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Title: Prevalence of complications identified on follow-up of children with sickle cell disease and fever after discharge from the Emergency Department.

A. STUDY PURPOSE AND RATIONALE

Background:

Patients with sickle cell disease (SCD) are at increased risk for complications such as serious bacterial infection (SBI), acute chest syndrome (ACS), and splenic sequestration. Given this risk, it is recommended that patients present for evaluation upon the development of fever, as this may be the first indicator of such complications. Although the prevalence of bacteremia per febrile event in a patient with SCD is low (2-4%), there can be substantial morbidity and mortality for those patients if left untreated.

Significant practice variation exists between centers regarding the safest disposition for SCD presenting to the Emergency Department (ED) with febrile events in the absence of other overt clinical symptoms. In a review of 3 children's hospitals, each with established comprehensive sickle cell centers, *Eisenbrown et al., 2018* showed that nearly all patients (>90%) receive a CBC, blood culture and antibiotics upon presentation with fever, which is in compliance with established NHLBI guidelines (NHLBI, 2014). These sites vastly differ however in their rates of admission (34-99% admitted depending on age). In our center, patients are typically stratified based on their clinical presentation and those who are deemed to be high risk for complications are admitted for further evaluation and observation, and those with lower risk features are often discharged from the ED after a dose of parenteral antibiotics and recommended to follow up for repeat examination the following day. *Wilimas et al., 1993* showed this strategy of outpatient treatment after initial presentation does not confer any increased risk of sepsis in their randomized clinical trial which randomized patients presenting with fever to inpatient treatment with parenteral antibiotics versus outpatient follow up for a subsequent dose of parenteral antibiotics. In this randomized trial, patients were considered safe for outpatient treatment if all "low risk criteria" (for example age >12mo, Temp <40C, no history of sepsis, WBC <30,000, Platelets >10,000) were satisfied. Additionally, it has been shown that among febrile patients with SCD, 90% of pathogens can be detected via blood culture within 24 hours (REF), thus a second dose of antibiotics at the follow up visit is not standard practice. This led to the development of clinical practice guidelines at many institutions attempting to decrease the hospital admissions among patients with SCD and fever (Ellison et al., 2018).

For such low risk patients, follow up within twenty-four hours for repeat clinical evaluation and a possible second dose of parenteral antibiotics has been standard practice in our center. However, for this subset of patients, there is little evidence to show whether this subsequent

follow up and additional dose of antibiotics confers any additional protection or aids in the identification of other complications. Furthermore, if the risk of complications is low, there may be potentially no need for in-person follow-up or this could be accomplished via telemedicine

Aim:
To determine the prevalence of complications and factors associated with these complications identified on follow-up of children with sickle cell disease and fever after discharge from the Emergency Department.

B. METHODOLOGY

Through retrospective chart review we will identify SCD patients who presented to the CHONY Emergency Department with the chief complaint of fever. Those patients who were deemed to be low risk (as defined above) and discharged from the ED will be included in the study; data from their follow up appointment will be reviewed to evaluate for risk factors newly identified at this subsequent visit. Exclusion criteria may include age <12 mo, no follow up within 24-48 hours. Collected data may include: disposition of follow up visit (discharge vs. admission), presence of any new physical exam findings (*i.e.* new splenomegaly), vital signs, fever duration, height of fever, clinical appearance, follow up laboratory studies, and imaging.

C. ANALYSIS

We will report the prevalence of readmission and subsequent development of adverse complications such as bacteremia, aplastic anemia, and ACS. We will compare the prevalence of risk factors identified at the subsequent follow up appointment to attempt to identify an association with the development of complications mentioned above. Presence of risk factors mentioned above will be compared between those patients requiring readmission versus discharge from the follow up appointment. Among patients who develop adverse outcomes such as SBI, ACS, or aplastic anemia, we will describe the clinical signs and symptoms and characterize at which time point they arose. Power analysis will be conducted. We will assume a p value of <0.05 for statistical significance and 80% power.

D. **STUDY DRUGS:** Not applicable

E. **MEDICAL DEVICES:** Not applicable

F. **STUDY QUESTIONNAIRES**: Not applicable.

G. **STUDY SUBJECTS**: Children with SCD presenting to the ED at CHONY with fever.

H. **RECRUITMENT**: No recruitment necessary as this is a retrospective chart review.

I. **CONFIDENTIALITY OF DATA:** Chart review will be performed on password protected devices. Patient information will be de-identified and each patient will be assigned a unique ID number. Data collected will only be accessible by study personnel.

J. **POTENTIAL CONFLICT OF INTEREST**: No conflict of interest to declare

K. **LOCATION OF STUDY:** MSCHONY Emergency Department

L. **POTENTIAL RISKS:** None identified.

M. **POTENTIAL BENEFITS**: Information collected could provide information regarding necessity of in person follow up after ED visits, potentially allowing for less missed work/school days as an example.

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