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Serum Lactate Dehydrogenase Level as an Early Predictor of Morbidity in Neonates with Transient Tachypnea of the Newborn

Sheikh Mohammad Aqib[1], Surendra Singh Meena[2], Amit Kumar[3], Sonam Yadav[4]

[1]Postgraduate Resident, Department of Paediatrics, NIMS University Rajasthan, Jaipur, India
[2]Assistant Professor, Department of Pediatrics, NIMS University Rajasthan, Jaipur, India
[3]Assistant Professor, Department of Pediatrics, NIMS University Rajasthan, Jaipur, India
[4]Postgraduate Resident, Department of Paediatrics, NIMS University Rajasthan, Jaipur, India

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Corresponding Author
Dr. Amit Kumar
Assistant Professor,
Department of Pediatrics,
NIMS University Rajasthan,
Jaipur, India.

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ABSTRACT

Background: Transient tachypnea of the newborn (TTNB) is a frequent cause of neonatal respiratory distress. Serum lactate dehydrogenase (LDH), a marker of cellular injury, may help predict disease severity and prognosis.
Objective: To evaluate serum LDH levels as an early predictor of morbidity in neonates with TTNB, defined by duration of NICU stay and incidence of complications.
Methods: A prospective observational study was conducted in the NICU at NIMS University Hospital, Jaipur, between May 2023 and October 2024. Neonates ≥34 weeks gestational age diagnosed with TTNB were included. Serum LDH was measured within 24 hours of admission. The correlation of LDH with NICU stay and complications was analysed using appropriate statistical tests.
Results: Among 140 neonates, 56.43% had elevated LDH (>750 IU/L). Elevated LDH was associated with prolonged NICU stay (8.15 ± 1.28 vs. 3.79 ± 1.32 days; $p<0.0001$) and higher complication rates (32.91% vs. 4.92%; $p<0.0001$). Strong correlation existed between LDH and NICU stay duration ($r=0.8439$), and moderate correlation with complications ($r=0.4677$).
Conclusion: Elevated serum LDH levels are associated with increased morbidity in neonates with TTNB. LDH may serve as a simple, early biochemical marker for risk stratification and prognostication in these patients. Further large-scale, multicentre studies are recommended to validate these findings.

Keywords: Transient tachypnea, newborn, lactate dehydrogenase, NICU, neonatal complications

INTRODUCTION

Transient tachypnea of the newborn (TTN) is a significant cause of respiratory distress in neonates, characterized by rapid breathing resulting from the delayed clearance of fetal lung fluid from the lungs after birth. Its incidence is reported at approximately 5.7 per 1,000 live births[1], and while TTN is generally regarded as a self-limited condition, it can sometimes lead to significant complications requiring prolonged hospitalization and advanced respiratory support. Early identification of neonates at risk of greater morbidity is essential for optimizing clinical management, allocating intensive care resources, and improving neonatal outcomes.

Biomarkers that predict disease severity at an early stage offer critical value in neonatal care. Among these, serum lactate dehydrogenase (LDH) has attracted considerable attention[2,3]. LDH is an enzyme released during tissue injury and hypoxia, both of which are integral to the pathophysiology of TTN. Elevated serum LDH in neonates with TTN reflects the increased anaerobic metabolism resulting from insufficient oxygenation in the early postnatal period. Recent studies have demonstrated that higher LDH levels upon admission are significantly associated with longer NICU stays and a greater risk of complications in TTN. Ozkiraz et al. specifically identified LDH as an effective predictor of prolonged oxygen support requirements, even for infants with normal Apgar scores, underscoring its practical value for NICU triage and referral decisions[4].

Further, LDH has been found not only to differentiate between TTN and more severe respiratory conditions[5,6,7] like respiratory distress syndrome (RDS), but also to possess prognostic utility in a broader spectrum of neonatal morbidities, including sepsis and perinatal asphyxia[8,9]. However, given that TTN and RDS often overlap in clinical presentation, integrating LDH levels into a multimodal assessment improves diagnostic precision and guides early intervention.

In summary, incorporating serum LDH measurements into the routine early evaluation of neonates with TTN could enhance the prediction of clinical course, support prompt and targeted therapy, and potentially reduce morbidity associated with respiratory distress in the newborn.

Methodology

Study Design: This prospective observational study was conducted at the NICU of NIMS University Hospital, Jaipur, from May 2023 to October 2024. The study aimed to assess serum lactate dehydrogenase levels in neonates with transient tachypnea of the newborn as an early predictor of morbidity.

Study Population: Patients were eligible for inclusion if they were

- All neonates of ≥34 weeks gestation admitted with the diagnosis of transient tachypnea of the newborn.
- Neonates with the diagnosis of transient tachypnea of the newborn for whom the parents/guardians provided their consent to participate in the study.

Exclusion Criteria:

- Premature neonates with respiratory distress syndrome
- Perinatal asphyxia
- Early onset neonatal sepsis
- Meconium aspiration syndrome
- Congenital pneumonia
- Congenital cardiac/ pulmonary abnormalities

Data Collection: Demographic data, mode of delivery, gestational age, serum LDH levels, duration of NICU stay, and complications were recorded. LDH was measured using a Siemens Dimension EXL 200 within 24 hours of NICU admission.

Statistical Analysis: The data was compiled and analysed using MS Excel (R) Office 365, GraphPad Prism 8.4.2, and SPSS version 25. Descriptive statistics were presented in the form of proportions/percentages for categorical variables and mean & standard deviation for continuous data variables. Fisher's Exact test/Chi-square test was used for the comparison of proportions (Categorical variables). Continuous variables were analysed using the Mann-Whitney test/Student T test (Independent group/Unpaired data) and Wilcoxon signed rank test/Paired T test (for paired data) based on the normality of the data. Correlation analysis for the univariate assessment was done using the Pearson R or Spearman's rho correlation coefficient. P-value of <0.05 was considered significant.

Ethical Considerations: The study protocol was approved by the Institutional Ethics Committee of the National Institute of Medical Science & Research, Jaipur. Informed consent was obtained from all participants before enrolment in the study.

Results

Gender Distribution

There was a notable male preponderance among the study population, with 94 out of 140 neonates being male (67.15%) and 46 (32.85%) being female. Table 2. Gender distribution of neonates in the study. Gender Number Percentage Female 46 32.85% Male 94 67.15

Mode of Delivery

Distribution of mode of delivery among study participants.

Gestational Age
The mean gestational age was 37.26 ± 1.08 weeks, with a median gestational age of 37 weeks and a range of 36 to 39 weeks

Serum LDH levels
The mean serum LDH level among the neonates was 824.90 ± 396.89 IU/L, with a median value of 831 IU/L. The observed range was 135–1492 IU/L.

Table 1. Descriptive statistics of serum LDH levels (IU/L).

Serum LDH	Values
Mean ± SD	824.90±396.89
Range (Min-Max)	135-1492
Median (IQR) 831	(471-1148)

A normal range for serum LDH was considered to be 135-750 IU/L in line with the internationally accepted standards. It was seen that 56.43% of neonates had a raised LDH as seen by a serum LDH level of >750 IU/L.

Table 2. Categorization of neonates based on serum LDH levels.

Serum LDH category	Number	Percentage
Normal LDH	61	43.57%
Raised LDH	79	56.43%

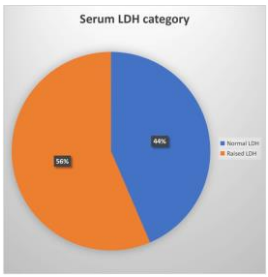


Figure 1. Pie chart illustrating the distribution of LDH categories

Duration of NICU stay
The mean duration of NICU stay was 6.25 ± 2.53 days, with a median duration of 7 days (range: 1–10 days). The majority (42.86%) stayed for 4–7 days, followed by 36.43% who stayed more than 7 days.
Table 3. Descriptive statistics of NICU stay duration

Duration of NICU stay	Values
Mean ± SD	6.25±2.53
Range (Min-Max)	1-10
Median (IQR)	7 (4-8)

Based on the duration of the study, categorisation of the neonates was done, with the majority (42.86%) staying for 4–7 days, followed by 36.43% who stayed more than 7 days.

Table 4. NICU stay duration categorized into groups.

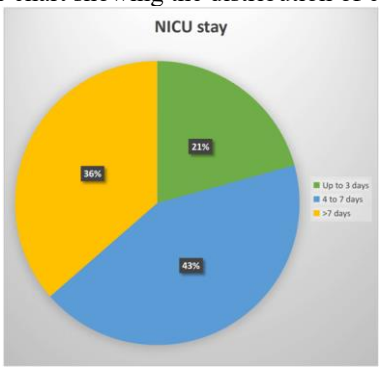
Duration category	Number	Percentage
Up to 3 days	29	20.71%
4 to 7 days	60	42.86%
>7 days	51	36.43%

Complications
Among the neonates, 29 (20.71%) developed complications (including respiratory support requirement for more than 72 hours), while 111 (79.29%) had no complications.

Table 5. NICU stay duration categorized into groups.

Complication	Number	Percentage
No complication	111	79.29%
Complication	29	20.71%

Figure 2. Pie chart showing the distribution of complications



A univariate correlation analysis revealed that serum LDH levels had a statistically significant and strong positive correlation with NICU stay duration ($\rho = 0.8439$, $P < 0.0001$) and a moderate correlation with the occurrence of complications ($\rho = 0.4673$, $P < 0.0001$). No statistically significant correlation was observed between serum LDH and gender, mode of delivery, or gestational age.

Table 6. Correlation analysis between serum LDH levels and clinical/demographic variables.

Parameters	Rho	95% CI	P value
Gender	0.02314	-0.1482 to 0.1931	0.7861
Mode of delivery	0.03524	-0.1363 to 0.2047	0.6793
Gestational Age	-0.1223	-0.2870 to 0.04948	0.1501
NICU duration	**0.8439**	**0.6905 to 0.9952**	**<0.0001**
Complication	**0.4673**	**0.3223 to 0.5909**	**<0.0001**

Serum LDH and NICU Stay

The mean NICU stay duration was significantly longer in the raised LDH group compared to the normal LDH group (8.15 ± 1.28 vs. 3.79 ± 1.32 days, $P < 0.0001$).

Table 7. Comparison of NICU stay duration between normal and raised LDH groups.

NICU stay	Normal LDH	Raised LDH	P Value
Mean ± SD	3.79±1.32	8.15±1.28	**<0.0001**
Range (Min-Max)	2-6	4-10	

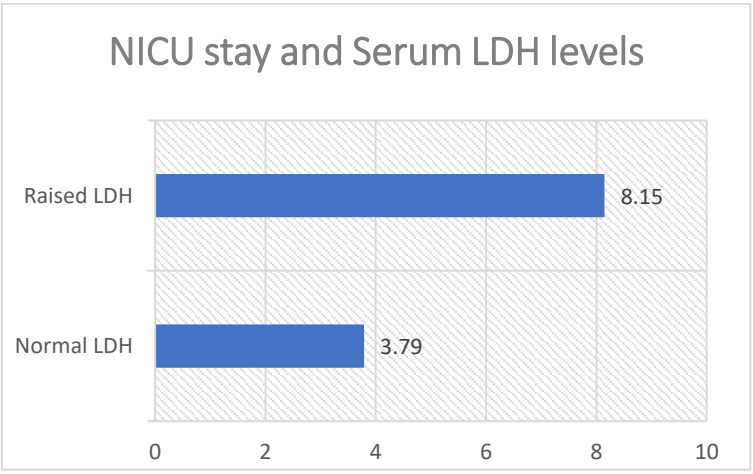


Figure 3. Bar chart comparing NICU stay durations across LDH categories.

Correlation analysis further confirmed a strong positive correlation ($R = 0.8439$, $R^2 = 0.7123$, $P < 0.0001$) between serum LDH levels and NICU stay duration, indicating that LDH levels explained approximately 71.23% of the variance in hospital stay duration.

Table 8. Correlation analysis of serum LDH levels with NICU stay duration.

Serum LDH levels	Value
R (Correlation coefficient)	0.8439
R square (Coefficient of determinance)	0.7123
P Value	<0.0001

Serum LDH and Complications

The complication rate was significantly higher in the raised LDH group (32.91%) compared to the normal LDH group (4.92%) ($P < 0.0001$).

Table 9. Incidence of complications in neonates stratified by LDH levels.

Complication	Normal LDH	Raised LDH	P Value
No	58 (95.08%)	53 (67.09%)	**<0.0001**
Yes	3 (4.92%)	26 (32.91%)	

A moderate positive correlation was found between LDH levels and complications ($R = 0.4677$, $P < 0.0001$), indicating that higher LDH levels were associated with a greater likelihood of complications.

Table 10. Correlation analysis of LDH levels with complications.

Serum LDH levels	Value
R (Correlation coefficient)	0.4677
P Value	<0.0001

Discussion

Transient Tachypnea of the Newborn is a significant neonatal respiratory condition primarily resulting from delayed absorption of fetal lung fluid. The retained fluid occupies alveolar space, impeding effective gas exchange and leading to respiratory distress. TTNB is more commonly observed in neonates delivered by cesarean section[10,11], owing to the lack of thoracic compression during delivery, which otherwise aids in the expulsion of lung fluid. Despite being generally self-limiting due to spontaneous absorption of fluid via pulmonary lymphatics, TTN can still lead to considerable neonatal morbidity [19,20]

Lactate dehydrogenase (LDH) being a ubiquitous intracellular enzyme essential in energy metabolism, particularly in anaerobic glycolysis. It is released into the bloodstream during cellular injury, including that caused by perinatal or neonatal hypoxia, and serves as a nonspecific marker of tissue damage[12,13,14]. Elevated serum LDH levels have been associated with a variety of neonatal conditions, especially respiratory disorders such as respiratory distress syndrome (RDS), where tissue hypoxia and damage are prominent features.

In light of this, the present study was undertaken in the Department of Paediatrics at the Neonatal Intensive Care Unit, National Institute of Medical Sciences, Jaipur, Rajasthan, India, and included 140 neonates diagnosed with TTNB. Serum LDH levels were measured and correlated with clinical morbidity indicators, including the duration of NICU stay and incidence of complications.

Conclusion

The study concluded that a majority of patients with Transient Tachypnea of the Newborn had elevated LDH levels. Close to half of the TTN patients had raised LDH levels. Elevated LDH was associated with longer NICU stays and higher complication rates. Therefore, LDH may be associated with increased morbidity in TTN patients and has the potential to serve as an early diagnostic marker in these newborns. The findings of this study are consistent with the existing literature, both nationally and internationally. Larger, multicentric studies are needed to confirm and expand upon these results.

Ethical Approval: This study was approved by the Institutional Ethics Committee.
Informed Consent: Written informed consent was obtained from parents/guardians.
Funding: Institutional support provided by NIMS University.
Conflict of Interest: None declared.
Data Availability: Data supporting the findings are available upon reasonable request from the corresponding author.
Author Contributions: SMA: Concept, data collection, manuscript drafting; MT: Study design, supervision, manuscript review. All authors approved the final manuscript.
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