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Comparison Between Septic Arthritis Alone and Coexisting with Other Bone and Joint Infections in Pediatric Patients

A Retrospective Review

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Investigation performed at Geneva University Hospitals, Switzerland

Background: It is unclear whether coexisting septic arthritis and osteomyelitis (CSAO) differs from septic arthritis (SA) alone in terms of susceptible age groups, clinical and paraclinical presentations, and prevalence. This study aimed to compare patients with isolated SA with those presenting with CSAO, determine the efficacy of different parameters used to distinguish those diagnoses, and investigate the prevalence of CSAO due to *Kingella kingae*.

Methods: The study retrospectively included all patients treated for SA over a 17-year period at Geneva University Hospitals. Clinical, biological, and bacteriological data were analyzed. Magnetic resonance imaging (MRI) was reviewed for all patients to identify those with coexisting osteomyelitis. Comparisons between patients with isolated SA and those with CSAO were performed using the unpaired Mann-Whitney *U* for continuous outcomes (reported with median [interquartile range]) and the Pearson χ^2 tests for dichotomous outcomes (reported with n [%]).

Results: Of 247 patients with osteoarticular infections, 177 with SA fulfilled our inclusion criteria. Of these, 124 had SA alone, and 53 (29.9%) had a CSAO. There were no statistically significant differences between the 2 groups regarding sex, age, and clinical and paraclinical results. When coexisting osteomyelitis was present, 51% of cases were acute and 49% were subacute. Bone infection was found in the metaphyses of 21 patients (39.6%), the epiphyses of 11 (20.8%), and was transphyseal in 10 (18.9%). Whatever the infection location, *K. kingae* was the most common pathogen found in both groups (48% of SA, 43% of CSAO, p = 0.651).

Conclusions: This study showed that CSAO is common in children, especially among those younger than 4 years, with an unexpectedly high prevalence of subacute osteomyelitis. This should encourage caregivers to use MRI more extensively in diagnostic processes. Clinical and paraclinical data did not contribute to differentiate CSAO from SA. The widespread presence of *K. kingae* as a pathogen in both groups supports the advice to systematically use polymerase chain reaction techniques in children younger than 4 years of age.

Level of Evidence: Level III. See Instructions for Authors for a complete description of levels of evidence.

Introduction

Septic arthritis (SA) and hematogenous osteomyelitis (HO) are among the most common severe childhood bacterial infections and remain challenging clinical issues for physicians. Diagnostic tools for identifying and managing them have multiplied and improved in recent decades. Notably, the large-scale use of nucleic acid amplification assays had a positive impact on diagnosing osteoarticular infections (OAIs)[1-3]. Concurrently, interest grew in using magnetic resonance imaging (MRI) to confirm diagnoses of OAIs and understand their local spread.

SA is frequently reported as a complication of HO in children due to the intracapsular position of the metaphysis allowing osteomyelitis to spread into the joint[4]. The widespread use of MRI showed that the proportional amount of concomitant infections of the bone and the joint was much higher than expected. Indeed, some studies have demonstrated that more than half of children

Disclosure: The **Disclosure of Potential Conflicts of Interest** forms are provided with the online version of the article (http://links.lww.com/JBJSOA/A803).

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(58%–68%) with SA presented with coexisting osteomyelitis[5-8]. Owing to their anatomical characteristics, some joints, such as hips and shoulders, are more often affected[7,9,10]. Patient age also seems to be a confounding factor as children younger than 6 months old and teenagers paradoxically display higher proportions of concurrent infections[9]. The early recognition of this condition is very important since many authors think that children with coexisting SA and osteomyelitis (CSAO) have less favorable outcomes, and require more surgical procedures and longer antibiotic therapies than patients with SA alone or HO alone[11].

We hypothesize that CSAO is found in a significant portion of children presenting with SA because their presenting vital signs, serological values, microbiological parameters, and outcomes do not differ much from each other. This can be explained by the fact that *Kingella kingae* is the most represented pathogen for these infections.

To investigate the differences between the 2 groups, (1) clinical variables such as age and sex, (2) microbiological parameters like white blood cell (WBC) count, platelet count (PLC), C-reactive protein (CRP) level and erythrocyte sedimentation rate (ESR), and (3) bacteriological characteristics were compared. Finally, (4) the involvement of *K. kingae* in CSAO was assessed.

Material and Methods

After approval by the Geneva Children's Hospital Review Board, the medical charts of pediatric patients aged 1 day to 16 years old admitted in our facility with SA (with or without coexisting osteomyelitis) from January 2007 to December 2023 were retrospectively reviewed[12]. Diagnosis codes for SA and CSAO were used to identify the study population from our institution's electronic medical records. The criteria established by Morrey were used to estimate children's risk of having a joint or bone infection[13,14]. The inclusion criteria were (1) SA with or without concomitant HO, (2) positive MRI evidence from the affected anatomical region, and (3) antibiotic treatment required. Excluded patients had had previous surgeries, presented with a traumatic wound or foreign body at the site of infection, had incomplete radiological investigations or did not fit in either group.

Epidemiological, Clinical, and Paraclinical Investigations

Collected data included age, sex, the joints, and/or bones involved. Clinical and paraclinical investigations included temperature at admission and laboratory values such as WBC count, PLC, ESR, and CRP level.

Microbiological Work-up

Blood cultures were collected systematically. Joint and bone aspirate samples were sent to the laboratory for immediate inoculation before starting antibiotic therapy. Two polymerase chain reaction (PCR) assays were also performed for bacterial identification when standard cultures were negative.

Radiological Investigations

Plain radiographs were performed for patients with signs and symptoms. MRI was performed within 24 hours of every admission. Images were acquired at 1.5-T (Avanto; Siemens) using tridimensional Short Tau Inversion Recovery (STIR), T1-weighted turbo spin-echo (one longitudinal plane); 2 orthogonal planes with T2-weighting plus fat suppression, STIR (longitudinal plane), and water-only fast spin-echo T2-weighted Dixon sequences (axial plane); Diffusion weighted imaging (DWI) (axial plane) and postcontrast injection T1-weighted spin echo with frequency-selective fat saturation (2 orthogonal planes)[12]. Postcontrast sequences were obtained after the injection of 0.2 mL/kg of gadoteric acid (Dotarem). To limit the difficulty of performing MRI in the pediatric population, anesthesia was performed before MRI and immediately followed by the surgical procedure, when required.

Both radiographs and MRI were independently and retrospectively reviewed by a board-certified pediatric radiologist and a senior pediatric orthopedist to find consensus diagnoses.

MRI has a primordial role in identifying joint effusion and locating abscesses, whether osseous or in the soft tissues. MRI for pediatric musculoskeletal infections has a sensitivity of 81%–100% and specificity 67%–94% compared with the CT scan (sensitivity of 67%–100% and specificity 50%)[15,16].

Bone involvement in osteomyelitis is defined by the presence of intramedullary low T1 signal intensity; increased signal intensity on fluid-sensitive sequences; findings attributable to edema, hyperemia, or exudate[17-21]; or evidence of contrast-enhanced enhancement of the vascularized inflamed tissue[22-24]. The presence of joint effusion was subjectively defined by visualization on MRI of a supraphysiologic amount of fluid in the joint space after injection, with contrast enhancement of the synovium after injection.

The diagnosis of osteomyelitis was based on laboratory studies, and culture of bone aspiration, with supportive MRI or surgical findings.

When there was a discrepancy between imaging and clinical diagnosis, imaging was reviewed, and surgical and microbiologic diagnosis were used as the reference.

Statistical Analysis

The characteristics of patients with SA were analyzed in the 2 diagnostic subgroups (SA alone & CSAO). The normality of the distribution of the clinical manifestations and laboratory test results was evaluated using the normal Q-Q plot and the Shapiro-Wilk test. Comparisons between patients with SA alone and those with CSAO were performed using Student t-tests for continuous outcomes with normal distribution reported with mean (SD), an unpaired Mann-Whitney *U* test for continuous outcomes with nonnormal distributions reported with median (interquartile range [IQR]), and a Pearson χ^2 test for dichotomous outcomes reported with n (%).

The proportions of children with SA alone and those with CSAO were assessed according to the number of parameters present at admission.

To predict CSAO, the clinical and laboratory parameters (temperature at admission, CRP, WBC, ESR, and PLC) were then included in a univariate and multivariate logistic regression model for which adjusted odds ratio (OR) and 95% confidence interval were calculated.

Statistical analysis was performed using R v.4.2.2 software (R foundation for statistical computing) with the RStudio interface (RStudio Team 2016; RStudio). Statistical significance was set at $p < 0.05$.

Results

The medical charts of 247 children treated for SA were analyzed retrospectively. Of 177 eligible for the study, 89 were male (50.3%) and the median age was 18 months (1-189 months).

Comparison Between SA Alone and CSAO

Our analysis showed no statistically significant differences between the clinical and paraclinical parameters of both groups. Sex, age, and temperature at admission were almost identical. Results showed no statistical differences in temperature ($p = 0.343$), WBC ($p = 0.598$), CRP ($p = 0.423$), and ESR ($p = 0.279$). Only PLC showed a statistically significant difference ($p = 0.024$) between the 2 groups showing a median (IQR) PLC of 357 (298-441) G/L in SA and 424 (316-520) G/L in CSAO with significantly ($p = 0.025$) less cases with PLC >400 G/L in SA (46/122 [37%]) compared with CSAO (30/53 [57%]) (Table I).

According to bacteriology, in both groups, *K. kingae* was the most frequently identified pathogen with no statistically significant difference ($p = 0.656$) (Table II). The CSAO group had more infections due to *Staphylococcus aureus* (5.7% of SA and 20.8% of CSAO cases, $p = 0.006$) or to other germs (12.9% of SA and 17% of CSAO). No bacteria were detected in 20% of cases of SA alone and in 13% of cases of CSAO (Table I).

The joints most affected by SA alone were, respectively, knees (41.1%), hips (20.2%), and ankles (9.7%), while in the CSAO group, respectively, ankles (20.8%), knees (18.9%), and elbows (15.1%) (Table II).

In the CSAO group, the coexisting osteomyelitis was defined as acute in 27 cases (51%) and subacute in 26 (49%). Infections were metaphyseal in 21 cases (39.6%), epiphyseal in 11 (20.8%), and transphyseal in 10 (18.9%) (Table II) (Figs. 1–3).

Predicted Coexisting SA and Osteomyelitis

The clinical and laboratory parameters distribution are shown in Figure 4. A clear overlapping of the density curve of the age (Fig. 4-A), temperature (Fig. 4-B), CRP level (Fig. 4-C), ESR (Fig. 4-D), and WBC count (Fig. 4-E) was found for SA and

TABLE I Comparison of the Demographic, Clinical and Biological and Bacteriological Characteristics Between the Patients with Septic Arthritis Alone (n = 124) and Coexisting Septic Arthritis and Osteomyelitis (n = 53)

	SA (n = 124)	CSAO (n = 53)	p	ES	95% CI
Demographic					
Age (months)	18 (14-30)	18 (11-42)	0.865	0.083	−5.5 to 4.0
Male, n (%)	62 (50)	27 (51)	>0.999	<0.001	−18% to 16%
Bacteriological					
Kingella kingae, n (%)	60 (48)	23 (43)	0.656	0.015	−12% to 22%
K. kingae suspicion, n (%)	16 (13)	4 (8)	0.440	0.045	−5% to 16%
Staphylococcus aureus, n (%)	7 (6)	11 (21)	0.006*	0.579	−28% to −2%
No germs, n (%)	25 (20)	7 (13)	0.375	0.059	−6% to 20%
Other germs, n (%)	16 (13)	8 (15)	0.881	0.002	−15% to 10%
Clinical and bacteriological					
Temperature, °†	37.3 (36.7-38.1)	37.4 (36.6-38.2)	0.724	0.045	−0.3 to 0.2
Temperature > 38.5, n (%)†	15 (12)	7 (13)	>0.999	<0.001	−13% to 13%
WBC count, 1,000/mm^3‡	12.1 (9.6-14.9)	11.7 (9.1-14.2)	0.454	0.009	−8.0 to 19.0
WBC count > 12, n (%)‡	62 (50)	24 (45)	0.681	0.013	−13% to 22%
CRP level, mg/L§	24.3 (11.8-50.3)	31.4 (9.8-78.0)	0.465	0.007	−15.0 to 5.0
CRP level > 20, n (%)§	69 (56)	28 (53)	0.857	0.002	−15% to 20%
ESR, mm/h#	34 (18-45)	35 (25-55)	0.290	0.042	−13 to 3
ESR > 40, n (%)#	37 (30)	16 (30)	>0.999	<0.001	−15% to 15%
PLC, 1,000/mm^3**	357 (298-441)	424 (316-520)	0.024*	0.149	−98 to −8
PLC > 400, n (%)**	46 (37)	30 (57)	0.025*	0.376	−37% to −2%

*Significance was set at p-value<0.05. Results are presented as median (IQR) where IQR is the interquartile range; group comparison is made with a Mann-Whitney *U* test. †Temperature was available for n = 123 SA and n = 52 CSAO. ‡White blood cell (WBC) count was available for n = 123 SA and n = 53 CSAO. §C-reactive protein level (CRP) was available for n = 124 SA and n = 48 CSAO. #Erythrocyte sedimentation rate (ESR) was available for n = 105 SA and n = 39 CSAO. **Platelet count (PLC) was available for n = 122 SA and n = 53 CSAO. CI = confidence interval, CRP = C-reactive protein, CSAO = coexisting septic arthritis and osteomyelitis, ES = effect size, ESR = erythrocyte sedimentation rate, IQR = interquartile range, PLC = platelet count, SA = septic arthritis, and WBC = white blood cell.

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TABLE II Infected Joint for Patients with Septic Arthritis Alone (n = 124) and Coexisting Septic Arthritis and Osteomyelitis (n = 53), with Type and Location of Osteomyelitis for Patients with CSAO

	SA (N = 124)	CSAO (N = 53)
Infected joint		
Hip	25 (20.2%)	7 (13.2%)
Knee	51 (41.1%)	10 (18.9%)
Ankle	12 (9.7%)	11 (20.8%)
Foot	6 (4.8%)	3 (5.7%)
Thorax	2 (1.6%)	3 (5.7%)
Spine	1 (0.8%)	0 (0%)
Sacroiliac	3 (2.4%)	0 (0%)
Shoulder	5 (4%)	7 (13.2%)
Elbow	9 (7.3%)	8 (15.1%)
Wrist	7 (5.7%)	3 (5.7%)
Hand	3 (2.4%)	1 (1.9%)
Type of bone infection		
Acute osteomyelitis		27 (51%)
Subacute osteomyelitis		26 (49%)
Bone infection location		
Epiphysis		11 (20.8%)
Metaphysis		21 (39.6%)
Transphyseal		10 (18.9%)
Tarsal bone		4 (7.6%)
Sesamoid bone		3 (5.7%)
Acetabulum		1 (1.9%)
Carpal bone		1 (1.9%)
Thorax		1 (1.9%)
Apophysis		1 (1.9%)

CSAO = coexisting septic arthritis and osteomyelitis and SA = septic arthritis.

CSAO patients. A tendency to have higher values of PLC (Fig. 4-F) was reported in CSAO patients.

Univariate logistic regression models demonstrated that PLC ($p = 0.024$) was significantly higher in CSAO patients compared with SA. In the multivariate analysis, only age (OR = 0.998 [0.996–1.000], $p = 0.088$) comes close to statistical significance with no significant clinical and biological outcomes ($p > 0.05$) (Table III).

Discussion

CSAO continues to be a real challenge as its clinical presentation is difficult to distinguish from SA alone. HO and SA can even be considered part of a single-infection event in which pathogens selectively infect 1 or both foci. For a long time, the CSAO was believed to occur essentially either in joints with an intracapsular metaphysis or in very young patients due to their transphyseal vessels connecting epiphyseal and metaphyseal circulation[25-29]. We now realize that it is much less clear whether this infection originates in bones or joints and whether it spreads through contiguous propagation or vascular dissemination[29-31] especially in older children since vessels do not penetrate the physeal plate anymore.

This study was designed to provide the most accurate results by systematically using MRI and optimal techniques to detect pathogens in OAI, such as PCRs in blood samples since all OAI in children arise from initial hematogenous seeding.

The incidence of CSAO in our study was 29.9%, which corresponds to the lower range values previously reported in the literature. Indeed, reported rates of CSAO among pediatric patients vary from 17% to 79%[5,7-10,27,32,33]. In the literature published after 2015, the frequency of CSAO was over 60%, reflecting greater recognition of this entity thanks to the increased use of MRI during the initial evaluation[5,7,8,10]. Our lower rate of coexisting osteomyelitis could be caused by the few OAIs due to *S. aureus*, which is a recognized risk factor for coexisting bone infections.

Our study highlighted that not all children are equally susceptible to CSAO. Age appears to be a determining factor. Nearly 80% of patients in our series were younger than 4 years old, and among them, 11.9% were younger than 6 months old. This suggests that children younger than 4 were more likely to present with CSAO. This observation is somewhat different from that made by Jackson et al., who found that most of their patients with coexisting infections (44%) were younger than 6 months old[32]. However, these observations go against many authors who consider the presence of CSAO to be associated with an older median age (>4 years)[9,34].

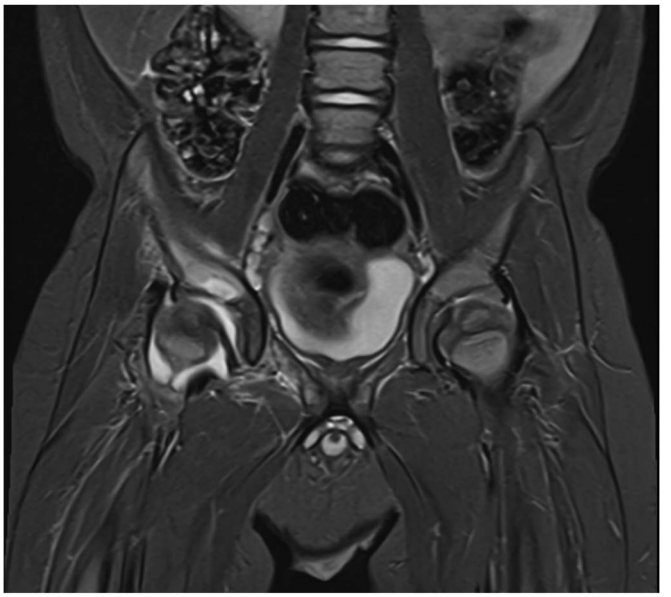

Fig. 1

MRI of a septic arthritis of the right hip with concomitant subacute osteomyelitis of the right acetabulum in a 17-month-old boy caused by *Kingella kingae*: Coronal STIR MR image shows hyperintense juxta articular lesion with peripheral bone marrow of the right acetabulum, right hip joint effusion, and ipsilateral soft tissue edema. MRI = magnetic resonance imaging.

Fig. 2

MRI of a septic arthritis of the left knee with concomitant subacute transphyseal osteomyelitis of the distal femur in a 26-month-old woman caused by *Kingella kingae*: Sagittal STIR MR image shows hyperintense transphyseal bone marrow and mild knee joint effusion. MRI = magnetic resonance imaging.

This study also confirmed that certain joints had a higher risk of displaying CSAO. Our results demonstrated that ankles and knees were more frequently affected than shoulders and hips. Intracapsular metaphyses in the shoulder, hip, radial head, and ankle facilitate the spread of bony infections to their adjacent joints[5]. For anatomical reasons, some joints are also more affected than others, notably hips and shoulders[7,9,10].

Regarding types of infections, our results were the first to show that subacute osteomyelitis was highly prevalent, constituting almost half (49.1%) of our osteomyelitis cases. Osteomyelitis in long bones was surprising; however, since only half of the cases of coexisting osteomyelitis affected metaphyses, 26.2% had an epiphyseal starting point, and 23.8% were both epiphyseal and metaphyseal, with transphyseal diffusion. Our findings highlighted that CSAO may result (in nearly a quarter of cases) in a significant damage to growth plates. Identifying and quantifying transphyseal lesions appears crucial to providing prognoses about potential growth arrest and proper monitoring.

Our study provided strong evidence that *K. kingae* was the most common pathogen responsible for CSAO. This is already the case for SA alone. Indeed, appropriate PCR use has demonstrated that *K. kingae* is currently the major bacterial cause of pediatric OAIs, ahead of *S. aureus*, especially among children younger than 4 years old. PCR assays should thus be used in routine microbiological evaluations to improve diagnostic performance.

Finally, this study's results did not confirm previously identified factors aiming to detect coexisting infections earlier. In our series, patients with CSAO and those with SA alone had similar age distribution and temperatures, blood parameters did not differ significantly except for PLC (meanly higher in CSAO cases), and *S. aureus* was not the principal pathogen responsible for their infections. However, children with CSAO may have a longer duration of symptoms due to the high prevalence of coexisting subacute osteomyelitis. This could explain the elevation of PLC in this group. Until now, CSAO was associated with an older median age, a longer duration of symptoms (especially fever), a more prevalent involvement of *S. aureus*, higher rates of bacteremia, and extended hospital lengths of stay[9]. Danilov et al. considered the following as independent predictors of coexisting osteomyelitis in children with SA of the hip: (1) refusal to bear weight or hip pain among nonambulatory children, (2) CRP > 20 mg/dL, (3) age > 4 years, and (4) symptoms for more than 4 days[34]. For other joints, the presence of CSAO was associated with older age, a longer duration of symptoms, bacteremia, and infection caused by *S. aureus*[5,34]. Finally, many authors consider that MRI should be performed for all pediatric patients with SA, particularly if they have been in pain for > 4 days, as 96% of these children have coexisting osteomyelitis[5]. All this is easily

Fig. 3

MRI of a septic arthritis of the right ankle with concomitant acute transphyseal osteomyelitis of the distal tibia in a 13-year-old boy caused by MSSA: Sagittal STIR image MR shows transphyseal hyperintense lesion with peripheral bone marrow and ankle joint effusion. MRI = magnetic resonance imaging; MSSA = methicillin-susceptible staphylococcus aureus.

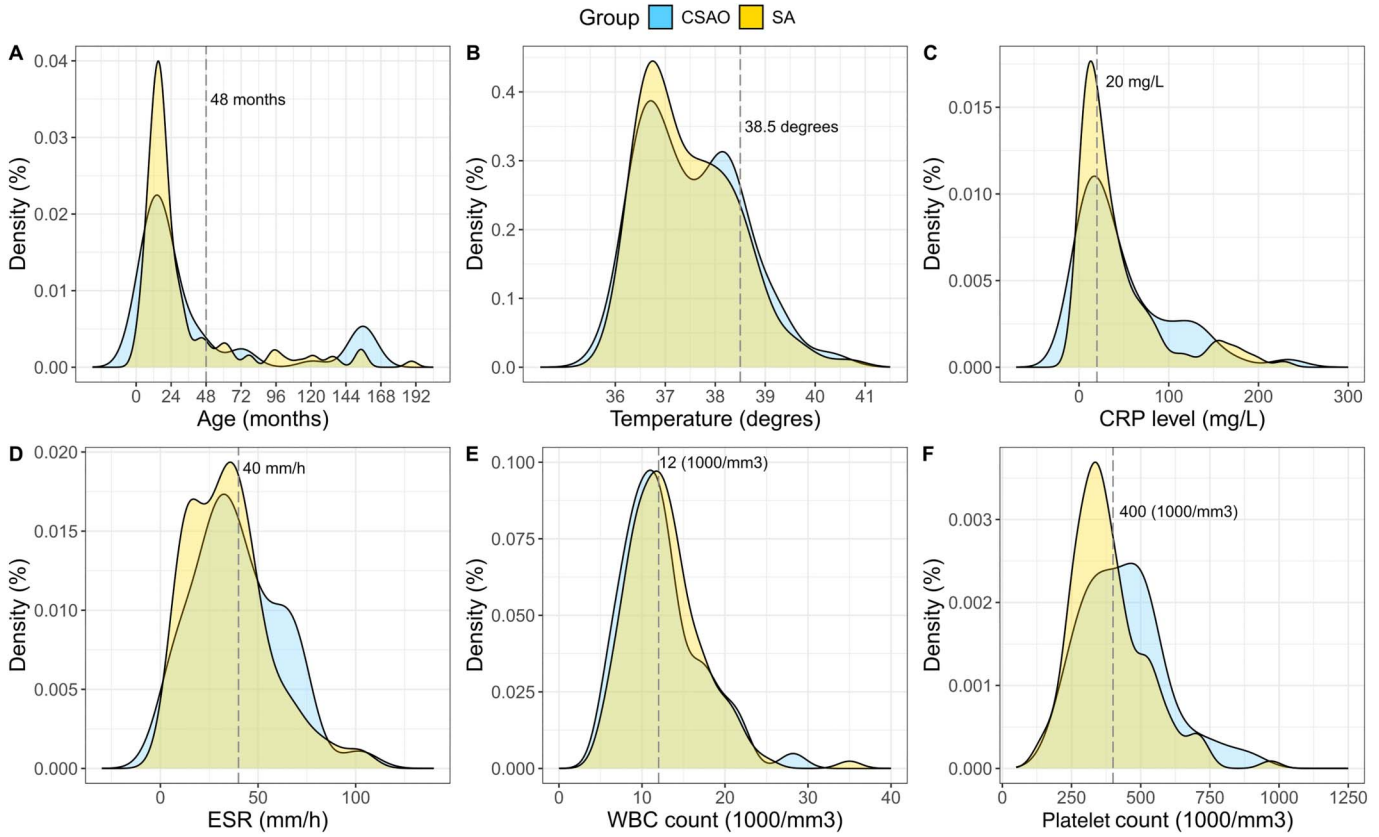

Fig. 4

Density curve of the (**Fig. 4-A**) age, (**Fig. 4-B**) temperature, (**Fig. 4-C**) C-reactive protein (CRP) level, (**Fig. 4-D**) erythrocyte sedimentation rate (ESR), (**Fig. 4-E**) white blood cell (WBC) count, and (**Fig. 4-F**) platelet count (PLC) for the patients with septic arthritis alone (SA, n = 124) and coexisting SA and osteomyelitis (CSAO, n = 53).

explained, however, because most of these studies neglected the 6 months to 4 years age group, which accounts for over 70% of all OAIs[35-37], and they focused solely on infections among older children caused by pyogenic pathogens, such as *S. aureus*, *Streptococcus pyogenes*, and *Streptococcus pneumoniae*. Our study's results suggest, therefore, that the parameters and cutoffs mentioned above should be re-evaluated using multicenter studies that consider the causal germs of SA.

TABLE III Univariate and Multivariable Logistic Regression with the Biological and Clinical Markers to Predict Patients with Septic Arthritis Alone (SA, n = 124) and Coexisting Septic Arthritis and Osteomyelitis (CSAO, n = 53)

		Univariate Logistic Regression		Multivariate Logistic Regression	
Predictors	Contrast	OR (95% CI)	p	OR (95% CI)	p
Age	1 mo-increase	0.999 (0.997-1.000)	0.208	0.998 (0.996-1.000)	0.088
T. admission†	1°C-increase	0.986 (0.918-1.060)	0.698	0.970 (0.892-1.050)	0.465
WBC count‡	1,000/mm^3-increase	1.000 (0.989-1.020)	0.592	1.020 (0.996-1.040)	0.121
CRP§	1 mg/L-increase	0.999 (0.998-1.000)	0.172	1.000 (0.998-1.000)	0.955
ESR#	1 mm/h-increase	0.998 (0.995-1.000)	0.263	0.998 (0.994-1.000)	0.283
Platelet count**	1,000/mm^3-increase	0.999 (0.999-1.000)	0.023*	0.999 (0.999-1.000)	0.114
Intercept	—	—	—	7.85 (0.359-172.0)	0.193

*The level of significance was set at $p < 0.05$. †Temperature was available for n = 123 SA and n = 52 CSAO. ‡WBC count was available for n = 123 SA and n = 53 CSAO. §CRP was available for n = 124 SA and n = 48 CSAO. #ESR was available for n = 105 SA and n = 39 CSAO. **Platelet count was available for n = 122 SA and n = 53 CSAO. CI = confidence interval, CRP = C-reactive protein, CSAO = coexisting septic arthritis and osteomyelitis, ES = effect size, ESR = erythrocyte sedimentation rate, IQR = interquartile range, OR = odds ratio, PLC = platelet count, SA = septic arthritis, and WBC = white blood cell.

The study has some limitations. Its retrospective nature increases the risk of missing certain cases due to medical coding errors and the likely proportion of missing data and patients lost to follow-up. Some children with SA did not benefit from an MRI investigation and thus had to be excluded from the study, generating a possible selection bias. Nevertheless, the descriptive material examined provided information about the types and locations of CSAO and pathogens involved. These results should be confirmed and enriched in a proper multicenter study that would allow to examine more patients and thus identify factors that may help diagnose coexisting infections earlier.

Conclusion

Since osteomyelitis coexists in almost 30% of cases of SA, performing MRI should be a valuable aid in diagnosing the associated involvement of bones and joints. Despite the descriptions in the literature, infants seem more likely to present with coexisting infections since our results revealed that 80% of our cohort were younger than 4 years old. This study highlighted that the admission values of traditional laboratory measures such as the WBC, CRP, and ESR were not predictive of CSAO. Subacute osteomyelitis was highly prevalent among our cases of coexisting osteomyelitis and may result in up to a quarter of cases having significant damage to the growth plate. There is strong evidence that *K. kingae* is the most common pathogen responsible for these CSAO.

Finally, the validation of predictive risk factors for CSAO in pediatric populations remains the subject of debate. Only a multicenter controlled trial study could properly solve this question. ■

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