Evaluation of creatine kinase and lactic dehydrogenase enzymes for the retrospective diagnosis of perinatal asphyxia

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ABSTRACT

Objectives: This study was conducted to diagnose perinatal asphyxia in babies delivered outside with a history of poor cry at birth and certain non specific signs of sickness admitted to NICU within 24 hours of birth. Serum CK-MB and LDH levels were done among the cases and compared with controls and their significance in diagnosing perinatal asphyxia retrospectively were studied.

Methods: a prospective study was conducted on 30 neonates comprising the cases(babies delivered outside) and 30 neonates comprising the controls (babies delivered intramural) meeting the inclusion and exclusion criteria for one year from November 2013 to November 2014. The blood samples were drawn at 24 and 72 hours of age and sent for analysis. A CK-MB level of above 92.6U/L at 24 hour and 39.15U/L at 72 hour was taken as cut off level and LDH above 580U/L at 24 and 72 hour taken as cut off level.

Results: CK-MB and LDH significantly raised in babies with perinatal asphyxia. The cut off CK-MB value of >92.6U/L at 24 hours has sensitively of 96.6% specificity of 86.6% and at 72 hours CK-MB >39.15U/L has sensitivity 83.3% specificity 30%. The cut off LDH value of >580U/L at 24 hours has sensitively of 100% specificity of 80% and at 72 hours LDH >580U/L has sensitivity 83.3% specificity 86.6%.

Conclusion: the area under ROC for LDH at 72 hours was 0.935 and area under curve of ROC for CK-MB at 72 hours was 0.778 with not much difference in area under the curve of ROC for CK-MB (0.984) and LDH (0.982) at 24 hours. So we conclude that LDH at 72 hours of life is most accurate at differentiating asphyxiated and non-asphyxiated symptomatic neonates.

KEYWORDS : Perinatal asphyxia, CK-MB, LDH

Introduction:
Perinatal asphyxia is a common neonatal problem which contributes significantly to neonatal morbidity and mortality. Only a third of deliveries in India are institutional(1) and many asphyxiated babies are brought late to hospitals. The signs of asphyxial injury are non-specific and overlap with other illnesses. In the absence of perinatal records, it is difficult to retrospectively diagnose perinatal asphyxia.

We conducted this study to ascertain whether common enzyme assays in neonates with non-specific sickness can distinguish an asphyxial from a non-asphyxial etiology

Materials and methods:
This study was done with newborn infants who were admitted to NICU over one year period in SDM College of Medical sciences and Hospital, Dharwad.

Inclusion criteria: Gestational age32 weeks or more, Birth weight 1.5kg or more, Age less than 24 hours at admission and with history of poor cry at birth, babies delivered outside and referred here were admitted to NICU for various symptoms suggestive of perinatal asphyxia

Exclusion criteria: Babies with obvious congenital anomalies, Babies Gestational age less than 32weeks birth weight less than1.5kg and babies with mothers who received pethidine or magnesium sulphate within 4 hours of delivery.

Controls: babies delivered in our hospital with gestational age 32 weeks or more birth weight 1500gms or more apgar score more than 7 at one minute, arterial blood pH more than 7.2 Sample size: 30 cases and 30 controls

The blood samples were drawn at 24 and 72 hours of age and sent for analysis. CK-MB level of above 92.6U/L at 24 hour and 39.15U/L at 72 hour was taken as cut off level and LDH above 580U/L at 24 and 72 hour taken as cut off level.

Results: CK-MB and LDH significantly raised in babies with perinatal asphyxia. The cut off CK-MB value of >92.6U/L at 24 hours has sensitively of 96.6% specificity of 86.6% and at 72 hours CK-MB >39.15U/L has sensitivity 83.3% specificity 30%. The cut off LDH value of >580U/L at 24 hours has sensitively of 100% specificity of 80% and at 72 hours LDH >580U/L has sensitivity 83.3% specificity

86.6%.

Discussion:
In India 260 lakh babies born every year but 9 lakh die during neonatal period. Out of this 7 lakh die in first week after birth(2) Major causes of neonatal mortality are perinatal asphyxia (23%), sepsis(33%), complications related to low birth weight and prematurity(27%) and congenital malformations (1-6%) (2).

Only a third of deliveries in India are institutional (1) and many asphyxiated babies are brought late to hospitals. The signs of asphyxial injury are non-specific and overlap with other illnesses. In the absence of perinatal records, it is difficult to retrospectively diagnose perinatal asphyxia.

We conducted this study to ascertain whether common enzyme assays in neonates with non-specific sickness can distinguish an asphyxial from a non-asphyxial etiology.

Our study showed CK-MB and LDH significantly raised in babies with perinatal asphyxia. Elevated CK-MB value of >92.6U/L at 24 hours has sensitivity of 96.6% specificity of 86.6% and at 72 hours CK-MB >39.15U/L has sensitivity 83.3% specificity 30%. Elevated CK-MB at 24 hour of life has high sensitivity and specificity than at 72 hours. Our study comparable to study by Primhak, *et al.*(3) the CK-MB in both normal (*n*=43) and asphyxiated (*n*=20) neonates, peaked at 8 hours and fell by 72 hours

The cut off LDH value of >580U/L at 24 hours has sensitivity of 100% specificity of 80% and at 72 hours LDH >580U/L has sensitivity 83.3% specificity 86.6%. Our study comparable to study by Sanath et al(4) which showed that LDH at 72 hours of life was the most accurate test for discriminating asphyxia from other illnesses among neonates who presented with non-specific signs of illness.

Lab data	Cases n=30	Control n=30	P value
CKMB at 24 hour U/L	Mean +/-SD 300.4+/-232.4	Mean+/-SD 49.9+/-12.7	0.0001
CKMB >60U/L at 24 hr	29(96.6%)	4(13.3%)	
CKMB at 72 hour U/L	Mean+/-SD 129+8+/-115	Mean+/-SD 44+/-8	0.0002
CKMB above 39 U/L at 72 hour	25(83.3%)	21(70%)	
LDH at 24 hour U/L	Mean+/-SD 1937+/-1132	Mean+/-SD 471+/-154	0.0001
LDH above 580U/L at 24 hour	30(100%)	6(20%)	

LDH at 72 hr U/L	Mean+/-SD 1129+/-545	Mean+/-SD 453+/-139	0.0001
LDH above 580U/L at 72 hr	24(80%)	7(23%)	

Table1- comparing CK-MB and LDH values between cases and controls

The results of the present study would be of utility to pediatricians in referral hospitals, who receive sick neonates, whose birth details are not well recorded. LDH could be used at 3 days of age to diagnose asphyxia retrospectively in such cases.

Conclusions: LDH at 72 hours of life is most accurate at differentiating asphyxiated and non-asphyxiated symptomatic neonates.

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Competing interests –none

Abbreviations: CK-MB= creatine kinase-myocardium LDH= lactic dehydrogenase ROC curve= receiver operating characteristic curve NICU=neonatal intensive care unit

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