



A COMPARATIVE STUDY ON PREDICTORS OF ADVERSE OUTCOME IN PERINATAL ASPHYXIA

Ashish Gupta¹, Amit Kr Singh², Ajay Arya³

¹Post Graduate student, Department of Pediatrics, GMC Haldwani (Nainital)

²Assistant Professor, Department of Pediatrics, GMC Haldwani (Nainital)

³Professor and Head, Department of Pediatrics, GMC Haldwani (Nainital)

Conflicts of Interest: Nil

Corresponding author: Amit Kr Singh

Abstract:

Perinatal asphyxia is a leading cause of mortality and significant morbidity. Mild cases does not have a significant problem but moderate to severe cases can lead to many short and long term complications Objectives: The present study was done to evaluate various markers of perinatal asphyxia and their role in predicting adverse outcome. Methods: 108 neonates suspected to have experienced perinatal asphyxia were included in the study and followed up until discharge/ death. Role of cord blood pH, APGAR at 5 min and 10 min were compared with outcome. Results: Out of 108 studied neonates, 78(72.2%) needed resuscitation whereas 30(27.78%) didn't need any form of resuscitation, 20(18.52%) were in HIE stage 1, 11(10.19%) were in stage 2 & 25(23.15%) were in stage 3 of hypoxic ischemic encephalopathy according to sarnat & sarnat staging. Correlation coefficient and P value was calculated for cord blood pH and APGAR as a predictor of ischemic brain injury among the newborns with hypoxic ischemic encephalopathy & it was observed that both are statistically significant (p value<0.001) & significant negative correlation with severity of birth asphyxia. The mean APGAR score at 5 min,10min and mean cord blood pH in the babies without HIE were 7.9±0.6,8.9±0.3 and 7.28±0.08, respectively. Whereas the mean APGAR at 5 min, 10min and mean cord blood pH in the babies with HIE-I were 6.3±1.3,8.35±0.58 and 7.04±0.04; HIE-II 4.54±0.52,6.09±0.30 and 6.99±0.01; HIE-III 3.6±1.1,5.44±0.96 and 6.84±0.04. Conclusion: Umbilical cord blood pH is with cut off <7.10 remains the best predictor for perinatal asphyxia & poor early neonatal outcome followed by 5 min APGAR score. Following APGAR to 10 min has no significant advantage over 5 min APGAR.

Keywords: Perinatal asphyxia, APGAR, Cord blood pH, HIE

Introduction

Perinatal asphyxia is a condition characterized by an impairment of exchange of the respiratory gases (oxygen and carbon dioxide) resulting in hypoxemia and hypercapnia, accompanied by metabolic acidosis. virtually perinatal asphyxia can affect any organ of the body, but neurological sequelae are widely studied and most important cause of long term morbidity. in response to persistent hypoxia during perinatal period & anaerobic metabolism, baby will develop acidosis. With the help of umbilical cord blood pH status at birth, we can assess the perinatal insult retrospectively.[1]

Despite the recent advances and protocols in perinatal care, Perinatal asphyxia is a leading cause of infant morbidity and mortality worldwide. Although the infant mortality due to infectious diseases have been significantly reduced but perinatal asphyxia is still one of challenging problem especially in rural population. As per latest estimates, perinatal asphyxia accounts for 9.4%(i.e., 0.72 million) of total under 5 child mortality worldwide. Along with prematurity and systemic infections, Perinatal asphyxia is one of three most common causes of neonatal deaths. [2,3] It is also an important cause of stillbirths and according to the National neonatal perinatal database (NNPD; 2002-2003), perinatal asphyxia is the commonest

cause of stillbirths, accounting for 45.1% of all such cases. [4] Almost all (98.2%) asphyxia related deaths occur in first week of life, with 73% occurring within 24 hours of birth.⁵ Various definitions and criteria to define birth asphyxia were given by World Health Organization (WHO), National Neonatal-Perinatal Database (NNPD), American Academy of Paediatrics (AAP) and American College of Obstetrician and Gynaecologists (ACOG). [6,7,8]

Although the umbilical blood gases measurement is used in many countries and as per some researchers measuring the acid base status is best method to assess the perinatal asphyxia & its short and long term complication, but some studies don't favor the same. Dijkhoorn et al showed that a large number of neurologically abnormal infants have low Apgar scores, but a normal cord arterial pH [9]. A later study on more than 150 000 live-born infants by Casey et al reported that when pH fell to 7.0 or less, the likelihood of neonatal death increased by 1400 folds in term newborns [10]

There are various markers which have been tested to identify the perinatal asphyxia including FHR monitoring, low APGAR, cord blood pH, EEG, MRI and Doppler studies. Currently the problem is our inability to precisely differentiate the false positive tested from truly asphyxiated newborn. Several studies have been done to

evaluate the better marker to identify the true asphyxiated cases and our study is done to evaluate the role of umbilical arterial cord blood pH & APGAR score as a predictor of birth asphyxia and early neonatal outcome.

Materials & methods

Present study was conducted at a tertiary care NICU in Dr Sushila Tiwari Hospital and GMC Haldwani from January 2018 to December 2018. Study was approved by the ethical committee and informed consents were taken from the parents.

The study included 108 neonates fulfilling the following criteria:- Singleton, live born neonates of Gestational age > 37 weeks, Appropriate for gestational age, The new born will be suspected to have experienced perinatal asphyxia when any of the following criteria is present: a) signs of Intrapartum fetal hypoxia, as indicated by non-reassuring Non-Stress Test on continuous electronic fetal monitoring. b) Thick meconium stained liquor c) Apgar score of <7 at one minute of life. d) A need for Resuscitation for >1 minute. Patients were excluded according to the following criteria:- Preterm & low birth babies, Multifetal gestation, IUGR babies, intrauterine or perinatal infections, gross congenital malformation, History of maternal intrapartum fever, Maternal drug addiction, anti-epileptics, Neonates born to mothers who are smokers or consuming alcohol in pregnancy time.

Immediately after the delivery of the neonate, cord blood sample was taken from doubly clamped umbilical artery following delivery by separating the umbilical cord segment. A syringe of 2 ml, flushed with 1/1000 of heparin solution was inserted into the umbilical artery and 1ml of blood sample was collected. The results of the blood gas were analysed by ABG Machine (GEM PRIMER).

A detailed maternal history, APGAR score, examination & investigation of enrolled baby was done. All babies were followed up until discharge/death and the data collected. Outcome variables studied were 1) Need for resuscitation 2) Need for NICU/Neonatal ward admission 3) Delay in attaining full feeds 4) Neurological examination 5) Death/discharge. Analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0 and P values less than 0.05 were considered statistically significant

Results:

Among 108 neonates, 61(56.48%) were male and 47(43.52%) were female, 95(87.90%) were term, 9(8.33%) were post-dated & 4(3.70%) were post term. 101(93.52%) babies were delivered by vertex presentation and 7 (6.48%) by breech. 84(77.78%) babies had birth weight between 2.5-3 Kg, 14.81% between 3-3.5 kg & 7.41% babies more than 3.5Kg. 48(44.44%) neonates were delivered normally, 60(55.56%) were delivered by

caesarean section. 15(13.89%) had Reassuring NST and 93 (86.11%) had Non-Reassuring NST suggestive of fetal distress. 26(24.07%) neonates had Thick MSAF and in 82(75.93%) the amniotic fluid was clear. Mean APGAR score at 1min was 3.27 and at 5min 6.27.

Neonatal outcome was studied by various parameters like need for resuscitation, NICU admission, neurological abnormalities, delay in feed, and final outcome i.e. death/discharge. These babies were not followed for long term neurodevelopmental sequelae. Out of 108 studied neonates, 78(72.2%) needed resuscitation whereas 30(27.78%) didn't need any form of resuscitation, 77(71.30%) babies were admitted in NICU for care & management as per protocols, whereas 31(28.70%) neonates were shifted to mother side & followed up till discharge. In neurological examination, 70(64.81%) neonates had normal tone, 25(23.15%) had flaccid tone & 13(12.04%) showed increased tone, 72(66.67%) had no seizures while 36(33.33%) had seizures as an abnormal neurological examination finding. 52(48.15%) were neurologically normal without encephalopathy, 20(18.52%) were in HIE stage 1, 11(10.19%) were in stage 2 & 25(23.15%) were in stage 3 of hypoxic ischemic encephalopathy according to sarnat & sarnat staging. Among 108 neonates, feed was started in 87 neonates, out of them 28(32.56%) had delay in attaining full feed whereas 59(67.44%) had attained feed timely. 21 neonates were too sick for feed to be started & they ultimately died during hospital stay and 87 (80.56%) babies were discharged from hospital.

Correlation coefficient and P value was calculated for cord blood pH and APGAR as a predictor of ischemic brain injury among the newborns with hypoxic ischemic encephalopathy & it was observed that both are statistically significant (p value < 0.001) & significant negative correlation with severity of birth asphyxia. (table 3) (Figure 1, 2 & 3)

The mean APGAR score at 5 min, 10min and mean cord blood pH in the babies without HIE were 7.9 ± 0.6 , 8.9 ± 0.3 and 7.28 ± 0.08 , respectively. Whereas the mean APGAR at 5 min, 10min and mean cord blood pH in the babies with HIE-I were 6.3 ± 1.3 , 8.35 ± 0.58 and 7.04 ± 0.04 ; HIE-II 4.54 ± 0.52 , 6.09 ± 0.30 and 6.99 ± 0.01 ; HIE-III 3.6 ± 1.1 , 5.44 ± 0.96 and 6.84 ± 0.04 . (Table 4)

Figure 4, 5 & 6 shows Umbilical cord pH value with cut off < 7.1 had highest area under ROC curve (0.998), standard error = 0.00149, sensitivity = 96.43%, specificity = 98.08%, positive predictive value = 98.2 & negative predictive value = 96.2. APGAR score at 5 minutes (cut off < 6) had area under ROC curve 0.943, SE = 0.025, Sn = 78.57%, Sp = 90.08%, PPV = 97.8 & NPV = 81. APGAR < 8 at 10 minutes had area

under ROC 0.902, SE=0.277, Sn=83.9%, Sp=90%, PPV=90.4 & NPV=83.9.

Table 1:

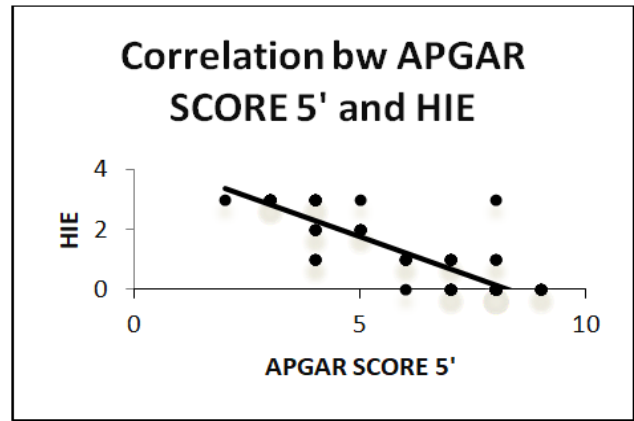
Clinical variable	Case =108
Birth weight	
2.5-3.0 kg	84(77.78%)
3.1-3.5kg	16(14.81%)
>3.5kg	8(7.41%)
Sex	
Male	61(56.48%)
Female	47(43.52%)
Gestation	
Term	95(87.96%)
Postterm and post dated	13(12.04%)
Mode of delivery	
NVD	48(44.44%)
LSCS	60(55.56%)
PRESENTATION	
VERTEX	101(93.52%)
BREECH	7(6.48%)
AMNIOTIC FLUID	
MECONIUM STAINED	26(24.07%)
CLEAR	82(75.93%)
APGAR	
MEAN APGAR AT 1 MIN	3.27
ME APGAR AT 5 MIN	6.27
NON STRESS TEST	
NON REASSURING	93(86.11%)
REASSURING	15(13.89%)

Table 2: NEONATAL OUTCOME

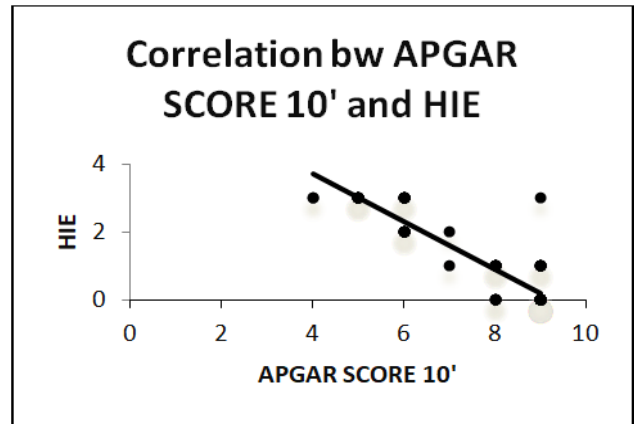
Resuscitation	Yes	72.2%
	No	27.78%
NICU admission	Yes	71.30%
	No	28.70%
Delay in feed	Yes	32.36%
	No	67.44%
Seizures	Yes	33.33%
	No	66.67%
Abnormal tone	Yes	35.19%
	No	64.81%
HIE	No HIE	48.15%
	STAGE 1	18.52%
	STAGE 2	10.19%
	STAGE 3	23.15%
Final outcome	DEATH	19.44%
	DISCHARGE	80.56%

Table 3: CORRERALTION COEFFICIENT OF APGAR SCORE AT 5MIN, APGAR ASCORE AT 10 MIN AND CORD BLOOD pH TO PREDICT THE SEVERITY OF BIRTH ASPHYXIA

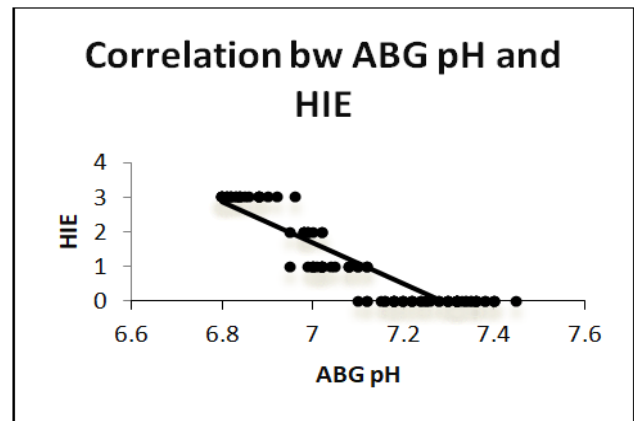
PARAMETER	P VALUE	CORRERALTION COEFFICIENT
CORD BLOOD Ph	<0.001	-0.926
APGAR AT 5 MIN	<0.001	-0.856
APGAR AT 10 MIN	<0.001	-0.870



Graph 1:



Graph 2:

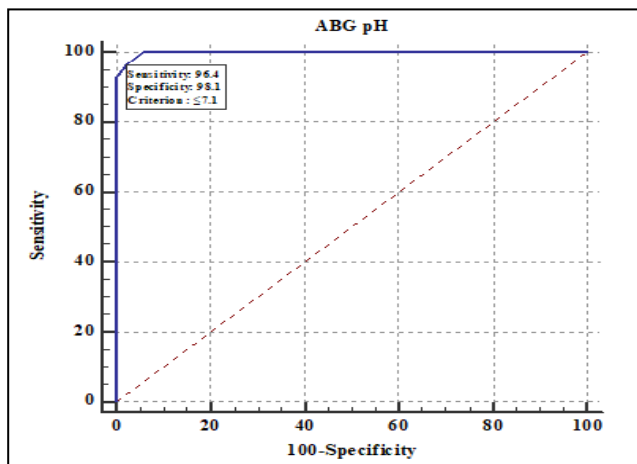


Graph 3:

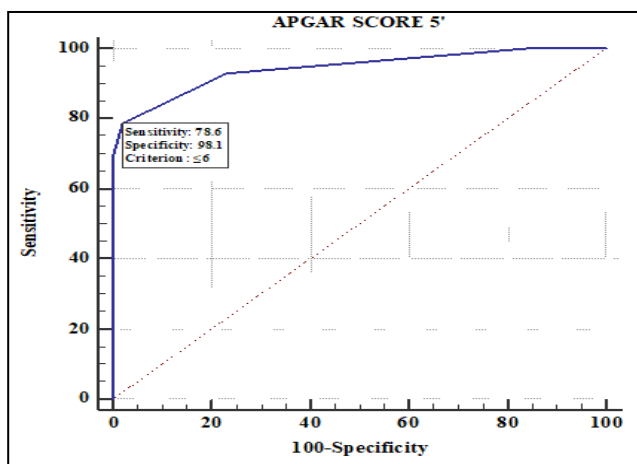
Birth asphyxia

Table 4:

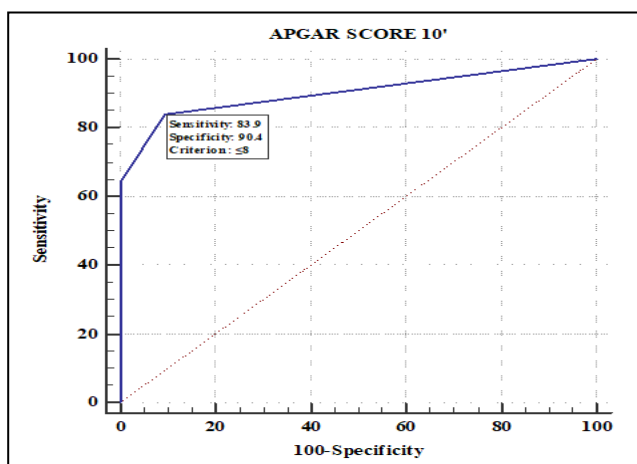
	Case(n)	Mean pH	APGAR at 5min	APGAR at 10min
NO HIE	52	7.28±0.08	7.9±0.6	8.9±0.3
HIE STAGE 1	20	7.04±0.04	6.3±1.3	8.35±0.58
HIE STAGE 2	11	6.99±0.01	4.54±0.52	6.09±0.30
HIE STAGE 3	25	6.84±0.04	3.6±1.1	5.44±0.96



Graph 4:



Graph 5:



Graph 6:

Discussion:

The goal of study was to find out the better predictor of poor short term neonatal outcome & HIE. Cases with inclusion criteria were analysed for APGAR score, cord blood pH and used to predict the outcome. Sex, parity,

mode of delivery, thick meconium stained liquor were also compared in terms of HIE sequelae but none of them had shown any significance in respect to neonatal outcome.

Even in resource limited healthcare facility, umbilical cord blood gas analysis & APGAR score is widely used to assess the severity of perinatal asphyxia.[11] In most of the previous studies, low cord blood pH correlates with the fetal hypoxia & anaerobic metabolism during perinatal period, role of APGAR is incoherent.[12,13,14] because low APGAR can be attributed to other factors like congenital malformation general anaesthesia, magnesium sulphate, intrauterine infection. Although the usefulness of APGAR is controversial, two major studies conducted on APGAR had shown that majority of (APGAR-5) below 4 and almost half of score 4-6 could be attributed to asphyxia. [15,16].

The mean APGAR score at 5 min,10min and mean cord blood pH in the babies without HIE were 7.9 ± 0.6 , 8.9 ± 0.3 and 7.28 ± 0.08 , respectively. Whereas the mean APGAR at 5 min,10min and mean cord blood pH in the babies with HIE-I were 6.3 ± 1.3 , 8.35 ± 0.58 and 7.04 ± 0.04 ; HIE-II 4.54 ± 0.52 , 6.09 ± 0.30 and 6.99 ± 0.01 ; HIE-III 3.6 ± 1.1 , 5.44 ± 0.96 and 6.84 ± 0.04 . Correlation coefficient for APGAR-5, APGAR-10 and cord blood pH was -0.856, -0.870 & -0.926 respectively. similar results were reported in previous studies.[17,18,19]

Umbilical cord pH value with cut off <7.1 had highest area under ROC curve (0.998), standard error=0.00149, sensitivity=96.43%, specificity=98.08%, positive predictive value=98.2 & negative predictive value=96.2. APGAR score at 5minutes (cut off <6) had area under ROC curve 0.943, SE=0.025, Sn=78.57%, Sp=90.08%, PPV=97.8 & NPV=81. APGAR <8 at 10 minutes had area under ROC 0.902, SE=0.277, Sn=83.9%, Sp=90%, PPV=90.4 & NPV=83.9.

As with these analysis, it is observed that sensitivity from APGAR at 5 to APGAR at 10min increases by only 5% thus rather than APGAR-10, 5min APGAR is enough to predict poor neonatal outcome.

Conclusion:

Umbilical cord blood pH is with cut off <7.10 remains the best predictor for perinatal asphyxia & poor early neonatal outcome followed by 5 min APGAR score. Following APGAR to 10 min has no significant advantage over 5 min APGAR.

References:

1. Bax MC, Flodmark O, Tydeman C. Definition and classification of cerebral palsy. From syndrome toward disease. Dev Med Child Neurol Suppl. 2007;109:39-41.]
2. Liu L, Johnson HL, Cousens S, perinJ, ScottS, Lawn JE, Rudan I, Campbell H, CibulskisR, Li M, Mathers C, Black RE. Global, regional, and national cause of child mortality: an updated systematic analysis for 2010 with time trends since 2000. Lancet 2012;379:2151-61.

3. Lawn JE, Blencowe H, Oza S, You D, Lee AC, Waisawa P, Lalli M, Bhutta Z, Barros AJ, Christian P, Mathers C, Cousens SN; Lancet Every Newborn Study Group. Every Newborn: progress, priorities, and potential beyond survival. *Lancet* 2014;384:189-205.
4. Report of the national neonatal perinatal database (national neonatology forum, India) 2003.
5. Sankar MJ, natrajan CK, Das RR, Agrawal R, Chandrashekharan A, Paul VK. *J Perinatol* 2016;36Suppl 1:S1-S11
6. National Neonatal and Perinatal Database Report; 2002- 2003:1-58.
7. World Health Organization. Neonatal and Perinatal Mortality; Country, Regional and Global estimates, 2004; WHO, Geneva; 2006:1-25.
8. American Academy of Pediatrics and American College of Obstetrician and Gynaecologists. In: Guidelines for Perinatal Care. Gilstrap LC, Oh W (Eds.) 5 th Ed. Elk Grove Village Ill. American Academy of Pediatrics; 2002:187
9. Dijkhoorn MJ, Visser GH, Fidler VJ, Touwen BC, Huisjes HJ. Apgar score, meconium and acidaemia at birth in relation to neonatal neurological morbidity in term infants. *Br J ObstetGynaecol*. 1986;93(3):217-222. doi:10.1111/j.1471-0528.1986.tb07896.x
10. Casey BM, McIntire DD, Leveno KJ. The continuing value of the Apgar score for the assessment of new born infants. *N Engl J Med*. 2001;344(7):467-471. doi:10.1056/nejm200102153440701
11. World Health Organization. Neonatal and Perinatal Mortality; Country, Regional and Global estimates, 2004; WHO, Geneva; 2006:1-25
12. Ruth VJ, Raivio KO. Perinatal brain damage: predictive value of metabolic acidosis and the Apgar score. *BMJ*. 1988;297: 24-5
13. Sykes GS, Johnson P, Ashworth F, Molloy PM, Gu W, Stirrat GM. Do Apgar scores indicate asphyxia. *Lancet*. 1982;27:494-6
14. Hogan L, Ingemarsson I, Thorngren-Jerneck K, Herbst A. How often is a low 5-min apgar score in term newborns due to asphyxia? *Eur J ObstetGynecolReprod Biol*. 2007;130:169-75
15. Hogan L, Ingemarsson I, Thorngren-Jerneck K, Herbst A. How often is a low 5-min apgar score in term newborns due to asphyxia? *Eur J ObstetGynecolReprod Biol*. 2007;130:169-75
16. Thorngren-Jerneck K, Herbst A. Low 5-minute apgar score: a population-based register study of 1 million term births. *Obstet Gynecol*. 2001;98:65-70
17. Kaveh M, Davari FT, Farhani MSH. APGAR score and arterial blood gas in the first hour of birth. *Iran J Pediatr*. 2004;14(1):27-32
18. Malin GL, Morris RK, Khan KS. Strength of association between umbilical cord pH and perinatal and long-term outcomes: systematic review and meta-analysis. *BMJ*. 2010;340:14-71
19. Field LM, Entman SS, Boehm FH. Correlation of the one-minute Apgar score and the pH value of umbilical arterial cord blood. *South Med J*. 1993; 46(12):1477-9