

Predictor of neonatal morbidity in birth asphyxia

Rabindran¹, Gedam DS²

¹Dr. Rabindran, Consultant Neonatologist, Sunrise Superspeciality Children's Hospital, Hyderabad., ² Dr D Sharad Gedam, Editor, IJMRR and associate with L N Medical college, Bhopal, MP, India.

Address for correspondence: Dr Rabindran, E mail: rabindranindia@yahoo.co.in

Abstract

Hypoxic ischaemic brain damage is a major cause of neonatal mortality and morbidity. Similar degrees of insult may completely spare one child and devastate another, so very sensitive prognostic parameters are needed. Conventional predictors like fetal heart rate patterns, Apgar scores, need for resuscitation and umbilical arterial blood gas analysis show variable predictive values of outcome in neonates with asphyxia.

Key words: birth asphyxia, Neonatal morbidity, Predictor of outcome

Conventional perinatal variables such as Apgar score and cord pH are not specific predictors of adverse outcome. The stage of encephalopathy in the first week of life is probably the single best clinical predictor of long-term outcome after acute perinatal asphyxia. However early prediction of HIE is needed for selection of newborn infants who could benefit from neuroprotective treatment like hypothermia.

Recent papers have drawn our attention to the prognostic value of lactic acidemia in newborns with severe hypoxaemia [1]. Serum lactate levels in the first 30 minutes of life do not predict the severity of the ensuing encephalopathy. In contrast, sustained lactic acidosis is associated with severe encephalopathy on EEG and correlates with seizure burden. Plasma lactate > 9 mmol/l was associated with moderate or severe encephalopathy with a sensitivity of 84% and a specificity of 67% [2]. Cerebral lactate & urinary lactate are correlated with neonatal outcome. LDH is a good predictor of HIE during the first 12 h after birth. A cut off level of 1049 U/L for LDH was the best predictor of HIE (sensitivity 100% and specificity 97%) [3]. Salivary LDH also provided an early and accurate diagnosis of HIE and could be used as a triage tool. Degree of metabolic acidosis correlated with the neonatal neurological outcome. However it may lack sensitivity when asphyxia occurs during the early stages of labour. Hyperglycemia in the first 12 hours of life is associated with poor gross motor outcome or death in asphyxiated term infants. NRBCs can be considered as a marker of perinatal asphyxia and significantly correlate with the degree of asphyxia.

Biomarkers of neonatal hypoxic ischemic encephalopathy predictive of abnormal outcomes include glial fibrillary acidic protein, brain-derived neurotrophic factor, S100b, serum and CSF concentrations of IL-1b, IL-6, and serum neuron-specific enolase (NSE). GFAP => than 0.15 ng/mL was predictive of an abnormal brain MRI [4]. Higher cord plasma BDNF levels among babies with HIE had poor outcome. Urinary S100b concentrations above 1 mcg/L predicted neonatal death with a sensitivity and specificity of 100%, and concentrations were not affected by renal failure [5]. Cord blood S100b > 2.02 mg/L has a

sensitivity of 87% and a specificity of 88% for predicting the development of moderate or severe HIE [6]. IL-1 α seems to be a better predictor of HIE than TNF-alpha. Interleukin-6 concentrations in CSF after hypoxia were significantly higher in the patients with adverse outcome. Serum NSE > 40 mcg/L obtained between 4 & 48 hours after birth can distinguish infants who have mild HIE from infants who have moderate or severe HIE [7]. Glutamate level has been shown to correlate with grade of HIE and outcome. VEGF system is up-regulated in response to placental hypoxia and is assumed to be a potential early indicator of severe birth asphyxia.

Cardiac biomarkers aid in long term neurodevelopmental outcome prediction following neonatal hypoxic-ischaemia. ECG changes were significantly associated with poor prognosis (p = 0.001), with negative predictive value of 90%, but poor positive predictive value of 53% & were associated with multi-organ involvement, low Apgar score at 5 min and severe grade of encephalopathy. Newborns with severe neonatal hypoxic ischaemia have significantly higher serum troponin-T concentrations than other asphyxiated groups (mild to moderate) and healthy neonates on day 1 of life. The optimal cut-off value of cord troponin-I for prediction of perinatal hypoxia was 0.35 lg /L and for prediction of serious risk of early mortality was 4.6 lg /L [8]. Cord troponin-I is the marker with highest specificity (86%), sensitivity (88%), NPV (85%), PPV (88%) for prediction of perinatal hypoxia and was identified as the most sensitive factor for predicting early death [8]. The levels of antioxidant enzymes like lipid peroxidase can reliably and significantly predict mortality and morbidity. Determining the serum levels of oxidative stress markers and protein carbonyl can be used as predictors of immediate outcome in perinatal asphyxia.

High CPK activity was noted as a sensitive indicator of conspicuous brain damage. Serum CK-BB activity determined in cord blood between 6 and 12 h post-partum is an effective predictor of neurological prognosis. CSF glycine, Glutamate & aspartate concentration correlated significantly with the severity of HIE. Hypoxanthine level is a better predictor of hypoxia-related sequelae than Apgar score or lactate level. Urinary microglobulin was

Editorial

the most sensitive indicator of systemic organ injury in perinatal asphyxia. N-acetylaspartate, a marker of neuronal integrity declines after asphyxial injury, and this decline is predictive of later neurologic deficits. Cerebral ultrasound scanning was the most commonly used predictor of the outcome previously. However it is a poor predictor of outcome, with a likelihood ratio of close to 1 because of a high false positive rate. With Doppler measurements, the false positive rate was 0 but the detection rate (sensitivity) was only 23.5%. MRI demonstration of involvement of subcortical gray matter structures, such as the basal ganglia and thalamus, a T1-weighted signal in the posterior limb of the internal capsule are adverse prognostic markers. Abnormal intracerebral lactate levels on magnetic resonance spectroscopy within 18 hours of birth in infants with HIE and correlate with neurodevelopmental outcome. Higher Glx- α /Cr value by proton magnetic resonance spectroscopy in basal ganglia and thalamus in neonates with HIE may predict a poor outcome.

Amplitude-integrated electroencephalography (EEG) pattern and voltage was found to have a good correlation with outcome in term infants who suffered from hypoxic-ischemic encephalopathy. Early EEG changes (within 48 hours of age) in the acute phase is highly predictive of very unfavorable short-term outcomes. During the first 6 hours after birth, a bi-parietal aEEG is the most sensitive and specific single indicator of long-term outcome after HIE. The cerebral function monitor (CFM) has been used in term neonates to evaluate prognosis after perinatal asphyxia. Cerebral haemodynamics showing higher CBF and CBV on the first day of life had adverse outcomes, and a CBV outside the normal range had a sensitivity of 86% for predicting death or disability. The value of CBF velocity changes to predict poor outcome in asphyxiated infants is low 2–6 hour after asphyxia, but increases by the age of 12 hour. Because of its noninvasive, easy-to-use nature, neonatal polysomnography has become an important assessment method for neurologically damaged infants. Polygraphic evidence of status epilepticus, hypovoltage, and burst suppression pattern plays an important role in predicting neurologic disabilities. The need for early prediction of outcome of birth asphyxia is particularly important because of the narrow window of effectiveness and possible side effects of neuro-protective interventions. With advanced technology, biochemical and clinical assessment it is possible to prognosticate asphyxiated babies early which helps in early intervention.

Pal et al in his study revealed that linear relationship between levels of cardiac troponin-I and birth asphyxia.

How to cite this article?

Rabindran, Gedam DS. Predictor of neonatal morbidity in birth asphyxia. *Int J Med Res Rev* 2015;3(4):364-365. doi: 10.17511/ijmrr.2015.i4.085.

Therefore cardiac troponin-I level may be useful in predicting the mortality and outcome in perinatal asphyxia [9].

References:

- Cheung PY, Robertson CMT, Finer NN. Plasma lactate as a predictor of early childhood neurodevelopmental outcome of neonates with severe hypoxemia requiring extracorporeal membrane oxygenation. *Arch Dis Child* 1996; 74: F47–503.
- Da Silva S, Hennebert N, Denis R, Wayenberg J-L. Clinical value of a single postnatal lactate measurement after intrapartum asphyxia. *Acta Paediatr* 2000; 89(3): 320–3. doi: 10.1111/j.1651-2227.2000.tb01334.x
- Mathias Karlsson, Eva Wiberg-Itzel, Ela Chakkarapani, Mats Blennow, Birger Winbladh, Marianne Thoresen. Lactate dehydrogenase predicts hypoxic ischaemic encephalopathy in newborn infants: a preliminary study. *Acta Paediatrica* 2010;99(8) : 1139–1144. Doi: 10.1111/j.1651-2227.2010.01802.x
- Martha Douglas-Escobar, Michael D. Weiss. Neonatal Biomarkers of Brain Injury; *NeoReviews* Vol.14 No.10 October 2013 e501. doi: 10.1542/neo.14-10-e501
- Gazzolo D, Frigiola A, Bashir M, et al. Diagnostic accuracy of S100b urinary testing at birth in full-term asphyxiated newborns to predict neonatal death. *PloS one*. 2009;Feb 4(2):e4298 doi: 10.1371/journal.pone.0004298
- Qian J, Zhou D, Wang YW. Umbilical artery blood S100b protein: a tool for the early identification of neonatal hypoxic-ischemic encephalopathy. *Eur J Pediatr*. 2009;168(1):71–77. doi: 10.3389/fneur.2012.00144 PMID: PMC3486976
- E Thornberg, K Thiringer, H Hagberg, I Kjellmer. Neuron specific enolase in asphyxiated newborns: association with encephalopathy and cerebral function monitor trace. *Arch Dis Child Fetal Neonatal Ed*. 1995 Jan; 72(1): F39–F42.
- Turker G, Babaoglu K, Gokalp AS, Sarper N, Zengin E, Arisoy AE. Cord blood cardiac Troponin I as an early predictor of short-term outcome in perinatal hypoxia. *Biol Neonate* 2004; 86: 131–7.
- Pal P, Goel M. ECG changes in birth asphyxia and its correlation with Cardiac troponin-I. *Int J Med Res Rev* 2015;3(4):400-403. doi: 10.17511/ijmrr.2015.i4.075.