ISSN (Print) : 2348–263X
ISSN (Online) : 2348-2648
MVP Journal of Medical Sciences, *Vol 4(1), 55–60, January-June 2017* DOI: 10.18311/mvpjms/2017/v4i1/701

Study of Platelet Count and Platelet Indices in Neonatal Sepsis in Tertiary Care Institute

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Abstract

Aims and Objectives: To correlate degree of thrombocytopenia and platelet indices with neonatal sepsis in our NICU set up. **Materials and Methods:** After taking approval from ethical committee of our institute, we studied total 150 cases over a span of 24 months, from August 2013 to August 2015. Peripheral blood was drawn from all the study subjects under aseptic precautions in EDTA bulb. A complete hemogram was performed using Beckman Coulter. Latex agglutination kit was used for CRP estimation. Different organisms were isolated by Bactecblood culture. **Results:** Out of 150 neonates 40(26%) cases were sepsis proven, 63 (42%) ases had suspected infection and 47(31%) cases were non infected. Male constituted 84(56%) cases and females constituted 66(44%) cases. 35(87.5%) cases out of proven sepsis were preterm neonates. Out of 40 sepsis proven cases CRP was increased in 31 (77.5%) neonates. Gram negative organisms were more common than gram positive organisms. Pseudomonas was most common organism, and was isolated in 16 (40%) cases. Staphylococcus organism isolated in 7 (17.5%) cases. 23 (57.5%) of sepsis proven cases showed severe degree of thrombocytopenia and was seen mainly with Pseudomonas organisms. In platelet indices PDW was significantly increased in newborns with sepsis. Whereas MPV was also increased in sepsis cases but was not significant. **Conclusion:** Variation in the degree of thrombocytopenia and platelet indices was seen in neonatal sepsis. Severe degree of thrombocytopenia associated with proven sepsis. PDW was significantly increased in newborns with sepsis. Gram negative organisms were common cause of neonatal sepsis.

Keywords: C Reactive Protein (CRP), Mean Platelet Volume (MPV), Platelet Distribution Width (PDW)

1. Introduction

1.1 Neonatal Septicemia- Definition

Neonatal septicemia is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia in the first month of life[1]. Sepsis is a common complication in the neonatal intensive care unit and is a major cause of neonatal mortality.It is caused by various organisms invading the blood stream, which may be by bacterial, viral, fungal and protozoal infections. It is characterized by positive blood culture, thrombocytopenia and elevated C-reactive protein. Septic shock is the most dangerous complication of septicemia[1].

The objective of this study is to correlate degree of thrombocytopenia and platelet indices with neonatal sepsis in our NICU set up of tertiary care institute.

1.2 Materials and Methods

After taking approval from ethical committee from our institute, we studied total 150 cases over a span of 24months, from August 2013 to August2015.

- Inclusion Criteria
  All neonates (<28 days) presenting with symptoms and signs of sepsis like poor feeding, lethargy, tachypnea, hypothermia, convulsion, etc. were included in the study.

- Exclusion Criteria
  All newborns with neonatal hyperbilirubinemia due to causes other than sepsis like physiological jaundice, Rh, ABO incompatibility, TTN, MAS without clinical or laboratory suspicion of sepsis were excluded from the study.

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2. Aims and Objectives

- To correlate the degree of thrombocytopenia with sepsis.
- To study correlation between sepsis and platelet indices in study group.
- To find out etiological agent causing neonatal sepsis.

Neonates were enrolled in the study if there were predisposing factors (i.e., maternal fever, significant PV leaking, maternal UTI, etc) or if there was clinical suspicion of sepsis[1]. Written and informed consent was taken from parents/guardian of neonate. Ethical committee approval was taken from institute for study. The blood samples were sent to the pathology laboratory collected by peripheral venipuncture using aseptic precautions in EDTA bulb, from which values of Haemoglobin, total leukocyte count, platelet count, haematocrit, RBC count, Plateletcrit, PDW (Platelet Distribution Width), Mean platelet Volume (MPV) were derived. In plain bulb sample was taken for C-Reactive Protein (CRP) which was processed using C-reactive protein kit. The routine haematological investigations performed on multichannel automated cell counter with standard calibration.

Special investigation: Blood culture and sensitivity - 1-3ml venous sample was taken in blood culture bottle under all aseptic precautions. The culture and sensitivity report was done by Bactec method. All the above tests were done in pathology and microbiology laboratory.
The study group was categorised in three groups.

- Proven Sepsis (Septicaemia[1])- It is characterised by positive blood culture with clinical and/or laboratory evidence of sepsis.
- Probable Sepsis- Blood culture negative, but having clinical criteria for sepsis as per IMCI /WHO criteria[1]. i.e., Neurologic-convulsions, drowsy/unconscious, decreased activity, bulging fontanel.

Respiratory - Respiratory rate>60 breaths/min, grunting, severe chest in drawing, central cyanosis.
Cardiac- poor perfusion, rapid and weak pulse.
Gastrointestinal - jaundice, poor feeding, abdominal distension
Dermatologic- skin pustules, periumbilical erythema or purulence.
Musculoskeletal - edema or erythema overlying bones or joints.
Other- Temperature > 37.7°C or < 35.5 C.

- No Sepsis – Babies without clinical or laboratory evidence of sepsis.

2.1 Grading of Thrombocytopenia[2]

Thrombocytopenia is graded to different severity for the risk assessment and management as following

- Severe degree of thrombocytopenia- <50,000 / µL.
- Moderate degree of thrombocytopenia- 50,000 -1,00,000 / µL.
- Mild degree of thrombocytopenia- 1,00,000-1,50,000 / µL.

2.2 Platelet Indices

Platelet indices are:

- Mean Platelet Volume (MPV).
- Platelet Distribution Width (PDW).
- Plateletcrit (MPV×platelet count).

The values of MPV and PDW were studied in relation to sepsis in all three categories. The findings of investigations were entered in proforma. The data were analysed using standard statistical software.

3. Observations

40 out of 150 neonates (26%) were classified as sepsis proven, as they have positive blood culture, 63 (42%) had probable infection and 47 (31%) were non-infected (Table 1).

Table 1. Infection status (based on blood culture)

Infection status	Number of neonates	Percentage (%)
Sepsis proven	40	26
Probable sepsis	63	42
No sepsis	47	31

4. C-Reactive Proteins

Normal reference range of CRP being 0 to 6 mg/liter as per our institute laboratory.

Out of 150 cases CRP value is negative i.e., below 6 mg/liter in 76 cases and positive in 74 cases. Out of positive 74 cases 31 (77.5%) cases are sepsis proven and 33 (52.38%) are of probable sepsis (Table 2).

Table 2. CRP and sepsis

CRP levels	Clinical diagnosis			Total
	Sepsis proven	Probable Sepsis	No Sepsis	
< 6 mg/ltr	9 22.5%	30 47.61 %	37 78.72%	76 50.67%
> 6 mg/ltr	31 77.5%	33 52.38%	10 21.28 %	74 49.33%
Total	**40 100%**	**63 100 %**	**47 100 %**	**150 100 %**

Gram negative organisms were more commonly isolated in neonatal sepsis cases. Pseudomonas aeruginosa was isolated in 16 cases out of 40 proven sepsis which was most common organism found in our NICU set up.

Other was Klebsiella, E coli. In gram positive organisms, staph aureus was most commonly found. The most common fungal organism isolated was Candida albicans.

The other less commonly isolated organism were acinetobacter, enterobacter etc [Table 3 and 4].

Table 3. Isolated blood culture

Organism isolated	Number of neonates	Percentage (%)
Pseudomonas	16	40
Staph. aureus	7	17.5
Candida	6	15
Klebsiella	4	10
Acinetobacter sp.	3	7.5
Escherichia coli	2	5
Enterobacter	2	5
Total	**40**	**100**

Table 4. Isolated blood culture

Organisms	Frequency	Percentage
Gram negative	27	67.5 %
Gram positive	7	17.5 %
Fungal	6	15.0%
Total	**40**	**100 %**

4.1 Degree of Thrombocytopenia and Sepsis

Out of 150 cases, 86 neonates (57.3%) had mild degree of thrombocytopenia, 22 neonates (14.7%) had moderate degree thrombocytopenia and 42 neonates (28%) showed severe degree thrombocytopenia.

23 out of 40 sepsis proven cases (57.5%) showed severe thrombocytopenia whereas 12 out of 63(19.1%) probable sepsis cases showed severe thrombocytopenia (Table 5).

45(43.69%) out 103 cases of proven and probable sepsis had increased Platelet Distribution Width (PDW) value (Table 6).

4.2 Chi Square Test Output

As a coefficient of significance value is positive i.e., 0.033, which indicates there is positive correlation between sepsis and PDW.

Chi-Square Tests			
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	8.712	3	0.033
N of Valid Cases	150		

a.1 cells (12.5%) have expected count less than 5. The minimum expected count is 3.45.

Here 37 cases (35.92%) out of 103 cases of sepsis had increased MPV. (Table 7).

Table 5. Degree of thrombocytopenia and sepsis

Status of sepsis	Thrombocytopenia			Total
	Mild (1.5L -1,00,000)	Moderate (50,000-1,00,000)	Severe (<50,000)	
Proven Sepsis	9	8	23	40
	22.5 %	20.0 %	57.5 %	100 %
Probable Sepsis	42	9	12	63
	66.7 %	14.2 %	19.1 %	100 %
No Sepsis	35	5	7	47
	74.5 %	10.6 %	14.9 %	100 %
Total	**86**	**22**	**42**	**150**
	57.3 %	**14.7 %**	**28.0 %**	**100 %**

Table 6. Relation of Sepsis with Platelet Distribution Width (PDW)

Sepsis	Platelet Distribution Width				Total
	Decreased (7.5)	Normal (7.5-11.5)	Increased (>11.5)	Not detected	
Present	6	19	45	33	103
	5.83%	18.45%	43.69%	32.04%	100.00%
Absent	5	13	9	20	47
	10.64%	27.66%	19.15%	42.55%	100.00%
Total	**11**	**32**	**54**	**53**	**150**
	7.33%	**21.33%**	**36.00%**	**35.33%**	**100.00%**

Table 7. Relation of sepsis with mean platelet volume

Sepsis	MPV category			Total
	Increased	Normal / Decreased	Not Detected	
Present	37	34	32	103
	35.92%	33.01%	31.07%	100.00%
Absent	11	16	20	47
	23.40%	15.53%	19.42%	45.63%
Total	**48**	**50**	**52**	**150**
	32.00%	**33.33%**	**34.67%**	**100.00%**

As coefficient of significance value is negative (0.244) which indicates there is no any significant association between sepsis and MPV.

Chi-Square Tests			
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	2.819	2	0.244
N of Valid Cases	150		
a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 15.04.			

5. Discussion

5.1 Neonatal Septicemia- Definition

Neonatal septicemia is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia in the first month of life. Neonatal survivors of sepsis can have severe neurological sequel dut to central nervous system infection as well as from secondary hypoxemia resulting from septic shock, persistent pulmonary hypertension and severe parenchymal lung disease[3]. The signs and symptoms suggesting neonatal sepsis are nonspecific and there is no rapid and reliable laboratory test finding for confirmation of etiological diagnosis. Although advances in neonatal care have improved survival and reduced complication in preterm infants, sepsis still contribute significantly to morbidity and mortality among very low birth weight infant in NICU[4].

It requires a minimum period of 48-72 hours for blood culture which is the gold standard for diagnosis of neonatal sepsis and yields positive results i n 25-70 % of cases[5,6].

5.2 Incidence of sepsis

Incidence of neonatal sepsis or bacteremia in asymptomatic infant is low, but not negligible[7]. The percentage of proven sepsis with positive blood culture was 26% and probable sepsis was 42% in our study.

Mirza sultan Ahmed[8] had blood culture positivity in 29 % and probable sepsis in 71%. In Rodwell's study[9] sepsis was confirmed in 9% of evaluations. Jack D. Guida[10] diagnosed sepsis in 16% of newborns and 28.5% culture positive cases in Franz A R et al.,[11] study.

5.3 Age and Sex Incidence

In our study, total numbers of male newborns were 84 and female 66. Several other workers such as Philip and Hevitt[12],Chandna et al., Ablin et al[13] have reported a similar finding. E.Guclu, Y Durmaz et al.[14] reported 61 female and 84 male out of 145 cases.

5.4 Gestational Age

Due to immunodeficiency in preterm neonates, the risk of sepsis is increased[15]. 87.5% of proven sepsis were preterm whereas 68% term neonates were non septic.

5.5 Onset of Symptoms

Late onset sepsis was more common than early onset sepsis, presented in study conducted by Rodwell et al[9]. In our study group, 73.3 % neonates presented with late onset sepsis whereas 26.7 % neonates presented with early onset sepsis.

Pseudomonas aeruginosa was the most common organism followed by staphylococcus aureus. Gram negative organisms (67.5%) were relatively higher than gram positive organisms (17.5%) and fungal organism (15%). Study conducted by Krishna et al[16] and Kumhar et al[17]. Klebsiella was the commonest organism identified. In Jack D Guida's study[10], gram negative were 16% whereas grams positive and fungal were 7.6% and 8%, respectively.

Even Group B Streptococcus was the most common organism in the studies conducted by Rodwell et al[9]. Sartaj A Bhat et al.,[18] identified gram negative culture positive in 67.5% and gram positive were 26.3%, remaining were fungal growth.

Parvez Rajnesh[19] proved in their study that gram negative were 54%, in that most common were Klebsiella, followed by pseudomonas then acinetobacter and gram positive were 40%, most common were staphylococcus followed by Enterococcus.

5.6 C-Reactive Protein

Out of total 40 sepsis proven cases, CRP raised in 77.5% neonates and 52.38% in probable sepsis. 21.28% raised CRP cases were non infected neonates.

Manucha et al[20]., have reported elevated CRP levels in 76% cases of neonatal sepsis.

5.7 Platelet Count and Platelet Indices

In our study group, out of total sepsis positive cases, severe thrombocytopenia was presented in 57.5%, while mild and moderate thrombocytopenia in 22.5% and 20.0% respectively. Non infected neonates had majority of mild thrombocytopenia in 74.5% and severe thrombocytopenia in 14.9 %. S.h. Arif et al.,[21] showed that thrombocytopenia was seen in 83.5% cases of neonates with sepsis.

In our study Pseudomonas aeruginosa was the commonest organism causing neonatal sepsis accompanying severe thrombocytopenia (64.7%) than mild or moderate thrombocytopenia. In Torkman N et al. study[22], Enterobacter was the commonest organism causing neonatal sepsis with thrombocytopenia.

E Guclu et al.,[14] found PDW as a significant parameter in neonates with sepsis. Ferhatcatal et al., found that there is significant differences between control and sepsis group in terms of platelet count, PDW/MPV($p<0.005$)[23].

Thrombocytopenia is also known to be of prognostic value. Thrombocytopenia was found to be consistently associated with poor prognosis, confirming the finding of other studies[22].

In our present study, 45 out of 103 cases (43.69%) of proven and probable sepsis showed increased PDW value. Patrick CH et al., reported that there is significantly increased presence of bacteremia in those neonates with MPV greater than 10.8f Land/or PDW greater than 19.1%[24].

Jack D. Guida[10] reported 54% neonates with thrombocytopenia, in that 61% neonates had increased MPV. In our study 37 out of 103 (35.92%) cases of proven and probable sepsis had increased MPV which does not show any co relation between sepsis and MPV.

6. Conclusion

In this observational study, we concluded that there was severe degree of thrombocytopenia in proven neonatal sepsis cases. Gram negative organisms were more commonly isolated than gram positive and fungal organisms. Fungal growth increased due to use of higher antibiotics in late onset sepsis. In gram negative organisms, pseudomonas aeruginosa was the most common organism while in gram positive organisms, staphylococcus aureus was the most common. Candida albicans was the most common fungal organism. Incidence of late onset sepsis was more than early onset sepsis. Risk of neonatal sepsis was more in preterm babies than full term babies. Prematurity, PROM and meconium stained liquor were found to be associated maternal risk factors. C reactive protein was raised in most of sepsis cases and proved to be a useful rapid diagnostic test especially if used in conjunction with other hematological parameters. Severe thrombocytopenia was more commonly present in sepsis proven cases than non-infected neonates. Platelet indices values MPV and PDW were increased in newborns with sepsis.

7. Acknowledgements

All authors thank and express appreciation to Head of Pediatric Department Dr. Ravindra Sonawane and our colleagues from Pediatric Department of Dr. Vasantrao Pawar Medical College and Research Center, Adgaon, Nashik for their immense help while doing the study. Authors also thank and express appreciation to Department of Community Health Medicine of the institute.

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