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PROGNOSTIC SIGNIFICANCE OF EARLY PLATELET COUNT DECLINE IN PRETERM NEWBORNS

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ABSTRACT

Background: Neonatal thrombocytopenia is common in both preterm and term neonates admitted to the neonatal intensive care unit (NICU), and is associated with significant morbidity and mortality. **Objective:** The aim of this study was to investigate the predictive value of an early decline in platelet count in relation to final outcomes, as well as the subsequent development of major comorbidities. **Patients and Methods:** A prospective analytic cohort study was conducted over one year (2023–2024) at Lattakia University Hospital, Syria. The study included four groups of premature neonates admitted to the NICU. Platelet counts were assessed on admission and on the seventh day of life. Group I consisted of 22 neonates (no thrombocytopenia, no decrease in platelet count), group II included 78 neonates (no thrombocytopenia, but a reduction in platelet count), group III had thrombocytopenia without a reduction in platelet count, and group IV had both thrombocytopenia and a reduction in platelet count. The final outcomes were compared among the four groups. **Results:** A total of 140 premature neonates were included (57 males [40.7%] and 83 females [59.3%]), with a mean gestational age of 29.5 ± 1.8 weeks. Gestational age and birth weight were significantly lower in group IV, which also had a higher frequency of cesarean deliveries (p < 0.05). Intraventricular hemorrhage (IVH) and necrotizing enterocolitis (NEC) were observed only in groups II and IV, with significantly higher rates in group IV (p < 0.05). Hospitalization was significantly longer in groups II (54.4 ± 8.2 days) and IV (49.9 ± 8.7 days) compared to group III (25.5 ± 3.2 days) and group I (18.1 ± 2.9 days) (p = 0.0001). A reduction in platelet count before the 7th day of life was associated with an increased risk of mortality (RR: 5.3, p = 0.0001). **Conclusion:** The current study demonstrates that a reduction in platelet count during the first week of life may be an independent predictor of mortality and morbidity in premature neonates.

KEYWORDS: Decline, early, neonates, mortality, platelet, Premature.

1. INTRODUCTION

Thrombocytopenia is defined as a platelet count less than 150.000/microL, which is considered one of the most prevalent hematologic conditions in NICU.[1,2] It is classified according to the time of occurrence after delivery into; early- onset occurring before 72 hours after birth and late-onset after the first 72 hours.[3] Thrombocytopenia can be categorized according to the severity into three groups: mild $(100\text{-}149*10^3/mm)$, moderate $(50\text{-}99*10^3/mm)$ and severe(less than $40*10^3/mm)$.[4] The prevalence of neonatal thrombocytopenia ranges from 1 to 5% with high frequency among neonates admitted to NICU which reaches to 18-35%.[5,6,7] In addition to, thrombocytopenia is encountered in approximately 70% of neonates with birth weight less than 1000 g.[8,9]

There are several mechanisms that are involved in neonatal thrombocytopenia including increase platelet destruction (observed more frequently), decrease platelet production or both mechanisms.[10,11,12] Increased consumption of platelets is seen in many cases, especially infections in premature neonates and is associated with significant mortality and morbidity such as intraventricular hemorrhage(IVH), necrotizing enterocolitis(NEC) and disseminated intravascular coagulation(DIC) so it is crucial to detect high risk neonates with initiation of management to prevent occurrence of complications.[13,14,15]

Thrombocytopenia in premature neonates might be transient or progress to severe form. Majority of studies focused on prognostic value of platelet count changes regarding final outcome in neonates with platelet count in the range $50\text{-}100*10^3/mm$.[16] Absence of local studies regarding decline in platelet count within the first 7 days of life prompted us to conducted this study, therefore the aims of the current study were: 1- to assess the relationship between decrease in platelet count ≥30% before the seventh day of life with morbidity, mortality

and duration of hospitalization. 2-to detect the predictive ability of reduction in platelet count for subsequent comorbidities.

2. PATIENTS AND METHODS
Study Population
After approval by local research ethics committee, an analytic -prospective cohort Study was conducted in neonates admitted at NICU in Lattakia University Hospital over a period of one year (April 2023 - April 2024).

Inclusion Criteria were as follows: neonates of both sexes, gestational age<37 week who admitted on their first day of life and survive for more than 7 days.

Exclusion Criteria: neonates with presence of one of the following: neonatal transfers before completing a full course of treatment, undetermined platelet levels on admission or transfusion any type of blood components during the first seven days of life. Gestational age was determined depending on the date of the last menstrual period, and if unavailable by postnatal assessment using the Ballard score. Laboratory investigations including complete blood count, C-reactive protein(CRP), blood glucose and blood culture were performed on admission. Platelets counts on admission were taken as baseline value to establish changes subsequently.

Thrombocytopenia was defined as a platelet count $<150*10^9$/L which confirmed by two serial measurements, whereas a decrease in platelet count was defined by a reduction in platelet count ≥30% from the baseline value. Patients were assigned according to the changes in platelet count as follows; group I(no thrombocytopenia, no decrease in platelet count), group II(no thrombocytopenia with reduction in platelet count), group III(thrombocytopenia without reduction in platelet count) and group IV(thrombocytopenia with reduction in platelet count). Characteristics of the study population as well as final outcome were compared between groups.

Statistical Analysis
Statistical analysis was performed by using IBM SPSS version25. Basic Descriptive statistics included means, standard deviations(SD), median, Frequency and percentages. To examine the relationships and comparisons between the two group, chi-square test was used. Paired t student test was used to compare 2 dependent groups. One way Anova was used to determine if there are statistically significant differences between the means of three or more groups. Logistic regression was used to calculate the odds of mortality in all groups. All the tests were considered significant at a 5% type I error rate(p<0.05), β:20%, and power of the study:80%.

3. RESULTS
The study included a group of 140 neonates who fulfilled the criteria of study. Gestational age ranged from 27 to 33 weeks, with mean age of 29.5±1.8 weeks. Birth weight ranged from 710 to 2500 g, with mean weight of 1371.2±298g, and males represented 40.7% of the study sample. Group I constituted of 22 cases(15.7%), group II of 78 cases(55.7%), group III of 25 cases(17.9%) and group IV of 15 cases(10.7%).

The baseline characteristics of neonates according to platelet counts were as shown in Table (1). Males represented 40.9% of group I, 38.5% of group II, 44% of group III and 46.7% of group IV whereas females represented 59.1% of group I, 61.5% of group II, 56% of group III and 53.3% of group IV, p:0.2. There were significant differences between groups regarding of gestational age; 30.3±1.9 weeks in group I, 28.8±1.4 weeks in group II, 29.3±1.5 weeks in group III and 28.1±0.9 weeks in group IV,p:0.01. In addition to, an average birth weight was significantly lower in group IV(995.5±240 g) and II(1150.9±140 g) compared to group III(1400.3±210 g) and I(1900.2±490 g),p:0.0001. Maternal antenatal corticosteroid was detected in 68.2%, 76.9%,88% and 93.3% of neonates in group I, II,III and IV respectively,p:0.06.

Table 1: The relationship between platelet count changes and demographic variables of the study population.

Variable	Group I	Group II	Group III	Group IV	p-value
Gender Male Female	9(40.9%) 13(59.1%)	30(38.5%) 48(61.5%)	11(44%) 14(56%)	7(46.7%) 8(53.3%)	0.2
Gestational age(weeks)	30.3±1.9	28.8±1.4	29.3±1.5	28.1±0.9	0.01
Type of delivery Vaginal Cesarean section	9(40.9%) 13(59.1%)	49(62.8%) 29(37.2%)	5(20%) 20(80%)	2(13.3%) 13(86.7%)	0.001
Birth weight(g)	1900.2±490	1150.9±140	1400.3±210	995.5±240	0.0001
Antenatal Corticosteroids Present Absent	15(68.2%) 7(31.8%)	60(76.9%) 18(23.1%)	22(88%) 3(12%)	14(93.3%) 1(6.7%)	0.06

As shown in table(2), gram- positive bacterial septicemia was present in one case(6.7%) of group IV, whereas gram- negative bacterial septicemia was detected in

13.3% of group IV and 6.4% of group II,p:0.08. IVH was significantly higher in group IV(20%) vs. 6.4% in group II without any case in group I and III, p:0.03. NEC was

detected in 26.7% of neonates in group IV vs. 7.7% in group II with presence of significant differences, p:0.002.

Table 2: The relationship between platelet count changes and comorbidities.

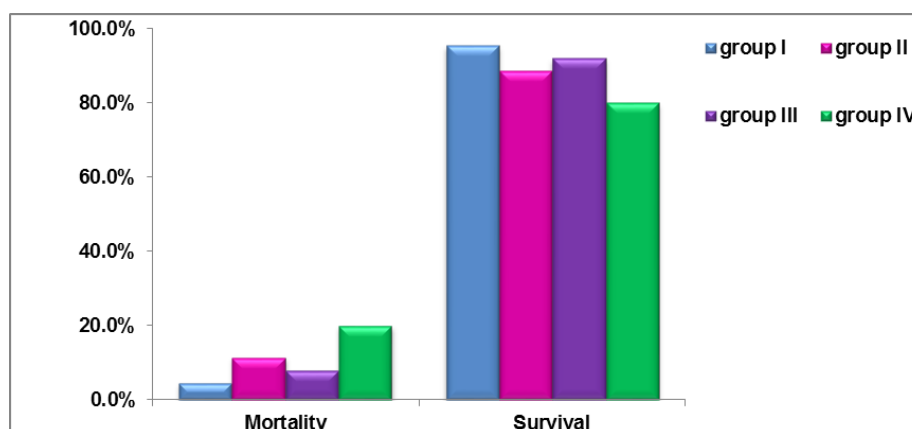| Variable	Group I	Group II	Group III	Group IV	p-value
Septicemia					
Positive gram	0(0%)	0(0%)	0(0%)	1(6.7%)	0.1
Negative gram	0(0%)	5(6.4%)	0(0%)	2(13.3%)	0.08
Hemorrhagic complications					
IVH	0(0%)	5(6.4%)	0(0%)	3(20%)	0.03
Others	0(0%)	0(0%)	0(0%)	2(13.3%)	0.2
NEC					
Present	0(0%)	6(7.7%)	0(0%)	4(26.7%)	0.002
Absent	22(100%)	72(92.3%)	25(100%)	11(73.3%)	

Length of hospital stay was significantly longer in group IV(49.9±8.7 day), followed by group II(54.4±8.2 day), group III(25.5±3.2 day) and group I(18.1±2.9 day),p:0.0001.
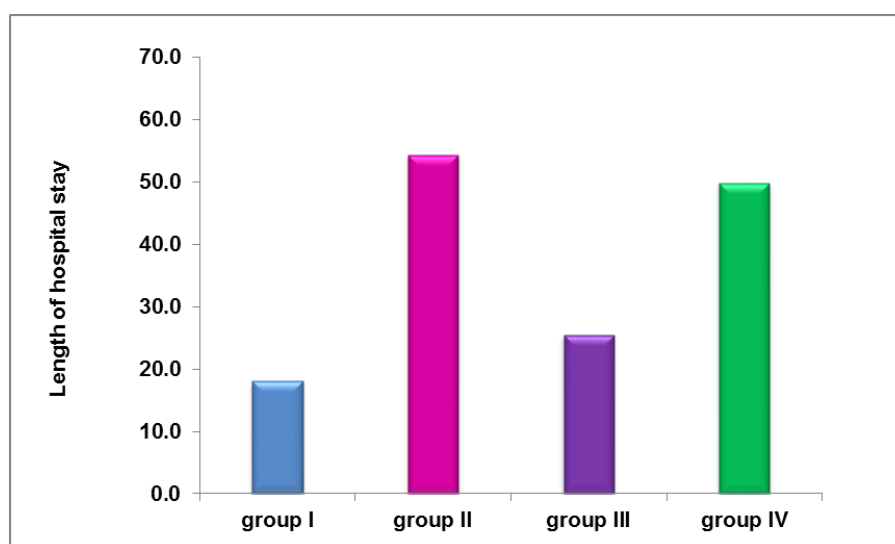
Figure 1: Duration of hospitalization according to platelet count changes.

Death rate was significantly higher in group IV(20%), followed by group II(11.5%), group III(8%) and group I(4.5%), p:0.004. By using the 1st group as a reference category, a decrease in platelet count with or without thrombocytopenia was associated with an independent risk for mortality; (RR: 5.3, p:0.0001) in group IV, (RR: 2.7, p:0.0001) in group II and (RR: 1.8, p:0.04) in group III.

Figure 2: Mortality rates according to platelet count changes.

Table 3: The relationship between thrombocytopenia and final outcome of the study population.

Variable	Group I	Group II	Group III	Group IV	p-value
Duration of hospitalization(days)	18.1±2.9	54.4±8.2	25.5±3.2	49.9±8.7	0.0001
Mortality					
Present	1(4.5%)	9(11.5%)	2(8%)	3(20%)	0.004
Absent	21(95.5%)	69(88.5%)	23(92%)	12(80%)	

4. DISCUSSION

Early thrombocytopenia might be an early prognostic marker for mortality and morbidity in preterm neonates admitted to NICU.

The current study of 140 premature neonates who admitted to NICU showed the main findings: first, mean of gestational age(GA) at delivery was 29.5±1.8 weeks and birth weight(BW) was1371±298 g. By comparison with previous studies regarding of demographic variables, Abeer et al study[17] included 188 cases with mean GA 28.3±1.6 weeks and BW 1025±385 g, whereas Rastogi et al study[18] included 286 cases with mean GA 26.3 weeks and BW 899±215 g.

Second, a decrease in platelet count before the seventh day was present in 66.4% of neonates, and this finding corresponds to Abeer et al and Rastogi et al; 61.7% and 68.1% respectively. Neonates were divided into four groups according to platelet count at admission as well as their changes before the seventh day in which demographic characteristics and final outcome were compared between groups. Third, there were no significant differences between groups regarding of gender(p:0.2) and antenatal corticosteroid therapy(p:0.06). In addition to, GA and BW were significantly lower(p<0.05) in neonates who developed a decrease in platelet count and this finding is in agreement with Abeer et al.[17] Fourth, IVH was detected only in neonates who developed a decrease in platelet count with presence of significant differences (p:0.03). These finding corresponds to Rastogi et al+ and Abeer et al[17], in which thrombocytopenia might lead to IVH or as a result of IVH by consumptive process.

Furthermore, other hemorrhagic complications were observed only in group 4(thrombocytopenia, decrease in platelet count) on average 13.3% which corresponds to Abeer et al[17] on an average 5.3%.

Fifth, NEC was detected in 26.7% of group 4(thrombocytopenia, decrease in platelet count) versus 7.7% in group II(no thrombocytopenia, decrease in platelet count) with presence of significant differences, p:0.001 and this finding is in agreement with Abeer et al[17] and Rastogi et al study.[18]

There were no significant differences between groups regarding of septicemia(p>0.05). In contrast to the current study, Abeer et al[17] found that decreasing in platelet count is an independent risk factor for development of gram-positive, negative-gram and fungal septicemia and this finding is in agreement with Rastogi et al study.[18] These differences might be explained by NICU circumstances such as nosocomial infections as well characteristics of the study population. Regarding of final outcome, duration of hospitalization was significantly longer in patients who developed a decrease in platelet count(p:0.0001) and this finding is in agreement with Abeer et al.[17] Finally, a decrease in platelet count represents an independent risk factor for mortality(RR:5) and this finding corresponds with Abeer et al.[17]

In summary, a decrease in platelet count before the seventh day of life in premature neonates can be used as an independent predictor for mortality and final clinical outcome.

REFERENCES
1. Roberts I, Stanworth S, Murray N., "Thrombocytopenia in the neonate" Blood Rev., 2008; 22: 173.
2. Wiedmeier S, Henry E, Christensen R., "Platelet reference range for neonates, defined using data

from over 47.000 patients in multihospital healthcare system" J Perinatol, 2009; 29: 130.

3. Donato H., "Neonatal thrombocytopenia: a review I. Definitions, differential diagnosis, causes, immune thrombocytopenia" Arch Argent Pediatr, 2021; 119: 202.

4. Shantanu R, Inan O, Alok B., "NCI classification of thrombocytopenia in extremely preterm neonates and its association with mortality and morbidity" J Perinat Med., 2011; 39: 65-9.

5. Baer V, Lambert D, Henry E., "Severe thrombocytopenia in the NICU" Pediatrics, 2009; 124: 1095.

6. Aparajita Gupta et al., "Incidence of thrombocytopenia in the neonatal intensive care unit" Med J Armed Forces India, 2011; 67: 234-6.

7. Boutaybi N, Steggerda S, Smits V., "Early onset Thrombocytopenia in near term and term infants with perinatal asphyxia" Vox Sang, 2014; 106: 361.

8. Delaney J, Nunes G, Simoneau J., "Thrombocytopenia and neonatal outcomes among extremely premature infants exposed to maternal hypertension" Pediatr Blood Cancer, 2023; 70: 301-31.

9. Del A., "Evaluation and management of thrombocytopenic neonates in the intensive care unit" Early Hum Dev, 2014; 90: 51-55.

10. Christensen R, Henry E, Wiedmeier S., "Thrombocytopenia among extremely low birth weight neonates: data from a multihospital healthcare system" J Perinatol, 2006; 26: 348.

11. Resch E, Hinkas O, Resch B., "Neonatal thrombocytopenia-causes and outcomes following platelet transfusions" Eur J Pediatr, 2018; 177: 1045.

12. de Alarcon P, Christensen R, Sola M., "Neonatal Hematology: pathogenesis, diagnosis and management of hematologic problems" Cambridge University Press, 2021.

13. Winkelhorst D, Oepkes D, Lopriore E., "Fetal and neonatal alloimmune thrombocytopenia: evidence based antenatal and postnatal management strategies" Expert Rev Hematol, 2017; 10: 729.

14. Ree I, Bekker V, Steggerda S., "Thrombocytopenia in neonatal sepsis, incidence, severity and risk factors" PLoS one, 2017; 12: e0185581.

15. Rozeta S, Petros M, Alexia P., "Diagnostic and prognostic value of hematological parameters in necrotizing enterocolitis: A systematic review" J Clin Med., 2025; 14: 1-42.

16. Sillers L, Van Slambrouck C, Lapping G., "Neonatal Thrombocytopenia: etiology and diagnosis" Pediatr Ann, 2015; 44: 175-180.

17. Abeer E, Mohammed Z, Eisa S., "Prognostic significance of early platelet count decline in preterm newborns" Indian Journal of Critical Care Medicine, 2015; 19: 456-461.

18. Rastogi S, Olmez I, Bhutada A., "Drop in platelet counts in extremely preterm neonates and its association with clinical outcome" Journal of Pediatric Hematology /Oncology, 2011; 33: 580-584.