Difference in Hospitalizations and Annual Bed Days for Patients With Sickle Cell Disease by Varying Levels of Anemia: A Retrospective Analysis of Linked Primary and Secondary Care Databases in England

Paul Telfer, MD, FRCP[1]; Judith Ruzangi, MSc[2]; Sara João Carvalho, PhD[2]; Giovanna Barcelos, MS[3]; Anne Beaubrun, PhD[3]; Caoimhe T. Rice, MSc, MRCP[2]

[1]Queen Mary, University of London, London, UK; [2]CorEvitas Specialty EMR, London, UK; [3]Global Blood Therapeutics, South San Francisco, CA, USA

INTRODUCTION

- Sickle cell disease (SCD) is an inherited disorder in which the underlying pathology is driven by sickle hemoglobin polymerization in the deoxygenated state.[1]
- Sickle hemoglobin polymerization causes red blood cell sickling, leading to chronic hemolytic anemia, painful vaso-occlusive crises, and end-organ damage.[1]
- Anemia in SCD is associated with both short- and long-term adverse outcomes; patients often require hospitalizations and the utilization of numerous healthcare resources, all of which contribute to heightened healthcare costs.[2,3]

OBJECTIVE

- To quantify the differences in hospitalizations and number of annual bed days by differing levels of anemia among patients with SCD.

METHODS

Patients

- Patients with SCD aged ≥12 years with ≥1 recorded hemoglobin (Hb) level were identified in the primary care English Clinical Practice Research Datalink (CPRD) and linked with a secondary care data set, Hospital Episode Statistics (HES), between January 2007 and March 2019.

Assessments and Analysis

- We used Hb records from primary care to categorize Hb intervals for each patient; patient intervals were divided by Hb level as <6 g/dL (severe anemia), 6 to <8 g/dL, 8 to 10.5 g/dL, or >10.5 g/dL.
  - Because Hb readings are highly variable, affected by hydration status, hemolysis and hematopoiesis, 30-day mean Hb levels were calculated to smooth this variation; each mean Hb was designated at the date of the first Hb value.
  - Hb intervals began with a new mean Hb level and ended with blood transfusion or a Hb level that was out of the Hb category range.
  - Patient index was the date of their first Hb value within the study period; patients were censored at the earliest of stem cell or bone marrow transplant, death, last CPRD-HES record date, end of study period, or 3 months before a record of pregnancy during the study period.
  - Patients could change Hb categories during the study period.
- We compared the significance of the categorical data distribution for hospitalizations using the Kruskal–Wallis test across Hb categories, extended with pairwise Wilcoxon rank sum testing; this method was repeated for hospitalizations due to any end-organ damage (EOD) and annual bed days.

RESULTS

Patient Demographics

- A total of 6018 patients with Hb records were included; the mean (SD) age was 37.1 (15.7) years, 64.8% were female, 72.9% were Black, and 5.2% were taking concomitant hydroxyurea (HU) (**Table 1**).

Table 1. Patient Demographics

	Patients (N=6018)
Age, years	
Mean (SD)	37.1 (15.7)
Range	12-92
Sex, n (%)	
Female	3897 (64.8)
Male	2121 (35.2)
Race or ethnicity, n (%)	
Black	4389 (72.9)
White	524 (8.7)
Unknown	355 (5.9)
Mixed	298 (5.0)
Other	202 (3.4)
South Asian	171 (2.8)
Other Asian	79 (1.3)
Concomitant HU, n (%)	
Yes	313 (5.2)
No	5705 (94.8)

HU, hydroxyurea.

- Of the 6018 patients with recorded Hb, 72.3% had intervals of Hb >10.5 g/dL, 44.3% had intervals of Hb of 8 to 10.5 g/dL, 15.3% had intervals of Hb of 6 to <8 g/dL, and 2.6% had intervals of Hb <6 g/dL (**Table 2**); categories were not mutually exclusive for patients.

Table 2. Mean Duration of Hb Intervals by Hb Category

Hb category, g/dL	Patients, n (%)[a]	Number of intervals	Mean (SD) duration, days	Median (IQR) duration, days
Hb <6	154 (2.6)	322	275.4 (482.3)	102 (254.2)
Hb 6 to <8	920 (15.3)	2654	389.1 (586.5)	166.5 (362)
Hb 8 to 10.5	2664 (44.3)	8702	415.1 (623.4)	179 (381)
Hb >10.5	4350 (72.3)	20,289	472.8 (615.1)	261 (429)

[a]Patients could change Hb categories during the study period.
Hb, hemoglobin; IQR, interquartile range.

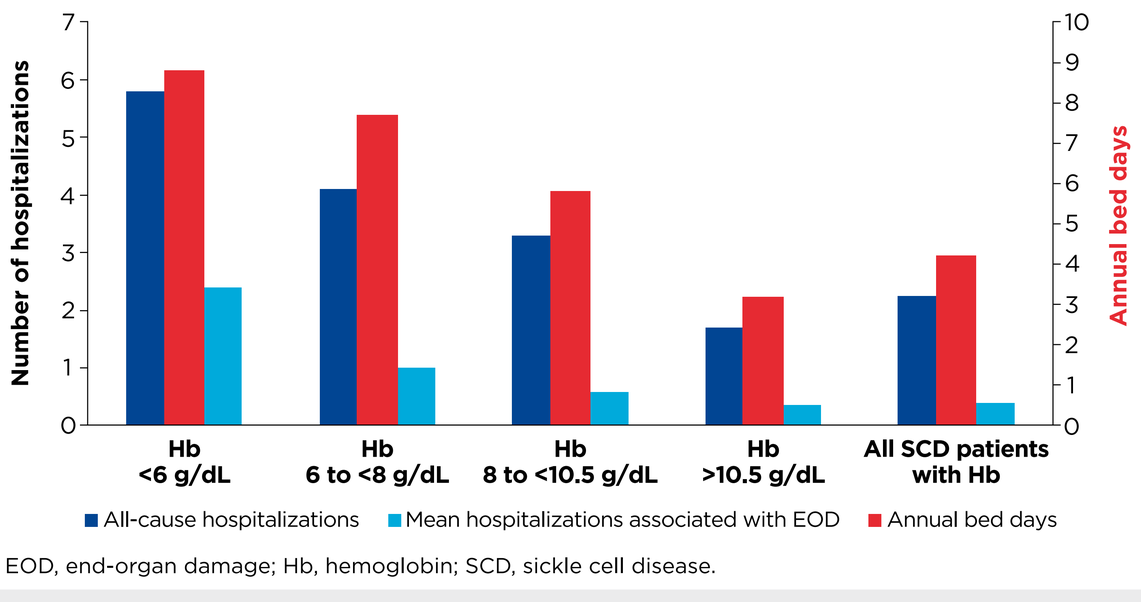
Hospitalizations

- The annualized rate of all-cause hospitalizations decreased as Hb category increased: 5.8 in patients with Hb <6 g/dL, 4.1 for 6 to <8 g/dL, 3.3 for 8 to 10.5 g/dL, and 1.7 for >10.5 g/dL (**Figure**).
- Hospitalizations were significantly lower for patients with a history of Hb >10.5 g/dL than for those with Hb <6 g/dL (P<0.001).
- Across Hb categories, the distribution of all-cause hospitalization was significantly different (P<0.001).
- A total of 385 (6.4%) patients had ≥1 hospitalization for any EOD.
- The annualized rate of hospitalizations for any EOD decreased as Hb increased: 2.4 in patients with Hb <6 g/dL, 1.0 for 6 to <8 g/dL, 0.6 for 8 to 10.5 g/dL, and 0.4 for >10.5 g/dL (**Figure**).
- Significantly fewer hospitalizations were attributable to any EOD in patients with intervals of Hb >10.5 g/dL compared to those with a history of Hb <6 g/dL (0.4 and 2.4 hospitalizations per patient interval per year, respectively; P<0.001).

Annual Bed Days

- Annual all-cause bed days decreased across increasing Hb categories, with a mean of 8.8 days in patients with a history of Hb <6 g/dL, 7.7 days with 6 to <8 g/dL, 5.8 days with 8 to 10.5 g/dL, and 3.2 days with >10.5 g/dL (**Figure**).
- A significant decrease in annual bed days was observed in patients with intervals of Hb >10.5 g/dL compared with Hb <6 g/dL (P<0.001).
- Across Hb categories, the distribution of the difference in bed days was significantly different (P<0.001).

Figure. Hospitalizations and Annual Bed Days by Hb Category



EOD, end-organ damage; Hb, hemoglobin; SCD, sickle cell disease.

CONCLUSIONS

- All-cause hospitalizations and annual bed days were progressively reduced in patients with intervals of higher Hb levels, whereas patients with severe anemia did not experience the same benefit.
- EOD-related hospitalizations were considerably less frequent for patients with intervals of Hb >10.5 g/dL compared with those for patients with intervals of Hb <6 g/dL.
- Our findings support the importance of the use of treatments that improve Hb, which may lead to a reduction in all-cause hospitalizations in patients with SCD.

ACKNOWLEDGMENTS

- We thank all the patients with sickle cell disease, families, caregivers, research nurses, study coordinators, and support staff who contributed to this study.
- Brittany Ulrich, PhD (Healthcare Consultancy Group, funded by Global Blood Therapeutics), provided editorial and writing assistance.

DISCLOSURES

- **Paul Telfer:** research funding: Bluebird Bio; honoraria: Global Blood Therapeutics, Terumo, Bluebird Bio; membership: Global Blood Therapeutics, Pfizer, ApoPharma. **Judith Ruzangi:** employee: CorEvitas Specialty EMR Data division, which was funded by Global Blood Therapeutics to conduct this research. **Sara João Carvalho:** employee: CorEvitas Specialty EMR Data division, which was funded by Global Blood Therapeutics to conduct this research. **Giovanna Barcelos:** employee: Global Blood Therapeutics. **Anne Beaubrun:** employee, equity ownership: Global Blood Therapeutics. **Caoimhe T. Rice:** employee: CorEvitas Specialty EMR Data division, which was funded by Global Blood Therapeutics to conduct this research.

REFERENCES

1. Kato GJ, Piel FB, Reid CD, et al. Sickle cell disease. *Nat Rev Dis Primers*. 2018;4:18010.
2. Brousseau DC, Owens PL, Mosso AL, et al. Acute care utilization and rehospitalizations for sickle cell disease. *JAMA*. 2010;303(13):1288-1294.
3. Campbell A, Cong Z, Agodoa I, et al. The economic burden of end-organ damage among Medicaid patients with sickle cell disease in the United States: a population-based longitudinal claims study. *J Manag Care Spec Pharm*. 2020;26(9):1121-1129.

Presented at the 17th Annual Academy for Sickle Cell and Thalassaemia (ASCAT) conference; October 20-22, 2022; London, UK.