Section: Pediatrics

Original Research Article

INCREASE IN MEAN PLATELET VOLUME AS AN INDICATOR AND PREDICTOR IN PEDIATRIC SEPSIS

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Abstract

Background: Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection. The main objective is to study the prevalence of increased mean platelet volume in sepsis and the association between an increase in mean platelet volume and the severity of sepsis, duration of hospital stay and the outcome. **Materials and Methods:** This prospective study was conducted in the general medical wards and PICU at the Institute of Child Health and Hospital for Children for 12 months. On admission, children suspected to have sepsis, fulfilling the inclusion criteria, were selected. All suspected and proven sepsis cases were categorized as sepsis, severe sepsis, septic shock and MODS. **Result:** Out of 175 children selected, most patients were males, 93 (53.1%). 64 (36.6%) of the study participants had sepsis, followed by septic shock in 36(20.6%) and severe sepsis in 34(19.4%). 41 patients in the study population had MODS, that is 23.4%. 82 patients (46.9%) stayed for less than one week. The mean duration of hospital stay was 9.36 ± 7.6. Mortality was seen among (75) 42.9% of the study participants. There is a significant difference in delta MPV, PRISM 3, duration of hospital stay and duration of mechanical ventilation between the dead patients and the survivors. There is a significant difference in MPV at 72 hours and delta MPV between the two categories. The MPV at 72 hrs had a strong positive correlation (R=0.365, P<0.001). Delta MPV has a stronger positive correlation (R=0.766, P<0.001). The AUC values of 0.761 and 0.870 indicate that Delta MPV and PRISM 3 scores have moderate to high predictive ability for pediatric sepsis outcome. **Conclusion:** Platelet indices can help in early identification of the risk of mortality and poor outcomes in patients with severe sepsis.

INTRODUCTION

Sepsis is a "life-threatening organ dysfunction caused by a dysregulated host response to infection".[1] Unless the sepsis is managed correctly, sepsis can result in complications such as multi-organ dysfunction and septic shock and may also result in death. Antimicrobial resistance is the significant factor influencing the treatment response, and Patient who has increased antibiotic resistance has increased mortality. Worldwide, the burden of sepsis is uncertain. Globally nearly 30 million are predicted to have sepsis which may lead to a mortality of 11 million per year.[2]

Hematologic and electrolyte abnormalities are the laboratory findings in sepsis. Hematologic changes can be prolonged PT and partial thromboplastin times, thrombocytopenia, increased fibrin split products, decreased serum fibrinogen level and anaemia. There can also be increased neutrophils and immature forms, vacuolation of neutrophils, associated with infection. The main warning sign of overwhelming sepsis is neutropenia or leukopenia. The common electrolyte abnormalities include hyper or hypoglycemia, hypocalcemia, hypoalbuminemia and metabolic acidosis.[3-5]

Platelets, a main component of blood, plays a pivotal role in pathological and physiological processes, like thrombosis, inflammation, coagulation, and preserving the vascular endothelial cell's integrity. Platelet activation results in inflammation-associated endothelial dysfunction and play a significant role in organ failure.[6] Due to this, platelet count alteration must be monitored regularly to assess the prognosis of critical paediatric patients. During the physiological state, the platelet amount in blood will be in equilibrium due to the elimination and regeneration. Hence the number and size remain unaltered. However, in a

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pathological state, any determinant inhibiting platelet regeneration increases activation, thereby overwhelming self-regulation capacity. This leads to changes in the number and morphology of platelets.[7]

As a result of thrombosis and inflammation, there occurs alteration in the size of platelets. The routinely used platelet index is the Mean platelet volume (MPV). It is calculated by the ratio of platelet crit to platelet count.[8] The normal mean platelet volume is 7.3 ± 1.4 fl. An increase in MPV results in an increased release of mediators because of the exogenous/endogenous stimuli. The main objective is to study the prevalence of increased mean platelet volume in sepsis and the association between an increase in mean platelet volume and severity of sepsis, duration of hospital stay and outcome.

MATERIALS AND METHODS

This prospective study was conducted in general medical wards and PICU at the Institute of Child Health and Hospital for Children, Madras Medical College, for 12 months. On admission, children suspected of sepsis, fulfilling the inclusion criteria, were selected. The study was started after obtaining Institutional ethical approval. The purpose and procedure of the study were explained to the parents/ guardian in their local language. The patient information sheet and informed written consent was obtained from the parents/ guardian before initiating the study.

Inclusion Criteria

Patients admitted for sepsis who stayed for more than 72 hours were included in the study. To diagnose sepsis, two of 4 criteria, 1 of which must be abnormal temperature or abnormal leukocyte count, were taken. The Criteria were Core temperature >38.5°C (101.3°F) or <36°C (96.8°F) (rectal, bladder, oral, or central catheter). Tachycardia: Mean heart rate >2 SD above normal for age in the absence of external stimuli, chronic drugs or painful stimuli or Unexplained persistent elevation over 0.5-4 hr or in children < 1-year-old, persistent bradycardia over 0.5 hr (mean heart rate <10th percentile for age in the absence of vagal stimuli, β- blocker drugs, or congenital heart disease).Respiratory rate >2 SD above normal for age or acute need for mechanical ventilation unrelated to neuromuscular disease or general anaesthesia. d) Leukocyte counts elevated or depressed for age (not secondary to chemotherapy), or >10% immature neutrophils.

Exclusion Criteria

Children with obesity, hyperlipidaemia, hypothyroidism, nephrotic syndrome, connective tissue disorder, malignancy, haematological disorders like bone marrow failure, and H/O platelet transfusion after admission were excluded.

MPV values were measured at admission (MPV adm) and at 72nd hour MPV (MPV72 hr), and the difference between them (delta MPV 72 –adm) was calculated. MPV values were confirmed with a peripheral smear study. In addition, the need for mechanical ventilation and length of hospital stay were also assessed. All suspected and proven sepsis cases were analysed and categorized as sepsis, severe sepsis, septic shock and MODS for further analysis.

The criteria used to calculate PRISM 3 score were Systolic blood pressure, body temperature, Glasgow coma score, heart rate, pupillary reflexes, parameters of blood gas, plasma glucose, potassium, blood urea nitrogen, creatinine, white blood cell (WBC) count, platelet count, prothrombin time and activated partial thromboplastin time. Case follow-up was done to see the outcome of the child. In survived children, the duration of the hospital stay was noted.

The collected data were checked for completeness before entering in the Microsoft Excel spreadsheet. The validation of the data was checked at regular intervals. The data analysis was performed with intention to treat the approach using Statistical Package for Social Sciences (SPSS IBM) 21. The quantitative data were expressed in frequency and percentage. The chi-square test and Mann Whitney U test/ Kruskal Wallis test were applied, and a p-value less than 0.05 was considered significant to test the association between the variables. Correlation analysis was performed for PRISM 3 score.

RESULTS

Out of 175, most of the study participants were males, 93 (53.1%). Seventy-one patients (40.6%) were less than one year old, 58 patients (33.1%) were between 1 and 5 years old, 36 patients (20.6%) were between 6 and 10 years old, and ten patients (5.7%) were between 10 and 12 years old. The mean age of the study participants was 3.54 ± 2.

Table 1: Demographic data of the study

Variables		Frequency	Percentage
Gender	Male	93	53.1
	Female	82	46.9
Age group	< 1	71	40.6
	1-5	58	33.1
	6-10	36	20.6
	10-12	10	5.7
Sepsis category	Sepsis	64	36.6
	Septic shock	36	20.6

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	Severe sepsis	34	19.4
	MODS	41	23.4
Duration of hospital stay	< 1 week	82	46.9
	1 week-1 month	91	52
	>1 month	2	1.1
Outcome	Death	75	42.9
	Discharged	100	57.1

Most study participants (36.6%) had sepsis, followed by MODS in 23.4%, septic shock in 20.6% and severe sepsis in 19.4%. 82 (46.9%) stayed for less than one week, 91 (52.3%) stayed between 1 week to 1 month, and only 2 (1.1%) stayed for more than one month. The mean duration of hospital stay was 9.36 ± 7.6, and mortality was seen among 42.9% of the study participants [Table 1].

Table 2: Mean values of the study

Variables	Mean	STD
MPV at admission	8.598	1.28
MPV at 72 hours	9.489	1.34
Delta MPV	0.889	0.41
PRISM 3	9.34	4.16
Duration of Mechanical ventilation	2.64	4.48

82.3% of the children had elevated MPV at admission. The mean MPV at admission was 8.598 ± 1.28, and at 72 hours was 9.489 ± 1.34. The mean Delta MPV was 0.889 ± 0.41, the mean PRISM 3 score was 9.34 ± 4.16, and the mean duration of mechanical ventilation was 2.64 ± 4.48 [Table 2].

Table 3: Comparison of parameters between outcomes

Variables		Outcome		P-value
		Death	Discharged	
Gender	Male	41(54.7)	52(52)	0.726
	Female	34(45.3)	48(48)	
Age	< 1	33(44)	38(38)	0.607
	1-5	26(34.7)	32(32)	
	6-10	12(16)	24(24)	
	10-12	4(5.3)	6(6)	
Sepsis category	Sepsis	7(9.3)	57(57)	<0.0001
	Septic shock	19(25.3)	17(17)	
	Severe sepsis	12(16)	22(22)	
	MODS	37(49.3)	4(4)	
MPV At admission		8.63(1.33)	8.57(1.25)	0.332
MPV At 72 hours		9.76(1.31)	9.28(1.33)	0.001
Delta MPV		1.109(0.41)	0.723(0.33)	<0.001
PRISM 3		12.4(3.1)	7.05(3.27)	<0.001
Duration of hospital stay		7.72(8.47)	10.59(6.70)	<0.001
Duration of Mechanical ventilation		4.96(5.38)	0.90(2.54)	<0.001

Mortality was higher among males, and mortality was higher among those less than one month of age. There was no significant difference in gender and age between outcomes.

Mortality was higher among MODS, followed by septic shock in 25.3%, which is statistically significant. 144 children (82.3%) of the study participants had MPV higher than 7.3 at admission. 61 (81.3%) out of 75 study participants who died had increased MPV at admission.

89.1% (156) of the study participants had MPV higher than 7.3 at 72 hours. 69 (92%) out of 75 study participants who died had increased MPV at 72 hours. There is a significant difference in delta MPV, PRISM 3, duration of hospital stay, and duration of mechanical ventilation between the dead and survivors ($p<0.001$) [Table 3].

Table 4: Comparison of parameters between sepsis category and hospital stay

Variables		Sepsis category				P-value
		Sepsis	Septic shock	Severe sepsis	MODS	
Age	< 1	27(42.2)	15(41.7)	13(38.2)	16(39)	0.110
	1-5	25(39.1)	12(33.3)	7(20.6)	14(34.1)	
	6-10	10(15.6)	4(11.1)	12(35.3)	10(24.4)	
	10-12	2(3.1)	5(13.9)	2(5.9)	1(2.4)	
Gender	Male	30(46.9)	20(55.6)	21(61.8)	22(53.7)	0.549
	Female	34(53.1)	16(44.4)	13(38.2)	19(46.3)	
MPV At admission		8.50(1.04)	8.73(1.21)	8.53(1.60)	8.68(1.42)	0.171
MPV At 72 hours		9.04(1.03)	9.61(1.20)	9.56(1.65)	10.01(1.41)	<0.001
Delta MPV		0.55(0.23)	0.89(0.30)	1.03(0.36)	1.28(0.35)	<0.001
Duration of hospital stay			< 1 week	1 week-1 month	> 1 month	P-value

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MPV At admission	8.62(1.21)	8.55(1.36)	9.4(0.00)	0.446
MPV At 72 hours	9.45(1.28)	9.48(1.39)	10.9(0.14)	0.116
Delta MPV	0.83(0.39)	0.92(0.42)	1.5(0.14)	0.055

There was no significant difference in gender and age between the sepsis category. MPV at admission and 72 hours were higher among those who had MODS.

MPV at admission and 72 hours were higher among those with a hospital stay of more than one month. There is a significant difference in MPV at 72 hours and delta MPV between the sepsis category ($p<0.001$). There was no significant difference in MPV at admission, 72 hours and delta MPV and the duration of hospital stay [Table 4].

Table 5: Correlation between MPV $_{adm}$, MPV 72 and delta MPV and PRISM 3 score

Variable	MPV $_{adm}$		MPV 72 hours		Delta MPV	
	R	P	R	P	R	P
PRISM 3 score	0.125	0.099	0.365	<0.001	0.766	<0.001

The MPV at adm has a weak positive correlation with the PRISM 3 score (R=0.125, P=0.099), while MPV 72hrs has a strong positive correlation (R=0.365, P<0.001). Delta MPV has an even stronger positive correlation (R=0.766, P<0.001) (Table 5). This suggests that an increase in mean platelet volume over the first 72 hours of hospitalization (as indicated by Delta MPV) may be a helpful indicator and predictor of the severity of illness in pediatric sepsis.

Table 6: The area under the curve values

Variable	Delta MPV	PRISM 3 score
AUC	0.761	0.870

The AUC values of 0.761 and 0.870 indicate that Delta MPV and PRISM 3 scores have moderate to high predictive ability for pediatric sepsis [Table 6, Figures 1 and 2].

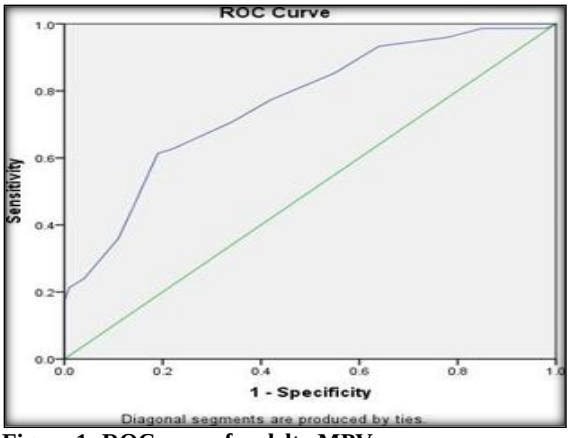

Figure 1: ROC curve for delta MPV

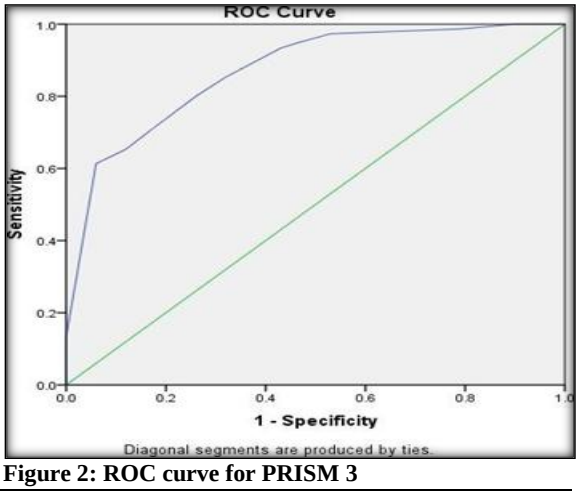

Figure 2: ROC curve for PRISM 3

DISCUSSION

Globally, sepsis remains the commonest cause of mortality in infants and children.[9] The incidence of childhood pneumonia is estimated to be 0.29 and 0.05 episodes per child-year in pre-developed and developed countries, respectively, making it the commonest cause of paediatric sepsis and the leading cause of mortality in children under five years of age.[10] Platelet indices are measurements that determine the morphology and count of platelets. Pathophysiological conditions such as coagulation system activation, thrombotic diseases, and inflammatory conditions can alter platelet indices.

The present study has shown that the mean age of the study participants was 3.54 ± 2, and most were males. This follows the study done by Nam et al,[11] and Dursun A et al,[12] who showed that most study participants were males. Literature has shown that male infants have increased hospitalization due to sepsis as in adults. Mortality was seen among 42.9% of the study participants. The PRISM 3 score of the study participants was 9.34. The mean PRISM 3 score among the non-survivor was 12.4 compared to 7.05 among the survivor group. Sayed SZ et al,[13] have shown that the median PRISM score was 11 and 26 among the survivors and non-survivors, respectively. PRISM score is a well-established score used to predict paediatric patients' mortality.

In the present study, 82.3% of participants had raised MPV at admission. The mean MPV at admission was 8.59, increasing to 9.48 at 72 hours. Similarly, a study done by Nam et al,[11] showed that the mean MPV in the sepsis group was 9.2 ± 1.4. Correspondingly, a study done by Dursun A et al,[12]

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showed that the median MPV value among the patients with sepsis was 8.4 MPV was significantly higher among the non-survivor group than the survivor group both at admission and at 72 hours. Delta MPV was higher among the non-survivor group than the survivor group, with an r value of 0.766, which is statistically significant.

A study by Zhang et al,[14] showed that MPV higher than 11.3 was an independent mortality risk factor among critically ill patients. Dursun A et al,[12] have shown an R-value of 0.243. Sayed SZ et al,[13] have shown that the median MPV score was higher among the non-survivors than the survivors. Another study by Cai N et al,[15] showed that the mean platelet volume was 11.40 in the non-survivor group, significantly higher than in the survivor group (10.7). The increased MPV among the non-survivors could be due to increased synthesis of cytokines, raised bone marrow suppression and endothelial damage.[16]

Golebiewska et al,[17] stated that MPV is an acute phase reactant in diverse inflammatory conditions. They also reported that increased MPV levels were associated with increased inflammation because of big platelets in circulation. Tajarernmuang P et al,[18] showed that a steady rise in MPV after admission was significantly associated with increased hospital mortality after a few days. Increased MPV suggests that the infection is uncontrolled and invasive and is associated with the disease severity and hence can be used as a helpful assessment tool for outcome prognosis. Besides, a study by Sezgi et al,[19] stated that the MPV level gradually increased since admission in the non-survivor group of septic patients. In contrast, the trend is reversed in the survivor group of septic patients.

Limitations

Since this is a single-centre study , the results of the study may not be broadly applicable to other institutions. Because of inclusion and exclusion criteria, we can only enrol a limited number of patients, so subgroup analysis could not be performed.

CONCLUSION

Platelet indices are sensitive, readily available, valuable prognostic indicators that can help identify the patients with severe sepsis with the poorest outcome. MPV, delta MPV values can be used as a quick and reliable indicator for early diagnosis and prognosis of sepsis. Large sample multicentric studies with frequent serial measurements of MPV can be done to give a still better picture of using MPV as a predictor of mortality.

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