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Prediction of Morbidity and Mortality in the Pediatric Intensive Care Unit of Suez Canal University using Pediatric Risk of Mortality (PRISM) Score, Neutrophil to Lymphocyte Ratio and Platelet to Lymphocyte Ratio

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Abstract:

Background: A reliable indicator of children's death is the Pediatric Risk of death (PRISM) score. Outside of America and Europe, there is relatively little information available about the predictive validity of the PRISM score, particularly in developing nations.

Aim: Detecting the role of using (PRISM) score, neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) in prediction of morbidity and mortality in the pediatric intensive care unit to improve the quality of care.

Patients and methods: A cross-section study was done among children in the pediatric intensive care unit of Suez Canal University Hospital.

Results: The study included 153 pediatric patients. The average age was 3.61 years, with 56.9% of them being infants. 62.1% were discharged without morbidity, 8.5% were discharged with morbidity and 29.4% died. The mean PRISM score for those patients who were discharged without morbidity and those died were 8.0 ± 6.44 and 19.04 ± 10.32 respectively. The length of hospital stay, readmission, mechanical ventilation, sedative and vasoactive drug use, nosocomial infection, feeding, blood transfusion, systolic blood pressure, temperature, mental status, pupillary reflex, and PT/PTT all had a statistically significant association with outcome among admitted patients ($P < 0.005$). Furthermore, the PRISM score was shown to have a statistically significant association with mortality outcomes but there was no statistically significant association with morbidity outcomes. Finally, there was no statistically significant association between PLR and NLR as risk factors with morbidity and mortality outcomes.

Conclusion: The PRISM score demonstrated good discriminatory capacity and calibration, making it a valuable tool for determining prognosis in pediatric patients admitted to pediatric intensive care unit. In contrast, NLR and PLR were insignificant in determining patient outcomes.

Keywords: PRISM score, Mortality, Neutrophil to Lymphocyte Ratio

1. Introduction

The pediatric intensive care units are an essential component of any healthcare facility, where technology and expertise are used to appropriately treat young patients' serious illnesses in order to lower the incidence of morbidity and death. Determining a patient's risk of death is thus useful for analyzing drugs that are essential for modifying treatment procedures, evaluating the patient's

prognosis, and figuring out how well PICUs use their resources. Additionally, it helps the doctors to classify and identify patients that need more resources and urgent treatment (1).

The Pediatric Risk of Mortality (PRISM) score is one of many grading systems that are used. First described by Pollack et al. in 1988, the third revision of the Physiologic Stability Index (PRISM-III) is a modified version of the index that predicts mortality through normal physiologic disturbances during the period of the disease. It has also been used to evaluate the performance of the same PICU or to compare how different PICUs function over time (2).

Utilizing hospitalization data from patients ranging in age from newborns to teenagers, the most current iteration of the PRISM Score (IV) was published in 2015. The PRISM score and mortality have a directly proportional connection, meaning that as the PRISM score rises, so does the death rate.

The ratios of neutrophils to lymphocytes and platelets to lymphocytes have been widely employed as mortality indicators in adult patients (3).

Fewer studies, meanwhile, have examined its use in the pediatric population. For evaluating systemic inflammation, the neutrophil-to-lymphocyte ratio (NLR) is a readily available biomarker. In addition to expressing the severity of the illness in critically sick patients, it is linked to a bad long-term prognosis for septic patients. Increased NLR in hospital mortality was still debatable, however. A new inflammatory measure called the platelet-lymphocyte ratio (PLR) is used to forecast the prognosis of a number of illnesses, including adult inflammatory disorders, cancer, and cardiovascular diseases (4–6).

2. Aim of the study

This study aimed to elaborate the role of using (PRISM) score, neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) in prediction of morbidity and mortality in the pediatric intensive care unit to improve the quality of care.

3. Patients and Methods

This is cross- section study done in the pediatric intensive care unit of Suez Canal University Hospital which was equipped with six beds with age ranging from one month to 18 years. The study included all patients admitted to the pediatric intensive care unit. Medical records were analyzed and the PRISM score was recorded within the first 12 hours of hospitalization. Patients who were discharged within 24 hours and those with history of burns or trauma was excluded from the study.

Additional data were gathered to better categorize the study population (age, gender, underlying disease, pre-existent chronic disorder, status of vaccination, weight, duration of stay and final outcome), prioritization criteria of admission, variables that occurred during admission such as the occurrence of nosocomial infection, mechanical ventilation, treatment with vasoactive drugs and tolerability to feeding. These variables were selected based on previous studies of risk factors for mortality in patients with similar characteristics who were admitted to the PICU. The PRISM score's 17 physiological and laboratory parameters were used (systolic blood pressure, heart rate, temperature, Glasgow coma scale, pupillary reflexes, acidosis or alkalosis, pH, Pao₂, Paco₂, total CO₂, serum creatinine, blood glucose, potassium, blood urea nitrogen, PT/PTT, TLC and platelet count). It ranges from 0 to 77 and each parameter recorded the highest severity value as shown in table (1) (7).

Data were tabulated and analyzed in a spreadsheet using IBM SPSS. Quantitative data was expressed as means and standard deviation while qualitative data was expressed as numbers and percentages. Categorical variables were analyzed using the chi-square test. Monte Carlo correction was used for correction chi-square test when more than 20% of the cells had expected count less than 5, Kruskal Wallis test was used for abnormally distributed quantitative variables and to compare between more than two studied groups and Post Hoc was used for pairwise comparisons. Finally, regression was used to identify the most independent and relevant factors that influence mortality. A probability value of p-value < 0.05 was considered statistically significant. The discriminative power of the model (i.e., its ability to distinguish patients who would survive from those who would die) was calculated based on the ROC curve.

4. Results

The present study included 153 patients admitted to the pediatric intensive care unit. The mean age of the patients was 3.61 years with 56.9% of them being infants. 88.9% of the patients were admitted for treatment of medical illnesses, with central nervous diseases being the most common cause of admission (27.5%). 11.1% of patients were admitted for treatment of surgical causes where gastrointestinal surgical causes being the most common cause (8.5%). Furthermore, seven patients were diagnosed as multisystem inflammatory syndrome associated with COVID 19 (MIS-C) with mortality rate being 42.8%. The characteristics of the sample population studied are listed in table (2).

We found that 108 pediatric patients were discharged from the hospital, with 95 patients (62.1%) were discharged without morbidity, 13 patients (8.5%) were discharged with morbidity and 45 patients (29.4%) died. Patients who were discharged with morbidity included four patients with spastic cerebral palsy, three paraplegic patients, and one hemiplegic patient, as well as one patient with lung fibrosis who is oxygen-dependent and one patient with tracheostomy. In addition, one patient has a colostomy, and two patients have a tracheostomy and a gastrostomy tube.

The mortality rate among pediatric patients admitted due to sepsis was the highest (31.1%) followed by patients admitted with central nervous system diseases (24.4%) while 69.2% of total morbid patients were discharged with neurological sequelae.

It was found that length of hospital stay, readmission, usage of mechanical ventilation, usage of sedative and vasoactive drugs, nosocomial infection, feeding and blood transfusion all had a statistically significant association with morbidity and mortality risk among admitted patients

In the present study as shown in table (3), the minimum PRISM Score of patients was 0 and the maximum score was 39. the mean PRISM score of those who were discharged without morbidity was 8.0 ± 6.44 (7.0), while was 19.04 ± 10.32 (18.0) among those who were died. Also, the proportion of deaths which was 4.4% among patients with the PRISM scores of ≤ 5 and increased gradually with increasing score value, reaching 100% among patients with a PRISM scores of ≥ 30 . There was a significant correlation between patients discharged without morbidity and those who were died and between patients discharged with morbidity and those who were died. However, there was no statistically significant difference between patients who were discharged without morbidity and those who were discharged with morbidity. As a result, it was determined that the PRISM score had a statistically significant association with mortality outcomes ($X^2 = 43.585$, $P = 0.001$) but no statistically significant correlation with morbidity outcomes.

It was seen that area under the receiver operating curve for PRISM score was 0.815 (95% confidence interval [CI], 0.742 – 0.888; $P < 0.001$) with a cutoff value >11 , indicating that it was a good predictor in the present study (Figure 1). The overall sensitivity was 71.11 and specificity was 73.15 while positive predictive value was 52.5 and negative predictive value was 85.9 at cut off point >11 as shown in Table (4).

In the present study, systolic blood pressure (SBP), temperature, mental status (GCS), pupillary reaction and PT/PTT had a statistically significant association with morbidity and mortality outcomes. While the remaining variables like heart rate (HR), (PaCO₂), (PaO₂), total CO, (pH), serum creatinine level, (BUN), platelet count, white blood cells and serum potassium, hadn't a statistically significant association with morbidity and mortality outcomes. Finally, the present study detected that there was statistically insignificant association between PLR and NLR with morbidity and mortality outcomes respectively as shown in Table (5).

The association of different factor and variables in the PRISM score with mortality was determined by using logistic regression, the study found that increasing the PRISM score by one unit increased mortality by 1.158 times as shown in Table (6).

Tables and figures

Table (1): Pediatric Risk of Mortality Scoring System in PICU

Variables	Infants	Children	Score
Systemic blood pressure (mmHg)	>65	>75	0
	45-65	55-75	3
	<45	<55	7
Heart rate	<215	<185	0
	215-225	185-205	3
	>225	>205	4
Temperature	33-40 c		0
	<33 or >40 c		3
Mental status	Glasgow coma score ≥ 8		0
	Glasgow coma score < 8		5
Pupillary reflex	Both reactive		0
	One pupil fixed, pupil >3 mm		7
	Both pupils fixed, pupil >3 mm		11
Blood glucose (mg%)	≤ 200		0
	> 200		2
Potassium (mmol/L)	≤ 6.9		0
	> 6.9		3
Creatinine (mg %)	≤ 0.9	≤ 0.9	0
	> 0.9	> 0.9	2
BUN (mg %)	≤ 14.9		0
	> 14.9		3
White blood cell count	≥ 3000 cells/mm ³		0
	< 3000 cells/mm ³		4
Platelets (cells/mm ³)	$> 200,000$		0
	100,000-200,000		2
	50,000-99,999		4
	$< 50,000$		5
PT (s) or PTT (s)	PT ≤ 22 and PTT ≤ 57		0
	PT > 22 or PTT > 57		3
Acidosis	pH > 7.28 or total co ₂ ≥ 17 meq/l		0
	pH 7.0 - 7.28 or total co ₂ 5-16.9 meq/l		2
	pH < 7 or total co ₂ < 5 meq/l		6

PaO ₂	≥ 50	0
	42-49.9	3
	<42	6
PCO ₂ (mmHg)	<50	0
	51-75	1
	>75	3
Total CO ₂ (mmol/L)	< 34	0
	≥ 34	4
pH	<7.48	0
	7.48-7.55	2
	>7.55	3

Table (2): Clinical data of patients enrolled in the present study.

Patients characteristics		N	%
Chronic illness	No	71	46.4%
	Yes	82	53.6%
Vaccination	Yes	130	85%
Weight	Below normal percentile (below 5th)	33	21.6%
	Normal percentile (between 5th to 85th)	116	75.8%
	Over Growth percentile (above 85th)	4	2.6%
Priority of admission	1	49	32 %
	2	43	28.1%
	3	27	17.6%
	4	34	22.2%
Duration of admission	Less than or equal to 3 days	39	25.5%
	4-7 days	51	33.3%
	8-15 days	33	21.6%
	More than 15 days	30	19.6%
Readmission	No admission	145	94.8%
	Within a week	8	5.2%
Mechanical ventilation	No	93	60.8%
	Yes	60	39.2%
Nosocomial infection	No	107	69.9%
	Yes	46	30.1%
Sedative drug	No	91	59.5%
	Yes	62	40.5%
Vasoactive drug	No	92	60.13%
	Yes	61	39.9%
Feeding	No	94	61.4%
	Yes	59	38.6%
Blood Transfusion	No	81	52.9%
	Yes	72	47.1%

Table (3): Distribution of morbidity and mortality according to PRISM score.

Prism Score	Final outcome			Test of sig.	p
	Discharge without morbidity (n= 95)	Discharge with morbidity (n= 13)	Mortality (n= 45)		

≤ 5	30 (31.6%)	5 (38.5%)	2 (4.4%)	X²= 43.585	MCp <0.001*
6 – 15	53 (55.8%)	6 (46.2%)	16 (35.6%)		
16 – 30	12 (12.6%)	2 (15.4%)	18 (40.0%)		
≥ 30	0 (0.0%)	0 (0.0%)	9 (20.0%)		
Significant	MC p₁=0.760,p₂<0.001*,MC p₃=0.005*				
Min. – Max.	0.0 – 29.0	0.0 – 28.0	3.0 – 39.0	H= 37.725	<0.001*
Mean ± SD.	8.0 ± 6.44	8.77 ± 4.02	19.04 ± 10.32		
Median (IQR)	7.0(3.0 – 11.50)	8.0(2.0 – 12.0)	18.0(10.0 – 27.0)		
Significant	p₁=0.877,p₂<0.001*,p₃=0.001*				

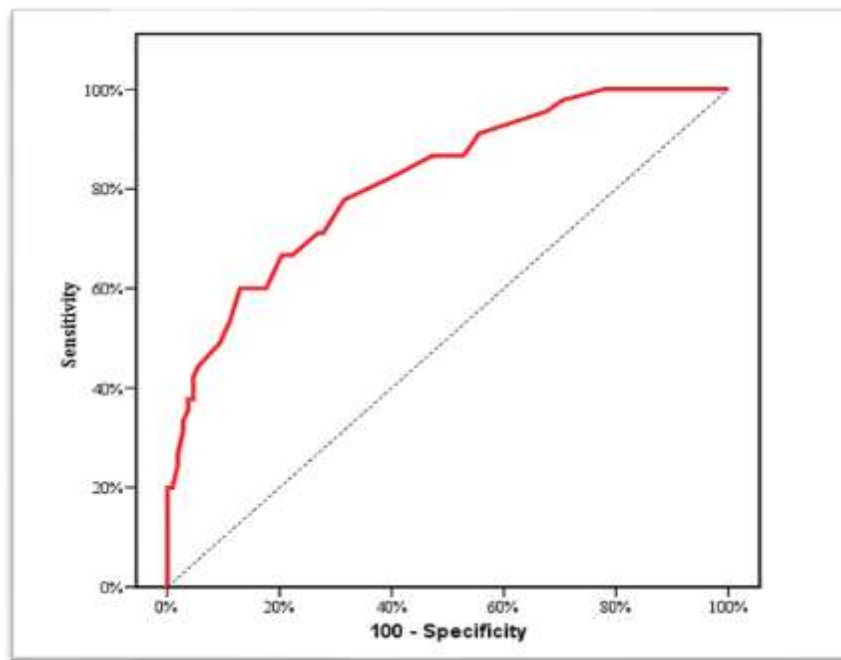


Figure (1): ROC curve for Prism Score to predict mortality versus discharge.

Table (4): Prognostic performance for Prism Score to predict mortality (n= 45) versus discharge (n= 108).

Prism Score	AUC	P	95% C.I	Cut off	Sensitivity	Specificity	PPV	NPV
	0.815	<0.001*	0.742 – 0.888	>5	91.11	44.44	40.6	92.3
				>11	71.11	73.15	52.5	85.9
				>15	60.00	87.04	65.9	83.9
				>25	31.11	97.22	82.4	77.2
				>29	20	100.0	100.0	75.0

Table (5): Risk factors of morbidity and mortality among admitted patients related to PLR ratio and NLR ratio variables.

	Final outcome			H	p
	Discharge without morbidity (n= 95)	Discharge with morbidity (n= 13)	Mortality (n= 45)		
PLR ratio					
Min. – Max.	5.0 – 2487.0	45.60 – 323.0	2.10 – 457.0	1.178	0.555
Mean ± SD.	144.03 ± 266.83	121.53 ± 88.42	99.49 ± 84.0		
Median (IQR)	89.40(60.80 – 145.30)	114.0(57.0 – 124.0)	88.0(36.70 – 131.0)		
NLR ratio					
Min. – Max.	0.06 – 21.10	0.31 – 17.0	0.32 – 22.70	1.310	0.520
Mean ± SD.	2.99 ± 3.40	3.26 ± 4.52	2.10(3.46 ± 4.05)		
Median (IQR)	1.80(0.89 – 3.85)	1.60(1.10 – 2.90)	2.10(1.1 – 4.20)		

Table (6): Logistic regression analysis for the significant PRISM score variables and other factors that affecting morality.

	B	SE	Wald	df	Sig.	Exp (B)	95% CI	
							LL	UL
Cause of admission (surgical)	1.139	0.523	4.740	1.000	0.029	3.125	1.120	8.716
Duration of admission	0.403	0.152	7.067	1.000	0.008	1.496	1.112	2.013
Mechanical ventilation	5.533	1.047	27.934	1.000	<0.001	253.000	32.506	1969.169
Sedative drug	1.705	0.386	19.513	1.000	<0.001	5.500	2.581	11.718
Feeding	-2.364	0.558	17.949	1.000	<0.001	0.094	0.031	0.281
Blood transfusion	4.070	0.755	29.044	1.000	<0.001	58.569	13.329	257.356
Prism Score	0.146	0.026	30.862	1.000	<0.001	1.158	1.099	1.219
Systolic BP	0.782	0.378	4.286	1.000	0.038	2.186	1.043	4.582
Temperature	0.864	0.370	5.449	1.000	0.020	2.374	1.149	4.905
GCS	0.539	0.088	37.370	1.000	<0.001	1.714	1.442	2.037
Pupillary reaction	0.307	0.064	23.236	1.000	<0.001	1.359	1.200	1.539
PT/PTT	0.870	0.172	25.566	1.000	<0.001	2.387	1.704	3.344

5. Discussion

The effectiveness of the prognostic scoring system to distinguish between survivors and those who died was proved in the current investigation by the fact that those who died had higher PRISM scores than those who survived. Whereas the percentage of fatalities among patients with PRISM scores of ≥ 5 was 4.4%, it progressively rose as PRISM score values climbed, reaching 100% among patients with PRISM scores of ≥ 30 (8).

Accordingly, the current research discovered that the chance of death rises noticeably as the PRISM score rises, suggesting that the PRISM score is a sensitive indicator of mortality outcomes. Nevertheless, no statistically significant association was found between morbidity outcomes and the PRISM score. Both the initial research by Pollack et al. (9) in the United States and the study by Naseem et al. (10) in Egypt revealed that a rise in PRISM score was linked to an increase in mortality, which is consistent with the current study.

Studies conducted in Pakistan with 70 patients (11), India with 411 patients (12), and the Kingdom of Saudi Arabia with 68 patients (13) all produced similar results. Additionally, in 2017 research of 723 patients in India, Varma et al. discovered that death rates for scores "0-10" were 0%, scores "36-40" were 94.44%, and scores "41" and above were 100%.

Additionally, Dey et al.'s (14) study in India, which included 225 patients, found that children with scores greater than 45 had a 94.7% mortality rate.

In contrast, Mirza et al.'s (15) study in Pakistan, which involved 407 patients, found that patients with scores greater than 20 had a 100% chance of dying. Either the more critical clinical state of admitted patients or hospital settings with limited resources may account for the difference in PRISM scores between the current research and other studies that corresponded to increased mortality risk.

The PRISM score underpredicted mortality in their PICU due to differences in their patient clinical profile, a lack of resources, and disparities in the quality of care compared to those PICUs where the score was established, according to a study by Thukral et al. (16) conducted in India.

Additionally, Patki et al. (17) discovered that the actual mortality (21.7%) was higher than the anticipated mortality (5.68%) using the PRISM score in a 2017 research including 120 patients in India. The PRISM score is thus not a reliable indicator of PICU death.

While Chauhan et al. (18) found that while PRISM scoring in patients with hepatobiliary and CNS diseases cannot predict mortality, it can be used to assess severity at the time of admission to PICU. In a study of 107 patients conducted in India, Kesici et al. (19) demonstrated that the PRISM score performed poorly for severity evaluation and failed to predict mortality risk in pediatric patients on mechanical ventilation. In contrast, the PRISM score proved to be a good predictor of mortality for children admitted with septicemia, renal diseases, and respiratory diseases. The area under the ROC curve in this investigation was 0.815. A model's overall accuracy in discriminating outcomes is expressed by its area under the curve, which is a useful indicator of its predictive power.

The prediction model is better if the ROC curve area is around 1.0. The ROC curves for studies Brady et al.(1), Korea by Jung et al.(20), India by Taori et al. (21) and Varma et al. (22), and Brazil by Martha et al. (23) were 0.80%, 0.82%, 0.826%, 0.851, 0.86, and 0.870, respectively. Their findings are almost identical to this. which were all thought to have accurate predictions. On the other hand, research in India by Dey et al.(14) had ROC curves with areas of 0.974, 0.903, and 0.987, respectively, whereas the original study by Pollack et al. (9) in the United States showed a ROC curve with an area of 0.958. These investigations, which included a large population, were thought to be highly predictive. Differences in patient clinical profiles, a lack of resources, and variances in the quality of treatment compared to the institution where the score was created were probably the main causes of the discrepancy in discrimination across trials.

Lastly, the current investigation discovered a statistically negligible association between PLR and NLR as risk factors for outcomes related to morbidity and death. At the time of admission,

critically ill patients with sepsis had substantially higher NLR levels than those without sepsis, according to an observational cohort research done in Cambridge by Salciccioli et al. (24) on 5056 patients. However, no statistically significant correlation was seen between those patients' NLR levels and their ultimate result.

Kutlucan et al. (25) found that PLR levels were marginally higher in patients who did not survive compared to those who did.

Another research (26) in Slovakia, which included 90 cancer patients, was the first to find that high NLR levels were linked to a bad prognosis and that NLR was a quick and easy indicator of inflammatory stress in critically sick patients.

Many investigations came to the same result, such as an observational cohort study done in China in 2016 with 333 septic patients enrolled in the intensive care unit (ICU) by Liu et al. (27) According to the results, NLR is a simple and affordable measure that may be used to assess septic patients in the ED. In contrast to the current research's findings, other study (28) of 654 children in Western Nepal who had lower chest infections revealed greater death rates among PICU patients with high NLR levels.

Although, our study had limitations as There was an insufficient pediatric patient's enrollment in the present study as the functional bed strength in the Pediatric Intensive Care Unit of Suez Canal University Hospital was six beds prior to renovation. Larger patients are required to support the results.

6. Conclusion

The present study showed that the PRISM score demonstrated good discriminatory capacity, making it a valuable tool for predicting mortality for pediatric patients admitted to Pediatric Intensive Care Unit. However, there was no association detected between the PRISM score and morbidity outcomes. Furthermore, NLR and PLR are insignificant in determining patient outcomes. More study including a larger sample size of patients is required to create and validate a mortality prediction score for our country. Furthermore, more research is needed to determine the precise value of NLR and PLR as a prognostic and diagnostic tool in pediatric patients. The PRISM score does not include any particular indicators of morbidity or the ultimate result in terms of disability following transfer from the PICU. It is necessary to develop newer scores that quantify disability and long-term consequences.

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