International Journal of Contemporary Pediatrics
Goudar VR et al. Int J Contemp Pediatr. 2017 May;4(3):1032-1036
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20171722

Original Research Article

A study of bacterial sepsis and its relation to thrombocytopenia in neonates

Vikram R. Goudar, Gautam M. Kabbin*, Suhas N. Joshi, Vinod P. Chavan, Shriharsha L. Badiger

Department of Pediatrics, SDM College of Medical Sciences and Hospital, Dharwad, Karnataka, India

Received: 09 March 2017
Accepted: 03 April 2017

***Correspondence:**
Dr. Gautam M. Kabbin,
E-mail: drkabbin@gmail.com

ABSTRACT

Background: In developing countries like India, the culture facilities are non-existent in most of the district hospitals, so the burden of identification of sepsis lies on hematological investigations like platelet count and white blood cells and very few indian studies have been done to show the association. Objectives: 1) To know the incidence of thrombocytopenia in babies with proven bacterial sepsis. 2) To find, if any, species specific differences in severity and incidence of thrombocytopenia. 3) Clinical outcomes in thrombocytopenic and nonthrombocytopenic septic babies.
Methods: It is a prospective observational hospital based study. All the neonates admitted to our NICU with probable sepsis were screened for sepsis and neonates with birth weight of 1000 grams and above with blood and/or Cerebrospinal Fluid (CSF) culture positivity for bacterial growth were recruited during the study period from November 2011 to October 2012. A total of 100 neonates with blood and/or CSF culture positivity for bacterial growth were considered convenient for the study.
Results: During the present study period of 1 year we had a total of 960 Neonates admitted to our NICU. 475 neonates were screened for sepsis. A total of 100 neonates with blood and/or CSF culture positivity for bacterial growth were considered for the study. *Klebsiella pneumoniae* sepsis was the highest contributor to the severe thrombocytopenia category (15 out of 29cases). Out of the 100 cases, 41 had normal platelet count and 59 had thrombocytopenia. Klebsiella positivity was more significantly associated with severe thrombocytopenia than MRCONS positivity or rest of the cultures combined together (p value <0.01). Although there was no significant association between thrombocytopenia and mortality (p=0.176), the proportion of children with severe thrombocytopenia was significantly higher in babies who expired (25% vs 9%) when compared to babies who survived.
Conclusions: Our study shows that in our setting bacterial sepsis is significantly complicated by thrombocytopenia. Severe thrombocytopenia in a suspected case of bacterial sepsis might predict *Klebsiella species* sepsis and hence it may be prudent to start empirical antibiotics covering the Klebsiella species.

Keywords: Bacterial sepsis, Neonate, Thrombocytopenia

INTRODUCTION

Neonates constitute the foundation of human life. As Neonates are unique compared to other age groups, so are their health issues and problems. This is due to structural and functional immaturity of various body organs depending upon their gestational age and birth weight.

Neonatal period (first 28 days of life) is considered the most vulnerable phase of life. This period accounts for

45% of all deaths of under 5 children. Of the estimated 5.9 million child deaths in 2015, almost 1 million occur in the first day of life and close to 2 million take places in the first week.[1] Neonatal mortality contribute significantly to the infant mortality rates in developing countries, various conditions are responsible for neonatal mortality among which is neonatal sepsis, which account for about 36% of neonatal mortality.[2] The current neonatal mortality rate in India is around 28 per 1000 live births.[3]

Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia in the first month of life.[4] The clinical presentation of sepsis is subtle and vary from neonate to neonate. So, early diagnosis of the condition and aggressive management has got better outcome in neonates with sepsis. Sepsis in neonate should be picked up with high index of suspicion based on their clinical signs and symptoms.

For confirmation of the sepsis and to know the hematologic changes occurring and organism responsible for the condition a battery of investigations need to be carried out. In developing countries like India, the culture facilities are non-existent in most of the district hospitals, so the burden of identification of sepsis lies on hematological investigations like platelet count and white blood cells.

Few studies have been done on these issues and have demonstrated a strong association of thrombocytopenia (platelet count <150,000/μL) with sepsis. A study done by Robert et al showed that about 22-35% of all babies admitted to Neonatal Intensive Care Unit (NICU) and in up to 50% of those admitted to NICUs who require intensive care develop thrombocytopenia of varying degree.[5]

So, in developing countries where the culture facilities are non- existent platelet count can be considered as one of the parameter in early diagnosis of sepsis in symptomatic infants.[6]

In past, there have been a lot of research studies done regarding the etiology, clinical profile and management of neonatal thrombocytopenia in the NICUs. The subject of influence of thrombocytopenia on the outcome of neonate has not been studied in detail in the past and neither have studies assessed the value of neonatal thrombocytopenia as a prognostic indicator in sick neonates.

On detailed search of various indexed medical literature, we found that only few articles have been published on this issue from India. So, as neonatal thrombocytopenia is one of the most common hematological problems encountered in the NICU, we designed a study to determine the frequency, etiological profile, predisposing factors and its influence on the neonate's outcome in our NICU.

METHODS

This single centre study was carried out prospectively on neonates admitted to SDM College of Medical Sciences and Hospital NICU during November 2011 to November 2012. A total of 100 consecutive neonates with positive blood culture or CSF culture for bacterial growth were considerd for the study.

Inclusion criteria

- Both males and females newborn
- Birth weight of 1 kg and above
- Blood and/or CSF culture positive cases

Exclusion criteria

- Blood culture negative
- Cases with blood culture positive for both bacterial and fungal sepsis
- Extremely low birth weight newborns (weight <1000 grams)
- Neonates >28 days
- Maternal history suggestive of placental insufficiency were excluded from study
- Cases with Family history of bleeding manifestations were excluded from study
- Cases of perinatal asphyxia were excluded from study
- Neonates whose parents or guardians did not agree to be a part of study

Collection of data

Babies who met our inclusion criteria and whose history and physical examination suggested possible sepsis were subjected Complete Hemogram (Hb, Total Leucocyte Count, Differential Count, ESR, Packed Cell Volume), platelet count, CRP, blood culture and sensitivity, CSF analysis was done if blood culture showed evident bacterial growth and in babies whose physical examination and history suggested meningitis.

Chest X-ray was done in selected cases IT ratio. ANC and micro ESR were not done. For study purpose that platlet count was considered which was drawn either along with positive blood culture or the one closest to the time the positive blood culture was drawn.

Objectives of present study are:

- To know the incidence of thrombocytopenia in babies with proven bacterial sepsis.
- To find, if any, species specific differences in severity and incidence of thrombocytopenia.

- Clinical outcomes in thrombocytopenic and nonthrombocytopenic septic babies.

Microbiological method

Collecting a blood sample for culture was carried out under strict aseptic conditions to avoid contamination. A 0.5 - 1 ml blood sample was considered adequate for blood culture bottle containing 5-10ml of culture media. BacT/ALERT^{R} PF Plus automated blood culture system was used to determine the growth of the organism. Blood culture reports were declared at 3-5 days of incubation period. Those babies with proven bacterial sepsis were included in the study and platelet counts, bleeding manifestations and causative organisms were noted. 2ml venous blood samples were taken in EDTA bulbs for platelet count analysis using automated analyser.

RESULTS

During the study period of 1 year we had a total of 960 neonates admitted to our NICU. Among them 570 neonates were inborn and 390 neonates were outborn. 475 neonates had some form of signs and symptoms which were suggestive of sepsis. So, all the 475 neonates were screened for sepsis. Among them 150 babies had positive blood culture. Out of the 150 cases with the positive blood culture 100 cases showed evident growth of bacteria only, 24 cases showed evident growth of fungi only, 26 cases showed evident growth of both bacteria and Fungi. As per the inclusion criteria of our study, cases which showed only bacterial growth in blood culture were considered for the study. Hence 100 neonates were included in the study.

Table 1 shows incidence of sepsis was slightly high in outborn neonates (52%) when compared with inborn neonates among those who required NICU admission. Bacterial sepsis was the commonest among different kind of sepsis. Baby boys (64%) had more sepsis in our cohort. Majority of our cohort were term babies (61%) and 69% of the babies in our study were delivered vaginally. Out of the 61 term neonates, 37 neonates had birth weight of ≥2500 grams and 63 neonates had birth weight <2500 grams, of which 12 weighed 1000-1499 grams and 51 weighed 1500-2499 grams in weight.

Early onset of sepsis was considered if neonates presented with signs and symptoms of sepsis within 72 hours of life and LOS was considered if signs and symptoms of sepsis presented after 72 hours of life. The incidence of EOS was more compared to LOS (61%).

Table 2 shows there is no significant difference between incidence of thrombocytopenia in babies with gram positive and gram negative sepsis (p value=0.218). Methicillin Resistant Coagulase negative *Staphylococcus aureus* (MR-CONS) was the commonest gram positive organism and *Klebsiella pneumoniae* was the commonest gram negative organism in both early and late onset sepsis groups. Out of the 100 cases, 41 had normal platelet count and 59 had thrombocytopenia, of which 15 each had mild and moderate and 29 were found to have severe thrombocytopenia. *Klebsiella pneumoniae* sepsis was the highest contributor to the severe thrombocytopenia category (15 out of 29 cases). Klebsiella positivity was more significantly associated with severe thrombocytopenia than MRCONS positivity or rest of the cultures combined together (p value <0.01).

Table 1: Demographic data of babies with bacterial sepsis.

	Gram positive	Gram negetive	Total
Sex			
Male	37	27	64
Female	18	18	36
Place of delivery			
Inborn	26	22	48
Outborn	29	23	52
Type of sepsis			
Early onset	34	27	61
Late onset	21	18	39
Gestation			
Term	40	21	61
Preterm	5	19	24
Late preterm	10	5	15
Weight			
>2500	23	14	37
2499- 1500	29	22	51
1499-1000	3	9	12
Mode of delivery			
Vaginal	38	34	72
Cesarean	17	11	28
ROM			
Absent	48	37	85
<18 hours	1	1	2
>18 hours	6	7	13
Thrombocytopenia			
No	36	24	60
Mild	10	8	18
Moderate	7	4	11
Severe	2	9	11
Outcome			
Improved	45	37	82
Unchanged	5	1	6
Expired	5	7	12

Of the 59 neonates who had abnormal platelet counts, 41 (69.49%) were found to have bleeding tendencies and 18 (30.51%) didn't have any bleeding. In comparison, of the 41 neonates with normal platelet count, only 5 (12.20%) had bleeding manifestations and 36 (87.80%) didn't have bleeding manifestation. Hence an abnormal platelet count was found to be significantly associated with bleeding tendencies (p<0.001).

CSF was done in 91 out of 100 neonates with blood culture positive for bacteria. Among them 85 babies (93.40%) had CSF within normal limits and 6 babies (6.60%) had features suggestive of meningitis.

9 neonates were not subjected to CSF examination as some were ventilated or died and other neonates died on the day of their admission to NICU.

Table 2: Frequency of microorganism causing mild to severe thrombocytopenia.

Type of organism	No of neonateswith thrombocytopenia				
	Normal (%)	Mild (%)	Moderate (%)	Severe (%)	Total
MR -CONS	22 (55)	4 (10)	6 (15)	8 (20)	40
Klebsiella pneumoniae	5 (19.23)	4 (15.39)	2 (7.69)	15 (57.69)	26
CONS	6 (54.54)	3 (27.27)	2 (18.18)	0 (0)	11
Nonfermenting GNB	1 (50)	1 (50)	0 (0)	0 (0)	2
Enterobacter cloacae	0 (0)	0 (0)	0 (0)	1 (100)	1
Pseudomonas aeruginosa	1 (33.33)	0 (0)	2 (66.67)	0 (0)	3
Staphylococcus aureus	4 (66.66)	1 (16.67)	0 (0)	1 (16.67)	6
Acinetobacter	2 (28.57)	1 (14.28)	2 (28.57)	2 (28.57)	7
E. coli	0 (0)	1 (25)	1 (25)	2 (50)	4
Total	**41**	**15**	**15**	**29**	**100**

Table 3: Thrombocytopenia and outcomes.

Thrombocytopenia	Expired	Unchanged	Improved	
No	5	51	4	60
Mild	3	15	0	18
Moderate	1	8	2	11
Severe	3	8	0	11

Table 3 shows there was no significant association between thrombocytopenia and mortality (p=0.176), the proportion of children with severe thrombocytopenia was significantly higher in babies who expired (25% vs 9%) when compared to babies who survived.

DISCUSSION

The total number of neonates admitted to NICU was 960 of which 150 neonates had sepsis. Among them 100 neonates had bacterial sepsis. Incidence of bacterial sepsis in our NICU was 21.75.

In present study, we found that low birth weight neonates were more prone to sepsis when compared to normal birth weight babies. 63 babies of our 100 babies with proven bacterial sepsis had either low birth or very low birth weight. This is comparable with the study conducted by Seyyed Mohammad Hassan Aletayeb et al who showed 73.3% were low birth weight and 26.7% were normal birth weight.[7]

Thrombocytopenia is a well-known complication of sepsis.[8] Responsible mechanisms include immune-mediated platelet destruction, decreased production, and DIC. In our study 59 babies (59%) had thrombocytopenia of which 15 babies had mild, another 15 babies had moderate and 29 babies had severe thrombocytopenia. This incidence of thrombocytopenia in our study is comparable with other studies conducted by Bashir et al (59.5%), Guida JD et al (54%).[9,10]

In current study, 9 organisms were isolated and all these organisms were associated with some form of thrombocytopenia. Methicillin Resistant Coagulase negative *Staphylococcus aureus* (MR-CONS) was the commonest gram positive organism and *Klebsiella pneumonia* was the commonest gram negative organism in both early and late onset sepsis groups.

Among them *Klebsiella pneumoniae* was the most common organism associated with thrombocytopenia (21%).total of 29 babies had severe thrombocytopenia out of which nearly 50% i.e. 15 babies were positive for *Klebsiella pnuemoniae*. Among all the organisms responsible for thrombocytopenia Enterobacter cloacae was the least organism causing thrombocytopenia (1%). A study done by Bashir et al showed that *Klebsiella pneumoniae* was the most common organism associated with thrombocytopenia (58%).[9] Another study done by Arif et al showed that *Klebsiella pneumoniae* was the most common organism associated with thrombocytopenia (73.3%).[11] *Klebsiella pneumoniae* expresses a smooth lipopolysaccharide (LPS with O antigen) and a capsular polysaccharide (K antigen), and both are important for its virulence. There is a variation in the genetic makeup of O antigen between *Klebsiella pneumoniae* and other Gram-negative organisms, which

allows *Klebsiella pneumoniae* strains to constitutively express a polysaccharide capsule critical for the organism's ability to resist complement-mediated opsonophagocytic killing. These genetic variations in *Klebsiella pneumoniae* may be responsible for the effects on platelet numbers seen in our study.

Although there was no significant difference in mean number of hospital stay (14.45 days Vs 14.60 days; p value=0.941) and mortality rates (p value=0.176) between non-thrombocytopenic and thrombocytopenic babies, the proportion of children with severe thrombocytopenia was significantly higher in babies who expired (25% vs 9%) when compared to babies who survived. These facts suggest that there may be no direct causality of thrombocytopenia over mortality and the fact that there was higher proportion of severe thrombocytopenia in babies who died merely points to the severity of the illness i.e. babies died because of the severe illness rather than severe thrombocytopenia. In study conducted by Zulfiqar Ahmed Bhutta et al the mortality was associated with birth weight, birth asphyxia, shock and metabolic derangements rather than thrombocytopenia.[12]

CONCLUSION

Our study shows that in our setting bacterial sepsis is significantly complicated by thrombocytopenia. Severe thrombocytopenia in a suspected case of bacterial sepsis might predict *Klebsiella species* sepsis and hence it may be prudent to start empirical antibiotics covering the Klebsiella species.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Committing to child survival: a promise renewed. 2015. Available from: https://www.unicef.org/publications/files/APR_2015_9_Sep_15.pdf
2. Newborn death and illness. Millennium Development Goal (MDG) 4. Available from: http://www.who.int/pmnch/media/press_materials/fs/fs_newborndealth_illness/en/
3. Mortality rate, neonatal (per 1,000 live births). The world bank. Available from: http://data.worldbank.org/indicator/SH.DYN.NMRT
4. Sankar MJ, Agarwal R, Deorari AK and Paul VK. Sepsis in the Newborn. Indian J Pediatr. 2008;75(3):261.
5. Roberts I, Murray NA. Neonatal thrombocytopenia: causes and management. Arch Dis Child Fetal Neonatal Ed. 2003;88: 359-64.
6. Sharma A, Krishna Kutty CV, Sabharwal U, Rathee S, Mohan H. Evaluation of Sepsis screen for diagnosis of Neonatal septicaemia. Ind J Pediatr. 1993;60:559-63.
7. Aletayeb SMH, Khosravi AD, Dehdashtian M. Identification of bacterial agents and antimicrobial susceptibility of neonatal sepsis: 54- month study in a tertiary hospital. Af J Microbiol Res. 2011;5(5):528-31.
8. Lee KH, Hui KP, Tan WC. Thrombocytopenia in sepsis: a predictor of mortality in the intensive care unit. Singapore Med J. 1993;34(3):245-6.
9. Charoo BA, Iqbal JI, Iqbal Q, Mushtaq S, Bhat AW, Nawaz I. Nosocomial sepsis-induced late onset thrombocytopenia in a neonatal tertiary care unit: a prospective study. Hematol Oncol Stem Cell Ther. 2009;2(2):349-53.
10. Guida JD, KunigAM, Leef KH, McKenzie SE, Paul DA. Platelet count and sepsis in very low birthweight neonates: is there an organism-specific response? Pediatr. 2003;111(6 Pt 1):1411-5.
11. Arif SH, Ahmad I, Ali SM, Khan HM. Thrombocytopenia and bacterial sepsis in neonates. Indian J Hematol Blood Transfus. 2012;28(3):147-51.
12. Bhutta ZA, Yusuf K. Neonatal sepsis in Karachi: factors determining outcome and mortality. J Trop Pediatr. 1997;43(2):65-70.

Cite this article as: Goudar VR, Kabbin GM, Joshi SN, Chavan VP, Badiger SL. A study of bacterial sepsis and its relation to thrombocytopenia in neonates. Int J Contemp Pediatr 2017;4:1032-6.