Predictive Factors for Hemoglobin Level Increases After Red Blood Cell Transfusion: The Role of BMI and BSA

Ali Habib[1], Firas Hussein[2], Suzanne Alshemali [3]

[1] Master's Student in the Hematology Department in Latakia University, Latakia, Syria (MD).
[2] Professor in the Hematology Department in Latakia University, Latakia, Syria (PhD).
[3] Lecturer in the Department of Laboratory Medicine in Latakia University, Latakia, Syria.

ABSTRACT:

Introduction: Red blood cell transfusion is a routine medical practice in hospitals. Currently, there is no reliable hypothesis to determine the optimal number of concentrates to transfuse or to accurately predict the increase in hemoglobin levels following transfusion in adults. Traditionally, it has been assumed that transfusing one unit of red blood cell concentrate in a hemodynamically stable adult will result in an increase of 1 g/dL in hemoglobin and 3% in hematocrit. However, this assumption is not consistently accurate, highlighting the need for additional indicators to assess each patient's specific requirements for red blood cell concentrates.

Objective: This study aims to evaluate the predictive value of (BMI) and (BSA) in determining the requirement for one or more units of red blood cell concentrates in hemodynamically stable adult patients, specifically to anticipate a 1 g/dL increase in hemoglobin levels..

Study design & Methods: A prospective cross-sectional study was conducted involving 99 patients who attended Latakia University Hospital in 2024. Participants were selected based on criteria for hemodynamic stability. BMI and BSA were calculated (using the Du Bois formula for BSA). The change in hemoglobin levels following a single red blood cell concentrate transfusion was assessed. A patient was classified as a positive (favorable) responder if there was an increase of 1 g/dL or more in hemoglobin levels post-transfusion.

Results: Among the 99 patients (66 males: 33 females) studied, 66 exhibited a positive response to the transfusion, while 33 demonstrated a negative response. BMI cutoff for achieving a 1 g/dL increase in hemoglobin was determined to be 23.55 kg/m² ($P < 0.0001$), with a sensitivity and a specificity of 75.8%, 57.6% respectively. BSA cutoff was found to be 1.88 m² ($P < 0.0001$), with a sensitivity and a specificity of 86.4%, 87% respectively. Therefore, our results show that patients with a BMI of 23.55 kg/m² or less and a BSA of 1.88 m² or less would require only one unit of red blood cell concentrate to achieve a 1 g/dL increase in hemoglobin. In contrast, patients with values exceeding these cutoffs would necessitate more than one unit to achieve similar increase.

Conclusion: BSA, as calculated using the Du Bois formula, is a more reliable predictor of post-transfusion hemoglobin improvement compared to body mass index in hemodynamically stable patients receiving a single unit of red blood cell concentrate. Therefore, BSA should be considered when determining transfusion requirements to minimize the risk of overtransfusion.

Key words: Blood transfusion, Red blood cell concentrate, BSA, BMI.

Introduction:

Blood transfusion is one of the most common medical practices worldwide and can be considered a straightforward form of organ transplantation. [1] However, it carries potential complications, including immunological reactions and hemolytic events. [2] The global demand for blood transfusions and their derivatives continues to rise, while the number of voluntary donors remains insufficient. For instance, in the United States alone, approximately 29,000 units of concentrated red blood cells are transfused daily, yet the donation rate is less than 3% of the population.[3] [4]

Blood transfusion is a critical intervention in cases of acute blood loss due to trauma, surgical procedures, or conditions such as hemolysis. It also plays a vital role in managing chronic anemia, providing symptomatic relief and allowing time for further diagnostic evaluation. [5] While maintaining a hemoglobin level between 7-8 g/dL is often deemed acceptable in hemodynamically stable patients, clinical judgment should guide transfusion decisions, prioritizing the patient's overall condition and specific indications over strict laboratory thresholds. [6]

Despite numerous studies aimed at identifying reliable predictors of hemoglobin increase post-transfusion, no universally accepted rule exists for adults. Research has suggested various factors that may influence hemoglobin response, including donor characteristics (such as age and gender), recipient demographics, body mass index (BMI), and body surface area (BSA). However, these findings remain inconclusive and cannot yet be generalized across diverse patient populations. [7] [8]

Currently, the prevailing guideline is the (3:1) rule, which posits that transfusing one unit of red blood cell concentrate in a stable adult will increase hemoglobin by approximately 1 g/dL and hematocrit by 3%. However, this rule has proven ineffective in many clinical scenarios. [9]

Given the escalating demand for blood products and the need to minimize waste, our study aims to evaluate the roles of BMI and BSA —readily available and cost-effective indicators— in determining their relationship with hemoglobin increases following transfusion. The goal is to establish threshold values that can help ascertain a patient's requirement for one or more units of red blood cell concentrate to achieve a target hemoglobin increase of 1 g/dL.

Patients and methods:

<u>Study design and patients selection:</u>

This study was conducted in the Hematology Department of Latakia University Hospital, a central university hospital in Syria. Data were collected from patients who received red blood cell concentrate transfusions between January 2024 and April 2024, adhering to the established inclusion criteria [Table 1].

All hemoglobin measurements were obtained using a single device, the Sysmex Automated Hematology Analyzer XP series (Japan, 2014). Pre-transfusion hemoglobin levels were recorded at least 12 hours prior to the transfusion, while post-transfusion hemoglobin levels were assessed within 6 to 24 hours after the procedure.

During the transfusion, red blood cell concentrates of 250 mL were administered, with an average transfusion duration of 2 hours for all patients. The following data were systematically recorded: patient age (years), sex, height (cm), weight (kg), hemoglobin levels before and after transfusion (g/dL), and the change in hemoglobin value (ΔHgb, g/dL). BMI and BSA-Du Bois were calculated.

Table1: The inclusion and exclusion criteria for the study.

Inclusion criteria	Exclusion criteria
• Age >18 years. • Hemodynamically stable patient (defined as consciousness, ability to swallow, mean blood pressure >80	• Active hemolysis or hemolysis. • Hypersplenism. • Hemoglobipathies. • Development of complications during transfusion.

mmHg, pulse between 60-100 beats/min, and oxygen saturation >92%).	• Failure to complete the transfusion. • Presence of a volume imbalance. (Dehydration, shock, overload, albumin or urea disorder.) • Use of diuretics during or prior to transfusion.

Body mass index (BMI; kg/m²) was calculated as weight (kg) divided by the square of height (m). Body surface area (BSA; m²) was determined using the Du Bois formula [Table 2]. The change in hemoglobin (ΔHgb) was defined as the post-transfusion hemoglobin level minus the pre-transfusion hemoglobin level (g/dL). Patients with $\Delta Hgb \geq 1$ g/dL were classified as "positive responders," while those with $\Delta Hgb < 1$ g/dL were classified as "negative responders.

Table2: The Du Bois formula.

Du Bois Formula
BSA (m^2) = 0.007184 × (height (cm))$^{0.725}$ × (weight (kg))$^{0.425}$

<u>Statistical analysis:</u>

Descriptive statistics, including mean and standard deviation, were calculated for continuous variables within the study group, with data presented as mean ± standard deviation. Patients were categorized into two groups based on their response to transfusion: the positive response group and the negative response group, as defined by the study variables.

Receiver Operating Characteristic (ROC) analysis was employed to determine the optimal cutoff values for both (BMI) and (BSA) in predicting improvements in hemoglobin levels following transfusion. All statistical analyses were conducted using IBM SPSS Statistics version 2024. A p-value of less than 0.05 was considered statistically significant.

Results:

The final research sample included 99 patients. There was 66 males (66.77%), 33 females (33.33). Demographic and clinical characteristics are presented in [table. 3]

Table.3: Demographic and Clinical Characteristics

Variable	(Mean±SD)
Age (years)	46.73±19.04
Body weight (kg)	69.32±19.96
Height (cm)	172.2±10.49
BMI (kg/m²)	23.38±6.24
BSA (m²)	1.825±0.211
PRBC age (days)	2.06±2.62
pre-transfusion Hgb check (hours)	10.26±2.45
hemoglobin increment (g/dl)	1.12±0.48

A total of 66 patients (66.67%) exhibited a positive response in hemoglobin levels following transfusion, while 33 patients (33.33%) demonstrated a negative response. To assess the predictive value of (BMI) and (BSA) for hemoglobin improvement, a Receiver Operating Characteristic (ROC) curve analysis was conducted, as illustrated in Figure 1

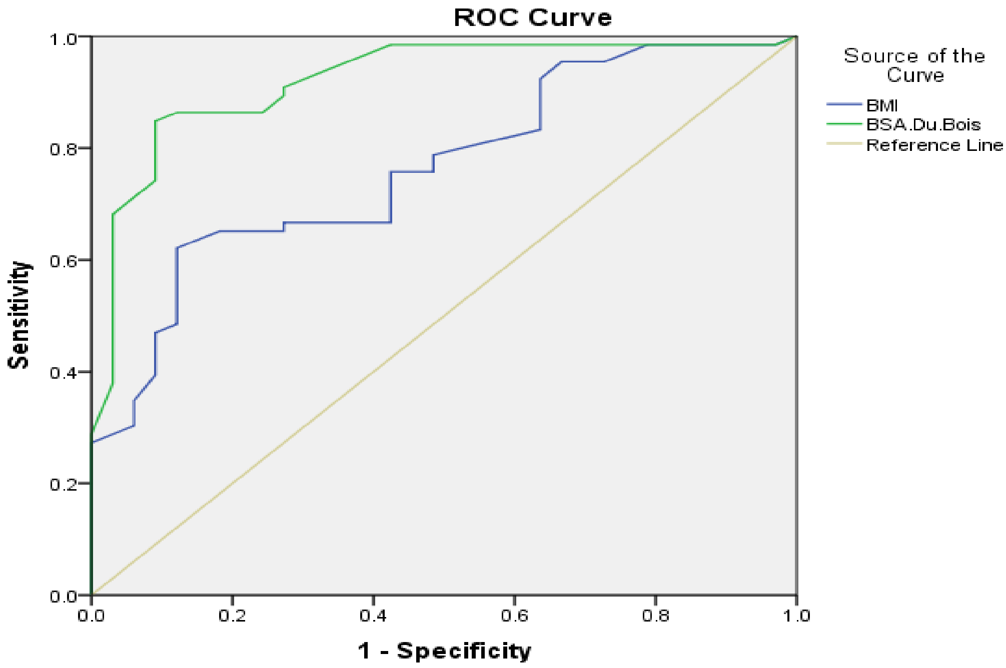

Figure 1: ROC curve for (BMI) and (BSA) calculated using the Du Bois formula for predicting hemoglobin improvement in patients following blood transfusion

Variable	Area Under the Curve (AUC)	Cut-off	Sensitivity	Specificity	p-value
BMI	0.765	**23.55**	75.8%	57.6%	**< 0.0001**
BSA – Du Bois	0.921	**1.88**	86.4%	87.9%	**< 0.0001**

Table 4: The significance of (BMI) and (BSA) in predicting hemoglobin improvement following a single unit transfusion in hemodynamically stable patients

[Table 4] presents the predictive value of (BMI) for improvement in hemoglobin levels following the transfusion of one unit of red blood cell concentrate. The area under the curve (AUC) for BMI was 0.765, with a cut-off value of 23.55 kg/m² yielding a sensitivity of 75.8% and a specificity of 57.6% ($P < 0.0001$) for an increase in hemoglobin of 1 g/dL.

In contrast, (BSA) demonstrated superior predictive capability for hemoglobin improvement, with an AUC of 0.921. At a cut-off value of 1.88 m², BSA exhibited a sensitivity of 86.4% and a specificity of 87.9% ($P < 0.0001$) for an increase in hemoglobin of 1 g/dL

Discussion:

The challenge of accurately predicting the increase in hemoglobin levels following blood transfusion in adults remains a significant obstacle in clinical transfusion medicine. Numerous studies have sought to establish reliable predictive models. Notably, the study by Huber et al. demonstrated an average increase in hemoglobin of 0.9 ± 0.1 g/dL in a cohort of 16 patients after a single transfusion of red blood cell concentrate. This finding led to the adoption of the 3:1 rule, which has been utilized for an extended period in clinical practice. [10]

In this study involving 99 patients (66.67% male, 33.33% female), we evaluated the predictive value of (BMI) and (BSA) for hemoglobin improvement following a single unit of red blood cell transfusion. A total of 66 patients (66.67%) exhibited a positive response in hemoglobin levels. ROC curve analysis revealed that BMI had an area under the curve (AUC) of 0.765, with a cut-off value of 23.55 kg/m², sensitivity of 75.8%, and specificity of 57.6% ($P < 0.0001$). In contrast, BSA demonstrated superior predictive capability with an AUC of 0.921, a cut-off value of 1.88 m², sensitivity of 86.4%, and specificity of 87.9% ($P < 0.0001$). These findings suggest that BSA is a more reliable predictor of hemoglobin improvement post-transfusion compared to BMI, highlighting its potential utility in clinical transfusion practices.

The increase in hemoglobin levels following the transfusion of a single unit of red blood cell concentrate in hemodynamically stable patients is inversely proportional to both body surface area (BSA) and body mass index (BMI). Specifically, patients with a BMI of 23.55 kg/m² or less and a BSA of 1.88 m² or less are expected to achieve an increase in hemoglobin of approximately 1 g/dL. Therefore, it is advisable to consider administering additional units of red blood cell concentrate for patients whose measurements exceed these cut-off values, as .their response to transfusion may be diminished

The indicators utilized in our study— (BMI) and (BSA)—are simple, readily available, cost-effective, and easy to apply in the management of hemodynamically stable patients. Previous research has explored the role of these indicators in predicting hemoglobin increases following red blood cell transfusion. For instance, Lee et al. investigated the relationship between BSA and hemoglobin increase in hemodynamically stable patients, finding a significant inverse correlation. This finding aligns with our results. However, their study derived an equation related to BSA using the Monsteller formula and baseline hemoglobin values, which may limit the generalizability of their findings due to its single-center design and a relatively small sample size of 137 patients. [11]

In a related study, Sharma et al. investigated the role of (BSA) in predicting elevated hemoglobin levels in children. Their findings corroborated our results; however, rather than establishing specific cut-off values, they developed a formula based on BSA, similar to the approach taken by Lee et al. [11] [12]

Similarly, Man et al. examined the role of BSA in predicting hemoglobin increases and identified a cut-off value of 1.97 m² using the Du Bois formula, which was associated with a 1 g/dL increase in hemoglobin. Their methodology differed from ours, as they employed a derivation group to establish a logarithmic function for determining the cut-off value, which was then validated in a separate cohort. Their model achieved a sensitivity of 84.6% and a specificity of 43.8%. Despite the differences in cut-off values and methodologies, both studies corroborate the inverse correlation between BSA and hemoglobin increase. [8]

Regarding BMI, Roubinian et al. also reported an inverse correlation between BMI and hemoglobin improvement, consistent with our findings. Their study developed a complex linear function that incorporates multiple variables to predict hemoglobin increases, which may complicate its application across various clinical settings. The reliance on numerous donor and recipient factors necessitates further research before such a model can be widely adopted. [7]

Stein et al. validated the role of body mass index (BMI) in blood transfusion by evaluating Roubinian findings using their own sample population, ultimately arriving at similar conclusions. Additionally, Roubinian conducted a follow-up study with a different sample to further investigate the impact of BMI and found no significant differences from his initial results. [13] [14]

While our study did not establish a definitive predictive model for hemoglobin increase, we successfully demonstrated a correlation between the indicators used and their inverse relationship with hemoglobin improvement. Although the limit values identified may not be generalizable at this stage, these findings provide a foundation for future research. Broader studies are warranted to refine these results and potentially develop an evidence-based guideline for blood transfusion practices in adults.

Conclusion:

This study underscores the significance of (BSA) and (BMI) as predictive indicators of hemoglobin improvement following red blood cell transfusion in hemodynamically stable patients. Our findings demonstrate a strong inverse correlation between BSA and hemoglobin increase, with BSA proving to be a superior predictor compared to BMI. While previous studies have established similar relationships, our research contributes to the growing body of evidence supporting the use of these parameters in clinical transfusion practices. Although we did not develop a definitive predictive model, the correlations identified provide a foundation for future investigations. Further studies with larger, diverse populations are warranted to refine these findings and potentially establish standardized guidelines for optimizing transfusion outcomes in adult patients

References:

1. Karaboue K. History of the first organ transplant: blood transfusions. Med History [Internet]. 2023 Dec. 20 [cited 2024 Aug. 24]; 7(3):e2023049.

2. Callum JL, Pinkerton PH, Lima A, et al. *Bloody Easy 4: Blood transfusion, blood alternatives and transfusion reactions—a guide to transfusion medicine*. 4th ed. Ontario Regional Blood Coordinating Network; 2016.

3. American Red Cross. "Importance of the Blood Supply." Redcrossblood.org, 2023, www.redcrossblood.org/donate-blood/how-to-donate/how-blood-donations-help/blood-needs-blood-supply.html

4. ADRP, ARC. *America's Blood Centers (ABC) and ADRP*: The Association for Blood Donor Professionals Thank the Following Groups for Their Support and Involvement in Developing This Guide: ADRP Marketing Resource Committee Statistics and Public Messaging Guide. 2024.

5. Burns, Carolyn D. "Anemia and Red Blood Cell Transfusion in the Adult Non-Bleeding Patient." Annals of Blood, vol. 0, Jan. 2021, https://doi.org/10.21037/aob-21-51

6. Australian Red Cross Lifeblood. Blood Book: Australian Blood Administration Handbook. Melbourne, Australian Red Cross Lifeblood - Victoria, Mar. 2020.

7. Roubinian, Nareg H., et al. “Effect of Donor, Component, and Recipient Characteristics on Hemoglobin Increments Following Red Blood Cell Transfusion.” Blood, vol. 134, no. 13, 26 July 2019, pp. 1003–1013, https://doi.org/10.1182/blood.2019000773.

8. Man, Louise, and H. Raymond Tahhan. “Body Surface Area: A Predictor of Response to Red Blood Cell Transfusion.” Journal of Blood Medicine, vol. Volume 7, Sept. 2016, pp. 199–204, https://doi.org/10.2147/jbm.s105063.

9. Whitman, Lucinda, et al. SINGLE RED BLOOD CELL UNIT TRANSFUSION (ADULTS) NLBCP-050 Office of Administrative Responsibility Medical Advisor to the Provincial Blood Coordinating Program Manager, Provincial Blood Coordinating Program Issuing Authority Government of Newfoundland and Labrador Department of Health and Community Services Provincial Blood Coordinating Program. 2019.

10. Huber H, Lewis SM, Szur L. The influence of anaemia, polycythaemia and splenomegaly on the relationship between venous haematocrit and red-cell volume. Br J Haematol. 1964; 10:567–575. doi: 10.1111/j.1365-2141.1964.tb00733.x.

11. Lee, Jae Hyuk MD; Kim, Dong Hoon MD, PhD; Kim, Kyuseok MD, PhD; Rhee, Joong Eui MD, PhD; Kim, Tae Youn MD; Jo, You Hwan MD; Lee, Jin Hee MD; Suh, Gil Joon MD, PhD; Hwang, Seung Sik MD, PhD; Lee, Christopher C. MD; Singer, Adam J. MD. Predicting Change of Hemoglobin after Transfusion in Hemodynamically Stable Anemic Patients in Emergency Department. The Journal of Trauma: Injury, Infection, and Critical Care 68(2): p 337-341, February 2010. | DOI: 10.1097/TA.0b013e3181c9f3aa.

12. Sharma, Sankalp, et al. “Standardizing Blood Dose Using Body Surface Area and Analyze the Effect of Blood Storage on Hemoglobin Increment within Pediatric Patients.” Acta Haematologica Polonica, vol. 53, No 4 (2022), no. ISSN 0001–5814, 5 June 2022, https://doi.org/10.5603/ahp.a2022.0029.

13. Roubinian, Nareg H, et al. “Donor Genetic and Nongenetic Factors Affecting Red Blood Cell Transfusion Effectiveness.” JCI Insight, vol. 7, no. 1, 11 Jan. 2022, https://doi.org/10.1172/jci.insight.152598.

14. Stein, Brady L, and Mhs. “Factors Influencing Hemoglobin Increments after Transfusion.” Journal Watch, vol. 2019, 9 Oct. 2019, https://doi.org/10.1056/nejm-jw.na50103.