

# A Study on Comparison of CK-MB, LDH and CRP Levels in Asphyxiated and Non-Asphyxiated Neonates

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## Abstract

**Background:** 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. There is a need to identify neonates with asphyxia who will be at high risk for hypoxic ischemic encephalopathy and multi-organ dysfunction. **Subjects and Methods:** The study was conducted on 60 neonates comprising the cases and 30 neonates comprising the controls meeting the inclusion and exclusion criteria. The blood samples for CK-MB and CRP, LDH was drawn at 24±2 and 72±2 hours of age respectively and sent for analysis. **Result:** CK-MB value of >60 U/L was found to 43(71.7%) of cases, LDH >580U/L was found in 40(66.7%) of cases and CRP >1mg/dl was found in 5(8.3%) cases. **Conclusion:** CK-MB and LDH were found to be elevated in asphyxiated neonates compared to non asphyxiated neonates.

**Keywords:** Perinatal asphyxia; Creatine kinase muscle-brain fraction (CK-MB); Lactate dehydrogenase (LDH); C-reactive protein (CRP); hypoxic ischemic encephalopathy (HIE).

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## Introduction

Perinatal asphyxia is a common perennial neonatal problem and contributes significantly to neonatal morbidity and mortality. Globally, hypoxia of the newborn (birth asphyxia) is estimated to account for 23% of the 4 million neonatal deaths and 26% of the 3.2 million stillbirths each year.<sup>[1]</sup> An estimated 1 million children who survive birth asphyxia live with chronic neurodevelopmental morbidities - cerebral palsy, mental retardation, and learning disabilities. Every hour, 104 children die as a result of asphyxia.<sup>[1]</sup> That is, approximately 8% of the total global pediatric mortality (age less than five years) making it a serious problem. Due to a lack of resources, developing countries are worse off.

In India, between 250,000 to 350,000 neonates die each year due to birth asphyxia, mostly within the first three days of life.<sup>[2]</sup> Data from National Neonatal Perinatal database (NNPD) suggests that perinatal asphyxia contributes to almost 20% of neonatal deaths in India.<sup>[2]</sup> Ante-partum and intra-partum asphyxia contributes to as many as 300,000 to 400,000 stillbirths.<sup>[2]</sup> In India, 8.4% of inborn babies have a one minute Apgar score less than 7 and 1.4% suffer from hypoxic ischemic encephalopathy (HIE).<sup>[2]</sup> Accurate estimates of the proportion of neonatal mortality attributable to birth asphyxia are limited by the lack of a consistent definition for use in community-based settings and the

absence of vital registration in communities where the majority of neonatal deaths occur.

Only a third of deliveries in India are institutional<sup>[3]</sup> and many asphyxiated babies have a delayed presentation to hospitals. The signs of asphyxial injury are nonspecific and overlap with other illnesses. In the absence of perinatal records, it is difficult to retrospectively diagnose perinatal asphyxia.

Although asphyxia is associated with multiple organ injuries, especially with adverse neurological outcomes, management still focuses on supportive care. So, if the adverse effects of hypoxia on the newborn are considered, there is a need to identify infants who will be at high risk for hypoxic ischemic encephalopathy and early neonatal death as a consequence of perinatal hypoxia. A variety of markers have been examined to identify perinatal hypoxia including electronic fetal heart monitoring, low Apgar scores, cord pH, electroencephalograms (EEG), computed tomography (CT) and magnetic resonance imaging (MRI) scans and Doppler flow studies. The current problem then is the inability to precisely distinguish the false positive affected from the true positive asphyxiated or compromised fetus. Several studies have been conducted to evaluate better markers that help distinguish an asphyxiated from a non-asphyxiated neonate.

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 occur in 50%, 28%, 25% and 23% cases respectively<sup>4</sup>. The extent of multi-organ dysfunction (MOD) determines the early outcome of an asphyxiated neonate with either the neonate succumbing as a consequence of organ damage or recovering completely. Generally there are no long term sequelae associated with these organ system derangements.

HIE refers to the central nervous system (CNS) dysfunction associated with perinatal asphyxia. 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) 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.<sup>[5]</sup>

Myocardial damage may also be determined by 2D Echo changes in ejection fraction (EF), fractional shortening (FS), Mitral or tricuspid regurgitation, ventricular hypokinesia. ECG also may depict changes in ST segment, T wave and Q wave changes.<sup>[6, 7]</sup>

## Subjects and Methods

Leakage of intracellular enzymes such as alanine aminotransferase (ALT), aspartate aminotransferase (AST) and lactate dehydrogenase (LDH) signaling multiorgan dysfunction is seen together with HIE after perinatal asphyxia.

Elevation in inflammatory mediators like interleukin 6, soluble intercellular adhesion molecule-1 and CRP is seen in stressful conditions like infection and perinatal asphyxia.

A sample of 60 neonates (>37 weeks) with perinatal asphyxia having base excess of -12mEq/L and above or at least 1 non-specific sign of sickness— tachypnea, chest retractions, grunt, lethargy, poor feeding, hypotonia, irritability, central cyanosis, cardiac gallop rhythm, cardiac murmur, shock and abdominal distension who were born and admitted to Neonatal Intensive care unit attached to Medical College. Controls were chosen in a ratio of 2:1.

The study included two groups

### The case group

It included 60 neonates fulfilling the following criteria

### Inclusion criteria

- Neonates [gestational age more than 37 weeks]- Normal/LSCS born and admitted at NICU of BTGH or STGH.
- Neonates weighing more than 2000grams
- Apgar of less than or equal to 5 at one min or less than 7 five min of birth.
- Failure to establish spontaneous respiration.
- Base excess of -12mEq/L or above at the time of admission

### Exclusion criteria

- Preterm neonates [gestational age < 36weeks].
- Neonates with internal congenital anomalies
- Neonates with syndromoid appearance.
- Neonates with congenital heart disease
- Neonates born at other than BTGH or STGH
- Neonates with birth weight of less than 2000grams

### The control group

It included 30 term apparently healthy neonates appropriate for gestational age without signs of perinatal asphyxia as evidenced by normal fetal heart rate patterns and one minute Apgar score  $\geq 7$ .

## Results

Table 1: Shows gender distribution of neonates studied.

Gender	Cases (n=60)		Controls (n=30)	
	No	%	No	%
Male	36	60.0	17	57.0
Female	24	40.0	13	43.0
Total	60	100.0	30	100.0

Among the 60 neonates in case group, there were 36 (60%) males and 24 (40%) females. Among the control group of 30 neonates, there were 17 (57%) males and 13 (43%) females. Gender distribution of neonates is statistically similar between two groups with  $P=0.993$ .

Table 2: Shows comparison of cut-off levels of CK-MB, CRP and LDH in cases and controls.

Variables	Study Group (N=60)		Control Group (N=30)		X2-test value	P-Value & Significance
	No.	%	No.	%		
CK-MB U/L	>60	43	71.7	0	0	X2 = 27.31 P < 0.001, VHS
	≤ 60	17	28.3	30	100.0	
CRP mg/dl	>1	5	8.3	2	6.7	X2 = 0.077 P > 0.05, NS
	≤1	55	91.7	28	93.3	
LDH U/L	≤580	20	33.3	29	96.7	X2 = 32.34 P < 0.001, VHS
	>580	40	66.7	1	3.3	

NS= not significant, S=significant, HS=highly significant, VHS=very highly significant

Among the 60 neonates in the case group, 17 (28.33%) had CK-MB levels <60 U/L and 43 (71.67%) had CK-MB levels >60U/L. In control group all had CK-MB levels <60 U/L. The number of neonates with CK-MB levels >60U/L is significantly more in cases when compared to controls with  $P<0.001$ .

Among the 60 neonates in the case group, 20 (33.33%) had LDH levels <580 U/L and 40 (66.7%) had LDH levels >580 U/L. Of the 30 neonates in control group 29(96.7%) had LDH levels <580 U/L and 1 (3.3%) had LDH level >580 U/L. The number of neonates with LDH levels >580 U/L is significantly more in cases when compared to controls with

P<0.001.

Among the 60 neonates in the case group, 5 (8.3%) had CRP levels >1mg/dl and 55(91.7%) had CRP levels <1mg/dl. Of the 30 neonates in control group 28(93.3%) had CRP levels <1mg/dl and 2 (6.7%) had CRP level >1mg/dl. There is no statistically significant difference in CRP levels among cases and control group (p > 0.05)

**Table 3: Shows comparison of CK-MB, CRP and LDH levels in cases and controls**

Variable	Study Group (N=60)		Control Group (N=30)		t-test value	P-value & sig.
	Mean ± SD	Median & Range	Mean ± SD	Median & Range		
CK-MB	75.3 ± 22.28	78 36-142	44.73 ± 10.99	46 26-60	t = 5.42	P<0.001, VHS
LDH	584.4 ± 89.3	565 154-881	396.1 ± 82.4	228 232-602	t = 9.67	P<0.001, VHS
CRP	0.21±0.38	0.1 0.1-1.8	0.18±0.33	0.1 0.1-1.6	t = 0.291	P=0.772, NS

NS= not significant, S=significant, HS=highly significant, VHS=very highly significant

Mean value of CK-MB is 75.3U/L in cases and 44.73U/L in controls. Mean value of LDH is 584.4U/L in cases and 396.1U/L in controls. Mean value of CRP is 0.21mg/dl in cases and 0.18mg/dl in controls. Mean values of CK-MB and LDH are more in cases compared to controls (p<0.001). There is statistically no significant change in CRP values among two groups (p=0.77).

**Table 4: Correlation of CK-MB, CRP and LDH with stages of HIE**

Variables		HIE stages			X2-test value	P-Value & sig
		Mild (1)	Moderate (2)	Severe (3)		
CK-MB	>60	22	17	4	X2=9.68	P <0.001, VHS
	≤ 60	16	1	0		
CRP	>1	2	2	1	X2=1.27	P =0.852, NS
	≤ 1	36	16	3		
LDH	>580	19	17	4	X2=12.95	P <0.001, VHS
	≤580	19	1	0		

In neonates with mild HIE 22 cases had CK-MB >60U/L and 16 had CK-MB <60U/L. In neonates with moderate HIE 17 had CK-MB >60U/L and 1 had CK-MB <60U/L. In neonates with severe HIE all 4 had CK-MB >60U/L. Raised levels of CK-MB was significant in neonates with moderate and severe HIE (p<0.001).

## Discussion

In the present study, gender distribution of neonates is statistically similar between two groups and the results are comparable to Reddy S et al.<sup>[8]</sup> The incidence of birth asphyxia is more in males in both the studies. There is neither a previous study available on this aspect nor a plausible mechanism has been proposed for the same. The social belief in the Indian setup that male babies are cared better and female babies are usually neglected and are managed at home even if they are very sick did not have any interference with the study population as none of the parents of the cases included in the study refused admission at birth. In the present study the number of neonates with CK-MB levels >60 U/L is significantly more in cases when compared to controls with P<0.001. 28.3% of the cases in the present study had CK-MB levels >60 U/L. This is comparable to Reddy S et al.<sup>[8]</sup> in which 36% of cases had CK-MB levels >60 U/L (P=0.006).

In the present study the mean CK-MB levels were significantly higher in cases compared to controls with P<0.001 which is comparable to Reddy S et al.<sup>[8]</sup> and Rajakumar PS et al.<sup>[9]</sup>

Raised levels of CK-MB among asphyxiated neonates was also observed in studies conducted by Primhak et al.<sup>[10]</sup>, Omokhodion SI et al.<sup>[11]</sup>, Fonseca E et al.<sup>[12]</sup>, Barberi et al.<sup>[13]</sup>. 66.7% of the cases in the present study had LDH levels >580 U/L. This is lower when compared to Reddy S et al.<sup>[8]</sup> in which 100% of cases had LDH levels >580U/L. In both the studies, the number of neonates with LDH levels >580 U/L is significantly more in cases when compared to controls. This is statistically significant in both the studies with P<0.001. In the present study the mean LDH levels in cases were significantly higher in cases compared to controls with P<0.001 which is comparable to Reddy S et al.<sup>[8]</sup>

In the present study CRP >1mg/dl was found only in 5(8.3%) of cases and 2(6.7%) of controls. There is no statistically significant difference in CRP levels among cases and controls. This is similar to study of Xanthouet al.<sup>[14]</sup> in which CRP levels were higher in infected neonates compared to asphyxiated neonates and controls.

## Conclusion

- Estimation of CK-MB at 24 hours of life and LDH at 72 hours of life can help distinguish an asphyxiated from a non-asphyxiated term neonate.
- Raised levels of CK-MB, LDH was more significant in cases with moderate to severe HIE.

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