

Study of Mean Platelet Volume as Predictive Index of Neonatal Sepsis

Rashmi Tiwari¹, Mahtabuddin¹, Qazi Rais Ahmed² and R. C. Sharma^{*2}

¹Assistant Professor, ²Professor, Department of Physiology, G.C.R.G. Institute of Medical Sciences, Lucknow, UP, India

QR Code



*Correspondence Info:

Dr. R. C. Sharma,
Professor,
Department of Physiology,
G.C.R.G. Institute of Medical Sciences,
Lucknow, UP, India

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Abstract

Background: Changes in platelet volume indices have been found in infectious diseases. Higher MPV [mean platelet volume] and PDW [platelet development width] values were observed in patients with sepsis compared to the patients who did not have sepsis. It is emphasized that indices might be helpful indices in predicting survival in sepsis.

Material and Methods: A total of 54 newborns (sepsis group) and 55 healthy newborns (control group) were evaluated in this study. The groups were evaluated in terms of significant differences in the values of mean platelet volume and platelet distribution width. A p value of <0.05 was considered statistically significant for all results.

Results: The study revealed statistically significant MPV and CRP in neonates with sepsis compared to healthy neonatal subjects on day 1 and 3.

Conclusion: It is concluded that increased level of MPV and CRP on day 1 and day 3 (p<0.001) and proposes that these observations can be useful in detecting inflammation in early neonatal life and mortality risk.

Keywords: Neonatal Sepsis, Platelet count, Mean platelet volume, C - reactive protein.

1. Introduction

Neonatal sepsis is potentially a life threatening condition and is one of the major causes of mortality and morbidity throughout the world. Higher Incidence of neonatal sepsis is reported in India especially in Uttar Pradesh [1]. Antoniette B *et al* reported early onset of sepsis within 24 hours in 85% cases [2]. The earliest signs of sepsis are often subtle and nonspecific and babies with sepsis may present with one or more of the symptoms and signs [3-7]. Since clinical signs of sepsis are poor, late and non-specific in neonates, particularly in preterm infants, the onset of sepsis may be acute or chronic hence clinical course can deteriorate quickly or may be delayed. Therefore, early diagnosis of a neonatal sepsis is the mandatory prerequisite for a timely treatment. Supreetha *et al* reported that definite diagnosis of septicemia by a

positive blood culture required a minimum period of 48-72 hours and yielded a positive result in 30-70% of cases [8].

Hisamuddin *et al* reported 70% diagnostic accuracy of C-reactive protein levels for diagnosis of neonatal sepsis and suggested that C-reactive protein levels alone is not specific enough to be relied upon as the only indicator of neonatal sepsis [9]. Lower platelet counts and higher MPV levels have been reported in patients with sepsis than in controls [10]. Few studies have reported no elevation or lower increase in non-survivors than survivors in first phase but in second phase, MPV levels increased and remained higher than survivors [11]. MPV levels have been notified to be statistically higher in non-survivors with septic shock on admission [12].

Wiwanitkit *et al* did not observed significant changes have been reported in MPV levels between early

and later onset sepsis in preterm infants [13]. Hence a critical study of association of MPV with neonatal sepsis is warranted to establish role of MPV as a laboratory tests for accurate & rapid diagnosis of neonatal sepsis. Present study is aimed to investigate mean platelet volume [MPV] and C-reactive protein [CRP] and their predictive value in diagnosis of neonatal sepsis, and to develop effective treatment for a successful outcome.

2. Material & methods

The present study was carried out in department of physiology in association with Pediatrics department after approval of institutional ethical committee. The study included 55 septic newborns (sepsis group) and 55 healthy newborns (control group). The subjects were drawn amongst delivered neonates. Sepsis group subjects were selected based on the signs and symptoms of suspected case of sepsis-bradycardia (<100/min), tachycardia (>200/min), hypotension, respiratory distress, irritability, lethargic, cyanosis, apnea, tachypnea, poor skin color and poor perfusion, feeding difficulty. Neonates with history of blood transfusion were not included in the study.

Blood samples of all the subjects were taken at birth [umbilical cord blood sample] on day 1 as well as on

day 3 [peripheral blood sample] after obtaining consent from mother. Analysis for CBC, Platelet count and Mean Platelet Volume, 2 ml blood was stored in EDTA vial and for analysis of C-reactive protein, 2 ml blood is taken in a plain vial. the samples were centrifuged @ 2000 rpm for 10 minutes within 2 hours of collection, Serum was labeled properly and separately stored at – 20 degree C till analyzed for CRP estimation. Blood samples were also analyzed for estimation of Hemoglobin, Total Leucocyte Count, Total Red Blood Cell Count, Platelet Count, and Mean Platelet Volume by automated cell counter machine (SYSMEX KX 21) in hospital laboratory services (HLS). C-reactive protein was estimated by ELISA method.

Statistical analysis of measurements was done using SPSS 16 software. Descriptive and appropriate tests such as unpaired 't' test and chi square test. Continuous variables are expressed as mean \pm S.D. The p-value >0.05 was considered significant.

3. Results and observations

The study results expressed in table1 indicates the mean \pm S.D of biochemical parameters between case and control group on day 1.

Table 1: Mean \pm S.D of biochemical parameters between case and control group on day 1

Parameter	Control Group	Sepsis group	P value
Haemoglobin [gm%]	17.52 \pm 2.19	15.18 \pm 1.52	P>.0001
Total Lecuocytes	9191.45 \pm 4180.18	8939.27 \pm 4178	P>0.75
Total Red Blood Cells	5.02 \pm 0.74	4.55 \pm 0.83	P>0.02
Total Platelet count	231527.30 \pm 344.40	199438.2 \pm 214.80	P>0.55
Mean Platelet Volume	9.13 \pm 0.64	11.66 \pm 1.36	P>0.0001
C-Reactive Protein	3.92 \pm 1.10	9.30 \pm 9.85	P>0.0001

Table shows that sepsis group subject shows statistically significant decreased in hemoglobin concentrtrion as compared to normal healthy neonates but significantly higher mean platelet volume and C-reactive

protein level on day 1. Similar observations were also found on day 3. Other hematological parameter e.g. total leucocytes count, total RBC count and platelet count demonstrated variations but not statistically significant.

Table 2: Mean \pm S.D of biochemical parameters between case and control group on day 3

Parameter	Control Group	Sepsis group	P value
Haemoglobin [gm%]	17.11 \pm 1.190	14.93 \pm 1.96	P>.0001
Total Lecuocytes [Nos/cmm]	8680.00 \pm 392.35	10338.91 \pm 816.284	P>0.45
Total Red Blood Cells [Nos/cmm]	5.01 \pm 0.73	4.61 \pm 0.80	P>0.009
Total Platelet count [Nos/cmm]	207212.70 \pm 1016.60	181229.11 \pm 234.20	P>0.45
Mean Platelet Volume [fL]	9.00 \pm 0.51	11.81 \pm 1.30	P>0.0001
C-Reactive Protein [mg/L]	3.93 \pm 1.10	9.56 \pm 9.41	P>0.0001

4. Discussion

We observed statistically significant decreased in hemoglobin concentrtrion in sepsis group as compared to normal healthy neonates on day and 3. We also found that total RBC on day 1 and 3 in sepsis group were reduced as

compared to healthy group. The strongest impairment of RBC deformability was observed in preterm infants. Hellerqvist and colleagues (14) observed that a GBS polysaccharide exotoxin binds only to developing or immature endothelium in neonates. Pauly and associates

(15) proposed that hydroxyl radicals may be involved in the rapid development of septic shock resulting from GBS in neonates. Increased peroxidation also may explain the more pronounced impairment of RBC deformability in neonates, particularly in preterm infants. Hence significant decreased in hemoglobin concentration on day 1 and 3 observed in present study may be attributed to impaired deformity of RBC associated with hemolysis.

Total leucocytes in neonates with sepsis revealed decreased on day 1 and increased on day 3 than healthy neonates but were not statistically significant. White blood cells accumulation outside blood vessels has been demonstrated in neonatal rat after ligation of the right common carotid artery and systemic hypoxia. [16]. Large numbers of mature and immature neutrophils are released from the bone marrow into the circulating blood following acute bacterial infection. Previous studies have reported activation of leukocytes attributed to several inflammatory mediators released from infected tissues [17]. These observations explain the leucopenia on day 1 and leukocytosis on day 3 in sepsis group as compared to healthy neonates as demonstrated in the present study.

The platelet is intimately involved in the pathogenesis of sepsis, participating in the immune response and inter-acting with bacteria. Platelet abnormalities occur frequently in critical illness, especially in septic patients, and are associated with poorer outcomes. In the present study the platelet count of the sepsis group were found to be lower than healthy neonatal group on day 1 as well day 3, though variation is statistically insignificant. Abdalla *et al.* reported that thrombocytopenia was present in 45 (42.8%) of all cases of neonatal sepsis [10]. Other studies reported mild thrombocytopenia (platelet count $51 - 100 \times 10^9/L$) in 39.4% of the neonates [18-19]. In a study done by Shirazi *et al.* thrombocytopenia had sensitivity of 61% and specificity of 82% [20]. Dhananjay *et al* observed that platelet count in subjects developing sepsis are significantly less than platelet count of those not developing sepsis [21].

We observed higher mean platelet volume [MPV] in sepsis group on day 1 as well as on day 3 compared to healthy group. The changes are statistically significant ($p < 0.0001$) which are in agreement with observation by other studies [10, 22]. Destructive thrombocytopenia known to be associated with high MPV levels while low level of MPV is reported in hypo-proliferative thrombocytopenia [23]. Accordingly, it is considered that MPV levels may increase in mild inflammation because of the raise of large platelets, or on the contrary, MPV levels may decrease in severe inflammation owing to the depletion of large platelets in inflammatory area [24]. These observations indicate that MPV may be a negative acute phase reactant as well as a positive acute phase reactant and may show

fluctuation in different phases of sepsis. Nelson and Kehl *et al* observed platelet consumption associated with increase in MPV in human subjects having acute infection [25]. Becchi *et al* suggested that MPV has an important prognostic value of early stage of sepsis [26].

In the present study the C-reactive protein levels in sepsis group were found to be statistically elevated as compared to normal healthy groups on day 1 and 3, which are in agreement with observation of other studies [18, 21, 22]. Haider Shirazi *et al* reported that C-RP was positive in 14/90 (16%) of babies with probable sepsis. Dhananjay *et al* observed that C-RP values of those developing sepsis are significantly greater than those not developing neonatal sepsis [20-22]. In view of findings of other studies as reported above and the changes in platelet count, C-reactive protein and mean platelet volume reported in present study might be beneficial to identify inflammation in early neonatal period prior to sepsis. These observations in sepsis group as compared to normal healthy neonates may also be used as index in predicting survival in sepsis, though we did not follow the patient after treatment.

5. Conclusion

Present study reported statistically significant increased level of MPV and CRP on day 1 and day 3 ($p < 0.001$), which can be useful in detecting inflammation in early neonatal life and mortality risk. In our study, we did not evaluate MPV after treatment, we therefore suggests that serial measurements of MPV and CRP before and after treatment in large population during different period of sepsis would be helpful index in the follow-up of patients.

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