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Original Research Article

Umbilical cord blood lactate dehydrogenase as a predictor of short-term outcomes in term neonates with meconium aspiration syndrome

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ABSTRACT

Background: Meconium aspiration syndrome (MAS) is an important cause of respiratory problems in term newborns. Early identification of infants at risk for adverse outcomes is essential for timely intervention. Umbilical cord blood lactate dehydrogenase (LDH), a marker of tissue hypoxia and cellular injury, may serve as an early prognostic biomarker in MAS.
Methods: A hospital-based cross-sectional observational study was conducted over 18 months at a tertiary care hospital in Mysore. One hundred term newborns with MAS born through meconium-stained amniotic fluid (MSAF) were enrolled. Umbilical cord blood samples collected immediately after birth were analysed for LDH levels using the UV assay method. The demographic, perinatal, and clinical data were collected. Appropriate statistical tests were performed to analyse associations between cord blood LDH levels and short-term neonatal outcomes, with $p<0.05$ considered statistically significant.
Results: Thick MSAF was seen in 64% of the newborns, and 72% required resuscitation at birth. The most frequent presentation was moderate MAS (50%); 30% had severe disease. 11% developed persistent pulmonary hypertension, 25% developed sepsis, and overall mortality was 8%. Higher cord blood LDH levels were significantly associated with adverse short-term outcomes, such as prolonged oxygen requirement and longer NICU stay.
Conclusions: Umbilical cord blood LDH is a simple, easily available, and promising biomarker for short term outcome prediction in term newborns with MAS. Its early assessment may be beneficial in risk stratification and management in tertiary care settings.

Keywords: Meconium aspiration syndrome, Umbilical cord blood, Lactate dehydrogenase, Neonatal outcomes, NICU stay

INTRODUCTION

Meconium aspiration syndrome (MAS) continues to be a major cause of respiratory distress in term and post-term neonates and an important contributor to neonatal morbidity and mortality, even with advances in obstetric and neonatal care. Infants born through MSAF who develop MAS, may have severe respiratory compromise requiring prolonged oxygen therapy, ventilatory support, and admission to the neonatal intensive care unit (NICU). Persistent pulmonary hypertension of the newborn (PPHN), pneumothorax, and respiratory failure contribute to adverse short-term outcomes. Early identification of newborns at risk for severe disease is therefore important to allow timely intervention and optimise management.[1,2]

The pathophysiology of MAS is closely associated with fetal hypoxia. Intrauterine hypoxia stimulates fetal gasping and passage of meconium into the amniotic fluid, resulting in aspiration before or during delivery. Aspirated meconium causes ventilation–perfusion mismatch, hypoxemia, and persistent pulmonary

hypertension via mechanical airway obstruction, chemical pneumonitis, surfactant inactivation, pulmonary inflammation, and pulmonary vasoconstriction.[3,4] Historically, foetal hypoxia has been assessed by Apgar scores, umbilical cord blood gas analysis and clinical evaluation.[5] Although umbilical cord arterial pH and base excess are useful indicators of intrapartum hypoxia, these investigations require specialized equipment and may not accurately reflect extent of tissue injury.[6,7] Consequently, there is need of biochemical markers that can identify hypoxic cellular injury and predict neonatal outcomes more reliably.[8,9]

LDH is an intracellular enzyme present in almost all body tissues and plays a key role in anaerobic glycolysis by catalysing the reversible conversion of pyruvate to lactate.[10] During hypoxia and cellular membrane damage, there is release of LDH into the circulation, resulting in elevated serum and umbilical cord blood concentrations. As umbilical cord blood reflects fetal metabolic status prior to birth and can be obtained without invasive procedures, estimation of cord blood LDH represents a simple, inexpensive, and readily available biomarker of perinatal hypoxic stress.[11,12]

Several investigators have demonstrated an association between elevated umbilical cord blood LDH or lactate levels and adverse neonatal outcomes, including respiratory distress, need for resuscitation, prolonged NICU stay, hypoxic-ischaemic encephalopathy, and neonatal mortality.[13,14] However, most studies have included heterogeneous populations of high-risk neonates or have primarily evaluated perinatal asphyxia rather than MAS. Evidence regarding the prognostic value of cord blood LDH specifically among term newborns with the MAS remains limited, particularly in the Indian population.[10,14]

Considering the burden of MAS and the need for an early, inexpensive, and widely available prognostic marker, assessment of umbilical cord blood LDH may facilitate early risk stratification and guide neonatal management.

Therefore, the present study was undertaken to evaluate the role of umbilical cord blood LDH in predicting short-term outcomes among term newborns with MAS admitted to a tertiary care hospital.

METHODS

Study design and setting

A hospital-based cross-sectional observational study was conducted in NICU, Department of Paediatrics, Cheluvamba Hospital, Mysore Medical College and Research Institute, Mysore, Karnataka, India, over a period of 18 months from March 2024 to September 2025 after obtaining approval from institutional ethics committee.

Study participants

The study included term neonates (gestational age ≥37 weeks) born through MSAF who subsequently developed MAS and were admitted to the NICU during the study period. Written informed consent was obtained from the parents or legal guardians before enrolment.

Neonates with Rh incompatibility, ABO incompatibility, congenital heart disease, congenital pulmonary malformations, respiratory distress syndrome, transient tachypnoea of the newborn, congenital anomalies, neonatal pneumonia, or any other identifiable cause of respiratory distress were excluded. Newborns born through MSAF without clinical or radiological evidence of MAS were also excluded.

Sample size and sampling

The sample size was calculated using the prevalence of MAS reported in previous studies, with a 95% confidence level and 5% absolute precision. Although the calculated minimum sample size was 87, a total of 100 eligible neonates were enrolled to improve study precision. Consecutive sampling was employed until the required sample size was achieved.[16]

Data collection

Maternal demographic characteristics, antenatal and intrapartum history, mode of delivery, and the consistency of MSAF were recorded. Neonatal variables included sex, birth weight, gestational age, Apgar scores, requirement for resuscitation at birth, Downes' score, severity of MAS, respiratory support required, duration of oxygen therapy, duration of NICU stay, and complications including PPHN, sepsis, pneumothorax, and mortality.

Umbilical cord blood LDH estimation

Immediately after delivery, the umbilical cord was doubly clamped and umbilical cord blood was collected aseptically before placental delivery. Samples were immediately transported to the central biochemistry laboratory where serum LDH levels were estimated using the ultraviolet (UV) kinetic enzymatic assay as per the manufacturer’s protocol. Standard laboratory quality-control procedures were followed throughout the study.

Outcome measures

The primary objective was to evaluate the association between umbilical cord blood LDH levels and short-term neonatal outcomes in term newborns with MAS. The primary outcome measures included duration of oxygen therapy, duration of NICU stay, and survival. Secondary outcome measures included severity of MAS, requirement for respiratory support, development of

PPHN, sepsis, pneumothorax, and need for mechanical ventilation.

Statistical analysis

Data were entered into Microsoft excel and analysed using the statistical package for the social sciences (SPSS) software. Continuous variables were expressed as mean±standard deviation or median with interquartile range, depending on data distribution, whereas categorical variables were expressed as frequencies and percentages. Comparisons between groups were performed using the independent Student's t test for continuous variables and the Chi-square test or Fisher's exact test for categorical variables, wherever appropriate. Receiver operating characteristic (ROC) curve analysis was performed to determine the optimal cord blood LDH cut-off value for predicting adverse short-term outcomes. Sensitivity, specificity, positive predictive value, negative predictive value, and area under the curve (AUC) were calculated. A $p<0.05$ was considered statistically significant.

Ethical considerations

The study was approved by the institutional ethics committee of Mysore Medical College and Research Institute before commencement of the study. Written informed consent was obtained from the parents or legal guardians of all enrolled newborns. Confidentiality of patient information was maintained throughout the study in accordance with the ethical principles of the Declaration of Helsinki.[17]

RESULTS

A total of 100 term newborn with MAS were taken in the study.

Most of the neonates in the study had a birth weight of 2.51-3.0 kg (62%). This shows that most of the infants were of normal birth weight. Lower birth weight 2-2.5 kg was seen in 17% cases and higher birth weight 3.01-3.5 kg was seen in 21%. Females represented 54% of cases, and males 46%, showing a slight female predominance in the study population.

The mode of delivery was almost equal, 51% neonates delivered vaginally and 49% caesarean section. MSAF was thick in 64% and thin in 36%. Resuscitation at birth was required in a large number of neonates (72%) and only 28% did not need it (Table 1).

Moderate MAS was the most common presentation (50%), followed by severe (30%) and mild (20%). Continuous positive airway pressure (CPAP) (50%) was the most common mode of respiratory support, followed by mechanical ventilation (30%) and oxygen hood (20%). Persistent pulmonary hypertension of newborn was observed in 11% cases. Sepsis was observed in 25% neonates. Pneumothorax was observed in 4% neonates. Most of the neonates (92%) were discharged successfully, 8% resulted in mortality (Table 2).

Birth weight demonstrated statistically significant association with outcome ($p=0.0224$). Neonates with lower birth weight (2-2.5 kg) exhibited a higher mortality rate (23.5%) compared to those in higher weight categories. Mode of delivery was statistically significantly associated with outcome ($p=0.0231$). Mortality was higher in neonates born by LSCS (14.3%) than in neonates born vaginally (2.0%). Thickness of meconium was found to have statistically significant association with outcome ($p=0.027$). There was a 12.5% mortality in neonates with thick MSAF, compared to no mortality in the thin MSAF group, which had a 100% discharge rate. The need for resuscitation was not statistically significantly associated with outcome ($p=0.0659$), although a clinically relevant trend is evident. Neonates who required resuscitation had a mortality rate of 11.1% compared with 0% among those who did not require resuscitation, all of whom were discharged (100%) (Table 1).

There was a statistically significant association between the severity of MAS and outcome ($p<0.001$). No mortality was reported in mild and moderate MAS cases, both showing 100% discharge rates. In contrast, severe MAS was associated with a markedly higher mortality rate of 26.7% and a reduced discharge rate of 73.3%. Type of respiratory support demonstrated statistically significant association with outcome ($p<0.001$). Neonates managed with CPAP and oxygen hood demonstrated 100% survival with no mortality. Those on mechanical ventilation, in contrast, had a significantly higher death rate of 26.7% with lowered discharge rate of 73.3%. Outcome was statistically significantly associated with PPHN ($p=0.0002$). The mortality rate was low (4.5%) and the discharge rate was high (95.5%) among the neonates without PPHN. In contrast, those with PPHN showed a substantially higher mortality rate of 36.4% and a reduced discharge rate of 63.6%. There was a statistically significant association of outcome with sepsis ($p=0.0007$). Neonates without sepsis had low mortality (2.7%) and high discharge rate (97.3%). Conversely, patients with sepsis had a significantly higher mortality rate of 24.0% and a significantly lower discharge rate of 76.0%. Pneumothorax was statistically significantly associated with outcome ($p<0.001$). The mortality rate of neonates without pneumothorax was relatively low (5.2%) and the discharge rate was high (94.8%). In contrast, the mortality rate was significantly higher at 75.0% and the discharge rate was grossly lower at 25.0% in patients with pneumothorax.

Cord LDH was significantly higher in the death group (mean 1812 IU/L) than the discharge group (mean 1007.55 IU/L) with a significant $p<0.0001$. A cut-off value of ≥1500 IU/L for cord LDH was related to death and values <1500 IU/L with discharge. (Table 3). The

diagnostic accuracy was excellent with a sensitivity of 87% and a specificity of 97% (Figure 1). Thus, cord LDH is a dependable biomarker in the prognosis of neonatal outcomes, with high specificity to minimize false positive results and good sensitivity for the detection of most high-risk cases.

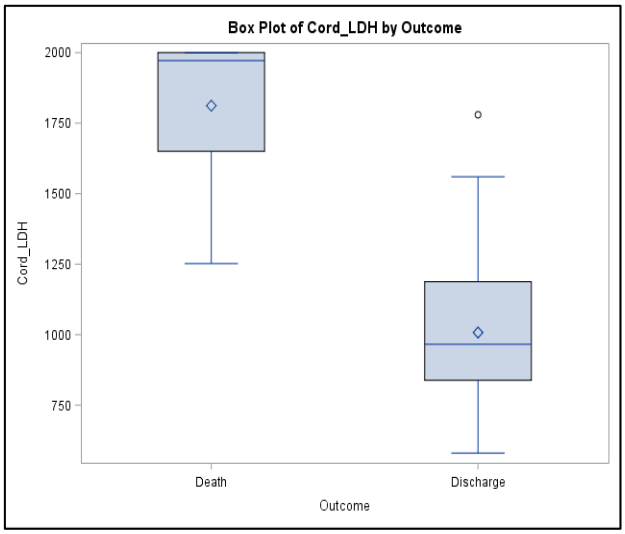

Figure 1: Cord LDH cut-off with diagnostic accuracy.

Table 1: Baseline demographic and perinatal characteristics of study participants with outcomes.

Characteristics	N (%)	Death, N (%)	Discharge, N (%)	P value
Birth weight (in kg)				
2.0-2.5	4 (23.5)	4 (23.5)	13 (76.5)	0.0224*
2.51-3.0	4 (6.5)	4 (6.5)	58 (93.5)	
3.01-3.5	0 (0)	0 (0)	21 (100)	
Sex				
Female	54 (54)	4 (7.4)	50 (92.6)	0.8129
Male	46 (46)	4 (8.7)	42 (91.3)	
Mode of delivery				
LSCS	49 (49)	7 (14.3)	42 (85.7)	0.0231*
Vaginal	51 (51)	1 (2.0)	50 (98.0)	
MSAF thickness				
Thick	64 (64)	8 (12.5)	56 (87.5)	0.027*
Thin	36 (36)	0 (0)	36 (100)	
Resuscitation required				
No	28 (28)	0 (0)	28 (100)	0.0659
Yes	72 (72)	8 (11.1)	64 (88.9)	

*P<0.05 is significant

Table 2: Clinical characteristics and severity of MAS with outcomes.

Clinical characteristics	N (%)	Death, N (%)	Discharge, N (%)	P value
Severity				
Mild	20 (20)	0 (0)	20 (100)	<0.001*
Moderate	50 (50)	0 (0)	50 (100)	
Severe	30 (30)	8 (26.7)	22 (73.3)	
Type of respiratory support				
CPAP	50 (50)	0 (0)	50 (100)	<0.001*
Mechanical ventilation	30 (30)	8 (26.7)	22 (73.3)	
Oxygen hood	20 (20)	0 (0)	20 (100)	
PPHN				
No	89 (89)	4 (4.5)	85 (95.5)	0.0002*
Yes	11 (11)	4 (36.4)	7 (63.6)	

Continued.

Clinical characteristics	N (%)	Death, N (%)	Discharge, N (%)	P value
Sepsis				
No	75 (75)	2 (2.7)	73 (97.3)	0.0007*
Yes	25 (25)	6 (24.0)	19 (76.0)	
Pneumothorax				
No	96 (96)	5 (5.2)	91 (94.8)	<0.001*
Yes	4 (4)	3 (75.0)	1 (25.0)	

*P<0.05 is significant

Table 3: Comparison of cord LDH levels with outcome.

Variables	Death mean	Death SD	Discharge mean	Discharge SD	P value
Cord LDH (IU/l)	1812	285.33	1007.55	254.07	<0.0001
Cutoff			Outcome		
≥1500			Death		
<1500			Discharge		

DISCUSSION

MAS remains an important cause of respiratory morbidity and mortality among term and post-term neonates despite advances in perinatal and neonatal care. Early identification of newborns at increased risk of adverse outcomes allows timely intervention and optimal utilization of neonatal intensive care resources. In the present study, umbilical cord blood LDH was evaluated as an early biochemical marker for predicting short-term outcomes in term newborns with MAS.

The majority of newborns in the present study were born through thick MSAF and required resuscitation at birth. Moderate MAS was the most common clinical presentation, followed by severe and mild disease. Similar observations have been reported by Wiswell and Cleary, who described thick meconium as an important risk factor for the development of clinically significant MAS and respiratory morbidity.[18,19]

CPAP was the most commonly used mode of respiratory support, whereas mechanical ventilation was required in neonates with severe disease. Infants with severe MAS were more likely to develop PPHN, sepsis and pneumothorax. These results are consistent with the pathophysiology of MAS, where airway obstruction, surfactant inactivation, inflammation and pulmonary vasoconstriction all contribute to respiratory failure and its complications.[20,21] The present study showed that high levels of LDH in the umbilical cord blood were significantly associated with adverse short-term neonatal outcomes. Higher LDH level in newborns was associated with longer oxygen requirement; longer NICU stay and more severe disease. These results lend support to the idea that the rise in LDH is an index of cellular damage from fetal hypoxia and tissue damage during the intrapartum period.

The results are similar to the observations of Kamath et al who found significantly higher cord blood LDH levels in neonates born through MSAF who subsequently developed adverse neonatal outcomes.[6] They concluded that cord blood LDH is a useful and inexpensive prognostic biomarker to identify the newborns requiring intensive neonatal care.

Similarly, Kumar et al observed that elevated cord blood LDH levels were significantly associated with prolonged hospitalization, increased respiratory support, and poorer neonatal outcomes in high-risk term pregnancies.[7] They proposed that LDH is a better indicator of tissue damage than isolated pH values of cord blood.

Mazouri et al reported elevated umbilical cord blood biochemical markers were linked with worser severity of MAS and respiratory complications, enhancing the role of early biochemical assessment in predicting neonatal outcome.[8]

Einikyte et al reported that elevated cord blood lactate levels were associated with multiple adverse outcomes including need for resuscitation and NICU admission.[11] This is in agreement with present study where neonates with high levels of LDH had higher clinical severity as well, indicating a consistent relationship between biochemical derangement and clinical compromise.

Patil et al reported that lactate in cord blood was more specific and predictive of adverse neonatal outcomes than pH.[12] The high specificity (97%) and sensitivity (87%) found in the present study for LDH ≥1500 IU/L support the use of biochemical markers as reliable predictors.

Hansen et al reported that cord blood biochemical abnormality correlate with increased neonatal morbidity and respiratory complications, emphasizing that biochemical markers reflect severity of disease and subsequent outcome.[13]

Rubak et al established that metabolic stress markers such as lactate increase in response to hypoxia, which provides

the physiological basis for the use of LDH as a surrogate marker of tissue injury and hypoxic insult.[9]

These findings suggest that cord blood LDH may be incorporated into the initial evaluation of newborns with MAS to identify infants at higher risk of prolonged oxygen therapy, extended NICU stay, and severe respiratory disease. Because LDH estimation is inexpensive, rapid, and available in most hospital laboratories, it may be particularly valuable in resource-limited settings.

The strengths of the present study include prospective data collection, uniform management protocols in a tertiary care NICU, and assessment of umbilical cord blood before initiation of neonatal treatment, thereby reflecting the fetal metabolic status immediately after birth.

The present study has certain limitations. It was conducted at a single tertiary care centre with a relatively small sample size, which may limit the generalizability of the findings. Serial postnatal LDH measurements were not analyzed and no long-term neurodevelopmental follow-up was performed. Further multicentre studies in larger populations are needed to confirm the optimal LDH cut-off value and to define its prognostic value in different clinical settings.

CONCLUSION

To summarize, LDH in umbilical cord blood is a promising, simple and inexpensive biomarker for the prediction of short-term outcome in term newborns with MAS. Increased LDH levels were significantly correlated with increased severity of disease, increased oxygen requirement and increased length of stay in NICU. Routine cord blood LDH measurement at birth may allow for early risk stratification and improved management of newborns with MAS.

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