Study of blood lactate levels at admission as a predictor of mortality and morbidity in critically ill children in a tertiary care pediatric intensive care unit

ABSTRACT

Background and Aim: Patients with severe illness are at an elevated risk of experiencing multiple organ failure, which in turn increases their likelihood of mortality. Hyperlactatemia is recognized as a distinct risk factor for the onset of organ dysfunction and mortality, as well as morbidity in children's. Present study aims to to determine threshold values for the prediction of in-hospital mortality in the larger cohort of critically ill children and to evaluate the predictive value of blood lactate levels at admission.

Methods: This prospective observational study was conducted with 202 critically ill children, ranging in age from one month to 18 years, admitted to the Pediatric Intensive Care Unit (PICU). Arterial blood samples were obtained upon admission, and subsequent measurements of lactate levels were conducted. The demographical data, clinical status and organ involvement were recorded. Statistical analysis was performed by using SPSS Version 21.0 and $P < 0.05$ was considered to be significant.

Results: Survivors geometric mean lactate levels at admission were lower (1.2 mmol/L) than non-survivors' (4.8 mmol/L), and higher lactate levels at admission were substantially linked to both mortality and morbidity (length of hospital stay, need for ventilator and inotropic support). The sensitivity and specificity of the blood lactate levels were 93.6% and 89.7%, achieved at the optimal cut-off value of 4.05 mmol/L. The incidence of multi organ dysfunction, need for ventilator and inotropic support, duration of hospital stay in critically ill children was significantly associated with increased blood lactate levels at admission ($P<0.01$).

Conclusion: A high level of blood lactate upon admission was independently predictive of in-hospital mortality in the pediatric population. The early identification of children who are at a high risk for mortality allows for prompt intervention, thereby enhancing the overall outcomes.

Key words: *Blood lactate, critically ill children, cut-off value, hospital stay, hospital outcome*

1. INTRODUCTION

Lactate is a metabolite generated during anaerobic glycolysis [1]. It has been employed as an indicator of tissue hypoperfusion and cellular hypoxia and an elevation in lactate levels is significantly correlated with mortality [2].

Hyperlactatemia has been identified as being associated with a more severe outcome in critically ill patients [3]. This was characterized by elevated levels of lactate in the blood, has been explored in certain clinical contexts such as cardiogenic shock, trauma, and sepsis. A blood lactate concentration below 1.5 mmol/L is considered normal, however, any elevation above this threshold, even to a slight degree, significantly elevates the risk of a poorer outcome [4]. Upon admission to a general

medical intensive care unit, the presence of hyperlactatemia served as a predictive marker, identifying those at a significantly increased risk of mortality [5]. To date, a limited number of studies have been conducted in pediatric populations to assess the significance of measuring lactate levels in the general critically ill pediatric inpatient population within the pediatric intensive care unit (PICU) [6].
This research aimed to assess the predictive utility of blood lactate levels upon admission and to establish threshold values for the prediction of in-hospital mortality within the broader cohort of critically ill children.

2. MATERIAL AND METHODS

2.1 Study Design: A prospective, observational study.
2.2 Study Sample: This prospective observational study included 202 Children.
2.3 Study site: The current study is a single-centre, hospital-based investigation conducted from August 2022 to July 2023 in the Department of Pediatric Critical Care, NICE Hospital for Women, Newborns and Children, Hyderabad.
2.4 Inclusion criteria: The study includes patients who require mechanical ventilation, patients who are risk of severe breathing problems, lung issues, brain infections, liver problems, cerebral malaria, head injuries, severe bleeding, unconscious patients and patients with shock and hemodynamic instability.
2.5 Exclusion criteria: The study excludes the children with inborn errors of metabolism, disorders of lactate metabolism, received bicarbonate (alkali) prior to admission elsewhere and who had not provided the written informed parental consent form.
Clearance of hospital's ethical committee and hospital research committees were obtained for this study. On admission detailed relevant historical data including history of inborn errors of metabolism (IEM) and prior treatment with any drugs or bicarbonate was obtained for each child. Detailed clinical examination was carried out. As per PICU protocol, for all Children at admission venous blood gas sample was obtained in pre-heparinized syringe and was sent to lab immediately for analysis. Blood gas was analyzed using automatic analyzer (ABL80 flex blood gas analyzer) and blood lactate was measured. Normal levels were 0.6 to1.6 mmol/L. Further specific investigations were carried out as per patient's clinical condition.
Patients were rigorously monitored by continuous recording of vitals, physical examinations for every 4-6 hours. In case of abnormal laboratory values, repeat investigations were carried out after instituting corrective therapy. This process was carried out till patient was stabilized; metabolic and electrolyte aberrations were corrected. The results of all investigations, further clinical progress including organ dysfunction, need for respiratory support, need for inotropic support was recorded in the proforma.
2.6 Statistical Analysis
The statistical analysis was performed using IBM SPSS V21. Mean ± SD was used to present the quantitative data, cronbach's alpha test was used if the data failed the normality test and the unpaired t-test was used if the data passed. Number (%) was used to present the results of categorical measurements. Fisher's exact test and the chi-square test with continuity correction were used to evaluate the associations between the qualitative variables in all two-by-two tables. A $p< 0.05$ was deemed significant for statistical significance.

3. RESULTS

Table 1 shows that out of 202 cases included in this study 84 were female and 118 were male, the mean age of the female group was 47.65 **months** and male group was 35.97months. Table 1 also shows that out of 202 cases, 141 children (70%) had hyperlactemia (>1.5 mmol/L), 61 children (30%) had normal lactate (0.6-1.5mmol/L).

Table 1 : Age and Gender distribution, Prevalence of hyperlactemia

Gender	N	Mean age (Months)	SD age (Months)		Lactate level ((mmol/L)	N	%
Female	84	47.65	55.67		≤1.5	61	30%
Male	118	35.97	45.10		>1.5	141	70%
Total	202	40.83	49.97		Total	202	100%

Table 2 shows that, of the 141 children with elevated lactate, the majority (34%) had lactate levels between 1.6 and 2.5 mmol/L, followed by 2.6 to 3.5 mmol/L in 32% of children, >4.5 mmol/L in 22% of children, and 3.6 to 4.5 mmol/L in 12% of children.

Table 2: Prevalence of hyperlactemia with severity

Range of lactate (mmol/L)	Frequency (%)
1.6-2.5	48(34%)
2.6-3.5	45(32%)
3.6-4.5	17(12%)
>4.5	31(22%)
Total	141(100%)

Table 3 revealed that among 202 children, infants were major group accounting to 43%. Among 141 children with hyperlactemia (>1.5mmol/L/), 51% were infants, 29% were between 1 to 5 years and 20% were between 6 to 12 years, <1% was between 13-18 years.

Table 3: Age and distribution of lactate levels

Lactate levels	Age Group				Total
	< 1 year	1-5 years	6-12 years	13-18 years	

(mmol/L)					
0.5-1.5	15	28	13	5	61
1.6-2.5	23	18	6	1	48
2.6-3.5	22	14	9	0	45
3.6-4.5	9	2	6	0	17
>4.6	19	7	5	0	31
Total	88	69	39	6	202

Table 4 shows that 83 children had multi organ dysfunction (MODS) involving 2 or more than 2 systems. The prevalence of MODS increased with severity of lactate. In 0.5-1.5 (mmol/L) group only 4 children had MODS and in ≥4.6 (mmol/L) group, 29 children (93.55%) had MODS.

Table 4: Distribution of MODS (Multi organ dysfunction syndrome) with lactate levels

Lactate levels(mmol/L)	MODS+	%	MODS-	%	Total
0.5-1.5	4	6.56%	57	93.44%	61
1.6-2.5	15	31.25%	33	68.75%	48
2.6-3.5	25	55.56%	20	44.44%	45
3.6-4.5	10	58.82%	7	41.18%	17
≥4.6	29	93.55%	2	6.45%	31
Total	83	41.09%	119	58.91%	202

Table 5 demonstrated that out of 202 children, 55 children needed inotropic support. With increasing severity need for inotropic support also increased. In 31 children with > 4.6 mmol/L of lactate, 90% children needed inotropic support, where as children with 0.5-1.5 mmol/L of lactate, only 3% needed inotropic support. Out of 202 children, 79% required ventilatory support. The need for ventilatory support increased with severity of lactate. Individuals with >4.6 mmol/L of lactate 100% of patients needed ventilation support. Among 202 children, 51% children had septic markers as positive which included increased WBC count with neutrophilic predominance. Prevalence of positivity for septic markers increased with severity of lactate levels. In 61 children with 0.5-1.5 mmol/L of lactate only 27% had septic markers positive and out of 31 individuals with >4.6 mmol/L of lactate, 93% children had positive septic markers.

Table 5: Distribution of Inotropic support, Ventilation, Septic markers with lactate levels

		Lactate level (mmol/L)										Total		*P*
		0.5-1.5		1.6-2.5		2.6-3.5		3.6-4.5		≥4.6				
		NO	YES	NO	YES	NO	YES	NO	YES	NO	YES	NO	YES	
Inotropes	N	59	2	43	5	34	11	8	9	3	28	147	55	*p* = 0.000
	%	40.1	3.6	29.3	9.1	23.8	45	5.4	16.4	2.0	50.9	100	100	
Total	N	61		48		45		17		31		202		
	%	30.2		23.8		22.3		8.4		15.3		100		
Ventilation	N	28	33	10	38	3	42	1	16	0	31	42	160	
	%	66.7	20.6	23.8	23.8	7.1	26.3	2.4	10	0	19.4	100	100	
Total	N	61		48		45		17		31		202		
	%	30.2		23.8		22.3		8.4		15.3		100		
Septic markers	N	44	17	30	18	17	28	6	11	2	29	99	103	
	%	44.4	16.5	30.3	17.5	17.2	27.2	6.1	10.7	2	28.2	100	100	
Total	N	61		48		45		17		31		202		
	%	30.2		23.8		22.3		8.4		15.3		100		

Table 6 explains 202 children were divided in to 3 groups depending on duration of hospital stay as 1-3days, 4-6 days and >7 days. Severity of lactate was compared to the duration of hospital stay. Though group with >4.6 mmol/L lactate had normal duration of stay, it was because the children had mortality also. But 30.2 % of children with 0.5-1.5 mmol/L of lactate had lesser duration of hospital stay of 1-3 days followed by 23.8% of children with 3.6-4.5 mmol/L of lactate had a duration of 4-6 days of hospital stay and >7 days of hospital stay was observed in 32.70% of individuals with lactate ≥4.6 mmol/L. Maximum survivors (34.7%) were recorded with lactate levels of 0.5-1.5 mmol/L and least (3.5%) were identified with ≥4.6 mmol/L.

Table 6: Distribution of Hospital Stay and Outcome with lactate levels

Lactate level (mmol/L)		Hospital stay (Days)			Outcome		Total
		1 TO 3	4 TO 6	> 7	Non survivors	Survivors	
0.5-1.5	N	44	14	3	1	60	61
	%	67.7	16.5	5.80	3.4	34.7	30.2
1.6-2.5	N	10	32	6	0	48	48
	%	15.4	37.6	11.50	0	27.7	23.8
2.6-3.5	N	1	28	16	1	44	45
	%	1.5	32.9	30.80	3.4	25.4	22.3
3.6-4.5	N	2	5	10	2	15	17
	%	3.1	5.9	19.20	6.9	8.7	8.4
≥4.6	N	8	6	17	25	6	31
	%	22.3	17.1	32.70	86.2	3.5	15.3
Total	N	65	85	52	29	173	202
	%	100	100	100	100	100	100

Table 7 shows that sensitivity and specificity of differing concentrations of blood lactate to predict in hospital mortality in critically ill children. Blood lactate showed a sensitivity

of 93.60% and a specificity of 89.70% for predicting in-hospital mortality at a value of 4.05 mmol/L.

Table 7: Predicting performance of admission blood lactate for in-hospital mortality

	AUC	95% CI	*P*	Cut off	Sensitivity	Specificity
Lactate levels (mmol/L)	0.951	0.887-1.0	0.00	4.05	93.60%	89.70%

4. DISCUSSION

In critically ill children, a high blood lactate level at PICU admission predicts in-hospital mortality. Data on blood lactate levels in critically ill children are presented in this study, which also shows a significant correlation between in-hospital mortality and the blood lactate level at admission to a general medical PICU. According to the current single-centric study, children admitted with hyperlactemia are not significantly impacted by age or gender, which is consistent with the studies of Abbas Q et al [7].

The incidence of hyperlactemia was found to be 70% in our study in contrast to the previous study conducted by Ozlem et al. reported a prevalence of 77.5%, align with our findings [8]. Conversely, a more recent study by Vinayak K et al observed a lower prevalence rate of hyperlactemia, yet it is important to note that the sample size of this study was comparatively smaller than that of ours [9]. The average age of the children included in this study was 40.83 months and hyperlactemia being notably higher in infants. In a comparative study conducted by Jat et al. the average age was found to be 16.4 months, which was lower than our study and also indicated that infants experienced severe hyperlactemia compared to other age groups, aligning with our findings [10].

The incidence of MODS increased with severity of lactate. In this study, children with severe lactate levels had multi organ dysfunction (MODS) involving two or more systems. Similarly, Channanayaka et al also concluded that higher lactate was associated with MODS [11]. But in contrast to our study Hatherill M et al observed no association between lactate to MOSF (Multi organ system failure) score [12].

In our research, it has been established that children exhibiting elevated lactate levels require a greater degree of inotropic support compared to those with lower lactate levels. It was observed that the requirement for ventilation support was proportional to the severity of lactate in our study. Murat Basaran et al. demonstrated a statistically significant correlation between mean lactate level and the inotropic score ($p < 0.0001$), lactate levels and ventilation needed ($p<0.001$) [13]. Jansen et al. also found that patients in the intensive care unit with low lactate clearance levels required less ionotropic support and fewer days of mechanical ventilation support [14]. These results are in concordance with the conclusions drawn from our research. In this study it was also observed that positive septic markers were inversely correlated with the severity of lactate levels. Conversely,studies conducted by de Souza et al and Odeta et al

reported a higher prevalence of sepsis with the severity of lactate compared to our findings [15, 16].

Bengt et al., reported that children with elevated lactate levels tended to have a longer hospital stay [17]. In our study, the group with severe lactate levels experienced a longer hospital stay and the group with low lactate levels had a shorter hospital stay. Our findings were also consistent with those of research by Richa Choudhary et al [18].

In our study, it was observed that lactate levels act as a reliable marker for predicting outcomes in hospitals. As the severity of lactate levels increases, there was a corresponding decline in survival rates. Koliski et al observed that patients with elevated blood lactate levels were more likely to die, whereas those with lower lactate levels had a higher chance of survival, these results were congruent with the outcomes observed in our research [19].

Current study shows that, the most effective threshold for the prediction of in-hospital mortality among critically ill children seems to be blood lactate concentration of 4.05 mmol/L which was associated with a sensitivity of 93.60% and a specificity of 89.70%. Our outcomes aligned closely with a study on children admitted to the pediatric intensive care unit (PICU) with septic shock diagnoses, whose blood lactate concentration was exceeding 4 mmol/L and proved to be a reliable indicator of mortality [20]. Lactate, acts as a useful marker for disease mortality and severity but an unreliable marker of tissue hypoxia/hypoperfusion in critically ill patients [21]. Analysis of our current data, in conjunction with prior research, indicates that infants who present to the hospital with elevated levels of blood lactate upon admission necessitate meticulous observation of clinical decline. Conversely, infants with blood lactate levels within the normal range should be subjected to additional scrutiny of blood lactate levels, as repeated lactate measurements might yield more accurate prognostic insights [22].

5. CONCLUSION

Blood lactate is a useful early predictor in identifying critically ill children who are at high risk of death in the pediatric intensive care setting. Increased blood lactate levels at admission were significantly associated with mortality and morbidity in critically ill children. Increased blood lactate levels at admission were also substantially correlated with the incidence of multiorgan dysfunction syndrome (MODS), need for ventilatory and inotropic support and the length of hospitalization in critically ill children.

Ethical Approval:

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

Disclaimer (Artificial intelligence)

We hereby declare that NO generative AI technologies such as Large Language Models and text to image generators have been used during writing or editing of this manuscript.

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