Original Research Article

A comparative study of serum creatine kinase muscle-brain fraction (CK-MB) and lactate dehydrogenase (LDH) levels among asphyxiated and Non-asphyxiated term neonates

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Abstract

Background and Objectives: Perinatal asphyxia is a common neonatal problem and contributes significantly to neonatal morbidity and mortality. Only a third of deliveries in India are institutional and many asphyxiated babies are brought late to hospitals. In the absence of perinatal records, it is difficult to retrospectively diagnose perinatal asphyxia. Hence, this study was conducted to compare the serum levels of creatine kinase muscle brain fraction (CK MB) and lactate dehydrogenase (LDH) among asphyxiated and nonasphyxiated term neonates and to ascertain whether these enzymes can identify asphyxiated neonates. **Methods:** A study was conducted on 50 neonates comprising the cases and 50 neonates comprising the controls meeting the inclusion and exclusion criteria born in Neonatal division of department of Pediatrics, Jawaharlal Nehru Medical College, Ajmer over a period of 12 months from July 2012 to June 2013. Cases and Controls comprised of asphyxiated and non-asphyxiated neonates, respectively. The blood samples for CK MB and LDH was drawn at 8±2 and72±2 hours of age respectively and sent for analysis. A serum CK MB value > 92.6 U/L at 8 hours and LDH value > 580 U/L at 72 hours was taken as the cut-off level. The sensitivity, specificity, Positive predictive value (PPV), Negative predictive value (NPV) was calculated for both CK-MB and LDH. **Results:** The cut-off CK-MB value of > 92.6 U/L has 32 % sensitivity with a specificity of 100%.CK-MB has a positive predictive value of 100% with a negative predictive value of 59.52%. The cut-off LDH value of >580 U/L has 52% sensitivity with a specificity of 96%. LDH has a positive predictive value of 92.86% with a negative predictive value of 66.67%. **Interpretation and Conclusion**: The diagnostic performance of LDH is better than CK-MB. Estimation of CK-MB at 8 hours of life and LDH at 72 hours of life can help distinguish an asphyxiated from a non-asphyxiated term neonate in correlation with history and clinical features in the neonate.

Key words: Perinatal asphyxia,Creatine kinase muscle-brain fraction(CK-MB),Lactate dehydrogenase (LDH), hypoxic ischemic encephalopathy(HIE)

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INTRODUCTION

Birth asphyxia / intrapartum-related neonatal deaths are the fifth most common cause of deaths among children under 5 years of age accounting for an estimated 814,000 deaths each year. It is also associated with significant morbidity, resulting in a burden of 42 million disability adjusted life years (DALYs). Incidence of severe birth asphyxia (no cry or breath absent, slow or gasping at five minutes) was estimated as 4.6% of all births in community based studies in India. Birth asphyxia is the cause of 20% of neonatal deaths in India.[(1)]The global

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burden of neonatal deaths is estimated to be 5 million of which 3.2 million deaths occur during the first week of life. Almost a quarter of the burden of neonatal mortality is shared by India with three babies dying every minute, and every fourth baby born being low birth weight .[(2)]*Hypoxic-ischemic encephalopathy* is an important cause of permanent damage to CNS cells that may result in neonatal death or be manifested later as cerebral palsy or mental deficiency. About 20-30% of infants with hypoxic-ischemic encephalopathy die in the neonatal period, and 33-50% of survivors are left with permanent neurodevelopmental abnormalities (cerebral palsy, mental retardation. The greatest risk of adverse outcome is seen in infants with severe fetal acidosis(pH<6.7)(90% of death/impairment) and base deficit >25mmol/lt(72% mortality.)[3] Perinatal asphyxia may result in adverse effects on all major body systems. Many of these complications are potentially fatal. In a term infant with perinatal asphyxia renal, neurologic, cardiac and lung dysfunction occurs in 50%, 28%, 25% and 23% cases respectively[4] Transient myocardial ischemia (TMI) with myocardial dysfunction may occur in any neonate with a history of perinatal asphyxia. An elevated serum creatine kinase muscle-brain fraction (CK-MB) fraction or cardiac troponin T (cTnT) level may be helpful in determining the presence of myocardial damage. An elevation of serum CK-MB fraction of >5% to 10% may indicate myocardial injury .[(5)]Leakage of intracellular enzymes such as alanine aminotransferase (ALT), aspartate aminotransferase (AST) and lactate dehydrogenase (LDH) signaling multi organ dysfunction is seen together with HIE after perinatal asphyxia .[(6-8)]This study will be conducted to compare the serum levels of CK-MB and LDH among asphyxiated and non asphyxiated term neonates and to ascertain whether these enzymes can distinguish an asphyxiated from a non asphyxiated neonate.

AIMS AND OBJECTIVES OF THE STUDY

1. To monitor the serum levels of CK-MB and LDH among asphyxiated and non-asphyxiated term neonates.
2. To ascertain whether these enzymes can distinguish an asphyxiated from a non-asphyxiated term neonate.
3. To compare the serum levels of CK-MB and LDH among asphyxiated from a non – asphyxiated term neonates.

MATERIALS AND METHODS

SOURCE OF DATA

The study will be a prospective study conducted on asphyxiated and nonasphyxiated term neonates recruited from Neonatal Intensive Care Unit (NICU) and Post natal wards of J.L.N. medical College, Ajmer. The blood samples from the 50 neonates comprising the cases and 50 neonates comprising the controls constituted the material for the study.

METHOD OF COLLECTION OF DATA

The study included two groups:

The case group: It included 25 neonates fulfilling the following criteria:

Inclusion criteria:

1) Gestational age ≥ 37 weeks.
2) Appropriate for gestational age.
3) The neonates will be identified to have experienced perinatal asphyxia when atleast 3 of the following are present:

A) Intrapartum signs of fetal distress, as indicated by non reassuring NST on continuous electronic fetal monitoring and/ or by thick meconium staining of the amniotic fluid.

B) Apgar score of <7 at one minute of life.

C) Resuscitation with >1 minute of positive pressure ventilation before stable spontaneous respiration.

D) Profound metabolic or mixed acidemia (pH<7.00) in an umbilical artery blood sample, if obtained.

E) Mild, moderate or severe hypoxic ischemic encephalopathy (HIE), as defined by Sernatstaging .

Exclusion criteria:

1) Congenital malformations.
2) Maternal drug addiction.
3) Neonates born to mothers who would have received magnesium sulphate
within 4 hours prior to delivery or opiods (pharmacological depression).
4) Hemolytic disease of the newborn.

The control group:

It included 50 term apparently healthy neonates appropriate for gestational age without signs of peinatal asphyxia as evidenced by normal fetal heart rate patterns, clear liquor and one minute Apgar score ≥7.

All neonates included in the study had the following done:

1) Detailed maternal history, assessment of intrauterine fetal well being by continuous electronic fetal monitoring, meconium staining of amniotic fluid, birth events, Apgar score, sex of the baby and weight of the baby were recorded on theprecoded proforma. Gestational age was assessed by New Ballard scoring system. Arterial blood gas analysis (ABG) will be done if umbilical arterial blood is obtained and also depending on the availability of the facility for analysis.

2) Thorough clinical and neurological examination will be done for all the neonates included in the study. The asphyxiated neonates (case group) were monitored for

seizures, hypotonia and HIE in the immediate neonatal period in the NICU. A clinical grading system by Sernat will be used to grade the severity of HIE. The cases will also be observed for other systemic effects of asphyxia.

3) Blood sample will be collected from the neonates and sent for:

A) Creatine Kinase Muscle-Brain fraction (CK-MB) levels.

B) Lactate Dehydrogenase (LDH) levels.Blood for CK-MB will be drawn at 8±2 hours. Blood for LDH will be drawn at 72±2 hours of age. Laboratory technicians performing the CK-MB and LDH tests will be masked to the identity and birth history of asphyxia of the neonate. The upper limit of the normal range of CK-MB at 5-8 hours of life is 7.9% of 1,175 U/L which is ~92.6 U/L 106. A serum CK-MB value >92.6 U/L at 8 hours will be taken as the cut-off level. The normal reference value of LDH in neonates and infants <1 year is 170- 580 U/L 106. A value >580 U/L at 72 hours will be taken as the cut-off level.

4) The case group also had other investigations and imaging studies done as required for post-resuscitation management of asphyxiated neonates. The causes for hypotonia, seizures, lethargy, poor feeding other than HIE will be ruled out with relevant investigations available. Peripheral smear for erythrocyte morphology and reticulocyte count will be used to document hemolytic disease of the newborn.

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