The Correlation of Platelet Indices; Platelet Count, Mean Platelet Volume (MPV), Platelet Distribution Width (PDW) and Platelet-Large Cell Ratio (P-LCR) with Mortality in Patients Admitted to PICU

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ABSTRACT

Objective: To determine the correlation of platelet indices; platelet count (PC), mean platelet volume (MPV), platelet distribution width (PDW) and platelet large cell ratio (P-LCR) with mortality in patients admitted to PICU.

Study Design: Comparative cross-sectional study.

Place and Duration of Study: Pediatric Intensive Care Unit (PICU) of CMH Lahore from Jun 2019 to May 2020.

Methodology: Cases (mortality group) were the 81 consecutive patients who died in the PICU during the study period and fulfilled inclusion criteria. The control group comprised 81 surviving patients admitted to PICU contemporarily. Both groups' mean values of platelet indices (PC, MPV, PDW and P-LCR) were compared.

Results: The mortality rate was 10.42%. Infants were the largest sub-group (45.68%) in the mortality group. Mean platelet counts were significantly low, while mean MPV, PDW and P-LCR were significantly higher in children in the mortality group compared to the control group (*p*-value <0.001). The correlation coefficient 'r' was -0.682,0.598,0.671 and 0.355 for platelet count, PDW, MPV and P-LCR, respectively, showing a negative correlation between platelet count and positive correlation of mean platelet volume (MPV), platelet distribution width (PDW) and platelet-large cell ratio (P-LCR) with mortality.

Conclusion: Deranged platelet indices, as manifested by lower platelet count and higher values of MPV, PDW and p-LCR, were significantly correlated with higher mortality in children admitted to PICU and can be used to predict/anticipate the severity of illness.

Keywords: Mortality rate, MPV, Platelet indices, Platelet count, PDW, P-LCR, PICU.

How to Cite This Article: *Nadeem MT, Hassan SA, Basit A, Siddiqui AW, Awan AA, Ahdi SG. The Correlation of Platelet Indices; Platelet Count, Mean Platelet Volume (MPV), Platelet Distribution Width (PDW) and Platelet-Large Cell Ratio (P-LCR) with Mortality in Patients Admitted to PICU. Pak Armed Forces Med J 2022; 72(3): 1060-1064. DOI: https://doi.org/10.51253/pafmj.v72i3.7509*

INTRODUCTION

Pediatric Intensive Care Units (PICUs) are recognized as a reflection of the quality of a country's healthcare for children.[1] PICUs have contributed tremendously to the health of children in the USA, resulting in an almost five-fold reduction in pediatric mortality.[2]

The biggest challenge in PICUs is how to reduce the mortality and long-term morbidity in survivors. The task becomes even more challenging in countries with scarce resources.[3] Pediatric intensivists have used different scores like Pediatric Risk of Mortality-III, Pediatric index of mortality-II and PELOD-2 to predict the risk of mortality,[4] but the use of multiple clinical and expensive laboratory variables in these scoring systems is a disadvantage for developing countries. Moreover, the direct cost of managing a critically ill child in a PICU is very high.[5]

A reliable and inexpensive predictor of mortality and morbidity in critically ill children admitted to PICUs is needed. Platelet indices; platelet count, mean platelet volume (MPV), platelet distribution width (PDW) and platelet-large cell ratio (P-LCR) might provide this answer and are being proposed as a promising prognostic indicator in critically ill patients.[6]

High PDW, MPV and P-LCR values have been linked to the disease activity in autoimmune, infectious, inflammatory and non-inflammatory conditions, e.g., IBD,[7] congenital and acquired heart disease and pulmonary hypertension in all age groups.[8]

Low platelet count, high MPV value, and high PDW value have been reported to be associated with more severe illness, shorter survival time and increased mortality in adults and children.[9]

Platelet indices are routinely measured with automatic cell counters without any extra cost but are usually not used to predict the severity of illness. There is a paucity of research in this field in Pakistan. This study aimed to evaluate the correlation between mortality and changes in platelet indices in critically ill children in the PICU. Establishing a correlation between platelet indices and mortality may help to

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Received: 10 Oct 2021; revision received: 24 Jan 2022; accepted: 26 Jan 2022

stratify and prioritize the patients in PICU and use the resources effectively. It may decrease mortality in critically ill children in PICUs and help reduce Pakistan's overall child mortality rate.

METHODOLOGY

This cross-sectional comparative study was conducted in the PICU of Combined Military Hospital (CMH) Lahore from June 2019 to May 2020. CMH Lahore is a tertiary care hospital. PICU in this hospital is a 12- bedded unit and admits one month to 12 years old children due to any pediatric emergency and critical illness. The Ethics Committee approved the study of CMH Lahore (102/2018).

The WHO sample size calculator calculated the sample size. The calculated sample size was 138 (69 Mortality ± 69 surviving Cases) with a 5% significance level and 95% power for 8-10% of pediatric patients' population proportion admitted to PICU. Therefore, we used a larger sample size of 162 (81 mortality cases ± 81 surviving cases). In Similar studies, Zainab *et al,*[10] and Samira et al,[11] used a sample size of 40 (20 non-survivors and 20 survivors) and 51, respectively, for a study power of 80% at a 5% confidence level. Informed consent was obtained from the parents prior to enrolment. The study population was selected by nonprobability consecutive sampling technique and was divided into two groups of 81 cases each; the "Mortality group" and the "Control group".

Inclusion Criteria: All the patients of either gender, aged one month to 12 years who died in PICU during the study period were included in the mortality group. The surviving patients of either gender with near matching age admitted to PICU contemporarily were included in the survival/control group.

Exclusion Criteria: The patients with haematological diseases, including aplastic anaemia, Idiopathic thrombocytopenic purpura, platelet function disorder, lymphoproliferative diseases, hemolytic anaemias, hypersplenia, storage disorders, the patients on anti-platelet drugs such as Clopidogrel or Aspirin (Acetylsalicylic acid), patients who had received blood or platelets transfusion in preceding two weeks and radiotherapy, chemotherapy or bone marrow transplantation within last four weeks.

The age of children in the control group was matched within one year, while infants were matched to within 2-months age of the index mortality cases of the mortality group. Data of patients were collected prospectively from the patient's hospital records.

Approximately 3 ml of blood was drawn by peripheral venipuncture under complete aseptic conditions at the time of admission to PICU and sent to the laboratory for complete blood count, including platelet indices (platelet count, MPV, PDW and P-LCR). The blood samples were drawn into tubes containing Ethylenediaminetetraacetic acid (EDTA-K2) and were thoroughly mixed. The blood sample was analyzed within one hour. Complete blood count was done using a haematology auto-analyzer (SYSMEX-XS 10000i, Sysmex Corporation, Kobe, Japan) using Beckman Coulter electrical impedance method. In addition, the demographic data (age, gender), platelet indices and outcome (Mortality/Survival) were documented.

The data was compiled and analyzed by using Statistical Package for the social sciences (SPSS) version 23.00 and MS Excel 2019 software. Mean ± SD was calculated for the continuous variable. Frequency and percentage were calculated for categorical variables. Chi-square test and t-test were used. The Pearson correlation coefficient 'r' was calculated to determine the strength and direction (negative or positive) of the correlation between the platelet indices (Platelet count, PDW, MPV, P-LCR) and outcome (Mortality/Survival). Scatter plots with linear regression lines for individual platelet indices were plotted. The *p*-value ≤ 0.05 was considered significant.

RESULTS

A total of 892 patients were admitted to PICU CMH Lahore during the study period from June 2019 to May 2020. Ninety-three patients died in PICU during the study period. Twelve patients were excluded because they did not meet the inclusion criteria. The "Mortality" group included 81 consecutive patients who died during their admission to PICU during the study period and fulfilled the inclusion criteria. The same number (81) of surviving patients admitted to PICU contemporarily were included in the "Survival or Control" group. The overall mortality rate was 10.42% in PICU during the 1-year study period. Statistically, there was no significant difference bet-ween the two groups per age and gender (Table–I).

Table-I: Demographic features of Mortality and Control groups.

Demographic Characteristic		Mortality Group (n=81)	Control Group (n=81)	*p*-value
Gender	Female	48 (59.26%)	42 (51.85%)	0.636
	Male	33 (40.74%)	39 (48.15%)	
Age (Months)	Mean ± SD	33.45 ±35.28	43.18 ±38.98	0.097

In the mortality group, 37 (45.68%) children were below the age of 1 year, 29 (35.80%) were 1 to 5 years, and 15 (18.51%) were 5 to 12 years old. 66 (81.42%) children in the mortality group were below five years old. The leading underlying illnesses causing mortality and morbidity in Mortality and Control groups were shown in Figure-1.

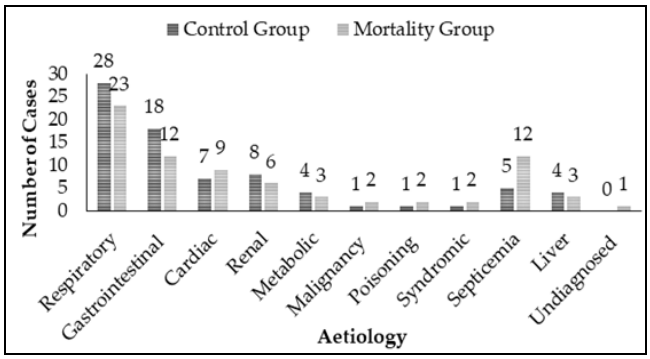

Figure-1: Basic underlying illnesses in mortality and control group.

Statistically, there was no significant difference between the two groups based on underlying aetiology (*p*-value 0.73). Respiratory failure secondary to respiratory diseases (e.g., pneumonia, acute bronchiolitis, asthma, aspiration pneumonia, cystic fibrosis) and cardiovascular disease was the leading cause of mortality. Twelve patients developed ventilator-associated pneumonia, and eight of them died. Eighteen patients (22.22 %) died within 24 hours of admission.

The statistical comparison of platelet Indices between the mortality and control groups is depicted in Table-II.

Table-II: Comparison of platelet Indices between the mortality and control groups.

Platelet Indices	Mortality Group	Control Group	*p*-value (t-test)
Platelet count Mean ± SD	200.38 x 109 /L ± 46.70	299.17 x 109 /L ± 59.08	<0.001
Platelet Distribution Width (PDW) Mean ± SD	17.33 fl ± 4.03	12.19 fl ± 2.78	<0.001
Mean Platelet Volume (MPV) Mean ± SD	16.30 fl ± 4.69	9.97 fl ± 1.64	<0.001
Platelet-Large Cell Ratio (P-LCR) Mean ± SD	32.86 % ± 7.80	27.03 % ± 7.47	<0.001

The Mean ± SD of platelet count in the morta-lity group was 200.38 x 109/L ± 46.70 and was significantly lower than the mean platelet count (299.17 x 109 /L ± 59.08) in the patients in the control group (*p*-value <0.001). The mean value of PDW in patients in the mortality group was 17.33 fl ± 4.03 and was significantly higher compared to the mean PDW of 12.19 fl ± 2.78 in the control group (*p*-value <0.001). The mean MPV± SD in patients in the mortality group was 16.30 fl ± 4.69 and was significantly higher than the mean MPV of 9.97 fl ± 4.69 in the control group (*p*-value <0.001). The mean ± SD value of P-LCR in the patient mortality group was 32.86 % ± 7.80 and was significantly higher compared to the mean P-LCR value of 27.03% ± 7.47 in the control group (*p*-value < 0.001).

The correlation coefficient 'r' was -0.682, 0.598, 0.671 and 0.355 for platelet count, PDW, MPV and P-LCR, respectively, showing that platelet count had a negative correlation (Table-III).

Table-III: Correlation of platelet indices with outcome (Mortality/Survival) in PICU patients.

Factors		Pearson Correlation Co-efficient (r) and *p*-value
Platelet Count	Pearson Correlation Co-efficient	-0.682
	p-value	<0.001
Platelet Distribution Width	Pearson Correlation Co-efficient	0.598
	p-value	<0.001
Mean Platelet Volume	Pearson Correlation Co-efficient	0.671
	p-value	<0.001
Platelet- Large Cell Ratio	Pearson Correlation Co-efficient	0.355
	p-value	<0.001

In contrast, mean platelet volume (MPV), platelet distribution width (PDW) and platelet-large cell ratio (P-LCR) had a positive correlation with mortality. Scatter plots with linear regression lines for individual platelet indices are depicted in Figure-2.

DISCUSSION

The objective of this study was to find out the correlation of derangement of platelet indices; platelet count (PC), MPV, PDW & P-LCR with mortality in PICU. For this purpose, we compared the platelet indices of mortality and control (survival) groups in PICU. We used the first blood sample after admission for analysis and found a significant correlation between admission platelet indices and outcome. Zainab *et al,*[10] and Samira *et al,*[11] have reported similar findings in their studies that the platelet indices; MPV, PDW and P-LCR in the first sample after admission were reliable predictors of poor outcomes in patients

admitted to PICU. In our study, no significant difference was detected (p-value>0.05) between the patients of the two groups based on age and gender.

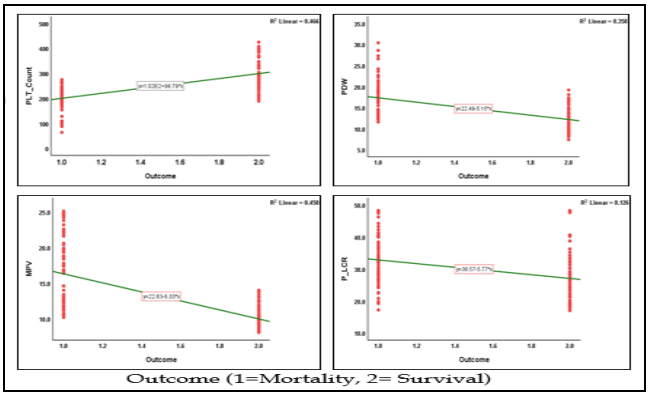

Figure-2: Scatter plots with linear regression line of platelet indices and outcome.

62.10% (554/892) of children admitted to PICU were under 05 years old. The mortality rate during the one-year study period was 10.42 %. Studies have reported a wide range of mortality rates in PICUs of Pakistan (11.9 to 35%),[12] which is comparable to India,[13] but very high compared to approximately 3% in the USA.[2] Infants were the largest sub-group (45.68%) in the mortality group. Similar results were reported by Nadir *et al,*[14] Twenty-eight (34.57%) patients died within the first 24 hours after admission in our study. Nahom *et al,*[15] reported in their study in Ethiopia that about 53.9% of deaths in PICU occur in the first 24 hours of admission.

In our study, the patients in the mortality group had significantly lower platelet count and higher MPV, PDW and p-LCR values compared to the Control group indicating that patients with deranged platelet indices were at greater risk of deteriorating into more severe illness and death. Many international studies on critically ill adults and children have shown similar findings. Gema *et al,*[16] concluded in their study that platelet profiles can be used as prognostic factors in critically ill children. Duran *et al,*[17] demonstrated in their study that patients with reduced platelet count and increased MPV and PDW had increased mortality and shorter length of survival before death compared to patients with normal values.

Zhang *et al,*[18] have reported in their study that low platelet count, increased MPV and PDW are independent risk factors for mortality. In their study in India, Varada *et al,*[19] found a statistically significant correlation between platelet indices and mortality in sick children.

In the present study, platelet count showed a significant decrease in the mortality group compared to the control (survivor) group. This appears to be consistent with the finding of a high number of patients (39, 48.15%) had systemic infections and septicemia in our study. Suneel *et al,*[20] described that thrombocytopenia is an important prognostic factor and can predict mortality in patients critically ill with septicemia. Peripheral destruction of platelets in septicemia increases platelet production and release of larger and younger platelets with high MPV and PDW into the circulation.

Hazwani *et al,*[21] reported in their study that the rise of MPV, P-LCR and PDW in patients with septicemia indicates a worse prognosis. Mishra *et al,*[22] have reported in their studies that platelet count decreases and MPV, PDW& P-LCR increase in neonatal sepsis and RDS.

Respiratory diseases, including pneumonia, were the most common (31.48%) underlying illness in both the groups under study. It was in line with the results of Qamar *et al,*[23] in their study in Pakistan. Respiratory failure was the terminal event, and fifty-four deaths (66.67%) occurred on mechanical ventilation during this study. Various local and international studies have presented similar observations. Sheng *et al,*[24] documented in their study in China that platelet volume indices are associated with increased pneumonia severity and high mortality in critically ill children receiving mechanical ventilation. Haque *et al,*[25] reported from their study in Karachi that 64.1% of patients required mechanical ventilation in their pediatric ICU.

RECOMMENDATIONS

We recommend further multi-centre studies with larger sample size. We also recommend studying the impact of the trend of values of platelet indices during admission to PICU on the outcome (mortality, morbidity and survival) of the patient.

CONCLUSION

The platelet indices are a group of platelet parameters determined together in automated CBC profiles without extra cost. Deranged platelet indices, as manifested by lower platelet count and higher values of MPV, PDW and p-LCR, are significantly correlated with higher mortality in children admitted to PICU. Therefore, platelet indices should be evaluated in all PICU patients to predict/anticipate the severity of illness and prioritize the management of critically ill children.

Conflict of Interest: None.

Authors' Contribution

MTN: Project leader in concept of study, patient selection, data collection and analysis, literature search and manuscript writing, SAH:, AWS:, AAA:, SGA: Substantial contribution in research, analysis and drafting of manuscript, AB: Substantial contribution in Data & amp, lab reports collection, analysis on excell and SPSS, manuscript, proof reading.

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