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ORIGINAL ARTICLE

Platelet Distribution Width to Platelet Count Ratio as an Index of Severity of Illness

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Abstract
Objective To prospectively validate association between the ratio of platelet distribution width (PDW)/platelet count (PCT) and pediatric intensive care unit (PICU) mortality.
Methods The study was done in the pediatric intensive care unit (PICU). Platelet indices in the first sample taken after admission were used. In this case control analysis, cases were the patients who died in PICU and the survivors served as controls. Consecutive 209 eligible patients over a period of 15 mo from January 2014 through March 2015 were included. Exposure was PDW/PC above 0.07. Of them 174 survived and 35 died.
Results The mean PDW for survivors was 16.77 (±0.92) and for those who died it was 17.33 (±1.03) (p 0.0015). Mean platelet count (PC) for survivors was 3,46,000 (±1,64,700) and for those who died it was 1,75,800 (±1,61,500) ($p < 0.001$). PDW/PC for survivors was 0.12 (±0.46) and for those who died it was 0.336 (±0.53) (p 0.0014). Using the cut-off of 0.07 for PDW/PC described by Golwala et al., 77.14% above the cut-off died, compared to 22.85% below that cut-off. The odds ratio (OR) for death was 10.6 (95% CI: 4.48 to 25.12). The area under the receiver operating curve (ROC) curve for PDW/PC ratio was 0.81.
Conclusions The ratio of PDW/PC, higher than 0.07 in the first sample after admission can be considered as an independent predictor of mortality with sensitivity and specificity of 77.1% and 77.5%, respectively. It may be a useful component for inclusion in composite scores for predicting mortality.

Keywords Platelet indices · Critical care in pediatrics · Predicting mortality in hospital

Introduction

Technological advancements have resulted in improvement in the comprehensive care of children and adolescents. These advancements have improved survival in pediatric intensive care units (PICU). However the costs of care have escalated and in spite of these improvements, a large number of sick children die in PICU each year. Predicting mortality of children admitted to PICU could help concentrate efforts on those that need intensive care the most and this could help improve outcomes further.

It is necessary to characterize the disease severity at admission, to assess prognosis. A number of scoring systems have been developed to predict mortality looking at the severity of illness at admission. The PRISM score is widely used in the pediatric population for predicting mortality [1]. It was developed looking at various physiological variables and laboratory parameters in children who died against patients who survived to discharge from PICU [2]. A drawback of this scoring system is that it looks at parameters in the first 24 h of admission and thus, is not available till the next day.

Platelets are the major and essential constituent of blood which play important roles in physiological and pathological processes such as coagulation, thrombosis, inflammation and maintenance of the integrity of vascular endothelial cells [3–5]. Thrombocytopenia is a known predictor of severity of

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illness [6–9]. Critically-ill patients with thrombocytopenia have higher MODS (Multi-Organ Dysfunction Syndrome) score, SAPS (Simplified Acute Physiology Score) and APACHE II (Acute Physiology and Chronic Health Evaluation II) score compared to patients admitted with normal platelet counts at the time of ICU admission [7, 8].

In critically-ill patients, the platelet count and also the morphology of the platelets are altered and these are reflected in changes in the platelet indices [10]. Platelet indices are routinely measured by automated blood analyzers. Platelets decrease in size as they age and an increased mean platelet volume (MPV) indicates an increased proportion of young platelets in the circulation. Increased MPV suggests that there is increased platelet production and/or increased platelet destruction [11, 12]. Plateletocrit (PCT) is the arithmetic product of platelet count (PC) and platelet volume. The platelet distribution width (PDW) is increased when there is variation in the size of cells in circulation implying that mature and immature cells are present simultaneously in circulation. Initially, animal studies demonstrated that MPV and PDW increases in early part of sepsis and at the same time PC and PCT decrease [13, 14]. Similar changes in the platelet indices have also been observed in human studies [15–20].

Golwala and colleagues did a retrospective analysis of various platelet indices and their ratios in PICU patients [21]. They concluded that PDW/PC above 0.07 was significantly associated with PICU mortality with an odds ratio of 3.86 (95% CI 1.53 9.75). The present study was done prospectively in a fresh cohort of PICU patients to validate the findings of Golwala et al. The authors hypothesized that PDW/PC > 0.07 can be used as a predictor of mortality.

Material and Methods

The study was conducted at a tertiary care PICU. Consecutive admissions over a period of 15 mo from January 2014 through March 2015 were included. Patients with age < 1 mo and >12 y and those requiring immediate surgery were excluded from the study. Patients referred to another hospital for further care like children referred for cardiac surgery *etc*. and those who left against medical advice were excluded from the study prior to analysis, as the outcome in them was not known. Age, gender, diagnosis and outcome (survived/died) were recorded. Platelet indices were recorded from the first sample drawn at the time of admission, collected in EDTA vials. The samples were processed immediately in the laboratory. Complete blood count was done using Baeckmen Coulter electrical impedance method. Platelet count, MPV, plateletocrit and PDW were noted. The laboratory personnel providing the data on the blood indices were not aware of the study hypothesis or the severity of illness of the child.

Approval by the institutional ethics committee was obtained for the study. Written consent from guardians of the children was obtained for inclusion of their data in the study. However, in 20 children admitted to the PICU, consent forms could not be located when the data was being consolidated for analysis, having been misplaced or it had not been obtained due to oversight. As the data was acquired routinely during PICU stay, separate permission of the ethics committee was sought and obtained, to include the data from 20 children whose consent forms could not be located, in this analysis.

Sample size calculation was done using data parameters from the previous study by Golwala et al. [21] Assuming an odds ratio of at least 3.6, and assuming 30% exposure (PDW/PC > 0.07) among controls, for an alpha risk of 5% and power of 90% with a control: case ratio of 3, the estimated sample size was 35 cases and 105 controls. In this prospective study the authors proposed to collect data from all eligible patients till 35 cases (deaths) were recruited. Data from survivors during the study period provided the parameters for controls.

The authors studied mortality where PDW/PC was higher than 0.07 and compared it to patients with levels below this cut-off. Chi square test was used to look for level of significance. p value <0.05 was considered significant. Receiver operating characteristic (ROC) was examined to look for the optimal cut-off with maximum sensitivity with least reduction in specificity, in this cohort. ROC for PDW/PC, PC, MPV, PCT and PDW were also prepared.

Results

A total of 270 patients were admitted to PICU from January 2014 through March 2015, of which 209 patients met the inclusion criteria. Data on all 209 patients was available. Of them, 174 survived and 35 died. At this point further recruitment to the study was stopped. Figure 1 gives the details related to recruitment and distribution of patients in the study. There were 146 boys and 63 girls and mortality among girls was higher (13.6% for boys and 23.8% for girls). The clinical conditions for which the children were admitted to ICU are summarized in Table 1. Neurological ailments (34.6%) followed by respiratory problems (21%) were the most common causes for admission to PICU. Mortality was highest in those admitted for cardiovascular problems including shock and in those progressing to multi-organ dysfunction syndrome.

The mean PDW for survivors was 16.77 (±0.92) and for those who died it was 17.33 (±1.02) (p 0.0015). Mean PC for survivors was 3,46,500 (±1,64,700) and for those who died it was 1,75,800 (±1,61,500) ($p < 0.001$). Mean MPV for survivors and non-survivors was 8.6 (±1.3) and 9.8 (±1.9), respectively (p 0.0008). Mean plateletocrit for survivors was 0.29 (±0.13) and for those who died it was 0.16 (±0.12)

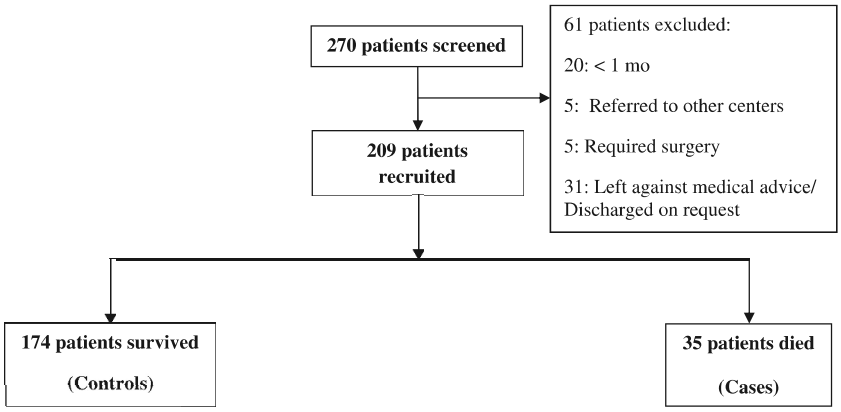

Fig. 1 Recruitment and distribution of patients

($p < 0.0001$). PDW/PC for survivors was 0.12 (±0.46) and for those who died it was 0.336 (±0.53) (p 0.0014). A comparison of various platelet indices between cases and controls is given in Table 2. Thrombocytopenia was evident in 54% of non-survivors and in 9.8% of survivors. Thrombocytosis was observed in 5.7% of non-survivors and 23% of survivors. Using the cut-off of 0.07 for PDW/PC described by Golwala and colleagues, 77.14% patients above the cut-off died compared to

Table 1 Clinical profile of included patients

Etiology	Survivors n = 174	Non survivors n = 35	Total n = 209 (%)
Respiratory	42	2	44 (21)
Pneumonia	20	0	
Bronchiolitis	21	0	
ARDS	1	2	
Cardiovascular	6	13	19 (9)
Congenital heart disease	3	1	
Myocarditis	1	3	
Refractory shock	2	9	
Neurological	66	6	72 (34.6)
Head injury	29	2	
Meningoencephalitis	11	3	
Status epilepticus	2	1	
Seizure	16	0	
Stroke	2	0	
Other	6	0	
Gastrointestinal (GI)	15	0	15 (7.2)
Diarrhea with dehydration	9	0	
Hepatic	6	0	
Hematological	1	1	2 (0.9)
Immune thrombocytopenia	1	0	
Malignancy	0	1	
Progressing to MODS	4	6	10 (4.2)
Surgical cases	2	0	2 (0.9)
Infection	14	7	21 (10)
Malaria	2	1	
Sepsis	8	5	
Dengue fever	3	1	
Enteric fever	1	0	
Endocrine	7	0	7 (3.4)
Diabetic ketoacidosis	7	0	
Others	17	0	17 (8.2)

ARDS Acute respiratory distress syndrome; *MODS* Multi-organ dysfunction syndrome

Table 2 Diagnostic parameters of ROCs and comparison of various indices between survivors and non-survivors

Indices	AUC	Optimal cut-off point	Sensitivity, %	Specificity, %	Survivors*	Non-survivors*	*p* value
PC	0.799	<2,46,000	77.1	75.8	3,46,000 (±1,64,700)	1,75,800 (±1,61,500)	<0.001
PCT	0.780	<0.23	82.8	71.4	0.29 (±0.13)	0.16 (±0.12)	<0.0001
MPV	0.682	>9.5	51.4	81	8.6 (±1.3)	9.8 (±1.9)	0.0008
PDW	0.665	>17.2	51.4	73.1	16.77 (±0.92)	17.33 (±1.02)	0.0015
PDW/PC	0.811	>0.067	80	75.2	0.12 (±0.46)	0.336 (±0.53)	0.0014

AUC Area under curve; *MPV* Mean platelet volume (fL); *PC* Platelet count (per mm^3); *PCT* Plateletocrit (%); *PDW* Platelet distribution width (fL); *ROC* Receiver operating curve

*Mean values (± SD)

22.85% below that cut-off. The OR for death was 10.6 (95% CI 4.4796 to 25.1167).

The ROC curve for PDW/PC ratio is shown in Fig. 2. The area under the curve was 0.811. The optimal cut-off value in present study was 0.067 with a sensitivity and specificity of 80% and 75.2%, respectively. However, at the cut-off value of 0.07, the specificity and sensitivity was 77.5% and 77.1%, respectively. Fig. 3 shows the comparison of ROC curves of various platelet indices (PC, MPV, PDW and plateletocrit) and Table 2 provides the data in tabular format.

Discussion

This validation study found that PDW/PC ratio of 0.07 can be used as a predictor of severity of illness. The area under the curve was 0.811. The odds ratio for mortality was 10.6 above this cut-off. This may be used in scoring systems to predict hospital survival. Further studies are needed to see if its inclusion in existing severity of illness scoring systems can further improve their predictive ability.

The study by Golwala et al. was a retrospective analysis of data whereas the present study is a prospective study evaluating the role of this ratio in predicting mortality. Having been planned prospectively it was possible to employ a standardized method for collection and evaluation of platelet indices with a minimum delay. It is known that platelet indices like MPV change with prolonged storage. This improves the internal validity of the findings.

Recently many other studies have also shown that platelet indices are one of the useful predictors of mortality in critically-ill adult patients. Zhang and colleagues, in their retrospective analysis in 1556 patients admitted in ICU, found that higher MPV and PDW were associated with increased risk of death, whereas, the decrease in plateletocrit was associated with increased risk in mortality [22]. Another retrospective analysis of 216 patients admitted in ICU, showed that low platelet count, high MPV value and high PDW value were associated with more severe illness and had higher risk of mortality [23]. All these studies confirm that platelet indices are useful to predict mortality. Golwala and colleagues in their original work also, found that platelet indices and their ratios were useful predictors of mortality [21].

In the present study, girls had a higher mortality. The sociocultural factors responsible for this have been studied previously but it is not the focus of the present study [24].

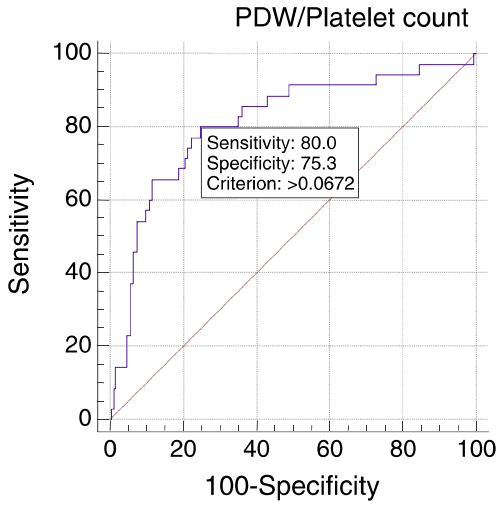

Fig. 2 PWD/PC ROC

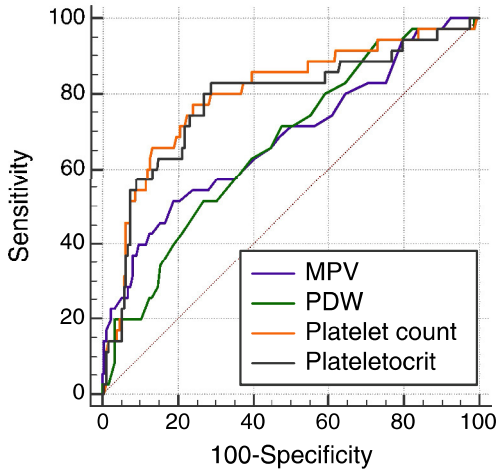

Fig. 3 Comparison of ROC curve

There are various limitations of the present study. The authors did not study the trend of the platelet indices with time after admission. There is recent research showing that in place of absolute values, trends of change in platelet indices are better prognosticator of disease outcome [25]. Secondly, the effect of treatment received by the patient prior to admission and duration of illness were not looked at in the present study. Further studies which address these limitations are necessary. Also a larger multi-center study is needed to confirm the external validity of present findings.

Conclusions

The ratio of PDW/PC, higher than 0.07 in the first sample after admission can be considered as an independent predictor of mortality with sensitivity and specificity of 77.1% and 77.5%, respectively. It may be a useful component for inclusion in composite scores for predicting mortality.

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Contributions PP: Collected and compiled the data for the study and drafted the manuscript; JMP: Conceptualized and designed the study and finalized the manuscript; ZMG and AM: Provided intellectual inputs from protocol stage and helped in drafting paper; VS: Did the sample size calculation and statistical analysis. All the authors performed critical review. JMP will act as guarantor for the paper.

Compliance with Ethical Standards

Conflict of Interest None.

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