#### **ORIGINAL PAPER**



# Ten-year retrospective review of paediatric septic arthritis in a New Zealand centre

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## Abstract

**Background** Paediatric septic arthritis, although a rare diagnosis in the developed world, remains a significant challenge in the New Zealand population. In recent years, there has been effort to characterize the nature of paediatric bone and joint infection for New Zealand due to rising incidence of osteomyelitis and staphylococcal sepsis [1, 2]. We have sought to identify trends in presentation, diagnosis and management of paediatric septic arthritis, with added focus on ethnicity and access to healthcare. **Methods** A ten year retrospective review of all cases < 16 years with presumed septic arthritis presenting to a tertiary referral centre between 2008 and 2018 was performed.

**Results** A total of 103 cases met inclusion criteria. Mean age was 5.9 years (SD +/- 4.17) with a male predominance (64%). Traditional laboratory culture method isolated an organism in 66% of cases: *Staphylococcus aureus* was the most common pathogen identified (61%). Incidence varied greatly by ethnicity 1:16,000 for NZ European children; 1:8760 for Pacifica and 1:4300 for Māori. Mean distance travelled by patients to reach the nearest emergency department was 38.3 km, ranging from 2 to 188 km. Assessment using NZ deprivation scores showed the Māori paediatric population were likely to reside in areas of worse socioeconomic deprivation (p = 0.0005). The majority (66%) of cases were treated surgically with a low recurrence rate (2.9%). Delayed presentation was associated with worse outcomes and more likely in patients residing > 20 km away from the nearest emergency department.

**Conclusion** The incidence of paediatric septic arthritis in New Zealand is concerningly high within Māori and Pacific populations. Future health interventions should consider environmental, socioeconomic, and microbiological trends in the burden of disease.

Keywords Paediatric septic arthritis · Epidemiology · Paediatric bone and joint infection

Level of Evidence: Retrospective study, Level II

No portion of this work has been published elsewhere or submitted elsewhere for review.

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# Introduction

The incidence of paediatric septic arthritis (SA) in Organisation For Economic Cooperation and Development (OECD) countries ranges from one to four cases per 100,000 children per year [3, 4]. The incidence is slightly higher in the very young particularly those aged under five years. Frequently clinical signs, such as fever, localized pain or limp, are present, and the key predictive features have been elicited by Kocher with the four modified criteria of raised Creactive protein, raised white cell count, limp and fever having an ever-increasing positive predictive value [4]. Although mortality as a result of SA is rare, many cases are managed with surgical intervention on an emergent basis as the developing joint is susceptible to irreversible damage by the infective cascade resulting in long term sequalae such as pain, stiffness, limb length discrepancy and loss of function [5]. Most epidemiologic reports detail microbiologic findings and *Staphylococcus aureus* remains a main causative organism. More recently, *Kingella kingae* has emerged as a common causative organism, particularly in the very young [2]. The opportunity to identify *K. kingae* as the causative organism may be missed if appropriate culture techniques are not utilized [2].

New Zealand is geographically isolated and as a result has unique population characteristics. The population is ethnically and socially diverse with multiple groups represented including the indigenous Māori who make up 16% of the population [6]. In New Zealand, *S. aureus* infection presents unique challenges due to variations in its molecular componentry [7–9]. Unusually high rates of Staphylococcal musculoskeletal infection have prompted further investigation [9].

To date, data is lacking on detailing the presentation and management of septic arthritis in the New Zealand setting. Our aim therefore is to characterize the presentation, diagnosis and management of acute septic arthritis in children presenting to our institution over a ten year period.

# Materials and methods

We reviewed all cases of septic arthritis presenting to our institution between 2008 and 2018 in children from newborn to age 15 years. The database was created via clinical coding with approval for analysis from the hospital Clinical Audit Support Unit.

Review of electronic clinical records was conducted on a total of 120 cases. We defined septic arthritis (SA) based on intra-operative culture results, culture results from aspirate or positive radiographic investigation in the setting of positive blood culture. We excluded cases of post-viral or reactive arthritis (n = 15), septic arthritis as a result of post-operative infection (n = 1) or patients with insufficient clinical data for analysis (n = 1) leaving a total of 103 patients.

Data was collected including patient demographics (age, gender, ethnicity), presenting complaint, time to presentation (grouped as < 24 hours, 24–72 h, 72 h–2 weeks, or > 2 weeks), and use of local primary care facilities (timeframe used previously [10]). The hospital catchment, although covering a relatively small catchment of 400,000 patients, traverses more than 21,000 km<sup>2</sup>. The demographics of this area are consistent with New Zealand as a whole, with the notable exception of ethnicity. The area serviced by the hospital has a higher proportion of Maori patients than the overall percentage for New Zealand (22% vs. 16%). Calculations for incidence included the broadest catchment area for paediatrics serviced by the hospital. Patient addresses were derived from electronic record at the time of admission and used to calculate distance travelled (kilometres; km) to reach the Emergency Department. The New Zealand deprivation index (NZDep 2013) separates geographical regions into 'meshblocks', which are used as a marker of socioeconomic status based on 2013 census data [11]. NZDep2013 provides a ten category ordinal scale from 1 (assigned to the 10% of NZDep2013 small areas with the least deprived NZDep2013 scores) to 10 (assigned to the 10% of NZDep2013 small areas with the most deprived NZDep2013 scores). Each patient address was scored using NZDep2013, and the score has been used in this analysis as a representation of socioeconomic status, and has been used in previous research for this purpose [2, 8].

Laboratory results at the time of presentation were collected including C-reactive protein (CRP mg/L), white cell count (-10<sup>9</sup>cells/L), haemoglobin (Hb g/dl) and albumin (Alb, mg/ L). Microbiological samples from either joint aspirate, blood culture or intra-operative specimen. Standard agar plate culture was used for synovial fluid aspirate, positive result defined by positive gram stain, cell count >  $50,000 \text{ mm}^3$ , or growth of pathogen on culture. No samples underwent 16sPCR during the period under review. Synovial fluid culture with BD Batec bottles has not been routinely undertaken at our institution [3]. Organism isolated, antibiotic type, route of therapy and duration were recorded. Decision regarding antimicrobial therapy was made by the treating team; in some cases, advice was sought from infectious disease specialists. Patients were followed up in either orthopaedic or paediatric clinic and complications noted including readmission rates at 30 days and 1 year.

Univariate statistical analysis of results was undertaken via simple *t* test or chi<sup>2</sup> accepting significance if  $p \le 0.05$ . The interaction between time to presentation, antibiotic duration and length of stay was assessed by one-way ANOVA and Fisher LSD.

## Results

The median age was 5.9 years with a range from one month to 15 years (IQR 8, SD 4.25) (Table 1). There was a male majority (64%). Ethnicity breakdown showed a majority were Māori (57%) followed by NZ European (33%). The annual incidence for our entire cohort was 1:7500. This varied greatly by ethnicity: 1:16,000 for NZ European; 1:8760 for Pacifica, and; 1:4300 for Māori (Table 2). The number of presentations rose over the course of the study, with a mean number of 4.5 cases in the first two years and 18 cases in the last 2 years. Patients were usually booked into orthopaedic or paediatric outpatient clinic following discharge; however, a large number failed to attend and were lost to follow-up (14%).

The overall mean distance to the emergency department was 38 km (+/- 42 km, range 2–188 km). Patients who needed to travel more than 20 km to present to hospital were more likely to wait 72 hours - two weeks before seeking medical attention (p = 0.03) (Table 3).

#### Table 1 Descriptive statistics

Demographics	Mean/ Median	IQR	Number	%	Range	SD
Age (range 0.01–15)	5.92	8			0.01–15	4.25
Male sex			66	64.1		
Ethnicity			50	57.2		
Maori NZE			59 34	57.3 33.0		
NZE Pacific			54 6	5.8		
Indian			2	1.9		
Asian			2	1.9		
Presenting complaint						
Fever			10	9.7		
Joint specific pain			73	70.9		
Swelling			7	6.8		
Unable to weight bear			8	7.8		
Irritability			3	2.9		
Other			2	1.9		
Febrile on arrival			71	68.9		
Time to presentation < 24 h			16	15.5		
< 72 h			39	15.5 37.9		
< 72 m <2 weeks			39	35.9		
> 2 weeks			11	10.7		
Sought primary care			34	33.0		
Joint of interest			5.	2210		
Knee			30	29.1		
Hip			32	31.1		
SI joint			10	9.7		
Ankle			13	12.6		
Wrist			4	3.9		
MCP			2	1.9		
Elbow			3 4	2.9 3.9		
Shoulder Primary osteomyelitis/other	secondary joint		4 5	3.9 4.9		
Diagnosis made	secondary joint		5	ч.)		
Clinically			36	35.0		
Surgically			21	20.4		
Radiographically			46	44.7		
MRI			53	51.0		
Laboratory results						
Haemoglobin	117.4	17			15.2	2.93
WCC	12.79	6.25			5.42	1.05
CRP	90.39	97.5			79	1.06
Albumin Positive blood culture	19.9	35	32	31.1	17.0	
S. aureus			42	61.8		
MRSA			1	1.5		
Group B Strep			2	2.9		
Kingella			4	5.9		
S. pneumoniae			2	2.9		
Propionibacterium			1	1.5		
Coagulase negative			3	4.4		
staphylococcus						
Enterococcus			1	1.5		
Nisseria meningiditis			1	1.5		
Streptococcus bovis			1	1.5		
Resistance			10	14.7		
Treatment			(0)	(7		
Surgical			69	67		
Antibiotics targeted Antibiotics broad			14 20	13.59 19.42		
Successful primary			20 86	83.49		
Converted to surgery			17	16.50		
Repeat procedures			28	27.18		
			3	2.91		
Recurrence						

The primary presenting complaint was joint-specific pain and difficulty weight-bearing (70%). Most were febrile on arrival (69%). Time to presentation was most frequently Table 2 Incidence of disease by ethnicity

Ethnicity	Number in cohort	Population	Incidence
NZE	34	54039	1:16000
Maori	59	25,374	1:4300
Pacific	6	5,256	1:8760
Total	103	77586.00	1:7500

between 24 and 72 hours (38%) or between 72 hours and two weeks following symptom onset (35%) (Table 1). Approximately one-third of patients sought medical attention from a primary care facility before coming into hospital. Up to 17% were discharged from the ED with an alternative diagnosis before re-presenting for evaluation and admission. Patients in our cohort who waited > two weeks to present to a tertiary centre had a statistically longer hospital stay and longer duration of antibiotics (Graph 1).

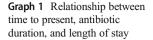
The mean white cell count in our cohort was  $12.8 \times 10^9$ /L (SD 5.4, IQR 6.25) with average CRP of 90 mg/L (std 78.9, IQR 97.5) (Table 1). Positive blood cultures were identified in 31%. An organism could be detected in 66% of patients from either blood culture, aspirate or intra-operative sample. The most common pathogen isolated was *S. aureus* (61%), followed by *Streptococcus pyogenes* (13%). *K. kingae* was seen in 5.9%. Methicillin-resistant *Staphylococcus aureus* (MRSA) was only seen in one. Antibiotic resistance was detected in ten, of which six cases were *S. aureus*.

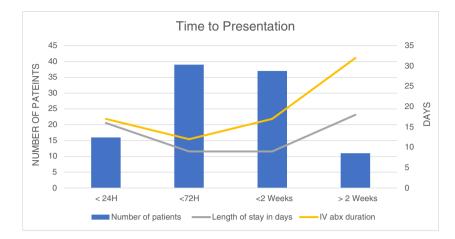
The majority of children in our study reside in the most deprived three deciles (deciles 8–10, 55%). Analysis of ethnic subgroups revealed that children of Māori ethnicity were still more likely to live in deprived areas (Table 4). Median NZdep score was 9 for Māori compared with mean score of 7 for NZ European (Mann-Whitney p = 0.0004). There was no other significant difference including no variation in time to presentation, dominant pathogen or length of stay (Table 4).

MRI use as a percentage of total cases increased over the course of the study, with an average of 10.5 scans used annually in the last two years of the study (2016–2018) and only 1.5 scans per year in the first two years (2008–2009) (Graph 2). Use of MRI scanning was associated with greater length of

 Table 3
 Relationship between distance from emergency department in kilometres and time taken to present, univariate statistical analysis

Patient distance from tertiary centre vs. time taken to present							
Time to present	$<20 \mathrm{~km}~(n=48)$	> 20  km (n = 55)	$\text{Chi}^2 (p = < 0.05)$				
24 h	8	7	0.57				
72 h	24	16	0.02				
< 2 weeks	12	25	0.03				
> 2 weeks	4	7	0.47				





ANOVA – Assessment of Relationship between time to present and length of stay (LOS)

Source of Variation	<i>d.f.</i>	SS	MS	F	p-value
Between Groups	3	1,285.09973	428.36658	2.78692	0.04466
Within Groups	99	15,216.88085	153.70587		
Total	102	16,501.98058			

ANOVA - Assessment of relationship between time to present and IV antibiotic

Source of Variation	<i>d.f.</i>	SS	MS	$\overline{F}$	p-value
Between Groups	3	3,855.82076	1,285.27359	3.68847	0.01473
Within Groups	92	32,058.01257	348.45666		
Total	95	35,913.83333			

antibiotic treatment (p = 0.0000005), greater average length of stay (15 days vs. 8 days, p = 0.003) and increased rate of surgical intervention (p = 0.01).

Adjacent musculoskeletal infection was identified in 47% of MRI scans, usually showing osteomyelitis (39%) or subperiosteal abscess (9%). An adjacent musculoskeletal infection on MRI dictated a statistically significant increase in mean length of antibiotic treatment (34 days vs. 48 days, p = 0.006); these patients also had higher mean CRP compared with those with isolated SA (122 mg/L vs 77 mg/L, p = 0.04).

The hip was the most commonly affected joint (31%) followed by the knee (29%). There were ten cases of SA involving the sacroiliac joint. Rarer areas of infection included metacarpal joint (2%) and elbow (3%).

Surgical intervention was the initial method of treatment (66%) in our cohort, usually via open or arthroscopic washout of the affected joint. Those who did not undergo surgery had either broad-spectrum antibiotics (19%) or targeted antibiotics (14%) where culture results were available. Once started on antibiotics with the intention of treating conservatively, 17% of patients converted to a surgical procedure due to worsening clinical picture, failure of laboratory markers to respond or interval radiographic result. Overall, this increased the rate of

surgical intervention to 83%. Twenty-eight patients required multiple washouts before infection control was achieved.

The primary antibiotic of choice was flucloxacillin (63%) followed by co-amoxiclav (11%). Mean duration of IV antibiotics was 15.7 days (+/- 19, range 3–70) with mean oral duration of 17 days (=/- 13.4, range 0–56). The average length of combined intravenous and oral antibiotic duration for patients with isolated SA was 34.2 days (+/-14.4) which exceeds the national guideline of 21 days [12].

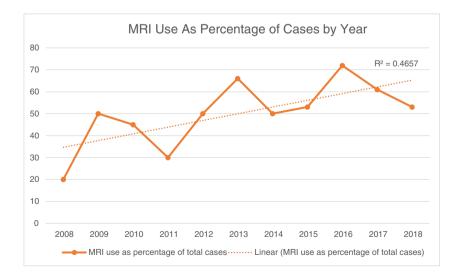
When assessing deprivation as a potential risk for worse clinical picture we used length of stay, days of IV antibiotics and need for repeat procedures to as surrogate markers of more severe disease (Table 5). Recurrent SA could not be used as because the rate was too low (only 3 patients had recurrent joint infection). Splitting the cohort into deciles one to four, five to seven, and eight to ten, we did not identify worse disease in those with greater socioeconomic hardship (Table 5).

Following discharge from hospital, 15 patients were readmitted within 30 days. The reason for readmission was related to their primary diagnosis of SA in only eight cases, of which four were due to issues with peripherally inserted central catheter (PICC) lines, three with ongoing pain, one child with fever, and one with a recurrence of infection.

# Table 4Subgroup analysis by ethnicity

Time to presentation	Maori ( $n = 59$ )	%	SD.	NZ European ( $n = 34$ )	%	SD	TTEST/Chi <sup>2</sup> / Mann-Whitney ( $p = <0.05$ )
< 24 h	9.00	15.25		5.00	14.71		0.89
< 72 h	24.00	40.68		11.00	32.35		0.94
< 2 weeks	20.00	33.90		15.00	44.12		0.64
> 2 weeks	6.00	10.17		3.00	8.82		0.83
Sought primary care	19.00	32.20		13.00	38.24		0.55
Mean distance from ED (km)	40.60	/	39.40	38.80	/	45.10	0.42
Median NZ Deprivation index	9.00	/	2.30	7.00	/	2.80	0.00048*
Positive blood culture	21.00	42.00		10.00	29.41		0.91
Mean age	5.90	/	4.17	5.77	/	4.40	0.88
Mean CRP	90.40	/	76.92	84.00	/	12.40	0.72
Mean WCC	12.60	/	5.05	13.30	/	6.11	0.60
MRI done	30.00	50.85		18.00	52.94		0.85
Primary treatment plan = surgery	39.00	66.10		23.00	67.65		0.87
Conversion to surgery	8.00	13.56		5.00	14.71		0.88
S. aureus	26.00	63.41		12.00	60.00		0.41
MRSA	1.00	2.44		/			/
S. pneumoniae		0.00		1.00	5.00		/
Organism identified	41.00	69.49		20.00	58.82		0.95
Multiple procedures	18.00	30.51		10.00	29.41		0.91
Isolated MRI SA	15.00	50.00		10.00	29.41		0.71
MRI positive for other	15.00	50.00		8.00	23.53		0.71
Mean oral abx	17.50	/	20.72	16.90	/	15.99	0.67
Mean IV abx	18.30	/	12.85	16.90	/	19.57	0.83
Mean total abx	33.70		18.83	34.00		18.60	0.93
LOS	12.30	/	13.41	10.60	/	13.20	0.56
> WNB to OPC*	12.00	20.34		2.00	5.88		0.06
Chronic osteomyelitis	4.00	6.78		1.00	2.94		0.43

\*WNB Was not brought



Graph 2 MRI use by year

Chi<sup>2</sup>/ Decile 1– Decile 5– Decile 8-4 7 10 ANOVA (p = < 0.05)19 Number 28 56 0.00001\* IV abx duration 18.16 14.94 15.67 0.83 LOS 11.26 12.15 11.71 0.84 Multiple 5 5 18 0.33 procedures S. aureus 9 22 0.82 12 % isolates 0.6 0.67 0.61

 Table 5
 NZ deprivation index stratification—markers of disease severity

The overall recurrence rate of primary joint infection was 2.9% after treatment. Five children developed chronic osteomyelitis; five also experienced growth disturbance secondary to their infection. There was one case of chronic pain subsequently referred to the regional pain service for further management.

## Discussion

We have found an increased incidence of SA compared with other OECD countries, irrespective of ethnicity. An earlier report focusing on paediatric acute haematogenous osteomyelitis in New Zealand found similar results; the rates of Staphylococcal infection in New Zealand for both children and adults are among the highest in the world [1]. Prevalence of Staphylococcal skin and soft tissue infection is up to 1:1000 [9]. Separating our population by ethnicity highlights the disparity between rates of SA in Māori patients (1:4300) compared with NZ European (1:16,000). Although some effort has been made to attribute variation by ethnicity solely to socioeconomic status and overcrowding, research in 2004 did not demonstrate increased risk of skin infection in young Polynesian children by decile [13].

Our findings raise concern as the incidence seen in Māori is similar to that seen in the developing world; in Malawi, where Salmonella is frequently identified as a causative organism, an incidence of up to 1:5000 has been reported [2]. A broader approach is required to address reasons for the inequitable burden of *S. aureus* disease [14]. Although Māori children within the cohort tended to reside in more deprived areas this is also a reflection of population trends [15]. In 2013, 23.5% of Māori lived in decile 10 areas (compared with 6.8% of non-Māori), while only 3.8% lived in decile 1 areas (compared with 11.6% of non-Māori) [11].

Late presentation is sometime cited as a reason for worse health outcomes; however, the data from our research confirms that Māori families did not present significantly later to hospital or seek less primary care. Previously, cultural factors in particular household overcrowding has been used as an explanation for higher rates of *S. aureus* carriage in both Māori and Pacific patients [16]. High rates of *S. aureus* colonization in New Zealand increase the likelihood of community-onset skin and soft-tissue infection [8]. However, regression analysis showed that ethnicity and socioeconomic status remain independent predictors of SSTI despite skin colonisation when examining the 'growing up in New Zealand' cohort [16].

Socioeconomic determinants of health do have a clear association with invasive community-onset *S. aureus*. We have been unable to suggest that those children experienced a stormier clinical course when addressing length of stay, duration of IV antibiotics and the need for repeat procedures. The association between distance travelled to the emergency department and length of stay/IV antibiotic duration demonstrates a key aspect of practical access to health. Our region, although covering a relatively small catchment of 400,000 patients, traverses more than 21,000 km<sup>2</sup>.

The presence of adjacent infection on MRI was more common in patients waiting > two weeks to present to hospital. The assessment and treatment of paediatric septic arthritis have evolved over the last few decades with advances in imaging modality and exploration into the optimal duration of antibiotics [6, 10, 17]. Given the closely aligned clinical pictures of septic arthritis and osteomyelitis, recent evidence supports increasing the use of MRI in diagnosis of SA [18]. Adjacent infection occurs more frequently than expected and understandably alters the mode and length of treatment [19]. Considering the range of distances families may be required to travel, some more than 150 km; care must be taken in prompt diagnosis and treatment. We would recommend raised index of suspicion for adjacent infection in patients who present to hospital in a delayed fashion.

The microbiology of S. *aureus* infection may have a role to play in ethnic variation of disease. Unlike the USA, New Zealand experiences invasive paediatric musculoskeletal disease in association with MSSA rather than MRSA [8]. Only one patient in our cohort had a positive finding of MRSA.

The inequitable burden of *S. aureus* infection seen in Māori patients of all ages has been well documented in the literature [20]. Maori are more likely to experience *S. aureus* bacteraemia, they have double the national point-prevalence of *S. aureus* infection, and are twice as likely to have a paediatric hospital admission for *S. aureus* skin and soft tissue infection (SSTI) [20, 21]. When typing a large cohort of *S. aureus* strains for virulence factors

work by Williamson et al. showed an extremely high prevalence of MSSA Panton-Valentin leucocidin toxin (lukSF-PV genes) which varied by ethnicity [22]. Systematic review of the role of *lukSF-PV* in musculoskeletal infection revealed an increased requirement for surgical intervention and possible increased morbidity in those exhibiting the gene [23]. Unfortunately, our laboratory does not provide typing of S. aureus virulence factors making it difficult to establish the precise role played by *lukSF-PV* in our cohort. However, it is clear that within New Zealand, there is suspicion that virulence factors may vary by ethnicity, and this can in turn cause worsened clinical picture. For instance, the incidence of *lukSF-PV* is higher in young children with community-onset SSTI as confirmed by typing done for > 400 cases in the Auckland region before 2010. In the SSTI population, presence of the lukSF-PV gene increased with non-European ethnicity (statistically significant for Pacific peoples) and mandated a 7.4× higher rate of surgical intervention. It is suspected that *lukSF-PV* may also play a role in the increased incidence of pelvic pyomyositis in children in non-tropical countries [24]. A recently published review of paediatric cases suggests a low threshold for MRI in these children due to low specificity of clinical examination and laboratory factors in distinguishing from isolated septic arthritis [24].

Limitations of our study include a relatively small sample size and retrospective nature of review. Reviewing a longer timeframe may have increased study numbers; however, we selected dates to ensure availability of electronic clinical and radiographic records. We are also limited by the use of traditional laboratory technique; having molecular pathogen analysis via methods such as 16SPCR will likely improve organism detection as demonstrated in other international studies [25]. As a surrogate measure of socioeconomic standing, the NZ deprivation index is broadly utilized; however, it must be recognized that significant variation exists within meshblocks. Not all patients living in deprived areas will be representative of the worst conditions within each suburb.

In summary, we have provided an analysis of trends in presentation, microbiology, and management of septic arthritis in our institution over a 10-year period reflecting a worrying variation in disease burden associated with ethnicity. Explanations of this variation must take into account socioeconomic, pathogen-related and environmental factors. The incidence of septic arthritis in New Zealand's indigenous paediatric population mandates additional resources.

## **Compliance with ethical standards**

**Conflict of interest** The authors declare that they have no conflict of interest.

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