Prognostic Factors Associated with Acute Hematogenous Osteomyelitis Complications in Children

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ABSTRACT

Background
The clinical presentation and management of acute hematogenous osteomyelitis (AHO) in children can vary significantly. Scores to predict acute complications utilize prolonged fever after antibiotics, bone abscess, suppurative arthritis, disseminated infection and delayed source control. By contrast, elevated CRP after 48-96 hours of therapy, disseminated disease and bone debridement are predictive of chronic complications. Such scoring systems have undergone limited validation. We examined factors associated with acute and chronic AHO complications at our center to identify other variables that may enhance published scores.
Methods
A retrospective chart review was conducted of all children 6 mo-18 years with AHO and with acute symptoms of ≤ 14 days at Texas Children's Hospital from January 2012 through December 2020. An acute complicated course was defined as treatment failure within 6 weeks of starting antibiotics, ≥ 2 bone debridements, prolonged admission (>14 days) and acute avascular necrosis. Chronic complications included growth arrest or limb leg discrepancy, pathologic fracture, avascular necrosis, chronic osteomyelitis or frozen joint. Statistical analysis was completed using STATA 17.
Results
418 patients met the inclusion criteria. 106 (25.4%) had an acute complicated course. 51 (13.5%) of 377 followed had a chronic complication. Clinical factors associated with acute and chronic complications were very similar. Factors associated with either an acute complicated course or chronic orthopedic complications included: older age, tibia involvement, infection due to *S. aureus*/MRSA, presence of multifocal or disseminated infection, DVT, fever for more than 48 hours after starting antibiotic therapy, admission laboratory values including higher absolute neutrophil count (ANC) and higher CRP, ICU admission, associated suppurative arthritis, bacteremia, bone abscess, surgical debridement and delayed source control.
Conclusion
In children with AHO, risk factors for acute and chronic complications are highly similar. Older age, tibia involvement, MRSA, higher ANC and bacteremia were linked to complications in our population and could be included in clinical scoring systems and may help guide management.

INTRODUCTION

- Acute hematogenous osteomyelitis (AHO) in children has the potential to develop into significant acute and chronic complications.
- Little is known about risk factors that may influence development of complications and optimal follow up time for these patients.
- Scores have been developed to assess the likelihood of complications based on clinical, laboratory and imaging criteria.

AIMS

1. Identify factors associated with complications in AHO.
2. Assess the performance of the Acute (A) and Chronic (C) scores published by Alhinai *et al.* (*Clin Infect Dis*. 2020; 71: e454-64) in Houston area children.
3. Evaluate if additional variables may improve the performance characteristics of the Alhinai *et al.* scores.

PATIENTS AND METHODS

- Patients were selected from a review of admissions to Texas Children's Hospital (TCH) with ICD9/10 codes for AHO from 2012-2020 in children 6 months to 18 years of age, with symptoms for ≤14 days prior to admission.
- Medical records were reviewed for clinical and laboratory parameters during admission and follow up.
- Definitions
  - Acute complicated course: Presence of treatment failure within 6 weeks of starting antibiotics requiring treatment change, undergoing ≥ 2 bone debridements, prolonged admission of >14 days and/or acute avascular necrosis.
  - Chronic complication: Development of growth arrest, pathologic fracture, avascular necrosis, frozen joint, joint deformity and/or chronic infection.
- Fisher's exact and Wilcoxon Rank Sum tests were performed to analyze different variables. A multivariable logistic regression model was used to examine predictors of complications.

RESULTS

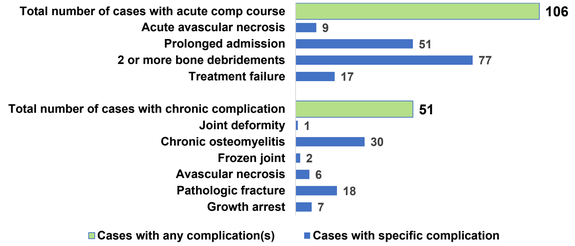
- 418 cases of AHO were included. The demographics and characteristics of the population are provided in **Table 1**.
- 106/418 (25.4%) had an acute complicated course and 51/377 (13.5%) patients followed had a chronic complication.
- The number of cases with each complication is shown in **Figure 1.**

Table 1. General Characteristics of Patients

Characteristic	All patients, N=418
Age, years	7.36 (3.5-11.2)*
Female	159 (38)
Race/ Ethnicity	
White non-Hispanic	165 (39)
Hispanic	136 (33)
African American	71 (17)
Asian	26 (6)
Other	20 (5)
No Comorbidities	322 (77)
Days of Symptoms at Presentation, median	5 (3.5-6.5)
ICU Admission	41 (10.5)
Multifocal-Noncontiguous Infection	24 (5.7)
Disseminated Infection	60 (14.4)
Concomitant Septic Joint	128 (30.6)
Most Common Sites of Infection**	
Tibia	103 (24.6)
Pelvis	103 (24.6)
Femur	97 (23.2)
Fibula	32 (7.7)
Humerus	27 (6.5)
Radius/ Ulna	22 (5.3)
Other bones (feet, hands, clavicle, ribs)	72 (17.2)

*All continuous variables expressed as medians with interquartile ranges (IQR), categorical variables as n (%).
** Patients may have presented with >1 site of infection.

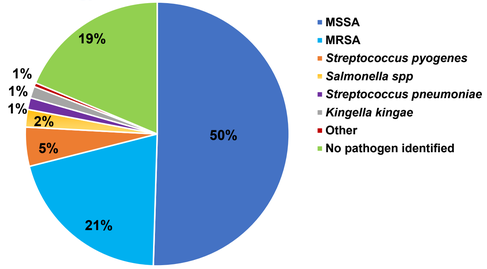
Figure 1. Cases per Acute Complicated Course and Chronic Complication



RESULTS

- The relative frequency of organisms is shown in **Figure 2.**
- The performance of A-score and C-score at TCH is shown in **Table 2**.
- C-score was not calculated for 24 patients lacking follow-up CRP and 41 patients lost to follow-up.
- Tibia involvement, multifocal infection, deep venous thrombosis, ICU admission, bacteremia, identification of causative organism, *S. aureus* infection, MRSA and elevated CRP on admission were each associated with both acute complicated course and chronic complication in our population with p <0.01. (**Figures 3 and 4).**
- We attempted to identify variables to improve on the published scores using a multiple regression backward elimination model. The incorporation of *S. aureus,* MRSA infection, need for ICU care and higher ESR, ANC and CRP on admission did not improve the AUC sufficiently to justify a modification of the published A and C scores.

Figure 2. Etiology of AHO, 2012-2020



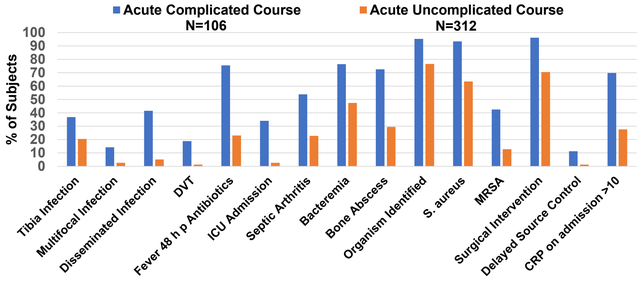
MSSA: methicillin-susceptible *S. aureus;* MRSA: methicillin-resistant *S. aureus*

Table 2. Calculation and performance of the A-score and C-score by Alhinai *et al.* vs TCH patients

Calculation A-score (points)	Performance A-score	Alhinai *et al.* (N= 225)	TCH (N= 418)
✓ Bone abscess (2) ✓ Fever after >48h of antibiotic therapy (2) ✓ Suppurative arthritis (3) ✓ Disseminated disease (4) ✓ Delayed source control (4) Cut-off: >3 points Maximum score: 15 points	Sensitivity	74	81
	Specificity	78	78
	PPV	52	55
	NPV	91	92
	AUC	0.82	0.87
Calculation C-score (points)	**Performance C-score**	**Alhinai *et al.* (N= 220)**	**TCH (N= 353)**
✓ CRP ≥10 mg/dL 2-4 days (+/- 12hr) after starting antibiotics (1) ✓ Disseminated disease (1) ✓ Bone debridement (2) Cut-off: >2 points Maximum score: 4 points	Sensitivity	63	64
	Specificity	89	86
	PPV	42	42
	NPV	95	94
	AUC	0.83	0.71

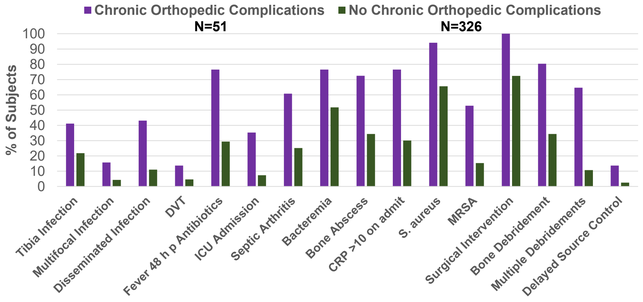
RESULTS

Figure 3. Clinical Variables Associated with an Acute Complicated Course



*All presented variables had a P < 0.01

Figure 4. Clinical Variables Associated with a Chronic Orthopedic Complication



*All depicted comparisons with P < 0.01

CONCLUSIONS

- Factors linked to AHO complications in children used by Alhinai *et al.* in predictive A and C scores like disseminated infection, presence of bone abscess, prolonged fever after starting antibiotics, concomitant septic arthritis and delayed source control were also associated with complications for a larger and different demographic population, with overall similar predictive performance.
- Tibia involvement, bacteremia, *S. aureus,* MRSA infection, higher CRP on admission and need for ICU care were each associated to both acute complicated course and chronic complications.
- Inclusion of additional parameters did not provide better predictive scores for our patients but could be considered to be used in the future for further studies.