Investigation of Chest X-Ray Use in the Emergency Department in Pediatric Patients with Sickle Cell Disease

Urania Dagalakis[1], Henna1 Butt[1], Natalie Davis[1], and Regina Macatangay[2]

[1]University of Maryland Medical Center
[2]University of Maryland School of Medicine

April 05, 2024

Abstract

Determining which patients are at highest risk of acute chest syndrome (ACS) is challenging for pediatric emergency department (PED) providers, resulting in more chest x-rays (CXR), increased radiation exposure, and higher healthcare costs. The objective of this study was to identify significant clinical predictors of ACS to better guide care. In this retrospective review, we included patients diagnosed with sickle cell disease (SCD), aged 2-12 years, who presented to the PED between 2016-2018. We compared patients who were febrile vs. afebrile on presentation, and those diagnosed with ACS vs. those who were not. A total of 424 patients met inclusion criteria, 25% presenting with fever. For febrile patients, 69% received a CXR on presentation vs. 42% of afebrile subjects (p=<0.0001). Overall, 10% of patients were diagnosed with ACS: 13% of febrile presentations vs. 9% of afebrile presentations. Patients diagnosed with ACS were significantly more likely to present with chest pain (p=0.003), tachypnea (p=0.001), hypoxia (p<0.0001), and a history of asthma (p=0.0085). Upon multivariable modeling the only significant predictors were chest pain (OR 3.3, CI 1.5-7.4) and hypoxia (OR 8.4, CI 4-17.9). Current guidelines recommend empiric treatment and a CXR for SCD patients presenting with fever, hypoxia, tachypnea, tachycardia or abnormal respiratory exam. Our data demonstrate that hypoxia and chest pain are significant predictors of ACS. Additionally, data indicated that CXRs were likely performed in excess in febrile patients. Further research is needed, but chest pain and hypoxia may focus the use of CXR on the appropriate patients.

Introduction

In sickle cell disease (SCD), acute chest syndrome (ACS) is a major cause of significant mortality and morbidity. It is responsible for an estimated 25% of sickle cell disease-related deaths, and is associated with prolonged hospitalization, increased risk of respiratory failure, future lung disease and 25% mortality in hospitalized patients[1,2]. ACS has a 40% incidence in the SCD population and is most commonly caused by infection and pulmonary infarction. Pediatric patients with SCD frequently present to the pediatric emergency department (PED) with complaints of fever, chest pain, and cough, all of which may or may not be associated with ACS.

Other studies have been conducted to evaluate the differences between adult and pediatric sickle cell patients in their presentation of ACS. Findings include a lower prominence of extrapulmonary findings in pediatric patients as compared to adult patients. Factors such as low hemoglobin (Hb) and oxygen tension fraction were predictors of ACS in pediatric patients[3]. Madhi et. al., also noted that oxygen saturation (SpO_2) level was significantly lower at admission for children with ACS when compared to adults.[4] Certain co-morbidities, such as asthma, have been shown to increase risk of ACS in pediatric patients.[5] Boyd et al. found that children with both asthma and SCD experienced almost twice as many ACS episodes vs. children with SCD without asthma.[6] Other risk factors for ACS include young age, severe SCD genotypes, low fetal Hb levels, high steady-state Hb levels, high steady-state leukocyte count, history of asthma, and a previous history of ACS[1].

Despite growing research in the field, it remains challenging for PED providers to determine which patients are at highest risk of ACS. In fact, a national hospital ambulatory medical care survey evaluated almost two-hundred thousand yearly emergency department (ED) visits by SCD patients from 1999-2007 and found that 37% of those aged 0-19 years ended up hospitalized[7]. This high frequency of ED visits and hospitalizations increased pediatric SCD patient exposure to nosocomial infections, radiation, and was associated with higher mortality.

Chest x-rays (CXR) are frequently ordered, increasing radiation exposure and healthcare costs. A Dallas Newborn cohort from 1996-2009 found that SCD patients had greater than 25 radiographic tests before age 18, and 5% of these patients had greater than 100 tests.[8]This is concerning since one CXR has an average effective radiation dose of 0.01-0.02 millisievert (mSv), comparable to 10 days of natural radiation exposure[9,10]. While there is currently no set limit on an acceptable radiation dose for pediatric patients, providers should make every effort possible to reduce unnecessary radiation exposure based on the principle of "as low as reasonably achievable" (ALARA).

Therefore, the objectives of this study were: 1) to identify incidence of CXR performance and ACS diagnosis in SCD patients, both with and without fever, presenting to our PED, and 2) to identify significant clinical and demographic predictors of ACS in this population in order to implement a diagnostic algorithm for PED providers with the goal of minimizing unnecessary CXR performance in this population.

Methods

This was an IRB-approved retrospective medical record review of subjects diagnosed with SCD. Individuals were initially identified from International Classification of Diseases, Tenth Revision, Clinical Modification 10 (ICD10) codes for PED visits in SCD patients from 2014 to 2019. Retrospective chart review was performed using PED and inpatient medical record documentation. Inclusion criteria were SCD patients aged 2-12 years who presented to the University of Maryland Medical Center (UMMC) PED between 2016-2018. Exclusion criteria included non-SCD patients, patients less than 2 years of age, or greater than 12 years of age, and patients evaluated at hospitals other than UMMC. Each PED encounter was counted as a separate data point.

We performed bivariate analyses comparing clinical and demographic variables between subjects who were febrile vs. afebrile on presentation to the PED, as well as those who were ultimately diagnosed with ACS compared to those who were not. Analysis of categorical variables was performed using Chi-square or Fischer exact test as appropriate. We performed multivariable logistic regression modelling to identify significant predictors of an ACS diagnosis. Analyses were performed using SAS 9.4 (Cary, NC).

Results

We identified 424 SCD subjects who presented to our PED meeting inclusion and exclusion criteria, with 25% (n=108) presenting with fever. Within the febrile group, 69% (n=74) of subjects received a CXR on presentation compared to 42% (n=133) of afebrile group ($p<0.0001$). Of the febrile subjects, 21% (n=23) had more than 2 febrile episodes of whom 100% received CXRs. Of the subjects who were ultimately hospitalized, 46% (n=50) within the febrile group received at least one inpatient CXR compared to 26% (n=82) of the afebrile group ($p<0.001$). Additional radiation exposure via x-ray imaging and CT scans during their hospitalization occurred in 26% (n=28) of the febrile group compared to 28% (n=90) in the afebrile group.

There were no significant differences between the febrile and afebrile subjects when it came to sex, asthma diagnosis/comorbidity, hydroxyurea use, folic acid supplementation, or pneumococcal prophylaxis (Tables 1 & 2). Overall, 10% of patients presenting to the PED were diagnosed with ACS (n=42), 13% (n=14) of those presenting with fever compared to 9% (n=28) of those presenting without fever. Those subjects diagnosed with ACS were significantly more likely to present with chest pain ($p=0.003$), tachypnea ($p=0.001$), and hypoxia ($p<0.0001$), and were more likely to have a history of asthma ($p=0.0085$). Sickle cell genotype, home medications, and history of splenectomy were not significantly associated with ACS diagnosis.

Upon multivariable modeling, when adjusting for known significant predictors of fever and pre-existing asthma diagnosis, the only significant predictors of ACS diagnosis were chest pain and hypoxia. Patients without chest pain had an odds ratio (OR) =0.3 of ACS diagnosis [95% Confidence Interval, CI 0.14-0.67], indicating they had 70% lower odds of ACS compared to patients with chest pain (Table 3). Patients without hypoxia had OR=0.12 of ACS compared to those with hypoxia [CI 0.06-0.25], indicating 88% reduced odds of ACS diagnosis (Table 3). Conversely, those with chest pain had 3.3-fold increased odds of ACS diagnosis [CI 1.5-7.4] and those with hypoxia had 8.4 times the odds of ACS diagnosis [CI 4-17.9] compared to those without these symptoms.

Discussion

In ACS, guidelines from the British Society of Hematology recommend that patients presenting with fever, hypoxia, tachypnea, tachycardia and abnormal respiratory exam findings should be treated empirically as well as receive a CXR[11]. However, radiological signs can be delayed compared to physical signs; a normal CXR does not preclude the diagnosis of ACS if there is clinical suspicion[11]. Vichinsky's study of 939 patients found that 35% had normal lung exams and 17% presented with lower extremity pain when they presented with ACS[12]. Our data demonstrate that clinical findings such as chest pain, tachypnea and hypoxia were most likely to correlate with a diagnosis of ACS. While 69% of our febrile patients received a CXR in the PED, only 13% were ultimately diagnosed with ACS, indicating that more CXRs and radiation exposure occurred in the febrile population than may have been necessary. When adjusting for fever and asthma, the most salient predictors of ACS were hypoxia and chest pain. When present, these findings were significant predictors of ACS; when absent, patients had significantly decreased odds of ACS.

While CXR remains a key diagnostic tool in the diagnosis of ACS, many studies have suggested that lung ultrasound may provide evidence for diagnosis and evolution of ACS. CXR can be normal in up to approximately 66% of early cases of ACS, including CXRs obtained in patients who were hypoxemic on presentation[13]. Historically, lung ultrasound diagnostic research had been primarily performed in adult patients; however, more recently, lung ultrasound has been evaluated in the pediatric population. Multiple studies in pediatric SCD patients have demonstrated that lung ultrasounds showed a higher number of ACS associated lesions than CXR[13]. In a study by Vetter et al., lung ultrasound was superior to CXR for diagnosing consolidations and pleural effusions in these patients.[13] Future investigations should evaluate whether lung ultrasound is at least equal to, if not superior, to CXR to support the broader use of radiation-sparing bedside alternatives for diagnosing ACS in pediatric patients.

Strengths of our study include a relatively large sample size; the total "n" of 424 was robust enough to allow for significant statistical analysis and supported a meaningful analysis stratifying by risk factors. Our study evaluated SCD in an understudied patient population, with a focus on children aged 2 to 12 years old due to the higher incidence and severity of ACS in this age group. One limitation is that our data may not be generalizable to patients under 2 years or older than 12 years. The retrospective study design can limit results due to risk of bias in documentation, but we evaluated all PED and inpatient notes and laboratory values to increase likelihood of capturing important clinical data. As with any retrospective study, we can only evaluate for associations and not causation, but we performed multivariable modelling, in addition to bivariate analysis, in order to control for confounders and better assess for significant predictors. In addition, we evaluated subjects presenting to the PED in 2016-2018, which is a more modern cohort than many studies on pediatric SCD and ACS diagnosis.

In conclusion, studies have demonstrated that the clinical presentation of ACS differ based on the age of patients. Prior studies have noted that children under the age of 10 tend to present with fever, cough and wheezing, whereas adults typically report chest pain and dyspnea.[14] Further research is needed to confirm, but based on our data, incorporating the presence or absence of chest pain and hypoxia in pediatric patients may help focus the use of CXR to the appropriate patient population at risk of developing ACS. By 18 years of age, most children with SCD will have had on average 26.7 (95% CI: 24.1-29.3; range 0-492.1) radiographic tests while 5% of these patients will have had more than 100 radiographic tests[15]. A high cumulative lifetime of radiation exposure is an established risk factor for serious life-threatening diseases such as cancer[16]. With

advancements in standards of medical care for patients with SCD, the life expectancy for SCD patients has improved to an average of 54 years old[8], which makes it even more important to reduce cumulative exposure to diagnostic radiation in this vulnerable population. Thus, this study provides evidence to support a more critical assessment of risk factors and presenting symptoms to better triage which pediatric patients warrant further imaging in the PED at initial presentation to investigate for possible ACS.

Conflict-of-interest statements

The authors have no conflicts of interest to disclose.

Acknowledgements

The authors sincerely thank the University of Maryland Department of Pediatrics for its support in pursuing this research work.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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