

Lactate Clearance as a Marker of Mortality in Pediatric Intensive Care Unit

A MUNDE, N KUMAR, RS BERI AND JM PULIYEL

From Department of Pediatrics, St. Stephens Hospital, Tis-Hazari, Delhi, India.

Correspondence to:

Dr Nirmal Kumar,

4, Rajpur Road, Qtr. B-2, Tis-Hazari,

Delhi 110 054, India.

nsk9_2000@yahoo.com

Received: January 15, 2014;

Initial review: January 20, 2014;

Accepted: May 13, 2014.

Objectives: To correlate lactate clearance with Pediatric Intensive Care Unit (PICU) mortality. **Methods:** 45 (mean age 40.15 mo, 60% males) consecutive admissions in the PICU were enrolled between May 2012 to June 2013. Lactate clearance (Lactate level at admission – level 6 hr later \times 100 / lactate level at admission) in first 6 hours of hospitalization was correlated to in-hospital mortality and PRISM score. **Results:** Twelve out of 45 patients died. 90% died among those with delayed/poor clearance (clearance $<$ 30%) compared to 8.5% in those with good clearance (clearance $>$ 30%) ($P < 0.001$). Lactate clearance $<$ 30% predicted mortality with sensitivity of 75%, specificity of 97%, positive predictive value of 90%, and negative predictive value of 91.42%. Predictability was comparable to PRISM score $>$ 30. **Conclusion:** Lactate clearance at six hours correlates with mortality in the PICU.

Keywords: In-hospital mortality, Lactate clearance, PRISM score.

Hyperlactatemia is an indicator of inadequate tissue perfusion, particularly in sepsis [1]. It reflects severity of illness with significant prognostic implications [2]. The severity and duration of lactic acidosis in critically ill patients correlates with overall oxygen debt, and increased production [3,4]. However, a single lactate measurement has not been correlated to mortality consistently [5].

Lactate clearance is the rate of fall in lactate after resuscitation is started. This has shown more promise in predicting mortality. Two studies in adult patients with shock showed that lactate clearance of $<$ 10% was related to mortality [5,6]. There are no pediatric studies looking at lactate clearance and mortality although Hatheril, *et al.* [7] showed that persistent hyper-lactatemia at 24 hours ($>$ 2 mmol/dL) was associated with mortality. We investigated whether lactate clearance in the early period of resuscitation (first 6 hours of hospitalization) could help predict mortality in pediatric patients.

METHODS

Admissions to the PICU (aged $>$ 1 month and $<$ 13 years) were studied between May 2012 and June 2013 after obtaining informed written consent from parents. Children with inborn error of metabolism and trauma were excluded. The study was approved by the hospital ethics committee. As a pilot study, a convenience sample of 45 patients admitted consecutively was enrolled. Heparinized syringe was used to collect venous blood. Lactate estimation was done by Radiometer Copenhagen

ABL 555 blood gas analyzer.

Lactate levels were estimated at admission and after six hours of admission and the clearance was calculated as follows: Lactate clearance = [Initial Lactate - Current Lactate] \times 100 / Initial Lactate].

A positive value denotes clearance of lactate, whereas a negative value denotes an increase in lactate after intervention. Routine ICU care and investigations were performed and Pediatric Risk of Mortality (PRISM) score was calculated. In-hospital mortality was the primary outcome of interest.

Survivors and non-survivors were compared by the Mann-Whitney test for continuous variables and by Fisher's exact test for categorical variables. For non-parametric data, pair-wise comparisons were made using Wilcoxon's signed-rank test. For continuous variable, we used t-test. A P value $<$ 0.05 was taken as statistically significant. SPSS version 16.0 was used.

RESULTS

Out of 45 children (mean age 40.15, range 1-144 months, M:F ratio 1.5:1), twelve died. The initial lactate was not significantly different between those who died and those who survived [8.44 (3.27) vs 7.29 (3.31), $P = 0.18$], but clearance at 6 hours was significantly lower in those who died (-4.01%) than those who survived (55.53) ($P < 0.001$). The mean (SD) PRISM score was also higher in those who died compared with those who survived [43.6 (7.27) vs. 21.7 (9.2), $P < 0.001$].

Where lactate clearance was <30% at 6 hours, nine out of ten died. In those with clearance >30% only three out of thirty-five died. ROC curve analysis for mortality prediction was 0.97 ($P < 0.001$) (**Fig. 1**). Three children died within 24 hours. Mean (SD) duration of hospital stay in those with lactate clearance >30% was 18.5 (8.44) d (range 3-40), against 3.1 (2.61) d (range 1-9) in those with clearance <30%.

An inverse relationship was observed between lactate clearance and PRISM score (**Table I**). Lactate clearance <30% at six hours predicted mortality with sensitivity of 75%, specificity of 97%, PPV 90%, NPV 91.42%. Observed and expected mortality was almost similar in those having PRISM score of >30.

DISCUSSION

Lactate clearance at 6 hours was significantly associated with mortality as was a PRISM score >35. The ROC curve shows mortality prediction of lactate clearance was 0.977.

The duration of stay was longer in those with good clearance because of early mortality in the ones with poor clearance. There were very few survivors among those with poor clearance to allow us to compare duration of stay in survivors in the two groups.

High admission lactate was a significant independent predictor of mortality in adult patients admitted to ICU [8-10] but it could not be replicated in other studies [6,11].

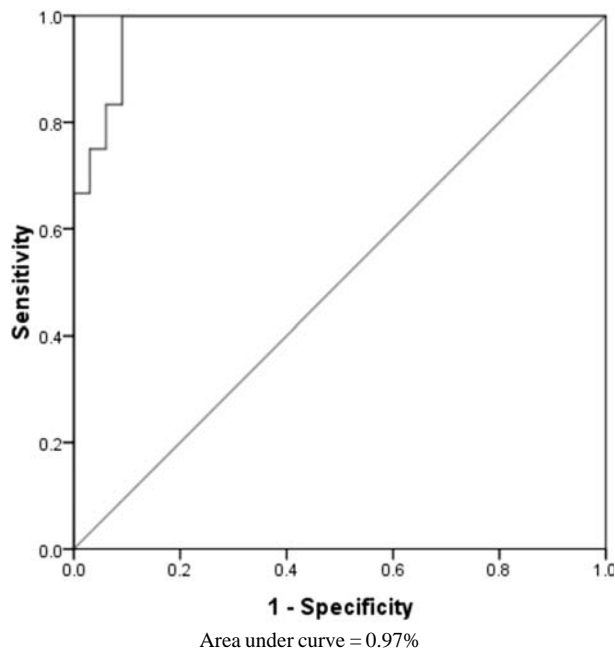


FIG.1 ROC curve for lactate clearance at 6 hours in relation to mortality prediction.

TABLE I CORRELATION OF PRISM SCORE WITH LACTATE CLEARANCE IN RELATION TO OBSERVED AND EXPECTED MORTALITY

PRISM score	Number of patients	Lactate clearance at 6 hrs (%)	Observed mortality (%)	Expected mortality (%)
01-05	0	–	–	09
06-10	4	60.9	–	15
11-15	5	51.0	–	23
16-20	6	54.4	–	35
21-25	9	61.3	–	49
26-30	3	48.0	–	63
31-35	6	42.3	33.3	75
>35	12	0.7	83.3	>75

Studies have suggested the value of monitoring for lactate clearance with hypo-perfusion [6,7]. One of these studies found a 41% higher mortality rate among those subjects who failed to reach a lactate clearance of 10% when compared with those that effectively cleared lactate (60% vs. 19% mortality) during the early resuscitative period. The only study in pediatric age group conducted by Hatheril, *et al.* [7], showed that persistent hyper-lactatemia >2 mmol/L after 24 hours was associated with 93% mortality, as compared to 30% in those children whose lactate level had normalized. Following the study in adults, we used lactate clearance at 6 hours [6]. We found that we can predict mortality as early as 6 hours. In our study PPV, NPV and ROC curve analysis for mortality prediction at 6 hours of lactate clearance are comparable to Hatheril, *et al.* [7] findings at 24 hours.

We found that a lactate clearance $\leq 30\%$ at six hours and PRISM score more than 30 have high prediction for mortality. Lactate clearance can probably be used as a screening tool to predict adverse outcome. We have provided stratification and cut-off values of lactate clearance which need validation by more studies with larger samples.

Acknowledgement: Dr DK Shukla for data analysis.

Contributors: AM: Design, Manuscript writing, Data-Collection and Data Interpretation; NK: Concept, Design, Manuscript drafting and guarantor of the study; RSB: Manuscript writing and JMP: Manuscript Drafting and Design of the study.

Funding: None; *Competing interest:* None stated.

REFERENCES

1. Weil MH, Afifi AA. Experimental and clinical studies on lactate and pyruvate as indicators of the severity of acute circulatory failure (shock). *Circulation*. 1970;41:989-1001.

WHAT THIS STUDY ADDS?

- Lactate Clearance <30% at 6 hours of admission predicts mortality in PICU admitted patients.
- Lactate clearance < 30% at 6 hours correlates well with PRISM score for mortality prediction.

- Bone RC, Balk RA, Cerra FB, Dellinger RP, Fein AM, Knaus WA, *et al.* Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis – The ACCP / SCCM Consensus Conference Committee. *Chest.* 1992;101:1644-55.
- Bakker J, Gris P, Coffernils M, Kahn RJ, Vincent JL. Serial blood lactate levels can predict the development of multiple organ failure following septic shock. *Am J Surg.* 1996; 171:221-6.
- Bernardin G, Pradler C, Tiger F, Deloffre P, Mattei M. Blood pressure and arterial lactate level are early indicators of short-term survival in human septic shock. *Intensive Care Med.* 1996;22:17-25.
- Arnold RC, Shapiro NI, Jones AE, Schorr C, Pope J, Casner E, *et al.* Multi-center study of early lactate clearance as a determinant of survival in patients with presumed sepsis. *Shock.* 2009;34:36-40.
- Nguyen HB, Rivers EP, Knoblich BP, Jacobsen G, Muzzin A, Ressler JA, *et al.* Early lactate clearance is associated with improved outcome in severe sepsis and septic shock. *Crit Care Med.* 2004;32:1637-42.
- Hatherill M, McIntyre AG, Wattie M, Dellofer P, Murdoch IA. Early hyperlactatemia in critically ill children. *Intensive Care Med.* 2000;26:314-8.
- Khosravani H, Shahpori R, Stelfox HT, Kirkpatrick AW, Laupland KB. Occurrence and adverse effect on outcome of hyperlactatemia in the critically ill. *Critical Care.* 2009;13:R90.
- Smith I, Kumar P, Molloy S, Rhodes A, Newman PJ, Groundi RM, *et al.* Base excess and lactate as prognostic indicators for patients admitted to intensive care. *Intensive Care Med.* 2001;27:74-83.
- Jansen TC, Bommel JV, Schoonderbeek FJ, Sleswijk visser SJ, Klooster JM, Lima AP, *et al.* Early lactate-guided therapy in intensive care unit patients: a multicenter, open-label, randomized controlled trial. *Am J Respir Crit Care Med.* 2010;182:752-61.
- Del Portal DA, Shofer F, Mikkelsen ME, Dorsey PJ, Gaieski DF, Synnestvedt M, *et al.* Emergency department lactate is associated with mortality in older adults admitted with and without infections. *Acad Emerg Med.* 2010;17:260-8.