

Predictors of Emergency Department Utilization and Hospitalization for Vaso-Occlusive Pain Crises in Pediatric Patients with Sickle Cell Disease

Christina Marbrey^{1*}, Justin Davis¹, Matthew Morris², Erin Jackson³, Cynthia Karlson³

¹Department of Pediatric Emergency Medicine, University of Mississippi Medical Center
State St. Jackson, MS, 39216, United States

²Department of Psychiatry and Human Behavior, University of Mississippi Medical Center
State St. Jackson, MS, 39216, United States

³Department of Hematology and Oncology, University of Mississippi Medical Center
2500 State St. Jackson, MS, 39216, United States

* **Corresponding author:** Christina Marbrey, Department of Pediatric Emergency Medicine, University of Mississippi Medical Center, State St. Jackson, MS, 39216, United States, Tel: (601) 984-2195; Email: cmarbrey@umc.edu

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Abstract

Vaso-occlusive pain crisis (VOC) is the most common complication in pediatric patients with sickle cell disease seen in the emergency department (ED). The purpose of this study was to identify demographic and disease-related predictors of VOC in pediatric patients with SCD who present to the ED for pain. A retrospective chart review was conducted over a 6 year period. We examined differences in high ED utilization (>3 visits in any year) versus low ED utilization. Using multilevel regression models, we identified the strongest predictors of high ED utilization as older age, HbSS subtype, lower hemoglobin, and history of severe disease.

Introduction

Sickle cell disease (SCD) affects 1 in every 365 Black/African American children in the United States¹. Vaso-occlusive pain crises (VOC) are the most common complication of SCD². Frequent VOC is associated with increased morbidity, mortality, and increased healthcare utilization^{3,4}. While the majority of VOC are managed at home, some patients present to the emergency department (ED) for pain management^{5,6}. Despite well-identified disease processes, ED utilization for VOC is highly variable and poorly explained by SCD's single genetic variant.

The objective of this study was to identify demographic and disease-related predictors of ED utilization and hospitalization for VOC in pediatric patients with SCD⁷. We hypothesized that HbSS genotype, male, public insurance, visit during winter months, and worse blood laboratory values would be associated with high ED utilization^{8,9} and predict total number of ED SCD visits and hospitalizations. We further examined whether ED length of stay, time till roomed, time till opioid analgesia, and total opioid dosage impacted healthcare utilization^[10-12].

Methods

Study design

Institutional IRB approval was obtained for an electronic health record-review from July 1, 2012 to October 25, 2018. Inclusion criteria: (1) SCD HbSS, SC, S β O thalassemia, or S β + thalassemia, (2) 5-19 years, and (3) admitted to pediatric ED for VOC only (ICD 9 and ICD 10 codes). An ED visit was included if the disposition was "discharge to home", "inpatient admission" or "inpatient observation". Patients who left against medical advice, eloped, or had non-VOC diagnosis were excluded (e.g., fever, acute chest syndrome, bone marrow failure).

Clinical investigation

Primary Outcomes. ED visit was defined as registered in the pediatric ED. Hospitalized was defined as ED disposition of "inpatient admission" or "inpatient observation". Total number of ED visits and total number of hospitalizations were summed across the six year study period. Patients had High ED Utilization if they had ≥ 3 ED visits during any year.

Demographic and Disease Predictors. Demographics included age at visit, sex, race, SCD genotype, time of year (Winter, Spring, Summer, Fall)¹³, and insurance. Body mass index¹⁴, hemoglobin (Hgb), hematocrit (Hct), reticulocyte count (retic), mean corpuscle volume (MCV), mean corpuscular hemoglobin concentration (MCHC), and mean corpuscular hemoglobin (MCH) were extracted for each visit¹⁵⁻¹⁷. Severe SCD disease severity [3,18,19] was defined as 5 or more hospitalizations over the six year study period.

Exploratory variables

We examined whether ED length of stay (minutes), ED time until roomed (minutes), time till initial opioid administration,

and total opioid dose (morphine equivalents/kilogram) were predictive of hospitalization for VOC [20,21].

Statistical analysis

Descriptive statistics, non-parametric one sample tests (males vs females; time of year), t-tests for continuous and chi-squared for categorical group differences were calculated in IBM SPSS 26 (IBM Corp). Linear and logistic regression models included mean values for predictors that varied across visits. Multilevel models for binary outcomes were specified using hierarchical linear models (HLM v.8) [22] to account for nesting of hospital visits within patients. ‘Visit number’ was included in all models, along with predictors that varied across visits: age, BMI, Hgb, Retic, MCV result, MCHC level, ED length of stay, ED time until roomed, time till initial opioid, and total opioid dose. Hct and MCH were highly correlated with other laboratory values ($r^2 > .7$) and were removed from regression and multilevel models. Genotype (1=SS/SB0 thalassemia; 2=SC/SB+ thalassemia), sex, and insurance (0=Federal/self-pay; 1=private) were included as between-person predictors.

Results

Participant Characteristics

Descriptive statistics for 248 patients across 1,363 ED visits are in Table 1. Patients were predominantly African American (99.6%). Mean age at first ED visit was 9.7 (SD=3.9). Thirty patients (12.1%) had one ED visit, 100 patients (40.3%) had two to five visits, and 118 patients (47.6%) had six or more visits. All patients had normal BMI, except for one visit reflecting obesity. ED visits were evenly distributed across time of year (Chi-Squared=1.23, $p=.75$). A subset of 61 patients (24.6%) were classified as severe SCD disease severity.

	Low ED Utilization N = 93	High ED Utilization N = 158	Test statistic (p-value)	Total Sample	Range
	n (%)	n (%)		n (%)	
Male	44	88		132 (52.6)	
Female	49	70	1.65 (.20)	119 (47.4)	
Hb, SS/β0 thalassemia	62	107		169 (67.3)	
Hb, SC/β + thalassemia	31	51	.03 (.86)	82 (32.7)	
Private/Military insurance	9	20		29 (11.6)	
Public/No insurance	84	138	.51 (.48)	222 (88.4)	

	M (SD)	M (SD)		M (SD)	
Age, years	10.10 (4.03)	11.84 (3.76)	-4.91 (<.001)	11.68 (3.81)	5-19
BMI	18.93 (5.41)	20.77 (5.76)	-3.09 (<.01)	20.61 (5.74)	11-99
Hgb, g/dL	8.89 (1.75)	9.18 (1.66)	-1.75 (.08)	9.16 (1.67)	4.1-16.8
Hematocrit	25.46 (4.64)	26.09 (4.74)	-1.32 (.19)	26.03 (4.74)	13.1-45.1
Reticulocyte percent	8.09 (4.71)	7.87 (4.38)	.44 (.66)	7.89 (4.41)	.1-18.1
MCHC level	34.87 (1.57)	35.26 (1.62)	-2.39 (.02)	35.23 (1.62)	29.3-39.7
MCV	79.56 (10.66)	83.08 (10.50)	-3.31 (<.01)	82.78 (10.55)	54.0-121.8
MCH	27.77 (4.13)	29.31 (4.05)	-3.76 (<.001)	29.18 (4.08)	18.1-44.5
ED length of stay (min)	205.52 (80.80)	229.91 (86.01)	-3.05 (<.01)	227.65 (85.81)	16-875
Time to first opioid (min)	61.89 (39.95)	62.99 (40.18)	-.26 (.79)	62.90 (40.14)	5-319
ED morphine equivalency dosage	.11 (.10)	.13 (.10)	-2.42 (.02)	.13 (.10)	0-0.61
Total ED visits per patientb	2.19 (1.13)	13.77 (13.66)	-8.15 (<.001)	9.48 (12.21)	1-94
Total hospitalizations per patientb	1.11 (1.08)	5.65 (6.61)	-6.56 (<.001)	3.96 (5.72)	0-39

Note: aInsurance payer was collected for first ED visit for each patient. bTotal ED and total hospitalizations per patient are summed over the six year study period.

Table 1: Demographics

High versus Low ED Utilization

A substantial subset (62.9%) of patients classified as having High ED Utilization. Patients with High ED Utilization were typically older, had severe SCD disease, had lower Hgb levels, had lower MCV, and had more hospitalizations than Low ED Utilization counterparts ($p^s < 0.05$; Table 1).

Predicting Total Number of ED Visits and Hospitalizations

SCD genotype, demographic (age at visit, sex), BMI, and laboratory values (Hgb, retic, MCV, MCHC) at ED admission were not significantly associated with total number of ED visits or

total number of hospitalizations in linear regression models (all p 's >0.05).

Predicting High ED Utilization

A logistic regression model revealed that age, BMI, and laboratory value were not significantly associated with High ED utilization (all p 's >0.05).

Predicting Hospitalization

The odds of being hospitalized decreased as patients' number of visits increased (Table 2). Higher BMI and lower Hgb level were associated with increased likelihood of hospitalization. No laboratory values were associated with hospitalization. Specific to the ED visit, longer ED visits were associated with decreased odds of hospitalization. However, longer time until receiving first opioid and higher total morphine equivalency dosage was associated with increased likelihood of hospitalization for VOC.

	b (SE)	OR (95% CI)	p-value
Genotype ^a	0.08 (.45)	1.09 (0.45, 2.64)	.86
Insurance ^a	0.48 (.49)	1.62 (0.61, 4.30)	.33
Visit number	-0.02 (.01)	0.98 (0.97, 0.99)	.03
Age	-0.00 (.17)	1.00 (0.72, 1.39)	.99
BMI	0.86 (.19)	2.36 (1.62, 3.43)	<.001
Hgb, g/dL	-0.46 (.17)	0.63 (0.46, 0.88)	<.01
Reticulocyte Percent	0.11 (.15)	1.11 (0.83, 1.51)	.47
MCHC Level	0.04 (.11)	1.04 (0.84, 1.28)	.74
MCV Result	0.06 (.13)	1.06 (0.81, 1.37)	.68
ED Length of Stay (min)	-0.49 (.16)	0.61 (0.45, 0.84)	<.01
ED time till roomed (min)	-0.15 (.09)	0.86 (0.72, 1.02)	.09
ED Time Till Opioid (min)	0.29 (.13)	1.34 (1.05, 1.71)	.02
ED Morphine equivalency	1.80 (.16)	6.03 (4.41, 8.26)	<.001

Table 2: Multilevel Logistic Regression Model Predicting Hospitalization (yes/no).

Discussion

Discussion of Results

Compared to their Low ED Utilization counterparts, patients with High ED Utilization (62.9%) tended to be older, have severe SCD disease, have lower Hgb levels, and have lower MCV result. Early identification and recognition of these higher risk patients in the outpatient setting may allow for earlier healthcare intervention and decreased hospital utilization [23,24].

Despite examining a range of demographic and medical laboratory predictors we did not identify any significant

predictors of total ED visits, total hospitalizations, or High ED Utilization in regression analyses. These null findings are consistent with previous literature⁵ and suggests that the frequency of SCD VOC complications is highly individual.

Lower Hgb level, requiring more opioid medications, and requiring a longer ED length of stay are reflective of the clinical picture leading to hospitalization¹¹. At our institution, time to initial opioid administration fell in line with the current National Lung Blood and Heart Institute (NHLBI) recommendations²¹ for opioid administration within 1 hour. However, initial opioid morphine equivalency dosage was frequently low for weight status, and may have been inadequate to treat VOC, contributing to a higher hospitalization rate.

Limitations

In this clinical setting, there is risk that patient diagnoses were misclassified, coding differences occurred between ICD 9 and ICD 10 codes, and changes in practice occurred after 2014 NHLBI recommendations published during this study period. While our institution is the only pediatric hospital in the state, it is likely not all VOC ED visits were captured due to patients being seen at their local ED and 16 years and older occasionally alternating care between the pediatric and adult ED.

Conclusions and Future Directions

Based on the current study and larger literature, the strongest predictors of high ED utilization in pediatric patients with SCD include older age, HbSS subtype, lower Hgb level, and prior history of complication (i.e., severe SCD disease). Additional studies are critically needed to identify novel predictors of high ED utilization and test standardized interventions in both the outpatient and ED setting.

References

- Centers for Disease Control and Prevention (2020) Sickle cell disease- data and statistics.
- Salman ZA, Hassan MK (2015) Hospitalization Events among Children and Adolescents with Sickle Cell Disease in Basra, Iraq. *Anemia* 195469.
- Hardy SJ, Bills SE, Wise SM, Hardy KK (2018) Cognitive abilities moderate the effect of disease severity on health-related quality of life in pediatric sickle cell disease. *Journal of Pediatric Psychology*, 43: 882-894.
- Aisiku IP, Smith WR, McClish DK et al. (2009) Comparisons of high versus low emergency department utilizers in sickle cell disease. *Annals of Emergency Medicine*. 5387-593.
- Carroll CP, Haywood C Jr, Fagain P, Lanzkron S, et al. (2009) The course and correlates of high hospital utilization in sickle cell disease: Evidence from a large, urban Medicaid managed care organization. *American Journal of Hematology* 84:666-70.
- Jacob SA, Mueller EL, Cochrane AR, Carroll AE, Bennett WE, et al. (2019) Variation in hospital admission of sickle cell patients from the emergency department using the Pediatric Health Information System. *Pediatr Blood Cancer* e28067.
- Mvundura M, Amendah D, Kavanagh PL, Sprinz PG, Grosse SD, et al. (2009) Health care utilization and expenditures for privately

- and publicly insured children with sickle cell disease in the United States. *Pediatric Blood Cancer* 53: 642-646.
8. Lanzkron S, Carroll CP (2010) The burden of emergency department use for sickle cell disease: analysis of the national emergency department sample database. *Am J Hematol* 85:797-799.
 9. Darbari DS, Onyekwere O, Nourai M, et al. (2012) Markers of severe vasoocclusive painful episode frequency in children and adolescents with sickle cell anemia. *J Pediatr* 160:286-290.
 10. Payne J, Aban I, Hilliard LM, et al. (2018) Impact of early analgesia on hospitalization outcomes for sickle cell pain crises. *Pediatr Blood Cancer* 65: e27420.
 11. Brandow AM, Nimmer M, Simmons T, et al. (2016) Impact of emergency department care on outcomes of acute pain events in children with sickle cell disease. *Am J Hematol* 91:1175-1180.
 12. Lin SM, Strouse JJ, Whiteman LN, Anders J, Stewart RW. Improving Quality of Care for Sickle Cell Patients in the Pediatric Emergency Department. *Pediatr Emerg Care*. 2016;32(1):14-16.
 13. Zivot A, Apollonsky N, Gracely E, Raybagkar D. Body Mass Index and the association with vaso-occlusive crises in pediatric sickle cell disease. *J Pediatr Hematol Oncol*. 2017;39(4):314-317.
 14. Centers for Disease Control and Prevention, Healthy Weight. (2020).
 15. Billett HH. Hemoglobin and Hematocrit. In: Walker HK, Hall WD, Hurst JW, editors. *Clinical Methods: The History, Physical, and Laboratory Examinations*. 3rd edition. Boston: Butterworths; 1990. Chapter 151.
 16. Bessman JD. Reticulocytes. In: Walker HK, Hall WD, Hurst JW, editors. *Clinical Methods: The History, Physical, and Laboratory Examinations*. 3rd edition. Boston: Butterworths; 1990. Chapter 156.
 17. Sarma PR. Red Cell Indices. In: Walker HK, Hall WD, Hurst JW, editors. *Clinical Methods: The History, Physical, and Laboratory Examinations*. 3rd edition. Boston: Butterworths; 1990. Chapter 152.
 18. Panepinto JA, Torres S, Bendo CB, et al. PedsQL™ sickle cell disease module: feasibility, reliability, and validity. *Pediatr Blood Cancer*. 2013;60(8):1338-1344.
 19. Loeffler P, Mueller T, Kutlar A. Frequency of emergency department visits for sickle cell disease vaso-occlusive crises and its contribution to hospital admission rates. *Blood* 2015; 26(23):5569.
 20. Kavanagh PL, Sprinz PG, Wolfgang TL, et al. Improving the management of vaso-occlusive episodes in the pediatric emergency department. *Pediatrics*. 2015; 136:e1016-1025.
 21. NHLBI. Evidence-Based Management of Sickle Cell Disease: Expert Panel Report. Bethesda, MD: NHLBI, U.S. Department of Health and Human Services; 2014.
 22. Raudenbush S, Bryk A, Cheong, Y, Congdon R, & du Toit, M. HLM 8: Hierarchical linear and nonlinear modeling. Skokie, IL: Scientific Software International; 2019.
 23. Brandow AM, Weisman SJ, Panepinto JA. The impact of a multidisciplinary pain management model on sickle cell disease pain hospitalizations. *Pediatr Blood Cancer*. 2011;56(5):789-793.
 24. Akenroye AT, Thurm CW, Neuman MI, et al. Prevalence and predictors of return visits to pediatric emergency departments. *J Hosp Med*. 2014;9(12):779-787.