Predictors Indicating the Need for Packed Red Cell Transfusion in Trauma Patients in a Referral Hospital in Tehran Iran

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Abstract

Background: Injury is one of the leading causes of death worldwide. Additionally, acute traumatic hemorrhage is one of the leading reasons for mortality in traumatic patients. This study aims to determine factors indicating Packed Red Cell (PRC) transfusion in traumatic patients.

Methods: This case-control study was conducted at Sina Hospital in Tehran, Iran, from July 24, 2016, to April 8, 2023. The case group included all trauma patients aged 18 *yrs* and older who received PRC transfusions within 72 *hr* after admission. The control group comprised trauma patients aged 18 *yrs* and older who received no blood transfusion during their hospitalization.

Results: Patients with PRC transfusion had lower Hemoglobin (Hb) levels, bicarbonate levels, Diastolic Blood Pressure (DBP), higher tachycardia rate, lower Mean Arterial Pressure (MAP), lower Base Excess (BE), higher positive Focused Assessment with Sonography in Trauma (FAST) results, and penetrating injuries than the control group. Multivariate logistic regression revealed Hb≤10 *g/dl* had 5.449 times more odds for PRC transfusion [OR: 5.449, p<0.001]. Also, DBP≤70 *mm/Hg* increased 1.563 times PRC transfusion's chance [OR: 1.563, p=0.036]. Patients with penetrating injury had 2.035 times more odds for PRC transfusion compared to the blunt victims [OR: 2.035, p=0.01]. Other predictors were MAP less than 65 and tachycardia [Pulse Rate (PR)>100] with 4.574 and 4.056 odds of ratio, respectively [OR: 4.574, 4.056, p=0.02, <0.001].

Conclusion: This study revealed hemoglobin levels, penetrating trauma, and shock indexes included DBP, MAP, and tachycardia as predictors for PRC transfusion.

Keywords: Blood transfusion, Hemorrhage, Trauma centers, Wounds and injuries

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Introduction

Trauma is the leading cause of death under the age of 40 *yr*s and one of the most important causes of death and disability at all ages (1). According to the World Health Organization (WHO) report entitled Road Traffic Injuries, released in February 2020, approximately 1.35 million individuals die each year due to road accidents solely. Also, 93% of the road deaths occur in low-to middle-income countries (2). Trauma is one of the four leading causes of death in Iran (3).

Acute traumatic hemorrhage is one of the leading reasons for mortality (4). The majority of deaths from traumatic hemorrhage occur within the first three *hr* of injury (5).

Relying only on vital signs may be insufficient for resuscitating trauma patients, since early shock can involve compensatory physiological mechanisms. A study showed that up to 80% of critically ill patients who are normotensive and have adequate urine output may still be in a state of compensated shock (6).

In-hospital acute resuscitation in trauma has evolved toward early and balanced resuscitation with transfusion-Packed Red Cells (PRC) (7). Literature suggests that 25% of trauma patients require a PRC transfusion (8). Therefore, additional biochemical markers of shock have been explored to evaluate tissue hypoxia and prevent under-resuscitation more promptly.

It has been believed that blood component values require *hr* to equilibrate; however, recent investigations regarding Hemoglobin (Hb) levels at the time of hospital admission of severe trauma patients have reported that peripheral levels of Hb can be lowered even during the very early stages of trauma (9).

Arterial Base Excess (BE) has become a crucial indicator for evaluating resuscitation efforts and predicting outcomes in trauma patients (10). Some studies demonstrated that Glasgow Coma Scale (GCS)≤8, age, Injury Severity Score (ISS) >16, the mechanism of injury, Blood Pressure (BP), Respiratory Rate (RR), Heart Rate (HR), abnormal corneal size, and cervical spinal fractures were independent predictors of outcome in trauma patients. GCS, blood pH, lactate dehydrogenase, coagulation disorders, and the need for intubation were also important factors associated with mortality (11-15).

In the context of traumatic injury, blood transfusion can markedly decrease mortality rates in trauma patients. Therefore, understanding the factors that indicate which patients will require packed red blood cells is crucial. This study aimed to investigate factors indicating pack cell transfusion in traumatic patients.

Materials and Methods

Study design and participants

This case-control study was conducted at Sina Hospital in Tehran, Iran, from July 24, 2016, to April 8, 2023. The study was performed within the framework of the National Trauma Registry of Iran (NTRI), which has been previously discussed regarding the registry process and data quality evaluation (16).

The case group included all trauma patients aged 18 *yr* and older who received PRC transfusions within 72 *hr* after admission. The control group comprised trauma patients aged 18 *yr*s and older who received no PRC transfusion during their hospitalization.

Measurements and tools

Variables studied included age, Hb, bicarbonate (HCO_3), Partial Thromboplastin Time (PTT), BE, Focused Assessment with Sonography in Trauma (FAST), abdominal-pelvic computed tomography (CT) scan, cause of injury, Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP), and Pulse Rate (PR). Information on the cause of injury and age was obtained through patient reviews conducted by a registered nurse. DBP, PR, and GCS was measured by a physician during the emergency room visit. Laboratory data, including Hb, bicarbonate, BE, PTT, and imaging data (FAST, CT scan), were gathered from the hospital information system.

The cause of injury is categorized into two groups: penetrating and blunt. Penetrating trauma included stabs/cuts and firearms (shotgun and gunshot). The blunt injuries had several causes, including Road Traffic Incidents (RTI), falls, and forces. BE equal and less than -10 was considered abnormal and BE>-10 was normal. DBP≤70 *mm/Hg* is considered as a hypotension. Hb level was divided into two groups: Hb>10 *g/dl*, and Hb≤10 *g/dl*. PR above 100 was cutoff for tachycardia. Also, MAP less than 65 considered as a hypotension. The mentioned formula

was used to calculate MAP (17).
MAP=SAP+2×DAP)3

Statistical analysis

Nominal and categorical variables were presented as counts and percentages, while continuous variables without a normal distribution were described using non-parametric Mann-Whitney tests. Univariate and multiple logistic regression models were applied to assess the PRC transfusion predictors. Variables with p-values<0.1 were entered into the multivariate model. A p-value<0.05 was considered statistically significant for the final model. Statistical analysis was performed by SPSS 26.

Results

There were had 140 victims with PRC transfusion in the case group and 640 traumatic individuals without PRC transfusion in the control group. The mean (SD) of age was 46.15 (20.33) and 47.41 (20.23) in the case and control groups, respectively. The case group had higher rate of Hb≤10 *g/dl* than control groups significantly [32 (22.9%) *vs*. 32 (5%), p<0.001]. Bicarbonate level was higher in the control group (400.63 *vs*. 317.09, p<0.001). Also, traumatic patients who had received PRC had DBP ≤ 70 *mm/Hg* more than control group in the initial visit at emergency [74 (52.9%) *vs*. 226 (35.3%), p<0.001]. Tachycardia was significantly different between the two groups [31 (22.1%) in case group *vs*. 35 (5.5%) in control group, p<0.001]. Additionally, MAP less than 65 was significantly higher in cases than controls [8 (5.7%) *vs*. 5 (0.8%), p=0.001]. We observed that 20 (14.8%) of study cases and 37 (5.9%) of the control group had BE≤-10 (p=0.001). Penetrating injuries were the cause of injury for 35 (25%) of injuries in patients with PRC transfusion, while 69 (10.8%) of the control group patients had penetrating injuries (p<0.001). Thirty-two (22.9%) of the PRC transfusion cases and 67 (10.7%) of the control group had a positive FAST report (p<0.001). Demographic and baseline characteristics of the case and control groups were shown in table 1.

The association between various clinical parameters and the need for PRC transfusion was evaluated using logistic regression to calculate Odds Ratios (OR) and 95% Confidence Intervals (CI). In the initial univariate

Table 1. Demographic and baseline characteristics of the case and control groups, N(%)

Variables	Case group N=140	Control group N=640	p-value
Age, mean (SD)	46.15(20.33)	47.41(20.23)	0.660
Hb (*g/dl*)			<0.001
Hb >10	108(77.1)	605(95)	
Hb ≤10	32(22.9)	32(5)	
PR			<0.001
PR ≤100	109(77.9)	605(94.5)	
PR >100	31(22.1)	35(5.5)	
HCO_3 (mean rank)	317.09	400.63	<0.001
Lactate (mean rank)	35.67	41.04	0.310
PTT (mean rank)	359.36	387.88	0.179
DBP *mm/Hg*			<0.001
DBP >70	66(47.1)	414(64.7)	
DBP ≤70	74(52.9)	226(35.3)	
MAP			0.001
MAP >65	132(94.3)	635(99.2)	
MAP ≤65	8(5.7)	5(0.8)	
BE			0.001
BE >-10	115(82.1)	594(92.8)	
BE ≤-10	20(14.2)	37(5.7)	
CT.scan			0.236
Not performed	97(69.2)	477(74.9)	
Positive	5(3.6)	10(1.6)	
Negative	35(25.5)	150(23.5)	
FAST			<0.001
Not performed	29(20.7)	137(21.8)	
Positive	32(22.9)	67(10.7)	
Negative	79(56.4)	425(66.4)	
Trauma			<0.001
Blunt	105(75)	571(89.2)	
Penetrating	35(25)	69(10.8)	

Hb: Hemoglobin; HCO3: bicarbonate; PTT: Partial Thromboplastin Time; DBP: Diastolic Blood Pressure; BE: Base Excess; CT: Computed Tomography; FAST: Focused Assessment with Sonography in Trauma; PR: Pulse Rate; MAP: Mean Arterial Pressure.

Table 2. Demographic and baseline characteristics of the case and control groups separated by the type of trauma

Variables	Case group N=140		Control group N=640	
	Blunt trauma	Penetrating trauma	Blunt trauma	Penetrating trauma
Age* (*yrs*)	50.95(20.66)	30.30(11.04)	49.53(20.19)	30.71(10.03)
Hb* (*g/dl*)	11.85(2.62)	11.99(2.79)	13.15(1.99)	13.56(2.12)
HCO_3* (*mmol/L*)	21.02(4.57)	19.95(4.34)	22.90(13.23)	22.60(4.67)
Lactate* (*mmol/L*)	20.68(11.41)	30.78(21.03)	23.83(19.42)	24.67(4.16)
DBP* (*mmHg*)	72.56(14.28)	67.62(14.45)	76.41(11.15)	75.88(12.32)
PR*				
PR >100	20(39.2)	11(75)	31(60.7)	4(25)
PR ≤100	85(13.6)	24(26.9)	540(86.4)	65(73.1)
MAP*				
MAP >65	101(15.1)	31(31.3)	567(84.8)	68(68.6)
MAP ≤65	4(50)	4(80)	4(50)	1(20)
BE**				
BE >-10	19(11.3)	5(16.1)	149(88.7)	26(83.9)
BE ≤-10	71(18.9)	27(44.3)	305(81.1)	34(55.7)
CT Scan**				
Positive	3(30.0)	1(20.0)	7(70)	4(80.0)
Negative	27(16.7)	13(46.4)	135(83.3)	15(53.6)
FAST**				
Positive	20(29.0)	22(53.7)	49(71.0)	19(46.3)
Negative	82(17.6)	12(24.0)	385(82.4)	38(76.0)

* Mean (SD), **n (%), Hb: Hemoglobin; PTT: Partial Thromboplastin Time; DBP: Diastolic Blood Pressure; BE: Base Excess; CT: Computed Tomography; FAST: Focused Assessment with Sonography in Trauma.

analysis, several factors were identified as significant, including Hb≤10 *g/dL*, penetrating trauma, BE≤-10, DBP≤70 *mmHg*, MAP≤65, tachycardia, positive FAST, and bicarbonate (Table 2).

The multivariate analysis revealed that low hemoglobin levels (Hb≤10 *g/dL*), penetrating trauma, low DBP (≤70 *mmHg*), lower MAP (≤65), and tachycardia remained significantly associated with an increased requirement for PRC transfusion (Table 3).

Discussion

The present study identified several key factors that are indicative of the need for PRC transfusion in trauma patients. Our results demonstrated that Hb levels (Hb≤10 *g/dl*), penetrative trauma, MAP≤65, tachycardia, and DBP (≤70 *mm/Hg*) are significantly related to the requirement for PRC transfusion. The mentioned findings highlight the importance of these parameters in guiding transfusion decisions and optimizing the patient outcomes in trauma care.

Negative BE in Venous Blood Gas (VBG) analysis indicates metabolic acidosis. It was observed that after adjustment with other factors, BE was not associated with the need for transfusion of PRC. Despite normal BP, HR, and urinary output, a large number of trauma patients have inappropriate tissue perfusion (18). Majority of trauma patients with a significant blood loss, often developed a condition known as the lethal triad. This syndrome includes acidosis, hypothermia, and coagulopathy, which are interconnected and related to each other (19). Therefore, it is crucial to monitor the patient's clinical status when it leads to severe acidosis.

Arterial BE is generally recognized as a surrogate

Table 3. Univariate Odds Ratio (OR) and 95% confidence interval (CI) of predictors of the need for packed red cell transfusion in trauma patients

Variables	OR	95% CI	p-value
BE >-10	Reference		0.001
BE ≤-10	2.792	1.564-4.984	
Hb >10 *g/dl*	Reference		<0.001
Hb ≤10	5.602	3.294-9.527	
HCO_3	0.933	0.896-0.972	0.001
Lactate	0.994	0.967-1.023	0.689
DBP >70 *mmHg*	Reference		<0.001
DBP ≤70 *mmHg*	2.039	1.409-2.95	
MAP >65	Reference		0.001
MAP ≤65	6.374	2.175-18.675	
PR ≤100	Reference		<0.001
PR >100	4.892	2.895-8.267	
PTT	1.002	0.989-1.015	0.805
Blunt trauma	Reference		<0.001
Penetrating trauma	2.744	1.738-4.333	
FAST (not performed)	Reference		0.001
FAST (negative)	0.878	0.55-1.401	0.586
FAST (positive)	2.256	1.262-4.035	0.006
CT (not performed)	Reference		
CT (negative)	1.147	0.748-1.76	0.529
CT (positive)	2.459	0.822-7.353	0.107
Age (*yrs*)	0.997	0.988-1.006	0.504

Hb: Hemoglobin; HCO_3: bicarbonate; PTT: Partial Thromboplastin Time; DBP: Diastolic Blood Pressure; BE: Base Excess; CT: Computed Tomography; FAST: Focused Assessment with Sonography in Trauma; MAP: Mean Arterial Pressure; PR: Pulse Rate.

laboratory marker for shock in trauma patients. A study indicated that both arterial and venous BE were critical and were significantly lower in non-survivors compared to survivors at 24 *hr* and one week after trauma (20). However, some studies suggested that when arterial and venous BE values did not align, venous BE could more accurately indicate early changes in tissue perfusion. Rudkin *et al* proposed that this discrepancy could be in terms of postcapillary acid-base status that more accurately reflecting tissue hypoperfusion (21).

Lactate is metabolized in the liver and kidneys to maintain acid-base balance. In traumatic hemorrhagic shock, reduced blood flow to these organs decreases lactate clearance, worsening acidosis and accelerating a "bloody vicious circle," which leads to a poorer prognosis (22). Analysis of the current study indicated that lactate levels were not a significant factor in the need for PRC transfusion. In contrast, most studies found that increased lactate concentration is an important predictor of the need for early massive transfusion (23,24).

Bicarbonate was significant in the univariate logistic analysis but not a significant factor in the multivariate analysis. Evidence on the impact of sodium bicarbonate on mortality in critically ill patients is controversial, with limited data available primarily from retrospective studies (25,26).

A study found that sodium bicarbonate infusion did not affect Intensive Care Unit (ICU) mortality in critically ill patients with metabolic acidosis (27). Sodium bicarbonate Ringer's solution has been shown to have a beneficial clinical effect in supplementing circulating blood volume and improving metabolic acidosis (28). It might be assumed that increasing bicarbonate levels is essential for better acid-base balance, but it does not significantly affect the need for PRC transfusion.

In trauma patients, the severity of acidosis correlates with the dysfunction of coagulation factors and predicts mortality (29). Since coagulopathy occurs in 25–35% of trauma patients and causes a major component of the lethal triad directly exacerbating hemorrhage, understanding the pathophysiology of trauma-induced coagulopathy is crucial for treating trauma patients with coagulopathy or its precursors to prevent the related deaths (30). Tissue factor

Table 4. Multivariate Odds Ratio (OR) and 95% Confidence Interval (CI) of predictors of the need for packed red cell transfusion in trauma patients

Variables	Multivariate OR	95% CI	p-value
Hb >10 *g/dL*	Reference	Reference	<0.001
Hb ≤10 *g/dL*	5.449	3.033–9.79	
MAP >65	Reference	Reference	0.02
MAP ≤65	4.574	1.268–16.504	
PR ≤100	Reference	Reference	<0.001
PR >100	4.056	2.066–7.262	
DBP >70 *mm/Hg*	Reference	Reference	0.036
DBP ≤70 *mm/Hg*	1.563	1.03–2.373	
Blunt trauma	Reference	Reference	0.01
Penetrating trauma	2.035	1.189–3.484	
BE >-10	Reference	Reference	0.522
BE ≤-10	1.3	0.582–2.903	
HCO_3	0.959	0.908–1.014	0.143
FAST (not performed)	Reference	Reference	0.057
FAST (negative)	0.985	0.589–1.646	0.953
FAST (positive)	1.925	0.999–3.711	0.05

Hb: Hemoglobin; MAP: Mean Arterial Pressure; DBP: Diastolic Blood Pressure; PR: Pulse Rate; FAST: Focused Assessment with Sonography in Trauma; BE: Base Excess; HCO3: Bicarbonate

interacts with activated factor VII, initiating the primary physiological process of clot formation. Both pathways subsequently converge to activate factor X, which converts prothrombin into thrombin. Thrombin then transforms fibrinogen into an insoluble fibrin clot (31). This is how PTT is important in coagulopathy. In the present study, no association was found between PTT levels and the requirement for PRC transfusion. In this line, a case-control study by Shaz *et al* revealed no differences in thrombin or fibrin generation between the cases and controls, nor was there any variance in the degree of fibrinolysis in early trauma-induced coagulopathy patients (32).

An optimal test for detecting ongoing bleeding should be quick, simple to administer, accessible at the patient's bedside, and capable of predicting whether intervention is necessary to control hemorrhage. Hb measurement is quick and minimally invasive, enabling early and repeated assessments within a short timeframe in the emergency department (33). Other tests typically necessitate an arterial blood sample and specialized laboratory analysis, which are usually unavailable at the bedside, time-consuming, and consume valuable minutes during the "golden hour." However, the physiological characteristics of acute blood loss indicate that the time required for Hb levels to stabilize would make it impractical to accurately assess the extent of blood loss and the necessity for intervention to control hemorrhage, especially since plasma and red blood cells are lost in equal proportions (34). Conventionally, it is believed that after the compensatory mechanisms for acute blood loss take effect, it takes a significant amount of time before Hb levels decrease (35). As it was suggested, Hb levels (Hb≤10 *g/dl*) are an essential factor indicating the need for PRC transfusion.

Due to the substantial differences in tissue damage extent and distribution, blunt and penetrating trauma patients exhibit distinct injury patterns and responses to resuscitation (36).

It was demonstrated that penetrative trauma was a strong factor indicating the need for PRC transfusion for traumatic patients. In contrast, another study found that patients with blunt injuries required more resources than those with penetrating injuries (37).

When the sample was stratified by blunt or penetrating trauma, mortality differed significantly; the mortality among blunt trauma patients was much more than penetrating trauma regarding their ISS (38). Although having significantly lower ISS compared to blunt trauma patients, a more significant proportion of penetrating trauma patients received a higher content of plasma. This result may be due to surgeons being more willing to administer plasma content to patients with penetrating trauma.

DBP was another factor related to requiring PRC transfusion. The aim was to keep arterial blood pressure low enough to prevent dislodging clots and worsening arterial bleeding while ensuring sufficient perfusion pressure. A meta-analysis indicated that patients treated with permissive hypotension had improved survival, required fewer blood transfusions, and experienced less estimated blood loss. However, many of the studies were underpowered, and the target systolic blood pressures were variable (39). FAST is a sonography used to determine hemoperitoneum and hemopericardium in case of trauma. Its results depend on operator skill, and it can predict the amount of bleeding. Thus, it has significant limitations without considering other shock predictor variables. The association between positive FAST and PRC transfusion was not observed. In contrast to Sandro Rizol *et al*'s study, positive FAST did not predict the need for PRC transfusion. The higher statistical significance in the positive group may attributed to the high incidence of non-abdominal traumas, such as direct head injuries and isolated limb fractures, resulting in a large number of cases with negative FAST outcomes (40).

According to Rowell *et al*, physicians should be alert to the possibility of significant intra-abdominal bleeding even when the FAST test is negative, as their study indicated that FAST has a high sensitivity and specificity (41).

Strengths and limitations

This study had several limitations. Firstly, it was a single-center retrospective study, which restricted the scope of data collection. Numerous factors influence the condition of trauma patients upon arrival at the hospital. For instance, it could not be determined whether respiratory or circulatory issues were responsible for the high lactate levels or low BE. Additionally, other factors that might affect the need for PRC transfusion, such as hypothermia, platelet count, hematocrit levels, the administration of intravenous crystalloids, drug effects, or management by the same group of trauma surgeons were not considered. Therefore, a large clinical trial with a sufficient sample size is required to address these limitations.

Conclusion

The current study identified key factors indicating the need for PRC transfusion in trauma patients. Hb levels, penetrating trauma, and shock indexes were significantly associated with increased PRC transfusion requirements. These findings emphasize the importance of these parameters in guiding transfusion decisions and optimizing patient outcomes in trauma care.

Ethical considerations

This study was performed according to the Declaration of Helsinki. The Research Ethics Committee of Tehran University of Medical Sciences approved it (Approval ID: IR.TUMS.MEDICINE.REC.1402.095). During the data collection process, informed consent was obtained from the patients.

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Conflict of Interest

There was no conflict of interest in this manuscript.

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