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## Lactate Clearance at 24 of Hours as Predictors of Outcome in Children with Shock

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### Abstract

**Background:** Monitoring of tissue perfusion markers like lactate and its clearance is necessary for early recognition of shock in sick children which will enable the caregiver to initiate an appropriate and timely therapy.

**Objective:** To study the blood lactate clearance at 24 hours of admission and its prognostic importance in predicting the outcomes in children with shock.

**Methods:** This was a “prospective observational” study, conducted in NICU and PICU at Sparsh multispeciality hospital, Bhilai and Jagannath hospital, Bhubaneswar over 80 children presented with shock, from January 2018 to December 2020. Blood lactate level at admission and after 24 hours were evaluated and lactate clearance was compared with mortality. **Results:** In lactate clearance >20% group, mortality was only 3.8% wherein LC<20% group, mortality was 52.17%. In Lactate clearance < 10% group, inotropes (p-0.0002), ventilator support (p-0.0015) were needed more than Lactate clearance > 20% group. When initial lactate >6mmol/dl, 35% of neonates died in comparison to 11.76% in the group having initial lactate <6mmol/dl. The

average lactate clearance among the survivors was 28.35% and among the non-survivors was 5.73% ( $P < 0.001$ ). AUC between lactate clearance and mortality was 0.73 suggestive of a good correlation. **Conclusion:** Lactate clearance of less than 10% at 24 hours of admission showed a good correlation in predicting the mortality in children with shock.

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**Keywords:** Lactate, lactate clearance, morbidity, mortality, children with shock

## **Introduction**

Lactate has been considered as a marker of tissue hypoxia and ischemia, hence reflects the microcirculatory status of the body. Normalization of blood lactate level is associated with improved survival in many studies conducted in adults (Aduen, J. 1994) as well as in children and newborns (Sauaia, A. 1994, Hebert, P. C et al 1993, Hatherill et al 1997). Lactic acid levels at the moment of the patient's admission to the ICU and its poor clearance have a positive correlation with the risk of death (Shimeet al 2001). Serial measurements of lactate concentrations are valuable in assessing the prognosis and response to treatment (VINCENT et al 1983).

## **Aims and objectives**

To study the blood lactate clearance at 24 hours of admission as a predictor of mortality in sick children.

## **Material and Methods**

**Centre For Study-** The study was conducted as a multicenter study at NICU and PICU of Sparsh multispecialty hospital, Bhilai and Jagannath Hospital, Bhubaneswar.

**Period-** January 2018 to December 2020

**Type of Study-** A “prospective observational” study conducted on data collected during the above-mentioned period from the intensive care units.

**Inclusion Criteria-** Sick children with shock, Age: day 1 to 1 year of life admitted to NICU and PICU, initial blood lactate  $> 2$ mmol.

**Exclusion Criteria-** Neonates with congenital abnormalities, children with metabolic diseases, Children died within 24 hours of admission, went LAMA, Post-surgical cases.

Blood lactate levels were obtained as a baseline at admission to the intensive care unit and then at 24 h of intensive care unit stay. The lactate

clearance in the study is defined by the equation  $([\text{lactate initial} - \text{lactate at 24 hrs}]/\text{lactate initial}) \times 100\%$ . Lactate clearance was determined at 24 hrs of admission. The primary outcome measured was mortality. Secondary outcomes measured were the duration of mechanical ventilation, inotropic requirement, and duration of stay at ICU. The information collected was tabulated and the data was analyzed using the software SPSS 18 for windows. P-value <0.05 was taken as statistically significant.

## Results

Among 80 sick patients, 64 survived and 16 deaths occurred. The weights of the enrolled patients were ranged from 0.90 to 11.98kgs with an average of  $4.467 \pm 0.70$ kgs. Among the survivors, average day of stay was  $8.35 \pm 5.47$  which was less than the non-survivors ( $11.36 \pm 5.51$  days).

Lactate at admission	Total No. of Patients	Mean lactate value	inotrope support	Death
2 –6mmol/dl	51(63.75%)	$3.95 \pm 1.14$	25(49%)	6(11.76%)
6-10mmol/dl	18(22.5%)	$7.74 \pm 0.95$	16(88.88%)	5(27.77)
>10mmol/dl	11(13.75%)	$13.66 \pm 2.95$	10(90.90%)	5(45.45)
P value		0.0001	0.010	0.001

**Table 1-**lactate levels at admission and outcomes

Among the 51 patients having initial serum lactate value 2-6mmol/dl, 25 patients required inotrope and vasopressor support, death occurred in 11.76%. In 11 patients, where initial lactate was >10 mmol/dl, 90.90% of them required inotrope support and 5 of them did not survive.

Group	LAC-0	LAC-24	LC(%)
Survivor	$5.41 \pm 2.65$	$3.78 \pm 1.73$	$28.35 \pm 20.47$
Non survivor	$9.08 \pm 5.57$	$9.57 \pm 4.99$	$5.73 \pm 11.71$
P value	<0.001	<0.001	<0.001

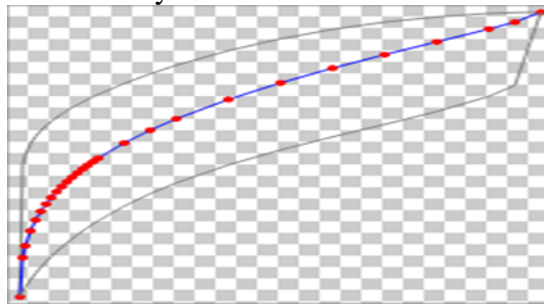
**Table 2-** lactate clearance in survivors and non-survivors

Among the survivors, the average initial lactate was  $5.41 \pm 2.65$ mmol/dl which was much less than the non-survivor group ( $9.08 \pm 5.57$ ). Mean lactate among the non-survivors was also high ( $9.57 \pm 4.99$ ). Mean lactate clearance at 24 hours among the survivors was 28.35% and among non survivors, it was only 5.73%.

LC	N	Death	RR	Mechanical ventilation	RR	I&V Support	RR	Duration of stay
<10%	29	14(48.27%)	12.31	26(89.65%)	1.43	25(86.20)	1.69	12.72±7.31
10-20%	9	1(11.11%)	0.52	4(44.44%)	0.58	3(33.33%)	0.49	7.77±3.52
>20%	42	1(2.38%)	0.06	28(66.66%)	0.88	23(54.76%)	0.74	9.97±4.04
P value	<0.001 HS		0.014		0.003		P=0.046	

**Table 3-**clinical outcomes of patients based on lactate clearance

In the group, lactate clearance less than 10% death occurred in 14 sick patients among 29. The relative risk was found to be 12.31. 26(89.65%) patients required mechanical ventilation with a relative risk of 1.43, 25(86.20%) patients required inotrope and vasopressor support. The duration of stay was 12.72 days. In the group where lactate clearance was 10% to 20%, only 1(11.11%) neonate died among 9 neonates. 4(44.44%) neonates required mechanical ventilation and 3(33.33%) of them required inotrope and vasopressor support. The mortality at lactate clearance more than 20% was only 2.38%, 28(66.66%) out of 42 patients required mechanical ventilation and 23(54.56%) required inotrope and vasopressor support. The duration of stay was 9.97 days.



**Figure 1-**ROC curve between lactate clearance and outcome

ROC curve analysis for the 24-hour lactate clearance <10% showed an area under the curve (AUC) of 0.71 (P<0.05), suggesting that the 24-hour lactate clearance measurement had good strength as a predictor of outcomes.

LC in Metabolic Acidosis	Not survived	Survived	Total	Risk ratio	P-value
<20%	12(52.17%)	11(47.83%)	23(100%)	13.56	0.0092
>=20%	1(3.8%)	25(96.20%)	26(100%)		

**Table 4-** Lactate clearance in presence of metabolic acidosis

In presence of metabolic acidosis, lactate clearance  $<20\%$  have 13.56 times more risk of not surviving than LC  $\geq 20\%$ . Only one patient did not survive with lactate clearance more than 20% with metabolic acidosis.

## Discussion

Blood lactate levels up to 2mmol/L are considered normal for adult patients which are regarded as the reference value. Studies by Jat, K. Ret al (2011) have shown that Initial lactate values of more than 5 mmol /dl are significantly associated with negative outcomes in pediatric patients with septic shock. Deshpande et al (1997) found that serial measurements of blood lactate are more useful than a single value. Point measurement of serum lactate does not reflect the events that occur after 24 to 48 hours of hospitalization. Interpretation of single lactate measurements has limitations as an increased level might indicate other mechanisms of hyperlactatemia like increased lactate production via catecholamine-driven pathways or decreased lactate clearance due to hepatic dysfunction. This might not necessarily point towards the ongoing hypoperfusion or hypoxia. This study shows that patients presented in shock having initial serum lactate value 2-6mmol/dl, 49% of them required inotrope and vasopressor support, death occurred in 11.76%. On the other hand, among 11 patients whose initial lactate was  $>10$  mmol/dl, 90.90% of them required inotrope support and death occurred in 45.45% of these patients. This suggests mortality and morbidity are significantly associated with higher initial lactate ranges. Among the survivor group, the average initial lactate was  $5.41 \pm 2.65$  mmol/dl which was much less than the non-survivor group.

Clearance of the initial lactate level depends on both the disease process and ongoing intervention. This is a more promising than initial lactate level. Studies in adult patients with shock showed lactate clearance of  $< 10\%$  was related to mortality. Marty et al (2013) suggested that during the first 24 hr in the ICU, lactate clearance was the best parameter associated with a 28-day mortality rate in septic patients. Out of 80 patients in our study, 64 survived and 16 died. Mean lactate clearance at 24 hours among the survivors was 28.35% and among non-survivors, it was only 5.73%. Those who died, could not clear their lactate well as compare to the survivors. Clearing lactate-directed therapy is being investigated among adults and the pediatric population. In septic patients, a lactate clearance directed therapy in the first 6 hours appeared as efficient as ScvO<sub>2</sub> by Jones et al (2010). Jansen et al (2010) suggested lactate clearance directed therapy at 8 hours reduced mortality rate in adult ICU population than who treated with standard therapy. The absence of lactate clearance to less than 20% after 8 hours of resuscitation leads to therapy intensification even in those who reach standard hemodynamically target in studies done by Well et al(1970). Less than 30 % clearance among

the pediatric population within the first 24 hours of admission correlated significantly with mortality as shown by Trzeciak et al(2007). In comparison to these studies, the present study demonstrates mortality was only 2.38% in the high lactate clearance group (>20%). Among the 29 sick patients having lactate clearance less than 10%, death occurred in 48.27% which was significantly higher than the lactate clearance>20%. ROC curve analysis for the 24-hour lactate clearance <10% showed an area under the curve (AUC) of 0.71 (P<0.05), suggesting that the 24-hour lactate clearance measurement has good strength as a predictor of outcomes. In presence of metabolic acidosis, the lactate clearance <20% has 13.56 times more risk of not surviving than LC >20%. Only one patient didn't survive with lactate clearance more than 20% with metabolic acidosis due to complications related to viral myocarditis.

Kapoor et al (2016) suggested that patients with lactate clearance of more than 10% from its baseline value in 6 hours, required less ventilator support, less inotrope, and vasopressor therapy, and had less duration of ICU stay. In the present study, 26 (89.65%) patients required mechanical ventilation, 25(86.20%) patients required inotropes and vasopressor support in the low lactate clearance group(<10%) which is significantly higher than sick children who cleared lactate >10% at 24 hours. High lactate clearance may indicate a resolution of hypoxia at the cellular level. As demonstrated here, lactate clearance at 24 hours seems to be a sensitive parameter to predict negative outcomes.

## Conclusion

The prognostic value of serial serum lactate monitoring at 24 hours for predicting morbidity and mortality in children with shock is confirmed in this study. The initial hyperlactatemia (>6mmol/dl) is significantly associated with mortality and a higher need for mechanical ventilation, inotrope support, and prolonged stay. Lactate clearance was significantly higher in the survivor group. Lactate clearance of less than 10% or an increase in lactate value at 24 hours could predict mortality in children with shock. High Lactate clearance (>20 %) at 24 hours of admission can be used as a marker of a good outcome with a good correlation irrespective of diagnosis. In presence of metabolic acidosis, lactate clearance <20% has 13.56 times more risk of not surviving than LC >=20%. This study recommends lactate clearance can be used for stratifying mortality risk among children with shock.

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