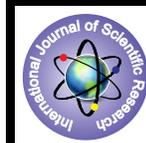


## Hyperlactatemia in critically ill newborns on presentation: Predictors, severity and outcome analysis



### MEDICAL SCIENCE

KEYWORDS : lactate, critically ill, newborns

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### ABSTRACT

#### Aim

To estimate levels of arterial lactate in critically ill newborns within 24 hours of hospitalization and to determine the severity and predictors of hyper-lactatemia and their effects on neonatal outcome.

#### Patients and Methods

Seventy-three neonates admitted to a tertiary care teaching hospital over a duration of 6 months requiring arterial blood gas analysis within the first 24 hours of hospitalization were enrolled in the study. Arterial lactate levels were estimated as a part of blood gas analysis. Hyperlactatemia was defined as lactate levels  $>2.5$  mmol/l while severe hyperlactatemia was a value  $>4.0$  mmol/l. Adverse outcome was defined as expiry or NICU stay of  $>7$  days.

#### Results

Hyperlactatemia was seen in 71.2%(52/73); levels were severe in 32.9%(24/73). Significant association was seen between early ( $<24$  hours of age) onset of symptoms ( $p=0.019$ ) and hyperlactatemia. Female sex ( $p=0.034$ ) and presence of hypoglycemia ( $p=0.052$ ) were significantly associated with presence of severe hyperlactatemia and absence of seizures ( $p=0.038$ ) with absence of the same. SNAP scores ( $p=0.014, 0.002$ ), were significantly associated with presence of both hyperlactatemia and severe hyperlactatemia respectively. Absence of severe hyperlactatemia ( $p=0.0001$ ) was significantly associated with good outcome.

#### Conclusion

Hyperlactatemia on admission correlates well with SNAP scores in critically ill newborns and its absence may predict good neonatal outcome.

### Introduction

Lactate is a glycolytic product that is either used within the cells or transported through the interstitium and vasculature to adjacent and anatomically distributed cells for utilization<sup>1</sup>. Both the production and the removal of lactate are active functions of every tissue of the body.

It has been used as a marker of cellular hypoxia and tissue malperfusion, though it is also found in inherited disorders of hepatic gluconeogenesis, disorders of pyruvate metabolism, and functional defects in the mitochondrial electron transport chain<sup>2</sup>. Elevated lactate levels in critically ill patients have been found to be determinants of poor prognosis.

Blood lactate concentrations are more easily obtained and measured than other monitoring variables, even before any invasive monitoring, such as mean arterial blood pressure, is available<sup>1</sup>. Lactate is now routinely measured by many blood gas analysers.

This study was done to find out the severity, predictors and outcome of hyperlactatemia in critically ill newborns on presentation to the hospital, by estimating arterial blood lactate levels during blood gas analysis.

### Patients and Methods

The study was done in a Level III NICU (Neonatal Intensive Care Unit) of a tertiary care teaching hospital. Critically ill neonates admitted to the NICU, who required arterial blood gas analysis during the first 24 hours of their hospitalization were included. Requirement of arterial blood gas analysis depended on the clinical discretion of the attending pediatrician. Neonates with major congenital malformations and those whose parents did not consent were excluded from the study. Ethical clearance was obtained from the institutional ethics committee.

Arterial lactate was estimated by the "OPTI CCA-TS2 Blood Gas and Electrolyte Analyzer". Hyperlactatemia was defined as lactate levels  $>2.5$  mmol/l while severe hyperlactatemia was levels  $>4.0$  mmol/l. Adverse outcome was defined as expiry or NICU stay of  $>7$  days. SNAP (Score for Neonatal Acute Physiology) scores were calculated for each of the patients<sup>5</sup>.

Data was collected on a standardized data collection sheet and

was later entered into MS-EXCEL spreadsheet. Analysis was done using Epi-info software version 3.5.1, with help from a biostatistician.

### Results

Ninety seven neonates were admitted in the hospital over 6 months. Of these 73 neonates were critically ill, requiring arterial blood gas analysis within 24 hours of hospitalization, and were included in the study. Their clinical profile and demographic details are mentioned in Table 1. Most common primary diagnosis was sepsis (36/73=49.3%) followed closely by perinatal asphyxia (27/73=36.9%).

Comparison of means was done by ANOVA and comparison of proportions was done by Chi-square test. Mean pH value was 7.33. Mean lactate value was 3.84 mmol/l. Hyperlactatemia was seen in 71.2%(52/73); levels were severe in 32.9%(24/73). Early ( $<24$  hours of age) onset of symptoms ( $p=0.019$ ) was found to be significantly associated with presence of hyperlactatemia. Female sex ( $p=0.034$ ) and presence of hypoglycemia ( $p=0.052$ ) were found to be significantly associated with presence of severe hyperlactatemia. Absence of seizures ( $p=0.038$ ) was significantly associated with absence of severe hyperlactatemia. Mean SNAP score was 21. SNAP score was significantly associated with both, presence of hyperlactatemia ( $p=0.014$ ) and presence of severe hyperlactatemia (0.002).

Thirty eight out of 52 neonates (73.1%), who had hyperlactatemia on presentation had a poor outcome. Of these, 22 expired and 16 had a prolonged stay in the NICU. Absence of severe hyperlactatemia ( $p=0.0001$ ) was significantly associated with good outcome.

**Table 1. Descriptive data of 73 patients**

Factor	Number of patients (n)	Percentage (%)
Male sex	48	65.8
Urban address	40	54.8
Caesarean delivery	28	38.4
Delayed cry at birth	32	43.8
Onset age $>24$ hrs	15	20.5

Delayed presentation (>24 hrs after onset)	14	19.2
Preterm	29	39.2
Low birth weight	50	68.5
RDS score>6	30	41.1
Oliguria	12	16.4
Hypotension	26	35.6
Hypothermia	34	45.6
Hypoglycemia	6	8.2
Seizures at presentation	12	16.4
Respiratory support required	69	94.5
Inotropic support required	39	53.4
Outcome measures		
Hyperlactatemia	52/73	71.2
Severe hyperlactatemia	24/73	32.9
Expiry	22/52	42.3
Prolonged hospital stay (>7 days)	16/52	30.7
Poor outcome	38/52	73.0

### Discussion

We analyzed data of 73 neonates. One study<sup>6</sup> had analyzed the acid base status of 50 critically ill newborns. No control group was taken as it would have been unethical to do arterial puncture in healthy neonates.

The most common primary diagnosis in neonates admitted was sepsis followed by perinatal asphyxia. The study<sup>6</sup> also showed higher lactate levels and hypoalbuminemia in sepsis. Mechanism of increased lactate production in both sepsis and perinatal asphyxia is increased glycolytic flux, secondary to hypermetabolism in the former, and to hypoxia in the latter respectively. Ortega et al<sup>7</sup> also concluded that lactate quantification is a useful indicator in neonatal asphyxia.

Studies in past have studied acid base imbalance in common pediatric diseases<sup>6</sup> and relation between common acid base parameters and blood lactate concentrations, and their prognostic importance in sick, ventilated neonates<sup>8</sup>. None of the studies in past has tried to determine *predictors* of hyperlactatemia in critically ill newborns, to the best of our knowledge. Early (<24 hours

of age) onset of symptoms ( $p=0.019$ ) was found to be significantly associated with presence of hyperlactatemia. Female sex ( $p=0.034$ ) and presence of hypoglycemia ( $p=0.052$ ) were found to be significantly associated with presence of severe hyperlactatemia. Absence of seizures ( $p=0.038$ ) was significantly associated with absence of severe hyperlactatemia.

Hyperlactatemia was seen in 71% of our patients. It was seen in more than half of the cases in a study by Lekhwaniet al<sup>6</sup>. Post-operative hyperlactatemia was seen in 38% of a cohort of 68 patients who underwent isolated atrial septal defect repair at Arkansas Children's Hospital between January 2001 and March 2006. In a study of adult patients, hyperlactatemia was present in 199 of 653 (30.47%) patients, admitted over 15 months to an 8-bed general ICU of a tertiary care hospital in India<sup>10</sup>. Some discrepancy may be attributable to the difference in the value of lactate taken as cut off for defining hyperlactatemia.

Mean SNAP score was found to be 21. It was 9 (range 0-41 points), in a study on 173 neonates within the 1st day of hospitalization. Elevated serum lactates were found even with SNAP as low as 8 points in this study<sup>11</sup>. SNAP score was significantly associated with both, presence of hyperlactatemia and presence of severe hyperlactatemia in our study also.

Thirty eight out of 52 neonates (who had hyperlactatemia on presentation) had a poor outcome, 22 expired and 16 had a prolonged stay in the NICU. Significant correlation between mortality and critical values of lactate was observed<sup>6</sup> but no such association with mortality was seen in our study.

Absence of severe hyperlactatemia was significantly associated with good outcome in this study. Nordstrom et al<sup>12</sup> also concluded that lactate is good at predicting neonatal outcome.

### Limitations and directions for future research

More studies with variable sample sizes need to be done to definitively conclude, predictors of hyperlactatemia, since, it is only the first study of its kind. Correlation with serial lactate levels is also desirable to look for any variation in predictors and outcome.

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