

Diagnostic Accuracy of Lactate Dehydrogenase for Diagnosis of Perinatal Asphyxia in Neonates with Non-Reactive CTG

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ABSTRACT

Background: Birth asphyxia is a major cause of mortality and morbidity in neonates. Lactate dehydrogenase (LDH) is an enzyme which can help in early prediction.

Aim: To assess the diagnostic accuracy of lactate dehydrogenase for diagnosis of perinatal asphyxia among neonates with non-reactive cardiotocography taking clinical diagnosis of birth asphyxia as gold standard.

Methods: This cross sectional study was done at Department of Pediatric Medicine, Services Hospital, Lahore for six months. 280 neonates with non-reactive CTG were included. Blood sample was taken within first 1 hr after birth. LDH level was noted and neonates were labeled as positive or negative. Neonates were followed-up for 72hours for signs of birth asphyxia.

Results: Mean gestational age was 39.45±1.73weeks and the mean weight was 2.75±0.48 kg. LDH was found positive in 179 (63.9%) patients and the birth asphyxia was observed positive in 176 (62.9%) patients. The diagnostic accuracy of LDH was 91.8% taking birth asphyxia as gold standard.

Conclusion: LDH is the appropriate and reliable predictor of perinatal asphyxia with diagnostic accuracy of 93% among neonates with non-reactive cardiotocography taking clinical diagnosis of birth asphyxia as gold standard.

Keywords: Lactate Dehydrogenase, LDH, Birth Asphyxia, Perinatal Asphyxia, Reactive Cardiotocography, CTG

INTRODUCTION

Birth asphyxia is a major cause of mortality and morbidity in neonates.¹ It is difficult to define birth asphyxia accurately and thus neonatal mortality data associated with birth asphyxia is also not reliable¹. Birth asphyxia was found in 0.5% of full term neonates¹. Locally, the frequency of birth asphyxia was found in 22% neonates born in a tertiary care hospital.² Birth asphyxia is mostly diagnosed on retrospective basis². But without the help of antenatal or birth records it is not possible to diagnose perinatal asphyxia retrospectively². Birth asphyxia causes hypoxemia which in turn affects different organ systems of body.³ After birth asphyxia enzyme leakage like lactate dehydrogenase occur due to cellular damage as a result of hypoxic ischemic injury⁴.

LDH is found in most body tissues⁵. It is released as a result of hypoxia and poor tissue perfusion⁵. LDH is a good predictor of birth asphyxia and can predict it in early stages when birth asphyxia can be prevented on early basis⁵. LDH level is high during first 12 hrs after birth in asphyxiated neonates⁴. This result is of clinical significance providing a cheap and reliable tool for predicting birth asphyxia in new born infants⁴. Reddy, Dutta and Narang conducted a study on 45 neonates and found that the sensitivity and specificity of LDH was 100% and 89% respectively⁵. However in another study conducted by Shah, Tracy and Smyth on 61 neonates, the sensitivity and specificity of LDH was 94% and 67% respectively⁹. Clinical diagnosis of HIE (hypoxic ischemic encephalopathy) based on cyanosis, tachycardia / bradycardia, tachypnea was taken as gold standard.

The rationale of this study is as not all patients with non-reactive cardiotocography develop birth asphyxia so this study will help to determine which patients will develop birth asphyxia on basis of serum LDH estimation within first 1 hr of birth. LDH is a good predictor of birth asphyxia and can predict it in early stages when birth asphyxia can be prevented on early basis. But due to lack of local evidence, assessment of LDH for prediction of birth asphyxia is not in practice. The study which has been mentioned above has small sample size so we cannot rely on results of that study. That is why I want to conduct this study to get more appropriate and reliable results and to implement the use of LDH for prediction of birth asphyxia in our population. This will help in early detection and intervention for birth asphyxia so that neonatal morbidity and mortality be minimized.

The objective of the study was to assess the diagnostic accuracy of lactate dehydrogenase for diagnosis of perinatal asphyxia among neonates with non-reactive cardiotocography taking clinical diagnosis of birth asphyxia as standard criteria.

MATERIAL AND METHODS

This cross sectional study was conducted in the Department of Pediatric Medicine, Services Hospital, Lahore during six months from 12-5-2015 to 12-11-2015. Sample size of 280 neonates was calculated by 95% confidence level and taking expected percentage of birth asphyxia i.e. 22%⁶ with margin of error 5% for sensitivity 94%⁶ and margin of error 8% for specificity 67%⁶ of LDH for diagnosis of perinatal asphyxia among neonates with non-reactive CTG taking clinical diagnosis as gold standard. Sampling technique used was Non probability (consecutive) sampling.

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1. Gestational age \geq 35weeks (on antenatal record through dating scan).
2. Either sex
3. Neonates with perinatal record of non-reactive CTG (CTG was considered non-reactive if sudden and sustained (>30 min) fetal bradycardia (heart rate < 110 beats/min) or absence of fetal heart rate variability (rapid fluctuations on base line fetal heart rate 110-160 beats/min) in the presence of late decelerations (slowing of heart rate >20 % after onset of uterine contraction) ,variable decelerations (vary in shape,timing and form) and persistent decelerations (depth >60 beats and duration >60 sec) during labour on 60 minute CTG record)

Exclusion

1. Very low birth weight neonates (birth weight <1.50 kg).
2. Babies with congenital malformations diagnosed on clinical examination.

Data Collection Procedure: After informed consent from parents, 280 neonates fulfilling the selection criteria with non-reactive CTG were included in this study from delivery room of Department of Obstetrics & Gynecology, Services Hospital, Lahore. Demographic profile (name, gestational age and birth weight) was also noted .Then blood sample was obtained from each neonate within first 1 hr after birth. All samples were sent to the laboratory for assessment of LDH level. Reports were assessed and neonates were labeled as positive (LDH \geq 580U/L) or negative (LDH<580U/L) for birth asphyxia. Neonates were considered to have birth asphyxia if \geq 2 of the following findings were present within 72 hours of birth:

1. Neurological abnormalities like irritability, lethargy, hypotonia (decrease tone of skeletal muscles on clinical examination) or seizures.
2. Abnormal heart rate bradycardia <100beats/min or tachycardia >160 beats/min.
3. Central cyanosis (blue color of lips, tongue).
4. Poor breathing, tachypnea (respiratory rate >60/min) or apnea (absence of breathing for >20 sec).
5. Then neonates were followed-up in NICU till 72 hours after birth for signs of birth asphyxia. All this information was collected on Proforma.

Data Analysis: Collected data was entered & analyzed by SPSS v.16. Numerical variables like gestational age, birth weight and LDH level were computed as mean \pm SD. Categorical variables like sex of neonate and birth asphyxia on LDH and clinically were presented as frequency and percentages. 2x2 table was generated to measure sensitivity, PPV, specificity, NPV & diagnostic accuracy of LDH taking clinical findings as standard criterion.

RESULTS

]The mean gestational age at birth was 39.45 \pm 1.73 weeks. There were 177 (63.2%) male neonates while 103 (36.8%) were females. The mean weight of neonates was 2.75 \pm 0.48 kg. The mean LDH of the patients was 591.65 \pm 58.09 (Table 1).

LDH was found positive in 179 (63.9%) patients and negative in 101 (36.1%) patients. Birth asphyxia was observed positive in 176 (62.86%) patients and negative in 104 (37.14%) patients (Table 2).

The sensitivity of LDH was 94.3% with specificity of 87.5%, PPV was 92.7%, NPV was 90.1% and the diagnostic accuracy was 91.8% taking birth asphyxia as gold standard. Table 3

Table 1: Baseline characteristics of neonates

n	280
Gestational age (weeks)	39.45 \pm 1.73
Male	177 (63.2%)
Female	103 (36.8%)
Weight (kg)	2.75 \pm 0.48
LDH level	591.65 \pm 58.09

Table 2: Distribution of positive and negative cases (n=280)

	Frequency	Percent
LDH	Positive	179
	Negative	101
Birth asphyxia	Positive	176
	Negative	104

Table 3: Comparison of LDH according to birth asphyxia

		Birth Asphyxia		Total
		Positive	Negative	
LDH	Positive	166	13	179
	Negative	10	91	101
Total		176	104	280

Sensitivity=94.3%, Specificity=87.5%, PPV=92.7%, NPV=90.1% & Diagnostic Accuracy=91.8%

DISCUSSION

Birth asphyxia oxygen insufficiency at the time of delivery of fetus can cause severe hypoxic ischemic organ damage in neonates. It may be followed by severe adverse outcome or severe life-long complications. Birth asphyxia is described as progressive injury to the organs or all organ systems, especially the nervous system. It can take about 72 hours for symptomatic neurological signs.⁷

According to our study LDH was found positive in 179 (63.9%) patients and birth asphyxia was observed positive in 176 (62.8%) patients. The sensitivity of LDH was 94.3% with specificity of 704%, PPV was 91.7%, NPV was 90.1% and the diagnostic accuracy was 91.8% taking birth asphyxia as gold standard. Ozkiraz et al., presented that LDH presented 88.9% PPV and showed the best predictive assessment method for prolonged oxygen requirement⁸.

In a study by Serdar Beken et al showed that the sensitivity of LDH was 79%, specificity was 56%, PPV was 76%, NPV was 62% and diagnostic accuracy of LGH was 71% for the prediction of HIE. ⁹ Reddy, Dutta and Narang conducted a study on 45 neonates and found that the sensitivity and specificity of LDH was 100% and 89% respectively.⁶ However in another study conducted by Shah, Tracy and Smyth on 61 neonates, the sensitivity and specificity of LDH was 94% and 67% respectively.(9) Clinical diagnosis of HIE (hypoxic ischemic encephalopathy) based on cyanosis, tachycardia / bradycardia, tachypnea was taken as gold standard.

In a study, it was proposed that LDH level after 72hours of life of neonate has best accuracy in differentiation of asphyxiated & non-asphyxiated neonates. They found through the study that LDH level after 72 hours of life was showed its best accuracy to differentiate asphyxiated neonates from other diseases in neonates,

who did not have any particular indications of the disease¹⁰. Sanjay et al demonstrated in their study that assessment of LDH level after 72 hours of life can support to differentiate the asphyxiated and non-asphyxiated neonates, born at term. It was found that with LDH > 580 U/L had sensitivity of 59.18% and specificity of 92%, PPV of 87.88% and NPV of 69.70%¹¹.

In 2010, Karlsson et al., done an experimental trial to examine organ damage in neonates with perinatal asphyxia. It was found that in asphyxiated neonates having conflicting degree of hypoxic ischemic encephalopathy and in neonates with fetal distress during birth and LDH > 1049 U/L, were the most suitable with 100% sensitivity and 97% specificity¹². Reddy et al., reported 100% sensitivity of LDH level after 72 hours of birth for detection of birth asphyxia¹⁰. Karlsson et al., found that in asphyxiated neonates with varying degree of hypoxic ischemic encephalopathy and in neonates with fetal distress during labor, the LDH > 1049 U/L was the most appropriate analyst for mild, moderate & severe hypoxic ischemic encephalopathy. It showed sensitivity of 100% & specificity of 97%¹³.

CONCLUSION

LDH is the appropriate and reliable predictor of perinatal asphyxia with diagnostic accuracy of 93% among neonates with non-reactive cardiotocography taking clinical diagnosis of birth asphyxia as gold standard.

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