was done in two case series, where findings included bone marrow edema, periosteal reaction, and joint effusion.

### Medical management

The mean duration of intravenous therapy followed by oral antibiotics was 2–6 weeks. Antibiotics alone were reported in only 12% (38 babies) of the cases.

**Table 4.** Presenting symptoms

No.	Authors (y)	Underlying Causes	Clinical Features	Organism
1	Uthraraj et al. 2022 [8]	Respiratory distress syndrome [5]; sepsis [5]; birth asphyxia [3]	Reduced active joint movements, raised temperature	<i>Pseudomonas</i> (56%), <i>Klebsiella pneumoniae</i> (25%), MS- <i>S. aureus</i> (19%)
2	Rubin et al. 2020 [13]	Total parenteral nutrition [25]; sepsis; Central venous catheterization [1]	Swelling (64%), erythema (56%), reduced movement (22%)	<i>Staphylococcus (methicillin-susceptible S. aureus &gt; methicillin-resistant S. aureus</i>
3	Salamon et al. 2020 [19]	Sepsis; umbilical catheterisation [1]	Irritability and feed intolerance, limited range of motion (87%), limb pain and swelling (75%)	<i>S. aureus &gt; Streptococcus agalactiae &gt; E. coli</i>
4	Sreenivas et al. 2016 [9]	Sepsis; birth asphyxia [16]	Pseudo-paralysis (69%), swelling (79%)	<i>K. pneumoniae &gt; S. aureus</i>
5	Li et al. 2016 [20]	Sepsis	Pseudo-paresis (50%), swelling (13.5%)	<i>S. aureus &gt; Klebsiella</i>
6	Khriesat et al. 2011 [10]	Neonatal intensive care unit admission; umbilical catheterisation [6]	No records	<i>K. pneumoniae &gt; S. aureus &gt; Enterobacter</i>
7	Kabak et al. 2002 [2]	Sepsis	Swelling/erythema/decreased range of motion	<i>S. aureus &gt; S. epidermidis</i>
8	Bos et al. 1998 [14]	Neonatal intensive care unit admission	Swelling, pyrexia, inability to use the involved arm	<i>S. aureus &gt; H. influenzae</i>
9	Merchant et al. 1997 [16]	Sepsis (candidiasis)	Tender swelling of the involved joint	<i>Candida</i>
10	Halder et al. 1996 [6]	Umbilical catheterisation [6]	Swelling (100%) Tenderness (90%) Limited movement (60%)	Methicillin-resistant <i>S. aureus &gt; Klebsiella</i>
11	Abuekteish et al. 1996 [11]	Sepsis	Joint tenderness, swelling, limitation of joint movement	<i>Klebsiella &gt; S. aureus</i>
12	Vidigal et al. 1994 [12]	Sepsis	Joint tenderness, pain of movement, pseudo-paralysis	<i>S. aureus Staphylococcus albus &gt; S. haemolyticus</i>
13	Adeyemo et al. 1993 [15]	Perinatal asphyxia [7] Sepsis	Local tenderness, swelling, limitation of movements	<i>Klebsiella, S. aureus &gt; Candida</i>
14	Frederiksen et al. 1993 [21]	Umbilical arterial catheters [15]; respiratory distress syndrome [15]; birth asphyxia [10]	Pseudo-paralysis, soft tissue swelling	<i>S. aureus</i>
15	Ho et al. [5]	Umbilical venous catheter [8]; sepsis [9]; meningitis [1]	Joint swelling, tenderness	<i>S. aureus &gt; Candida</i>
16	Pittard et al. [22]	Respiratory distress syndrome; birth asphyxia; sepsis	Swelling, tenderness, abnormal positioning of the affected leg	<i>S. aureus &gt; Candida</i>

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### Surgical management

Open surgery i.e. a throtomy was performed on 16% of the 49 babies. The rest of the babies responded to joint aspiration and irrigation, with or without immobilization (Table 6).

### Complications or sequelae

Five case series were documented to have no sequelae on follow-up (Table 6), which cited early diagnosis and prompt management as the reasons for this result. The rest of the case series included limb length discrepancy as the most common complication, a possible rea-

son being a joint subluxation, dislocation, or avascular necrosis of the femoral head (Table 6).

### Discussion

Our review included 16 articles for a total of 307 neonates with the involvement of 313 joints. It included neonates with a prematurity (<37 weeks) proportion of 66% (7%-100%). These are in line with Kleinman et al., who demonstrated that preterm and low birth weight infants are 3-10 times more likely to develop septic arthritis 12 case series mentioned the gender proportion of which males comprised 136/228 cases (60%), and females comprised 92/228 (40%), immunological differences in gender may explain above findings. The age

Table 5. Investigations

No.	Authors (y)	CRP/ESR	WBC	X-ray Findings	USG Findings
1	Uthraraj et al. 2022 [8]	Elevated (100%)	Elevated >20000 (100%)	-	Fluid pockets > 7x11 mm MRI-bone marrow edema, periosteal reaction, joint effusion
2	Rubin et al. 2020 [13]	NR	18200 cells	Periosteal reactions, lytic lesions, joint swelling, or effusion	No fluid, simple effusion, complex effusion, MRI - metaphyseal involvement, subperiosteal abscess
3	Salamon et al. 2020 [19]	Elevated (87%)	NR	Osteolytic lesions, soft tissue edema, periosteal reaction	Joint effusion, thickened periosteum, thickened synovium, elevated synovium, sub-periosteal abscess
4	Sreenivas et al. 2016 [9]	NR	Elevated (100%)	-	Effusion/subperiosteal abscess, positive 22(75.9%),negative 7(14.1%)
5	Li et al. 2016 [20]	NR	Elevated (75%)	Joint dislocation or subluxation, damage to metaphysis or epiphysis	-
6	Khriesat et al. 2011 [10]	28.5+17 mg/dL	Elevated (15%)	-	-
7	Kabak et al. 2002 [2]	ESR 55+16 52.6 mg/dL ESR 68.9 mm/h	>12000 cells/mm <sup>3</sup>	Widening of joint space, swelling of soft tissue	Synovial effusion
8	Bos et al. 1998 [14]	NR	Normal range	Radiological changes in epiphysis and metaphysis	-
9	Merchant et al. 2011 [16]	NR	Normal range	Soft tissue swelling—changes in the metaphysis	-
10	Halder et al. 1996 [6]	NR	~19000 cells/mm <sup>3</sup>	Soft tissue swelling (90%), bone lesions (60%), periosteal bone formation (10%)	-
11	Abuekteish et al. 1996 [11]	ESR high (42-137 mm/h)	Normal range	Periosteal reaction or lytic lesion	-
12	Vidigal et al. 1994 [12]	NR	Normal range	Subluxation/pathological dislocation of the hip	-
13	Adeyemo et al. 1993 [15]	NR	Soft tissue swelling, widened joint space, increased bone density, periosteal elevation, and osteomyelitis lesions		
14	Frederiksen et al. 1993 [21]	Normal range	Normal range	Soft tissue swelling followed by periosteal new bone formation	
15	Ho et al. 1989 [5]	NR	NR	-	-
16	Pittard et al. 1976 [22]	NR	Not consistent >25000 [3] <12000 [3]	Soft tissue swelling/synovial thickening/small effusion	

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Abbreviations: CPR: C-reactive protein; ESR: Erythrocyte sedimentation rate; WBC: White blood count; USG: Ultrasonography; NR: No records; MRI: Magnetic resonance imaging.

of onset of symptoms was predominantly in the third week, at an average of 20 days (8-40 days). The delayed presentation explained by low immunity in the preterm neonate to cause inflammation and late-onset sepsis catheterization and hospital admissions were the major risk factors [23].

The presence of initial symptoms was vague and less reported, which included fever and irritability. Fever, even though considered common in septic arthritis, is difficult to document in neonates because of physiological neonatal hypothermia [24]. This review emphasizes the importance of susceptibility to septic arthritis with

the above signs. However, most of the neonates presented with joint swelling, tenderness, erythema, and a reduced range of movements of the affected joint, with or without pseudo-paralysis, in variable order. The most important cause documented is neonatal intensive care unit admission, with the reasons being respiratory distress syndrome, sepsis, and birth asphyxia.

Umbilical catheterization has been a documented risk factor in 36 cases in 4 case series [2, 5, 6, 19]. Accordingly, diagnosis is difficult [25]. Kabak et al. mentioned that intravenous canulation (3/14) is a risk factor for septic arthritis [2]. Bergdahl and Woong. also reported that in-

Table 6. Treatment and sequelae

No.	Authors (y)	Antibiotics	Surgical Management	Complications/Sequelae
1	Uthraraj et al. 2022 [8]	Amoxicillin with clavulanate	Arthrotomy	No sequelae
2	Rubin et al. 2020 [13]	Nafcillin/oxacillin, cefazolin, vancomycin, rifampin	Drainage of joint and bone	Limb length discrepancy [3]; elbow deformity [1]; knee deformity [1]
3	Salamon et al. 2020 [19]	Cefotaxime, flucloxacillin	Drainage of pus and irrigation of affected bone/joint	No sequelae
4	Sreenivas et al. 2016 [9]	Ceftriaxone, gentamicin	Emergency arthrotomy, joint lavage	Hip dislocation [5]
5	Li et al. 2016 [20]	Cephalosporin+clindamycin based on sensitivity reports (2+2)	Open surgical drainage (72%)	Avascular necrosis of femoral head [6]; joint dislocation [4]
6	Khriesat et al. 2011 [10]	Imipenem, vancomycin (4-6 weeks)	Irrigation, drainage, and immobilization (4-6 weeks)	NR
7	Kabak et al. 2002 [2]	Antistaphylococcal drugs (3-4 weeks)	Irrigation, drainage, and immobilization (4-6 weeks)	Hip subluxation and destruction of the femoral head [1]
8	Bos et al. 1998 [14]	NR (8-14 weeks)	NR	Shortening of limbs [3]
9	Merchant et al. 1997 [16]	Fluconazole (3 weeks)	NR	No sequelae
10	Halder et al. 1996 [6]	Cephalosporin/clindamycin/vancomycin	NR	Abnormal joint function and growth [1]
11	Abuekteish et al. 1996 [11]	Nafcillin/Oxacillin	Surgical drainage procedure (42%)	No sequelae
12	Vidigal et al. 1994 [12]	NR	Arthrotomy	Limp [5], limited movements, pathological dislocation
13	Adeyemo et al. 1993 [15]	Cloxacillin, gentamicin	NR	Unstable hip joint with shortening of limb
14	Frederiksen et al. 1993 [21]	Dicloxacillin, methicillin, gentamicin, benzyl penicillin	Joint aspiration	Sequelae [4] subluxation, displacement, femoral head destruction
15	Ho et al. 1989 [5]	NR	Joint aspiration	Shortening of limbs, no sequelae [1]
16	Pittard et al. 1976 [22]	Methicillin, ampicillin, gentamicin, amphotericin	NR	Full recovery

NR: No records.

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travenous canulation is a major risk factor. In our study, intravenous canulation-induced septic arthritis was not uncommon [25, 26].

In the reported case series, CRP and erythrocyte sedimentation rates are elevated. The white blood cell count also showed variability, with five cases showing a normal range and seven cases showing elevated levels. Thus, measuring erythrocyte sedimentation rate and CRP may slightly improve sensitivity and negative predictive value for diagnosis; however, further investigation is necessary to establish a certain diagnostic role in septic arthritis. In our review, most of the cases were not reported. In some cases, they were also normal.

The important findings in radiographs were changes in epiphysis and metaphysis, soft tissue swelling, bone lesions, periosteal bone formation, joint dislocation, or subluxation, in variable order and depending on the day of diagnosis. Subsequently, ultrasonography has become the imaging modality, where findings include joint effusion, thickened periosteum, thickened synovium, el-

evated synovium, and subperiosteal abscess. Magnetic resonance imaging was done in seven patients in two case series [13, 19], where findings included bone marrow edema, periosteal reaction, and joint effusion. This is to emphasize that imaging plays a crucial role in establishing early and timely diagnosis, which is subsequently helpful in management, thus decreasing the incidence of long-term sequelae [19].

*S. aureus* (40%) was the most commonly cultured pathogen, followed by *Klebsiella* (18%). One case series, which included 8 cases, exclusively reported the cases of *Candida* [16]. Other microorganisms reported were *Pseudomonas* [8], *Streptococcus*, and *S. hemolyticus*, *H. influenzae*, *E. coli*, *Proteus*, and so on. This is in concordance with the published literature [27]. An increase in methicillin-resistant *S. aureus* has been reported in the pediatric population and should be considered when deciding on empiric antimicrobial treatment. Four of the reviewed case series [9-11, 15] highlighted the increasing incidence of *Klebsiella*-related septic arthritis, citing the possibility of using contaminated equipment

[28], which is an important reason for nosocomial infection. Another reason noted was a severe shortage of water supply [15], which, when corrected, led to no recurrence of this infection. *Pseudomonas* reported in Utharaj et al. [8] was important because of its nosocomial nature. The main cause of this outbreak was inadequate infection control by staff members. Thus, guidelines formulated to mitigate the risk led to no further outbreak [8]. *H. influenzae* was cultured in only one case [14], which is consistent with the drastic decrease in the cases of osteomyelitis secondary to *H. influenzae* after the introduction of large-scale vaccinations [27]. The culture and identification of the offending pathogen allow for definitive therapy with a narrow spectrum representing the cost-effective and responsible use of antibiotic resources [29].

Administration of antibiotics alone was reported in only 12% (38 babies) of the cases. Initial choices were mainly anti-staphylococcal drugs with a combination of aminoglycosides, followed by cephalosporins. Also, for fungal arthritis, fluconazole was effective [16]; however, amphotericin was helpful in another case series [22]. Open surgery was performed in 16% (49 babies). The rest of the babies responded to joint aspiration and irrigation, with or without immobilization.

There is still no consensus as regards the management of septic arthritis, let alone neonatal arthritis. Some advocate arthrotomy [8, 9, 11, 12, 20], while others prefer aspiration of infected joints [2, 10, 13, 19, 21, 22]. Conservative therapy was elected in small premature infants, while a surgical approach was done in newborns with larger joints [22]. Another discussion to decide on the choice of therapy based on the site of pus detection. If the pus is superficial and swelling is easily visible and monitored, repeated careful aspirations are the preferred method for decompression, and when it is deep-seated, especially in hip joints, an arthrotomy is the preferred method [5].

The importance of this review lies in the fact that an early diagnosis and appropriate management would decrease the incidence of sequelae in newborn babies with septic arthritis. 5 case series are documented to have no sequelae on follow-up [8, 11, 16, 19, 22]. The rest of the case series included limb length discrepancy as the most common complication, a possible reason being a joint subluxation, dislocation, or avascular necrosis of the femoral head. This is also seen in septic arthritis of the shoulder joint [14]. According to Diana et al. infants with lupus may have weakened immunity, making them more vulnerable to septic arthritis [30].

Parmar et al. reported a case of a 5-week-old baby presenting with septic arthritis in the knee and temporomandibular joint believed to be caused by omphalitis [31].

## Conclusion

Unexplained fever and irritability in a newborn with a significant neonatal intensive care unit course should raise suspicion of neonatal septic arthritis, which, on examination, if associated with any joint swelling, tenderness, or decreased range of movements, should be advised for further radiographic evaluation. Although laboratory screening tests may be normal, radiographs can help reduce the delay in diagnosis and improve outcomes. For focused treatment, blood and tissue cultures are to be performed. A prolonged stay is a major concern as it may involve invasive procedures like simple intravenous cannula insertion. Improvements in our microbiological diagnosis have the potential to improve antibiotic selection. Local methicillin-resistant *S. aureus* prevalence must be taken into consideration when starting empiric antibiotic treatment. Follow-up is a must as complications are common in delayed cases.

## Study limitations

This study is not without its limitations. Due to the rarity of neonatal septic arthritis, this systematic review was limited to case series and is thus of level IV evidence. Due to heterogeneous data and variable follow-up, we are limited in the interpretation of our data about presenting symptoms, choice of treatment, and complications, so we are unable to do a meta-analysis. The follow-up period was very short in comparison. Some studies were in single numbers. The time frame of the studies was very wide. Only three studies were of good quality.

## Ethical Considerations

### Compliance with ethical guidelines

The preferred reporting items for systematic reviews and meta-analyses protocol guidelines were strictly followed. Additionally, the review was registered by [International Prospective Register of Systematic Reviews \(PROSPERO\)](#) (Code: CRD42021281293).

### Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

### Authors contributions

All authors equally contributed to preparing this article.

### Conflicts of interest

The authors declared no conflict of interest.

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