Clinico etiological profile of Hypoxic ischemic encephalopathy in preterms and their outcome

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ABSTRACT

Background: Neonatal Mortality is still an issue of concern in developing countries. Perinatal asphyxia is one of the common causes of neonatal mortality. One of the important complication seen in perinatal hypoxia is Hypoxic ischemic encephalopathy (HIE).

Aims & Objectives: To study the epidemiology, aetiology and early outcome of preterm newborns with birth asphyxia and admitted with HIE and their relation with the outcome of the newborn.

Materials & Methods: This study was conducted at teaching cum tertiary care general hospital in rural area of Telangana between Oct 2013 to Oct 2014. Sarnat and Sarnat HIE staging, Levene Staging and Thompson Score and Neurosonogram were used in all preterm babies and it was compared with all the variables in relation to outcome.

Results: Of the total 2700 newborn, 796 were preterm and amongst them, 30 infants had HIE. Our study observed Pregnancy Induced Hypertenstion (36.6%), antepartum haemorrhage (16.6%) as risk factors. Seizures were observed in 12 newborns (40%). Out of 30 preterm infants, 16 (53.4%) recovered and 14 (46.6%) babies could not survive.

Conclusion: Male babies are more at risk of developing HIE compared to female babies. PIH, Oligohydramnios are common risk factors for causing HIE and lower the gestational age, more the chances of developing HIE and even mortality is very high.

Keywords : Perinatal hypoxia, preterm infants, Hypoxic Ischemic Encephalopathy, Levene staging, Thompson score, antenatal risk factors.

INTRODUCTION

HIE is an important cause of acute neurologic injury at birth, affecting approximately 2 to 3 cases per 1000 live births in developed countries[1,2] with a higher incidence in developing countries. It accounts for 20% of the perinatal deaths. Perinatal asphyxia refers to a condition during the first and second stage of labour in which impaired gas exchange leads to foetal hypoxemia and hypercarbia. The definition of perinatal asphyxia remains controversial with different authorities suggesting various definitions. The National Neonatal and Perinatal Database (NNPD) 2002-2003 has defined birth asphyxia as an Apgar score less than 7 at 1minute of age with moderate birth asphyxia being Apgar score between 4 to 6 or slow gasping respiration at 1 minute and severe asphyxia as Apgar of 3 or less or no breathing at 1 minute [3].

Risk factors for birth asphyxia in hospital based settings in developing countries have been categorised into antepartum, intrapartum and postnatal characteristics. Perinatal asphyxia, hypoxic ischemic encephalopathy and subsequent morbidity and mortality, is seldom reported in preterm infants. Criteria used in term infants to support a diagnosis of HIE occur for other reasons in preterm infants, where sub-optimal Apgar scores, a need for respiratory support and an inability to suck feed are common. Clinical seizures are often subtle in preterms and defining encephalopathy may be difficult [4].

MATERIALS AND METHODS : This study was conducted at teaching cum tertiary care general hospital in rural area of Telangana between Oct 2013 to Oct 2014. In the present study total number of newborns delivered during the study period was 2700. Term babies were 1904 and Preterm Babies were 796. New borns with Gestational age < 37 weeks were considered as preterm. Inclusion Criteria includes : (1) Newborns with gestational age less than 37 weeks (2) New born with delayed cry for more than one minute and (3) babies with Apgar score <4 at 1 min or 5 min or 10 min or later[5,6,7,8.]

Exclusion Criteria includes: (1) New borns with Congenital anomalies, infections and sepsis (2) babies with severe Respiratory Distress Syndrome.

A total of 37 preterm HIE cases were identified during the study period of which 30 asphyxiated preterm babies who met the inclusion criteria were enrolled in the study. 7 babies

were excluded as 3 babies suffered with severe Hyaline Membrane Disease, 2 babies had congenital Cardiac Malformations and in two babies there was severe early onset sepsis.

The total number of live births in the hospital during the study period was obtained from Obstetric Register. Detailed antenatal and natal history was taken along with clinical examination for each neonate. Assessment and staging were done clinically using Sarnat and Sarnat staging system, Levene staging system and scoring done according to Thompson Scoring system on Days 3 and 7 of life. Neurosonography was done in all babies.

RESULTS

Total number of neonates delivered during the study period was 2700. Among them, 796 were preterm of which 37 cases were admitted with perinatal asphyxia and HIE. The birth ratio for male to female babies was 1:1. The incidence of HIE was 4.6% among the preterms and 1.3% among all new borns (Table 1). In preterms with HIE, males were 19 (63.33%) and female babies were 11 (36.66%) but the mortality was 63.33% in female preterms with HIE and 36.8% in male babies. Among the preterm babies, Antenatal care (ANC) history revealed that 18 cases were booked and 12 were unbooked. Among the 30 cases, primies were 21 (70%), Gravida 2 were 5 (16.6%) and Gravida 3 were 3 cases and one was gravida 5 which suggests that HIE is more in Primi gravida. (Table 1).

According to gestational age 16 cases (53.33%) were between 28-32 weeks and 14 cases (46.6%) were between 32 weeks and 37 weeks. 10 out of 16 (62.5%) cases with lower gestational age had poor outcome resulting in mortality. And the mortality in preterms with gestational age greater than 32 weeks was 28.5% which is comparatively low. The infants with HIE were given as per the score Sarnat and Sarnat HIE staging. Among the study sample, 8 cases (26.66%) were of Stage 1 and Stage 2 comprised 14 cases (46.66%) and Stage 3 HIE was observed in 8 cases. The mortality is 100% in cases with Stage 3, 35.71% with Stage 2 and with stage 1, it was 12.5%. (Table 2).

According to Levene staging system, 13 cases were of mild HIE (43.33%), 4 were moderate HIE and 13 were severe HIE. Severe HIE had 92.3% mortality, 25% mortality was observed with moderate HIE and only one death was observed out of 13 mild HIE cases. (Table 2).

Thompsons score was administered in all these infants. It was found that Thompsons score less than 10 had good prognosis as there was only one death out of 17 cases. But if the score was more than 10, the outcome was very poor as all 13 cases died i.e. 100% mortality. (Table 2).

It was observed in our study that Pregnancy Induced Hypertension (PIH) was the common antenatal cause for HIE in as much as 11 cases, oligohydromnios was observed in 8 cases. Eclampsia and Antepartum Haemorrhage (APH) were the next common causes. The mortality of preterm newborn with HIE is more with APH as antenatal risk factor followed by eclampsia, oligohydramnios and PIH. (Table 3). Though the incidence is more with PIH, the mortality is high with APH as an antenatal risk factor.

Neurosonogram (NSG) was done for all the cases and most of the Stage 1 HIE babies had normal study. Intraventricular haemorrhage was seen in 5 babies with Stage 2 and 25 % with stage 3. Diffuse parenchymal echoes were seen in 75% newborns in Stage 3. Seizures were observed in 40% of the preterm babies with HIE. Mortality was high (50%) in newborns with HIE with seizures (Table 4). The overall mortality in our study was 46.6% and remaining 43.4% cases had recovered and were discharged home.

DISCUSSION

Perinatal hypoxia continues to be the leading cause of perinatal mortality, the resulting HIE leading to the developmental and neurological handicaps. Currently, neonatal deaths account for 40% of under 5 year mortality. This proportion is steadily increasing due to the annual rate of decline in childhood mortality without a corresponding decrease in neonatal mortality. Birth asphyxia has for long time been estimated to account for around 25% of neonatal deaths[9]. However the definition is imprecise in part because of Apgar score, often used as indicator to identify birth asphyxia, is inaccurate or unreliable[10].

Our study reveals a higher incidence of HIE in preterm babies when compared to studies done by John W Schmidt et al[11] and Chandra S and Ramji et al[12]. The incidence rate of HIE in preterm in our study is 4.6%. This is higher than that of another study by Dongol S and Singh J et al[13]. The high incidence in our study might be because of the fact that our hospital is a tertiary care referral hospital which caters to high risk pregnancies.

The sex distribution in our study shows more incidence in male babies as compared to the female babies, i.e., 63.33% were males against 36.6% female babies. Similar findings are seen with other studies like Dongol et al, Azam M et al[14] study. But in a study by Nayeri et al[15] and Chandra S and S Ray, incidence was found to be higher in female newborns.

Associations of HIE with small for gestational age (SGA) babies is more in our study. 19 out of 30 cases were SGA and remaining 11 were Approximate for Gestational Age (AGA). This indicates that intrauterine factors which are not favourable for the growth of foetus are

responsible for perinatal asphyxia and HIE. There are number of factors which are responsible for chronic placental insufficiency which inturn lead to hypoxia and ischemia. When further analysed, more number of cases with SGA are related to PIH. Mortality is 47% among these babies and 45% among AGA babies. In our study PIH is the most common antenatal etiological factor causing Perinatal Asphyxia with HIE followed by Oligohydramnios, Eclampsia, and APH. With respect to mortality, APH is more fatal as we have observed 100% mortality. This is consistent with studies done by Anne CC Lee et al[16] and Dongol S et al.

The incidence of HIE is more in primi gravida i.e., 70%, in gravida 2 the incidence was 16.6%. the figures indicate that birth asphyxia is more common in babies born to primi gravidae. This is consistent with Azam M study where it was 47%.

Pushpa chaturvedi et al[17], Cliffard and Batra et al in their studies have shown that HIE was found high in preterm and SGA babies. In a study done by Dongol S and Singh J et al, the incidence of birth asphyxia in preterm babies is 19.6% compared to 48.7% in term babies. When total babies were considered, preterm babies were quiet less than term babies. When only preterm babies were considered, birth asphyxia was much commoner among them.

In our study, though Sarnat and Sarnat[18] staging is mainly for term babies, it was applied here for preterm HIE staging. The mortality in HIE stage 3 was high (100%) which is consistent with the findings of Dongol S et al while in another study by Haidery et al[19] , it was only 60%.

The recovery rate is high with HIE Stage 1 followed by Stage 2 which is consistent with Dongol et al. Similar findings were observed in study done by Ladakhi GM et al[20]. By considering Levene Staging, cases were divided into mild, moderate and severe. The incidence of mild HIE was 43.33%, moderate HIE 13.33% and Severe HIE was 43.4% and recovery was also good for mild and moderate staging. Levene staging[21] can be applied for both preterm and term babies.

Thompson scoring system was used for all preterm HIE cases. Scoring was done on day 3 and day 7. Socre on day 7 was considered for all babies who survived till 7th day. For remaining score on day 3 was considered. Based on score, babies were divided into two groups, one with score less than ten and the other with score equal to or more than ten. The mortality was 100% in babies with score more than ten. Studies comparing Thompson scoring system and outcome are very few and there are no studies in relation to preterm HIE. One study by R Mittal and A Holzinger,[22] Thompson score on day 7 of life and outcome have shown that score of more than ten is suggestive of bad prognosis and score with less than 5 on day 7 of life is strongly predictive of outcome without severe handicap.

Seizures were observed in 12 cases in our study. Mortality in preterm babies with seizure association was found in 50%.

Neurosonogram (NSG) was done for all the cases. It was found that most babies with stage 1 had normal study while intraventricular haemorrhage was seen in 5 babies of stage 2 and diffuse parenchymal echoes were seen in 75% in stage 3. In similar study of NSG by Anand N K et al[23], NSG findings were normal in all cases of HIE stage 1, Diffuse parenchymal echoes were found in all babies with HIE stage 3 which is consistent with our study as well.

When we compare these NSG findings to Thompsons scoring system, the higher score is correlated with IVH and diffuse parenchymal echoes and when compared with Levene staging, more severe cases have shown diffuse parenchymal echogenicity and IVH. This indicates poor outcome with diffuse parenchymal echoes and IVH.

The overall mortality in our study was 46.6% and recovery rate was 53.33% which is very high when compared to studies done by S J Etuk and I S Etak et al and Dongol et al and Ladakhi GM in India. But in a similar study conducted in preterm infants of gestation age 32-36 weeks by John Schmidt et al, the mortality was 58.33%. The high incidence of mortality might be due to considering only preterm babies.

CONCLUSION

The present study yields that male babies are more at risk of developing HIE as compared to the female babies and PIH, Oligohydramnios are common risk factors for causing HIE. Lower the gestational age, more the chances of developing HIE and even mortality is very high.

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Table 1: Demographic characteristics and outcome of preterm babies with HIE

Total no of live births		2700
Term babies		1904
Pre term babies		796
Preterm babies with HIE		30
Sex	Male	19 (63.33%)
	Female	11(36.66%)
Gravida		

Primi	21 (70%)	
G2	5 (16.6%)	
G3	3 (10%)	
G5	1 (3.33%)	
Gestational age		Mortality
≤ 32 weeks	16 (53.3%)	10 (62.5%)
≥ 33 weeks	14 (46.6%)	4 (28.57%)
Mode of delivery	Normal vaginal delivery=6	8 (50%)
	Emergency LSCS=7	5 (71.42%)
Birth Weight	Elective LSCS=7	1 (14.2%)
	AGA:11 (36.66%)	5 (45.45%)
	SGA:19 (63.33%)	9 (47.36%)

Table 2: Sarnat and Sarnat staging, Levene staging and Thompsons score with relation to outcome.

Sarnat & Sarnat staging	Number (%)	Mortality
	Stage 1:8 cases (26.66%)	1 (12.5%)
	Stage 2:14 cases (46.66%)	5 (35.7%)
	Stage 3:8 cases (26.66%)	8 (100%)
Levene staging	Mild: 13 (43.33%)	1 (8%)
	Moderate: 4 (13.33%)	1 (25%)
	Severe: 13 (43.33%)	12 (92%)
Thompson scoring	< 10:17 (56.66%)	1 (6%)
	> 10:13 (43.33%)	13 (100%)

Table 3 : Risk factors and incidence of preterm babies with HIE and outcome.

Factors	No of Cases	Percentage	Mortality
PIH	11	36.6	3 (27.7%)
Oligohydramnios	8	26.66	3 (37.5%)
Eclampsia	5	16.6	3 (60%)
APH	5	16.6	5 (100%)
Gestational Diabetes	1	3.3	NIL

Table 4: Incidence of seizures, abnormalities on NSG and their relation to outcome.

Total no. of cases 30	Incidence of seizures	12	6 recovered
			6 died
	Neurosonogram	Nomal : 8	Abnormal : 22
	Outcome	Recovered : 16	Deaths : 14

REFERENCES

1. Wyatt JS, Gluckman PD, Liu PY, Azzopardi D, Ballard RA, Edwards AD et al. Determinants of outcomes after head cooling for neonatal encephalopathy. Paediatrics 2007;119:912-921.
2. Dixon G, Badawi N, Kurinczuk JJ. Early developmental outcomes after newborn encephalopathy. Paediatrics 2002;109:26-33.
3. National Neonatal Forum NNPD Network. National Neonatal Perinatal Database Report 2002-2003. New Delhi:NNF2005.
4. Pavithra Logitharajah, Mary A. Rutherford. 2009 Hypoxic Ischemic Encephalopathy in preterm infants: Antecedent factors. Brain imaging and outcome. Paediatric Research 0031-3998/09/6602-0222.
5. Committee on Foetus and Newborn; American Academy of Paediatrics; Committee on Obstetric Practice; American College of Obstreticians and Gynaecologist. Use and abuse of Apgar score. Paediatrics, 1996;98:141-142.
6. Lawn JE, Manandar A, aws R, Darmstadt GL. Reducing one million child deaths from birth asphyxia-policy and programme gaps and priorities based on an international survey-Health Res Policy Systems 2007;5;40.
7. Report of National Neonatal Perinatal Database (National Neonatal Forum, India), 2000.
8. Shankaran AS, Laptook AR, Ehraenkranz RA, Tyson JE, Mc Donald SA, Donovan TF et al. Whole body hypothermia for neonates with HIE, NEJM 2005;353: 1574-1584.
9. S. Ramji, R. Rasaily, P.K. Mishra et al ;Neonatal morbidity and mortality: Report of the National neonatal perinatal database. Indian Pediatr 1999; 36; 167-169.
10. Hege Langli Ersdal, Estoih Mduma, Erling Svensen and Jeffery Perlman Paediatrics 2012; 129; e1238; originally published online April 16; 2012; DOI: 10.1542/Peds.2011-3134

11. John W Schmidt, William F, Walsh, Hypoxic Ischemic Encephalopathy in preterm infants, Journal of Neonatal and Perinatal Medicine, 2010; Vol 3 (4); 277-284.

12. Chandra S, Ramji S, Thirupuram S, Perinatal asphyxia; Multivariate analysis of risk factors in hospital birth. Indian Pediatr 1997; 34:206-12.

13. Dongal S, Singh J, Clinical profile of Birth Asphyxia in Dhulikhel Hospital: A retrospective study. J Nepal Paediatr Soc 2010;30(3):141-46.

14. Azam M, Malik F, Khan P. Birth asphyxia risk factors. The Professional 2004;(4):416-23.

15. Nayeri F, Shariat M Dalil H, Adam LB Mehrjerdi FZ. Perinatal risk factors for neonatal asphyxia in Vali-e-Asr Hospital, Tehran, Iran- J Reprod Med 2012;10:137-40.

16. Anne CC-Lee et al, Risk factors for neonatal mortality due to Birth Asphyxia in Southern Nepal, Paediatrics 2008;121(5):1381-90.

17. Pushpa Chatrurvedi, Nisha Shah, Foetal correlates and mode of delivery in asphyxia neonatarum, Indian J Paediatrics. 1991; 58: 63-67.

18. Sarnat HB, Sarnat MS: Neonatal encephalopathy following foetal distress: A clinical and electroencephalographic study. Arch Neurol. 2000; 33:695-706.

19. Haidary MH, Hussia A, Ahmed S, Kasem A. Clinical Profile of Birth Asphyxia in Rajshahi Medical College Hospital. J Teachers Assoc. 2005; 18:106-8.

20. Ladakhi GM, Mubak M, Nabi B, Hassan M, Sethi AS. Neonatal risk factors and outcome of Birth asphyxia. J K Practitioner 2000; 7(4): 267-70.

21. Levene MI. The asphyxiated newborn infant. In: Levee MI, Lilfor RJ, Fetal and neonatal neurology and neurosurgery. Edinburgh: Churchill Livingstone. 1995; 17: 405-426.

22. R Mittal, A Holzinger, R Muche, Simbruner S. Usefulness of Thompson score on day 7 of life in predicting outcome at 18 months in neonates with Hypoxic Ischemic Encephalopathy due to birth asphyxia. 1996; 15: 446 – 50.

23. Anand N K, Gupta A K, Neurosonographic abnormalities in neonates with Hypoxic Ischemic Encephalopathy, Indian Paediatrics, July 1994;31:767-73.

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