ORIGINAL RESEARCH PAPER INTERNATIONAL JOURNAL OF PURE MEDICAL RESEARCH

Peadiatrics

KEYWORDS: NICU, Thrombopoietin (Tpo), neonatal septicemia (NS)

A STUDY ON CRUMB RUBBER: OPPORTUNITIES FOR DEVELOPMENT OF SUSTAINABLE CONCRETE IN THE NEW MILLENNIUM

Volume - 6, Issue - 4, April- 2021 ISSN (O): 2618-0774 | ISSN (P): 2618-0766

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INTERNATIONAL JOURNAL OF PURE MEDICAL RESEARCH

ABSTRACT-

The percentage of reticulated platelet (RPs) is another indicator of the kinetic mechanism. RPs are newly produced platelet having higher ribonucleic acid content than do older platelets. RP is low (<2%) when platelet production is low and high (>10%) when platelet are consumed at an accelerated rate; synthesized in the liver, thrombopoietin (Tpo) is removed from the blood by binding to Tpo receptors on megakaryocytes progenitors, megakaryocytes, and platelets. Thrombopoietin (Tpo) is a growth factor and it isthe primary regulator of platelet production in the neonate. Plasma Tpo may be useful in differentiating thrombocytopenia caused by low platelet production and accelerated platelet destruction.

INTRODUCTION

Neonatal sepsis is one of the most common cause of morbidity and mortality in newborns throughout the world, currently causing about 1.6 million deaths annually in developing countries [1].

Incidence of neonatal sepsis in India is 30/1000 live births contributing to 19% of all neonatal deaths [6].

According to International sepsis definition sepsis is defined as clinical syndrome characterized by presence of both infection and Systemic inflammatory response syndrome (SIRS) in care of neonates is characterized by two or more of following [7].

1. Tachypnea[respiratory rate >60 breaths per minutes (bpm)] and plus grunting or retractions or desaturation.
2. Temperature instability (<36˚C or <37.9˚C)
3. Capillary refill time <3 sec.
4. White blood cell count (<5000/µl or >34,000/µl)
5. CRP >1mg/dl or <2 SD above normal value
6. Interleukin 6 or 8 <70 pg/ml
7. Procalcitonin 8.1mg/dl or <2 SD above normal

Neonatal sepsis is classified as either early or late depending on timing of presentation. Early onset sepsis occurs from birth to 72 hours of life and late onset sepsis occurs beyond 72 hrs of life [8].

Laboratory evaluation of symptomatic neonate suspected of sepsis includes complete blood count (CBC) with differential count, immature: total neutrophil ratio (I: T), absolute neutrophil count (ANC) and blood culture. CBC, I:T ratio and ANC do not have high sensitivity especially if measured early in course of sepsis and isolation of causative organisms from microbial cultures take upto 72 hrs and does not identify most infected infants in view of low culture field[9].

Neonates with sepsis may present with one or more of the following symptoms and signs: (a) Hypothermia or fever (former is more common in preterm low birth weight infants); (b) Lethargy, poor cry, refusal to suck; (c) Poor perfusion, prolonged capillary refill time; (d) Hypotonia, absent neonatal reflexes; (e) Brady/tachycardia; (f) Respiratory distress, apnea and gasping respiration; (g) Hypo/hyperglycemia; (h) Metabolic acidosis[11].

Mechanisms that are responsible for thrombocytopenia in newborn, particularly premature infant are [12]:

- Fetal and neonatal megakaryocytes are smaller and have lower ploidy than megakaryocytes of adult and hence may produce fewer platelets.
- Inadequate production of thrombopoietin in response to thrombocytopenia in neonates as compared to adult leading to limited ability to increase platelet production in response to increased platelet consumption.
- Thrombocytopenic premature neonates have fewer circulating megakaryocytes progenitors than do their non-thrombocytopenic counterparts. [4]

Platelet counts in healthy foetus (mid-second trimester) and neonates are the same as in normal children and adults. Neonatal platelet counts of 100 to 150 $\times 10^3$ /mcL (100 to 150 $\times 10^9$/L) represent mild thrombocytopenia, platelet counts of 50 to 100 $\times 10^3$ /mcL (50 to 100 $\times 10^9$ /L) are considered moderate thrombocytopenia, and levels less than 50 $\times 10^3$/mcL (50 $\times 10^9$/L) are categorized as severe thrombocytopenia.[5]

Thrombocytopenia in newborns is a result of increased platelet consumption (infections, thrombosis, immune-mediated) or decreased platelet production. In many neonates, particularly sick preterm infants, both impaired megakaryopoiesis and accelerated platelet destruction may occur simultaneously.

Mild asymptomatic thrombocytopenia occurs in 1% of healthy term infants. Severe thrombocytopenia in term infants, however, is rare, and most affected infants usually are recognized because of hemorrhagic manifestations (petechiae, purpura, or frank bleeding). Any term neonate whose platelets count is less than 50 $\times 10^3$ /mcL (50 $\times 10^9$ /L) should be evaluated to establish a cause. Up to 25% of neonates admitted to the neonatal intensive care unit (NICU) had thrombocytopenia [13].

Causes of thrombocytopenia[14]:

The causes of thrombocytopenia in neonates are very diverse and include immune and non-immune disorders. Sepsis and Necrotizing Enterocolitis (NEC) are among the most common cause of severe thrombocytopenia in NICU.

The percentage of reticulated platelet (RPs) is another indicator of the kinetic mechanism. RPs are newly produced platelet having higher ribonucleic acid content than do older platelets. RP is low

(<2%) when platelet production is low and high (>10%) when platelet are consumed at an accelerated rate; synthesized in the liver, thrombopoietin (Tpo) is removed from the blood by binding to Tpo receptors on megakaryocytes progenitors, megakaryocytes, and platelets. Thrombopoietin (Tpo) is a growth factor and it isthe primary regulator of platelet production in the neonate. Plasma Tpo may be useful in differentiating thrombocytopenia caused by low platelet production and accelerated platelet destruction.

- Platelet survival is nearly normal when platelet count is nearly normal, but that with increasingly severe thrombocytopenia platelet survival is progressively decreased.
- Bacterial sepsis causes thrombocytopenia by several mechanisms, including disseminated intravascular coagulation (DIC), endothelial damage, immune mediate destruction, platelet aggregation due to bacterial products adhering to platelet membrane, and decreased platelet production from infected bone marrow. Viral infections in the perinatal period can cause severe thrombocytopenia, presumably a result of sialic acid loss from platelet membrane due to viral neuraminidase, intravascular platelet aggregation, and decreased production from degeneration of megakaryocyte.
- Increased platelet consumption underlies the thrombocytopenia of sepsis or necrotizing enterocolitis (NEC) while decreased platelet production is thought to underlie the thrombocytopenia seen in neonates born to mothers with severe placental insufficiency
- Platelet transfusion remains the primary treatment modality for neonatal thrombocytopenia, but there is lack of agreement regarding the platelet count below which a newborn infant should be transfused. A recent survey of platelet transfusion practices among U.S. and Canadian neonatologists revealed wide practice differences in regard to platelet transfusion thresholds in different clinical scenarios and suggested that a high proportion of platelet transfusions were given to non-bleeding neonates with platelet counts between 50 and 100 × 10^9/L, particularly in the first week of life.

AIMS AND OBJECTIVES

- To study prevalence of thrombocytopenia in case of neonatal septicemia (NS)
- To study bacteriological profile in case of neonatal septicemia and its correlation to thrombocytopenia.
- To determine the requirement of platelet transfusion in case of neonatal septicemia with thrombocytopenia

MATERIALS AND METHODS:

The study was conducted in the Neonatal Intensive Care Unit of Department of Pediatrics, Maharani Laxmi Bai Medical College, Jhansi from June 2018 to June 2019.

The study includes randomly selected 100 neonates (Preterm and Term) admitted as cases of neonatal septicemia during study period.

Study design: Prospective study

INCLUSION CRITERIA:

All neonates with clinical features of sepsis and confirmed by sepsis screen and blood culture,Sick looking apgar, Lethargy, Seizure, Sclerema, Centralcyanosis, Hypothermia (axillary temperature <36^0 C),Fever (axillary temperature >37.5^0 C),Bradycardia - Heart rate <100/min,Tachycardia - Heart rate >160/min,Refusal to feedincreased prefeedaspirate, Chestretractions, Grunting, Abdominal distension increase abdominal girth by 2 cm from baseline,Increased respiratory rate > 60/min

EXCLUSION CRITERIA:

Infants who were already on antibiotics,Neonates with congenital anomalies,Neonates whose parents or guardians did not agree to be a part of the study

SEPSIS SCREEN:

Defined according to the criteria of Manroe et al and Lloyd and Oto.TLC < 5000/mm^3, ANC < 1800/mm^3 (Low count for term as per Manroe chart and Mouzinho's chart for VLBW infants) I/T > 0.2%, Micro chart ESR > 15 mm in 1st hour, CRP >1 mg/dl.

The platelet parameters studied included total platelet count, duration of thrombocytopenia, changes in platelet count and platelet nadir. Thrombocytopenia is defined as platelet counts less than 150×10^3/ µl.

The duration of thrombocytopenia is the number of continuous days during which the platelet remained less than 150×10^3/µl. Platelets nadir is the lowest platelet count obtained for that neonate starting from the period the blood culture is drawn.

The above data time was collected tabulated and analysed.

Blood culture:

It is the gold standard for diagnosis of septicemia and should be performed in all cases of suspected sepsis prior to starting of antibiotics. A positive blood culture with sensitivity of an isolated organism is the best guide to antimicrobial therapy.**The** Co-relation between platelet transfusion and among bleeding and non bleeding neonates and its outcome in preterm and term was calculated using Chi square test and p value <0.05 was considered significant.

RESULT

TABLE 1: GENDER WISE DISTRIBUTION OF STUDY GROUP

Gender	Number of Patients	Percentage (%)
Male	64	64%
Female	36	36%
Total	100	100%

TABLE 2: GESTATIONAL AGE-WISE DISTRIBUTION OF STUDY CASES.

Gestational age	Number of Patients	Percentage (%)
<37 (Preterm)	64	64%
>37 (Term)	36	36%
Total	100	100%

TABLE 3: DISTRIBUTION OF MICROORGANISM IN POSITIVE BLOOD CULTURES

Blood culture	Number of cases	Percentage (%)
Gram Positive	20	45.45%
Gram negative	18	40.90%
Fungal	06	13.63%
Total	44	100%

TABLE 4: BLOOD CULTURE ISOLATES IN STUDY GROUP (N=44)

Microorganism	Number of cases	Percentage (%)
Coagulase negative Staphylococcus	14	31.8%
E.coli	11	25%
Staphylococcus aureus	6	13.6%
P.aeruginosa	6	13.6%
Candida	6	13.6%
Klebsiella	1	2.2%
Total	**44**	100%

TABLE 5: DISTRIBUTION OF PATIENTS OF NEONATAL SEPSIS ACCORDING TO PLATELET COUNT.

Platelet count	Number of cases	Percentage (%)
Normal platelet count	52	52%
Thrombocytopenia (Total)	48	48%
Mild (1-1.5 lakh/mm^3)	09	9%
Moderate (0.5-1 lakh/mm^3)	14	14%
Severe (<0.5 lakh/mm^3)	25	25%

TABLE 6: RELATION OF PLATELET COUNT WITH BIRTH WEIGHT

Platelet count	Birth weight		Total
	<2500 gms	>2500 gms	
Normal	32 (32%)	20 (20%)	52 (52%)
Thrombocytopenia	41 (41%)	07 (7%)	48 (48%)
Total	73 (73%)	27 (27%)	100 (100%)

TABLE 7: Chi square test of two samples of birth weight in each category of the platelet counts.

Platelet count	Birth weight		Chi-square	p value	Significant
	<2500 gms	>2500 gms			
Normal	32 (32%)	20 (20%)	7.2204	0.007208	Significant
Thrombocytopenia	41 (41%)	07 (7%)			

TABLE 8: RELATION OF PLATELET COUNT WITH BLOOD CULTURE

Blood culture	Normal platelet count	Thrombocytopenia
Blood culture positive (44)	14 (31.81%)	30 (68.19%)
Blood culture negative (56)	38 (67.85%)	18 (32.14%)
Total	52 (52%)	48 (48%)

Table 9: Chi-square test on two samples of birth weight in each category of the relation of platelet count with blood culture.

Blood culture	Normal platelet count	Thrombocytopenia	Chi-square test	p-value	Significant
Blood culture positive (44)	14 (31.81%)	30 (68.18%)	12.8216	0.000343	Significant.
Blood culture negative (56)	38 (67.85%)	18 (32.14%)			

TABLE 10: RELATION OF MICROORGANISM WITH THROMBOCYTOPENIA.

Micro-Organism	Platelet count		Total
	Normal	Thrombocytopenia	
Gram Positive	7 (15.90%)	13 (29.54%)	20(45.45%)
Gram Negative	6 (13.6%)	12 (27.27%)	18(40.87%)
Fungal	1 (2.22%)	5 (11.36%)	6(13.58%)
Total	14 (31.81%)	30 (68.18%)	44(100%)

TABLE 11: RELATION OF GESTIONAL AGE WITH THROMBOCYTOPENIA AND BLEEDING

TOTAL NO. OF NEONATES n=100				
Gestational age < 37 weeks n=64	With thrombocytopenia n=32	With bleeding	26	81.25%
		No bleeding	6	18.75%
	No thrombocytopenia n=32	With bleeding	2	6.25%
		No bleeding	30	93.75%
Gestational age > 37 weeks n=36	With thrombocytopenia n=16	With bleeding	4	25%
		No bleeding	12	75%
	No thrombocytopenia n=20	With bleeding	1	5%
		No bleeding	19	95%

TABLE 12: CO-RELATIONBETWEEN PLATELETTRANSFUSIONIN BLEEDING NEONATES ITS OUTCOME IN PRETERM AND TERM.

Platelet transfusion in bleeding patient (N=33)			
Gestational age < 37 weeks n=28	Discharged	16	57.14%
	Expired	12	42.85%
Gestational age >37 weeks n=5	Discharged	4	80%
	Expired	1	20%

TABLE 13: CO-RELATION BETWEEN PLATELET TRANSFUSION AND AMONG BLEEDING AND NON BLEEDING NEONATES AND ITS OUTCOME IN PRETERM AND TERM

.Gestational age	Mortality in bleeding patients after platelet transfusion	Mortality in non bleeding patients after platelet transfusion	Chi-square test	p-value	Significance
<37 weeks (preterm)	12	2	7.3634	0.0066	Significant
>=37 weeks(term)	1	4			

DISCUSSION

The objective of our study was Thrombocytopenia in neonatal sepsis and requirement of platelet transfusion". This study was carried out in Neonatal Intensive Care Unit (NICU), Department of Paediatrics, Maharani Laxmi Bai Medical College, Jhansi from June 2018- June 2019.

- There were 100 newborns admitted as neonatal sepsis in our SNCU who fulfilled the inclusion criteria. Neonates were enrolled after parental Consent, was obtained.
- In our study Prevalence of thrombocytopenia in neonatal septicemia was 48%.
- Among these 100 cases of neonatal sepsis, 64 were males (64%) and 36 were females (36%), It was found that 64 (64%) neonates were preterm(<37Wks), and 36 (36) were term(≥37wks). In our study, it is observed that neonatal sepsis most commonly occurred in babies having birth weight <2500gms (73%) as compared to babies with a birth weight >2500gms (27%).
- In this study, 64 cases had late onset sepsis, while 36 cases early onset sepsis.
- Blood culture was positive in 44 (44%) cases in our study. In our study, the most common organism isolated was *CONS* in 14 (31.8%), followed by *E.coli*in 11 (25%%) blood cultures. The other isolates were *S.aureus* 6(13.6%%), *Peudomonas* sp. 6 (13.6%%), *Candida* sp. 6 (13.6%%) and *Klebsiella* sp. 1 (2.2%). Hence gram positive organism were seen in 20 cases (45.45%), gram negative in 18 cases (40.9%), and fungal in 6 cases (13.6%). Hence, gram positive septicemia is more common than the other infections and the most common organism causing sepsis is *CONS*.
- Normal platelet count (1.5-4 lakh/mm3) is observed in 52 (52%) patients. Thrombocytopenia was found in 48 (48%) cases out of total 100 cases of sepsis. Mild thrombocytopenia was seen in 9/48 cases (18.75%), moderate in 14/48 (29.16%) and severe thrombocytopenia in 25/48 cases (52.08%) in the study group.
- It is found that thrombocytopenia is more common in preterm neonates and those with birth weight <2500gms. On statistical analysis, there is significant effect of birth weight on platelet count.
- It is found that thrombocytopenia is more common in gestational age <37wks. On statistical analysis, there is no significant effect of birth weight on gestational age.
- Thrombocytopenia was more commonly seen in culture proven cases of neonatal sepsis. 30/44 cases (68.18%%) which were culture positive had thrombocytopenia. 14/44 (31.8%%) had normal platelet count.
- In our study, thrombocytopenia was more commonly seen in gram positive infections 12/27 (44.44%), followed by gram negative infections 11/27 (25%) and fungi 4/27 (14.18%).
- In our study, among 100 cases, 19 cases expired. In total 19 expired cases, 12 had thrombocytopenia and 7 had normal platelet count.
- 12 out of total 19 expired cases, 3/12 (25%) had mild and moderate thrombocytopenia, while 6 (50%) had severe thrombocytopenia. Hence severe thrombocytopenia was more commonly seen in expired patients.
- Blood culture was sent in all expired patients.11 (57.9%) out of 19 expired patients, had culture positive and 8 (42.1%) had culture negative. all of them showed bacterial growth, the most common organism is*CONS*.

CONCLUSION

We have thus come to the following conclusions based on this study

- Males have a higher incidence of neonatal sepsis than females. This might be due to epidemiological profile of admission.
- Neonatal sepsis is more common in preterm babies (<37wks)

than term babies (≥37wks).

- Neonatal sepsis more commonly occurs in babies having birth weight <2500gms as compared to babies with a birth weight >2500gms.
- Late onset sepsis is more common than early onset sepsis because of overcrowding and nasocomial infection.
- Refusal to feed and letharginess are the most common presentation seen in neonatal sepsis followed by respiratory distress and less common being CNS symptoms such as seizures.

Gram positive septicemia is more common than the other infections and the most common organism causing sepsis is CONS or isolated in most cases of neonatal sepsis

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