Summary of i2b2 Data: Spirometry in Pediatric Sickle Cell Populations

Melissa Sue Loscalzo

University of Florida College of Nursing

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Abstract

Comorbidity of sickle cell disease (SCD) and asthma puts individuals at increased risk of acute chest syndrome, the leading cause of premature death in patients with sickle cell disease (Miller, 2011). Prompt diagnosis via pulmonary function testing (PFT) may reduce the incidence of acute chest syndrome (ACS). The purpose of this study is to analyze i2b2 data obtained from four major academic medical centers (Harvard, Texas Medical Center, Indiana State, and the University of Florida) to observe the incidence of children comorbid with sickle cell disease, asthma, and acute chest syndrome. Data revealed that among the four centers, only 30.9% of patients with sickle cell, asthma, and acute chest syndrome received spirometry treatment. Additionally, we can begin to explore the care provided to patients comorbid with these conditions and determine if revision of the standard of care is necessary. The scope of this study pertains to pediatric sickle cell patients comorbid with asthma and is limited to identifying whether there is reason to pursue further research on this topic and develop alternative standard care measures. Prompt management of asthma can improve quality of life and life expectancy for this population and is therefore imperative to their care.

Introduction

Within the United States, approximately 100,000 individuals have been diagnosed with sickle cell disease (Hassell, 2010). Sickle cell disease is a common genetic disorder primarily affecting African American populations, with 1 in 500 of these individuals being diagnosed with the disease (Hassell, 2010). According to the Centers for Disease Control and Prevention, approximately 25 million US individuals have been diagnosed with asthma, a condition that is influenced by both genetic and environmental factors (2018). A common complication for sickle cell patients is acute chest syndrome, which is characterized by chest pain, tachypnea, fever,

respiratory distress, and lung infiltrates (Gladwin & Rodgers, 2000). Acute chest syndrome is caused by sickling within the microvasculature and subsequent vaso-occlusion. These vaso-occlusive episodes result from the sickled cells characteristic of the disease process- their rigid and sticky nature can cause them to block small vessels, thus impairing the flow of blood, which carries vital oxygen and nutrients throughout the body (Gladwin & Rodgers, 2000). Without supportive care, acute chest syndrome can quickly progress to death, and has actually been identified as the most common cause of death in sickle cell patients (Quinn, Rogers & Buchanan, 2004). With this being said, early identification and rapid management of this condition can be a matter of life or death within this patient population. A correlation has been identified between age and pulmonary function, with younger children being more predisposed to deteriorating lung function and acute chest syndrome episodes (Greenough & Knight-Madden, 2018). This interrelationship places even greater emphasis on implementing treatment measures as early as possible in these patients' lives in order to manage symptoms and prevent exacerbation.

A relationship has been identified among patients comorbid with asthma and sickle cell disease, with pediatric patients being five times more likely to experience respiratory symptoms during a vaso-occlusive episode if asthma is present as well (Jain, Bakshi & Krishnamurti, 2017). With a correlation this strong, appropriate interventions in regards to the asthma are imperative to not only managing, but also preventing pathologic progression of a patient's condition. The prognosis of pediatric populations is characteristically unpredictable and at times fragile, so the coexistence of an asthmatic condition in a sickle cell patient greatly increases their likelihood of complications arising. Although more emphasis has been placed on the importance of adequate management in patients comorbid with these conditions in recent years, a gap still persists in relation to proper screening, diagnosis, and appropriate intervention.

In this study, numerical statistics have been extracted from four major academic medical centers, evaluating the number of patients with sickle cell disease, asthma, acute chest syndrome, and those who received spirometry treatment. This data can be used to compare and contrast the frequency of asthma screening and diagnosis among sickle cell populations and the development of acute chest syndrome. The information provided by this study can present the reality of the frequency of asthma screening and subsequent symptom management within this patient population. By identifying relevant relationships and contributing factors to this potentially fatal condition, this study can advance the care that is provided to this patient population. By evaluating the effectiveness of spirometry interventions, this study can provide health care professionals with a greater understanding of how to manage care for these individuals. The purpose of this study is to identify the incidence of pediatric patients comorbid with sickle cell disease, asthma, and acute chest syndrome and to evaluate the frequency of interventional spirometry utilization as treatment for symptom management. The objectives of this study are as follows: to analyze the coexistence of asthma diagnosis among this patient population and its relationship to the development of acute chest syndrome, to determine the frequency of interventional spirometry utilization among patients with sickle cell, asthma, and acute chest syndrome, and to explore the reasoning behind our findings.

Narrative

Data from four large academic medical centers has been gathered and evaluated for the prevalence of sickle cell disease (SCD), asthma, and acute chest syndrome (ACS) among patients 5-34 years of age spanning from December 2010 through December 2015 using i2b2, an IRB approved de-identified database. The four academic medical centers include Harvard, Texas Health Center, Indiana University, and UF Health Shands at the University of Florida. These

medical centers are labeled A, B, C, and D, respectively, throughout the study. The data collected from the four centers includes total sickle cell patients, those patients comorbid with asthma, those patients who developed acute chest syndrome, and those who received interventional spirometry treatment. Data was then organized into a table according to the following criteria:

(1) total sickle cell patients

(2) sickle cell and asthma

(3) sickle cell and acute chest syndrome

(4) sickle cell, asthma, and acute chest syndrome

(5) sickle cell, asthma, acute chest syndrome, and spirometry treatment.

Queries to cross-reference those patients with the current procedural terminology (CPT) code for pulmonary function testing (PFT) was then completed. The gathered information is organized into data tables that are referenced throughout the study and can be located within Appendices A, B, and C. From the collected data, we are able to compare and contrast the incidence of acute chest syndrome development among these patients as it relates to asthma diagnosis and the implementation of spirometry treatment measures. This data has been manipulated to yield percentages regarding the following:

(i) sickle cell patients presenting with asthma

(ii) sickle cell patients who developed acute chest syndrome

(iii) sickle cell patients with both asthma and acute chest syndrome

(iv) sickle cell patients with asthma, acute chest syndrome, and received spirometry treatment for each academic medical center.

From this data and the identified trends, we can begin to explore the processes behind the statistics. We can begin to question the reasoning behind our findings, and whether the results are due to inadequate screening measures, a gap in documentation, or a variety of other contributing factors. Understanding the contributing factors that led to the statistics at hand is the first step to deriving meaning from this data set.

The project described in this study was initiated as a University of Florida College of Nursing Honors research project by honors student Melissa Loscalzo (traditional BSN senior) along with research preceptor Dr. Laurie Duckworth, PhD, ARNP in Gainesville, Florida. The project includes the analysis of i2b2 data obtained from four academic medical center organizations: Harvard, Texas Health Center, Indiana University, and UF Health Shands at the University of Florida. Meetings between the honors student and research preceptor took place from May 2017 through April of 2018 within the University of Florida College of Nursing in regard to the scope of the project, organization, data acquisition, research design, stakeholder analysis, and review of the finished project. Rough drafts of the project have been provided to the mentor for feedback and guidance. Additionally, the final draft of the thesis and e-poster have been submitted to the mentor for approval prior to submission/presentation for the UF honors course as well as the 2018 University of Florida Nursing Research Summit and Malasanos Lectureship on Friday, April 13th, 2018.

This study required a great deal of collaboration among multiple parties, and several key stakeholders can be identified. Stakeholder involvement includes Dr. Laurie Duckworth, PhD, ARNP, who gathered and organized the data from the i2b2 de-identified data base, constructed the initial data table along with accompanying calculations, conducted literature review, and presented findings at the 2017 Sigma Theta Tau International Nursing Research Congress held in

Dublin, Ireland and served as the UF CON honors research preceptor for this project. Additionally, Melissa Loscalzo, a University of Florida College of Nursing Honors student completed summary of the numerical i2b2 data to covert the quantitative data into descriptive statistics. Significant correlations among the data have been identified and significant findings have been summarized. The reasoning behind the findings of this study have been explored and given thoughtful consideration in order to interpret the data and derive meaning. Lastly, the four academic medical centers (Harvard, Texas Health Center, Indiana University, and UF Health Shands at the University of Florida) from which i2b2 data has been extracted are key stakeholders for this study as well.

A potential barrier to this research study would be rejection from the academic medical centers in regard to participating in the study. Without the data obtained from these facilities, we would have either needed to explain in more detail why participation is so vital to the study in order to persuade the centers or seek participation from different facilities entirely. Another barrier to this study is the ability to account for unmeasurable factors and how they have contributed to the extracted data for each medical center within their unique geographical locations. Some of these factors include weather/environment, lifestyle factors, diet, family history, patient noncompliance, or health literacy level. An actual barrier related to this study involved the initial delineation of what aspect of the study for the honors student to focus on. This barrier was resolved by reviewing materials provided by the honors research mentor, including data tables (appendices A, B, and C) as well as the research preceptor's abstract for the study (refer to appendix D). The title and IRB approval number for Laurie Duckworth's study is as follows: Exploring Spirometry Use to Measure Asthma Control in Patients with Sickle Cell Disease: A Multicenter Study (IRB 201601125). The honors student and preceptor met several

times within the UF College of Nursing throughout the course of the mentorship in order to determine the scope of the nursing honors thesis and provide assistance as needed.

Results and Discussion

The following i2b2 data was obtained for academic medical centers labeled A, B, C, and D. Refer to Appendix A to view the data table for the following criteria:

(1) Total sickle cell patients: A=428, B=378, C=1202, D=74

(2) Sickle cell and asthma: A=79, B=57, C=377, D=64

(3) Sickle cell and acute chest syndrome: A=72, B=78, C=142, D=117

(4) Sickle cell, asthma, and acute chest syndrome: A=37, B=43, C=146, D=23

(5) Sickle cell, asthma, acute chest syndrome, and spirometry treatment: A=1, B=18, C=52, and D=6.

Using this data, we can yield the following quantitative data (refer to Appendices B and C and to compare and contrast these values within a bar graph):

(i) Percentage of sickle cell patients comorbid with asthma, which can be obtained by dividing the values from item (2) by item (1): A=18.5%, B= 15.1%, C=31.4%, D=8.6%

(ii) Sickle cell patients who developed acute chest syndrome, obtained by dividing item (3) by item (1): A=16.8%, B=20.6%, C=11.8%, D=15.8%

(iii) Sickle cell patients with both asthma and acute chest syndrome, obtained by dividing item (4) by item (1): A=8.6%, B=11.4%, C=12.1%, D=3.1%

(iv) Sickle cell patients with asthma, acute chest syndrome, and received spirometry treatment, obtained by dividing item (5) by item (4): A=2.7%, B=41.9%, C=35.6%, D=26.1%.

Among the four medical centers, a total of 249 patients fell under item (4) sickle cell, asthma, and acute chest syndrome, and of those patients, only 77 received pulmonary function testing (item 5), therefore only 30.9% of patients with SCD, asthma, and ACS utilized pulmonary function testing. A notable correlation among the data is that medical center C had the highest value for item (i), with a value of 31.4% of sickle cell patients diagnosed with asthma, which is almost double the value of any other center that was evaluated. Additionally, medical center C had the lowest value for item (ii) out of the four centers, with only 11.8% of sickle cell patients who had developed acute chest syndrome . The highest percentage of patients comorbid with sickle cell, asthma, and ACS receiving spirometry treatment was found within medical center B with a value of 41.9%, which is not even half of the patient population for this particular center. Also, the percentage of patients receiving interventional spirometry varied greatly, with the highest value being 41.9% (medical center B), and the lowest being 0.2% (medical center A).

Based on these findings, it raises the question of how this data came to be: is there a lack of pulmonary and asthma evaluation among this patient population, or are these patients indeed being evaluated for this condition and there is just a gap in documentation? Additionally, we can explore the reasoning as to why only 30.9% of patients with sickle cell, asthma, and acute chest syndrome received interventional spirometry, or if this reveals yet another gap between implementation of interventions and proper documentation. Another notable finding is seen within medical center C, in which there was the highest percentage of sickle cell patients diagnosed with asthma but also the lowest percentage of acute chest syndrome development among this patient population. This leaves us with the question of what measures have been set in place within this particular facility to ensure asthma screening and diagnosis takes place, and

if this is the reason for the low incidence of acute chest syndrome among the patients within this facility.

Given the results found in this single study, it is important to evaluate our findings compared to current literature that relates to the topics we explored. According to the Center of Disease Control and Prevention, approximately 12.7% of children had received an asthma diagnosis within their lifetime (Akinbami, 2006). Another study conducted by the American Society of Hematology, found that 17% of the participants with sickle cell disease were comorbid with asthma (Boyd, Macklin, Strunk, & Debaun, 2006). Within our study, the percentage of sickle cell patients with asthma is not too far off from these statistics. The exception to this would be within academic medical center C, which we have already pointed out as having the highest rate of asthma diagnosis among these sample populations. This leaves us to further consider how this statistic came to be- is there a significant abundance of environmental or genetic factors within the geographic region of medical center C, or is it related to prompt screening and documentation within this facility? Another study found that there is an association between sickle cell children who both currently have asthma or have ever experienced asthma with recurrent acute chest syndrome episodes (Knight-Madden, Forester, Lewis & Greenough, 2005). The correlation of these two conditions furthers the argument of this study, that sickle cell patients with asthma require prompt pulmonary intervention measures for symptom management and in order to prevent exacerbation of their condition. Although the amount of research exploring the use of spirometry in sickle cell patients is limited, a study conducted by Scott. T. Miller (2011) has shown that the implementation of spirometry prescribed for ten times every two hours while awake has shown to reduce the occurrence of acute chest syndrome for sickle cell patients during a hospital stay. The findings of Miller's study reveal that

pulmonary function testing and treatment can indeed manage the symptoms of patients presenting with sickle cell disease, as well as prevent the onset of more serious pulmonary complications.

Summary and Conclusion

By conducting this study, we aimed to quantify the comorbidity of asthma and acute chest syndrome among pediatric sickle cell populations. Among these groups, we examined the utilization of interventional spirometry treatments for these patients. Lastly, we were left to explore the reasoning behind such findings, and how the data came to be. By extracting i2b2 data from four academic medical centers, we were able to identify trends among the data and possible correlations. It was discovered that among the four centers, less than one third (30.9%) of sickle cell patients comorbid with asthma and acute chest syndrome received interventional spirometry. It was also discovered that the medical center with the highest incidence of asthma had the lowest incidence of acute chest syndrome, causing us to question the interventions in place that seems to be saving these patients from the exacerbation of their pulmonary status. Percentages of patients receiving spirometry varied greatly from one center to the next. The information gathered from this study can help us to learn more about this patient population and the proper interventions to be included in their care.

Comorbidity of sickle cell disease and asthma increases an individual's risk for the development of acute chest syndrome, one of the leading causes of fatality among this patient population. Utilization of PFT's in patients with SCD may aid in early diagnosis and subsequent symptoms management of asthmatic symptoms. Early diagnosis facilitates effective management of symptoms, can reduce exacerbations and, consequently, the development of acute chest syndrome. From this data, we can infer that medical center C is actively screening and

diagnosing sickle cell patients for asthma and following through with subsequent treatment measures for their pulmonary status. As a result, the occurrence of acute chest syndrome is decreased in this patient population. Exploring this center's strategies and protocols that have been set in place could be beneficial for other medical providers and this patient population as a whole. From the data obtained from the four medical centers, we can infer that there is a gap between adequate pulmonary screening measures for sickle patients and/or proper documentation.

An increased level of attention should be brought to this issue, and a revised standard of practice implemented in order to ensure adequate care of this patient population and prevention of complications. This can alter the way that nursing professionals and other healthcare providers care for sickle cell patients, which can lead to an entirely new standard of care for those diagnosed with having asthma or other pulmonary symptoms. This can lead to a decrease in mortality among this patient population, as well as an overall improvement in their quality of life and overall prognosis.

As an aspiring pediatric nurse, the findings of this study will impact my professional development as I encounter children with sickle cell throughout my career. Due to my experience with and the knowledge I have gained through this research study, I will have a heightened awareness in regard to identifying pulmonary symptoms and now that I know the impact of such comorbidities in these individuals, I will be able to make conscientious, prudent decisions in regard to their care. I hope to pursue my doctorate in nursing practice here at the University of Florida in the near future, and during that time, I will have the opportunity to continue my participation in this study and expound upon the knowledge that has been identified within this project.

This study has the set the stage for further research to take place in order to examine the effect of pulmonary function testing on this patient population. This study's research preceptor is currently devising a pilot study to evaluate the use of interventional spirometry treatment in pediatric sickle cell populations, which is expected to span over six months for data collection. The plan for this study includes the establishment of a cohort divided into two groups: a control group receiving standard of care asthma treatment and an experimental group participating in interventional spirometry treatments with regular follow up and evaluation. Collection of data regarding symptoms, peak flow, quality of life, and frequency of hospitalizations can reveal the effectiveness of interventional pulmonary treatment in comparison to the standard of care treatments in place currently.

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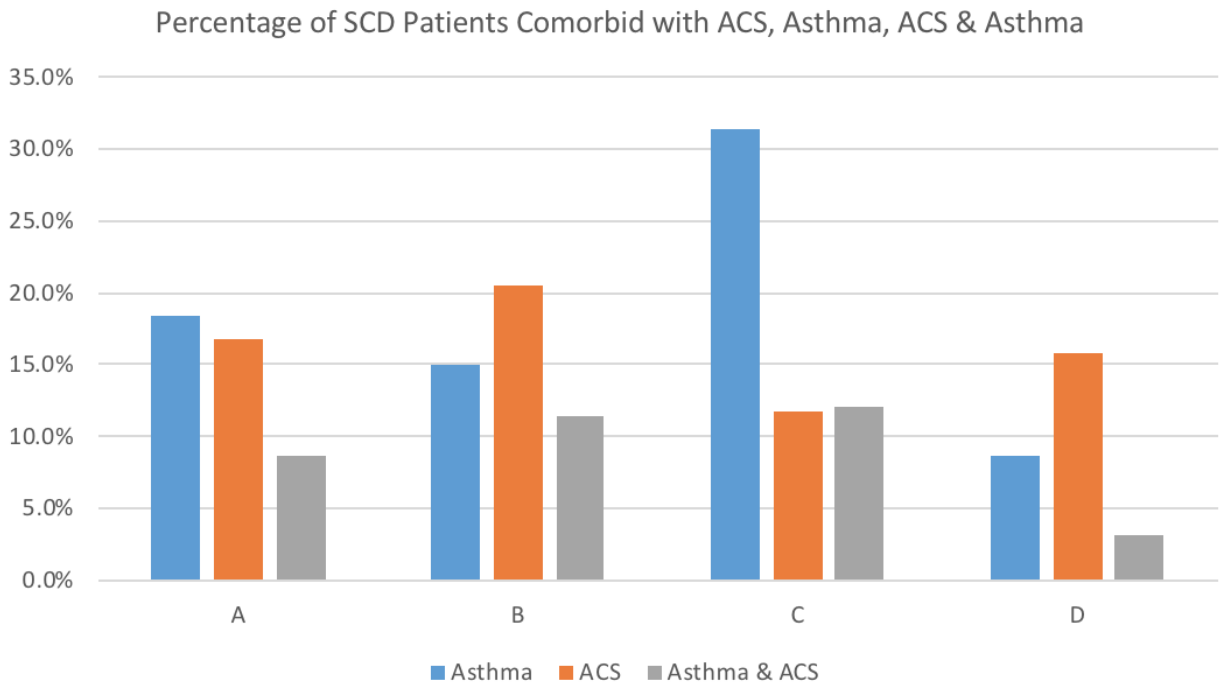
Appendix A

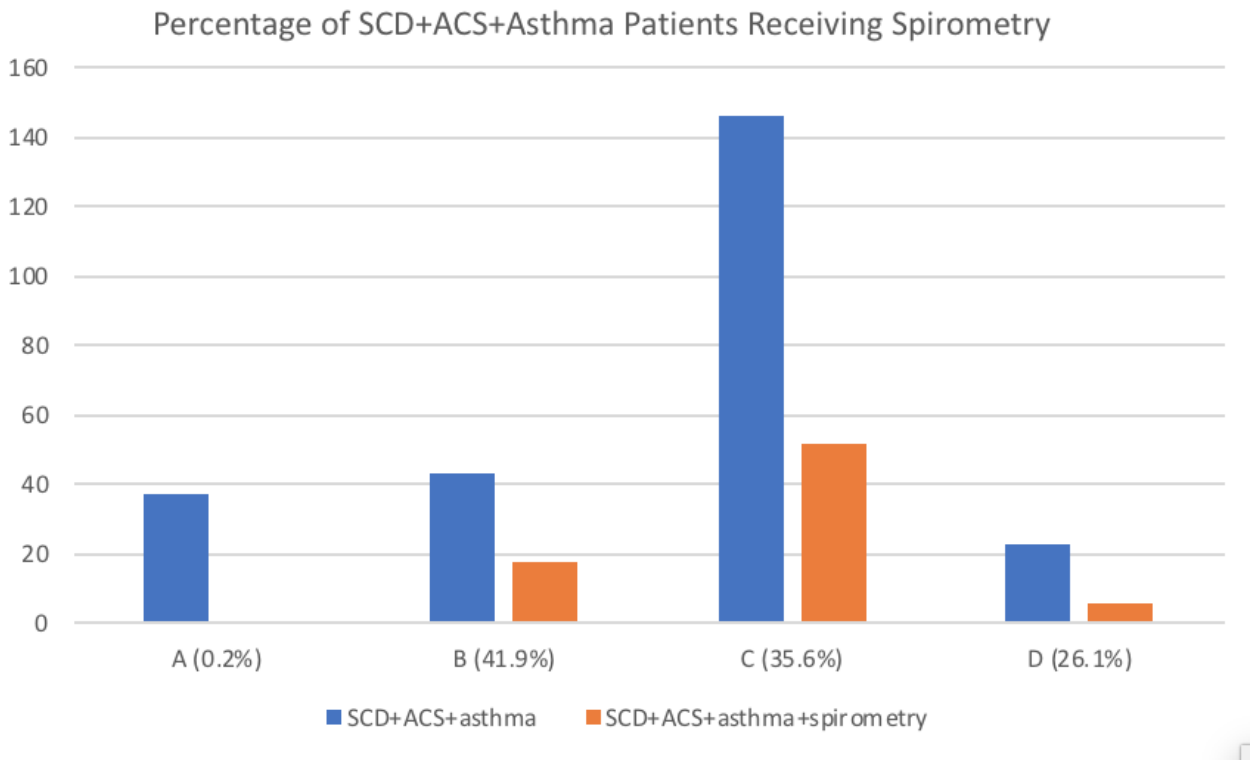
SCD Comorbidity with Asthma and/or ACS vs. Those Receiving Spirometry

	Query	Total	A	B	C	D
1	SCD	2749	428	378	1202	741
2	SCD+Asthma	577 (21.0%)	79 (18.5%)	57 (15.1%)	377 (31.4%)	64 (8.6%)
3	SCD+ACS	409 (14.9%)	72 (16.8%)	78 (20.6%)	142 (11.8%)	117 (15.8%)
4	SCD+ACS+Asthma	249 (9.1%)	37 (8.6%)	43 (11.4%)	146 (12.1%)	23 (3.1%)
5	SCD+ACS+Asthma+Spirometry	77	1	18	52	6
6	Spirometry/(SCD+ACS+Asthma)	30.9%	0.2%	41.9%	35.6%	26.1%

Appendix B



Appendix C



Appendix D

Use of Spirometry to Measure Asthma Control in Patients with Sickle Cell Disease

Purpose

The purpose of this study is to determine the use of spirometry testing to monitor and evaluate asthma control in patients with asthma, sickle cell disease and acute chest syndrome, ages 5 to 34 years.

Background

Sickle Cell Disease (SCD) is a common inherited genetic disorder and affects approximately 100,000 people in the United States annually and one in 400 African American births (CDC, 2016). Asthma affects 23 million people in the US alone. African American

children are disproportionally affected having a greater prevalence rate for asthma compared to Caucasians, in addition to a higher rate of hospitalization and higher mortality rate. SCD, when combined with a diagnosis of asthma, increases the risk of Acute Chest Syndrome (ACS), which can lead to significant morbidity and mortality. Findings from The National Heart Lung and Blood Institute (NHLBI) funded Sickle Asthma Cohort (SAC) study confirm that asthma is a risk factor for ACS in patients with SCD and that one early life ACS episode was a significant predictor for future ACS events (DeBaun et al., 2014). It has been reported that as many as 28% of children with SCD may have asthma {Strunk et al., 2014). While there seems to be increasing recognition of the importance of co-morbid asthma and SCD, asthma continues to be underdiagnosed and undertreated (DeBaun, Strunk, 2016). NHLBI Guidelines for the Diagnosis and Management of Asthma should be followed for patients with SCD and asthma (EPR 3, 2007). This would include routine follow up by a pulmonology provider to ensure proper management of asthma. Part of this routine care would include Spirometry testing to evaluate effectiveness of asthma medications and subtle changes in pulmonary function. Early detection of a decrease in pulmonary function may lead to changes in management, which may decrease the incidence of an asthma exacerbation and possibly prevent an occurrence of ACS. The number of spirometry procedures conducted may be indicative of how many patients with Asthma and SCD are receiving routine pulmonology management. Data gleaned from the EMR database may show that although a significant number of patients with SCD and ACS carry the diagnosis of asthma, very few have spirometry testing to evaluate the effectiveness of asthma treatment or to provide early detection of worsening lung function.

Methods

A descriptive cross-sectional study design was utilized to identify the number of patients with SCD, ACS, Asthma and the number of spirometry procedures performed. The Electronic Medical Record (EMR) using i2b2, (a de-identified data repository) for 4 Academic Medical Centers (AMC) was queried for the count of patients 5-34 years of age seen between 12/01/2010 and 12/01/2015 having co-morbid diagnoses of Asthma, Sickle Cell Disease and Acute Chest Syndrome. Queries to cross-reference those patients with the CPT code for spirometry was then performed. The i2b2 query included; (1) Number of patients with SCD + ACS + Asthma + Spirometry, (2) Number of patients with SCD, (3) Number of patients with SCD + Asthma, (4) Number of patients with SCD + ACS, and (5) Number of patients with SCD + ACS + Asthma. The percentage of SCD + ACS+ Asthma patients having spirometry testing was calculated by dividing SCD + ACS + Asthma +Spirometry by the number of patients with SCD + ACS+ Asthma. The four AMC's were labeled as A, B, C, D.

Results

The combined total number of patients for 4 AMC (A,B,C,D) for categories (1) SCD+ACS+Asthma+Spirometry,(2) SCD,(3) SCD+Asthma, (4) SCD+ACS, (5) SCD+ACS+Asthma are respectively; (1)77, (2)2749, (3) 577, (4) 409, and (5) 249. Number of patients for each AMC for these five categories; (1) Number of patients with SCD + ACS + Asthma + Spirometry, A =<10, B= 18, C= 52, D= <10. (2) Number of patients with SCD, A=428, B=378, C=1202, D=741. (3) Number of patients with SCD+Asthma, A=79 (18.4%), B=57 (15.0%), C=377 (31.3%), D=64 (8.6%). (4) Number of patients with SCD+ACS, A=72 (16.8%), (B) =78 (20.6%), C=142 (11.8%), D=117 (15.7%). (5) SCD+ACS+Asthma, A=37 (8.6%), B=43 (11.4%), C=146 (12.1%), D=23(3.1%). The percent of patients with SCD+ACS+Asthma who also had spirometry performed for each AMC was calculated

(SCD+ACS+Asthma+Spiro/SCD+ACS+Asthma = %); A=<10%, B=41.8%, C=35.6%, D=26%. The total number of patients with SCD+ACS+Asthma for all 4 AMC= 249, those having spirometry = 77, thus (77/249) 30.9% of patients with SCD+ACS+Asthma had spirometry performed.

Conclusion

Asthma is prevalent in children with SCD and may result in episodes of ACS. Across 4 AMC only 30.9% of patients with SCD, ACS, and asthma received spirometry testing. In addition there is considerable variation among the 4 AMC ranging from <10% to 41.8% receiving spirometry. Despite the NHLBI recommendations for children with asthma it appears that only a third of these patients with co-morbid SCD, ACS, and Asthma receive this procedure. Very few are being routinely tested for changes in pulmonary function, or those tests are not being coded and documented appropriately. Better coding and documentation practices for spirometry testing in those with sickle cell disease and asthma will allow better access for providers to utilize those test results for asthma management. If the testing is not being done routinely, further research should be done to determine if there are barriers to obtaining appropriate pulmonology evaluation and management.