

Predictors of Corrected Count Increment after Pooled Platelet Concentrate Transfusion in Thrombocytopenic Patients: A Cohort Study

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ABSTRACT

Introduction: Platelet transfusion is essential in managing thrombocytopenic patients to prevent or control bleeding. Corrected Count Increment (CCI) is a key measure of transfusion efficacy. Although apheresis Platelet Concentrates (PCs) from Single Donor Platelet (SDP) offers the highest platelet yield, they require more time, higher costs, specialised equipment, trained personnel and extensive donor counselling. In contrast, pooled PCs prepared by the Platelet-Rich Plasma (PRP) method serve as a practical and feasible alternative for blood centres with component separation facilities. The present study explores predictors influencing CCI following pooled PCs transfusion prepared by the PRP method.

Aim: To assess the CCI after pooled RDP transfusion.

Materials and Methods: A prospective observational cohort study was conducted in the Department of Immunohaematology and Blood Transfusion, Kalinga Institute of Medical Sciences (KIMS), Bhubaneswar, Odisha, India, for a period of two years (January 2023 to January 2025). A total of 205 thrombocytopenic

patients were included in the study who received pooled Random Donor Platelet (RDP) prepared by the PRP method. Patient demographics, diagnosis, transfusion history and platelet component characteristics were recorded. Pre-transfusion Total Platelet Counts (TPC) of the patients and the TPC of pooled RDP bags was analysed using calibrated Sysmex seven part analyser (XN3100 model) in the Department of IHBT, KIMS. Pre and post-transfusion platelet counts were measured to calculate CCI at one hour and 24 hours.

Results: Out of total 205 thrombocytopenic patients only 69 (33.65%) patients developed refractoriness. Logistic regression analysis revealed significant influence of active bleeding ($p<0.001$), drugs ($p=0.011$), days of storage of platelets ($p<0.001$) and ABO non identical platelet transfusions ($p=0.001$) on refractoriness.

Conclusion: Identifying the predictors can optimise transfusion strategies and improve patient outcomes. A modest yet potentially clinically significant benefit was noted with the transfusion of pooled platelets concentrate by PRP method in thrombocytopenic patients.

Keywords: Platelet refractoriness, Platelet-rich plasma, Random donor platelet, Thrombocytopenia

INTRODUCTION

Platelets play a crucial role in primary haemostasis. An estimated number of 7.1×10^9 platelets per litre in a day are needed to sustain vascular integrity. Platelet transfusion remains a cornerstone in the management of thrombocytopenia, which may arise due to bone marrow suppression, peripheral destruction, or splenic sequestration. A judicious use of platelet products having good quality, lesser storage effects, minimal risk of alloimmunisation and transfusion transmitted diseases with adequate post-transfusion platelet improvement is highly essential in this scenario. The various types of PCs administered in thrombocytopenia can be RDP by Buffy Coat method (BC-PCs), PRP-PCs from whole blood and SDP by apheresis [1]. SDP is generally preferred in contemporary transfusion practice due to reduced donor exposure and a higher platelet yield. However, the higher cost and resource-intensive nature can limit its widespread use in developing countries. In this context, pooled platelets prepared by combining four to six units of PRP-PC have emerged as a practical and cost-effective alternative to SDPs. Studies have demonstrated that PRP-pooled platelets offer comparable efficacy to SDPs in terms of post-transfusion platelet increment [2]. It is time-efficient, requires less donor counselling and is beneficial in urgent requirements [2]. The Drugs and Cosmetics Act amended in 2020 officially has listed it as a distinct blood component which can be prepared in all blood centres having component separation facilities [3].

The CCI is a crucial quantitative indicator for effective platelet transfusion evaluation [4]. Suboptimal increase in platelet count following repeated platelet transfusion leads to platelet refractoriness [5]. Platelet refractoriness is defined as CCI of $<7,500/\mu\text{L}$ and $<5000/\mu\text{L}$

after one hour and 24 hours of post-transfusion, respectively after two sequential ABO compatible transfusion [5]. The therapeutic efficacy of platelet transfusion is influenced by various patient, donor and product-related factors [4]. In Western countries, BC-PC is a commonly used method [6]. However, there are few studies regarding the use of PRP-PC in India and other developing countries [2,7,8]. The present study has aimed to identify predictors of successful CCI in thrombocytopenic patients receiving pooled RDP prepared by the PRP method.

MATERIALS AND METHODS

The present was a prospective observational cohort study conducted in the Department of Immunohaematology and Blood Transfusion in KIMS Hospital, Bhubaneswar, Odisha, India for a period of two years from January 2023 to January 2025). Approval from the Institutional Ethics Committee (KIIT/KIMS/IEC/1164/2023) was obtained and informed consent from all the patients was taken before conducting the study.

Inclusion criteria: This study included cases of thrombocytopenia in adults (≥ 18 years) requiring platelet transfusion, in which patients were transfused with pooled RDP-PC obtained from male donors; all units sharing the same day of expiry. Rh compatibility testing was performed for female patients of reproductive age. Patient related factors influencing CCI studied were fever, bleeding, medications, parity, sepsis, DIC, splenomegaly and past history of transfusions. Drug-related platelet response was categorised as "Decrease" or "No Change" based on post-transfusion platelet trends. Various product related factors like duration of storage, ABO compatibility and volume of platelet yield affecting the CCI were also studied.

Exclusion criteria: Products pooled from donors with mismatched ABO compatibility and differing sex; patients requiring less than four units of transfusion or requiring multiple components at a single time or with history of ≥ 10 units of transfusion in last two months were excluded from the study.

Study Procedure

Preparation and issue of platelets: RDPs were prepared from 450 mL of whole blood in a triple bag (MITRA, Mitra Industries Private Limited, Haryana, India) with citrate-phosphate-saline-adenine-glucose-mannitol by PRP method as per the departmental Standard Operating Procedures (SOPs). During collection, the bag was continuously and gently agitated to ensure thorough mixing of blood with the anticoagulant. The collected unit was then stored in an air-conditioned environment at 22-24°C until processing.

After tapping port of the primary bag, it was placed inside the bucket of the refrigerated centrifuge with the label facing the flat surface, while the attached secondary bags were neatly folded on the opposite side. The two buckets were then balanced accurately using a weighing double pan balance (CBZ-50 plus, REMI). Adapter was kept in the centrifuge cup and was first centrifuged at 1800 rpm with acceleration and deceleration curves of nine and six, respectively, for 15 minutes at a temperature of 22°C. SorvallRc 4 refrigerated centrifuge manufactured by Thermo Fisher Scientific, Germany, was used. The supernatant platelet-poor plasma was expressed into the second satellite bag, leaving approximately 40-50 mL of plasma with the platelets. The tubing was then sealed using a dielectric tube sealer (WELDON-B, REMI) and the bags were detached. The PRP-PC was allowed to stand undisturbed for one hour at 20-24°C. After one hour, the platelets were re-dispersed through gentle agitation of the bag. The operational flowchart is described in [Table/Fig-1].

Pooling of four units of RDP of same blood group with the same day of expiry was done in a closed system using sterile connecting device (TSCD-IT, Terumo Penopol). The final pooled PC [Table/Fig-2] was leucodepleted with the help of a lab-side leukofilter (MITRA labside filter). Each pooled RDP was assigned a unique identification number with the platelet content of $>2 \times 10^{11}$ /unit [9]. The storage duration of the RDPs was documented, with a maximum shelf life of five days at 20-24°C under continuous agitation in a platelet agitator [9]. ABO identical or non identical platelet products were issued based on availability. Volume reduction was performed when an ABO non identical pooled platelet was administered. RhD-positive platelets were avoided in RhD-negative female recipients of reproductive age whenever possible. A first-in, first-out policy was followed to minimise wastage of RDP units [4].

Platelet transfusion plan: The British Committee for Standards in Haematology (BCSH) transfusion guidelines were followed for platelet transfusions [10].

Body Surface Area (BSA) was calculated using Schlich formula depending on the gender of the patient [11]:

$$\text{Female: BSA} = 0.000975482 \times W^{0.46} \times H^{1.08}$$

$$\text{Male: BSA} = 0.000579479 \times W^{0.38} \times H^{1.24}$$

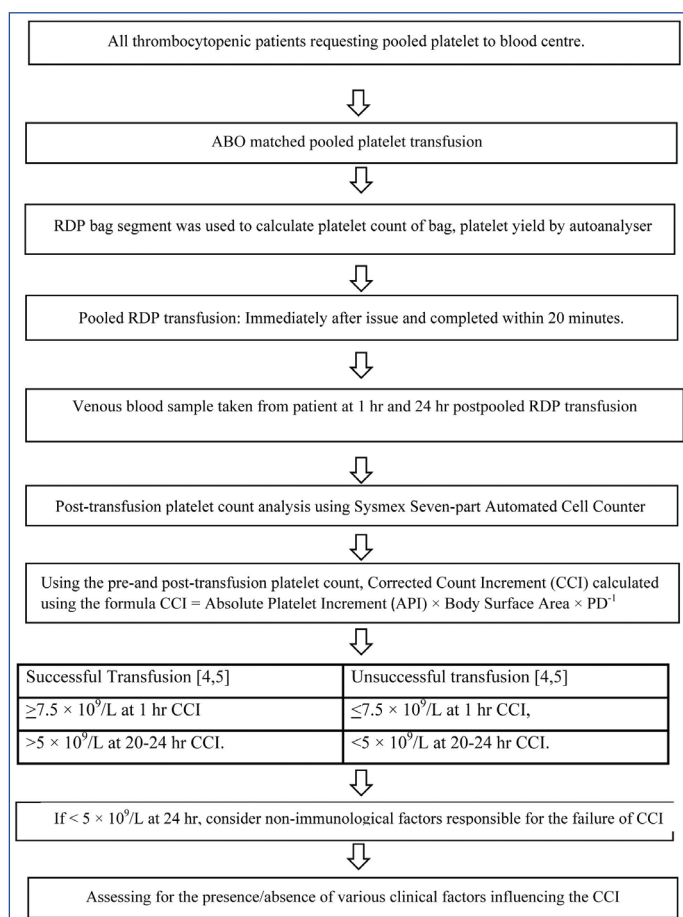
Total Blood Volume (TBV) was calculated using Nadler equation [12]:

$$\text{Male: Blood Volume} = (0.3669 \times H^3) + (0.03219 \times W) + 0.6041$$

$$\text{Female: Blood Volume} = (0.3561 \times H^3) + (0.03308 \times W) + 0.1833$$

Calculation of Platelet Dose (PD) was by the following formula:

PD = volume of platelets transfused in litres $\times$ platelet count of the platelet product ($\times 10^{11}$ /L) and platelet dose per body surface area (i.e., PD/BSA) was finally taken as the actual platelet dose transfused to the patients [13]. The storage days of PCs at the time of transfusion were categorised into two groups: ≥ 3 days and < 3 days. Adverse events after platelet transfusion were monitored for up to six hours' post-transfusion.



[Table/Fig-1]: Operational flowchart.



[Table/Fig-2]: Pooled platelet bag.

Pre and post-transfusion platelet count: Pre-transfusion TPC of the patients and the TPC of pooled RDP bags was analysed using calibrated Sysmex seven part analyser (XN3100 model) in the Department of IHBT, KIMS. Venous blood samples from the patients were collected after one hour and 24 hours of post-transfusion in sterile EDTA vacutainers and TPC was done using the above automated analyser.

Response to platelet transfusions: Absolute Platelet Increment (API) and CCI were calculated using following formula [14]:

$$\text{API} = \text{Post-transfusion platelet count} - \text{Pre-transfusion platelet count.}$$

$$\text{CCI} = \frac{\text{Absolute platelet Increment (API) } \mu\text{L} \times \text{Body surface area (m}^2\text{)}}{\text{Number of platelet transfused (10}^{11}\text{)}}$$

Platelet refractoriness: Platelet refractoriness characterised by a suboptimal increase in platelet count following repeated platelet transfusion. Platelet refractoriness is defined as CCI of $< 7,500/\mu\text{L}$

and <5000/ μ L after one hour and 24 hours of post-transfusion, respectively after two sequential ABO compatible transfusion [5].

Quality control: Quality control of the RDP by PRP method was maintained as per DGHS guidelines [15].

STATISTICAL ANALYSIS

Statistical analysis was done by using Microsoft Excel and Statistical Package for Social Sciences (SPSS) version 26.0. Comparison of CCI between subgroups was performed using the Mann-Whitney U test. Pearson's correlation was used to assess the association between platelet dose and CCI. The Chi-square was used as significance test for qualitative data. Binary logistic regression analysis was performed using SPSS and R software to determine the influence of various factors on CCI with platelet refractoriness. The p-value of less than 0.05 was considered to be statistically significant.

RESULTS

During the study period, 205 patients received pooled RDP transfusion by PRP method. 79 (38.5%) and 126 (61.5%) patients were males and females respectively. The distribution of cases according to demographic profiles like age, weight, BSA, Body Mass Index (BMI) blood volume, pre and post-transfusion platelet counts of all the patients were recorded [Table/Fig-3]. The characteristics of pooled PC (volume, duration of storage, pH, mean platelet yield, pre and post-transfusion TPC) were also noted [Table/Fig-3].

Parameters	Mean	SD	Percentile 25	Percentile 75
Age (years)	50	17	39	63
Height (in cm)	164	7	158	168
Weight (in kg)	65	10	58	72
Blood volume (in mL)	3894.644	449.744	3619.244	4168.110
BSA (in m ²)	1.631	0.163	1.533	1.731
BMI (kg/m ²)	24.245	3.980	21.671	26.446
Pre platelet count per microliter	22083.9	31039.8	9000.0	28000.0
Post-platelet count 24 hr	49780.0	47605.8	19000.0	68000.0
No of transfusion	5	3	3	8
Next transfusion (days)	4	3	2	7
TPC of the bag ($\times 10^3$)/ μ L	1370.2	228.2	1226	1477
Volume of bag (mL)	233.8	20.2	215	250
Platelet yield ($\times 10^{11}$)	3.101	0.542	2.719	3.415
pH	6.84	0.232	6.8	7
Days of storage	2	1	1	4

[Table/Fig-3]: Demographic profile and characteristics of pooled Random Donor Platelets (RDP) by platelet-rich plasma method.

Among the various causes of thrombocytopenia in the present study, the neoplastic conditions accounted for 88 cases (42.9%), with Acute Myeloid Leukaemia (AML) being the most common, constituting 45 cases (22%) of the total cases. The other neoplastic conditions included Acute Lymphoblastic Leukaemia (ALL), Chronic Myeloid Leukaemia (CML), Non-Hodgkin's Lymphoma (NHL) and Myelodysplastic Syndrome (MDS). The various non neoplastic causes were observed in 117 cases (57.1%); dengue fever was most frequent comprising 32 cases (15.6%), followed by aplastic anaemia 28 cases (13.7%), kidney disease 15 cases (7.3%) and sepsis 11 cases (5.4%) [Table/Fig-4].

Out of 205 pooled RDP transfusion episodes, 137 cases (67%) were prophylactic whereas 68 cases (33%) were therapeutic transfusions in cases of active bleeding. A total of 163 patients (79.5%) received ABO identical platelet transfusions whereas 42 patients (20.5%) received ABO non identical platelet transfusions. Only six transfusion reactions were reported. Out of which two were allergic reactions and four were febrile non haemolytic transfusion reactions.

Clinical conditions	Diagnosis	n (%)
Neoplastic	ALL	15 (7.3)
	AML	45 (22.0)
	CML	11 (5.4)
	MDS	8 (3.9)
	Multiple myeloma	2 (1.0)
	Non-Hodgkin's lymphoma	7 (3.4)
	Total	88 (42.9)
Non neoplastic	Kidney disease	15 (7.3)
	Aplastic anaemia	28 (13.7)
	Beta thalassaemia	1 (0.5)
	COPD	4 (2.0)
	DCLD	2 (1.0)
	Dengue fever	32 (15.6)
	Enteric fever	1 (0.5)
	ITP	4 (2.0)
	RHD	1 (0.5)
	Scrub typhus	1 (0.5)
	Sepsis	11 (5.4)
	SLE	2 (1.0)
	Surgery	9 (4.4)
	TTP	1 (0.5)
	Tuberculosis	2 (1.0)
	UGI bleed	3 (1.5)
	Total	117 (57.1)
Total no. of cases		205 (100)

[Table/Fig-4]: Distribution of cases according to various diseases causing thrombocytopenia (N=205).

COPD: Chronic obstructive pulmonary disease; DCLD: Diffuse chronic liver disease; ITP: Immune thrombocytopenia; RHD: Rheumatic heart disease; SLE: Systemic lupus erythematosus; TTP: Thrombotic thrombocytopenic purpura; UGI: Upper gastrointestinal bleeding

The distribution of gender, blood group (ABO and RhD) and various predictors of CCI like fever, sepsis, active bleeding, DIC, splenomegaly, history of transfusion, parity history in females, ABO identical and non identical transfusion and days of storage of PC is shown in [Table/Fig-5].

Parameters	Variables	n (%)
Patient blood group	A Positive	46 (22.4)
	AB Negative	1 (0.5)
	AB Positive	11 (5.4)
	B Negative	2 (1.0)
	B Positive	60 (29.3)
	O Positive	85 (41.5)
Gender	Male	79 (38.5)
	Female	126 (61.5)
Fever	Absent	17 (8.3)
	Present	188 (91.7)
Sepsis	Absent	188 (91.7)
	Present	17 (8.3)
Active bleeding	Absent	137 (66.8)
	Present	68 (33.2)
DIC	Absent	202 (98.5)
	Present	3 (1.5)
Splenomegaly	Absent	129 (62.9)
	Present	76 (37.1)
History of transfusion	Absent	13 (6.3)
	Present	192 (93.7)

Parity	≤2	57 (27.8)
	>2	20 (9.8)
	NA	128 (62.4)
Days of storage	≤3	141 (68.8)
	>3	64 (31.2)
ABO	Identical	163 (79.5)
	Non identical	42 (20.5)
Mismatch	Bidirectional	10 (4.9)
	Major	18 (8.8)
	Minor	14 (6.8)
	NA	163 (79.5)

[Table/Fig-5]: Various risk factors influencing Corrected Count Increment (CCI) (N=205).

A total of 69 patients (33.65%) out of total 205 cases developed refractoriness and 136 patients (66.34%) were non refractory to pooled platelet transfusion.

Key predictors of CCI included pre-transfusion platelet count, recipient's BSA, underlying diseases (haematological malignancies, sepsis, DIC), fever, splenomegaly, use of medications (chemotherapy, antibiotics and antifungals), ABO compatibility, storage conditions of platelets and transfusion dose.

These factors significantly impact platelet survival and function, influencing transfusion efficacy. Sepsis, active bleeding, splenomegaly, drug history, non identical ABO blood group platelet transfusion, ABO mismatch transfusion (major, minor or bidirectional) and prolonged storage of PC contributed to refractoriness having statistical significance ($p=0.046$, $p<0.001$, $p=0.004$, $p<0.001$, $p<0.001$, $p<0.001$ and $p<0.001$, respectively) [Table/Fig-6,7].

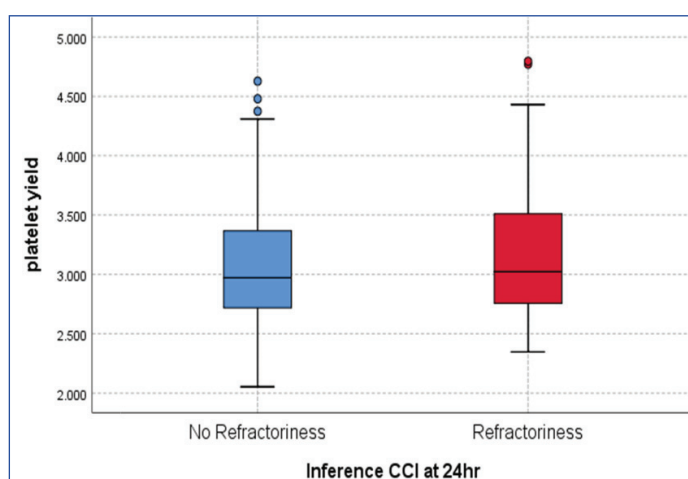
Parameters	Variables	Refractoriness		p-value
		Absent	Present	
		n (%)	n (%)	
Gender	Female	54 (34.40)	25 (52.10)	0.028
	Male	103 (65.60)	23 (47.90)	
Fever	Absent	10 (6.40)	7 (14.60)	0.071
	Present	147 (93.60)	41 (85.40)	
Sepsis	No	143 (91.10)	45 (93.80)	0.558
	Present	14 (8.90)	3 (6.30)	
Active bleeding	No	123 (78.30)	14 (29.20)	<0.001
	Present	34 (21.70)	34 (70.80)	
DIC	No	154 (98.10)	48 (100.00)	0.335
	Present	3 (1.90)	0	
Splenomegaly	No	106 (67.50)	23 (47.90)	0.014
	Present	51 (32.50)	25 (52.10)	
History of transfusion	Absent	11 (7.00)	2 (4.20)	0.354
	Present	146 (93.00)	46 (95.80)	
Parity	≤2	42 (26.80)	15 (31.30)	0.543
	>2	115 (73.20)	33 (68.80)	
Drug effect on platelet	Decrease	93 (59.20)	45 (93.80)	<0.001
	No Change	64 (40.80)	3 (6.30)	
ABO	Identical	131 (83.40)	32 (66.70)	0.012
	Non identical	26 (16.60)	16 (33.30)	
Mismatch	Bidirectional	5 (3.20)	5 (10.40)	0.06
	Major	12 (7.60)	6 (12.50)	
	Minor	9 (5.70)	5 (10.40)	
	No mismatch	131 (83.40)	32 (66.70)	
Days of storage	≤3	117 (74.50)	24 (50.00)	<0.001
	>3	40 (25.50)	24 (50.00)	

[Table/Fig-6]: Predictors of Corrected Count Increment (CCI) at one hour.

Parameters	Variables	Refractoriness		p-value
		Absent	Present	
		n (%)	n (%)	
Gender	Female	47 (34.60)	32 (46.40)	0.1
	Male	89 (65.40)	37 (53.60)	
Fever	Absent	9 (6.60)	8 (11.60)	0.222
	Present	127 (93.40)	61 (88.40)	
Sepsis	Absent	121 (89.00)	67 (97.10)	0.046
	Present	15 (11.00)	2 (2.90)	
Active bleeding	Absent	123 (90.40)	14 (20.30)	<0.001
	Present	13 (9.60)	55 (79.70)	
DIC	Absent	133 (97.80)	69 (100.00)	0.214
	Present	3 (2.20)	0	
Splenomegaly	Absent	95 (69.90)	34 (49.30)	0.004
	Present	41 (30.10)	35 (50.70)	
History of transfusion	Absent	12 (8.90)	1 (1.40)	0.119
	Present	124 (91.20)	68 (98.60)	
Parity	≤2	35 (25.70)	22 (31.90)	0.353
	>2	101 (74.30)	47 (68.10)	
Drug history	Present	73 (53.70)	65 (94.20)	<0.001
	Absent	63 (46.30)	4 (5.80)	
ABO	Identical	123 (90.40)	40 (58.00)	<0.001
	Non identical	13 (9.60)	29 (42.00)	
Mismatch	Bidirectional	3 (2.20)	7 (10.10)	<0.001
	Major	5 (3.70)	13 (18.80)	
	Minor	5 (3.70)	9 (13.00)	
	NA	123 (90.40)	40 (58.00)	
Days of storage	≤3	116 (85.30)	25 (36.20)	<0.001
	>3	20 (14.70)	44 (63.80)	

[Table/Fig-7]: Predictors of Corrected Count Increment (CCI) at 24 hours.

The details of dose of platelets transfused to refractory and non-refractory patients is given in [Table/Fig-8]. Patients who were found to be refractory received a mean dose of platelets 3.188×10^{11} (SD: 0.598); the non-refractory group received a mean dose of platelets 3.056×10^{11} (SD: 0.508). This difference was not statistically significant ($p=0.306$).



[Table/Fig-8]: Dose of platelet transfused to refractory and non-refractory patients.

In multivariable logistic regression analysis, active bleeding (adjusted OR 138.22; 95% CI 27.76-688.20; $p<0.001$), storage duration >3 days (adjusted OR 25.35; 95% CI 5.73-112.11; $p<0.001$) and ABO incompatibility (adjusted OR 10.56; 95% CI 2.52-44.33; $p=0.001$) were independently associated with 24-hour platelet refractoriness (CCI $<5 \times 10^9/L$). Drug-related platelet decrease was also significantly associated with refractoriness ($p=0.011$), whereas

splenomegaly did not show independent significance ($p=0.503$) [Table/Fig-9].

Variables	Adjusted Odds Ratio (OR)	95% CI of OR	p-value
Active bleeding (Present)	138.22	27.76 - 688.20	<0.001
Storage duration >3 days	25.35	5.73 - 112.11	<0.001
ABO non identical	10.56	2.52 - 44.33	0.001
Splenomegaly (Present)	1.48	0.47 - 4.72	0.503
Drug-related platelet response (No change vs decrease)	0.14	0.03 - 0.64	0.011

[Table/Fig-9]: Multivariable logistic regression analysis for predictors of 24-hour platelet refractoriness.
Reference categories: Active bleeding (No), Storage duration ≤ 3 days, ABO identical, Splenomegaly absent, Drug-related platelet decrease

The regression model was refined to avoid overfitting by limiting predictors to clinically relevant variables. The association between active bleeding and refractoriness remains strong and statistically significant. Confidence intervals are reported to reflect estimate precision [Table/Fig-9].

Sepsis was assessed in the univariate analysis; however, during multivariable modeling, variables were selected based on statistical significance, clinical relevance and avoidance of multicollinearity. Sepsis overlapped with other variables reflecting systemic illness and did not remain an independent predictor after adjustment. Therefore, it was not retained in the final model to maintain model stability and avoid overfitting [Table/Fig-9].

DISCUSSION

The CCI remains a widely accepted indicator of platelet transfusion efficacy [16]. It indicates the rise in platelet count after transfusion. It serves as a quantitative indicator of how well transfused platelets recover and persist in the recipient's bloodstream [16]. The TRAP Trial database provides various patient and product related factors affecting the CCI [17]. Successful transfusion is defined as a CCI >5000 at 24 hours [5]. The present study underscores considerable CCI at one hour and 24 hours following pooled RDP transfusion prepared by the PRP method in thrombocytopenic patients. Platelet refractoriness was identified in 33.65% of patients in the present study [4,18-21].

The present study noted various demographic, clinical and transfusion-related parameters that influence post-transfusion CCI in thrombocytopenic patients, highlighting factors that affect platelet transfusion efficacy and refractoriness to optimise transfusion strategies.

Several clinical variables like fever, sepsis, splenomegaly, history of bleeding and drug exposure affect the CCI. Fever and infections can accelerate platelet destruction through immune-mediated mechanisms, while splenomegaly leads to sequestration of platelets in the enlarged spleen, reducing their circulating lifespan. Haematologic malignancies, particularly those involving the bone marrow, not only reduce platelet production but also increase the likelihood of alloimmunisation, which can result in refractoriness to platelet transfusions [4].

Although fever was present in 88.4% of patients exhibiting platelet refractoriness, the association between fever and 24-hour refractoriness was not statistically significant ($p=0.222$). This finding was consistent with the reports of Shastry S and Chaudhary R, and Chenna D et al., suggesting a variable impact of fever on platelet consumption and transfusion efficacy [18,19]. In contrast, other studies by Slichter SJ et al., Kumawat V et al., and Sahu DP et al., have identified fever as a contributing factor for platelet refractoriness [4,20,21].

Sepsis was a significant determinant of platelet refractoriness in the present study ($p=0.046$), corroborating findings of Slichter SJ et al.,

Hussein E and Bishop JF et al., [4,22,23]. Similarly, active bleeding demonstrated a strong association with refractoriness, with 79.7% of refractory patients experiencing ongoing haemorrhage ($p<0.001$). This reflects enhanced platelet consumption and ongoing loss during active bleeding, as also noted by Slichter SJ et al., and Kumawat V et al., [4,20].

Splenomegaly was observed in a substantial proportion of our cohort (37.1%) and was significantly associated with lower post-transfusion CCI ($p=0.014$). This is likely due to increased sequestration and pooling of transfused platelets within the enlarged spleen, thereby diminishing the effective circulating platelet count.

The very high odds ratio observed for active bleeding in the multivariate analysis adjusted (OR 138.22) is clinically plausible. Active bleeding is a major indication for urgent and repeated transfusion of blood components, leading to greater exposure to transfusions and related complications. Such patients are often critically-ill and may have underlying coagulopathy or haemodynamic instability, which further strengthens this association. Additionally, the relatively smaller number of patients without active bleeding in the cohort may have contributed to an inflated odds ratio in the regression model. Overall, this finding highlights active bleeding as a strong clinical predictor in the study population.

Donor-related factors also play a significant role in CCI. Donor platelet quality, including platelet viability, pH and storage duration, affects post-transfusion recovery [4]. Additionally, donor-specific antigens may contribute to the development of alloimmunisation in recipients, further diminishing the efficacy of subsequent transfusions. HLA-matched platelets demonstrate higher CCI compared to RDPs in refractory patients. Platelet refractoriness is characterised by a suboptimal increase in platelet count following repeated platelet transfusion [5]. It has been the subject of extensive research across diverse patient populations.

In the present study, 94.2% of refractory patients were receiving treatments such as chemotherapy, antibiotics and antifungal agents. Platelet refractoriness was significantly associated with concurrent drug therapies ($p<0.001$). This finding was similar with those reported by Shastry S and Chaudhary R Shastry S et al., and Chenna D et al., underscoring the suppressive effects of various drug regimens on platelet increment [4,18,19].

Transfusion-related factors, such as the dose of platelets transfused, transfusion timing and the presence of concurrent medications, also influence CCI [4]. Studies have shown that platelets stored for longer durations exhibit reduced viability, leading to lower CCI [4]. Higher platelet doses generally result in better increments, though the response may plateau beyond a certain threshold. The timing of transfusion in relation to ongoing bleeding or chemotherapy administration impacts platelet survival and function. Chemotherapy-induced endothelial damage and radiation therapy can adversely affect platelet adhesion and aggregation, thereby reducing post-transfusion platelet recovery [6,10]. Moreover, certain medications, including antibiotics and antiplatelet drugs, interfere with platelet function and contribute to suboptimal CCI [9].

Several transfusion-related variables that significantly influence post-transfusion platelet increment were identified in the present study. Notably, ABO non identical platelet transfusions were strongly associated with platelet refractoriness. Among patients receiving ABO non identical platelets, 42% exhibited suboptimal CCI ($p<0.001$), whereas 79.5% of those receiving ABO-identical transfusions did not develop refractoriness ($p<0.001$). These findings imply the clinical importance of ABO compatibility in platelet transfusion, supporting the hypothesis that immune-mediated clearance of incompatible platelets contributes to reduced platelet survival. The present study results were congruent with the observations of Pavenski K et al., and Zaffuto BJ et al., who emphasised the benefits of ABO-identical platelet transfusions [24,25].

Additionally, prolonged storage (>3 days) was significantly associated with platelet refractoriness ($p < 0.001$). Among patients with refractoriness, 44 patients (63.8%) had received platelets stored beyond three days, in contrast to 116 patients (85.3%) of non-refractory patients who received platelets stored ≤ 3 days. This supports the findings by Slichter SJ et al., highlighting the detrimental effects of storage-related changes on platelet function and viability [4]. However, the present study findings differ from those of Ahmed A et al., and Das N et al., who reported that storage duration did not consistently affect post-transfusion platelet increments, indicating the need for further investigation into patient-specific responses and storage-related variables [26,27].

Alloimmunisation remains a key challenge in achieving satisfactory CCI [19]. Strategies such as leukoreduction, cross-matched or HLA-HPA compatible platelet transfusions have demonstrated superior efficacy in managing alloimmune refractoriness [4,19,20]. Thus, clinical and platelet product-related variables were significantly associated with suboptimal post-transfusion platelet increments in our study. Interestingly, baseline patient characteristics such as age ($p = 0.849$) and gender ($p = 0.852$) did not show significant association with post-transfusion CCI. These results were concordant with studies by Sharma S et al., suggesting that intrinsic patient demographics may play a less critical role in determining transfusion outcomes compared to clinical status and product-related factors [28]. Multiple studies conducted by various authors, indicating the prevalence of platelet refractoriness between 13.3% and 75%, have been summarised in [Table/Fig-10] [4,18-21,29,30].

Authors	Year	Sample size	Cases of unsuccessful CCI	Rate of refractoriness (%)
Slichter SJ et al., [4]	2005	533	144	27%
Shastri S and Chaudhary R [18]	2012	40	9	22.5%
Agarwal N et al., [30]	2014	340	127	37.5%
Kumawat V et al., [20]	2015	30	17	56.6%
Mangwana S and Simon N [29]	2016	30	3	13.33%
Chenna D et al., [19]	2020	339	102	30.1%
Sahu DP et al., [21]	2023	60	45	75%
Present study	2025	205	69	33.65%

[Table/Fig-10]: Comparison of rates of platelet refractoriness among various studies [4,18-21,29,30].

Limitation(s)

Despite its valuable findings, the present study has certain limitations. It was a single-centre study with a smaller sample size and short term follow-up which were insufficient to detect relevant statistical associations. Parameters like HLA alloimmunisation, presence of platelet-specific antibodies and pathogen reduction were not evaluated. Also the study did not account for the use of SDP and buffy coat-derived platelets.

CONCLUSION(S)

Despite a relatively high success rate of platelet transfusions, refractoriness remains a significant challenge, particularly in patients with underlying inflammatory conditions, those receiving frequent transfusions and older platelet units. Multiple factors like active bleeding, splenomegaly, medication, ABO non identical transfusion and prolonged platelet storage are associated with lower CCI and higher refractoriness rates in post-transfusion of pooled RDP by PRP method in thrombocytopenic patients. Larger studies and improved CCI-based prediction models are needed, along with evaluation of strategies such as pathogen reduction, HLA/HPA matching and growth factor therapies to enhance transfusion outcomes.

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