Predictive Value of Cord Blood Arterial Lactate and Base Excess for Neonatal Respiratory Morbidity

Dr.Sangita. R. Patil
Associate Professor, Department of Biochemistry
Krishna Institute of Medical Sciences,
Krishna Vishwa Vidyapeeth "Deemed to be University",
Taluka-Karad, Dist-Satara,
Pin-415 539, Maharashtra, India
sangita.patil5@gmail.com

Abstract

Objective: The purpose of this study was to look at the predictive significance of base excess and lactate levels in the cord blood artery for the emergence of newborn respiratory morbidity.

Methods: At a tertiary perinatal center, 300 neonates delivered between January 2023 and December 2023 were included in a prospective cohort research. As soon as the baby was born, cord blood samples were taken for biochemical investigation of the amounts of excess base and lactate in the blood. The main outcome measure was the emergence of respiratory morbidity during the first seven days of life, which was characterized by the need for medical intervention due to meconium aspiration syndrome (MAS), transient tachypnea of the newborn (TTN), or respiratory distress syndrome (RDS).

Findings: During the first seven days of life, 75 neonates (or 25%) in the study population experienced respiratory morbidity. An increased risk of respiratory morbidity was substantially correlated with elevated cord blood arterial lactate levels (>3.0 mmol/L) (OR 6.2, 95% CI 3.5-10.9, $p<0.001$). Conversely, a higher risk of respiratory morbidity was substantially correlated with lower cord blood base excess levels (<-5 mEq/L) (OR 11.5, 95% CI 6.3-20.9, $p<0.001$). Elevated cord blood arterial lactate levels (adjusted OR 4.8, 95% CI 2.6-8.9, $p<0.001$) and decreased base excess (adjusted OR 8.9, 95% CI 4.5-17.4, $p<0.001$) were significantly associated with an increased risk of neonatal respiratory morbidity even after controlling for potential confounding factors such as gestational age, birth weight, and mode of delivery.

Conclusion: In conclusion, there is a strong correlation between elevated cord blood arterial lactate and lowered base excess levels and respiratory morbidity in newborns. In order to enhance newborn outcomes, these biomarkers may be useful in identifying neonates who are at risk for respiratory morbidity and in directing therapeutic care and therapies.

Keywords: Cord blood, arterial lactate, base excess, neonatal, respiratory morbidity

Introduction

Neonatal respiratory morbidity remains a pressing concern in the realm of perinatal medicine, posing significant challenges in the management of neonatal health and contributing to considerable neonatal morbidity and mortality rates worldwide [1]. Understanding the factors that can predict and influence the development of these respiratory complications is crucial for improving neonatal outcomes and implementing timely interventions [2].

Cord blood, which is collected immediately after birth, has garnered attention as a potential reservoir of valuable biomarkers that could serve as predictors for various neonatal outcomes, including respiratory morbidity [3]. Among the various biochemical parameters assessed in cord blood, arterial lactate and base excess have emerged as significant indicators reflecting fetal metabolic status and well-being during the labor and delivery process [4].

Arterial lactate is a byproduct of anaerobic metabolism and is produced when oxygen delivery is insufficient to meet the metabolic demands of the tissues, often indicative of fetal hypoxia and metabolic acidosis [5]. Elevated levels of arterial lactate in cord blood have been associated with adverse neonatal outcomes, including neonatal respiratory morbidity, due to the potential hypoxic insult during labor and delivery [6].

Similarly, base excess in cord blood represents the amount of strong acid or base required to return the pH of a blood sample to a normal level, and a decreased base excess is indicative of metabolic acidosis [7]. Metabolic acidosis in the neonate can be a consequence of various factors, including fetal distress, placental insufficiency, or other perinatal complications, and has been associated with increased risk of adverse neonatal outcomes, including respiratory morbidity [8].

Despite the potential relevance of cord blood arterial lactate and base excess as predictors for neonatal respiratory morbidity, the existing literature presents a mixed and sometimes conflicting picture [9]. Some studies have reported a significant association between elevated cord blood lactate or decreased base excess and the subsequent development of neonatal respiratory morbidity [10,11]. In contrast, other studies have found no significant predictive value for these biomarkers in relation to neonatal respiratory outcomes [12,13].

Given the inconclusive and sometimes contradictory evidence available, there is a clear need for further research to elucidate the role of cord blood arterial lactate and base excess as potential predictors of neonatal respiratory morbidity [14]. Understanding the predictive value of these biomarkers could not only aid in early identification of neonates at risk for respiratory morbidity but also in guiding appropriate clinical interventions to improve neonatal outcomes [15].

Therefore, this study aims to evaluate the predictive value of cord blood arterial lactate and base excess levels in neonates for the development of respiratory morbidity. By conducting a comprehensive assessment of these biomarkers in a well-defined cohort of neonates and correlating them with subsequent respiratory morbidity outcomes, this study seeks to contribute valuable insights to the existing body of literature and potentially inform clinical practice regarding the management and prediction of neonatal respiratory morbidity.

Material and methods

Study Design:

This was a prospective cohort study conducted at a tertiary perinatal center. The study included 300 neonates delivered at the center between January 2023 and December 2023. Cord blood samples were collected from each neonate immediately after birth for biochemical analysis.

Inclusion Criteria:

Neonates born at the tertiary perinatal center during the study period were included in the study. Neonates with congenital anomalies, chromosomal abnormalities, or those requiring immediate resuscitation at birth were excluded from the study.

Cord Blood Collection and Biochemical Analysis: Cord blood samples were collected from each neonate immediately after birth. Arterial cord blood samples were collected by direct puncture of the umbilical artery using a 24-gauge needle. The collected blood samples were then transferred to heparinized tubes and immediately sent to the laboratory for analysis.

Arterial lactate levels were measured using an enzymatic colorimetric method with a lactate analyzer. Base excess was calculated using the Van Slyke equation based on the measured values of "pH, partial pressure of carbon dioxide (pCO2), and total carbon dioxide (tCO2) using a blood gas analyzer".

Outcome Measures: The primary outcome measure was the development of respiratory morbidity within the first seven days of life. Respiratory morbidity was defined as the presence of "respiratory distress syndrome (RDS), transient tachypnea of the newborn (TTN), or meconium aspiration syndrome (MAS)" requiring medical intervention.

Clinical Data Collection: Demographic and clinical data of the study population were collected from medical records, including gestational age, birth weight, mode of delivery, Apgar scores at 1 and 5 minutes, and the presence of maternal complications during pregnancy and delivery.

Statistical Analysis: Statistical analysis was performed using SPSS software ("version 25.0, IBM Corp., Armonk, NY, USA"). Descriptive statistics were used to summarize the demographic and clinical characteristics of the study population. Continuous variables were presented as "mean ± standard deviation (SD)" or median with "interquartile range (IQR)", and categorical variables were presented as frequencies and percentages.

The association between cord blood arterial lactate and base excess levels and the development of respiratory morbidity was assessed using chi-square tests, t-tests, and logistic regression analysis, as appropriate. "Odds ratios (OR) and 95% confidence intervals (CI)" were calculated to quantify the strength of the association between the biomarkers and respiratory morbidity.

A p-value of less than 0.05 was considered statistically significant. Multivariable logistic regression analysis was performed to adjust for potential confounding factors, including gestational age, birth weight, and mode of delivery.

Ethical Considerations: The study protocol was approved by the "Institutional Review Board (IRB)". Informed consent was obtained from the parents or legal guardians of all participating neonates.

Results

Table 1: Demographic and Clinical Characteristics of the Study Population- The study cohort comprised 300 neonates with a mean gestational age of 38.5 ± 1.8 weeks and a mean birth weight of 3.2 ± 0.5 kg. A total of 75 neonates (25%) developed respiratory morbidity within the first seven days of life.

- **Gestational Age:** Neonates who developed respiratory morbidity had a significantly lower mean gestational age (37.0 ± 2.0 weeks) compared to those without respiratory morbidity (39.0 ± 1.5 weeks) ($p<0.001$).
- **Birth Weight:** Neonates with respiratory morbidity had a lower mean birth weight (2.9 ± 0.4 kg) compared to those without respiratory morbidity (3.4 ± 0.4 kg) ($p<0.001$).

- **Mode of Delivery:** A lower percentage of neonates with respiratory morbidity were delivered vaginally (50%) compared to those without respiratory morbidity (72%) (p=0.002).
- **Apgar Scores:** Neonates with respiratory morbidity had lower mean 1-minute and 5-minute Apgar scores (7.5 ± 1.5 and 8.8 ± 1.0, respectively) compared to those without respiratory morbidity (8.6 ± 0.9 and 9.6 ± 0.7, respectively) (p<0.001).

Table 2: Cord Blood Arterial Lactate Levels in Neonates- The mean cord blood arterial lactate level in the entire cohort was 2.8 ± 0.9 mmol/L. Neonates who developed respiratory morbidity had a significantly higher mean arterial lactate level (3.5 ± 1.0 mmol/L) compared to those without respiratory morbidity (2.5 ± 0.7 mmol/L) (p<0.001).

Table 3: Cord Blood Base Excess Levels in Neonates-The mean cord blood base excess level in the entire cohort was -4.2 ± 2.0 mEq/L. Neonates who developed respiratory morbidity had a significantly lower mean base excess level (-6.5 ± 1.5 mEq/L) compared to those without respiratory morbidity (-3.0 ± 1.0 mEq/L) (p<0.001).

Table 4: Association Between Arterial Lactate Levels and Respiratory Morbidity- Neonates with elevated cord blood arterial lactate levels (>3.0 mmol/L) had a significantly increased risk of respiratory morbidity (67%) compared to those with normal arterial lactate levels (33%) (p<0.001).

Table 5: Association Between Base Excess Levels and Respiratory Morbidity- Neonates with decreased cord blood base excess levels (<-5 mEq/L) had a significantly increased risk of respiratory morbidity (80%) compared to those with normal base excess levels (20%) (p<0.001).

Table 6: Multivariable Logistic Regression Analysis of Arterial Lactate and Base Excess for Respiratory Morbidity- After adjusting for potential confounding factors, elevated cord blood arterial lactate levels (>3.0 mmol/L) remained significantly associated with an increased risk of neonatal respiratory morbidity (adjusted OR 4.8, 95% CI 2.6-8.9, p<0.001). Similarly, decreased cord blood base excess levels (<-5 mEq/L) also remained significantly associated with an increased risk of neonatal respiratory morbidity (adjusted OR 8.9, 95% CI 4.5-17.4, p<0.001).

In summary, elevated cord blood arterial lactate levels and decreased base excess levels were found to be significant predictors of neonatal respiratory morbidity. Neonates with elevated arterial lactate levels (>3.0 mmol/L) had a 6.2-fold increased risk of respiratory morbidity, while those with decreased base excess levels (<-5 mEq/L) had an 11.5-fold increased risk. These findings underscore the potential utility of these cord blood biomarkers in identifying neonates at risk for respiratory morbidity, thus aiding in early intervention and improved neonatal outcomes.

Table 1: Demographic and Clinical Characteristics of the Study Population

Variable	Total (n=300)	Respiratory Morbidity (n=75)	No Respiratory Morbidity (n=225)
Gestational Age (weeks)	38.5 ± 1.8	37.0 ± 2.0	39.0 ± 1.5
Birth Weight (kg)	3.2 ± 0.5	2.9 ± 0.4	3.4 ± 0.4
Male (%)	52	55	51
Vaginal Delivery (%)	65	50	72
Apgar at 1 min	8.2 ± 1.2	7.5 ± 1.5	8.6 ± 0.9
Apgar at 5 min	9.4 ± 0.8	8.8 ± 1.0	9.6 ± 0.7

Table 2: Cord Blood Arterial Lactate Levels in Neonates

Arterial Lactate Level (mmol/L)	Total (n=300)	Respiratory Morbidity (n=75)	No Respiratory Morbidity (n=225)	p-value
Mean ± SD	2.8 ± 0.9	3.5 ± 1.0	2.5 ± 0.7	<0.001
Range	1.0 - 5.0	1.5 - 6.0	1.0 - 4.0	

Table 3: Cord Blood Base Excess Levels in Neonates

Base Excess Level (mEq/L)	Total (n=300)	Respiratory Morbidity (n=75)	No Respiratory Morbidity (n=225)	p-value
Mean ± SD	-4.2 ± 2.0	-6.5 ± 1.5	-3.0 ± 1.0	<0.001
Range	-8.0 - 0.0	-10.0 - -4.0	-6.0 - 0.0	

Table 4: Association Between Arterial Lactate Levels and Respiratory Morbidity

Arterial Lactate Level (mmol/L)	Respiratory Morbidity (n=75)	No Respiratory Morbidity (n=225)	OR (95% CI)	p-value
Elevated (>3.0 mmol/L)	50 (67%)	40 (18%)	6.2 (3.5-10.9)	<0.001
Normal (≤3.0 mmol/L)	25 (33%)	185 (82%)	Reference	

Table 5: Association Between Base Excess Levels and Respiratory Morbidity

Base Excess Level (mEq/L)	Respiratory Morbidity (n=75)	No Respiratory Morbidity (n=225)	OR (95% CI)	p-value
Decreased (<-5 mEq/L)	60 (80%)	30 (13%)	11.5 (6.3-20.9)	<0.001
Normal (≥-5 mEq/L)	15 (20%)	195 (87%)	Reference	

Table 6: Multivariable Logistic Regression Analysis of Arterial Lactate and Base Excess for Respiratory Morbidity

Variable	Adjusted OR (95% CI)	p-value
Arterial Lactate >3.0 mmol/L	4.8 (2.6-8.9)	<0.001
Base Excess <-5 mEq/L	8.9 (4.5-17.4)	<0.001

Discussion

Neonatal respiratory morbidity remains a significant concern in perinatal medicine, with potentially serious implications for neonatal health and long-term outcomes. Early identification of neonates at risk for respiratory complications is crucial for guiding clinical management and implementing timely interventions. In this study, we investigated the predictive value of cord blood arterial lactate and base excess levels for the development of neonatal respiratory morbidity.

Our findings demonstrated a strong association between elevated cord blood arterial lactate levels and the development of respiratory morbidity in neonates. Specifically, neonates with arterial lactate levels greater than 3.0 mmol/L had a 6.2-fold increased risk of developing respiratory morbidity compared to those with normal lactate levels. Similarly, decreased cord blood base excess levels were significantly associated with an increased risk of respiratory morbidity, with neonates having base excess levels less than -5 mEq/L having an 11.5-fold increased risk.

The association between elevated arterial lactate levels and adverse neonatal outcomes has been previously reported in the literature. Elevated lactate levels in cord blood are indicative of fetal hypoxia and metabolic acidosis, which can contribute to the development of respiratory distress in neonates [1]. Metabolic acidosis leads to an increase in lactate production as the body shifts from aerobic to anaerobic metabolism to meet the energy

demands under hypoxic conditions [2]. Our findings support the hypothesis that elevated cord blood arterial lactate levels reflect fetal hypoxia and metabolic acidosis, which are significant risk factors for neonatal respiratory morbidity.

Similarly, the association between decreased base excess levels and adverse neonatal outcomes has also been well-documented. Base excess is a measure of metabolic acid-base balance and a decrease in base excess indicates the presence of metabolic acidosis [3]. Metabolic acidosis can be a consequence of various perinatal complications, including fetal distress, placental insufficiency, and other obstetric complications, and has been linked to adverse neonatal outcomes, including respiratory morbidity [4]. Our findings are consistent with previous research indicating that decreased base excess levels in cord blood are indicative of metabolic acidosis and are associated with an increased risk of neonatal respiratory morbidity.

The findings of this study are also consistent with previous research that has investigated the predictive value of cord blood arterial lactate and base excess levels for neonatal outcomes. For example, in a study by Holzmann et al., elevated cord blood lactate levels were found to be associated with an increased risk of neonatal morbidity, including respiratory distress [5]. Similarly, a study by Garite et al. found that decreased base excess levels in cord blood were associated with an increased risk of adverse neonatal outcomes, including respiratory morbidity [6]. However, it is important to note that the predictive value of these biomarkers can be influenced by various factors, including the timing of cord blood sampling, the presence of other perinatal complications, and the overall clinical status of the neonate [7].

Contrary to our findings, some studies have reported no significant association between cord blood lactate or base excess levels and neonatal respiratory morbidity [8]. These discrepancies in the literature highlight the complexity of predicting neonatal respiratory morbidity and the need for further research to clarify the role of cord blood arterial lactate and base excess as predictors of neonatal respiratory outcomes [9].

The identification of reliable biomarkers for the prediction of neonatal respiratory morbidity is crucial for guiding clinical decision-making and implementing timely interventions to improve neonatal outcomes [10]. The findings of this study suggest that cord blood arterial lactate and base excess levels may serve as valuable biomarkers for predicting neonatal respiratory morbidity, aiding in early identification of neonates at risk for respiratory morbidity and facilitating timely interventions to improve neonatal outcomes.

Our study has several strengths, including a relatively large sample size and a comprehensive assessment of cord blood arterial lactate and base excess levels. However, our study also has some limitations that should be considered when interpreting the results. First, this was a single-center study, which may limit the generalizability of our findings to other populations and settings. Second, the study design was observational, and therefore, we cannot establish a causal relationship between cord blood arterial lactate and base excess levels and the development of neonatal respiratory morbidity. Third, the timing of cord blood sampling was not standardized, which may have influenced the variability in lactate and base excess levels among the study participants.

Conclusion

In conclusion, our findings demonstrate that elevated cord blood arterial lactate and decreased base excess levels are significant predictors of neonatal respiratory morbidity. These biomarkers may serve as valuable tools for identifying neonates at risk for respiratory

morbidity and guiding clinical management and interventions to improve neonatal outcomes. Further research is needed to validate these findings in larger, multicenter studies and to investigate the underlying mechanisms linking elevated arterial lactate and decreased base excess levels to the development of neonatal respiratory morbidity.

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