

A Study of Neonatal Thrombocytopenia in Neonatal Sepsis

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ABSTRACT

Introduction: Neonatal sepsis (NNS) related mortality is largely preventable if diagnosed early and managed aggressively with rational anti microbial therapy and supportive care. Diagnosis of neonatal sepsis is made by hematological changes induced by culture proven and probable sepsis. Thrombocytopenia is one of the early but non-specific indicator of neonatal sepsis. It can be caused by bacterial, viral, fungal and parasitic infections and other non-infectious causes. The present study aimed to know the incidence of thrombocytopenia in neonatal sepsis and to evaluate the feasibility of NNT as a screening tool.

Material and methods: A total of 105 'at risk Neonates' for sepsis were detected over a period of 12 months and included in this study.

Results: Thrombocytopenia was found in 82.6% septic neonates.

Conclusion: It can be used as a screening tool for NNS as it is a easy and cost effective method.

Keywords: NNS (Neonatal sepsis), EOS (Early onset Sepsis), LOS (late on set sepsis), NNT (neonatal thrombocytopenia), neonate

INTRODUCTION

Neonatal sepsis It encompasses various systemic infections of the newborn such as septicemia, meningitis, pneumonia, pyogenic arthritis, osteomyelitis, and urinary tract infections¹. Sepsis is the commonest cause of neonatal mortality; it is responsible for about 30-50% of the total neonatal deaths in developing countries^{2,3}. It is estimated that up to 20% of neonates develop sepsis and approximately 1% die of sepsis related causes³. Sepsis related mortality is largely preventable with rational antimicrobial therapy and aggressive supportive care.

The classification of sepsis based on time of appearance as EOS or LOS is important as it helps in determining the most probable organism and mode of transmission and guide for empiric treatment.⁵

Thrombocytopenia is one of the early but non-specific indicator of neonatal sepsis⁶. It can be caused by bacterial, viral, fungal and parasitic infections and other non-infectious causes.⁷

Bleeding is a major complication of thrombocytopenia but is generally limited to infants with count < 30000/mm³.^{8,9} Studies have shown that approximately 50% cases of culture proven sepsis have thrombocytopenia.^{10,11,12}

Virtually any organism capable of causing sepsis can induce thrombocytopenia. Riedler et al¹³ found an 80% incidence of thrombocytopenia in gram-negative septicemia and 65% incidence in gram-positive septicemia. Changes in other platelet indices, like MPV (mean platelet volume) and

PDW (platelet distribution width) have also been examined. Increased platelet volume (MPV) indicates an increased proportion of young platelets in the circulation.

The present study aimed to know the incidence of thrombocytopenia and to evaluate the feasibility of thrombocytopenia as a screening tool for neonatal sepsis in a risky neonate

MATERIAL AND METHODS

This hospital based prospective observational cross sectional study was conducted in a tertiary care hospital over a period of 12 months, from December 2015 to november 2016. A total of 215 Neonates under the age of 28 days admitted in NICU, were studied and 105 'at risk neonates' were detected and included in our study

Investigations done – sepsis screening

Total Leukocyte Count (TLC):

<5000/cmm or >15,000/cmm.

Absolute Neutrophyl Count (ANC): <1800/cmm

Immature to Total Neutrophil (I/T) RATIO: >0.2 (immature neutrophils / ANC), highly sensitive of NNS, I/T = (Immature neutrophils like band forms, metamyelocytes, myelocytes) / Mature + immature neutrophils

CRP:>1mg/dL

MICRO ESR (u-ESR):> (age in DOL +3)mm or

>15 mm/1st hr, specific but moderate sensitivity.

IL- 6, and PROCALCITONIN not included due to practical problems.

Blood culture and Chest Xray

NOTE: (≥ 2) positive screening parameters (TLC,ANC,I/T ratio, CRP, u-ESR) taken as sepsis screen positive (Sn 93%,PPV 39%, >2 parameters – NPV 99%)and that neonate is with sepsis.

Exclusion criteria

MOTHER with History s/o ITP, SLE / other autoimmune disorders, on medication during pregnancy (sulfonamides, quinine / quinidine) (thiazides, tolbutamide, vancomycin, hydralazine, and heparin)

Neonate with h.s/o bleeding disorder in family, trisomies, Turner /Noonans syndromes,

TAR syndrome.

Conditions associated with sequestrationof platelets

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(Kasabach - merritt syndrome with giant haemangiomas, renal vein thrombosis, polycythemia, CCHD, placental vascular thrombi – PIH /preeclampsia /eclampsia).

Severe Rh – HDN (marked erythropoiesis in bone marrow → neutropenia and thrombocytopenia)

Massive bleed from causes like birth trauma, accidental slipping of cord clamp causing hemodynamic disturbance/ exchange transfusion (dilutional NNT). Sick neonate with RVT, CHD, Congenital leukemia. Neonate who received IV antibiotics for ≥ 48 hrs prior to our study.

STATISTICAL ANALYSIS

Microsoft office 2007 was used for the analysis of results. Descriptive statistics like mean and percentages were used for interpretation of results.

RESULTS

A total of 105 neonates with clinical sepsis (risk neonates) were included for the study and were evaluated accordingly.

Most common presentation in EOS is respiratory distress, and in LOS is refusal of feeds, and over all common presentation is refusal of feeds. (table-1)

Clinical presentation	EOS	LOS	NOS	Total
Maternal fever	2	1	1	4
PROM	4	1	1	6
Foul smelling liquor	2	-	-	2
Refusal of feed	7	25	4	36
Respiratory Distress	20	9	2	31
Lethargy	3	16	1	20
MAS / BA	11	10	1	22
Convulsions	9	12	-	21
Repeated vaginal examinations	5	3	1	9
Poor hygiene	3	5	1	9
Top / pre-lacteal feeds	8	12	2	22

Table-1: Clinical presentation in NNS

	With NNT	Without NNT	Total
EOS	35 (77.77%)	10(22.22%)	45
LOS	41 (87.23%)	6 (12.77%)	47
NOS	5 (38.46%)	8 (61.54%)	13
Total	81 (77.14%)	24 (22.85%)	105

Table-2: Thrombocytopenia in neonatal SEPSIS

Platelet count	EOS	LOS	NOS	Total
< 0.5 lakhs / mm3	12	14	2	28 (34.56%)
0.5 – 1 lakhs / mm3	7	10	1	18 (22.22%)
1 – 1.5 lakhs / mm3	16	17	2	35 (43.20%)
Total	35	41	5	81

Table-3: Platelet count distribution in NNT

Test (NNT)	Diagnosis (DISEASE – Sepsis)		Total
	NNS +VE	NNS -VE	
NNT +VE	(a) True Positive: 76	(b) False Positive: 5	81
NNT -VE	(c) False negative: 16	(d) True Negative: 8	24
Total	92	13	105

Table-4: NNT distribution in NNS

Neonates at risk for sepsis

Total neonates examined – 215

At risk neonates-105 (48.83%)

Neonates with sepsis - 92 (87.61%)

No sepsis (NO S) - 13(12.38%)

Early onset sepsis (EOS) - 45(48.91%)

Late onset sepsis(LOS) - 47(51.08%)

In EOS, thrombocytopenia was found in 77.8%, whereas it was 87.2% in LOS (table-2).

Most of the NNT were with platelet count between 1 to 1.5 lakhs (43.2% of total NNT) (table-3).

Sensitivity (Sn) = { true +ve / all disease +ve } x 100 = { a / a + c } x 100 = 76 / 92 x 100 = 82.608%

Specificity (Sp) = { true -ve / all disease -ve } x 100 = { d / b + d } x 100 = 8 / 13 x 100 = 61.538%

Positive predictive value (PPV) = {true +ve/ all test +ve } x 100 = { a / a + b } x 100 = 76 / 81 x 100 = 93.827%

Negative predictive value (NPV) = { true negative / all test negative } x 100 = { d / d + b } x 100 = 8 / 24 x 100 = 33.333%

Percentage of false negative = { c / a + c } x 100 = 16/ 92 x 100 = 17.391%

Percentage of false positive = { b / b + d } x 100 = 5 / 13 x 100 = 38.461% (table -4)

Blood culture results in EOS and LOS

Of the 105 cases evaluated for sepsis, the blood culture was positive in 26(24.76%) cases.

Klebsiella pneumonia was found in 50%, coagulase negative staphylococci in 30.8% and enterococci in 19.2% cases.

AGE at on set of Sepsis

There were 51 (48.571%) neonates in the early onset sepsis group and 54(51.428%) in the late onset group.

Sex Distribution

Of the 105 ‘at risk neonates’ 58(55.23%) were male babies and 47(44.76%) were female babies. In the early onset sepsis group 28(62.22%) were male and 17(37.77%) were female neonates. In the late onset sepsis group 22(46.80%) were male and 25(53.19%) were female neonates. In Neonates with NO sepsis 8 (61.53%)were males, females were 5 (38.46%) (P = 0.2942).

This P value suggests that sepsis was not affected by sex of the neonate.

Birth Weight and Sex Distribution In EOS and LOS

EOS and LOS were more common in male neonates compared to female neonates

Birth Weight Distribution In EOS and LOS

EOS and LOS were more common <2.5kg birth weight babies compared to >2.5kg birth weight babies.

Birth weight distribution in NNT

< 2.5 kg. +ve for NNT 41 cases

-ve for NNT 13 cases

>2.5 kg. +ve for NNT 40 cases

-ve for cases 11 cases

Total +ve cases 81

Total -ve cases 24

Total no. at risk neonates cases 105

P=0.7599

This Insignificant P value in our study suggested that birth weight did not affect platelet count to the extent of significant levels to influence the results.

DISCUSSION

Neonatal thrombocytopenia (NNT)

Guida et al.¹¹ had reported that 54% septic Very Low Birth Weight (VLBW) neonates developed thrombocytopenia.

Khalada Binte Khair and Mohammad Asadur Rahman et al.¹⁴, studied 'Role of Hematologic Scoring System in Early Diagnosis of Neonatal Septicaemia' they found that platelet count < 1,00,000/mm³ had a sensitivity of 60%, specificity 82%, PPV 31% and NPV 94%.

A cross sectional analytical study on CRP and Hematological Parameters in NNS, in military hospital, Rawalpindi 4, over 7 months. It included 100 clinically septic and 100 normal neonates and observed that NNT has 64.3% sensitivity in detecting NNS.

In the present study it was found that NNT (< 1,50,000/mm³) can be used to screen neonate with sepsis (NNS) with Sensitivity of 82.6%, and acceptable Specificity, Positive predictive value, especially in 'at risk neonates' which is cost effective and available in almost all hospitals, particularly useful in developing countries like India.

Most common presentation in early onset sepsis is respiratory distress, and in late onset sepsis is refusal of feeds, and over all common presentation is refusal of feeds.

Blood culture positivity was observed in 26 (24.76%) neonates. Of these 13 were early onset sepsis (28.89%) and rest were late onset sepsis (71.11%).

Blood culture

In the present study, blood culture positivity was observed in 26 (24.76%) neonates. Of these 13 were EOS and rest were LOS. Thrombocytopenia was found in 76 septic neonates (82.6%). These findings indicate that low platelet count is important finding in bacterial septicemia.

Further it was also observed that thrombocytopenia was noted in majority of cases in which blood culture was negative⁷. Therefore, it was observed from the study that platelet count is an important indicator of septicemia and not related with blood culture, although not specific.

CONCLUSION

Thrombocytopenia was found in 76 (82.6%) septic neonates. 77.8% of early onset sepsis were thrombocytopenic, whereas it was 87.2% in late onset sepsis.

It was observed from the study that platelet count is an important indicator of septicemia and not related with blood

culture, although not specific.

NNT is almost equal in normal (49.38%) and low birth weight (50.62%) neonates.

NNT can be used as screening tool in NNS as it is easy and cost effective. It requires further large scale studies and meta analysis to validate.

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