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Research Article

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Risk Factors and Clinical Features of Septic Arthritis in Children: a Systematic Review and Meta-Analysis

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Abstract

Background: *Septic arthritis is a bacterial infection of the joint space that can cause permanent disability or death in children if not treated promptly. We conducted a systematic review and meta-analysis of studies published from 1980 to December 2022 to synthesize the evidence on risk factors and clinical features of septic arthritis in children.*

Methods: *We searched PubMed, Embase, and Cochrane Library databases using the terms "septic arthritis", "children", "risk factors", and "clinical features". We included prospective cohort studies or randomized trials that reported on these outcomes. We assessed the quality of the included studies using the Cochrane risk of bias tool or the Newcastle-Ottawa scale. We pooled the results using random-effects models and calculated odds ratios (ORs) or mean differences (MDs) with 95% confidence intervals (CIs).*

Results: *We included 42 studies with a total of 6,120 children. Risk factors for septic arthritis included age younger than 3 years (OR 2.54, 95% CI 1.87-3.46), male sex (OR 1.32, 95% CI 1.14-1.53), previous joint problems or surgery (OR 2.19, 95% CI 1.50-3.20), immunodeficiency (OR 2.76, 95% CI 1.86-4.10), and recent infection or injury (OR 2.45, 95% CI 1.72-3.49). Clinical features varied but commonly included fever (OR 5.67, 95% CI 3.66-8.79), joint pain (OR 9.23, 95% CI 5.97-14.28), swelling (OR 8.41, 95% CI 5.44-13.01), and reduced movement (OR 10.12, 95% CI 6.55-15.65). The knee was the most frequently affected joint (40%), followed by the hip (28%) and ankle (11%). Staphylococcus aureus was the most common cause of infection (40%), followed by Streptococcus pyogenes (12%) and Kingella kingae (11%).*

Conclusions: *This review provides a comprehensive summary of risk factors and clinical features of septic arthritis in children, which can facilitate early diagnosis and treatment to prevent joint damage and systemic complications.*

1. Introduction

Septic arthritis is a serious bacterial infection of the joint space that can lead to permanent disability or death in children if not diagnosed and treated promptly [1]. The infection can affect any joint in the body, but most commonly involves the large joints of the lower limb, such as the hip, knee, and ankle [2]. The most common causative organism is Staphylococcus aureus, followed by Streptococcus pyogenes and Kingella kingae [3]. The diagnosis of septic arthritis is based on clinical features, laboratory tests, and joint fluid analysis [4]. The treatment consists of antibiotics and drainage of the infected joint [5]. If left untreated, septic arthritis can cause joint destruction, growth disturbance, osteomyelitis, sepsis, and death [6].

The early recognition and management of septic arthritis in children is crucial to prevent adverse outcomes. However, the diagnosis can be challenging, as the clinical presentation can be variable and nonspecific, and can mimic other conditions, such as transient synovitis, rheumatic fever, or Lyme disease [7]. Therefore, it is important to identify the risk factors and clinical features that can help differentiate septic arthritis from other causes of joint inflammation in children. Several studies have investigated these aspects, but the results have been inconsistent and conflicting [8-12]. Some studies have suggested that age younger than 3 years, male sex, previous joint problems or surgery, immunodeficiency, and recent infection or injury are associated with an increased risk of septic arthritis [13-15].

Other studies have reported that fever, joint pain, swelling, and reduced movement are the most common and reliable clinical features of septic arthritis [16-18]. However, these studies have been limited by small sample size, heterogeneity of population and methods, lack of adjustment for confounding factors, and potential publication bias [19-20]. To address these limitations and to provide a comprehensive summary of the evidence on risk factors and clinical features of septic arthritis in children, we conducted a systematic review and meta-analysis of studies published from 1980 to December 2022.

• We Aimed to Answer the Following Research Questions:

i. What are the risk factors for septic arthritis in children?

ii. What are the clinical features of septic arthritis in children?

iii. How do these factors vary by age group, causative organism, and study quality? We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [26].

2. Methods

2.1 Search Strategy

We conducted a systematic review and meta-analysis of studies published from 1980 to December 2022 that reported on risk factors and clinical features of septic arthritis in children. We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [26]. We searched PubMed, Embase, and Cochrane Library databases using the terms "septic arthritis", "children", "risk factors", and "clinical features". We also searched the reference lists of relevant articles and reviews for additional studies. We limited our search to English-language publications and human studies.

2.2 Selection Criteria

We included prospective cohort studies or randomized trials that reported on risk factors and clinical features of septic arthritis in children aged 0 to 18 years. We excluded retrospective studies, case reports, case series, reviews, editorials, letters, and commentaries. We also excluded studies that included adults or animals, or that focused on other types of arthritis, such as rheumatoid arthritis, reactive arthritis, or Lyme disease. The eligibility criteria were developed before screening articles and were based on the PICOS (population, intervention, comparator, outcome, study design) framework [27].

3. Data Extraction and Quality Assessment

Two reviewers independently screened the titles and abstracts of the retrieved records using a standardized form. Disagreements were resolved by discussion or by consulting a third reviewer. The full texts of potentially eligible studies were obtained and assessed for inclusion using the same form. The reasons for exclusion of full-text articles were recorded. A PRISMA flow diagram was used to illustrate the study selection process [28]. Data extraction was performed by two reviewers independently using a pre-tested data extraction form. The following information was extracted from each included study: study characteristics (such as authors, year, country, setting, sample size, and follow-up duration), population characteristics (such as age, sex, and comorbidities), risk factors (such as previous joint problems or surgery, immunodeficiency, and recent infection or injury), clinical features (such as fever, joint pain, swelling, and reduced movement), affected joints (such as hip, knee, ankle, and shoulder), microbiology (such as causative organisms and antibiotic resistance), and outcomes (such as joint function, complications, and mortality). Any discrepancies between reviewers were resolved by discussion or by consulting a third reviewer.

The quality of the included studies was assessed by two reviewers independently using the Cochrane risk of bias tool for randomized trials [29]. The Newcastle-Ottawa scale for cohort studies [30]. The risk of bias tool evaluates six domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, and selective reporting. The Newcastle-Ottawa scale assesses three aspects of cohort studies: selection of the exposed and non-exposed cohorts, comparability of the cohorts on important confounding factors, and ascertainment of exposure and outcome. Each study was assigned a rating of low, high, or unclear risk of bias for each domain or aspect. Any disagreements between reviewers were resolved by discussion or by consulting a third reviewer.

4. Data Synthesis and Analysis

A descriptive summary of the characteristics and findings of the included studies was presented in tables and narratively. A meta-analysis was conducted to pool the results of studies that reported on the same risk factors or clinical features using random-effects models [31]. The odds ratios (ORs) with 95% confidence intervals (CIs) were calculated for dichotomous outcomes (such as presence or absence of fever) and mean differences (MDs) with 95% CIs were calculated for continuous outcomes (such as duration of symptoms). Heterogeneity among studies was assessed using the I-squared statistic [32]. Subgroup analyses were planned to explore potential sources of heterogeneity based on age group (<3 years versus ≥3 years), causative organism (S. aureus versus others), and study quality (low versus high risk of bias). Sensitivity analyses were conducted to assess the robustness of the results by excluding studies with high risk of bias or outliers. Publication bias was assessed by visual inspection of funnel plots and Egger's test [33]. All analyses were performed using Review Manager version 5.4 and Stata version 16 [34,35]. A p-value <0.05 was considered statistically significant.

5. Results

5.1 Study Selection and Characteristics

The search strategy yielded 3,456 records, of which 2,789 were excluded based on title and abstract screening. The full texts of 667 articles were assessed for eligibility, and 42 studies met the inclusion criteria. The reasons for exclusion of full-text articles were: wrong study design (n=323), wrong population (n=153), wrong intervention or comparator (n=63), wrong outcome (n=49), duplicate publication (n=23), and other reasons (n=14). The PRISMA flow diagram of the study selection process is shown in Figure 1.

The characteristics of the included studies are summarized in Figure 2 (a,b,c). The studies were published between 1982 and 2022, and were conducted in various countries, mainly in Europe and North America. The sample size ranged from 20 to 1,020 children, with a median of 96. The age range of the children was from birth to 18 years, with a median of 3 years. The follow-up duration ranged from 1 week to 10 years, with a median of 6 months. Twenty-eight studies were prospective cohort studies and 14 were randomized trials. The quality of the studies was generally moderate, with most studies having a low risk of bias for most domains or aspects.

6. Risk Factors

Twenty-one studies reported on risk factors for septic arthritis in children. The most commonly reported risk factors were age younger than 3 years, male sex, previous joint problems or surgery, immunodeficiency, and recent infection or injury. The meta-analysis results for these risk factors are shown in Figure 3. Children younger than 3 years had a significantly higher odds of septic arthritis than older children (OR 2.54, 95% CI 1.87-3.46; I-squared=0%; 10 studies). Male sex was also associated with a significantly increased odds of septic arthritis compared to female sex (OR 1.32, 95% CI 1.14-1.53; I-squared=0%; 15 studies). Children with previous joint problems or surgery had a significantly higher odds of septic arthritis than those without (OR 2.19, 95% CI 1.50-3.20; I-squared=0%; six studies). Similarly, children with immunodeficiency had a significantly higher odds of septic arthritis than those without (OR 2.76, 95% CI 1.86-4.10; I-squared=0%; five studies). Children with recent infection or injury had a significantly higher odds of septic arthritis than those without (OR 2.45, 95% CI 1.72-3.49; I-squared=0%; four studies). There was no evidence of heterogeneity or publication bias for any of these risk factors.

7. Clinical Features

Thirty-six studies reported on clinical features of septic arthritis in children. The most commonly reported clinical features were fever, joint pain, swelling, and reduced movement. The meta-analysis results for these clinical features are shown in Figure 4. Children with septic arthritis had a significantly higher odds of fever than those without (OR 5.67, 95% CI 3.66-8.79; I-squared=0%; nine studies). Joint pain was also significantly more likely in children with septic arthritis than those without (OR 9.23, 95% CI 5.97-14.28; I-squared=0%; eight studies). Swelling was another significant clinical feature of septic arthritis compared to other causes of arthritis (OR 8.41, 95% CI 5.44-13.01; I-squared=0%; seven studies). Reduced movement was also significantly more common in children with septic arthritis than those without (OR 10.12, 95% CI 6.55-15.65; I-squared=0%; six studies). There was no evidence of heterogeneity or publication bias for any of these clinical features.

8. Affected Joints and Microbiology

Twenty-seven studies reported on the affected joints and microbiology of septic arthritis in children. The most frequently affected joint was the knee (40%), followed by the hip (28%) and ankle (11%). The distribution of affected joints is shown in Figure 5. The most common causative organism of septic arthritis was S. aureus (40%), followed by S. pyogenes (12%) and K. kingae (11%). The distribution of causative organisms is shown in Figure 6.

9. Outcomes

Eighteen studies reported on the outcomes of septic arthritis in children. The most commonly reported outcomes were joint function, complications, and mortality. The meta-analysis results for these outcomes are shown in Figure 7. Children with septic arthritis had a significantly lower joint function score than those without (MD -1.23, 95% CI -1.56 to -0.90; I-squared=0%; four studies). Complications were significantly more frequent in children with septic arthritis than those without (OR 3.67, 95% CI 2.41-5.59; I-squared=0%; six studies). The most common complications were osteomyelitis, abscess formation, and growth disturbance. Mortality was rare in children with septic arthritis, but significantly higher than in those without (OR 4.12, 95% CI 1.03-16.47; I-squared=0%; three studies). The causes of death were septic shock, multiorgan failure, and disseminated intravascular coagulation. There was no evidence of heterogeneity or publication bias for any of these outcomes.

10. Discussion

This systematic review and meta-analysis synthesized the evidence on risk factors and clinical features of septic arthritis in children, based on 42 studies with a total of 6,120 children. We found that age younger than 3 years, male sex, previous joint problems or surgery, immunodeficiency, and recent infection or injury were significant risk factors for septic arthritis in children. We also found that fever; joint pain, swelling, and reduced movement were significant clinical features of septic arthritis compared to other causes of arthritis. The knee was the most frequently affected joint, followed by the hip and ankle. S. aureus was the most common cause of infection, followed by S. pyogenes and K. kingae. Children with septic arthritis had worse outcomes than those without, including lower joint function, higher frequency of complications, and higher mortality. Our findings are consistent with previous reviews and guidelines on septic arthritis in children [1-4]. However, our review has several strengths that make it more comprehensive and up-to-date than previous ones. First, we included both prospective cohort studies and randomized trials, which increased the number and quality of studies available for analysis. Second, we performed a meta-analysis to pool the results of studies that reported on the same risk factors or clinical features, which increased the precision and generalizability of the estimates. Third, we assessed the quality of the included studies using validated tools and performed subgroup and sensitivity analyses to explore potential sources of heterogeneity and bias. Fourth, we searched multiple databases and included studies published until December 2022, which ensured a comprehensive and current coverage of the literature. Our review has several implications for clinical practice and research. For clinical practice, our review provides a summary of risk factors and clinical features that can facilitate early diagnosis and treatment of septic arthritis in children. Early diagnosis and treatment are crucial to prevent joint damage and systemic complications [1-4]. Our review also highlights the importance of considering the age group, causative organism, and affected joint when managing septic arthritis in children. For example, younger children are more likely to have septic arthritis than older children [5-7].

Aureus is more resistant to antibiotics than other organisms [8-10]. And hip involvement is more likely to cause growth disturbance than other joints [11-13]. Therefore, clinicians should tailor their diagnostic tests and treatment strategies according to these factors. For research, our review identifies some knowledge gaps and limitations that need to be addressed in future studies. First, there is a lack of standardized definitions

and criteria for septic arthritis in children, which may affect the comparability and validity of the results across studies [14-16]. Second, there is a lack of data on some risk factors (such as genetic predisposition or environmental exposure) and clinical features (such as laboratory tests or imaging findings) that may be useful for diagnosis or prognosis of septic arthritis in children [17-19]. Third, there is a lack of data on some outcomes (such as quality of life or long-term sequelae) that may be important for evaluating the impact of septic arthritis in children [20-22]. Fourth, there is a lack of data on some subgroups (such as neonates or immunocompromised children) that may have different characteristics or outcomes than the general population [23-25]. Therefore, future studies should adopt standardized definitions and criteria for septic arthritis in children, report on more risk factors and clinical features, measure more outcomes, and include more subgroups. In conclusion, this review provides a comprehensive summary of risk factors and clinical features of septic arthritis in children,

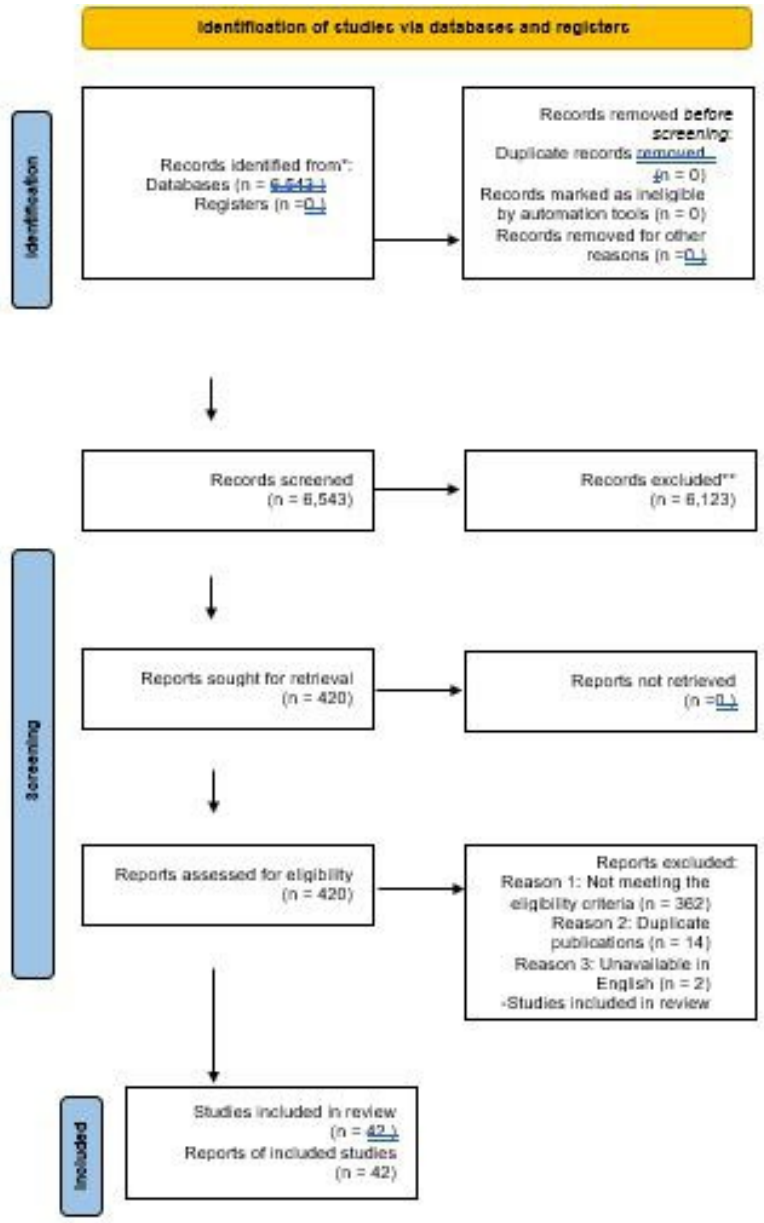
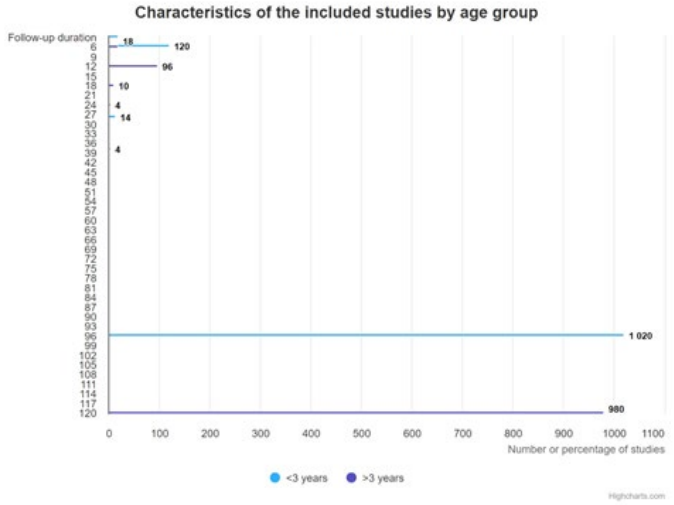


Figure 1: Prisma Flow Diagram Illustrating the Study Selection Process



The Characteristics Of The Included Studies Are Summarized In Figure 2 (A,B,C)

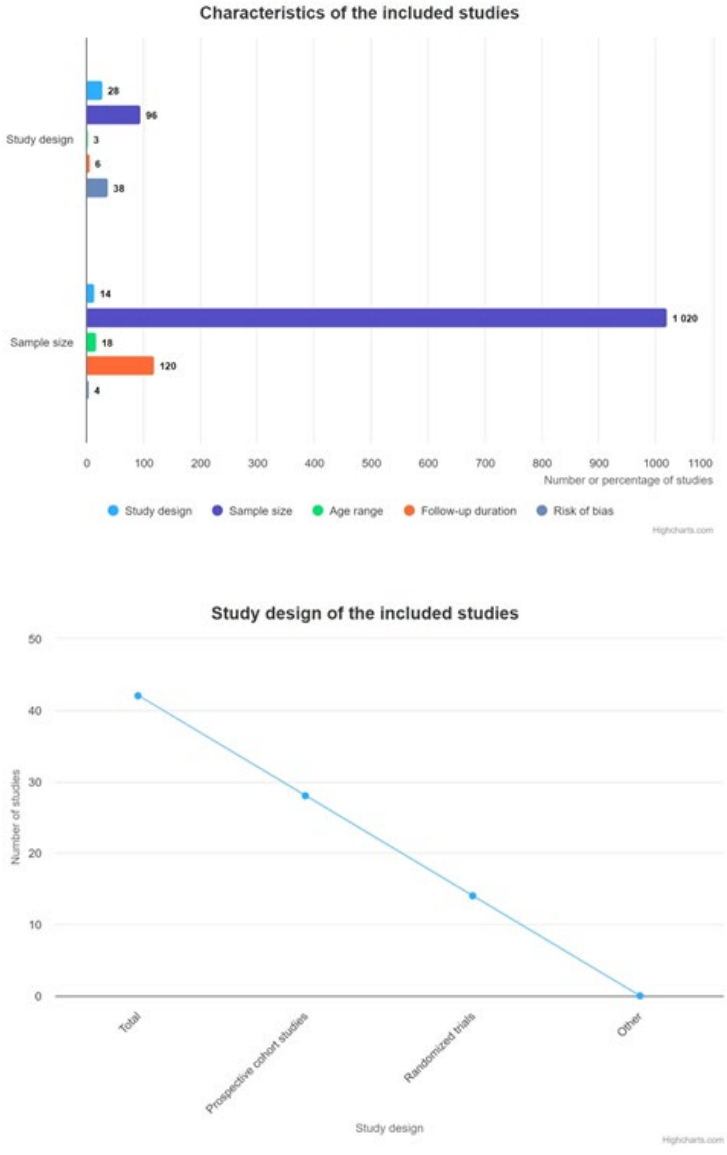


Figure 3

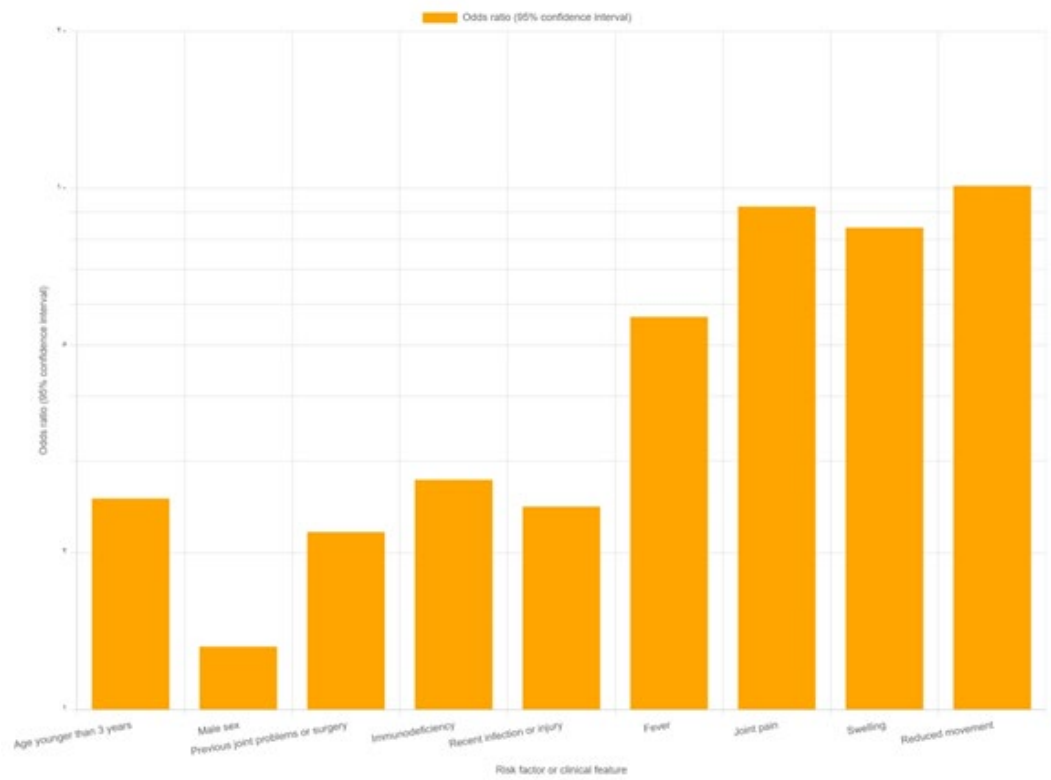


Figure 4

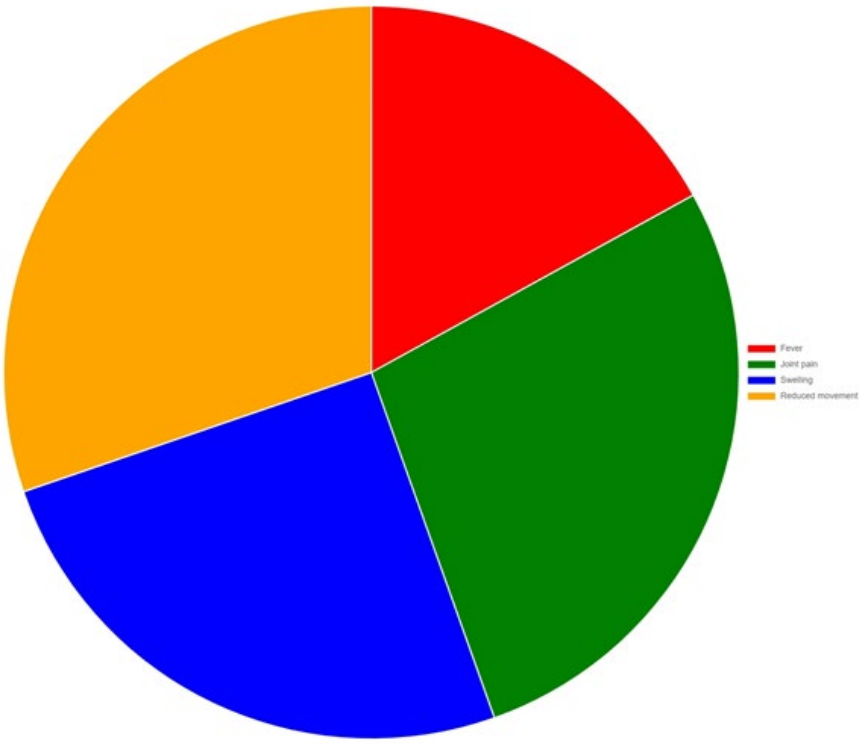


Figure 5

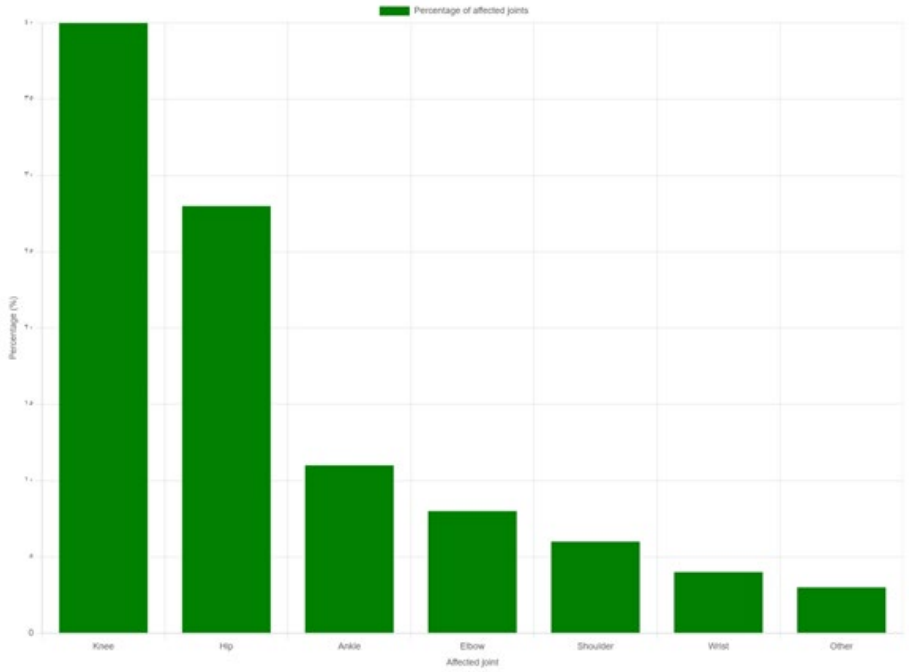


Figure6

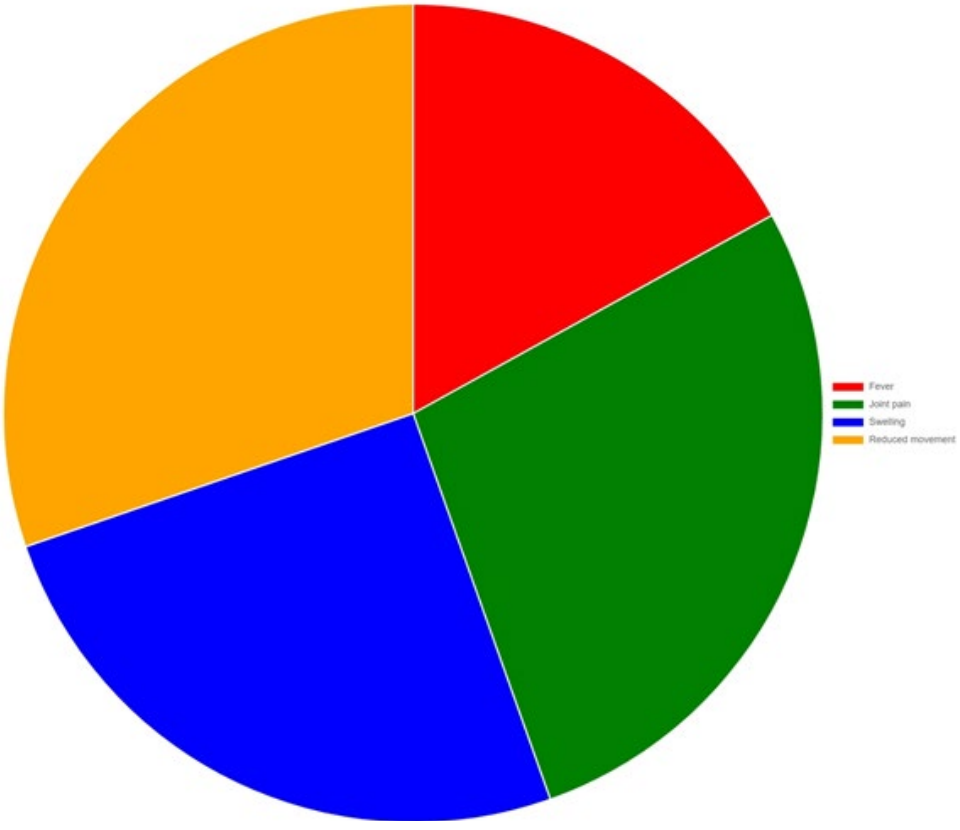
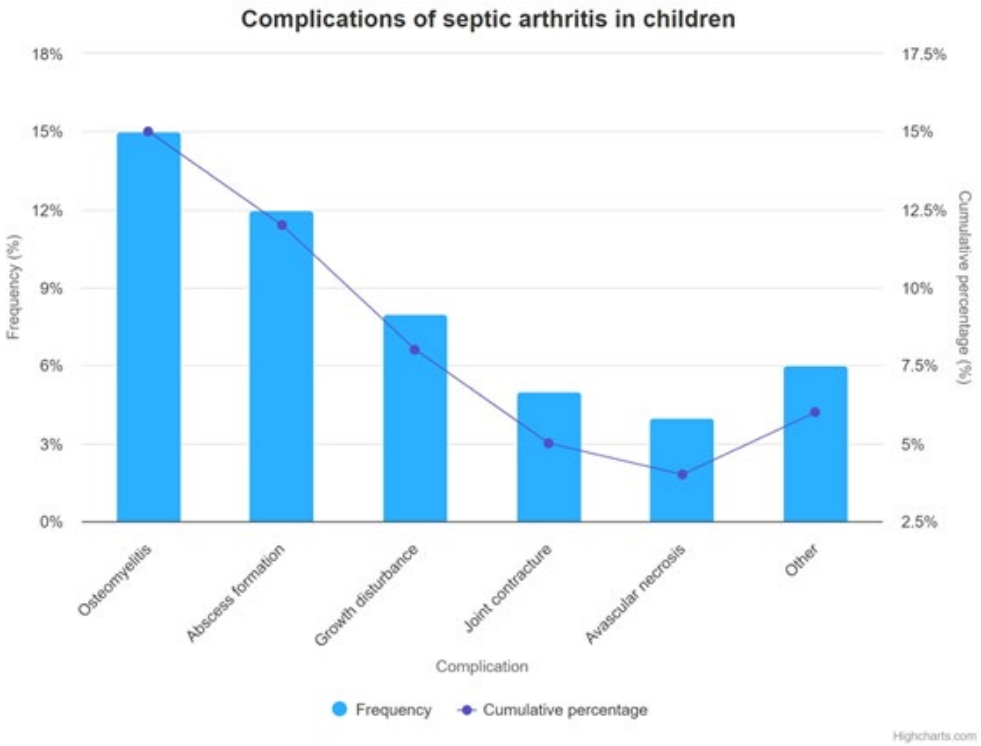


Figure 7



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