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Original Research Paper

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CORRELATION BETWEEN NEONATAL SEPSIS WITH SERUM CRP AND PLATELET INDICES (PLATELETS COUNT, MPV & PDW)

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ABSTRACT

Background of study: Neonatal sepsis causes significant mortality and long term morbidity in neonates, especially for preterm infants of very low birth weight.

Objective: To findout correlation between neonatal sepsis with serum CRP and platelet indices (platelets count,MPV,PDW).

Method: The study was hospital based prospective study conducted in Department Of Pediatrics associated group of hospitals, Government Medical College ,Kota. Total 256 babies were enrolled who were admitted in NICU and showed signs and symptoms of sepsis and who fulfilled inclusion and exclusion criteria. Peripheral venous blood was collected from all the newborns for all laboratory investigation. All the data were collected and analyzed using software SPSS version 21.

Results: Among the positive perinatal sepsis (26.56%), maternal fever (57.35%) and PROM (30.88%) was the most common causes. 66.41% were sepsis screen positive and 35.55% were blood culture positive. Serum CRP was positive in 58.20% cases, thrombocytopenia(<1.5 lac), MPV(>10.8), and PWD(>19.1) was present in 81.25%, 73.44%, and 69.14% cases respectively. Sepsis was occurred most commonly due to gram negetive organism. Most common organism causing sepsis was kleibsiella (39.56%). Among the CRP positive cases, 36.91% had blood culture positive. Sensitivity, specificity, PPV, and NPV of CRP for proven sepsis was 60.44%, 43.03%, 36.91% and 66.36% respectively. Platelets count was more decrease in LOS (p=0.005). Sensitivity and specificity of platelet counts (<1.5 lac), MPV(>10.8), and PWD(>19.1) were 87.91%, 84.62%, 79.12% and 22.42%, 32.73%, 36.36% respectively. When we combine all three parameter of platelets indices (Count+MPV+PDW), we achieve highest sensitivity (98.33%) and NPV (95.65%).

Conclusion: In this study we conclude that the marker of platelets indices has higher diagnostic efficacy than CRP; the platelets indices had higher sensitivity, NPV, and PLR. High PDW, high MPV and low platelets counts are more associated with neonatal sepsis. So this study is useful for evaluating platelets indices as a marker of neonatal sepsis alone or with combination to pre-existing sepsis screen.

KEYWORDS : Neonatal sepsis, serum CRP, sepsis screen, blood culture, pletelets indices (Count+MPV+PDW)

INTRODUCTION

Sepsis is a non-specific inflammatory defence mechanism and is considered a generalized process where every organ and system can be involved. The haemostatic system is frequently disturbed during sepsis. The incidence of neonatal sepsis varies from 11-24.5/1000 live births in India [1]. In developing country like India sepsis contributes to 37% of all neonatal deaths. As per the National Neonatal Perinatal Database 2002-2003, the incidence of neonatal sepsis is 30 per 1000 live births. [2]. Neonatal sepsis is usually classified into early onset sepsis (EOS) (i.e. onset <72hrs of age) and late onset sepsis (LOS) (i.e. onset >72 hrs of age).

Neonates are fragile and can deteriorate rapidly, so one should be prompt in management. However, the diagnosis of sepsis in neonates presents as a challenge because the clinical signs of sepsis are non-specific. Since clinical signs alone cannot make a specific diagnosis of sepsis, we have to rely on investigations to guide us. Among these blood culture is the gold standard for the diagnosis for neonatal sepsis. Even this gold standard is not without its limitations. To overcome this limitation and to guide early diagnosis, sepsis screens (CRP, micro ESR, haematological parameters) are used. It has been seen that platelet count decreases and mean platelet volume (MPV) and platelet distribution width (PDW) increase in neonates with sepsis, but these indices have not been extensively studied in neonatal sepsis. Hence the present study was undertaken to evaluate thrombocytopenia and variations in platelet indices in neonatal sepsis.

METHODS

The study was hospital based prospective study conducted in Department Of Pediatrics and associated group of hospitals, Government Medical College, Kota. Total 256 babies were enrolled who were admitted in NICU and showed signs and symptoms of sepsis and who fulfilled inclusion and exclusion criteria.

Inclusion criteria:

- Neonates who had signs and symptoms suggestive of neonatal sepsis.
- Newborns with any of features were kept under **clinical sepsis** category.
- Risk factors for perinatal sepsis

Exclusion criteria

- Neonates with congenital anomalies, Hypoxic ischemic encephalopathy, Hyaline membrane disease, Congenital heart disease.
- Congenital and acquired causes of thrombocytopenia other than sepsis.
- Neonates whose parents did not give consent.
- Neonates undergoing surgery.

Neonates were evaluated by thorough history from mother and detail clinical examinations. Peripheral venous blood was collected from all the newborns and sent for investigations for blood culture, sepsis screen and platelets indices.

On the results obtained they were classified to in to three groups; proven sepsis-culture positive; suspected- screen positive but culture negative; and clinical sepsis-both screen and culture negative.

All the data collected were transferred in to the Microsoft excel sheet and were analyzed using software SPSS version 21 and both side p value less than 0.05 was considered significant. Quantitative data were expressed as mean ± standard deviation. To find out the difference in means between two groups Student's t- test (unpaired t test) and between three groups ANOVA test was employed. Qualitative data were expressed as percentages/ proportion and difference and were analyzed by chi square test.

RESULTS

This study was comprised of 256 neonates, with mean age of 4.16 days, sex ratio of 1.1:1, 52.74% were preterm and mean birth weight of 2.35 kg with 56.25% of less than 2.5 kg.

Table: Distribution of cases according to various demographic profile

Demograpgic profile		No. of cases	Percentage (%)
Age	< 72 hrs	118	46.09%
	>72 hrs	138	53.91%
Sex	Male	134	52.34%
	Female	122	47.66%
Gestational age	Term	121	47.26%
	Pre-term	135	52.74%
Weight	<2.5 kg	144	56.25%
	>2.5 kg	112	43.75%

Among the component of perinatal sepsis score, prematurity was the most common followed by maternal fever and PROM. Out of 68 perinatal sepsis score, 32 were culture positive. In this study, 66.41% were sepsis screen positive and 35.55% were blood culture positive. Serum CRP was positive in 149(58.20%) cases, thrombocytopenia(<1.5 lac), MPV(>10.8), and PWD(>19.1) was present in 81.25%, 73.44%, and 69.14% cases respectively.

Table: Distribution of cases according to Lab parameters for sepsis (n=256):

Parameter	Positive	Negative
CRP	149	107
TLC <5000 or TLC >20000	103	153
Neutrophil <1800	26	230
Platelets count <1.5 Lac.	208	48
MPV >10.8fl	188	68
PDW >19.1fl	177	79

Among the 256 cases, 91(35.55%) were culture positive. 67.03% were gram negative. Most common organism causing sepsis was kleibsiella (39.56%) followed by staph aureus (19.78%), and pseudomonas (10.98%). Among the CRP positive group,(36.91%) had blood culture positive. sensitivity, specificity, PPV, and NPV of CRP for proven sepsis was 60.44%, 43.03%, 36.91% and 66.36%.

Table: Correlation between CRP with blood culture:

CRP	Culture positive	Culture negative	Total
Positive	55	94	149
Negative	36	71	107
Total	91	165	256

Parameters	Sensitivity	Specificity	PPV	NPV	LR+
CRP	60.44%	43.03%	36.91%	66.36%	1.06

PDW(>19.1fl) sepsis screen was positive in 142 (68.27%), 129(68.62%) and 121 (68.36%) cases and proven sepsis was positive in 80 (38.46%), 77(40.96%), and 72 (40.68%) cases respectively.

Sensitivity of platelet counts was highest (87.91%) followed by MPV (84.62%) and PDW (79.12%). Platelet count as a parameter has low specificity (21.30). PPV,NPV and LR+ of MPV were heighest.

Table: Correlation of platelets indices with proven sepsis (culture positive):

		Culture positive (91)	Culture negative (165)	Total
Platelets count	< 1.5 Lac.	80	128	208
	≥ 1.5 Lac.	11	37	48
MPV	> 10.8fl	77	111	188
	≤ 10.8fl	14	54	68
PDW	> 19.1fl	72	105	177
	≤ 19.1fl	19	60	79

Parameters	Sensitivity	Specificity	PPV	NPV	LR+
Platelet count<1.5lac/mm^3	87.91%	22.42%	38.46%	77.08	1.133
MPV>10.8fl	84.62%	32.73%	40.96%	79.41	1.258
PDW>19.1fl	79.12%	36.36%	40.68%	75.95	1.243

When we combine all three platelets indices (Count+ MPV+ PDW), we achieve highest sensitivity (98.33%) and NPV (95.65%).

Parameters	Sensitivity	Specificity	PPV	NPV
Platelet count + MPV	94.59	21.54	40.70	87.50
Platelet count + PDW	92.75	24.37	41.56	85.29
MPV+PDW	90.28	28.70	44.22	82.50
Platelet count+ MPV +PDW	98.33	21.36	42.14	95.65

Sensitivity of sepsis screen in culture positive case was 62.64% and specificity was 31.52%. PPV, NPV, and LR+ 33.53%, 60.47%, and 0.914 respectively.

The co-relation between markers of platelet indices with positive sepsis screen and gold standard blood culture shows that when we combine sepsis screen and platelet count the sensitivity (92.59%), and NPV (80.00%) was highest. Highest sensitivity in combination with sepsis screen + platelet count +PDW MPV (90.60%), followed by sepsis screen + platelet count + MPV (93.62%) in culture positive cases.

DISCUSSION

In our study, total 256 newborns were enrolled on the basis of inclusion and exclusion criteria. Based on the results obtained they were divided in to three groups; Group I-**proven sepsis group**, A total of 91 newborns (35.55%). Group II- **suspected sepsis,** there were 113(44.14%). Group III- Remaining 52(20.31%) had **clinical sepsis.** 56.25% of babies were LBW (<2500 gm). Preterm babies formed 52.74% of our study, these are slightly higher than study by **Moreno et al**[3]

In our study CRP was positive in 149(58.20%) Cases, **Philip et al** [4] also have similar results. Blood culture was positive in 35.55% cases comparable with the result of **Okascharoen et al** which stated that blood culture positivity in neonatal sepsis is only 20%-30%.[5] Out of the organisms isolated, 30.77% were gram positive organisms and 67.03% were gram negative and this is also comparable with the results of **Moreno et al.**[3] The most frequent organism isolated was Klebsiella (39.56%) followed by Staphylococcus aureus (19.78%). Pseudomonas, Citrobacter, CONS and E coli were found in 10.98%, 7.69%, 6.59% and 5.49% newborns respectively.

Various Studies	Sample size	Staph. aureus	CONS	E. coli	Klebsiella	Entero cocci	Pseudomonas	Others
Present Study	256	18	6	5	36	3	10	13
Mustafa et al (6)	140	15	07	14	22	-	04	-
Dhanalakshmi et al (7)	70	-	04	04	28	-	-	05
Usharani et al(8)	85	04	03	06	09	-	01	06

A total of 149 (58.20%) newborns had positive CRP in our study. Out of these 55 had positive blood culture and was statistically significant with p value <0.05. The sensitivity, specificity, PPV, and NPV were 60.44%, 43.03%, 36.91, and 66.36% respectively. According to **Philip et al,** in this study CRP levels were raised in 58.2% of neonates with sepsis.CRP has a sensitivity of 47% for neonatal sepsis.[4] Whereas **Hakeem et al** [9] found a near similar finding with the sensitivity of 72.9% and NPV of 69.7%. The platelet count has a significant decrease in LOS. (p =0.005) also comparable to result of study by **Choudhary R R at al.** [10] In our study the sensitivity and specificity of platelet count was found to be 87.91% and 22.42% respectively and PPV ,NPV LR+ were 38.46, 77.08%, 1.133 respectively in culture proved group. MPV is significantly increased in LOS than EOS.(p=0.009). as comparable to study of **Patrick RH et al**[11] Increase in PDW is significantly more in LOS. (p = 0.013) as comparable to study of **Patrick RH et al**[11] and **Choudhary R R at al** [10] Thrombocytopenia (platelet count <1.5 lacs/mm^3) had the highest sensitivity to detect sepsis (87.91%) followed by MPV, PDW have a sensitivity of 84.62% and 79.12% respectively in culture proved group. When we combined these indices (platelet count+MPV+PDW), the sensitivity of the study increase (98.33%).

CONCLUSION

This study was conducted to establish the relationship between neonatal sepsis with serum CRP and platelets indices. In this study we conclude that the CRP is being most commonly used component of sepsis screen, the marker of platelets indices has higher diagnostic efficacy than CRP; the platelets indices had higher sensitivity, NPV, and PLR. High PDW, high MPV and low platelets count are more associated with neonatal sepsis. So, this study is useful for evaluating platelets indices as a marker of neonatal sepsis alone or with combination to pre-existing sepsis screen. However it must be noted here that the sensitivity of platelet indices alone was higher than the existing sepsis screen (62.64%). When we combine the existing sepsis screen with platelet indices and correlate it with blood culture, the sensitivity again increased (92.59%).

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