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## Background

- Pediatric acute hematogenous osteoarticular infections (AOI), including hematogenous osteomyelitis (OM) and/or hematogenous septic arthritis (SA), are a frequent cause of hospitalization and morbidity.
- In well-resourced countries, OM estimates range from 1.2 - 13 per 100,000 children per year; SA estimates range from 40 – 80 per 100,000 children per year.
- Between 15 – 50% of AOI involve both bone and joint; and over 80% of AOI occur in lower extremities
- Staphylococcus aureus* is the most common etiology; with *Kingella kingae* common in < 5 years.
- In OM, positivity rate of blood cultures is estimated at ~ 33%, addition of bone/tissue culture increases identification of pathogen to ~ 55%.
- Standard cultures of bone/tissue identify an etiology in ~ 65% cases; and joint fluid in ~ 42%.
- Surgical intervention is indicated for source control (abscess drainage), preservation of maximal function and if feasible, microbiologic diagnosis.
- Patients who respond to initial intravenous therapy (IV) can transition to appropriate oral antibiotic.

## Objective

- We aim to describe the epidemiology, presentation, microbiology and management of children admitted and diagnosed with acute hematogenous osteoarticular infections at University of Missouri (MU), a Midwest academic center in central Missouri (MO).

## Methods



- Study site:** MU Children's Hospital is a 100+ bed inpatient pediatric facility within MU Health Care, that has a 25-county service area in MO.
- Study design:** Retrospective observational study
- Study period:** July 2015 to March 2021 (5.75 years)
- Inclusion:** Pediatric patients (age: 1 month to <18 years) hospitalized and diagnosed with AOI (both OM and SA) based on ICD-10 codes.

- Exclusion:** neonatal intensive care patients, infections related to penetrating trauma and orthopedic surgery, subsequent diagnosis of chronic recurrent multifocal osteomyelitis.
- Systematic review of electronic medical records (EMR)** was performed to collect data on demographics, site of infections, microbiology and management.
- REDCap** electronic data capture tools hosted at MU were used to manage study data.
- Analyses:** Descriptive statistics were used to analyze patient characteristics including median, and interquartile range (IQR) for continuous variables; frequency and percentages for categorical variables. Categorical variables were compared using Fisher exact test (antibiotic pretreatment and culture results) and quantitative variables with the Mann-Whitney U test (seasonal trend).

Characteristics of patients with acute hematogenous osteoarticular infections	1 mo to 18 yr n=73 (%)	Cases <1 yr n=5 (7%)	Cases 1 to < 5 yr n=21 (29%)	Cases 5 to 18 yr n=47 (64%)
Age in yr	6.9 (2.8 – 11.9)	0.5 (0.1 – 0.6)	2.2 (1.4 – 3.6)	10.5 (7 – 12.9)
Gender – Male	46 (63)	3	14	29
Presenting symptoms				
Localized pain	72/73 (99)			
Refusal to move or bear weight	64/73 (88)			
Fever	49/73 (63)			
All 3 symptoms	42/73 (56)			
Peak inflammatory markers at initial diagnosis				
CRP (mg/dL)	7.6 (2.5 – 15.5)			
ESR (mm/hr)	63 (40 – 81)			
Last CRP prior to oral transition	2.1 (0.6 – 5.1)			
Osteoarticular infection type				
Osteomyelitis (OM)	32/73 (44)	4	8	20
Septic arthritis (SA)	17/73 (23)	1	8	8
Both OM & SA	24/73 (33)	0	5	19
Site of OM (with or without concurrent SA)				
Femur	10	0	5	5
Tibia	10	1	0	9
Pelvis	9	0	1	8
Calcaneum	6	0	2	4
Fibula	4	0	3	1
Multifocal (Lower extremity – LL, upper extremity – UL)	6	1(LL)	0	4 (LL), 1(UL+LL)
Other	11	Radius 1, rib 1	Rib 1, metatarsus 1,	Humerus 2, 1 each (fibula, lumbar vertebra, midfoot, clavicle)
Site for SA (without concurrent OM)				
Hip	8	0	3	5
Knee	4	0	3	1
Ankle	3	1		2
Other	2	0	Midfoot 1, elbow 1	0

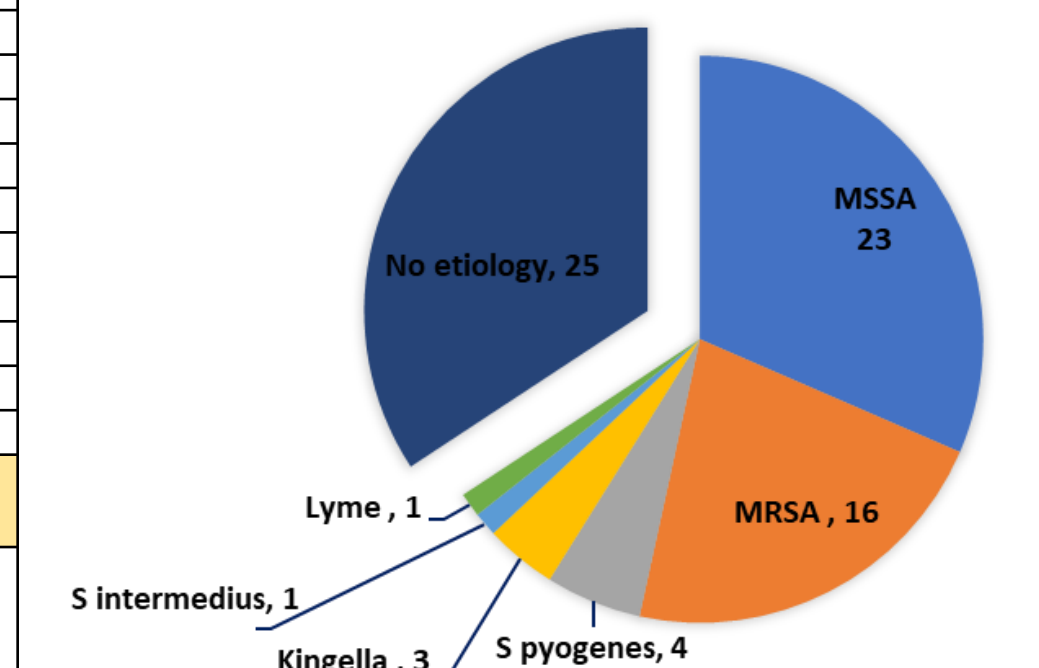
\* Continuous variables expressed as median (IQR), CRP – C-reactive protein, ESR – erythrocyte sedimentation rate, Bcx – blood culture, cx – culture, MSSA – methicillin susceptible *Staphylococcus aureus*, MRSA – methicillin resistant *Staphylococcus aureus*

## Results

Characteristics of patients with acute hematogenous osteoarticular infections	1 mo to 18 yr n=73 (%)	Cases <1 yr n=5 (7%)	Cases 1 to < 5 yr n=21 (29%)	Cases 5 yr to 18 yr n=47 (64%)
Definitive etiology identified	48* (64#)	1/48(2)	13/48 (27)	33/48 (68)
MSSA	23/73 (32)	1	4	18
Positive Bcx only			2	6
Positive tissue/synovial cx		1		5
Positive Bcx & tissue/synovial cx			2	7
MRSA	16/73 (22)	0	3	13
Positive Bcx only			0	5
Positive tissue/synovial cx			3	3
Positive Bcx & tissue/synovial cx				5
Streptococcus pyogenes	4/73 (5#)		2 (blood)	2 (synovial)
Kingella kingae	3/73 (4#)		3 (by PCR)	
Other	2/73 (3)		Lyme (1)	Streptococcus intermedius (1)
No etiology identified	25/73 (34)	4/25 (16)	8/25 (32)	13/25 (52)
		[16S PCR – 1/1 neg, No Bcx – 1]	[Kingella PCR – neg 3, not sent 5; No Bcx – 3]	[Kingella PCR – 1/1 neg, 16S PCR – 1/1 neg]
Surgical intervention				
In operating room	44/73 (60)	3	16	25
Non-operative intervention only (aspiration/biopsy only)	13/73 (18)	1	2	10
Median hospitalization, Median Intensive care stay	5 (4-8)			
Empiric intravenous antibiotic at admission	5/73 (7)			
Cefazolin monotherapy	22/73 (30)			
Clindamycin monotherapy	23/73 (32)			
Other monotherapy or combination antibiotics	28/73 (38)			
Transition from IV to oral antibiotics	62/73 (85)			
Definitive oral antibiotics	Cephalexin – 35 Clindamycin – 24 Amoxicillin – 3			
Peripherally inserted central catheter	14/73 (19)	Complications 4 – clotted, insertion site rash, dislodged, rash + dislodged		
IV antibiotics at discharge	10* (13%)	Plus 1 infant (0.1 yr) completed full IV treatment as inpatient		

# Revised (Erratum in abstract)

## Etiology of 73 AOI cases



Antibiotics prior to surgical intervention	Positive tissue/synovial culture	Negative tissue/synovial culture
Pretreatment	14	3
No antibiotics	7	10

- Pretreatment with antibiotics did not decrease yield of culture positivity from surgical intervention [Fisher's exact test (p = 0.034)]

## Discussion

- 73 patients** meeting study criteria were identified during the study period.
- For some analyses, cohorts were divided in 3 subgroups by age for analysis due to unique anatomy of blood supply of bone in infants and *Kingella* being a known common etiology in 1-5yr and does not grow well in culture.
- Table 1** lists patient characteristics.
- No risk factors** for osteomyelitis were identified (sickle cell disease, immunosuppression, diabetes mellitus or sensory neuropathy, immunodeficiency, prior hematologic or rheumatologic diagnoses)
- There was no seasonal variation in incidence of cases although a peak in July.
- Magnetic resonance imaging (MRI)** was most common imaging for diagnosing AOI - 88% (64/73) and radionuclide bone scan was performed in one patient with multifocal OM.

- Localized pain and refusal to move or bear weight were most common symptoms**, followed by fever. Only 56% had all three symptoms.
- 44% had OM, 23% had SA and 33% had both OM and SA.
- Blood culture identified an etiology in 29 of the 69 obtained, (42%;17# MSSA, 10# MRSA, 2 S pyogenes)**
- Surgical management in an operating room was performed in 44 (60%).**
- Median hospitalization was for 5 days (IQR 4-8), and 5 cases (7%) required intensive care, with no mortality.
- In 38%, cefazolin or clindamycin were not first line empiric monotherapy.
- Clindamycin resistance was only detected in 2 cases (1 MSSA, 1 S pyogenes) and Trimethoprim-sulfamethoxazole resistance in 2 cases (1 MSSA, 1 MRSA)**
- 62 (85%) successfully transitioned from intravenous (IV) antibiotics to oral at discharge** – 10 were discharged with IV antibiotics.
- 8 (11%) required hospital readmission for various reasons.

# Revised (Erratum in abstract)

Component	Status	Order Com...	Dose ...	Details
PED Osteomyelitis and Septic Arthritis SP (Planned Pending)				
Communication				
Click HERE for IDSA Guideline on Diagnosis and Management of Acute Hematogenous Osteomyelitis in Pediatrics				
Activity				
Weight Bearing				
Medications				
IMPORTANT: Please assess your patient for MRSA risk factors - patient/family history of recurrent skin abscesses OR previous MRSA infection				
Antimicrobials				
For well appearing patients WITHOUT MRSA risk factors OR for children < 3 years of age with concern for Kingella infection				
cefAZolin				Select an order sentence
For well appearing patients WITH MRSA risk factors OR cefAZolin allergy				
clindamycin (clindamycin IV)				Select an order sentence
For patients who meet pediatric severe sepsis criteria (Also please consult Infectious Disease)				
Pharmacist Vancomycin Dosing Protocol (VANCOMY...)		Vancomycin...	1 Each, form: Consult, Message, As Indicated...	
cefTRIAxone				Select an order sentence

EMR Order Set template: (partial)

## Conclusions

- Our trends in AOI presentation and microbiology are comparable to literature.
- Blood cultures remain key in identifying etiology** and empiric therapy should target *S aureus*.
- Pretreatment with antibiotics does not decrease culture positivity at surgical intervention.**
- We had **high success with transition to oral antibiotics.**
- We have since implemented an EMR order set that includes antimicrobial guidance to standardize empiric antibiotics.

## References

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