Characterization of Thrombocytopenia and the Immature Platelet Fraction in Neonatal Sepsis

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Introduction

Neonatal sepsis is a major cause of neonatal morbidity and mortality in the NICU. Its incidence ranges from 1-4 infections per 1,000 live births and has an estimated overall mortality of 16%.[1] Blood culture remains the gold standard for diagnosis of sepsis, but new parameters are under investigation to diagnose sepsis earlier, prognosticate the trajectory of illness and predict outcomes.

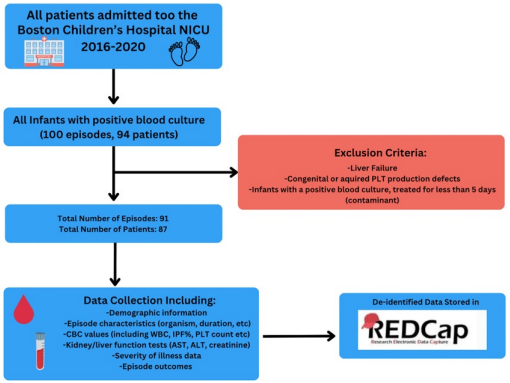
A common complication of neonatal sepsis is thrombocytopenia, which is defined as a platelet count < 150,000/μL.[2] Thrombocytopenia can be defined as mild (platelet count between 100,000 and 150,000), moderate (platelet count between 50,000-100,000) or severe (platelet count <50,000). Studies examining the incidence of neonatal sepsis-induced thrombocytopenia found that 17-54% of septic neonates will experience at least one episode of thrombocytopenia.[3,4] Severe thrombocytopenia can lead to the need for platelet transfusions, which recently has been associated with increased morbidity and mortality in neonates.[5]

One new biomarker of particular interest to help predict the course of neonatal thrombocytopenia is the IPF.[6] The IPF is the percentage of the newly released platelets in circulation. The IPF can characterize changes in platelet production from the marrow.[6] Elevations in the IPF indicate increased platelet production and decreases in the IPF are indicative of reduced production.[8] Previous studies have proven that the IPF is a good indicator of platelet production in neonates and could help determine the etiology of thrombocytopenia and predict the course.[6,7]

Aims and Objectives

The goal of this study was to characterize the time course and patterns of thrombocytopenia and the IPF in neonates with culture positive sepsis, investing associations with clinically relevant neonatal variables.

Methods



Results

1. Cohort Characteristics

Table 1. Cohort Characteristics n=86	
	N (%) or Median [min-max]
Sex	
Male	47 (55%)
Female	39 (45%)
Race	
White	32 (37%)
Black	12 (14%)
Asian	2 (2%)
Other	40 (47%)
Ethnicity	
Hispanic	15 (17%)
Non-Hispanic	44 (52%)
Unknown	27 (31%)
Birth weight, g	1750 [440-4520]
Gestational age, weeks	34 [22-41]
Surgical Patient	
Yes	40 (46%)
No	46 (54%)
IVH present	
Yes	21 (24%)
No	65 (76%)

Table 1: Patient Characteristics of subject in our cohort.

2. Severe thrombocytopenia and the need for platelet transfusion occurred more often in septic episodes caused by gram negative bacteria and fungal organisms compared to gram positive bacteria.

Table 2. Septic Episode Characteristics n=91					
N (%) or Median [min-max]					
	All (n=91)	Gram Positive (n=52)	Gram Negative (n=34)	Fungal (n=5)	p-value *
Postnatal age at time of episode, days	51 [0-274]	52.5 [2-195]	50 [0-234]	49 [3-274]	0.82
Weight at the time of episode, grams	3010 [580-7700]	3190 [860-7700]	2905 [900-6780]	3720 [580-6300]	0.92
Thrombocytopenia					
None	37 (40%)	28 (54%)	9 (26%)	0 (0%)	0.008
Mild	10 (11%)	5 (10%)	3 (9%)	2 (40%)	
Moderate	10 (11%)	6 (12%)	3 (9%)	1 (20%)	
Severe	34 (38%)	13 (25%)	19 (55%)	2 (40%)	
Positive blood cultures	1 [1-7]	1 [1-7]	1 [1-5]	3 [1-7]	0.04
Episodes with PLT Tx	30 (33%)	10 (19%)	17 (50%)	3 (60%)	0.004
PLT Tx administered (if >0)	3.5 [1-23]	1 [1-10]	5 [1-23]	2 [1-13]	0.22
Mortality	7 (8%)	3 (6%)	3 (9%)	1 (20%)	0.31
*Ho: equal percentages (Fisher exact test] or medians (Kruskal-Wallis test].					

Table 2: Septic episode characteristics. Fisher exact test or Kruskal-Wallis test used to test for analysis.

3. Sepsis induced thrombocytopenia occurred in neonates with younger gestational age, lower birth weights, and with lower weights at the time of the septic episode. There were no differences in the incidence of thrombocytopenia by sex, race, or ethnicity.

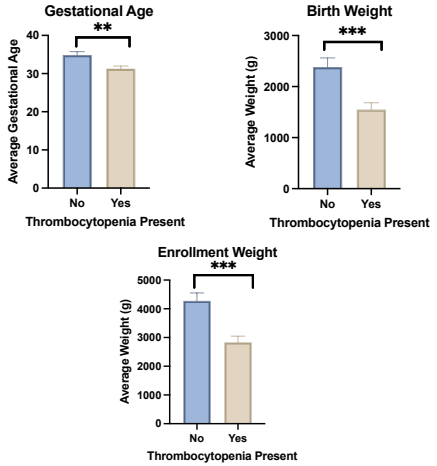


Figure 1: Average gestational age, birth weight, and episode weight in infants with and without thrombocytopenia. T-test comparisons, p<0.05 for significance.

4. The IPF response to thrombocytopenia differs by organism type, with gram negative infections having the lowest IPF values in the face of severe thrombocytopenia.

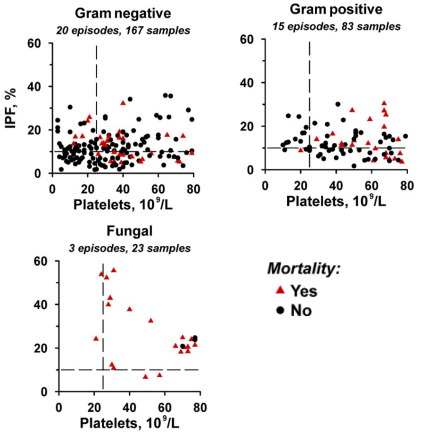


Figure 2: Graphic depiction of simultaneously measured IPFs and platelet counts for all platelet counts <80,000.

Conclusions

- Thrombocytopenia occurred in ~60% of septic neonates in our cohort
- There is a higher incidence of thrombocytopenia in infants of younger gestational ages, lower birth weights, and with lower weights at the time of sepsis.
- Severe thrombocytopenia occurs more often in infants with gram negative and fungal sepsis compared to gram positive sepsis.
- Episodes of gram-negative sepsis had lower IPF percentages in the face of severe thrombocytopenia compared to gram positive or fungal sepsis, suggestive of a relative hypo proliferative state.

Next Questions

- Can the IPF be used to predict:
  - Platelet count recovery in sepsis?
  - Sepsis induced severity of illness?
  - Sepsis induced mortality?

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