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Prognostic Value of Lactate Level in Critically-ill Children

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Abstract

Introduction: Disturbances in homeostasis, leading to single or multiple organ injury or reversible or irreversible organ failure, are hallmarks of critical illness. In critical illness, whether organ failure can be reversed or not depends largely on how long the affected organ was exposed to the damaging stimuli or conditions.

Aim of the study: The study aims at measuring serum lactate levels in critically-ill kids and to assess prognostic value of lactate level in critically-ill kids using (PRISM IV) score

Subjects and Methods: This study was conducted as a prospective cross-sectional study on 100 critically ill children who came to the PICU at Fayoum University Hospital for a period of 12 months (from October 2020 to October 2021). Over a 12-month period, around 200 children were admitted to the pediatric ICU at Fayoum University Hospital. For the purpose of statistical analysis, a sample of 100 children was chosen using the single population proportion formula, with an assumed incidence rate of hyperlactatemia of 50%. A confidence interval of 90% and a margin of error of 5% were used to determine the appropriate sample size.

Results: According to our findings, the blood lactate level at 24 hours after a patient's admission to the PICU was the most sensitive and specific predictor of mortality. Research is needed to prove lactate's prognostic significance in pediatric ICU admissions. Blood lactate can be used as a predictive diagnostic until other biochemical markers are established.

Conclusions: The occurrence of hyperlactatemia has been linked to unfavorable outcomes in critically ill kids brought to the PICU. A noticeable association was found between blood lactate level at admission to the PICU and mortality in critically ill kids, even after accounting for age, gender, and illness severity. An elevated blood lactate level at admission was identified as an independent predictor of in-hospital mortality among the pediatric population. These consequences contribute to the understanding of blood lactate as a clinical biomarker for predicting mortality in critical disease.

Key words: Lactate Level; Critically-ill Children; PRISM IV score.

1. Introduction

Diminished tissue perfusion (DTP) is a known symptom among critically ill children with various underlying diseases. Failure to recognize hypoperfusion promptly

can lead to multi-organ dysfunction syndrome (MODS), which is linked to increased morbidity and mortality rates [1]. Blood lactate, which results from anaerobic metabolism, is an effective predictor of mortality in cases of severe sepsis or septic shock in pediatrics [1]. The blood lactate concentration is a known indicator of altered tissue perfusion in critically ill patients [2].

Muscles, intestine, red blood cells, brain, and skin contribute to the daily total of roughly 1500 mmol of lactate, which is metabolized primarily by the liver (about 60%) and secondarily by the kidneys (30%) and other organs [3]. The typical blood lactate concentration is approximately 1 mEq/1 [4]. Even small increments in lactate levels to more than 1.5 mEq/1 are directly proportional to high mortality rates [5]. In critically ill children, the early recognition of sepsis and MODS is crucial for initiating effective therapeutic interventions [6]. High lactate levels at admission to the PICU are linked to in-hospital mortality [7].

Lactate normalization within six hours of admission to the PICU is directly proportional to high hospital survival rates compared to normalization beyond that period [8]. The CPCCRN's Trichotomous Outcome Prediction in Critical Care (TOPICC) study indicated that the physiologic status measured by the pediatric risk of mortality score (PRISM) physiologic variables and their ranges were directly proportional to increased morbidity and death rates. So, algorithms were devised to forecast all newly diagnosed cases of critical illness and deaths [9].

The inability to eliminate lactic acid has been proven in recent research to be preferable to a single lactic acid value [10]. During sepsis, metabolic changes might increase blood lactate (caused by elevated glycolysis and catecholamines stimulating the Na-K pump), change pyruvate dehydrogenase activity, and decrease lactate clearance due to liver hypoperfusion. Despite these underlying mechanisms, elevated lactate remained a key feature of shock states [11].

So, the current study aimed to measure serum lactate levels in critically-ill kids and to assess the prognostic value of lactate levels in critically-ill kids using (the PRISM IV) score.

2. Subjects and methods

2.1. Subjects

A prospective cross-sectional study was done on 100 critically ill kids who came to the PICU at Fayoum University Hospital for a duration of one year (from October 2020 to October 2021).

Over the course of 12 months, about 200 children came to the pediatric ICU at Fayoum University Hospital. A sample size of 100 was selected for the study using the single population proportion formula, which assumed a 50% incidence of hyperlactatemia, a confidence interval of 90%, and a margin of error of 5%.

The study collected venous blood samples from the critically ill children upon admission and 24 hours later and measured their serum lactate levels. The patients'

outcomes were then observed, and the PRISM IV score was used to determine the degree to which their sickness had progressed.

Inclusion criteria

Severely ill kids have been brought to the PICU located in Fayoum governorates, ages 28 days to 13 years, and both genders.

Exclusion criteria

Age: less than 28 days (neonatal age), death During the initial 24-hour period of PICU admission, discharge from PICU occurred 24 hours after PICU admission, including children who were admitted for postoperative surgical care and children with road traffic accidents.

2.2. Study design

The critically-ill children who participated in the study underwent various assessments, including a comprehensive medical history and clinical examination. At the time of admission to the PICU, as well as after 24 hours, blood lactate levels were taken. The PRISM physiologic variables were used to measure the physiologic status, with a shortened time interval for laboratory data (from 2 hours before PICU admission to 4 hours after admission) and the initial four hours of care in the pediatric intensive care unit for other physiological factors. Cardiovascular, neurological, respiratory, chemical, and hematologic aspects make up the PRISM components. Separate neurologic and non-neurologic sub-scores were calculated from the total PRISM score.

2.3. Statistical Methods

SPSS software, a statistical computer package, version 18 was utilized to organize, tabulate and analyze the acquired data (SPSS Inc, USA). Calculations of the mean, standard deviation (SD), median and interquartile range were all part of the statistical analysis of the numerical data (IQR). Independent t-test or Mann-Whitney U test when appropriate was utilized as a test of significant. The categorical data were expressed as counts and percentages, and the significance of the differences among groups was tested using the chi-square ($\chi 2$) test. The receive operating characteristic (ROC) curve was utilized to establish the discrimination value of blood lactate and PRISM score for predicting mortality. The optimal cut-points for sensitivity, specificity, PPV and NPV were defined using Youden index. $P<0.05$ was chosen as the threshold for statistical significance to be used in interpreting test findings.

3. Results and discussion

The clinical and laboratory findings of cases upon admission to ICU can provide valuable information on their pathophysiological state. These findings, including changes in laboratory parameters and clinical status, have been utilized to predict the danger of death in both adult and pediatric ICU patients. Blood lactate levels are often used as an indicator of illness severity and risk of mortality [12]. In cases who are critically ill, several indicators have been identified as predictive of mortality risk, including albumin, lactic acid, procalcitonin, glucose, PaO2, and nutritional status [13].

The aim of the current study was to assess the significance of blood lactate levels as a prognostic indicator in critically ill children by measuring these levels and analyzing them in conjunction with the PRISM IV score. This research was carried out as a prospective cross-sectional investigation involving 100 critically-ill children who were admitted to the PICU at Fayoum University Hospital between October 2020 and October 2021. The study revealed that the average age of the children was 27.2±42 months, with 47% being female and 53% male. Additionally, our findings showed no significant differences among survivors and non-survivors relative to either age or gender (Table 1). This did not come in agreement with Srigiri *et al.* (2019), who illustrated that out of 100 patients, (22%) expired [14].

The study also found that 30% of the critically-ill children had pneumonia, 17% had gastro-enteritis, 13% had COVID-19 pneumonia, 13% had CNS infection, 10% had heart failure, 5% had renal failure, 5% had diabetic ketoacidosis (DKA), 3% had convulsion, 3% had sepsis, 2% had stridor, and 2% had hematemesis. However, there was no significant difference among survivors and non-survivors with regards to any of these diagnoses. Srigiri *et al.* (2019) reported that pneumonia was the most common diagnosis (7.5%) among the non-survivor group, followed by meningitis and shock [14].

Table 1: Demographics and clinical characteristics of all patients.

Variables		**Frequency (N=100)**
Age (years)		27.2±42
Gender	**Female**	47 (47%)
	Male	53 (53%)
Type of disease	**Pneumonia**	30 (30%)
	Gastro-enteritis	17 (17%)
	COVID-19 pneumonia	13 (13%)
	CNS infection	13 (13%)
	HF	10 (10%)
	renal failure	5 (5%)
	DKA	5 (5%)
	CHD	4 (4%)
	Convulsions	3 (3%)
	Sepsis	3 (3%)
	Others	3 (3%)
	Hematemesis	2 (2%)
	Stridor	2 (2%)
	Shock	2 (2%)

According to the current study, mortality was the highest in the 10-16 age group (7%) and the least in the 1-4 years age group (4%). In our investigation, we observed no significant difference in length of hospital stay (LOS) among survivors and non-survivors. The average LOS was 9.4 days with a standard deviation of 8 (Table 2). Our findings were in line with the research by Koliski *et al.* (2005), which also found no significant difference in LOS between the two groups. Lactic acid (LA) is a biochemical product of anaerobic metabolism and it can serve as a useful marker for tissue hypoxia [15].

Tissue hypoxia is commonly caused by respiratory or circulatory problems, and elevated LA levels can indicate its occurrence [16]. Our study found a significant difference amongst survivors and non-survivors in terms of lactate levels at admission and 24 hours after admission.

Similarly, a previous study reported that serum lactate was higher among deceased patients than among those who survived [19], consistent with several studies that have linked admission lactate or peak lactate levels to mortality [19, 20, 21].

Additionally, our results align with multiple studies that have demonstrated the utility of hyperlactatemia as a prognostic index in critically ill kids admitted to the PICU [15, 22]. In this study, it was found that the mean lactate levels at admission and after 24 hours were (35.9±22.8) and (37.2±25.5), respectively. The research also showed that the mean lactate levels of survivors and non-survivors at admission and after 24 hours were significantly different.

Table 2: Estimated probability of mortality using PRISM4 score.

Variables			**Frequency (N=100)**
Estimated probability of mortality			10.3±10.7
Length of stay (LOS: days)			9.4±8
Mortality		**Non-survivor**	32 (32%)
		Survivor	68 (68%)
Relation between socio-demographics characteristics and mortality			
		Non-survivor	**Survivor**	***P-value***
Age		30.5±43.5	25.7±41.5	0.889
Gender	**Female**	38.8%	61.7%	0.204
	Male	26.4%	73.6%	
Mortality in relation to diagnoses				
Pneumonia	**Yes**	30.8%	69.2%	1.000
	No	32.2%	67.8%	
Gastro-enteritis	**Yes**	50.0%	50.0%	0.283

	No	30.0%	70.0%	
COVID-19 pneumonia	**Yes**	20.0%	80.0%	1.000
	No	32.6%	67.4%	
CNS infection	**Yes**	0.0%	100.0%	0.174
	No	33.8%	66.3%	
HF	**Yes**	50.0%	50.0%	0.591
	No	31.3%	68.7%	
renal failure	**Yes**	33.3%	66.7%	1.000
	No	32.0%	68.0%	
DKA	**Yes**	66.7%	33.3%	0.239
	No	30.9%	69.1%	
CHD	**Yes**	66.7%	33.3%	0;239
	No	30.9%	69.1%	
Convulsions	**Yes**	100.0%	0.0%	0.100
	No	30.6%	69.4%	
Sepsis	**Yes**	0.0%	100.0%	1.000
	No	32.7%	67.3%	
Others	**Yes**	50.0%	50.0%	0.540
	No	31.6%	68.4%	
Hematemesis	**Yes**	30.8%	69.2%	1.000
	No	32.2%	67.8%	
Stridor	**Yes**	50.0%	50.0%	0.283
	No	30.0%	70.0%	
Shock	**Yes**	20.0%	80.0%	1.000
	No	32.6%	67.4%	
Pneumonia	**Yes**	0.0%	100.0%	0.174
	No	33.8%	66.3%	

Other studies have also demonstrated the utilization of lactate levels as a prognostic index in critically ill patients, with higher levels of lactate being linked with amplified mortality.

Mortality was observed to be higher in cases where lactate levels were higher than 22 mg/dl [24], while shock patients whose lactate levels dropped dramatically within an hour of resuscitation had the best prognosis [2].

Hyperlactatemia can identify cases at risk of death and be utilized as a signal for ICU admission, as shown by research by Smith *et al.* (2001), who showed that only 11% of patients with blood lactate levels more than 36 mg/dl survived [24].

No statistically significant difference in outcomes was detected among the 2 groups [15]. For the purposes of this investigation, there was a high significant difference amongst survivors and non-survivors as regards the Estimated probability of mortality, with a mean of (10.3±10.7)

(Table 3).

Table 2: Estimated probability of mortality according to outcome.

Variables	**Frequency (N=100)**		
Lactate admission (mg/dl)	35.9±22.8		
Lactate 24 hours (mg/dl)	37.2±25.5		
Difference in Lactate level according to outcome			
	Non-survivor	**Survivor**	***P-value***
Lactate admission (mg/dl)	45.9±26	31.2±19.5	<0.0001
Lactate 24 hours (mg/dl)	57.5±43.5	27.6±18.7	<0.0001
Estimated probability of mortality	16.8±12.2	7.3±8.5	<0.0001
LOS	10.8±8.9	8.8±7.5	0.485

Different studies found that the PRISM score and predicted death rate were greater in non-surviving cases, which agrees other [18, 25, 26, 27]. Another study found that lactate and the Pediatric Index Mortality, Children in critical care can have their survival predicted by a (PIM) score [28].

In a study of children with sepsis, they discovered that lactate levels were able to differentiate between those who would and would not survive [29].

If hyperlactatemia is present upon admission and persists after 24 hours of treatment, it may be a fatal sign [30]. The risk of complications and death was most reliably predicted by lactate levels and the length of time the child was on extracorporeal circulation after cardiac surgery. Koliski *et al.* (2005) showed that lactate levels greater than 30 mg/dl did not significantly increase the risk of death, while lactate levels decreasing or normalizing within 24 hours were associated with improved survival rates [15]. In the present study, we found that lactate levels on admission and at 24 hours had high sensitivity and specificity for predicting survival.

The cut-off for lactate on admission was 26.8, while the cut-off for lactate at 24 hours was 32.8. The estimated probability of mortality had a sensitivity of 75%, a specificity of 72.1%, a positive predictive value of 55.9%, and a negative predictive value of 86% at a cut-off of 8.5.

Srigiri *et al.* (2019) found that lactate levels measured after 24 hours have higher sensitivity and specificity in predicting death in cases with high lactate levels (≥4 mmol/L) compared to admission lactate levels in the same group [14].

This is in line with the findings of a research by Koliski *et al.* (2005), which found that high lactate levels on admission and after 24 hours are associated with an increased positive likelihood ratio for predicting death, while low lactate levels are associated with a decreased positive likelihood ratio [15]. Several studies have reported that increasing lactate cut-off values lead to higher positive predictive values [28, 30], and the lactate cut-off level increases,

the positive predictability of death increases [14]. The positive likelihood ratio for predicting death is higher with high lactate levels compared to intermediate and low levels. Additionally, the area under the receiver operating characteristic curve values for admission lactate levels and lactate levels after 24 hours are 0.86 and 0.96, respectively.

Conclusion

Reduced survival rates have been linked to elevated blood lactate levels in critically ill infants in pediatric intensive care units (PICU). Even after correcting for confounding variables such as age, gender, and severity of illness, researchers discovered that the quantity of blood lactate on admission to the PICU strongly correlates with death in critically ill children. A greater blood lactate level at admission was linked to an increased risk of death in children while hospitalized. These findings support the use of blood lactate as a clinical biomarker for predicting death in pediatric intensive care unit patients. High blood lactate levels have been associated with an increased risk of death in the critically unwell, and these findings have been confirmed.

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Ethical approval and consent to participate: The Faculty of Medicine's Research Ethics Committee approved the research before it was conducted. The researcher was explaining the study's goals, the exam's format, and the results of the inquiry to the participants. In addition, their ability to opt out of the study will be protected and their privacy would be protected from disclosure.

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