

Racial differences in red blood cell transfusion in hospitalized patients with anemia

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Abstract

Background: Guidelines recommend transfusion of red blood cells (RBC's) when a hospitalized patient's hemoglobin (Hb) drops below a restrictive transfusion threshold, either at 7 or 8 g. Hospitals have implemented transfusion policies to encourage compliance with guidelines and reduce variation in transfusion practice. However, variation in transfusion practice remains. The purpose of this study was to examine whether there is variation in the receipt of transfusion by patient race.

Methods: Hospitalized general medicine patients with anemia (Hb < 10 g/dL) were eligible. Chi-squared tests were used to compare the percent of patients receiving a transfusion by race overall and within strata of their nadir Hb. Linear regression was used to test the association between a patient's race, their nadir Hb, receipt of an RBC transfusion, and the number of units transfused.

Results: Four thousand nine hundred and fifty-one patients consented, including 1363 (28%) who received a transfusion. 71% of patients were African American, 25% were White, and 4% were Other Race. Overall African Americans were less likely to be transfused compared to Whites (25% vs. 30%, $p < .01$), and within Hb strata below a Nadir Hb of 9 g/dL (Hb 8.0–8.9 g/dL 1% vs. 7%, $p < .01$; 7.0–7.9 g/dL 15% vs. 28%, $p < .01$; <7 g/dL 80% vs. 86%, $p < .01$). African Americans also received fewer units of RBC's ($\beta = -.17$, $p < .01$) overall and at lower Hb levels ($\beta = .14$, $p < .01$) compared to Whites.

Discussion: The Hb level at which patients are transfused at and the total number of RBC units received during hospitalization differ by patient race.

KEYWORDS

hematology—red cells, RBC transfusion, transfusion practices

Abbreviations: CCI, Charlson comorbidity index; EHR, electronic health record; GI, gastrointestinal; Hb, hemoglobin; RBC's, red blood cells; SC, sickle cell anemia; UCMC, university of Chicago medical center.

1 | INTRODUCTION

The two most recent red blood cell (RBC) transfusion guidelines from the Association for the Advancement of Blood and Biotherapies (AABB), recommend transfusion

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when a hospitalized patient's hemoglobin (Hb) drops below a restrictive transfusion threshold, either at 7 or 8 g/dL.^{1,2} These guidelines are supported by a body of clinical trial evidence,³⁻¹⁰ and clinicians have responded by largely adopting restrictive transfusion practices and only transfusing patients when their Hb drops below a restrictive threshold. Reducing the use of transfusion to comply with restrictive transfusion guidelines has also resulted in a preference for single unit transfusions, compared to transfusing ≥ 2 units at a time.^{11,12} Together these practices have now become standard of care for clinicians when treating anemia in hospitalized patients.¹³⁻¹⁵ Since transfusion is a common inpatient procedure,^{16,17} hospitals have utilized the electronic health record to implement these transfusion policies in an attempt to increase compliance with guidelines and standardize transfusion practice across providers.¹⁸⁻³¹ Moreover, improving compliance with and reducing variation in the use of transfusion outside of restrictive transfusion practices has become a hospital quality metric.^{26,28,31-33}

However, despite the widespread acceptance and adoption of restrictive transfusion practices, variation in transfusion practice does exist,³⁴⁻³⁹ including variation in transfusion practice by patients' race.⁴⁰⁻⁴⁵ Variation in transfusion practice by race is concerning because it may represent a healthcare disparity, since it is not supported by empiric data or guidelines. Previous studies in adult surgical patients where restrictive transfusion practices would be standard of care have found that African Americans receive more perioperative transfusions when undergoing major surgery (CABG, Hip replacement) than do Whites,⁴⁰ and are less likely to receive an autologous transfusion (rather than allogenic) when undergoing orthopedic surgery than are Whites.⁴¹ However, the data from these studies do not address whether there is variation outside of restrictive transfusion practices by race, and these studies were conducted before the widespread implementation of uniform restrictive transfusion policies enacted to discourage practice variation. Moreover, these studies were limited to narrow surgical patient populations and their findings may not be generalizable, since the largest volume of inpatient transfusions occurs in general medicine patients.⁴⁶ As a result, whether there is variation in the use of transfusion by race and outside of standard of care restrictive transfusion practices remains unknown.

Therefore, the purpose of this study was to examine transfusion practices in hospitalized general medicine patients, and test for differences in the Hb level at which patients are transfused at and the total number of RBC units received by patients' race.

2 | METHODS

2.1 | Study design and eligibility

The data for this study comes from an ongoing (2018-) prospective observational study of quality of life and symptoms in hospitalized general medicine patients with anemia at the University of Chicago Medical Center (UCMC). Any hospitalized adult (≥ 18 years old) general medicine patient with a Hb < 10 g/dL at any point during their hospitalization was eligible for study participation, and all participating subjects provided written informed consent. At UCMC the general medicine services do not care for or include surgical, trauma, pediatric, obstetrics/gynecology, cardiology, or oncology patients, and as such those patients were not eligible for this study. Patients with sickle cell anemia were eligible for study participation, but excluded from this analysis because they have different transfusion practices and guideline recommendations than other hospitalized general medicine patients.⁴⁷ Patient's identifying as Jehovah Witness (2%) were included in the sample because some of them received transfusion (4%), not all of them identified as African American (3%), and a sensitivity analysis removing them did not change any results. This study was approved by the University of Chicago Institutional Review Board.

2.2 | Patient demographic data

Hospital administrative data (including: electronic health record [EHR] and diagnosis codes) was used to determine patients' age, sex, race/ethnicity, length of stay (LOS), receipt of red blood cell transfusion, Hb levels, and comorbidities. Race and ethnicity were self-reported and optional for all patients, with the available racial and ethnic categories matching those defined by the NIH (Race: American Indian or Alaskan Native, Asian/Mideast Indian, Black/African American, More than One Race, Native Hawaiian/Other Pacific Islander, Patient Declined to Identify Race, Unknown, and White; Ethnicity: Hispanic or Latino, Not Hispanic or Latino, Patient Declined to Identify Ethnicity, and Unknown). A Charlson Comorbidity Index (CCI) score was calculated for all patients using International Classification of Disease 10 codes. Health Care Utilization Project diagnosis categories were used to identify patients with sickle cell anemia (SC) and/or gastrointestinal (GI) bleeding, since these diagnoses are not included as part of the Charlson Comorbidity Index. Given the low number of non-African Americans and non-Whites cared for at our institution and enrolled in this study ($< 5\%$), racial categories were condensed and analyzed as a categorical variable including African American, White, and Other.

2.3 | Restrictive transfusion policies

The EHR at UCMC utilizes a transfusion specific computerized provider order entry form, and the ordering form highlights a Hb <7 g/dL as a restrictive transfusion threshold.

2.4 | Statistical analysis

Descriptive statistics were used to characterize the demographic and clinical characteristics of study participants, including patients' Hb levels during hospitalization, whether they received a transfusion, and how many units of RBC were transfused. After reviewing the descriptive data on the number of RBC units transfused in all study participants, a decision was made to limit all analyses to the 95% of patients in the study who received ≤ 7 units of RBC transfusion (0–7) during hospitalization. This was to account for and minimize any spurious statistical effect stemming from the 5% of patients with a very large number of transfused RBC units.

Chi-squared tests were used to compare the percent of patients receiving or not receiving a transfusion by race overall during their hospitalization, and within strata of their nadir Hb during hospitalization (Hb 10–9 g/dL, 8.9–8.0 g/dL, 7.9–7.0 g/dL, <7 g/dL). Among patients receiving a transfusion, Kruskal–Wallis tests were used to compare the average number of RBC units received during hospitalization by race overall during their hospitalization, and within strata of their nadir Hb during hospitalization.

A linear regression model was specified to test the association between a patient's race, their nadir Hb, whether they received an RBC transfusion, and the number of units transfused. The primary dependent variable in this model was the total number of RBC's units transfused during hospitalization, and the independent variables of interest included patient's race, nadir Hb level during hospitalization, and an interaction between patient's race and nadir Hb level during hospitalization. For ease of interpretation nadir Hb was mean centered (7.9 g/dL) in the model, so that the intercept for patient's race could be interpreted at the mean nadir Hb rather than at a Hb = 0 g/dL. The model controlled for patient's age, gender, ethnicity, and Charlson Comorbidity Index score. We also performed a stratified analysis using this model in patients with GI bleeding and without GI bleeding. Last, ethnicity was removed in the final reported models because it was collinear with race, and removing it did not affect the size or direction of the coefficients for the other independent variables.

Statistical analysis was performed using the Stata statistical software, version 17, StataCorp, College Station, TX.

3 | RESULTS

3.1 | Patient characteristics

A total of 5028 patients provided consent for study participation and did not have a diagnosis of sickle cell anemia. Of these, 77 (5%) patients were transfused ≥ 8 units of RBC's during their hospitalization and excluded from analysis, leaving 4951 patients in the analytic sample. In the analytic sample 1363 (28%) patients received at least 1 unit of RBC transfusion. The overall average age of the sample 60 years old, 58% were female, and 94% were not Hispanic or Latino. The average admission Hb was 9.7 (± 1.9), and the average nadir Hb was 7.9 (± 1.3). Overall 9% ($n = 443$) of the patients in the sample had a diagnosis of GI bleeding.

The racial breakdown of the sample was 71% ($n = 3519$) African American, 24% ($n = 1168$) White, and 5% ($n = 264$) Other. The average age of African Americans and Whites was slightly older than patients of Other race. There were fewer White females and females of Other race than African Americans females, and a higher percentage of patients of Other race were also Hispanic or Latino, than either African Americans or Whites in the sample. There were no differences in the average admission Hb ($p = .49$) or Nadir Hb ($p = .69$) between patients of African American, White, and Other race. There were however a higher percentage of White and Other race admitted for GI bleeding than African Americans ($p < .01$). All patient characteristics, both overall and by race, are reported in Table 1.

3.2 | Transfusion percentages by race and nadir Hb

Figure 1 reports the percentage of patients transfused overall and within each Hb strata. Overall 25% ($n = 861$) of African Americans in the study received a transfusion, compared to 30% ($n = 352$) of Whites and 28% ($n = 73$) of Other patients ($p < .01$). For patients with a nadir Hb <7 g/dL, for which restrictive transfusion guidelines would suggest any patient be transfused, 80% of African Americans, 86% of Whites, and 92% of Other patients received a transfusion ($p < .01$). Similarly, for patients with a nadir Hb between 7.0 and 7.9 g/dL which is within restrictive transfusion threshold ranges and for which a transfusion would be considered consistent with transfusion guidelines, 15% of African Americans, 28% of Whites, and 12% of Other patients received a transfusion ($p < .01$). For patients with a nadir Hb between 8.0 and 8.9 g/dL which is above

TABLE 1 Patient characteristics

	All patients (n = 4951)	African American (n = 3519)	White (n = 1168)	Other (n = 264)
Age (years) mean, (SD)	60 (16)	60 (17)	61 (16)	56 (16)
Female n, (%)	2847 (58)	2179 (62)	526 (45)	142 (54)
Ethnicity				
Not Hispanic or Latino	4647 (94)	3497 (99)	1049 (90)	101 (38)
Hispanic or Latino	304 (6)	22 (1)	119 (10)	163 (62)
Length of stay (days) median (IQR)	6.1 (3.8–11)	6.0 (3.7–10)	7.1 (4.0–13)	5.9 (3.7–12)
Charlson comorbidity index n, (%)				
0	529 (11)	358 (10)	142 (12)	29 (11)
1–2	1366 (28)	991 (28)	302 (26)	73 (28)
3–4	1096 (22)	812 (23)	231 (20)	53 (20)
>5	2960 (39)	1358 (39)	493 (42)	109 (41)
Hemoglobin (Hb) mean, (SD)				
Admission Hb g/dL	9.7 (1.9)	9.7 (2.0)	9.6 (1.8)	9.7 (1.9)
Nadir Hb g/dL	7.9 (1.3)	7.9 (1.3)	7.9 (1.2)	7.9 (1.3)
GI bleeding n, (%)	443 (9)	285 (8)	124 (11)	34 (12)

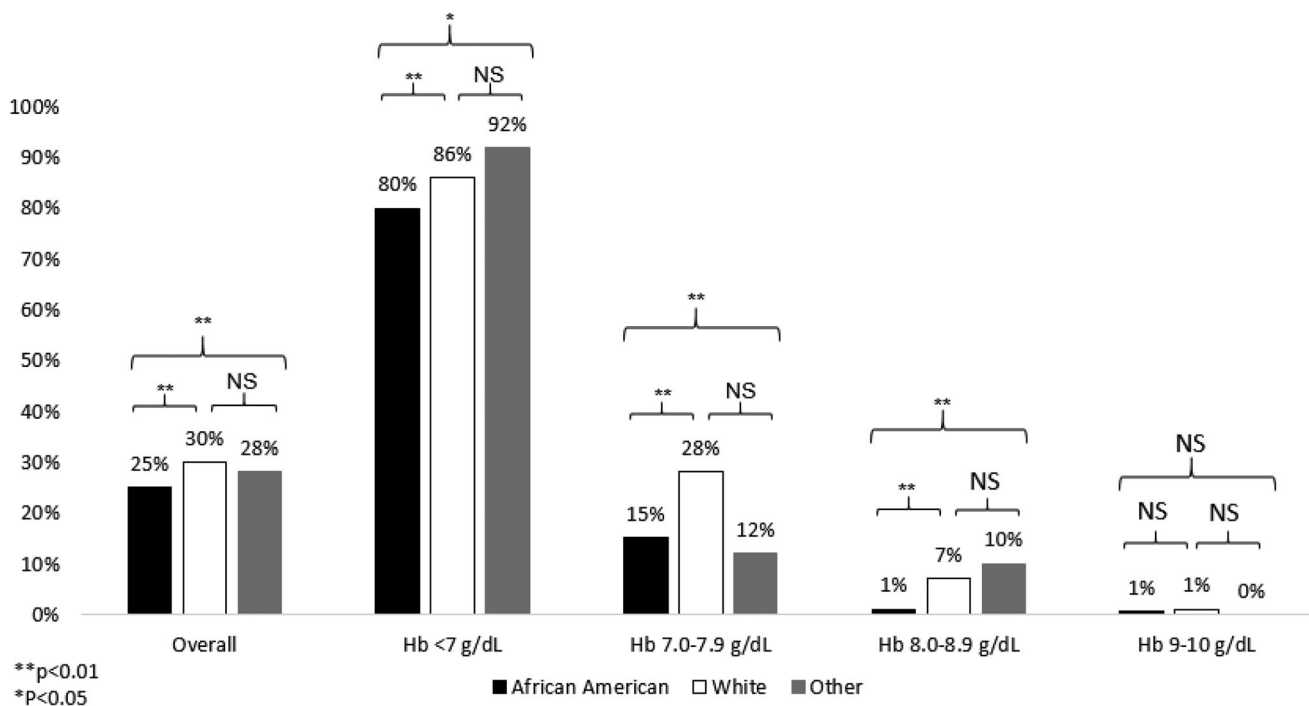


FIGURE 1 Percent of patients transfused by race and nadir Hb level

restrictive transfusion threshold, 1% of African Americans, 7% of Whites, and 10% of Other patients received a transfusion ($p < .01$). Last, consistent with restrictive transfusion guidelines, almost no patients of any race received a transfusion with a nadir Hb between 9 and 10 g/dL (African American 1%, White 1%, Other Race 0%, $p = .39$).

3.3 | Association between race, nadir Hb and transfusion

Despite differences in the percentage of patients transfused by race, among patients that were transfused in unadjusted analysis there were not differences in the

TABLE 2 Mean (SD) number of RBC's transfused by hemoglobin level and race

	All patients (n = 1286)	African American (n = 861)	White (n = 352)	Other (n = 73)	p-value ^a
Overall	2.1 (1.4)	2.1 (1.3)	2.2 (1.5)	2.2 (1.4)	.43
Hb 10–9 g/dL	1.3 (0.49)	1.5 (0.6)	1 (0)	No Data	.18
Hb 8.9–8.0 g/dL	1.8 (1.3)	1.4 (0.5)	2.1 (1.6)	1.5 (0.5)	.58
Hb 7.9–7.0 g/dL	1.5 (0.96)	1.6 (1.1)	1.4 (0.6)	1.8 (1.6)	.96
Hb <7.0 g/dL	2.2 (1.4)	2.1 (1.4)	2.5 (1.6)	2.1 (1.1)	.06

Note: Sample includes only patients receiving a transfusion and is restricted to patients with seven or less transfusions during hospitalization.

^ap-values represent Kruskal–Wallis test comparing the average number of RBC units transfused across Hb level (rows) by racial group.

TABLE 3 Association between race and units of RBC transfusion during hospitalization

	All patients (n = 4951)	Excluding patients with GIBL (n = 4508)	Only patients with GIBL (n = 443)
African American ^a	−0.17 (−0.23, −0.11)**	−0.13 (−0.19, −0.07)**	−0.28 (−0.60, 0.03)
Other ^a	−0.08 (−0.21, 0.04)	−0.03 (−0.15, 0.10)	−0.33 (−0.85, 0.18)
Nadir Hb ^b	−0.68 (−0.72, −0.64)**	−0.60 (−0.64, −0.55)**	−0.88 (−1.1, −0.70)**
African American × Nadir Hb ^a	0.14 (0.09, 0.19)**	0.09 (0.04, 0.14)**	0.26 (0.05, 0.46)*
Other × Nadir Hb ^a	0.08 (−0.14, 0.18)	0.02 (−0.07, 0.13)	0.30 (−0.03, 0.64)

^aReferent category is white. Columns report estimated β coefficient and (95% CI).

^bNadir Hb variable is mean centered. Models control for age, gender, and Charlson comorbidity index score and are limited to patients who received seven or less units of RBC's during hospitalization. ** $p < .01$, * $p < .05$.

number of units transfused by patient race either overall or within any Hb strata (Table 2).

In the adjusted regression models, African Americans received less units of RBC's overall compared to Whites ($\beta = -.17$, $p < .01$) at any nadir Hb level, and the amount of transfusion varied across nadir Hb levels compared to Whites (African American × Nadir Hb, $\beta = .14$, $p < .01$). The interaction term between African American and Nadir Hb can also be interpreted as African Americans receiving less transfusion at decreasing and lower Nadir Hb values compared to Whites. Although patients of Other race also received less transfusion overall ($\beta = -.08$, $p < .19$) and at decreasing and lower nadir Hb levels compared to Whites ($\beta = .08$, $p < .09$), the effects were not statistically significant (Table 3).

In the model that included only patients with GI bleeding, the differences in the number of units transfused by race were larger than in the overall model. Both African Americans ($\beta = -.28$, $p = .08$) and patients of Other race ($\beta = -.33$, $p = .21$) received less units of RBC's compared to Whites, but the effect of these lower order variables were not statistically significant. However, African Americans received fewer RBC's units compared to Whites across lower levels of nadir Hb ($\beta = .26$, $p = .01$), and this interaction effect was statistically significant. In the stratified model excluding patients with GI bleeding, the effects where the

same as in the overall model and the model with only GI bleeding patients, but the difference in the amount of RBC units African Americans received compared to Whites was smaller (Table 3).

4 | DISCUSSION

These data suggest that there are differences by race in the Hb level at which hospitalized patients are transfused and the total number of RBC units they receive. African Americans were less likely to be transfused overall and within each decreasing Hb strata during hospitalization below 9 g/dL compared to Whites. African Americans also received fewer units of RBC transfusion overall during hospitalization and fewer RBC units at lower Hb levels compared to Whites. This effect was greater in patients with GI bleeding.

These observed differences in the receipt of transfusion by race do meet the definition of a healthcare disparity.⁴⁸ However, when interpreted in the context of restrictive transfusion guidelines, it is less clear whether these differences represent worse care for any single racial group compared to others. Restrictive transfusion guidelines have been informed by clinical trial data showing that transfusion at liberal (or higher) Hb thresholds does not

improve mortality compared to transfusion at restrictive Hb thresholds (7–8 g/dL). Since transfusion does include some risk of a transfusion reaction and other adverse events,⁴⁹ any transfusion above restrictive threshold levels is perhaps not only unnecessary, but also potentially harmful. As such, the greater use of transfusion observed in patients of White and Other race with a Hb between 8.0 and 8.9 g/dL is discordant with guidelines, and would be considered unnecessary over-transfusion. Additionally, although the use of transfusion in patients with a Hb between 7 and 8 g/dL is consistent with restrictive transfusion guidelines, for most stable hospitalized patients there is stronger data to support and our electronic health record encourages a <7 g/dL Hb threshold. Therefore, the significantly higher percentage of Whites receiving transfusion between a Hb 7.0–7.9 g/dL could be considered harmful over-transfusion, rather than under-transfusion of African Americans and patients of Other race. Similarly, the greater number of RBC's units that Whites received compared to African Americans or Other patients may actually be over-transfusion, if the extra units of RBC's were transfused when the patients Hb was already above the restrictive transfusion threshold of 7 g/dL, including in GI bleeding patients.⁸ However, in the Hb <7 g/dL group where guidelines would suggest all patients receive transfusion, 20% of African Americans did not receive transfusion. While a non-trivial amount of White and Other patients also were not transfused within this Hb strata, there is no obvious explanation for why African Americans should have the lowest rate of transfusion among the racial groups examined. Not receiving transfusion with a Hb <7 g/dL during hospitalization is guideline discordant, and African Americans were the racial group most affected by under-transfusion. Regardless, while some patients in this study were over-transfused (whites), and some were under-transfused (African Americans), the differences detected in transfusion by race represent poor adherence to transfusion standards, and are concerning because they are not supported by empiric data or guidelines.

These data and the differences in transfusion practice by race raise several issues with respect to the quality of care and the use of transfusion in hospitalized patients with anemia. First, despite the widespread acceptance of restrictive transfusion practices, clinicians still transfuse outside of guideline recommendations. Although it has been suggested that the EHR can be a tool for standardizing clinical processes, our data suggest that even with concise practice guidelines embedded into the EHR to promote guideline adherence and practice uniformity, variation in practice still exists. Moreover, even if overall adherence to restrictive transfusion practices is high, variation in care by patient and provider level factors still

occur and can result in disparities in care. Since both improved quality of care and reducing healthcare disparities are national priorities, health systems should be attentive to and ensure that variation in transfusion practice is not occurring by patient level factors not supported by empiric data, such as patient's race. Second, better understanding and data on why clinicians may still vary in their use of transfusion, particularly outside of restrictive transfusion practices may be useful. For example, there is a body of observational data suggesting that transfusion at higher Hb levels may alleviate patients' symptoms of anemia,^{50–55} and the clinical transfusion trials to date have not adequately studied the effect of restrictive transfusion on patient-reported outcomes like symptoms.^{56,57} If clinicians are incorporating individual clinical factors, such as the severity of a patients' symptoms and patient preference, into the decision to transfuse outside of restrictive transfusion guidelines, requiring global adherence to uniform restrictive transfusion may not be optimal care for all patients. Therefore, more specific data on the clinical factors that clinicians consider when transfusing a patient may help identify important scientific and clinical questions to study, or targets for further standardizing clinical processes.

5 | LIMITATIONS

This study has several limitations. First, it is an observational study from a single academic medical center, and the results may not be generalizable to other institutions. Second, while we measured and adjusted for potentially confounding variables that could influence transfusion decisions, there may be additional confounding variables that we did not consider and control for. Third, we did not have provider level data to compare to patient level transfusion data. Providers recommend to and order transfusion for hospitalized patients, and so provider level data would improve understanding of whether transfusion was offered but declined, and could help explain some variation by race in the receipt of transfusion for hospitalized patients. Fourth, although shortages of RBC's have not resulted in any limits on transfusion at our institution, we do not have allo-immunization data on individual patients in our study that could account for some patients not receiving transfusion due to a lack of available matched RBC's. Fifth, we had a limited number of non-African American non-White racial groups in our study, and as a result in our model we could not compare the transfusion patterns in specific other racial groups, or account for the possibility of intersectionality with ethnicity and/or other sociodemographic factors that may influence transfusion patterns.

6 | CONCLUSION

The Hb level at which patients are transfused at and the total number of RBC units received during hospitalization differ by patient race, with African Americans being less likely to be transfused overall and receiving less RBC units during hospitalization than Whites. These differences in transfusion practices by race represent poor adherence to transfusion standards, and further work needs to be done understand the cause of these differences and their impact on patients.

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CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest.

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