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PAEDIATRICS

Clinical characteristics and prognosis of children with culture-negative osteoarticular infections: a meta-analysis based on cohort studies

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- *Purpose:* Pediatric osteoarticular infections (OAIs) are an orthopedic emergency that can lead to severe sequelae if not treated appropriately. Approximately half of the patients with OAIs in clinical practice fail to obtain microbiological results even after undergoing aspiration or surgery, which presents a significant challenge in clinical practice. The inability to identify pathogens can lead to incorrect antibiotic usage or under-treatment, increasing the risk of adverse outcomes. This study aims to investigate the clinical characteristics and prognosis of culture-negative OAIs compared to culture-positive OAIs through a meta-analysis, providing insights to optimize treatment strategies.
- *Methods:* A systematic search was conducted to identify cohort studies comparing the clinical characteristics and prognosis of children with culture-negative OAIs to those with culture-positive OAIs. The search encompassed the databases of Wanfang Data, China National Knowledge Infrastructure, China Biology Medicine disc, Excerpta Medica Database, PubMed and the Cochrane Library, with the literature review extending up to March 2024. Data were extracted from eligible articles and assessed using the Newcastle–Ottawa scale, and the articles were selected based on predefined inclusion and exclusion criteria.
- *Results:* Twelve literature reports covering 1630 patients were included in this meta-analysis. Publication bias did not significantly affect the results. The incidence of long-term sequelae, temperature before admission, baseline laboratory indicators and possibility of surgery in the culture-negative group of patients were significantly lower than those in the culture-positive group. In addition, there were no significant differences in gender, age, race, trauma history, patient delay, antibiotic usage before admission or clinical symptoms between the two groups.
- *Conclusions:* Children diagnosed with culture-negative OAIs generally demonstrated less severe systemic inflammatory responses, required shorter treatment durations, exhibited a reduced likelihood of requiring surgical intervention and were less prone to experience long-term functional impairments compared to children with culture-positive OAIs. However, no differences in patient characteristics and clinical symptoms were found between the two groups. Further large-scale studies are still required to validate these findings.
- *Type of study:* Meta-analysis.
- *Level of evidence:* Level III.

Keywords: child; osteoarticular infections; culture negative; meta-analysis as topic; clinical characteristics; prognosis; osteomyelitis; septic arthritis

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Introduction

Osteoarticular infections (OAIs) occur when pathogenic microorganisms invade bone tissue or joints, triggering an inflammatory response (1). This condition predominantly affects children and can lead to serious complications, including chronic osteomyelitis, growth arrest, joint deformities and impaired limb function. In severe cases, it may progress to sepsis, potentially resulting in death (2). Antibiotics play a crucial role in managing OAIs, with empirical antibiotic therapy typically initiated upon suspected infection in pediatric patients (3, 4). Timely adjustment to appropriate antibiotics based on bacterial culture and antibiotic sensitivity testing is essential for effective treatment.

However, despite the critical role of bacterial culture, approximately 40–60% of pediatric patients with OAIs fail to obtain positive microbiological results after aspiration or surgery (5, 6, 7). This condition is referred to as culture-negative OAIs. It usually manifests with evident signs of infection, yet conventional bacterial culture fails to identify pathogens (8). The occurrence of culture-negative OAIs can be attributed to factors such as prior antibiotic usage, issues with specimen collection and handling or the presence of fastidious pathogens, such as *K. kingae* (9).

The clinical presentation and prognosis of culture-negative OAIs remain uncertain, leading to considerable debate regarding their optimal management (10, 11, 12). Although culture-negative and culture-positive OAIs often present with similar clinical symptoms, including pain, fever, swelling and functional impairment, some studies (13, 14, 15) indicate that culture-negative OAIs might exhibit milder clinical symptoms and carry a lower risk of long-term complications. However, the absence of a definitive pathogen complicates treatment, potentially leading to inappropriate antibiotic regimens or under-treatment, which in turn increases the risk of prolonged recovery, treatment failure or long-term sequelae. Lavie and coworkers (16) and Paz and coworkers (17) highlighted the diagnostic and therapeutic challenges posed by culture-negative OAIs, while Pääkkönen and coworkers (18) argued that these patients often exhibit milder clinical symptoms and have more favorable outcomes.

To address this controversy and improve treatment efficacy, it is essential to delineate the differences in clinical presentation and prognosis between culture-negative and culture-positive OAIs. Therefore, we conducted a meta-analysis synthesizing cohort study data to compare the clinical characteristics and prognosis of children with culture-negative versus culture-positive OAIs. We hypothesize that children with culture-negative OAIs have a lower risk of long-term sequelae and may benefit from different management approaches.

Materials and methods

Protocol

This study adhered to the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

Search strategies

We performed a comprehensive literature search across multiple databases, including Wanfang Data, China National Knowledge Infrastructure (CNKI), China Biology Medicine disc, Excerpta Medica Database (Embase), PubMed and the Cochrane Library. The literature review spanned the period up to March 2024. These searches adopted various combinations of the following keywords: culture negative, osteoarticular infections (OAIs), bone and joint infection (BJI), Septic arthritis (SA) and osteomyelitis. Search results were confined to studies involving individuals aged 0–18 years, focusing on children or pediatrics. Both subject headings and free-text terms were utilized in all searches, with search strategies formulated following multiple pre-searches. In addition, we examined the references of the included articles and other relevant studies. No language restrictions were applied.

Study selection

In accordance with the systematic evaluation manual of the Cochrane Collaboration Network, we established strict inclusion and exclusion criteria based on the principles of population, intervention, comparison, outcomes and study design for this meta-analysis.

The inclusion criteria were as follows: studies including participants who were children diagnosed with OAIs, studies comparing culture-negative with culture-positive patients with relevant observed indicators, studies reporting data that could be directly extracted from the literature or calculated, and studies with a cohort design.

The exclusion criteria were as follows: descriptive studies, case–control studies, duplicate reports (inclusion or exclusion determined by literature quality), reviews, conference papers or abstracts without available full texts; studies with incomplete or challenging-to-extract data; studies lacking statistical analysis; and Newcastle–Ottawa scale score <7 (http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp).

Data extraction and quality assessment

For each study, two authors independently extracted the data and assessed their quality. Any disagreements were resolved by the corresponding author. A standardized data extraction form was employed, which included

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baseline characteristics of the literature and observed indicators.

The primary indicator of this meta-analysis was long-term sequelae, including osteonecrosis of the femoral head, limb length inequality, restricted joint motion, deformities, nonunion of bones and pseudoarthrosis (19, 20, 21). Secondary indicators included gender, age, trauma history, patient delay, temperature before admission, antibiotic usage before admission, race (white and black), clinical symptoms (fever, pain/tenderness, limitation of motion, limp and swelling), initial laboratory indicators (white blood cell count (WBC), C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)), likelihood of surgery and time-related indicators (duration of hospitalization, duration of intravenous antibiotic therapy and total duration of antibiotic therapy).

Statistical analysis

Publication bias was assessed using Egger's test using the Stata 15.0 software (StataCorp LLC, USA). Statistical analysis was conducted using the RevMan 5.4 software (The Cochrane Collaboration, London, UK). The *Q* test and I^2 index were used to assess the heterogeneity of odds ratios (ORs) or mean differences (MDs). In cases where no heterogeneity was observed (*Q* test $P > 0.1$ or $I^2 < 50\%$), the fixed-effects model based on the Mantel–Haenszel method was used for pooling. Otherwise, a random-effects model utilizing the DerSimonian–Laird method was applied. Stability analysis was conducted by comparing the consistency of results between the random-effects model and the fixed-effects model (22, 23). Some selected continuous variables were represented by the median (interquartile range). We calculated their mean and standard deviation (SD) based on the sample size using a calculator (24, 25), followed by meta-analysis. A *P* value <0.05 was considered significant.

Result

Description of studies

A total of 1107 articles were retrieved from all databases, including 48 in Chinese and 1059 in English. Upon reviewing the titles and abstracts, 1013 articles were excluded. The full text of the remaining 104 abstracts was analyzed, revealing that 83 articles were incomplete due to unavailable outcome data or population repetition. After additional evaluation, 12 articles met the inclusion criteria, with 1 included for cross-referencing purposes. The flow chart of the search strategies (26) is presented in Fig. 1.

A total of 1630 children were involved in the 12 studies (3, 9, 10, 13, 14, 18, 27, 28, 29, 30, 31, 32), as summarized in Table 1. All of these studies were retrospective cohort studies. The quality assessment scores of these studies ranged from 7 to 9, indicating moderate quality for cohort studies. The proportion of patients with culture-negative OAIs was approximately 41.29% (673/1630), with variability observed across studies, ranging from 23.19 to 68.99%.

Primary indicator

A total of seven studies, involving 1195 patients, were included in the analysis, revealing a long-term sequelae incidence of approximately 9.12% (109/1195). Specifically, in the culture-negative group, it was 6.59% (29/440), while in the culture-positive group, it was 12.38% (80/646).

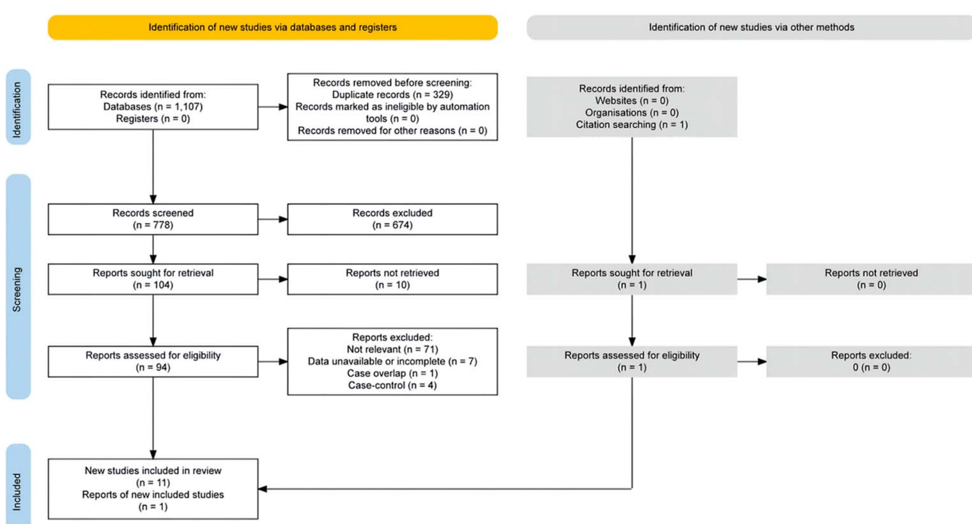

Figure 1

Flow chart of the paper screening process.

Table 1 Baseline analysis and results of quality evaluation for the 12 articles included.

Study	Year	Region	Research span	Infection type	Culture result	Cases	Gender M	Gender F	Age, years	NOS score
Baldwin *et al.* (27)	2016	Pennsylvania, USA	2005–2013	SA	Negative	26	13	13	2.1 ± 1.7	9
					Positive	23	12	11	5.6 ± 1.6	
Chen *et al.* (9)	2021	Taiwan, China	2003–2019	OAIs	Negative	33	21	12	6.5 (1.5, 10.5)	9
					Positive	37	25	12	3.6 (0.9, 11.36)	
Feng *et al.* (28)	2023	Beijing, China	2010–2020	OAIs	Negative	39	24	15	0.75 (0.25, 2.58)	9
					Positive	37	21	16	2.5 (0.88, 8.96)	
Floyed & Steele (29)	2003	Louisiana, USA	1998–2001	OAIs	Negative	40	24	16	8 ± 6.8	9
					Positive	45	28	17	6.3 ± 4.6	
Jia *et al.* (30)	2023	Shandong, China	2017–2021	OAIs	Negative	20	14	6	4.17 (0.98, 7.75)	8
					Positive	49	29	20	2.67 (1.13, 6)	
Osei *et al.* (13)	2017	French Guiana	2010–2015	OAIs	Negative	7	3	4	1.22 ± 0.54	8
					Positive	4	4	0	1.19 ± 0.8	
Özcan *et al.* (31)	2021	Istanbul, Turkey	2011–2019	OAIs	Negative	42	24	18	8.1 ± 4.5	7
					Positive	30	17	13	7.3 ± 5.5	
Pääkkönen *et al.* (18)	2013	Turku, Finland	1983–2005	OAIs	Negative	80	49	31	8 (4, 13)	8
					Positive	265	161	104	8 (4, 11)	
Saavedra-Lozano *et al.* (3)	2008	Texas, USA	1999–2003	OAIs	Negative	125	73	52	6 (2, 11)	9
					Positive	165	101	64		
Searns *et al.* (10)*	2021	Colorado, USA	2014–2018	OAIs	Negative	43	28	15	2.3	7
					Positive	127	78	49	9.8	
Spyridakis *et al.* (32)	2018	Pennsylvania, USA	2002–2014	SA	Negative	89	35	54	3.6 (1.7, 6.4)	8
					Positive	40	24	16	4.1 (1.1, 9.7)	
Williams *et al.* (14)	2011	Tennessee, USA	2002–2008	OAIs	Negative	129	64	65	3.2 (1.4, 8.1)	8
					Positive	135	85	50	6.8 (1.4, 11.2)	

F, female; M, male; NOS, Newcastle–Ottawa scale; OAIs, osteoarticular infections; SA, septic arthritis.
*Six cases of concurrent pyogenic myositis.

Results of Egger's test (Z = 0.86, P = 0.39) indicated no significant publication bias. The incidence of long-term sequelae in the culture-negative group of patients was significantly lower than that in the culture-positive group (OR = 0.41, 95% confidence interval (CI): 0.26–0.64, P < 0.001) (Fig. 2).

Secondary indicators

The temperature before admission (MD = −0.20, 95% CI: −0.25 to −0.16, P < 0.001), initial WBC (MD = −1.78, 95% CI: −2.61 to −0.94, P < 0.001), initial CRP (MD = −39.91, 95% CI: −57.52 to −22.30, P < 0.001), initial ESR (MD = −4.99, 95% CI: −5.68 to −4.29, P < 0.001) and likelihood of surgery (OR = 0.22, 95% CI: 0.07–0.70, P < 0.001) were significantly lower in the culture-negative group compared to the culture-positive group. The duration of hospitalization (MD = −2.26, 95% CI: −4.32 to −0.20, P < 0.001), duration of intravenous antibiotic therapy (MD = −5.66, 95% CI: −10.77 to −0.55, P < 0.001) and total duration of antibiotic therapy (MD = −5.66, 95% CI: −10.77 to −0.55, P = 0.03) were shorter in the culture-negative group compared to the culture-positive group. In addition, there were no significant differences in gender, age, race, trauma history, patient delay, antibiotic usage before admission or clinical symptoms between the two groups (P > 0.05) (Table 2).

Publication bias and stability analysis

All indicators underwent Egger's test, which revealed a significant publication bias in patient delay (Z = 2.33, P = 0.02) and ESR (Z = 4.53, P < 0.001). No significant publication bias was observed for other indicators

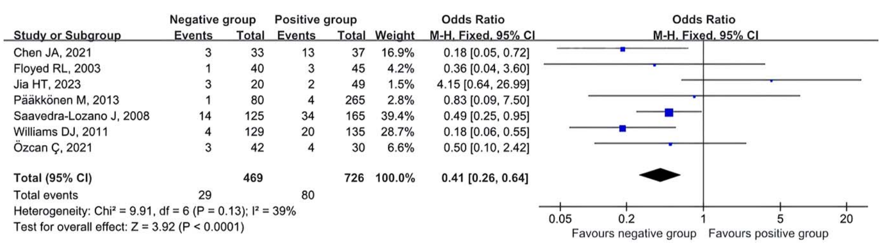

Figure 2

Forest plot of long-term sequelae for the 7 articles included (3, 9, 14, 18, 29, 30, 31).

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Table 2 Meta-analysis of comparisons between culture-negative and culture-positive groups.

Indicators	Studies	Heterogeneity I^2	Heterogeneity *P* value	PE model	OR or MD (95% CI)	*P* value
Gender (male vs female)	12	0	0.48	F	0.84 (0.68, 1.03)	0.10
Age (years)	10	83%	<0.001	R	−0.63 (−1.92, 0.66)	0.34
Trauma history (yes vs no)	4	60%	0.06	R	0.79 (0.38, 1.63)	0.52
Patient delay (days)	5	51%	0.09	R	0.40 (−0.43, 1.23)	0.35
Temperature before admission (°C)	4	43%	0.15	F	−0.20 (−0.25, −0.16)	<0.001*
Antibiotic usage before admission (yes vs no)	4	0	0.59	F	0.74 (0.49, 1.12)	0.15
Race						
White (white vs non-white)	3	2%	0.36	F	1.30 (0.94, 1.80)	0.11
Black (black vs non-black)	3	36%	0.21	F	1.24 (0.89, 1.73)	0.20
Clinical symptoms (yes vs no)						
Fever	8	59%	0.02	R	0.79 (0.47, 1.32)	0.37
Pain/tenderness	3	0	0.74	F	1.11 (0.49, 2.52)	0.80
Limitation of motion	3	72%	0.03	R	0.87 (0.15, 5.13)	0.88
Limp	2	13%	0.28	F	0.89 (0.43, 1.82)	0.75
Swelling	2	0	0.43	F	1.16 (0.58, 2.30)	0.68
Initial laboratory indicators						
WBC (×10⁹/L)	7	0	0.84	F	−1.78 (−2.61, −0.94)	<0.001*
CRP (mg/L)	8	82%	<0.001	R	−39.91 (−57.52, −22.30)	<0.001*
ESR (mm/H)	6	43%	0.12	F	−4.99 (−5.68, −4.29)	<0.001*
Surgery (yes vs no)	3	82%	0.004	R	0.22 (0.07, 0.70)	0.01*
Time-related indicators (days)						
Duration of hospitalization	6	97%	<0.001	R	−2.26 (−4.32, −0.20)	0.03*
Duration of intravenous antibiotic therapy	3	95%	<0.001	R	−10.68 (−21.04, −0.33)	0.04*
Total duration of antibiotic therapy	3	73%	0.02	R	−5.66 (−10.77, −0.55)	0.03*
Long-term sequelae (yes vs no)	7	39%	0.13	F	0.41 (0.26, 0.64)	<0.001*

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; F, fixed-effects model; MD, mean difference; OR, odds ratio; PE, preferred effect; R, random-effects model; WBC, white blood cell count.
*indicates signifacnt *P* value.

(*P* > 0.05). Stability analysis conducted on indicators with significant heterogeneity revealed unstable results for age, trauma history and fever. Therefore, caution should be exercised in interpreting these indicators. In addition, some heterogeneity was observed among the included studies. The source of this heterogeneity could not be determined. Therefore, further literature would be necessary to draw definitive conclusions (Table 3).

Summary of bacterial culture results

These 12 studies involved a total of 957 cases with culture-positive results. *Staphylococcus aureus* was the most commonly isolated microorganism, accounting for 69.70% (667/957) of cases, with variability observed across studies ranging from 57.50 to 95.92%. Among them, methicillin-resistant *Staphylococcus aureus* accounted for 14.94% (143/957) of the cases with culture-positive results and 21.44% (143/667) of the cases with positive *S. aureus*. Following *S. aureus* were *S. pyogenes* (6.17%, 59/957), *S. pneumoniae* (4.39%, 42/957) and *H. influenzae* (3.24%, 31/957). The proportion of other microbial species was less than 1%, as shown in Fig. 3.

Discussion

In this study, we conducted a comprehensive analysis of cohort studies involving children with culture-negative OAIs from 2003 to 2023. The primary outcome measure was the incidence of long-term sequelae. This meta-analysis found that the incidence of long-term sequelae, temperature before admission, baseline laboratory indicators and possibility of surgery in the culture-negative group of patients were significantly lower than those in the culture-positive group. In addition, there were no significant differences in gender, age, race, trauma history, patient delay, antibiotic usage before admission or clinical symptoms between the two groups.

Advances in the understanding of the pathogenic microbiology of OAIs have revealed significant variations in onset age, clinical manifestations, serological indicators and prognosis depending on the pathogen involved (33). Traditionally, *S. aureus* was considered the predominant pathogen responsible for OAIs across all pediatric age groups (34, 35). However, recent studies have demonstrated that *K. kingae* has emerged as the leading pathogen in OAIs among

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Table 3 Stability analysis and publication bias of comparisons between culture-negative and culture-positive groups.

Indicators	Studies	Stability analysis				Egger's test	
		Effect model*	OR or MD (95% CI)	*P* value	Result stability	*Z* value	*P* value
Gender (male vs female)	12	NA				−0.16	0.87
Age (years)	10	F	−1.16 (−1.64, −0.68)	<0.001**	Unstable	−0.70	0.48
Trauma history (yes vs no)	4	F	0.67 (0.45, 0.98)	0.04**	Unstable	1.11	0.27
Patient delay (days)	5	F	0.08 (−0.41, 0.57)	0.75	Stable	2.33	0.02**
Temperature before admission (°C)	4	NA				−0.46	0.64
Antibiotic usage before admission (yes vs no)	4	NA				0.92	0.36
Race							
White (white vs non-white)	3	NA				−0.11	0.91
Black (black vs non-black)	3	NA				0.04	0.97
Clinical symptoms (yes vs no)							
Fever	8	F	0.67 (0.50, 0.90)	0.007**	Unstable	1.75	0.08
Pain/tenderness	3	NA				0.78	0.44
Limitation of motion	3	F	0.73 (0.36, 1.47)	0.38	Stable	1.40	0.16
Limp	2	NA				NA†	
Swelling	2	NA				NA†	
Initial laboratory indicators							
WBC (×10^9/L)	7	NA				−0.85	0.40
CRP (mg/L)	8	F	−29.10 (−30.10, −28.11)	<0.001**	Stable	−0.20	0.84
ESR (mm/H)	6	NA				4.53	<0.001**
Surgery (yes vs no)	3	F	0.21 (0.14, 0.32)	<0.001**	Stable	−0.41	0.68
Time-related indicators (days)							
Duration of hospitalization	6	F	−2.89 (−2.98, −2.80)	<0.001**	Stable	−0.55	0.58
Duration of intravenous antibiotic therapy	3	F	−17.10 (−18.46, −15.74)	<0.001**	Stable	0.15	0.88
Total duration of antibiotic therapy	3	F	−4.41 (−6.59, −2.23)	<0.001**	Stable	−0.43	0.67
Long-term sequelae (yes vs no)	7	NA				0.86	0.39

*F, fixed-effects model; NA, not available (stability analysis is not necessary for those that prefer fixed-effects models); †Egger's test cannot be conducted for only two articles included.

toddlers aged 6–48 months (36, 37). The limitations of traditional bacterial culture techniques often result in false-negative findings, particularly with *K. kingae* in this age group (38, 39, 40, 41). Fortunately, *K. kingae* infections typically respond well to antibiotics, leading to milder infections and favorable outcomes (42).

In our study, even after excluding the research by Osei and coworkers (13), which focused on children under 36 months old, the rate of culture negativity among children with OAIs remained high across all age groups (41.14%), with no significant change in the occurrence of long-term sequelae. The low detection rate of *K. kingae* in older

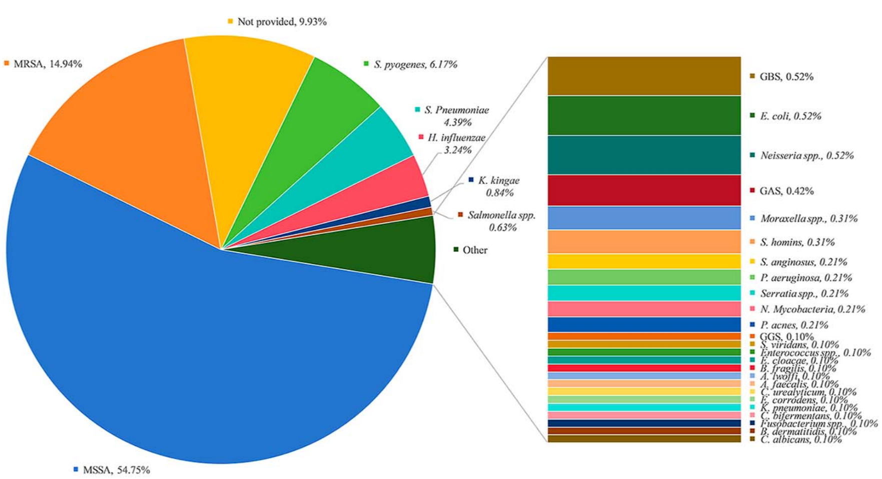

Figure 3

Pie chart for pathogen distribution in children with OAIs of the 12 articles included. MSSA, methicillin-sensitive *Staphylococcus aureus*; MRSA: methicillin-resistant *Staphylococcus aureus*.

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children (43), combined with the predominance of *S. aureus* in culture-positive cases (nearly 70%), suggests that the elevated rate of culture-negative results among children over 4 years old cannot be solely attributed to *K. kingae*. In addition, newly identified and other unidentified pathogens might also contribute to culture-negative results (9).

Enhanced antimicrobial immunity in children may suppress bacterial growth (44), leading to culture negativity and milder inflammatory responses, as indicated by lower WBC, CRP and ESR levels in culture-negative patients (30, 45). Consequently, these patients might experience less severe local damage and improved clinical outcomes due to relatively smaller bacterial loads (10). At the same time, Feng and coworkers (28) suggested that a brief delay in seeking medical care might contribute to culture negativity and the interval between symptom onset and medical care initiation impacts laboratory indicators. Although our meta-analysis did not find significant differences in this interval between patient groups, the variable remains noteworthy.

Empirical antibiotic use prior to hospital admission may inhibit bacterial growth and reduce tissue damage, potentially delaying medical care, which reduces the urgency for immediate medical attention. Some scholars (30, 46) demonstrated that empirical antibiotic usage could directly impact bacterial culture outcomes after admission. However, Chen and coworkers (9) and Lansell and coworkers (11) found no association between pre-admission antibiotic usage and culture outcomes, which was consistent with the findings of our meta-analysis. Upon exclusion of studies (3, 9, 27, 29) involving patients with pre-admission antibiotic usage, subsequent subgroup analysis revealed alterations solely in the duration of intravenous antibiotic therapy and total antibiotic therapy duration, with other metrics remaining unchanged. Therefore, based on the consistent findings in this meta-analysis, it can be concluded that pre-admission antibiotic usage may not influence culture outcomes.

In addition, the technical aspects of surgical or aspiration procedures and microbiological culture techniques may influence culture outcomes (14). Surgery can reduce local bacterial load, lower toxin concentration and alleviate local tissue damage (47). However, the procedures themselves might also lead to sequelae development (9, 15). Our findings indicate that culture-positive patients are more likely to undergo surgery and experience worse prognoses. Therefore, it is essential to consider the potential risks and benefits of surgical intervention carefully and to use appropriate microbiological culture techniques to improve culture outcomes.

Researchers (3, 9, 10, 18) have examined the differences in clinical manifestations and imaging findings among the patient groups. However, due to inconsistent criteria for positive results in the original studies, a meta-analysis on imaging examinations could not be performed. This meta-analysis did not reveal significant differences in various clinical symptoms between the patient cohorts, which was inconsistent with some studies suggesting that culture-negative patients exhibit milder symptoms (3, 32). The discrepancy may be attributed to inconsistent symptom descriptions and the retrospective nature of the included studies, leading to overlooked or unrecorded complaints/symptoms. Prospective cohort studies in the future may provide deeper insights into this matter.

This study has limitations. Due to the limited number of randomized controlled trials, the inclusion of retrospective cohort studies may have impacted the level of evidence in this study. Therefore, multi-center, large-sample and high-quality long-term follow-up trials are necessary to validate these findings. The reasons for culture-negative results in children with OAIs are complex and involve several confounding factors, making the analysis of their interactions challenging. Further research is needed to investigate the underlying mechanisms and potential risk factors associated with culture-negative OAIs. The limited availability of research information in published studies constrained our evaluation to pertinent research only, and complete elimination of potential publication bias is not feasible. Future studies should aim to include a more comprehensive range of studies to minimize the impact of publication bias. Some observed indicators exhibited significant heterogeneity, and the use of different models results in instability, necessitating cautious interpretation for subgroups with different age ranges, records of trauma history and fever symptoms.

Nonetheless, to our knowledge, this is the first study to comprehensively summarize the relevant literature and systematically analyze the outcomes of culture-negative OAIs through meta-analysis. These findings hold clinical significance and may provide valuable insights, laying a foundation for future research.

Conclusion

Children diagnosed with culture-negative OAIs generally demonstrated less severe systemic inflammatory responses, required shorter treatment durations, exhibited a reduced likelihood of requiring surgical intervention and were less prone to experiencing long-term functional impairments compared to children with culture-positive OAIs. However, no differences in patient characteristics and clinical symptoms were found between the two groups. Further large-scale studies are still required to validate these findings.

ICMJE Statement of Interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the work.

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Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

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