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TRANSFUSION

ORIGINAL RESEARCH

Transfusion Practice

Use of group A thawed plasma in emergency transfusions at a pediatric quaternary care center

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Abstract

Background: Balanced plasma/red blood cell transfusions have shown survival benefit in emergency scenarios. To improve plasma availability, we implemented 5-day group A thawed plasma at our pediatric hospital in February 2021.

Study Design and Methods: We maintain thawed group A plasma units (5-day shelf-life) ready for immediate issue in the blood bank (since February 2021) and trauma code room (since August 2022). Group A plasma (un-titered) is issued for patients with unknown blood type during emergencies. We retrospectively reviewed records and laboratory results of recipients to assess safety and identify possible adverse events related to incompatible plasma.

Results: Between February 2021 and December 2023, 173 emergency plasma requests occurred for 161 patients. Ninety-one occurred with massive transfusion protocol activations. Thirty-six patients (22.4%) were blood group B or AB, and 23 received incompatible plasma (age 0–21.3 years, weight 0.74–149.8 kg, incompatible plasma dose 4.0–428.4 mL/kg). These patients did not have any differences in survival outcomes or hospital lengths of stay (LOS) compared with compatible plasma recipients, mirroring the adult experience. None experienced adverse events related to group A plasma. No transfusion reactions were reported. No increase in wastage/outdate occurred upon thawed plasma implementation (2020 versus 2021 to 2023, 7.73% [133/1721] vs. 8.58% [497/5792], $p = .284$).

Conclusions: We implemented 5-day group A thawed plasma. Units are rapidly available from the blood bank and trauma code room without increased wastage. We did not identify any transfusion-associated adverse events in pediatric recipients of incompatible group A plasma.

KEYWORDS

emergency transfusion, group A plasma, pediatric transfusion, transfusion safety, trauma

Abbreviations: EBV, Estimated blood volume; EMRL, Emergency blood request/release; FDA, United States Food and Drug Administration; IQR, Interquartile range; LOS, Length of Stay; TAT, Turnaround time.

1 | INTRODUCTION

Life-threatening hemorrhage is a leading cause of death in children, with mortality rates between 20 and 50% depending on the study.[1–3] Causes include falls/injuries, motor vehicle accidents, and surgical bleeding. These scenarios may require initiation of massive transfusion to counteract exsanguination and trauma-induced coagulopathy. Adult studies, both in military and civilian environments, have shown benefit of balanced resuscitation, in which red blood cells, plasma, and platelets are all transfused as early as possible, and in ratios that approximate whole blood.[4]

Early provision of plasma poses a challenge because it is stored frozen and must first be thawed before transfusion. This process usually requires 20–30 min. Once thawed, plasma can only be stored for up to 5 days as prolonged storage leads to decreases in labile coagulation factors.[5] An alternative is to store plasma liquid from the time of donor phlebotomy; in this case, the shelf-life is 26 days.

Pediatric patients have been hypothesized to have an increased risk of hemolysis due to incompatible plasma, leading to an increased reliance on AB donors for plasma products. This puts strain on the availability of AB plasma products for other indications as AB donors represent only 4% of the population.[6] Adult studies have demonstrated that group A plasma products can be safely used in a massive transfusion/trauma setting; however, this practice has had limited uptake in pediatric hospitals due to the risks of hemolysis in patients with lower total blood volume.

Our hospital is a 320-bed tertiary care, freestanding pediatric hospital that serves as the level 1 pediatric trauma center for our region. Over the past few years, the transfusion medicine and trauma teams have been collaborating to minimize the time between patient arrival and balanced transfusion start. To increase availability of plasma for trauma patients, we introduced several changes in February 2021: (1) relabeling of plasma as thawed plasma to increase expiration date after thawing from 24 h to 5 days, (2) availability of at least 2 thawed plasma units in the blood bank at all times for emergencies, (3) use of group A plasma for emergency transfusions in the trauma bay when the recipient's blood type is unknown. This practice is based on the description in adults from the safety of the use of group A plasma in trauma (STAT) study.[7]

We describe this emergency plasma program's performance over the course of 35 months and assessed the safety and efficacy of these changes, as well as product wastage.

2 | STUDY DESIGN AND METHODS

This is a single institution retrospective study spanning the period between February 2021 and December 2023, inclusive. We reviewed all instances of emergency release of plasma. The hospital's institutional review board approved the study as minimal risk.

Since August 2019, prior to the implementation of thawed plasma, the blood bank has maintained two remote refrigerators: one located in the trauma code room and one located closer to the pediatric and cardiac intensive care units. The blood bank supplies these refrigerators with three fresh O negative red blood cell units each. In February 2021, we began storing two units of pre-thawed group A plasma in the blood bank for emergency release. In August 2022, we began additionally storing two units of pre-thawed group A plasma in the emergency department's remote refrigerator. We decided not to store plasma in the intensive care units' refrigerator because their emergency plasma use was lower than in trauma. We do not currently provide liquid plasma or whole blood at our institution for any patients.

Thawed plasma is stored in the blood bank with a five-day shelf-life and is considered equivalent to fresh frozen plasma and plasma frozen within 24 h after phlebotomy. We do not perform isohemagglutinin titers. Once plasma units are ≥3 days old, they can be used to fill nonemergency, ABO compatible orders (usually surgical) to prevent wastage. Whenever a B or AB patient received incompatible group A plasma, clinical charts and laboratory results were retrospectively reviewed to identify possible adverse events related to incompatible plasma. Initially, this was performed on a weekly basis. Once the protocol had been in place for 4 months, this review was performed each month. In addition, all massive transfusion cases are reviewed quarterly by the transfusion committee for quality improvement. Turnaround time (TAT) for emergency blood issue, as well as blood product usage and wastage are regularly monitored.

We collected the following data: demographic information, etiology of bleeding (trauma, surgery, medical), ABO/Rh blood type, volume of plasma transfused, whether incompatible plasma was transfused, 24-h mortality, in-hospital mortality, and laboratory values (creatinine, total bilirubin, and lactate dehydrogenase) up to 48 h after emergency transfusion. To determine the plasma dose administered, the patients' estimated blood volumes (EBVs) were calculated using Nadler's equation when both height and weight were provided. If only the weight was available, the EBV was calculated as 100 mL/kg for neonates (<1 year), 80 mL/kg for children (1–12 years), and 70 mL/kg for adolescents (>12 years).

TABLE 1 Patient demographics for all pediatric patients receiving emergency release during the 3-year period.

Total patient cases (Feb 2021–Dec 2023)	173 total cases, 161 unique patients
Patients with multiple events	7 (ranging from 2 to 4 events)
Gender ($n = 161$)	58 females (36%), 103 males (64%)
Etiology ($n = 161$)	60 medical (37%), 65 trauma (41%), 36 cardiac including extracorporeal membrane oxygenation (22%)
Blood type (ABO) ($n = 161$) Rh ($n = 161$)	27 B (17%), 33 A (20%), 9 AB (6%), 78 O (48%), 14 unknown (9%) 123 Rh pos (84%), 24 Rh neg (16%) (excluding 14 unknown)
Age ($n = 161$) Subcategories: Infants (0- < 1 years) Young children (1- < 12 years) Adolescents/adults (12 years and above)	Median 5.7, IQR 0.5–13.2, range 0–44 years 47 61 53
Weight ($n = 146$, 15 patients excluded due to unavailable weight)	Median 24 kg, IQR 8–53 kg, range 8.15–53 kg
EBV ($n = 146$)	Median 1738 mL, IQR 687–3430 mL, range 53–7153 mL
Plasma transfused (avg 225 mL/unit) Incompatible Compatible Total	 13,704 mL (∼61 units) 90,010 mL (∼400 units) 103,714 mL (∼461 units)

For patients with multiple bleeding events, only the first event was analyzed.

Patients were compared based on whether they received (1) only compatible plasma, (2) any incompatible plasma, or (3) no plasma during their emergency transfusion. Patients with an unknown blood type due to early death or transfer outside of our institution were separately analyzed from patients known to be groups B or AB. Plasma product transfusion data were collected for the 24 h following an emergency transfusion activation.

Data and statistical analysis were performed using Microsoft Excel 365 (Version 2308, Microsoft, Redmond, WA), R (4.2.3, R Foundation for Statistical Computing, Vienna, Austria), and R survival package (3.5–3). Survival rates were compared using Kaplan–Meier estimates with p-values obtained from χ^2 statistic. Between group hospital lengths of stay (LOS) were compared using Wilcoxon rank sum test.

3 | RESULTS AND FINDINGS

3.1 | Patient demographics and indications for emergency plasma transfusion

During the study period, 173 emergency release plasma requests occurred for 161 patients. Seven patients had multiple events (range 2–4). Ninety-one of the emergency requests occurred as part of massive transfusion protocol initiations.

The study population (161 patients) included the entire pediatric age range from newborns to adolescents (median 5.7 years, interquartile range [IQR] 0.5–13.2 years) (Table 1). On occasion, adult patients with trauma are treated on an emergency basis at our institution until they are stable enough for transfer to an adult facility. One such patient was 44 years old. Forty-seven of 161 patients (29%) were younger than 1 year. Patient weight ranged from 0.5 to 176 kg (median 24 kg, interquartile range 8.15–53 kg). The EBV ranged from 53 to 7153 mL (median 1738 mL, IQR 687–3430 mL).

A majority of patients received blood for cardiac indications and medical issues (including noncardiac surgery). Trauma accounted for 41% of emergency transfusion requests.

3.2 | Plasma transfusion characteristics

Thirty-nine patients received no plasma during emergency transfusions. For plasma recipients, the median transfused volume was 523.5 mL. After factoring in weight (when available), the median total plasma dose was 33.1 mL/kg (average 8.5 mL/kg, range 1.8–448.6 mL/kg, IQR 15.2–74.4 mL/kg). Doses were also analyzed by patient subgroups looking at compatible and incompatible plasma transfusions (see Table 2). Thirty-six patients

TABLE 2 Comparison among plasma recipients (incompatible and compatible transfusions) and non-recipients.

Patient categories	Only received compatible plasma ($n = 93$)	Received incompatible A plasma ($n = 23$)	Known blood type, received no plasma ($n = 31$)	Unknown blood type (due to early death or transfer to adult institution), received plasma ($n = 6$)	Unknown blood type (due to early death or transfer to adult institution), no plasma ($n = 8$)
Median plasma dose (mL/kg), with IQR and range	$n = 86$**	$n = 23$	$n = 31$	$n = 5$**	$n = 8$
Compatible	32.1, IQR 16.9 to 72.9, range 1.8 to 392.0	17.5, IQR 6.3 to 25.4, range 0 to 75.6	0	195.8 (1 pt)	0
Incompatible	N/A	14.1, IQR 6.6 to 28.6, range 4.0 to 428.4	0	51.2, IQR 35.0 to 62.0, range 5.7–74.7 (4 pts)*	0
Total	32.1, IQR 16.9 to 72.9, range 1.8 to 392.0	32.8, IQR 12.6 to 75.6, range 4.0 to 448.6		57.7, IQR 44.8 to 74.7, range 5.6–195.9 (5 pts)	
24-h mortality	14 of 93 (15%)	4 of 23 (17%)	2 of 31 (6%)	5 of 6 (83%)	8 of 8 (100%)
30-day mortality	29 of 93 (31%)	10 of 23 (43%)	3 of 31 (10%)	5 of 6 (83%)	8 of 8 (100%)
In-hospital mortality	34 of 93 (37%)	10 of 23 (43%)	6 of 31 (19%)	5 of 6 (83%)	8 of 8 (100%)
Hospital length of stay (days)	Median 15, IQR 4–42, range 0–300 Excludes two patients still admitted as of 2/14/2024	Median 12, IQR 2–18, range 0–98	Median 7, IQR 2–24, range 0–234	Median 0, IQR 0–1, range 0–3	Median 0, range 0–1
Creatinine change (mg/dL)				Insufficient laboratory data for analysis	Insufficient laboratory data for analysis
Admission to day 1	$n = 78$ pts: +0.07	$n = 19$ pts: −0.04	$n = 20$ pts: −0.22		
Admission to day 2	$n = 75$ pts: +0.09	$n = 17$ pts: +0.03	$n = 20$ pts: −0.05		
Total bilirubin change (mg/dL)				Insufficient laboratory data for analysis	Insufficient laboratory data for analysis
Admission to day 1	$n = 58$ pts: +0.48	$n = 16$ pts: +1.04	$n = 14$ pts: +0.09		
Admission to day 2	$n = 55$ pts: +0.61	$n = 15$ pts: +0.91	$n = 14$ pts: +0.06		

*Group A plasma is treated as incompatible in this column but approximately 85% of these patients are expected to be A or O (see discussion).
**Patients missing measured weights were excluded.

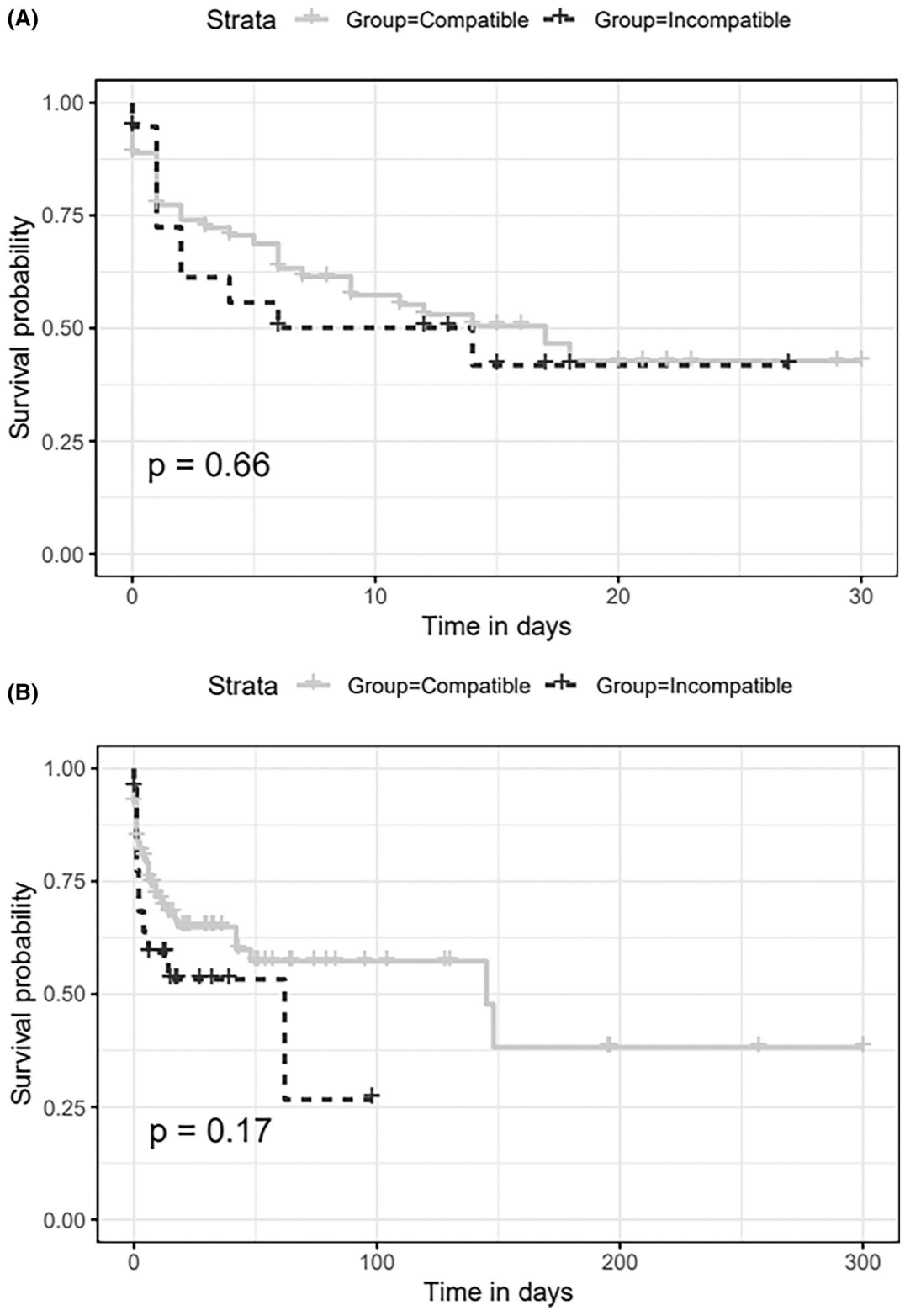

FIGURE 1 Survival curves for (A) 30 days after transfusion and (B) overall course until discharge or death.

(22.4%) were blood group B or AB, and 23 received incompatible plasma (age 0–21.3 years, weight 0.74–149.8 kg, incompatible plasma dose 4.0–428.4 mL/kg). The proportion of B and AB patients was slightly overrepresented in our urban population compared with the general United States population.

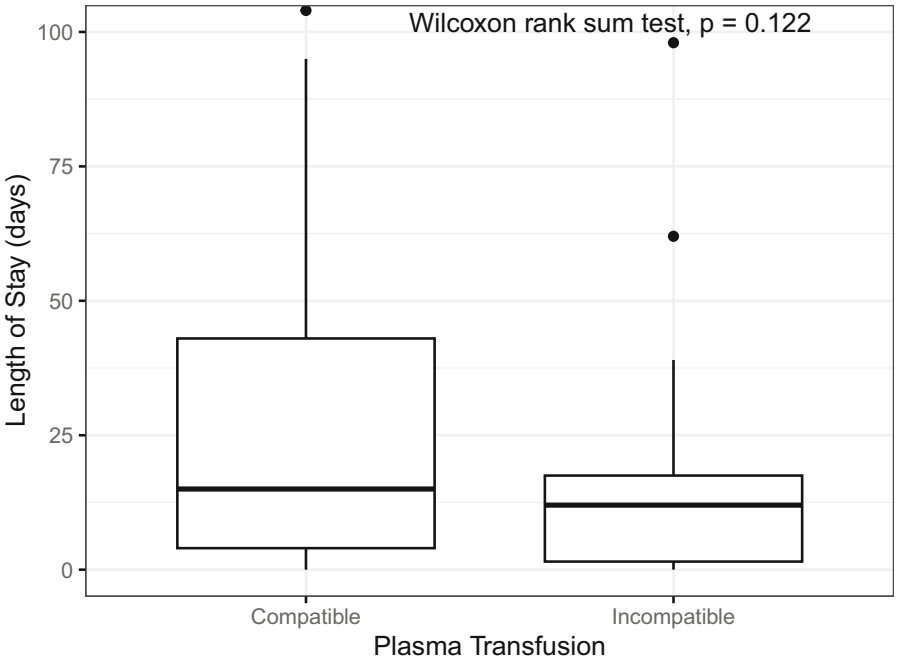

FIGURE 2 Comparison of overall hospital length of stay (LOS) between recipients of incompatible plasma and recipients of only compatible plasma.

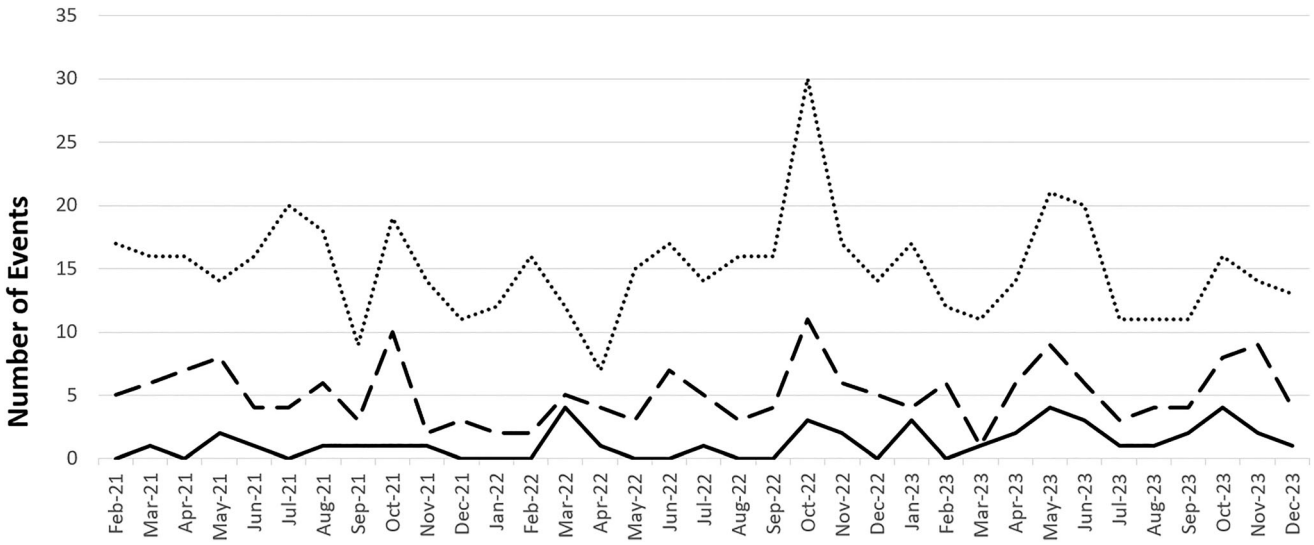

FIGURE 3 Frequency of emergency release blood and thawed plasma requests over time. The graphs display (1) the total number of patients with emergency blood transfusion and massive transfusion requests (dotted line) compared with (2) the number of patients requiring emergency thawed plasma (dashed line) and (3) events where a patient with blood type B, AB or unknown received thawed plasma (solid line).

No transfusion reactions were reported among emergency plasma recipients. No complications were attributed clinically to the plasma transfusions.

3.3 | Mortality and hospital course after transfusions

Mortality at 24 h was higher among patients with unknown blood types ($\chi^2 = 9.4$, $p = .0022$) compared with the patients with known blood types. Laboratory testing including type and screen could not be completed for patients who died quickly. Among patients with an established blood type, mortality rates at 24 h were similar among plasma recipients, whether they received incompatible plasma or not ($\chi^2 = .4$, $p = .5$). Early mortality was higher in patients who had an established blood type and received plasma transfusions compared with the patients with an established blood type but who were not transfused ($\chi^2 = 7.3$, $p = .007$).

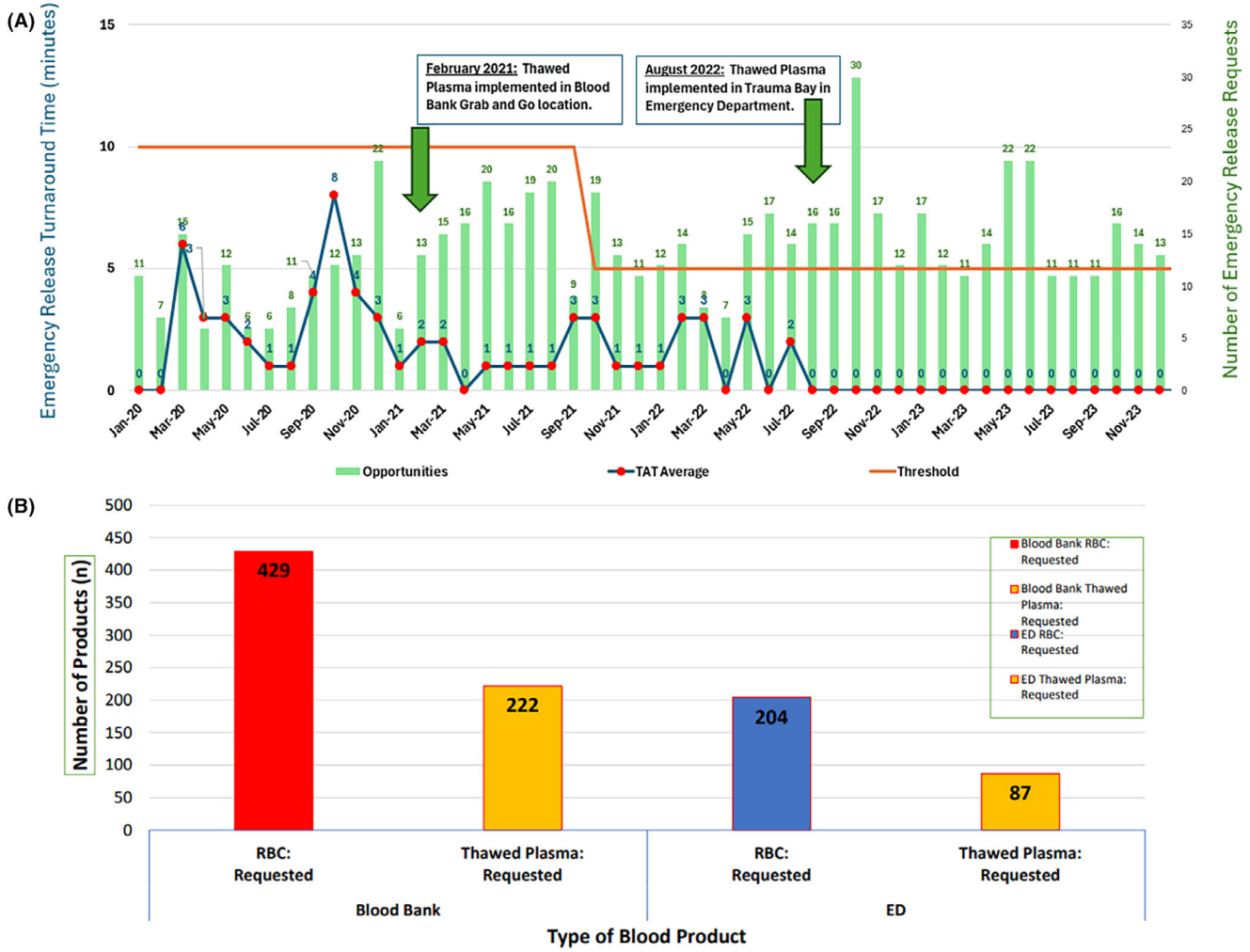

FIGURE 4 (A). Monthly average turnaround time (TAT) for emergency blood releases (both red blood cells and thawed plasma). In October 2021, we tightened our quality benchmark from ten to five minutes. The introduction of thawed plasma in February 2021, stored within the Transfusion Services department for quick access, further streamlined our process. From August 2022, storing thawed plasma in the trauma bay's remote refrigerator significantly enhanced our TAT. (B). Monthly use of emergency red blood cells and thawed plasma units from the blood bank and emergency department (trauma bay). Number of units issued includes both those ultimately transfused or those returned to the Transfusion Services department due to patient status change. [Color figure can be viewed at wileyonlinelibrary.com]

Comparison of 30-day survival and overall survival rates for patients with a known blood group was not different between compatible and incompatible plasma transfusion groups ($\chi^2 = .2$, $p = .66$; $\chi^2 = 1.9$, $p = .17$, respectively) (Figure 1). For patients with known blood group, there was no difference for the median hospital LOS between compatible and incompatible plasma transfusion groups (compatible = 15 days vs. incompatible = 12 days; $p = .122$) (Figure 2).

When creatinine and total bilirubin levels were available up to 48 h after emergency transfusion request (whether plasma was transfused or not), patients who received incompatible plasma did not show large changes in parameters compared with those who only received compatible plasma.

3.4 | Plasma usage and wastage—wait time

Thawed plasma requests fluctuated in alignment with total emergency transfusion and massive transfusion events (Figure 3). Particularly busy months were October 2022, May 2023, and October 2021. Our average TAT (from order receipt until emergency blood release from the blood bank) was below two minutes during the

35-month period (Figure 4A). Plasma usage throughout the entire hospital during calendar years 2020 through 2023 was 1721 units, 1922 units, 1824 units, and 2028 units, respectively. Emergency plasma use from the blood bank and the emergency department is shown in Figure 4B. No increase in plasma unit wastage (issued plasma not transfused), outdate (expired in blood bank), or discards (other reasons) occurred upon thawed plasma implementation (7.73% [133/1721] during calendar 2020 versus 8.58% [497/5792] in calendar years 2021–2023, chi-squared test, $\chi^2 = 1.1$, $p = .284$).

4 | DISCUSSION

We report a single institution experience with implementation of group A thawed plasma for emergency transfusions. Our 161 patients cover a wide range of patient weights (0.5–176 kg), from infants to adults. Although implemented to provide faster plasma availability in trauma patients, 59% of patients had other indications for emergency transfusions. The time to wait for emergency plasma was short throughout the study (on average, less than 2 min).

There were no significant differences in mortality or laboratory values (creatinine, total bilirubin) for patients who received only compatible plasma from those who received incompatible group A plasma.

Cases where a blood type could not be established for a patient were usually due to mortality soon after presentation, often in the setting of severe traumatic injuries. We separated out these patients from the incompatible plasma analysis as approximately 85% of them are expected to be A or O. In addition, their early death would skew statistical analysis. The overall mortality rate in our study was 86% when blood type remained unknown but 34% when it could be determined.

We found that group A plasma transfusions were safe and well tolerated in pediatric patients, even when their blood group was B or AB. No suspected transfusion reactions were reported among our study population. Laboratory results did not show differences in measures of hemolysis including creatinine or total bilirubin between patients receiving incompatible group A plasma and those receiving only compatible plasma. The incidence of reported adverse events is consistent with other publications examining out of group emergency transfusions.[7,8]

The strengths of our study include its broad patient representation and high number of emergency plasma recipients. For most patients, we were able to monitor creatinine and total bilirubin as hemolysis markers similar to other studies.[8,9]

Patients received blood soon after the decision for emergency transfusion, as recommended by guidelines.[10] The trauma team aims for a time interval of less than 10 min between decision to transfuse and start of transfusion. They obtain blood products first from the remote refrigerator in the emergency department before requesting units from the blood bank and/or initiating the massive transfusion protocol. The blood bank TAT for providing emergency release red blood cells or thawed plasma was usually less than 2 min and has been consistently less than 1 min since August 2022.

Our retrospective study has some limitations. We were not able to evaluate other hemolysis markers such as lactate dehydrogenase, direct antiglobulin test, or haptoglobin because these data elements were not prospectively collected. We relied on passive reporting of transfusion reactions. However, when patients are critically injured or ill, it can be difficult for the clinical team to identify concerning symptoms and signs of a possible reaction. As with the STAT study, we did not collect data on the ABO group of platelets transfused.[7] This study was not designed to identify either patient outcome benefits or harms.

The plasma wastage data pertains to all transfusions. We were not able to separate out wastage related specifically to emergency department/trauma use. Emergency units are issued whole instead of aliquoted to expedite blood release from the transfusion service. Thus, plasma volumes may be overestimated during initial resuscitation, especially for younger and smaller patients. Actual transfused volumes are at the discretion of the clinical team. However, because these are frequently recorded on paper code sheets, the documentation was not easily available for our review.

5 | SUMMARY

For the past three years, we have used group A thawed plasma for emergency transfusions in patients with unknown blood type in order to rapidly provide balanced resuscitation while preserving rare group AB plasma units. Our data show that this approach is well tolerated in pediatric patients. Mortality rates were similar among all plasma recipients and laboratory values remained overall stable. The benefit of whole blood use in children remains under investigation. For health care systems aiming to increase plasma availability for bleeding children, use of group A plasma should be considered.

CONFLICT OF INTEREST STATEMENT

The authors have disclosed no conflicts of interest.

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