

# **ORIGINAL ARTICLE**

# Validity of Platelet Mass Index in Platelet Transfusion in Management of Neonatal Thrombocytopenia

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#### **ABSTRACT**

**Keyword**: : NT, NICU, PMI Guideline, PC Guideline.

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Background: Platelets serve as the primary defense mechanism against hemorrhage. Neonatal thrombocytopenia is a common hemostatic abnormality among newborns in the neonatal intensive care unit (NICU), and using prophylactic platelet transfusion resulted in a higher rate of death or significant bleeding. Objectives: This study aimed to compare the outcome of using Platelet Mass Index (PMI) versus Platelet Count (PC) guidelines in prophylactic platelet transfusion. Methodology: This single-blinded, randomized controlled trial was conducted on 140 neonates with a <100,000/ml platelet count admitted to the NICU. Results: A significantly higher percentage of patients needed platelet transfusion in the PC guideline group vs. the PMI guideline group (77.1% vs 17.1%). Further, there was a statistically significantly higher percentage of hemorrhage, pulmonary hemorrhage, and mortality in the PC group vs. the PMI group (24.3% vs 10%, p=0.025, 17.1% vs 5.7%, p=0.034v 22.9% vs 10%, pvalue=0.040, respectively). **Conclusion:** This study demonstrated that transfusion strategies based on PMI guidelines resulted in higher post-transfusion platelet counts compared to the PC approach. Also, significant improvements in clinical outcomes were observed in the PMI group, including lower bleeding rates, intracranial hemorrhage, and mortality.

## INTRODUCTION

Platelets act as the main defense against hemorrhage brought on by both microvascular and macrovascular injuries by adhering and aggregating to maintain endothelial integrity. If your platelet count (PC) is less than  $150 \times 10^{\circ}$  you have thrombocytopenia (1).

A common hemostatic abnormality among newborns in the Neonatal Intensive Care Unit (NICU) is neonatal thrombocytopenia (NT), which rises in proportion with prematurity. Numerous immunologic and non-immunologic factors have been found to contribute to NT (2).

There was a higher risk of death or significant bleeding when prophylactic platelet transfusion was used based on a platelet-count threshold of 50,000 as opposed to 25,000 (3). Platelet transfusion rates in the NICU may be decreased by using criteria based on the platelet mass index (PMI), but more information from prospective studies is needed (4).



The primary objective of this study was to assess the efficacy of utilizing PMI criteria as a predictive tool to optimize the administration of prophylactic platelet transfusions in neonates with NT admitted to the NICU at Aswan University Hospital (AUH).

#### PATIENTS AND METHODS

This single-blinded Randomized Controlled Clinical Trial (RCT) was conducted on 140 neonates with NT, admitted to the NICU at AUH from April 2022 to October 2023. The sample size was calculated using Stata 16. The alpha error = 0.05, power 80%, and the reduction of prophylactic blood transfusion from 92% to 73% (5). The minimum required sample was 124 participants. To compensate for attrition and drop-outs, the sample was raised by 20% to 140 (i.e., 70 per group).

Cases admitted to NICU with NT with a <100,000/ml PLT count were included. On the other hand, those with significant congenital anomalies, hydrops fetalis, family history of thrombocyte diseases, or coagulation disorders were excluded. The patients were grouped according to the onset of thrombocytopenia. Thrombocytopenia before 72 h was defined as early-onset thrombocytopenia and after 72 h as late-onset thrombocytopenia(4).

#### **Randomization:**

Random numbers were generated at the computer center. Eligible cases were randomly assigned into two equal groups: Group I, which included 70 neonates with platelet transfusion according to the PLT count-based guideline, and Group II, which included 70 neonates with platelet transfusion according to the PMI-based guideline. Allocation was contained in opaque, sequentially numbered, sealed envelopes.

PMI is determined by multiplying platelet count by mean platelet volume (MPV), and the recommendation for transfusion based on PMI is as follows: PMI is < 800 in pre/postoperative patients, < 400 in unstable patients, and < 160 in stable patients (4).

## **Procedure**

All cases underwent entire history taking, clinical examination, and complete blood count (CBC). The number of PLT transfusions in both groups was recorded.

Clinical conditions of patients were classified into stable patients, unstable patients and immediate pre or postoperative patients.

Stable patients: premature (heart rate: 120-170 beats/minute, blood pressure: 55-75/35-45 mm Hg, respiratory rate: 40-70 breaths/minute). Full-term (heart rate: 100-150 beats/minute, blood pressure:65 -85/45-55 mm Hg, respiratory rate: 35-55 breaths/minute).

Unstable patients (neonates<1500 g birth weight in the first week of life or patients with heart rate or blood pressure or respiratory rate below the expected level for age and need resuscitation including mechanical ventilators or receiving continuous vasopressors) (6).

The PLTs were extracted from whole blood donations, which underwent leucofiltration. After matching, they were given in a dosage of 10–20 milliliters per kilogram of body weight.

PLT counts and MPVs were determined using a Sysmex Xn 1000 Hematology Analyzer and a Mindray Hematology Analyzer BC-5150. Venous blood sample (3ml) anticoagulated with ethylene diamine tetra acetic acid (EDTA).

Morbidity and mortality in both groups were recorded. Morbidity included infections, birth asphyxia, prematurity, low birth weight, necrotizing enterocolitis and hyperbilirubinemia. In addition, hemorrhages (pulmonary, gastrointestinal and mucocutaneous) in both groups were evaluated.



Major hemorrhage is defined as a hemorrhage requiring prompt, sustained nursing intervention (e.g., pulmonary hemorrhage requiring repeated endotracheal tube suctioning) or medical evaluation/intervention (e.g., red blood cell transfusion within 24 h).

# Statistical analysis

Data analysis was undertaken using IBM-SPSS version 26 (7). Categorical data were presented as frequencies and percentages. Numerical data were checked for normality by the Shapiro-Walk test and presented as mean and standard deviation (SD) or median and range according to their distribution. The Independent Sample T-test/Mann-Whitney U test was used to compare the mean/median difference between the two groups as appropriate. A Paired Sample T-test/Wilcoxon Sign test was used to compare the mean/median within the group before vs. after transfusion. The chi-square test/Fisher's exact test was used to compare proportions between groups as convenient. The level of significance was considered at p-value < 0.05.

#### **Ethical considerations**

The institutional Ethics and Research Review Board (IRB) of the Faculty of Medicine at Aswan University approved the study's methodology. The newborn enrolled in this study signed a written informed consent before the trial execution. Our team adhered to the World Medical Association Declaration of Helsinki (1964), which discusses the ethical conduct of research involving humans and/or animals. The study was not based on any incentives or rewards for the participants or their caregivers and abided by the Helsinki Declaration (8) guidelines and the STROBE guidelines for observational studies (9).

#### **RESULTS**

**Table 1** shows the baseline characteristics of the studied cohort. The mean gestational age was 34.9  $\pm$  2.9 weeks, ranging from 26 to 40 weeks. The mean weight was 2061.6  $\pm$  766.4 grams and ranged from 800 to 4200 grams. 57.1% were males, and 42.9% were females.

Table 1: Demographic data of studied neonates with thrombocytopenia.

Variables	Total (n=140)	
Gestational age (weeks)	Mean $\pm$ SD (range)	34.94 ± 2.9 (26 - 40)
Weight (gm)	Mean $\pm$ SD (range)	2061.57 ± 766.4 (800 - 4200)
Sex	N	%
Males	80	57.1
Females	60	42.9

**Table 2** compares the demographic and clinical data of the studied groups. Both groups were matched for age (p=0.074), weight (p=0.108), and sex (p=0.495). Likewise, non-significant differences regarding neonatal and maternal risk factors were observed between the two studied groups.



Table 2: Baseline Demographic and Clinical Data Differences Between Groups

Variables	PC guideline (n=70)	PMI guideline (n=70)	P-Value
Gestational age (weeks)			
$Mean \pm SD$	$34.50 \pm 2.9$	$35.37 \pm 2.8$	0.074*
(range)	(26 - 40)	(30 - 40)	0.074
Weight (gm)			
Mean $\pm$ SD	$1956 \pm 709.2$	$2167.14 \pm 829.9$	0.108*
(range)	(800 - 3500)	(900 - 4200)	0.108
Sex			
Males	42 (60.0%)	38 (54.3%)	0.495**
Females	28 (40.0%)	32 (45.7%)	0.493
Neonatal risk factors			
Respiratory distress syndrome	36 (51.4%)	47 (67.1%)	0.058**
Prematurity	39 (55.7%)	34 (48.6%)	0.398**
Sepsis	34 (48.6%)	26 (37.1%)	0.172**
Hyperbilirubinemia	13 (18.6%)	16 (22.9%)	0.532**
Blood incompatibility	8 (11.4%)	5 (7.1%)	0.562**
Premature rupture of membrane	13 (18.6%)	15 (21.4%)	0.673**
Necrotizing enterocolitis	12 (17.1%)	12 (17.1%)	0.999**
Intrauterine growth restriction	8 (11.4%)	11 (15.7%)	0.459**
Maternal risk factors			
Pre-eclampsia	10 (14.3%)	17 (24.3%)	0.134**
38467Diabetes mellites	3 (4.3%)	6 (8.6%)	0.493***
Hepatitis B, C	3 (4.3%)	1 (1.4%)	0.620***
ITP	1 (1.4%)	2 (2.9%)	0.999***
SLE	2 (2.9%)	1 (1.4%)	0.999***
COVID-19	1 (1.4%)	2 (2.9%)	0.999***

<sup>\*</sup>Independent Sample T-test compares mean between two groups

**Table 3** presents the comparison of thrombocytopenia characteristics between the studied groups. An insignificant difference was found regarding the onset of thrombocytopenia, day of onset, and severity of thrombocytopenia (p>0.05). On the other hand, a significantly (p<0.001) higher percentage of patients needed platelet transfusion in the PC guideline group vs. the PMI guideline group (77.1% vs 17.1%, respectively). Likewise, the median number of platelet transfusions for patients in the PC guideline group was significantly higher (p<0.001) than the PMI guideline group. Likely, the mean total number of transfusions was significantly higher (p<0.001) compared to the PMI guideline group.

<sup>\*\*</sup>Chi-square test compares proportion between groups

<sup>\*\*\*</sup> The Fisher Exact test was used to compare proportions between groups



Table 3: Comparison of thrombocytopenia characteristics among studied groups.

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	PC guideline	_	P-Value
	(n=70)	(n=70)	1 value
Onset of thrombocytopenia			
Early onset	26 (37.1%)	33 (47.1%)	0.221*
Late onset	44 (62.9%)	37 (52.9%)	0.231*
Day of onset:			
Mean $\pm$ SD	$3.97 \pm 2.5$	$4.14 \pm 3.4$	0.856**
Median (range)	4.00 (1 - 13)	4.00 (1 - 20)	0.830***
Severity of thrombocytopenia			
Moderate (50,000-100,000)	33 (47.1%)	41 (58.6%)	0.176*
Server (Less than 50,000)	37 (52.9%)	29 (41.4%)	0.176
Patients need platelets transfusion			
Not needing a platelet transfusion	16 (22.9%)	58 (82.9%)	۵۰ ۵۵1 ×
Need platelet transfusion	54 (77.1%)	12 (17.1%)	<0.001*
Number of platelets transfusions			
for patient			
$Mean \pm SD$	$1.33 \pm 1.3$	$0.24 \pm 0.6$	۰۸ ۸۸1**
Median (range)	1.00 (0 - 7)	0.00 (0 - 2)	<0.001**
The total number of transfusions in patients who need platelet transfusion			
Mean ± SD	$93.22 \pm 9.1$	$17.92 \pm 1.8$	<0.001**
Median (range)	93 (77 - 97)	17 (10 - 22)	

<sup>\*</sup>Chi square test was used to compare proportions between groups

Table 4: Effect of Transfusion on the Laboratory Findings among studied groups.

	PC guideline	PMI guideline	P-value*
	(n=70)	(n=70)	
White blood cells (×1000)			
Before transfusion	11.80 (2.3-35.0)	9.30 (1.2-68.0)	0.128
After transfusion	10.00 (3.0-36.0)	10.10 (3.9-32.8)	0.707
P-Value**	0.021	0.505	
Neutrophils (×1000)			
Before transfusion	6.45 (1.2-20.6)	4.90 (0.4-65.5)	0.145
After transfusion	5.00 (0.09-22.00)	5.30 (2.00-25.00)	0.144
P-Value**	0.039	0.872	
Lymphocytes (×1000)			
Before transfusion	3.00 (0.10-10.00)	3.15 (0.70-20.00)	0.395
After transfusion	3.25 (0.27-11.40)	3.20 (1.10-18.30)	0.419
P-Value**	0.639	0.758	
Hemoglobin (g/dl)			
Before transfusion	$13.42 \pm 2.2$	$14.17 \pm 2.8$	0.081
After transfusion	$13.20 \pm 2.2$	$13.64 \pm 2.4$	0.303
P-Value**	0.425	0.064	

<sup>\*\*</sup>Mann-Whitney U-test compares median between two groups



	PC guideline (n=70)	PMI guideline (n=70)	P-value*
Mean corpuscular volume (Um)			
Before transfusion	$93.36 \pm 8.9$	$97.66 \pm 8.5$	0.001
After transfusion	$91.47 \pm 7.7$	$95.97 \pm 7.9$	< 0.001
P-Value**	0.017	0.007	
Platelets (×1000)			
Before transfusion	48.50 (10.0-99.0)	49.00 (5.0-96.0)	0.943
After transfusion	125.00 (10.0-348.0)	162.50 (8.0-312.0)	< 0.001
P-Value**	<0.001	<0.001	
Mean platelet volume (Fl/nl)			
Before transfusion	$10.31 \pm 1.4$	$10.49 \pm 1.7$	0.281
After transfusion	$9.66 \pm 1.1$	$9.44 \pm 1.2$	0.232
P-Value**	<0.001	<0.001	
Platelet mass index			
Before transfusion	513.60 (88.0-1138.5)	502.90 (60.0-1035.5)	0.717
After transfusion	1239.0 (80.0-3828.0)	1489.0 (96.0-2808.0)	0.002
P-Value**	<0.001	<0.001	
<b>Prothrombin time (sec.)</b>	$12.11 \pm 0.6$	$12.01 \pm 0.7$	0.357
Partial thromboplastin time	$34.25 \pm 4.9$	$33.78 \pm 4.5$	0.549
(sec.)	34.23 ± 4.9	33.78 ± 4.3	0.549
International normalization	$1.09 \pm 0.1$	$1.05 \pm 0.1$	0.155
ratio			
C-Reactive protein	5.0 (.50-276.0)	4.75 (0.50-130.0)	0.423
For infants with hyperbilirubinemia			
Total bilirubin	22.0 (7.8-38.0)	21.75 (9.6-30.9)	0.948
Direct bilirubin	1.0 (0.30-16.60)	1.95 (0.50-8.40)	0.124
Indirect bilirubin	19.50 (6.0-34.0)	19.00 (8.6-29.9)	0.878

<sup>\*</sup>Independent Sample t-test/Mann-Whitney U test compares mean/median between groups.

\*\*Paired Sample T test/Wilcoxon Sign test compares mean/median between groups in each group before and after transfusion

Table 4 shows no significant difference between groups or within each group (before vs. after transfusion) regarding WBCs, neutrophils, lymphocytes, and hemoglobin. However, there was a significant reduction (p=0.039) in neutrophilic ratio within the PC guideline group. Moreover, there was a higher mean MCV among the PMI vs. PC group, and within each group, there was a significant reduction in mean MCV after transfusion.

For platelet count, there was an insignificant difference between groups before transfusion, while there was a significantly higher mean platelet count among the PMI group after transfusion vs the PC group, and within each group, there was a statistically significant increase in mean platelet count after transfusion

Regarding MPV, each group had a significant reduction after the transfusion. Also, there was a statistically significant higher PMI among the PMI group after transfusion vs. the PC group. Within each group, there was a significant rise in PMI after transfusion. Conversely, both groups were comparable concerning coagulation profile and C-reactive protein. Also, insignificant differences



were found among infants with hyperbilirubinemia regarding total, direct, and indirect bilirubin before transfusion.

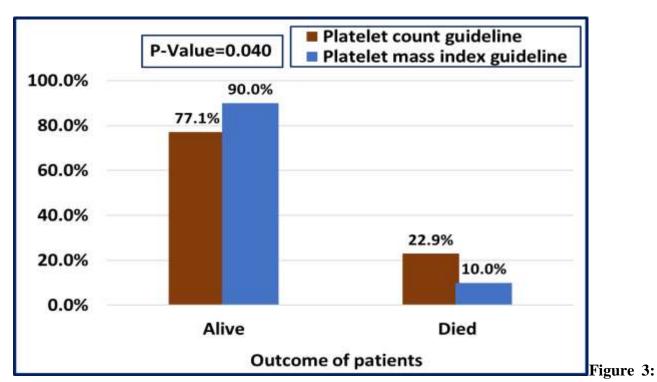
**Table 5** and **Fig 3** compare outcome measures among the studied groups. There was a non-significant difference between the two studied groups regarding blood culture results. For the imaging findings, there was a significantly higher percentage of positive signs for respiratory distress (RD) in chest x-rays among the PMI group vs. PC group (70% vs. 50%, p-value=0.016). However, no significant difference was delineated regarding plain erect and transcranial ultrasound. Furthermore, the PC group had a statistically significant higher percentage of hemorrhage than the PMI group (24.3% vs. 10%, p=0.025). Likewise, the PC group had a higher percentage of pulmonary hemorrhage than the PMI group (17.1% vs. 5.7%, p=0.034). Also, there was a statistically significant higher percentage of mortality in the PC group compared with the PMI group (22.9% vs. 10%, p-value=0.040) (**Fig. 3**).

Table 5: Comparison of Outcome results among studied groups

Variables	PC guideline (n=70)	PMI guideline (n=70)	P-value*
Blood culture			
No growth	39 (55.7%)	44 (62.9%)	0.390
Gram-negative organism	27 (38.6%)	17 (24.3%)	0.069
Gram-positive organism	4 (5.7%)	9 (12.9%)	0.243
Chest X-ray			
Positive signs of RD	35 (50.0%)	49 (70.0%)	0.016
Plain erect			
No abnormal signs	45 (64.3%)	52 (74.3%)	0.200
Necrotizing enterocolitis	11 (15.7%)	12 (17.1%)	0.820
Intestinal obstruction	14 (20.0%)	6 (8.6%)	0.054
Transcranial ultrasound			
Hemorrhage	6 (8.6%)	2 (2.9%)	0.145
Hemorrhage Type of hemorrhage	17 (24.3%)	7 (10.0%)	0.025
Pulmonary	12 (17.1%)	4 (5.7%)	0.034
Intracranial hemorrhage	6 (8.6%)	2 (2.9%)	0.275
Cutaneous	2 (2.9%)	2 (2.9%)	0.999
Gastrointestinal	3 (4.3%)	0 (0.0%)	0.245
Outcome			
Alive	54 (77.1%)	63 (90.0%)	0.040
Dead	16 (22.9%)	7 (10.0%)	



### \*Chi square test was used to compare proportions between groups



Comparison of outcome among studied groups

#### DISCUSSION

About one-fourth of neonates in NICUs have thrombocytopenia, which is defined as a platelet count below 150,000/mm<sup>3</sup>. The incidence of thrombocytopenia rises with decreasing gestational age, and it affects about 70% of very low birth weight neonates (11, 12). Despite the lack of evidence linking platelet counts to the risk of bleeding in neonates, prophylactic platelet transfusions are used in hospitalized neonates as part of clinical practice (13).

Increased mortality and morbidities, including severe intraventricular hemorrhage, necrotizing enterocolitis, retinopathy of prematurity and acute kidney injury in preterm infants, are linked to platelet transfusion (3, 14). Therefore, the use of a restrictive neonatal platelet transfusion guideline is advocated to decrease potentially hazardous platelet transfusions in NICUs, while the benefits of prophylactic platelet transfusions in neonates are disputed (15).

IS PMI harboring a chance that platelet transfusions in the NICU will decline? The only specific treatment for thrombocytopenia, a common issue in NICU, is platelet transfusion, which carries known risks (16). There are no documented Egyptian or Arabic randomized clinical trials about the role of platelet mass index in platelet transfusion in neonatal thrombocytopenia. Hence, the current work aimed to determine if PMI guidelines would lead to decreased transfusions. This single-blinded RCT was conducted on 140 neonates with thrombocytopenia at NICU, Pediatric Department, Aswan University Hospital, Egypt.



Among the studied group, the mean gestational age was  $34.9 \pm 2.9$  weeks, the mean weight was  $2061.6 \pm 766.4$  grams, and 57.1% were males and 42.9% were females. Likely, a Turkish retrospective study that was conducted by Kasap et al. (4) on 395 neonates with at least one recorded platelet count  $< 150 \times 109$ /L detected that the mean gestational age was  $34.4 \pm 4.5$  weeks, the median weight was 2322 grams, and 56% were males and 44% were females. In a Turkish retrospective cross-sectional study conducted by **Okbay et al.** (17) on 28 neonates who received prophylactic platelet transfusion, the median gestational age and weight values of the neonates were 34.5 (26–37) weeks and 2450 (740–3100) grams, respectively. About 53.6% of them were males.

As for the comparison of demographics and risk factors between studied patients among studied groups (PC group and PMI group), both groups were matched for gestational age, weight, sex, and neonatal and maternal risk factors. Similar to our results a Turkish study that was conducted by Yavuzcan Öztürk et al. (16) detected that demographic characteristics and risk factors of the infants in both groups showed insignificant differences.

Furthermore, in the current study, an insignificant difference was found regarding the onset of thrombocytopenia and the severity of thrombocytopenia. However, the number of patients who needed platelet transfusion was higher in the PC group vs. the PMI group (77% vs 17%, p<0.001). Moreover, there was a significantly higher median number of platelets transfusions for the PC vs PMI group (p<0.001). This was in agreement with an American study done by **Gerday et al. (5)**, the incidence of PLT transfusion was lower when the PMI guideline was used. The number of PLT transfusions administered per transfused patient was the same in both groups, but significantly fewer PLT transfusions were given for prophylaxis when the PMI guideline was used and there was no recognized increase in hemorrhagic problems. In another Turkish retrospective study done by **Kahvecioglu et al. (18)**, they found that 53% of the babies transfused according to the PC -based guidelines were transfused beyond the current guideline indications and an additional 11.5% would not be transfused if the PMI guideline was used.

On the other hand, our results disagreed with an American pilot study by **Zisk et al.** (19), in which neonates were randomized to receive PLT transfusions based on PMI vs. PC, and no difference was found in the number of platelet transfusions received. Notably, more infants (47% vs 38%) were transfused in the group where the PMI guideline was used. A small sample of this pilot study may explain this. Moreover, **Yavuzcan Öztürk et al.** (16) detected no significant difference between the two studied groups regarding the mean number of platelets transfusion and the median age of transfusion.

This study observed insignificant differences between groups regarding WBC, neutrophils, or lymphocytes before and after platelet transfusion. However, there was a significant reduction in WBC and neutrophils post-transfusion in the PC group, suggesting that transfusion may influence these specific immune cell counts in this group. The lack of significant change in lymphocytes between and within groups indicates that lymphocyte levels remain relatively unaffected by platelet transfusion. This pattern could be related to the selective impact of transfusion on different immune cells, or the underlying conditions being treated.

In the current study, hemoglobin levels remained consistent, showing non-significant differences between the groups or within each group before and after transfusion. This indicates that the platelet transfusion did not significantly impact hemoglobin levels.

In contrast, MCV was significantly higher in the PMI group compared to the PC group. Additionally, MCV decreased significantly after the transfusion in both groups. This suggests that platelet transfusion may influence red blood cell size, particularly reducing MCV, which could



reflect changes in the characteristics of circulating red blood cells, possibly due to the dilution effect or shifts in red blood cell production post-transfusion. Platelet counts showed no significant differences between groups before transfusion; however, the PMI had significantly higher platelet counts after transfusion than the PC group, with both groups showing a significant increase in mean platelet counts post-transfusion.

MPV did not differ significantly between groups before or after transfusion, but there was a significant decrease in MPV within each group following transfusion, indicating a potential reduction in platelet size. Regarding PMI, there were no significant differences before transfusion, but it demonstrated significantly higher values after transfusion compared to the PC group, with both groups showing a significant increase in PMI post-transfusion, highlighting the effectiveness of transfusions in elevating both platelet counts and overall platelet mass in circulation. Yavuzcan Öztürk et al. (16) detected no significant difference between the two studied groups regarding platelets and platelet mass index.

As regards blood culture, there was an insignificant difference between the groups regarding blood culture results. Since infections are a significant cause of NT, this uniformity in blood culture results suggested that both groups were similarly affected by the infectious component, which did not bias the platelet response, clinical condition, or outcomes related to transfusion. It also implies that infection management strategies likely remain consistent across groups, with similar interventions for sepsis or other infection-related complications. Therefore, any differences in other clinical outcomes between the groups would be more likely attributed to factors other than infection, such as transfusion protocols or underlying clinical conditions.

Regarding imaging, the PMI group had a significantly higher percentage of positive signs for RD in chest X-rays than the PC group (70% vs. 50%, p=0.016). However, there was an insignificant difference between the groups regarding plain erect and transcranial ultrasound results. This could be explained by the fact that ARDS is associated with several clinical disorders, including direct pulmonary injury from pneumonia and aspiration and extra-pulmonary injury from sepsis, traumas, and multiple transfusions (20).

As regards the comparison of outcomes, there was a statistically significant higher percentage of hemorrhage in the PC compared with the PMI group (24% vs 10%, p=0.025. Moreover, there was a statistically significant higher percentage of pulmonary hemorrhage in the PC vs PMI group (17% vs 5.7%, p=0.034), nevertheless, other types of hemorrhage did not show any significant difference. Additionally, there was a statistically significant higher percentage of mortality in the PC vs PMI group (23% vs 10%, p=0.040).

Yavuzcan Öztürk et al. (16) detected that there was a significant difference between the two studied groups as regards gastrointestinal bleeding (P= 0.08) while other types of hemorrhage showed non-significant between groups. Also, they reported no statistically significant difference as regards mortality. Zisk et al. (19) detected that no difference was found in bleeding episodes or mortality between the studied groups. Similarly, Kahvecioglu et al. (18) revealed that there was no recognized increase in hemorrhagic problems.

## **CONCLUSION**

In conclusion, this study provides important insights into managing neonatal thrombocytopenia, demonstrating that transfusion strategies based on PMI guidelines resulted in significantly higher post-transfusion platelet counts than the traditional PC approach. Also, compared to the PC group,



significant improvements in clinical outcomes were observed in the PMI group, including lower bleeding rates, intracranial hemorrhage, and mortality. Overall, these findings supported using a PMI-based approach for more precise transfusion management, potentially reducing complications and improving survival rates in NT.

## **Study Limitations**

The current study had some limitations. First, it was a single-center study, which limited its external validity (generalization). Second, possible confounding factors (presence of alloimmunization, platelet refractoriness, etc.) were not accounted for when matching between groups.

**Conflict of interest:** All authors declare no conflicts of interest.

Financial Disclosures: None

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#### REFERENCES

- 1. Saran K, Vidya K, Seema K, Prasad A & Prakash J (2022): Study of platelet indices and their role in the evaluation of thrombocytopenia. Journal of Family Medicine and Primary Care, 11(10): 6236-6242.
- 2. **Lookzadeh MH, Mirjalili SR & Ekraminasab S (2020):** Immune and Non-Immune Etiology of Thrombocytopenia: Neonatal and Maternal Causes. World Journal of Peri & Neonatology, 3(2): 78-86.
- 3. Curley A, Stanworth SJ, Willoughby K, Fustolo-Gunnink SF, Venkatesh V, Hudson C, et al. (2019): Randomized trial of platelet-transfusion thresholds in neonates. New England Journal of Medicine, 380(3): 242-251.
- 4. **Kasap T, Takçı Ş, Irak BE, Gümüşer R, Sönmezgöz E, Gül A, et al. (2020):** Neonatal thrombocytopenia and the role of the platelet mass index in platelet transfusion in the neonatal intensive care unit. Balkan Medical Journal, 37(3): 150-159.
- 5. Gerday E, Baer VL, Lambert DK, Paul DA, Sola-Visner MC, Pysher TJ, et al. (2009): Testing platelet mass versus platelet count to guide platelet transfusions in the neonatal intensive care unit. Transfusion, 49(10): 2034-2039.
- 6. **American Heart Association (2006):** AHA guidelines for cardiopulmonary resuscitation (CPR) and emergency cardiovascular care (ECC) of pediatric and neonatal patients: pediatric advanced life support. Pediatrics, 117(8): e1005–e1028.
- 7. **IBM Corp.** Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp.
- 8. **World Medical Association.** World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013 Nov 27;310(20):2191-4.
- 9. **Moher D, Hopewell S, Schulz K, et al. (2010).** CONSORT 2010 explanation and elaboration: Updated guidelines for reporting parallel group randomized trials. BMJ. 2010;340:c869.



- 10. **Abd El Moktader AM, Ezzat GM, Mohamed WS & Hashem NS (2020):** Impact of phototherapy on platelet count in neonates with indirect hyperbilirubinemia. Fayoum University Medical Journal, 7(1): 36-40.
- 11. **Sola-Visner M & Bercovitz RS (2016):** Neonatal platelet transfusions and future areas of research. Transfusion medicine reviews, 30(4): 183-188.
- 12. **Çetinkaya M, Atasay B & Perk Y (2018):** Turkish Neonatal Society guideline on the transfusion principles in newborns. Turkish Archives of Pediatrics/Türk Pediatri Arşivi, 53(Suppl 1): S101.
- 13. **Hasan R & Saifee NH (2021):** Benefits of lower neonatal platelet transfusion thresholds. Transfusion, 61(6): 210-9.
- 14. Elgendy MM, Durgham R, Othman HF, Heis F, Abu-Shaweesh G, Saker F, et al. (2021): Platelet transfusion and outcomes of preterm infants: a cross-sectional study. Neonatology, 118(4): 425-433.
- 15. Davenport PE, Chan Yuen J, Briere J, Feldman HA, Sola-Visner MC & Leeman KT (2021): Implementation of a neonatal platelet transfusion guideline to reduce non-indicated transfusions using quality improvement framework. Journal of Perinatology, 41(6): 1487-1494.
- 16. Yavuzcan Öztürk D, Erçin S, Gürsoy T, Karatekın G & Ovalı F (2016): Platelet mass index: is it a hope for reduction of platelet transfusion in NICU? The Journal of Maternal-Fetal & Neonatal Medicine, 29(12): 1926-1929.
- 17. **Okbay Gunes A, Geter S & Avlanmis ME** (2023): The Usability of Platelet Mass Index Thresholds to Assess the Repeated Platelet Transfusion Requirements in Neonates. Indian Journal of Hematology and Blood Transfusion, 39(3): 464-469.
- 18. **Kahvecioglu D, Erdeve O, Alan S, Cakir U, Yildiz D, Atasay B, et al. (2014):** The impact of evaluating platelet transfusion need by platelet mass index on reducing the unnecessary transfusions in newborns. The Journal of Maternal-Fetal & Neonatal Medicine, 27(17): 1787-1789.
- 19. Zisk JL, Mackley A, Clearly G, Chang E, Christensen RD & Paul DA (2014): Transfusing neonates based on platelet count vs. platelet mass: a randomized feasibility-pilot study. Platelets, 25(7): 513-516.
- 20. Wang T, Liu Z, Wang Z, Duan M, Li G, Wang S, et al. (2014): Thrombocytopenia is associated with acute respiratory distress syndrome mortality: an international study. PLoS One, 9(4): e94124.