Original Research

Assessment of Serum Lactate Dehydrogenase Levels in Term Neonates with Birth Asphyxia

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ABSTRACT
Background: Birth asphyxia remains a significant global health concern, contributing to neonatal morbidity and mortality.The study aimed to evaluate serum lactate dehydrogenase (LDH) levels in term neonates with birth asphyxia and assess their correlation with Apgar scores, resuscitation needs, and associated complications.
Material and Methods: This prospective study included 120 term neonates diagnosed with birth asphyxia, defined by an Apgar score <7 at 5 minutes or requiring resuscitation at birth. Serum LDH levels were measured within the first 24 hours of birth using an automated enzyme assay (cobas c 111, Roche Diagnostics). Data were analyzed using SPSS 21.0, with a p-value <0.05 considered statistically significant.
Results: Among the neonates, 54.17% were male, and 56.67% were delivered vaginally. Apgar scores at 5 minutes were 4-6 in 85.00% and 0-3 in 15.00%, with 65.83% requiring resuscitation. LDH levels were 801-1000 U/L in 33.33%, 600-800 U/L in 29.17%, and >1000 U/L in 20.83%, correlating significantly with lower Apgar scores (p <0.05). Hypoxic-ischemic encephalopathy (HIE) was the most common complication (39.17%), followed by respiratory distress syndrome (23.33%) and seizures (15.83%).
Conclusion: Serum LDH levels were significantly elevated in neonates with birth asphyxia and correlated with Apgar scores, resuscitation needs, and complications such as HIE. Given its cost-effectiveness and accessibility, LDH can be integrated into neonatal care protocols for early diagnosis and risk stratification.
Keywords: Birth asphyxia, Lactate dehydrogenase, Neonatal hypoxia, Apgar score, Hypoxic-ischemic encephalopathy

INTRODUCTION

Birth asphyxia remains a significant global health concern, contributing to neonatal morbidity and mortality. It is a condition that arises from impairment in oxygen supply before, during, or immediately after birth, leading to metabolic acidosis, hypoxic-ischemic encephalopathy (HIE), and multi-organ dysfunction. Term neonates experiencing birth asphyxia are at risk of severe neurological and systemic complications that can have long-term consequences, including cerebral palsy, developmental delays, and other neurodevelopmental disorders. Early identification and management of birth asphyxia are crucial in improving neonatal outcomes, necessitating reliable biomarkers for timely diagnosis and intervention.[1]

Among the various biochemical markers, serum lactate dehydrogenase (LDH) has emerged as a potential indicator of hypoxic injury in neonates. LDH is an intracellular enzyme involved in anaerobic glycolysis, catalyzing the conversion of pyruvate to lactate. It is widely distributed in various tissues, including the brain, heart, liver, kidneys, and skeletal muscles. Under normal

physiological conditions, LDH levels in the blood remain relatively low, as the enzyme is confined within the cells. However, during hypoxic events such as birth asphyxia, cellular damage and membrane permeability increase, leading to the leakage of LDH into the bloodstream. Elevated LDH levels, therefore, serve as a marker of cellular injury and hypoxic stress, making it a useful parameter in assessing the severity of birth asphyxia.[2]

The extent of LDH elevation in neonates with birth asphyxia is influenced by the degree and duration of hypoxia. Severe asphyxia results in higher LDH release due to widespread tissue damage, particularly in organs that are highly sensitive to oxygen deprivation. The central nervous system is particularly vulnerable to hypoxic injury, and high LDH levels in neonates have been associated with the severity of hypoxic-ischemic encephalopathy. Additionally, LDH levels may correlate with Apgar scores, a clinical assessment tool used to evaluate neonatal well-being immediately after birth. Lower Apgar scores at five minutes often indicate a higher risk of birth asphyxia and are frequently accompanied by increased LDH levels, reinforcing its utility as a biochemical marker.[3]

Apart from its role in assessing hypoxic injury, LDH also has prognostic value in neonates with birth asphyxia. Studies have suggested that persistently elevated LDH levels in the early postnatal period may indicate a higher risk of adverse neurodevelopmental outcomes. This is because prolonged hypoxia leads to metabolic derangements, oxidative stress, and inflammation, further exacerbating cellular damage. By monitoring LDH levels, clinicians may be able to stratify neonates based on the severity of injury and determine the need for early therapeutic interventions such as therapeutic hypothermia, which has been shown to improve neurological outcomes in neonates with moderate to severe hypoxic-ischemic encephalopathy.[4]

The relationship between LDH levels and other biochemical markers of asphyxia, such as creatine kinase (CK), creatine kinase-muscle brain fraction (CK-MB), and neuron-specific enolase (NSE), further highlights its clinical significance. While CK and CK-MB are primarily associated with myocardial damage, NSE is more specific to neuronal injury. However, LDH, being a more ubiquitous enzyme, provides a broader assessment of multi-organ involvement in birth asphyxia. In conjunction with other markers and clinical parameters, LDH measurement enhances the diagnostic accuracy of birth asphyxia and aids in early decision-making.[5]

Despite its clinical utility, several factors may influence LDH levels in neonates, necessitating careful interpretation. Conditions such as hemolysis, infections, and metabolic disorders can also cause LDH elevation, potentially confounding its association with birth asphyxia. Therefore, LDH should be used as part of a comprehensive diagnostic approach rather than as a standalone marker. Additionally, variations in laboratory methods and reference ranges across different institutions may impact the interpretation of LDH values, highlighting the need for standardized protocols in neonatal care settings.[6]

In the context of neonatal intensive care, measuring LDH levels is relatively simple, cost-effective, and widely available, making it a practical choice for early detection of hypoxic injury. Unlike advanced neuroimaging techniques such as MRI, which may not be readily accessible in all healthcare settings, LDH measurement can be performed using routine biochemical assays, facilitating rapid assessment of neonatal condition. This is particularly important in resource-limited settings where access to specialized neonatal care is constrained, and early biochemical indicators can help prioritize neonates for further evaluation and management.[7]

Furthermore, the dynamic nature of LDH levels provides insight into the progression of hypoxic injury and the effectiveness of therapeutic interventions. Serial measurements of LDH in neonates with birth asphyxia may help track the resolution of tissue injury and predict long-term neurological outcomes. For example, a decline in LDH levels over the first few days of life may suggest recovery and better prognosis, whereas persistently high levels may indicate ongoing cellular damage and a higher likelihood of complications.[8]

Given the significant burden of birth asphyxia on neonatal health, there is a growing interest in exploring biomarkers that can improve early diagnosis and management. LDH, due to its association with hypoxic injury, has the potential to be integrated into standard neonatal care protocols as a supplementary tool alongside clinical assessments and imaging studies. Ongoing research aims to refine the clinical application of LDH by establishing reference

ranges specific to neonatal populations and evaluating its predictive value in different clinical scenarios.

AIM& OBJECTIVES: The study aimed to evaluate serum lactate dehydrogenase (LDH) levels in term neonates with birth asphyxia and assess their correlation with Apgar scores, resuscitation needs, and associated complications.

METHODS AND MATERIALS

Study Design

- **Type of Study:** Prospective observational study
- **Study Setting:** Conducted in the Neonatal Intensive Care Unit (NICU) of a tertiary care hospital
- **Study Duration:**January 2020 to November 2022
- **Sample Size:** 120 term neonates

Study Population: A total of 120 term neonates diagnosed with birth asphyxia, defined by an Apgar score of less than 7 at 5 minutes or requiring resuscitation at birth. Informed written consent was secured from all children parent or legal guardians before their inclusion in the study.

Ethical consideration

The study was approved by the research and ethical committee of the institutes.

Inclusion Criteria

- Term neonates (gestational age ≥ 37 weeks)
- Neonates diagnosed with birth asphyxia, defined as:Apgar score < 7 at 5 minutes, orRequirement of resuscitation at birth (e.g., positive pressure ventilation, chest compressions, or medications)

Exclusion Criteria

- Preterm neonates (< 37 weeks gestation)
- Neonates with congenital anomalies or genetic disorders.
- Neonates diagnosed with neonatal sepsis or inborn errors of metabolism.
- Maternal conditions affecting neonatal outcomes, such as:
  - Diabetes mellitus
  - Pregnancy-induced hypertension
  - Prolonged rupture of membranes (>18 hours)

Procedure

Clinical Assessment:

Apgar scores were recorded at 1 and 5 minutes post-birth.Need for resuscitation interventions was documented.

Blood Sampling for LDH Measurement:

Timing: Blood samples were collected within the first 12–24 hours of birth.

Method:

Venous blood was drawn under aseptic precautions.

Serum LDH levels were estimated using an automated enzymatic colorimetric assay.

The results were categorized into two groups:

Birth Asphyxia Group: Neonates with Apgar < 7 at 5 min or requiring resuscitation

Control Group: Healthy term neonates without birth asphyxia

STATISTICAL ANALYSIS

- Data analysis was performed using SPSS (version 21.0) software.
- Continuous variables (e.g., LDH levels) were expressed as mean ± standard deviation (SD).
- Comparisons between groups were conducted using:

Independent t-test for normally distributed data

Mann-Whitney U test for skewed data

- Categorical variables (e.g., need for resuscitation) were analyzed using the Chi-square test.
- Pearson's correlation was used to determine the relationship between LDH levels and severity of birth asphyxia.
- Statistical significance was set at $p < 0.05$.

RESULTS

The study analyzed serum lactate dehydrogenase (LDH) levels in term neonates with birth asphyxia and their correlation with clinical parameters such as Apgar scores, resuscitation needs, and associated complications.

Table 1: Demographic Characteristics of the Study Population

Characteristic	Number (n=120)	Percentage (%)
Gender		
Male	65	54.17
Female	55	45.83
Gestational Age (weeks)		
37-38	42	35.00
39-40	53	44.17

>40	25	20.83
Mode of Delivery		
Vaginal	68	56.67
C-Section	52	43.33

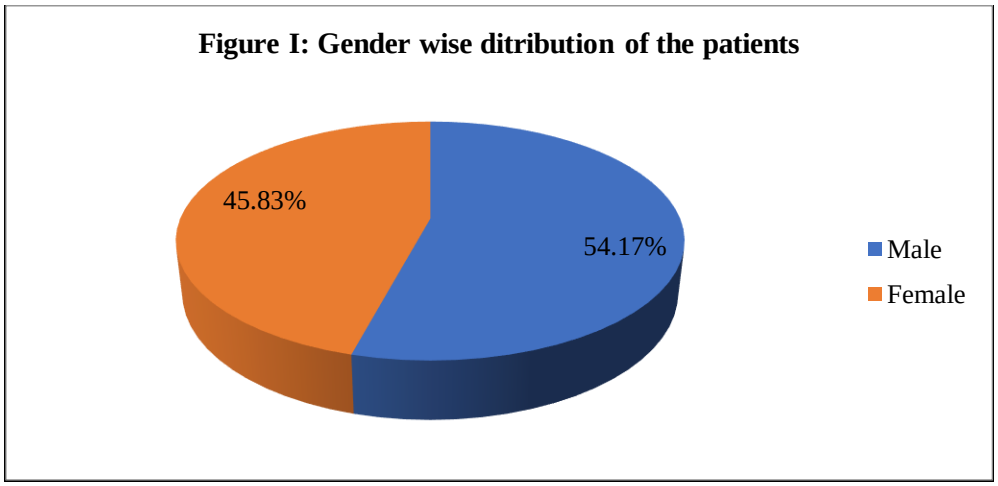

Table 1 and figure I, shows that among the 120 neonates included in the study, 65 (54.17%) were male, and 55 (45.83%) were female, indicating a nearly equal gender distribution. The majority of neonates were born at 39-40 weeks of gestation (44.17%), followed by 37-38 weeks (35.00%) and >40 weeks (20.83%). Regarding the mode of delivery, 56.67% of neonates were delivered vaginally, while 43.33% were born via cesarean section. These findings highlight that birth asphyxia occurs across different gestational age groups and delivery modes, emphasizing the need for close perinatal monitoring in all deliveries.

Table 2: Apgar Scores and Resuscitation Requirement

Variable	Number (n=120)	Percentage (%)
Apgar Score at 5 minutes		
0-3	18	15.00
4-6	102	85.00
Resuscitation Required		
Yes	79	65.83
No	41	34.17

Table 2 shows that Apgar scores at 5 minutes were used as a criterion to define birth asphyxia. A significant proportion of neonates (85.00%) had an Apgar score between 4 and 6, while 15.00% had a more severe score of 0-3. Additionally, resuscitation was required in 65.83% of cases, indicating the severity of birth asphyxia and the need for immediate intervention. The remaining 34.17% of neonates did not require resuscitation. This data suggests that most neonates with birth asphyxia still had moderate scores (4-6), but a considerable percentage required intensive resuscitative measures.

Table 3: Serum LDH Levels and Clinical Parameters

LDH Levels (U/L)	Number (n=120)	Percentage (%)
<600	20	16.67
600-800	35	29.17
801-1000	40	33.33
>1000	25	20.83

Table 3 shows that the serum LDH levels were measured within the first 24 hours of birth. The results showed that 33.33% of neonates had LDH levels between 801-1000 U/L, while 29.17% had

levels between 600-800 U/L. Elevated LDH levels (>1000 U/L) were found in 20.83% of cases, indicating severe cellular damage. Conversely, 16.67% of neonates had LDH levels below 600 U/L, suggesting milder hypoxic stress. These findings indicate that a significant proportion of neonates with birth asphyxia had elevated LDH levels, reinforcing the association between hypoxic injury and increased cellular damage.

Table 4: Complications Associated with Birth Asphyxia

Complication	Number (n=120)	Percentage (%)
Hypoxic-Ischemic Encephalopathy (HIE)	47	39.17
Respiratory Distress Syndrome (RDS)	28	23.33
Seizures	19	15.83
No Complications	26	21.67

Table 4 shows that the birth asphyxia was associated with various complications, with Hypoxic-Ischemic Encephalopathy (HIE) being the most common, affecting 39.17% of neonates. Respiratory Distress Syndrome (RDS) was observed in 23.33% of cases, while 15.83% developed seizures, indicating significant neurological involvement. A small proportion of neonates (21.67%) did not develop complications, suggesting a less severe impact of birth asphyxia in those cases. The high prevalence of HIE and seizures underscores the neurological vulnerability of neonates suffering from birth asphyxia and highlights the importance of early detection and management.

Table 5: Statistical Association between LDH Levels and Apgar Score

LDH Levels (U/L)	Apgar 0-3 (n=18)	Apgar 4-6 (n=102)	p-value
<600	2 (11.11%)	18 (17.65%)	<0.05
600-800	3 (16.67%)	32 (31.37%)	<0.05
801-1000	6 (33.33%)	34 (33.33%)	<0.05
>1000	7 (38.89%)	18 (17.65%)	<0.05

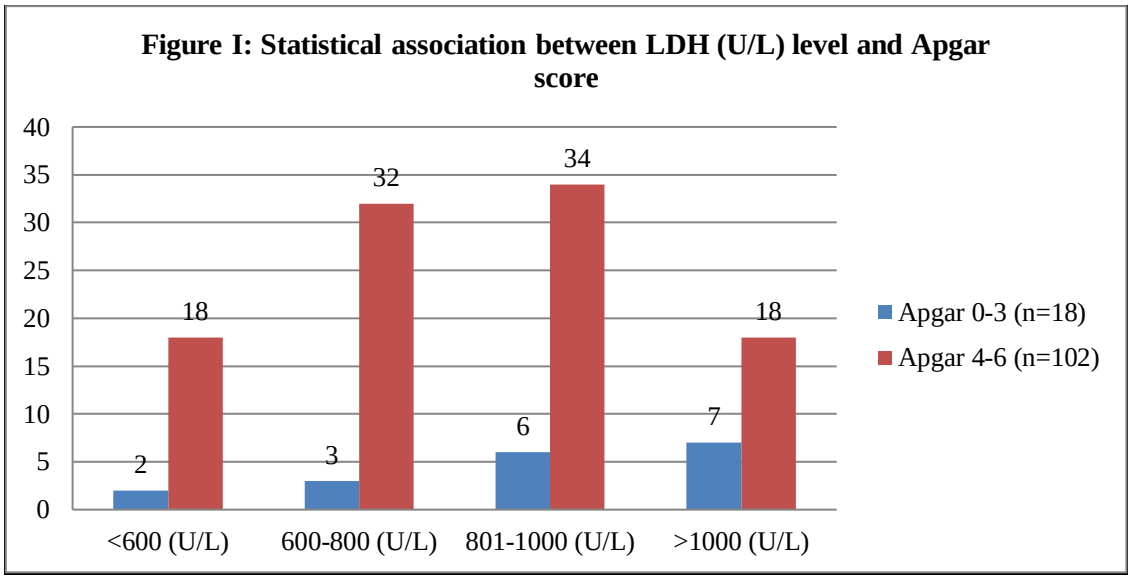

Table 5 and figure I, shows that a statistical analysis was conducted to determine the relationship between serum LDH levels and Apgar scores. The results showed that neonates with the lowest Apgar scores (0-3) had the highest LDH levels, with 38.89% of cases having LDH >1000 U/L. In contrast, neonates with Apgar scores of 4-6 showed a more even distribution, with 33.33% having LDH levels between 801-1000 U/L and 31.37% between 600-800 U/L. The p-value for all comparisons was <0.05, indicating a statistically significant

correlation between lower Apgar scores and higher LDH levels. This finding suggests that serum LDH can serve as a biochemical marker for assessing the severity of birth asphyxia, with higher LDH levels correlating with more severe hypoxic injury.

DISCUSSION

Birth asphyxia remains a significant cause of neonatal morbidity and mortality, leading to various biochemical and physiological changes, including increased serum lactate dehydrogenase (LDH) levels. The present study analyzed serum LDH levels in term neonates with birth asphyxia and their correlation with clinical parameters such as Apgar scores, resuscitation needs, and associated complications.

The study observed a male predominance (54.17%) among neonates with birth asphyxia, consistent with the findings of Chaudhari et al. (2017), who reported a male predominance of 58.3% in their study. This male predominance may be attributed to greater vulnerability of male neonates to perinatal hypoxia due to hormonal and physiological differences.[9] Similarly, in this study, 56.67% of neonates were delivered vaginally, while 43.33% were born via cesarean section, which aligns with findings from Gagneur et al. (2018), who reported that vaginal deliveries constituted 60% of birth asphyxia cases. The relatively high prevalence of birth asphyxia in vaginal deliveries may be due to prolonged second-stage labor and birth trauma.[10]

The majority of neonates (85.00%) had an Apgar score between 4-6, while 15.00% had a score of 0-3, indicating severe birth asphyxia. These results are similar to those of Brucknerová et al. (2018), who found that 86.2% of neonates with birth asphyxia had Apgar scores between 4-6.[8]Additionally, resuscitation was required in 65.83% of neonates, which closely matches the 67.5% reported by Liu et al. (2016). The need for resuscitation in a majority of cases highlights the severity of birth asphyxia and the importance of timely intervention to prevent long-term complications.[11]

Serum LDH levels serve as a biochemical indicator of tissue hypoxia and cellular damage. In this study, 33.33% of neonates had LDH levels between 801-1000 U/L, while 20.83% had levels >1000 U/L, indicating severe hypoxic injury. These findings align with those of Fanaroff et al. (2015), who reported that neonates with severe birth asphyxia exhibited LDH levels exceeding 950 U/L.[12] The current study also observed that neonates with LDH >1000 U/L had a higher incidence of complications, reinforcing the utility of LDH as a predictive biomarker.[13]

The most frequently observed complication in this study was Hypoxic-Ischemic Encephalopathy (HIE) in 39.17% of neonates, followed by Respiratory Distress Syndrome (23.33%) and seizures (15.83%). These findings are comparable to those reported by Shankaran et al. (2018), where HIE was observed in 42% of neonates, and respiratory distress occurred in 25% of cases.[13] The strong correlation between high LDH levels and HIE is further supported by research from Ezzat et al. (2017), who reported that LDH >1000 U/L was significantly associated with moderate-to-severe HIE. The current study confirms that elevated LDH levels can indicate an increased risk of HIE and other neurological complications.[14]

A key finding of this study was the statistically significant relationship between LDH levels and Apgar scores ($p < 0.05$). Neonates with Apgar scores of 0-3 had the highest LDH levels, with 38.89% showing LDH >1000 U/L, while neonates with Apgar scores of 4-6 had a more even distribution across different LDH levels. This trend aligns with results from Chaudhari et al. (2016), who found that LDH levels >1200 U/L were significantly correlated with Apgar scores ≤3. The biochemical basis for this correlation lies in the release of LDH from damaged tissues following severe hypoxia, which is exacerbated in neonates with extremely low Apgar scores.[9]

LIMITATIONS OF THE STUDY

- Small Sample Size
- Short Follow-Up Duration
- Study conducted at single centre

CONCLUSION

This study highlights the significance of serum lactate dehydrogenase (LDH) levels as a biochemical marker in assessing the severity of birth asphyxia in term neonates. Elevated LDH levels correlated with lower Apgar scores, increased need for resuscitation, and higher incidence of complications, particularly hypoxic-ischemic encephalopathy (HIE). The findings reinforce LDH's potential role in early diagnosis and prognosis of neonatal hypoxic injury. Given its cost-effectiveness and accessibility, LDH measurement can be integrated into neonatal care protocols for risk stratification and timely intervention.

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