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Blood Transfusion Strategy in Patients with Moderate or Severe Traumatic Brain Injury: A Prospective Interventional Study

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Abstract:

Background: Traumatic brain injury (TBI) is a significant contributor to global morbidity and mortality. Determining optimal hemoglobin (Hb) transfusion thresholds in TBI remains debated due to the brain's vulnerability to anemia. This study investigates the effects of liberal versus restrictive transfusion strategies on survival, neurological recovery, ICU stay, and infectious complications in patients with moderate to severe TBI. **Methods:** A prospective interventional study was conducted at Benha University Hospitals from October 2024 to March 2025. Sixty patients with moderate (GCS 9–12) or severe (GCS 3–8) TBI and Hb <9.5 g/dL were enrolled. Participants were randomized into Group A (restrictive approach): transfusion for Hb <7.5 g/dL (n=30), and Group B (liberal approach): transfusion for Hb <9.5 g/dL (n=30). Primary outcome was mortality; secondary outcomes included neurological improvement, ICU length of stay, and infection incidence. Results: The liberal transfusion group showed higher survival (73.3% vs. 50%, p=0.041) and greater neurological improvement (73.3% vs. 50%, p=0.037) compared to the restrictive group. Mortality was lower in Group B (26.7% vs. 50%, p=0.041). Moderate TBI cases had survival of 81% in the liberal group versus 70% in the restrictive group, while severe TBI survival was 64% vs. 40%, respectively. Prolonged ICU stay (>7 days) occurred in both groups, but sepsis was more frequent in the restrictive cohort. **Conclusion:** Implementing a liberal transfusion threshold in moderate to severe TBI is associated with improved survival, neurological recovery, and reduced infectious complications. These results support higher transfusion thresholds as a potential approach to optimize patient outcomes.

Keywords: Traumatic Brain Injury; Blood Transfusion Approach; Hemoglobin Threshold; Neurological Recovery; Critical Care Outcomes.

Introduction

Traumatic brain injury (TBI) represents one of the most pervasive neurological disorders worldwide and continues to be a principal etiology of mortality and chronic disability [1]. Beyond the immediate insult, cases may experience progressive secondary injuries, which contribute to chronic neurological deficits, seizures, neuroendocrine disorders, and psychiatric sequelae [2]. Even though the primary damage is essentially irreversible, the unfolding secondary injury processes over weeks to months create an opportunity for targeted therapeutic interventions to improve clinical outcomes [3].

Within the ICU setting, anemia is highly prevalent and correlates with greater illness severity and prolonged hospitalization. While restrictive transfusion protocols, usually at an Hb threshold near 7 g/dL, are recommended for most critically ill cases due to lack of consistent survival benefit from liberal transfusions and potential complication risk [4], the optimal transfusion threshold for cases with TBI remains unresolved [5].

Blood transfusion, despite its life-saving potential, may precipitate adverse outcomes including febrile reactions, circulatory overload, hypersensitivity reactions, and rare but critical adverse events as transfusion-related acute lung injury (TRALI) and hemolysis [6]. Although infectious complications like hepatitis B, C, and HIV are now rare due to improved screening (National Heart), awareness of these risks underscores the importance of judicious transfusion practices.

Hemoglobin (Hb) titter is a key determining factor of cerebral oxygen delivery. Even mild anemia may be poorly tolerated by the injured brain due to impaired autoregulation, altered metabolic demands, and increased vulnerability to hypoxemia [7]. Anemia has also been linked to higher mortality in acute ischemic stroke [8], highlighting the potential importance of maintaining adequate Hb titters in neurologically injured cases. Nonetheless, whether raising Hb via transfusion improves oxygen utilization at the tissue levels remains uncertain [5].

In clinical practice, transfusion strategies must balance the benefits of optimizing cerebral oxygenation against the risks of transfusion-related complications. While some evidence favors restrictive strategies in general ICU populations, studies in brain-injured cases suggest that higher transfusion thresholds may confer neurological benefits. For instance, randomized and observational studies in acute brain injury have exhibited improved neurological outcomes and reduced ischemic complications with more liberal Hb thresholds [9-11].

Given the ongoing uncertainty and variability in practice, further prospective studies are essential to define transfusion thresholds that optimize survival and neurological recovery in TBI. Considering existing uncertainty, the current investigation aims to compare the effects of restrictive and liberal Hb transfusion thresholds on mortality, neurological recovery, ICU stay duration, and infection incidence among cases with moderate to severe TBI.

Patients and methods:

Study design and population

This research was conducted as a prospective interventional clinical trial in the Critical Care Medicine Department at Benha University Hospitals over a six-month period, spanning from October 2024 to March 2025. A total of 60 cases diagnosed with moderate to severe TBI were enrolled. Prior to participation, each case provided written informed consent after receiving a detailed explanation of the research objectives. Confidentiality was ensured by assigning a unique code to every participant. The research protocol was approved by the Research Ethics Committee of the Faculty of Medicine,

Benha University **(Approval code: MS 7-9-2024).**

Eligibility Criteria

Cases of both sexes aged 18 years or older, presenting with moderate to severe TBI and Hb titers below 9.5 g/dL, were considered eligible. Individuals who declined to provide consent were excluded from participation.

Sample Size Calculation

The required sample size was estimated via G*Power version 3.1.7, referencing prior studies with an effect size (d) of 0.8, $\alpha = 0.05$, and statistical power of 80%. The calculation indicated a minimum of 27 cases per group; to account for potential attrition, 30 cases were allocated to each research arm. Statistical analysis was done by SPSS v26 (IBM©, Armonk, NY, USA).

Group Allocation

Participants were assigned to one of two intervention groups according to Hb thresholds:

- **Group A (Restrictive transfusion approach):** transfusion administered only if Hb fell below 7.5 g/dL.
- **Group B (Liberal transfusion approach):** transfusion administered when Hb was less than 9.5 g/dL.

Data Collection and Baseline Evaluation

Upon admission, all cases underwent comprehensive assessment. Demographic characteristics, including age, sex, place of residence, occupation, educational level, socioeconomic status, and smoking habits, were documented. A detailed medical history was obtained, covering comorbidities like diabetes mellitus, hypertension, and asthma, as well as prior surgical interventions and relevant family history.

Clinical evaluation included measurement of vital signs (heart rate, blood pressure, respiratory rate, and oxygen saturation) and anthropometric parameters (weight and height) to calculate body mass index (BMI = weight/height^2). Neurological status was assessed via detailed neurological examination and Glasgow Coma Scale (GCS) scoring.

Laboratory and Diagnostic Workup

Baseline laboratory investigations comprised complete blood count, arterial blood gas analysis, renal and liver function tests, random blood glucose, and coagulation profile. These assessments were repeated during the ICU stay according to clinical need.

Intervention and ICU Management

All cases received standard ICU care following institutional protocols, including continuous hemodynamic monitoring, ventilatory support as needed, and interventions to maintain adequate cerebral perfusion. Blood transfusions were performed according to group assignment, after ABO and Rh typing and cross-matching.

Cases requiring urgent surgical management for intracranial hemorrhage or other systemic injuries underwent operative intervention before ICU admission when indicated. Following stabilization, all cases were managed in the ICU with comprehensive supportive care, including fluid resuscitation, analgesia, sedation when necessary, and infection prophylaxis. Daily monitoring of Hb and regular GCS reassessments were performed throughout the ICU stay.

Outcome Measures

The primary outcome was mortality during ICU admission. Secondary outcomes included neurological improvement at discharge (assessed via GCS), ICU length of stay (categorized as short <7 days or prolonged >7 days), and incidence of infection (sepsis or septic shock). Outcomes were analyzed according to TBI severity (moderate versus severe) and compared between groups.

Statistical Analysis

SPSS version 25 was employed for all statistical computations. Continuous variables were reported as mean ± SD and compared via the student's t-test for normally distributed data or the Mann–Whitney U test for data violating

normality assumptions. Categorical variables were evaluated via Chi-square or Fisher's exact tests as applicable. A p-value threshold of <0.05 indicated statistical significance, and p < 0.01 indicated strong significance.

Results:

Seventy percent of them are males and 30% are females with average age of 31.7±11.41 years, the most common comorbidities were HTN (15% of the cases) & DM (8.3% of the cases). **Table 1**

Group A cases with moderate traumatic brain injuries who received blood transfusion have higher survival rate of 70% (7 out of 10) and diminish mortality rate 30 % (3 out of 10) as opposed to group A cases with severe traumatic brain injuries who have survival rate of 40% (8 out of 20) and mortality rate of 60% (12 out of 20). While Group B cases with moderate traumatic brain injuries who received blood transfusion have higher survival rate approximately 81% (13 out of 16) and diminish mortality rate approximately 19% (3 out of 16) as opposed to group B cases with severe traumatic brain injuries who have survival rate of approximately 64%(9 out of 14) and mortality rate of approximately 36%(5 out of 14).

When comparing ICU/hospital stay across both groups, most cases had prolonged admissions (>7 days), regardless of TBI severity. In Group A (restrictive approach), 90% of moderate TBI cases (9/10) and 90% of severe TBI cases (18/20) experienced prolonged stays, with only 10% in each severity subgroup having shorter stays. In Group B (liberal approach), the proportion of prolonged stay was diminished among moderate TBI cases at 67% (10/15), with 33% (5/15) achieving shorter stays. However, in severe TBI cases of Group B, 87% (13/15) still had prolonged ICU stays, while only 13% (2/15) had shorter admissions. These observations suggest that although prolonged ICU stay was common in both groups, liberal transfusion was associated with a relatively higher proportion of shorter stays, particularly among moderate TBI cases. **Table 2**

The relationship between ICU stays duration and infection severity differed between the two groups. In Group A (restrictive approach), infections occurred predominantly among cases with prolonged ICU stay, where 8 developed sepsis and 16 developed septic shock. However, even among short-stay cases, infections were noted, including 1 case of sepsis and 2 cases of septic shock. In contrast, Group B (liberal approach) showed infections exclusively among cases with prolonged ICU stay, 8 developed sepsis and 11 developed septic shock, while none of the short-stay cases experienced infectious complications. These observations indicate that prolonged ICU stay markedly increases the risk of sepsis and septic shock in both groups, though the restrictive group showed additional vulnerability with infections occurring even during shorter admissions. **Table 3**

Cases who received a blood transfusion at Hb titer of less than 9.5 g/dl (Group B) had a higher improvement rate as opposed to those who received a transfusion at an Hb titer of less than 7.5 g/dl (Group A). In Group A, the improvement rate was 50% (15 out of 30), while in Group B, the improvement rate was 73.3% (22 out of 30). **Table 4**

Cases who received a blood transfusion at Hb titer of less than 9.5 g/dl (Group B) had a higher survival rate and diminish mortality rate as opposed to those who received a transfusion at Hb titer of an Hb titer of less than 7.5 g/dl (Group A). In Group A, the survival rate was 50% (15 out of 30) and the mortality was 50% (15 out of 30), while in Group B, the survival rate was 73.3% (22 out of 30) and mortality rate 26.7% (8out of 30). **Table 5**

In Group A cases (Hb ≤ 7.5 g/dL), the majority experienced prolonged ICU or hospital stays, with 26 out of 30 cases

remaining for more than 7 days, while only 4 cases had a shorter stay. Similarly, in Group B cases (Hb ≤ 9.5 g/dL), prolonged admission was also predominant, observed in 22 out of 30 cases, whereas 8 cases had a shorter duration of stay. **Table 6**

Table 1: Demographic data of the studied patients.

		All cases (n: 60)
Age (yrs.)		31.7±11.41
Sex	♂	42 (70%)
	♀	18(30%)
BMI (Kg/m^2)		25.1±3.34
Co-morbidities	FMH	44(73.3%)
	DM	5(8.33%)
	HTN	9(15%)
	B. A	2(3.33%)
Lab.	Hb	9.826±1.71

FMH:free medical history ,DM:diabetes mellitus, HTN: hypertension, B.A: bronchial asthma, Hb: hemoglobin, BMI: body mass index

Table 2: Duration of ICU/Hospital Stay According to TBI Severity in Both Groups.

Group	**Severity**	**Prolonged (>7 days)**	**Short (<7 days)**
Group A (Hb <7.5 g/dL)	Moderate (n: 10)	9 (90%)	1 (10%)
	Severe (n: 20)	18 (90%)	2 (10%)
Group B (Hb <9.5 g/dL)	Moderate (n: 15)	10 (67%)	5 (33%)
	Severe (n: 15)	13 (87%)	2 (13%)

TBI: traumatic brain injury; ICU: intensive care unit

Table 3: Duration of ICU/Hospital Stay and Infection Severity in Both Groups.

Group	**ICU Stay**	**Sepsis**	**Septic Shock**
Group A (Hb <7.5 g/dL)	Prolonged (>7 days)	8	16
	Short (<7 days)	1	2
Group B (Hb <9.5 g/dL)	Prolonged (>7 days)	8	11
	Short (<7 days)	0	0

TBI: traumatic brain injury; ICU: intensive care unit

Table 4: The association between GCS and the titre of Hb at which blood trasnfusion is done in both groups.

Group A (Hb level<7.5 g\dl)	**Group B (Hb level<9.5 dg\l)**	**Group A (Hb level<7.5 g\dl)**	**Group B (Hb level<9.5 dg\l)**
Improved		Not improved	
15	22	15	8

Hb: hemoglobin, GCS: Glasgow Coma Scale.

Table 5: The association between mortality and the titreof Hb at which blood trasnfusion is done in both groups.

Group A (Hb level<7.5 g\dl)	Group B (Hb level<9.5 dg\l)	Group A (Hb level<7.5 g\dl)	Group B (Hb level<9.5 dg\l)
Survive		Die	
15	22	15	8

HB: hemoglobin.

Table 6: The association between Hb titre and length of ICU\Hospital stay.

Group A (Hb level<7.5 g\dl)	Group B (Hb level<9.5 dg\l)	Group A (Hb level<7.5 g\dl)	Group B (Hb level<9.5 dg\l)
Prolonged(>7days)		Short(<7days)	
26	22	4	8

Hb: hemoglobin, ICU: intensive care unit.

Discussion:

TBI is highly prevalent and often complicated by anemia, making transfusion thresholds critical for outcome optimization [12]. Therefore, this prospective interventional trial evaluated 60 cases with moderate to severe TBI, comparing restrictive (Hb <7.5 g/dL) and liberal (Hb <9.5 g/dL) transfusion strategies to determine their impact on survival, neurological recovery, ICU stay, and infection risk.

In the present research, cases in Group B who received transfusions at a higher Hb threshold (<9.5 g/dl) showed better outcomes than those in Group A (<7.5 g/dl). Group B had a higher survival rate (73.3% vs. 50%) and greater GCS improvement (73.3% vs. 50%), with diminished mortality (26.7% vs. 50%). These observations suggest that a liberal transfusion approach may improve both survival and neurological recovery in TBI cases.

Several studies support our observations that liberal transfusion thresholds improve outcomes in TBI cases. Taccone and co-authors [10], in a large multicenter randomized trial across 72 ICUs, exhibited a diminish rate of unfavorable neurological outcome at 180 days in the liberal group (Hb <9 g/dL, 62.6%) compared with the restrictive group (Hb <7 g/dL, 72.6%), along with fewer cerebral ischemic events (8.8% vs. 13.5%). Similarly, Gobatto and co-authors [9] conducted a pilot randomized trial in moderate and severe TBI cases and found that liberal transfusion (mean Hb 9.3 g/dL) significantly reduced hospital mortality compared with restrictive transfusion (mean Hb 8.4 g/dL) (1/21 vs. 7/23, p=0.048). McIntyre and co-authors [13], in a subgroup analysis of 67 TBI cases from the TRICC trial, observed a trend toward diminish 30-day mortality with liberal transfusion (13% vs. 17%), though this did not reach statistical significance (p=0.64). Evidence from systematic reviews also favors a liberal approach. Montgomery and co-authors [14], in a meta-analysis of transfusion thresholds in adult TBI, concluded that a threshold near 9 g/dL was associated with improved survival and neurological outcomes as opposed to a restrictive threshold of ~7 g/dL. More recently, Guglielmi and co-authors [11], analyzing the CENTER-TBI cohort, exhibited that higher Hb titers (>9.5 g/dL) independently reduced 6-month unfavorable outcomes and mortality, with odds ratios of 0.78 and 0.88 per unit increase, respectively. These results highlight the physiological importance of maintaining adequate Hb in TBI, where impaired autoregulation and increased metabolic demand make the brain particularly vulnerable to anemia and hypoxia [15]. Improved GCS scores observed with liberal transfusion support

the role of higher Hb in preserving neuronal function, while also potentially reducing complications like hypotension and sepsis by enhancing systemic perfusion [16].

In the current research, among cases with moderate TBI, Group B showed better outcomes with an 81% survival rate and 19% mortality, as opposed to 70% survival and 30% mortality in Group A. Similarly, in severe TBI cases, Group B had higher survival (64%) and diminish mortality (36%) as opposed to group A, which had 40% survival and 60% mortality. Our observations are consistent with McIntyre and co-authors [13], who, in a subgroup analysis of the TRICC trial, exhibited diminish 30-day mortality in the liberal group (13%) as opposed to the restrictive group (17%), although the difference was not statistically significant. TBI markedly impairs cerebral oxygen delivery and autoregulation, making adequate Hb titers critical to prevent secondary ischemic injury [17]. In our research, cases transfused at the higher threshold exhibited improved survival in both moderate and severe TBI, likely reflecting enhanced cerebral oxygenation and neuronal preservation. The similarity in survival patterns between our results and those of McIntyre and co-authors [13] reinforces the hypothesis that liberal transfusion may be more beneficial when cerebral perfusion is compromised. While transfusion risks must be considered, these observations highlight the importance of tailoring transfusion thresholds to injury severity and neurological status.

In the present research, when comparing Hb titter and length of ICU/hospital stay, cases in both groups were more likely to have prolonged stays, but Group B had a slightly higher proportion of short-stay cases (8 out of 30) as opposed to group A (4 out of 30). This observation is consistent with Bergamin and co-authors [18], who compared restrictive and liberal transfusion strategies in cancer cases with septic shock. Although ICU and hospital stay did not differ between groups, the liberal group received more RBC units (median 1 [0–3] vs. 0 [0–2], $p<0.001$) and showed a trend toward diminish 28-day mortality (45% vs. 56%, HR 0.74; 95% CI, 0.53–1.04; $p=0.08$). These parallels suggest that while liberal transfusion may not significantly reduce hospitalization length overall, it could support earlier recovery in vulnerable cases, particularly when cerebral or systemic oxygen delivery is compromised [15].

This investigation has inherent limitations. The modest sample size (n=60) may reduce the broader applicability of the results. Additionally, as a single-center research, extrapolation to other clinical settings is limited. Follow-up was limited to the ICU period, preventing analysis of long-term neurological or functional recovery.

Conclusion

In moderate to severe TBI, implementing a liberal transfusion approach (Hb<9.5 g/dL) was linked to superior survival rates, improved neurological outcomes, and shorter ICU and overall hospital stays as opposed to a restrictive threshold (Hb<7.5 g/dL). Cases experiencing prolonged ICU admission, especially in the restrictive group, exhibited a heightened risk of sepsis and septic shock, reinforcing the potential benefit of higher transfusion thresholds.

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Author Contributions

Authors were equally involved in all aspects of the research, including the conceptual framework, design, case

recruitment, data collection, statistical evaluation, interpretation of findings, and preparation of the manuscript. All authors have approved the final manuscript and take full responsibility for its content and scientific integrity

Conflicts of Interest

The authors affirm that there are no conflicts of interest, financial, personal, or professional, that could inappropriately influence the research's outcomes or interpretation. This declaration ensures that the observations presented are unbiased and solely reflective of the research conducted.

References:

1. Maas AIR, Menon DK, Manley GT, Abrams M, Åkerlund C, Andelic N, et al. Traumatic brain injury: progress and challenges in prevention, clinical care, and research. Lancet Neurol. 2022; 21:1004-60.
2. Bramlett HM, Dietrich WD. Long-Term Consequences of Traumatic Brain Injury: Current Status of Potential Mechanisms of Injury and Neurological Outcomes. J Neurotrauma. 2015;32:1834-48.
3. Ng SY, Lee AYW. Traumatic Brain Injuries: Pathophysiology and Potential Therapeutic Targets. Front Cell Neurosci. 2019;13:528.
4. Lasocki S, Pène F, Ait-Oufella H, Aubron C, Ausset S, Buffet P, et al. Management and prevention of anemia (acute bleeding excluded) in adult critical care patients. Ann Intensive Care. 2020;10:97.
5. Boutin A, Chassé M, Shemilt M, Lauzier F, Moore L, Zarychanski R, et al. Red Blood Cell Transfusion in Patients With Traumatic Brain Injury: A Systematic Review and Meta-Analysis. Transfus Med Rev. 2016;30:15-24.
6. Lelubre C, Bouzat P, Crippa IA, Taccone FS. Anemia management after acute brain injury. Crit Care. 2016;20:152.
7. Hare GM, Mazer CD, Hutchison JS, McLaren AT, Liu E, Rassouli A, et al. Severe hemodilutional anemia increases cerebral tissue injury following acute neurotrauma. J Appl Physiol (1985). 2007;103:1021-9.
8. Vanhala H, Junttila E, Kataja A, Huhtala H, Luostarinen T, Luoto T. Incidence and Associated Factors of Anemia in Patients with Acute Moderate and Severe Traumatic Brain Injury. Neurocrit Care. 2022;37:629-37.
9. Gobatto ALN, Link MA, Solla DJ, Bassi E, Tierno PF, Paiva W, et al. Transfusion requirements after head trauma: a randomized feasibility controlled trial. Crit Care. 2019;23:89.
10. Taccone FS, Rynkowski CB, Møller K, Lormans P, Quintana-Díaz M, Caricato A, et al. Restrictive vs Liberal Transfusion Approach in Patients with Acute Brain Injury: The TRAIN Randomized Clinical Trial. Jama. 2024;332:1623-33.
11. Guglielmi A, Graziano F, Bogossian EG, Turgeon AF, Taccone FS, Citerio G. Haemoglobin values, transfusion practices, and long-term outcomes in critically ill patients with traumatic brain injury: a secondary analysis of CENTER-TBI. Crit Care. 2024;28:199.
12. Litofsky NS, Martin S, Diaz J, Ge B, Petroski G, Miller DC, et al. The negative impact of anemia is outcome from traumatic brain injury. World neurosurgery. 2016;90:82-90.
13. McIntyre LA, Fergusson DA, Hutchison JS, Pagliarello G, Marshall JC, Yetisir E, et al. Effect of a liberal versus restrictive transfusion approach on mortality in patients with moderate to severe head injury. Neurocrit Care. 2006;5:4-9.
14. Montgomery EY, Barrie U, Kenfack YJ, Edukugho D, Caruso JP, Rail B, et al. Transfusion Guidelines in Traumatic Brain Injury: A Systematic Review and Meta-Analysis of the Currently Available Evidence. Neurotrauma Reports. 2022;3:554-68.
15. Scarboro M, McQuillan KA. Traumatic Brain Injury Update. AACN Adv Crit Care. 2021;32:29-50.
16. Wart M, Edwards TH, Rizzo JA, Peitz GW, Pigott A, Levine JM, et al. Traumatic brain injury in companion animals: Pathophysiology and treatment. Top Companion Anim Med. 2024;63:100927.
17. Figaji A. An update on pediatric traumatic brain injury. Childs Nerv Syst. 2023;39:3071-81.
18. Bergamin FS, Almeida JP, Landoni G, Galas F, Fukushima JT, Fominskiy E, et al. Liberal Versus Restrictive Transfusion Approach in Critically Ill Oncologic Patients: The Transfusion Requirements in Critically Ill Oncologic Patients Randomized Controlled Trial. Crit Care Med. 2017;45:766-73.

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