ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at:www.ijmacr.com

Volume – 6, Issue – 6, December - 2023, Page No. : 42 - 50

Platelet indices in determining illness severity and mortality in children

[1]Dr. Shruti Patil, MBBS, MD Pediatrics, Associate Professor, Department of Pediatrics, M.S. Ramaiah Medical College, Bangalore, India

[1]Dr. Sangeetha Shenoy, MBBS, MD Pediatrics, Associate Professor, Department of Pediatrics, M.S. Ramaiah Medical College, Bangalore, India

Corresponding Author: Dr. Shruti Patil, MBBS, MD Pediatrics, Associate Professor, Department of Pediatrics, M.S. Ramaiah Medical College, Bangalore, India

How to citation this article: Dr. Shruti Patil, Dr. Sangeetha Shenoy, "Platelet indices in determining illness severity and mortality in children", IJMACR- December - 2023, Volume – 6, Issue - 6, P. No. 42 – 50.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Objectives: Aim of this study was to determine platelet indices as a predictor of mortality and severity of illness as using, Pediatric Risk of Mortality-III (PRISM-III) and Pediatric Logistic Organ Dysfunction-2(PELOD-2). Methods: A retrospective cohort study, of critically ill children aged 1month to 18years admitted PICU January 2018 to October 2021. Platelet indices were compared among survivors and non survivors and among high PRISM-III and PELOD-2 scores. Results: 329 critically ill children were included with a mean (SD) age of 6(5) years and a male: female ratio of 0.8:1. MPV, PDW and PCT were significantly higher among the non survivors compared to the survivors. (8.7 vs. 9.8, p value 0.006, 17.1 vs. 10.75, p value < 0.001 and 0.08 vs 0.21 p value 0.002 respectively). After adjustment for well-established clinical risk factors, PDW >17.1% (R: 7.434 [3.5–15.36], P <0.005), MPV >9.4 fl (R: 2.6 [1.3–5.34], P = 0.007) were identified as the independent risk factors for mortality. MPV/PCT, PDW/PLT PDW/PCT and platelet index were significantly higher among the non survivors compared to the survivors. A positive correlation with PRISM III scores were seen with MPV, MPV/PLT, MPV/PCT, PDW/PLT, PDW/PCT and Platelet index. On grouping based on their severity of illness using at admission PRISM III and PELOD-2 scores, MPV was seen higher in the severe group (PRISM III 9.7fl vs. 8.5fl, PELOD-2 9.6fl vs. 8.7fl, p<0.001).

Conclusions: A high MPV > 9.4fl and PDW >17.1 are factors independently associated with mortality. The ratios MPV/PCT, PDW/PLT, PDW/PCT and Platelet index are also associated with severity of the disease. MPV is good marker for mortality and severity of illness.

Keywords: Platelet indices, Mean platelet volume (MPV), PRISM-III, PELOD-2, Pediatric Critical illness.

Introduction

Platelet (PLT) indices are a measure platelet numbers and their morphology. The circulating PLTs in blood are in equilibrium by continuous regeneration and elimination. However, during illness, both PLT count and its morphology are altered, which in turn alter the PLT indices (1). Studies (2, 3, 4) have shown that several conditions in children, such as severe sepsis, trauma, and systemic infections like malaria and dengue, could all change PLT indices.

Plateletocrit (PCT) is the volume occupied by the PLT in blood expressed as a percentage. Hence la low PCT indicates degree PLTs consumption. Mean platelet volume (MPV) is a measures thrombocyte volume. Increase consumption of platelets leads to marrow producing immature PLTs, having increase volume compared to mature PLTs. Hence, larger immature PLTs increase MPV and platelet distribution width (PDW) which is a measure of PLT size variation, during an acute illness (5).

Prognostic and descriptive scores like Pediatric risk of mortality-III (PRISM III) and Pediatric logistic organ dysfunction-2 (PELOD 2) have good decimating and calibration power between predicted and observed mortality (7). The scores have many biochemical variables, and computation requires a computer with other logistic support, which may not be available in rural healthcare centers. Another drawback of these scoring systems is inter-observer variation. Hence, there always is a search for a reliable, rapid, and inexpensive bedside markers for use in our sub-continent. PLT indices may be vital as they are routinely available parameters and can assist in prompt referrals.

Recent research has suggested the possibility of platelet indices as a marker for severity of illness and mortality but with inconsistent results. Studies assessing platelet indices as markers of illness severity and comparing them with validated scoring systems are limited. Hence, this study aimed to assess PLT indices as an indicator of the severity of illness and predictor of mortality using PELOD-2 and PRISM-III scores, respectively.

Methods

A retrospective cohort study was conducted in the Pediatric intensive care unit (PICU) of a 13 bedded tertiary referral hospital. All consecutive critically ill children aged one month to 18 years were admitted to the PICU during January 2020 to October 2021 were included in the study. Children with chronic platelet disorders were excluded from the study. Data regarding demographic details, diagnosis, PRISM-III and PELOD-2 score at admission, laboratory investigations (total count, differential count, and platelet count and platelet indices), mechanical ventilation, and outcome measures (death, discharge, length of hospital stay) were retrieved from hospital records and entered in a predesigned proforma. PLT indices done at admission were taken for analysis. Platelet ratios such as, MPV/PCT, MPV/PLT, PDW/PLT, PDW/ PCT, and platelet index were calculated and recorded. Institutional ethical committee approval was obtained. Informed consent was not required due to the retrospective nature of the study.

PELOD-2(9) has ten variables, including Glasgow coma score (GCS), pupillary reaction, high lactate, mean arterial pressure, creatinine, PaO2 /FiO2, PaCO2, ventilation, total leucocyte count, and PLT count, with a maximum score of 33. PRISM-III (8) has a total of 17 variables, including blood pressure, pulse rate, temperature, GCS, pupillary response, acidosis, pH, PaCO2, total CO2, PaO2, blood sugars, potassium, creatinine, BUN, total leucocyte count, platelet count, and

prothrombin or partial thromboplastin time. Both were scored, taking the most abnormal parameter in the first 24 hours. The scores were considered high if the PELOD -2 and PRISM III values were more than 7.5 and 9.5, respectively, as derived from a previous study (10).

Sample size justification: In study by Golwala et al. (6), it was observed that the sensitivity of predicting mortality based on platelet indices and the ratio was 77.1 %. In the present study expecting similar results with a 95% confidence level and 6% absolute precision, the study required a minimum of 188 subjects.

Statistical methods: Data normality was tested with Kolmogorov Smirnov. Continuous variables like age, length of PICU stay, total leucocyte count, and PLT count are expressed as mean (SD) or median (IQR). Categorical values like gender and systemic involvement are described in percentages. The non-parametric test compared the median values of PLT indices, PLT ratios, PELOD-2, and PRISM-III between the survivors and the non-survivor group. The area under the Receiver operating curve (AUROC) with a 95% confidence interval (CI) was used to assess the ability of the indices and ratios to differentiate between the survivors and the non-survivors. Analysis was done using SPSS. Inc. 2009. PASW Statistics for Windows version 18.0. Chicago. A "P" value of <0.05 was taken as significant.

Results

There was a total of 412 critically ill patients admitted to PICU from January 2020 to October 2021. After excluding patients with chronic hematological illnesses like malignancy and ITP (n=28) and non-availability of platelet indices data (n= 55), a total of 329 patients were included in the study. The mean (SD) age of the study population was 6 (5) years with a male: female ratio of 0.8:1. The mortality rate in our study was 12.7% (n=42). Sixty-nine (20.9%) patients required mechanical ventilation. Infections were the most common reason for admission in 138 cases (41.9%), followed by respiratory diseases in 70 (21.2%), neurological diseases in 45 (13.6%), renal diseases in 26 (7.9%), metabolic diseases in 17(5.1%), gastrointestinal diseases in 13 (4%) and others 20 (6.3%).

On univariate analysis, low total leucocyte count, high MPV, high PDW, high PCT, MPV/PCT, PDW/PLT, PDW/PCT, mechanical ventilation, high PRISM III and PELOD 2 scores were associated with mortality (Table 1). Platelet count did not show any association with mortality. On multivariate analysis after controlling for confounding factors, MPV >9.4 fl (R: 2.6 [1.3–5.34], p = 0.007) and PDW >17.1 (R: 7.434 [3.5–15.36], p <0.005, were identified as independent predictors for mortality (Table 2).

Receiver operating curves (ROC) were constructed to predict platelet indices' mortality. The AUROC for PDW was 0.751(95% CI -0.619 to 0.811), for MPV was 0.630(95% CI - 0.519 to 0.742), for PCT was 0.650(95% CI was 0.568 to 0.730). For predicting mortality MPV with a cut-off of more than 9.55, had a sensitivity of 73% and specificity of 54.8% (Figure 1, Tables 3). Likewise, PDW, with a cut off > 17.1, had a sensitivity of 50% and specificity of 89.2%. MPV had the highest diagnostic accuracy of 73.5%.

The ROC of PLT ratios for predicting mortality (Table 3 and Figure 1). With a cut of more than 144, PDW/PCT had the highest sensitivity of 58.9% among the PLT ratios. With a cut-off of more than 0.09, PDW/PLT and a higher specificity of 73.8% in predicting mortality.

We correlated the said markers with PRISM III scores, we found a positive correlation between MPV (r= 0.148, p= 0.004) and a negative correlation for PCT (coefficient r=-

0.305, p <0.001). MPV/PLT, MPV/PCT, PDW/PLT, PDW/ PCT, and platelet index positively correlated with PRISM III scores, which were all statistically significant (Table 4).

Calculating the correlation of the platelet indices and ratios with PELOD 2 scores. MPV, PDW, and PCT showed no significant correlation with PELOD -2. Among platelet ratios, MPV/PLT, MPV/PCT, and platelet index (r=0.161, r=0.043, r=0.199, all p=<0.001) respectively had a positive correlation (Table 4).

On grouping the study subjects based on their severity of illness using at-admission PRISM III and PELOD-2 scores, using cut-off 9.5 and 7.5, respectively, based on our center study (10), we found the mean MPV values to be higher in the severe group than the non-severe group (PRISM III 9.7fl vs. 8.5fl, PELOD-2 9.6fl vs. 8.7fl, p<0.001 in both) which was statistically significant.

Discussion

The above study was conducted to determine MPV, PDW, and PCT as a marker of the severity of illness and mortality in critically ill children. The results of our study show a high MPV and PDW values are independent risk factors of mortality. High MPV values of > 9.4fl and high PDW values > 17.1fl have 2.6 times and 7.4 times, respectively, higher risk of mortality when compared to children with normal. Elevated values of MPV also had a good correlation with PRISM III scores. Our study also showed that platelet ratios good markers for predicting mortality.

Our findings were similar to a study done by Sayyed et al. (13) in children with severe sepsis, where mean MPV values (9.3fl) was significantly higher in non-survivors (95%CI 1.005-2.4 p= 0.004). The study also showed MPV/PLT, MPV/PCT, PDW/PLT, and PDW/PCT ratios were significantly higher in the non-survivors. (p < 0.001 in all). Another study done by Golwala et al. (6) done in critically ill children showed platelet ratios, MPV/PCT, PDW/PLT, and MPV/PLT were predictor of mortality with an odds ratio of 4.31(95% CI, 1.69–10.99), 3.86 (95% CI, 1.53–9.75), 3.45 (95% CI, 1.38–8.64) respectively. An Egyptian study by Osama et al. (12) on pediatric patients found that the change in MPV over 48 hrs of PICU admission was higher among non-survivors (p = 0.006). A study by Purbiya et al. (16) described a cut-off PDW/PCT higher than 0.07 with a sensitivity and specificity of 77.1% and 77.5%, respectively, for predicting mortality.

An increase in MPV suggests an invasive infection and said correlates with severity of the disease. Platelet activation increases both platelet number and size, this is reflected as an increase in PDW value. Both of which were verified in our study.

The performance of PRISM III and PELOD 2 scores has been well documented in recent studies, with good discrimination and calibration for mortality. A study conducted by Zhang et al. (7) on 1253 pediatric patients showed significantly higher PRISM III, PELOD-2, and P-MODS scores [PRISM III: 18 (12, 23) vs. 11 (0, 16); PELOD-2, 8 (4, 10) vs. 4 (0, 6); and P-MODS: 5 (4, 9) vs. 3 (0, 4), all p < 0.001] between survivors and non-survivors. A similar study (10) was done at our center with 550 pediatric patients, which showed AUC was 0.992 for PELOD-2 and 0.98 for PRISM- III (95% CI 0.00325 to 0.0204) with a p-value of 0.007 for predicting mortality and also the goodness of fit test showed good calibration in predicting mortality for both scoring systems (PELOD-2: $\chi 2$ = 6.051, a p-value of 0.301, PRISM-III - $\chi 2$ = 9.391, p value= 0.153). In our study, mean MPV values correlated well with PRISM III. Elevated MPV values were seen in patients with elevated

PRISM III and PELOD-2 scores at admission. MPV/PLT, MPV/PCT, and platelet index all significantly correlated with PELOD 2 scores. In the study by Sayyed et al. (13), the PRISM III score had significant negative and positive associations with platelet count and platelet crit (r=-0.420, p=0.001), and CRP respectively. This finding suggests that a simple, cost-effective blood test can be used as a surrogate for scoring systems requiring advanced biochemical analysis and computation, which may not be available in rural parts of developing countries like ours.

The main strength of our study is its sample size. One of the significant limitations of our study is that we did not have a disease-specific cohort, as each disease process affects inflammation and, finally, the marrow. Future studies estimating the markers' probable cut-off values will be more valuable and definitive.

Conclusion

MPV and PDW are independent risk factors of mortality. Critically ill children with high MPV values had high PRISM III and PELOD-2 scores at admission. MPV/PLT, MPV/PCT, and platelet index also indicate the severity of the illness.

Platelet indices MPV and PDW, are routine parameters which can be effectively used for morbidity and mortality indicators in critically ill children.

What is already known?

PRISM III and PELOD -2 established descriptive scoring systems extensively used in ICU's. The study adds that the use of an available blood parameter MPV, PDW and Platelet ratios can be used as a surrogate for the above scores in PICU triaging.

What is the implication, and what should change now?

Platelet indices MPV and PDW are routinely available blood parameters, can be effectively used as a morbidity and mortality indicators in critically ill patients.

References

1. Sachdev R, Tiwari AK, Goel S, Raina V, Sethi M. Establishing biological reference intervals for novel platelet parameters (immature platelet fraction, high immature platelet fraction, platelet distribution width, platelet large cell ratio, platelet-X, plateletcrit, and platelet distribution width) and their correlations among each other. Indian Journal of Pathology and Microbiology. 2014 Apr 1;57(2):231.
2. Choi S J, Ha E, Jhang W K, Jong Park S. Platelet Indices as Predictive Markers of Prognosis in Pediatric Septic Shock Patients. Iran J Pediatr. 2017;27(3):e7212. doi: 10.5812/ijp.7212
3. Mukker P, Kiran S. Platelet indices evaluation in patients with dengue fever. Int J Res Med Sci. 2018 Jun;6(6):2054.
4. Yusuf AA, Abdullahi SA, Idris IM, Jobbi YD. Platelet count and indices in acute uncomplicated Malaria in Kano, Nigeria. Niget J Basic Clin Sci 2019;16:46-50
5. Zhang S, Cui YL, Diao MY, Chen DC, Lin ZF. Use of Platelet Indices for Determining Illness Severity and Predicting Prognosis in Critically Ill Patients. Chin Med J (Engl). 2015 Aug 5;128(15):2012-8. doi: 10.4103/0366-6999.161346.
6. Golwala ZM, Shah H, Gupta N, Sreenivas V, Puliyel JM. Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), Platelet Count and Plateletcrit (PCT) as predictors of in-hospital paediatric mortality: a case-control Study. Afr Health Sci. 2016;16(2):356-62.

7. Zhang L, Wu Y, Huang H, et al. Performance of PRISM III, PELOD-2, and P-MODS Scores in Two Pediatric Intensive Care Units in China. Front Pediatr. 2021;9:626165. Published 2021 Apr 28. doi:10.3389/fped.2021.62616
8. Pollack MM, Patel KM, Ruttimann UE. PRISM III: an updated Pediatric Risk of Mortality score. Crit Care Med. 1996 May;24(5):743-52. doi: 10.1097/00003246-199605000-00004. PMID: 8706448
9. Leteurtre S, Duhamel A, Salleron J, Grandbastien B, Lacroix J, Leclerc F, et al. PELOD-2: an update of the PEdiatric logistic organ dysfunction score. Crit Care Med. (2013) 41 :1761–73.
10. Shenoy S, Patil S, Karunakar BP, Mangalgi S, Samaga V. Comparison between paediatric risk of mortality III and paediatric logistic organ dysfunction-2 as mortality predictor in paediatric intensive care. Sri Lanka Journal of Child Health. 2023 Mar 5;52(1):45-51.
11. Gadó K, Domján G. Thrombocytopenia. Orvosi Hetilap. 2014 Feb 1;155(8):291-303.
12. Osama E. Bekhit, Hanaa H. Mahmoud, Hoiyda A. Abdelrasol, and Ahmed M. The Relation between Mean Platelet Volume and Mortality in Critically Ill Children Egyptian Journal of Pediatrics Vol. 36, No 1&2 (March & June), 301-311, 2019
13. Sayed, S.Z., Mahmoud, M.M., Moness, H.M. et al. Admission platelet count and indices as predictors of outcome in children with severe Sepsis: a prospective hospital-based study. BMC Pediatr 20, 387 (2020).
14. Yoon SH, Kim EH, Kim HY, Ahn JG. Presepsin as a diagnostic marker of sepsis in children and adolescents: a systemic review and meta-analysis. BMC Infect Dis. 2019 Aug 30;19(1):760. doi: 10.1186/s12879-019-4397-1.
15. Samuel D, Bhat AN, Prabhu VM. Platelet Indices as Predictive Markers of Prognosis in Critically Ill Patients: A Prospective Study. Indian J Crit Care Med. 2020 Sep;24(9):817-822. doi: 10.5005/jp-journals-10071-23574. PMID: 33132566; PMCID: PMC7584825
16. Purbiya P, Golwala ZM, Manchanda A, Sreenivas V, Puliyel JM. Platelet Distribution Width to Platelet Count Ratio as an Index of Severity of Illness. Indian J Pediatr. 2018 Jan;85(1):10-14. doi: 10.1007/s12098-017-2432-z. Epub 2017 Aug 26. PMID: 28842812.

Legends Figures and Tables

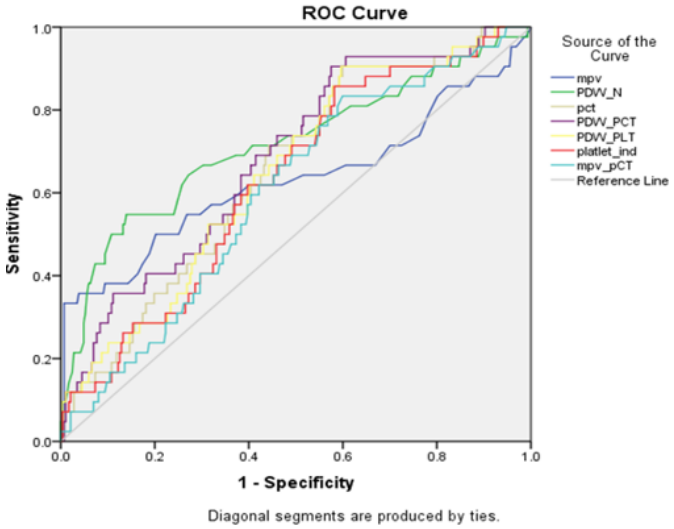

Figure 1: ROC for platelet indices and ratios in predicting mortality. The area under ROC (AUC) for MPV, PCT, and PDW were (0.63, 0.65, 0.715). For PDW/ PLT, PDW/PCT, MPV/PLT, PLATELET INDEX was (0.68,0.64,0.602,0.629) ROC: Receiver operating curve; AUC: Area under the ROC curve; MPV: Mean platelet volume; PCT: Plateletocrit; PLT: Platelet; PDW: Platelet distribution width percentage.

Table 1: Demographic characteristics of the survivors and non-survivor

Variable	Survivors (n=287)	Non survivors (n=42)	*p* value
Age, years, median (IQR)	6 (2,12)	2(0.2-9)	**0.002**
Gender n (%) Male Female	 177, (61.7) 110, (38.3)	 27, (64.3) 15, (37.5)	
Mechanical ventilation n, %	31, (10.8%)	38, (90.5%)	**<0.001**
System: N, % Neurological Infectious Respiratory Cardiac Renal Trauma Metabolic Gastro Miscellaneous	 36, 12.5 127, 44.3 60, 20.9 4, 1.4 11, 3.8 7, 2.4 24, 8.4 3, 1 31, 10.8	 9, 21.4 11, 26.2 10, 23.8 3, 7.1 2, 4.8 1, 2.4 2, 4.8 2, 4.8 2, 4.8	
Lab investigations:	median (IQR)	median (IQR)	
WBC mm^3	12785 (7982-16872)	9300(6000-14200)	**0.005**
PLT $10^9/l$	191(134-328)	204(71.5-392)	>0.05
PCT %	0.08(0.03-0.27)	0.21(0.06-0.37)	**0.002**
PDW fl	10.75(9.1-16.12)	17.1(15.9-9.18)	**<0.001**
MPV fl	8.7(8.1-9.7)	9.8(8-16.12)	**0.006**
MPV/PCT	109.9(30.5-294.1)	48.9(25.5-140.4)	**0.033**
MPV/PLT	0.1(0.02-0.27)	0.04(0.02-0.2)	>0.05
PDW/PLT	0.05(0.03-0.22)	0.16(0.04-0.50)	**0.002**
PDW/PCT	64.35(25.11-197.45)	167.7(54.1-573.3)	**<0.001**

Platelet index	18.9 (1.2-141.8)	2.8 (0.64-31.6)	**0.007**
PELOD-2	2(2-3)	10(7.75-13)	**<0.001**
PRISM -III	5(3-6)	13.5(10-18.25)	**<0.001**

WBC: white blood count; MPV: Mean platelet volume; PCT: Plateletocrit; PLT: Platelet; PDW: Platelet distribution width percentage.

Table 2: Diagnostic parameters of Platelet Indices and Platelet Ratios in predicting mortality.

Variables	AUC	95% CI	p value	Best Cut off values	Sensitivity (%)	Specificity %
MPV	0.630	0.519-0.742	0.006	9.55	73	54.8
PDW	0.715	0.619-0.811	0.000	17.1	50	89.2
PCT	0.650	0.568-0.733	0.002	0.18	57.1	63.4
PDW/PLT	0.684	0.602-0.766	<0.001	0.09	54	73.8
PDW/PCT	0.649	0.566-0.732	0.002	144	58.9	64.3
MPV/PCT	0.602	0.517-0.687	0.033	77	53.7	66.7
Platelet Index	0.629	0.545-0.713	0.007	16.5	50.9	71.4

MPV: Mean platelet volume; PCT: Plateletocrit; PLT: Platelet; PDW: Platelet distribution width percentage

Table 3: correlation of platelet indices for mortality after adjustments.

Platelet indices	R value	P value for R	95% C.I.	
			Lower	Upper
MPV > 9.4 fl	2.641	**0.007**	1.304	5.349
PDW >17.1%	7.434	**0.00**	3.598	15.3
PCT > 0.18 fl	1.178	.682	.538	2.579

MPV: Mean platelet volume; PCT: Plateletocrit; PLT: Platelet; PDW: Platelet distribution width percentage.

Table 4: Co-relation of platelet indices and ratios with PRISM III and PELOD 2 score.

Variables	MPV	PDW	PCT	MPV/PLT	MPV/PCT	PDW/PLT	PDW/PCT	Platelet Index
PRISM III								
R,	0.158	0.050	-0.305	0.363	0.347	0.306	0.273	.324
p value	0.004	0.364	<0.05	<0.05	<0.05	<0.05	<0.05	< .000
PELOD 2								
R,	0.079	-0.075	-0.113	0.161	0.143	0.104	0.081	0.199
p value	>0.05	>0.05	>0.05	0.003	0.01	>0.05	>0.05	0.03