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The Maternal Risk Factor for HIE Progression in Infants

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Abstract **Original Research Article**

Background*:** Perinatal asphyxia, or more accurately, hypoxic-ischemic encephalopathy (HIE), remains a devastating illness, producing considerable death and long-term morbidity despite great breakthroughs with sophisticated monitoring technologies and understanding of fetal and neonatal pathology. ***Objective*:** In this study our main goal is to evaluate the maternal risk factor for HIE progression in infants. ***Method*:** This case control study was conducted in the Department of the Paediatrics, Jalalabad Ragib Rabeya Medical College Hospital, Sylhet during the period from 1 st January 2014 to 30 th June 2014. Ninety-six normal birth weight term babies with HIE were selected as case; Ninety six sex and birth weight matched, term singleton baby without HIE born in Jalalabad Ragib Rabeya Medical College Hospital, Sylhet were taken as control. ***Results: Maternal age (<20 years) [15 (15.6%) versus 6 (6.2%); OR=3.165; 95% of CI=1.176-8.518; p=0.037]; maternal height (<145 cm) [37 (38.5%) versus 24 (25.0%); OR=1.881; 95% of CI=1.014-3.492; p=0.044), primiparity [45 (46.9%) versus 31 (32.3%); OR=1.850; 95% of CI=1.029-3.325; p=0.039], irregular or no antenatal care [41 (42.7%) versus 27 (28.1%); OR=1.905; 95% of CI=1.044-3.476; p=0.035]; pregnancy induced hypertension [38 (39.6%) versus 22 (22.9%);OR=2.204; 95% of CI=1.777-4.128; p=0.013]. ***Conclusion***: Maternal risk factors of development of hypoxic ischemic encephalopathy are maternal age (& lt;20 years), primigravida mother, absence or irregular antenatal care, pregnancy induced hypertension is associated with HIE.

Keywords: Hypoxic-ischemic encephalopathy (HIE), neonatal, maternal risk factor.

INTRODUCTION

Perinatal asphyxia is defined as the failure to initiate and sustain breathing at birth [1]. It causes impaired gas exchange leading to progressive hypoxemia and hypercapnoea with significant metabolic acidosis. Its severity has been related to the degree of depression of the Apgar score or by presence of cord blood acidosis [2]. Perinatal asphyxia, one of the most devastating neurological processes is characterized by different degrees of hypoxia-ischemia during labour and delivery, with the outcome depending on the severity of the underlying neuronal damage [3].

Neonatal hypoxic ischemic encephalopathy is a clinical syndrome of disturbed neurologic function of the term and near term infant in the early neonatal period following severe perinatal asphyxia with secondary cerebral ischemia [2]. It is characterized by clinical and laboratory evidence of acute or sub-acute brain injury due to asphyxia leading to hypoxia and acidosis [4]; and manifested by respiratory difficulties, depression of tone and reflexes, obtundation, and frequently by seizures resulting from intrapartum asphyxia. It is classified as mild, moderate or severe (or stage 1, 2 or 3) according to the criteria by Sarnat and Sarnat [5], and is based on the baby's response to handling, consciousness level, abnormalities of tone or reflexes, presence of seizures and the duration of the symptoms after birth [6]. It is an important cause of permanent damage to the central nervous system (CNS) which may result in neonatal death or manifest later as cerebral palsy or mental deficit. It has long been known

that survivor of HIE are at increased risk of neurological handicap [2].

Birth asphyxia, hence HIE is clearly a problem where prevention should be the aim [4]. Various risk factors e.g. sub-optimal intrapartum obstetric care has been associated with the HIE. These were maternal age (<20 years), height (<145cm), nulliparity, occupation, complicated pregnancy, inadequate antenatal care, gestational age, presentation other than vertex, induction of labour, instrumental delivery, emergency caesarean section and general anaesthesia [6, 7].

Bangladesh is among those countries with limited resources especially in the labour ward which make perinatal asphyxia to be one of the leading cause of the infant mortality and there are very few study done in our setting to show the maternal risk factors and hospital outcome of infants with HIE.

OBJECTIVE

In this study our main goal is to evaluate the maternal risk factor for HIE progression in infants.

METHODOLOGY

This was a case control study was done in the Department of Paediatrics, Jalalabad Ragib Rabeya Medical College Hospital, Sylhet from 1st January 2014 to 30th June 2014. Ninety six patients with HIE admitted in the neonatal unit of the Department of Paediatrics, Jalalabad Ragib Rabeya Medical College Hospital, Sylhet during the period and fulfilling the inclusion and exclusion criteria were enrolled in this study as case group. For the control group sex and birth weight matched, 96 term singleton baby without major malformations and HIE born in Jalalabad Ragib Rabeya Medical College Hospital, Sylhet was taken for each patient. 96 Term Newborns with history of delayed cry (for more than 5 minutes after birth, clinical picture of HIE at birth on the basis of changes in the level of consciousness, muscle tone, primitive and deep tendon reflexes and development of seizures were included as sample population. Immediately after admission a proper history and clinical examination were done in all cases. Birth weight of the babies was taken. Babies with a gestational age of 37 completed weeks or more those were admitted with the clinical picture of HIE at birth on the basis of delayed cry at birth, changes in the level of consciousness, muscle tone, primitive and deep tendon reflexes and development of seizures were included. HIE was diagnosed clinically based on following criteria: (1) First cry delayed more than 5 minutes, (2) Resuscitation need for >1 minute, (3) Neonatal encephalopathy characterized by altered consciousness, abnormal tone, posture and reflexes; abnormality in respiration (apnoea), seizure etc. HIE was considered in the presence of two or more of above criteria. Information was collected for the possible risk factors for HIE such as maternal age, parity, presence or absence of antenatal care, maternal hypertension, gestational diabetes, antepartum hemorrhage (APH), diseases related to pregnancy and other chronic illnesses, on mode of delivery, presence of meconium stained amniotic fluid and prolonged 2nd stage of labour.

Data were processed and analyzed with the help of computer program SPSS (Statistical Package for Social Sciences) version 16. Quantitative data were presented as mean and standard deviation; and comparison between before and after was done by unpaired "t" test. Qualitative data were presented as frequency and percentage; and were compared by Chi square test if needed or Fisher exact test. Odd ratio (OR) with 95% confidence interval was calculated to determine significance of risk factors. The stepwise multiple logistic regression analysis was used to determine the independent factors that may predispose an infant to HIE. A probability (p) value of < 0.05 ($p<0.05$) was considered statistically significant.

RESULTS

Table-1 shows comparison of baseline characteristics between HIE group and control group. The mean age at admission was 3.60 ± 1.99 days in HIE group and 4.24 ± 1.51 days in control group. The mean birth weight was 2.73 ± 0.24 Kg in HIE group and 2.78 ± 0.18 Kg in control group. In HIE group, 52 (54.2%) babies were male and 44 (45.8%) babies were female; whereas in control 50 (52.1%) babies were male and 46 (47.9%) babies were female.

Table 1: Comparison of baseline characteristics between HIE group and control group

Baseline characteristics of baby	Case group (n=96)	Control group (n=96)	p value
Age (years)	3.60 ± 1.99	4.24 ± 1.51	†p=0.014
Birth weight (Kg)	2.73 ± 0.24	2.78 ± 0.18	†p=0.127
Sex			
Male	52 (54.2%)	50 (52.1%)	*p=0.772
Female	44 (45.8%)	46 (47.9%)	

*Chi-square (χ^2) test and †unpaired t test were employed to analyse the data.

Figure-1 shows maternal age distribution where Maternal age (<20 years) significantly increased the risk of development of HIE than those with maternal age (20 years or above) [15 (15.6%) versus 6

(6.2%); OR=3.165; 95% of CI=1.176-8.518; χ2=4.331; p=0.037).

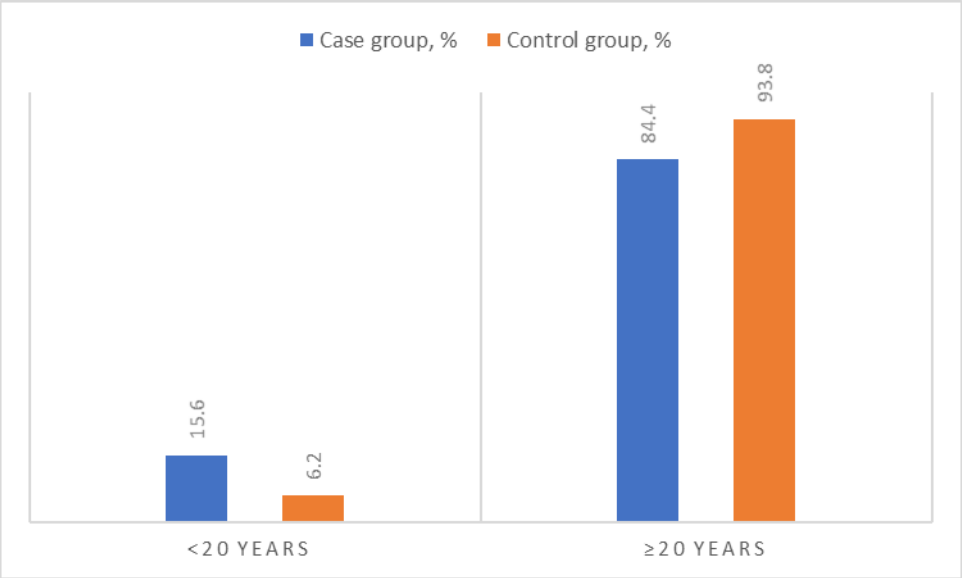

Figure 1: Maternal age distribution

Table-2 shows Comparison of height of the mother between HIE group and control group. Maternal height (<145 cm) significantly increased the risk of development of HIE than those with maternal height (≥145 cm) [37 (38.5%) versus 24 (25.0%); OR=1.881; 95% of CI=1.014-3.492; χ^2=4.061; p=0.044).

Table 2: Comparison of height of the mother between HIE group and control group

Height of the mother	Case (n=96) No (%)	Control (n=96) No (%)	Odds Ratio (95% of CI)	*p-value
<145 cm	37 (38.5)	24 (25)	1.881 (1.014-3.492)	p=0.044
≥145 cm	59 (51.5)	72 (75)		

OR: Odds ratio, CI: Confidence interval, SD: standard deviation
*Chi-square (χ^2) test was employed to analyse the data.

Table 3 shows Parity of the mother between HIE group and control group.

Primiparity was 45 (46.9%) in HIE group and 31 (32.3%) in control group. Primiparity was significantly increased the risk of development of HIE than those with multiparity (OR=1.850; 95% of CI=1.029-3.325; χ^2=4.269; p=0.039).

Table 3: Parity of the mother between HIE group and control group

Parity of the mother	Case (n=96) No (%)	Control (n=96) No (%)	Odds Ratio (95% of CI)	*p value
Primipara	45 (46.9%)	31 (32.3%)	1.850 (1.029-3.325)	p=0.039
Multipara	51 (53.1%)	65 (67.7%)		
Total	**96 (100)**	**96 (100)**		

OR: Odds ratio, CI: Confidence interval
*Chi-square (χ^2) test was employed to analyse the data.

Table-4 shows Comparison of gestational age between HIE group and control group where mean gestational age was 37.93 ± 0.93 weeks (range, 37-40 weeks) in HIE group and 38.16 ± 1.01 weeks (range, 37-40 weeks) in control group; difference was not significant (t=-1.635; p=0.104)..

Table 4: Comparison of gestational age between HIE group and control group

Gestational age (weeks)	Case (n=96)	Control (n=96)	p value
Mean	37.93	38.16	p=0.104
Standard deviation	± 0.93	± 1.01	
Range	37-40	37-40	

*Unpaired t test was employed to analyse the data.

Table-5 shows Comparison of status of antenatal care between HIE group and control group where Irregular or no antenatal care during pregnancy was 41 (42.7%) in HIE group and 27 (28.1%) in control group. Irregular or no antenatal care during pregnancy significantly increased the risk of development of HIE than those with regular antenatal care (OR=1.905; 95% of CI=1.044-3.476; χ^2=4.463; p=0.035).

Table 5: Comparison of status of antenatal care between HIE group and control group

Status of antenatal care	Case (n=96) No (%)	Control (n=96) No (%)	Odds Ratio (95% of CI)	*p value
Irregular or no	41 (42.7%)	27 (28.1%)	1.905 (1.044-3.476)	p=0.035
Regular	55 (57.3%)	69 (71.9%)		
Total	**96 (100)**	**96 (100)**		

OR: Odds ratio, CI: Confidence interval
*Chi-square (χ^2) Test was employed to analyse the data.

Table 6 shows the comparison of pregnancy induced hypertension between HIE group and control group:

Presence of pregnancy induced hypertension was 38 (39.6%) in HIE group and 22 (22.9%) in control group. Presence of pregnancy induced hypertension significantly increased the risk of development of HIE than that of mother without pregnancy induced hypertension (OR=2.204; 95% of CI=1.777-4.128; χ^2=6.206; p=0.013).

Table 6: Comparison of pregnancy induced hypertension between HIE group and control group

Pregnancy induced hypertension	Case (n=96) No (%)	Control (n=96) No (%)	Odds Ratio (95% of CI)	*p value
Present	38 (39.6%)	22 (22.9%)	2.204 (1.777-4.128)	p=0.013
Absent	58 (60.4%)	74 (77.1%)		
Total	**96 (100)**	**96 (100)**		

OR: Odds ratio, CI: Confidence interval
*Chi-square (χ^2) Test was employed to analyse the data.

DISCUSSION

Despite major advances in diagnostic and therapeutic improvements, hypoxic-ischemic encephalopathy (HIE), remains a serious condition that causes significant neonatal mortality and morbidity, including long-term neurodevelopmental sequelae of childhood [8]. It is importantly associated with early neonatal mortality and long term neurodevelopmental sequelae in countries of both high and low income [9]. HIE is reported to be responsible for 17% of total mortality and 15-20% of cerebral palsy in newborns [10, 11]. The causes of hypoxic-ischemic encephalopathy are heterogeneous, and many start in the antepartum period [9], and have been related to maternal and obstetric risk factors.

Thus it is important to be aware of factors that may predispose a newborn to hypoxic insult at birth with the aim of formulating preventive strategies. In settings where many mothers are stunted, do not have access to antenatal care, and receive poor obstetric care, it seems likely that intrapartum factors remain important in neonatal encephalopathy [10]. Any preventive strategy should be based on local facts and figures to be effective. It is, therefore, vital to collect local data about the problem and to use that information to formulate guidelines aimed at reducing the incidence of birth asphyxia and its sequel. The magnitude and impact of this preventable condition and the paucity of local data provided the impetus for this study to determine risk factors of hypoxic ischemic encephalopathy in newborn infant.

In this study the mean age on admission was significantly lower in HIE group than that of control group (3.60 ± 1.99 days versus 4.24 ± 1.51 days; p=0.014). Similarly Butt *et al.*, [4] reported that age at admission was significantly different between cases and control group (p<0.001). Shireen *et al.*, [10] reported the mean age on admission was 13.4 hours for cases and 2.6 days for the control group.

This study showed that the mean birth weight of the patients on admission did not differ between case group and control group (2.73 ± 0.24 Kg versus 2.78 ± 0.18 Kg; p=0.127). Similar findings was reported in the study of El Farargy and Ghoname [11] that birth weight of HIE baby and control group did not differ significantly.

In the present study male babies were predominant in both groups (54.2% and 52.1% respectively) and there no significant difference of sex between HIE and control group (p=0.772). This result was almost similar to the study of Elliss *et al.*, [12] that there were 61% male and 39% female in the case group; difference was not significant (OR 1.383; 95% CI 0.4-1.26). Male preponderance of HIE was reported in several other strudies [4, 11-14].

In this study the mean age of the mother was significantly higher in control group than that of case group (23.65 ± 4.01 years versus 25.15 ± 3.68 years; p=0.008). Itoo *et al.,* [14] found that age of the mother was 26.05 ± 6.9 years in HIE and 26.33 ± 6.1 years in control group; difference was not statistically significant (p=0.799). Kurinczuk *et al.,* [15] also did not found any significant difference maternal age between HIE and control group (p>0.05). This study showed that maternal age (<20 years) significantly increased the risk of development of HIE than those with maternal age (20 years or above) [15 (15.6%) versus 6 (6.2%); OR=3.165; 95% of CI=1.176-8.518; p=0.037). The above mentioned two studies did not mention the maternal age below 20 years as a risk factor for development of HIE.

In the present study maternal height (<145 cm) by 1.9times increased the risk of development of HIE (OR=1.881; 95% of CI=1.014-3.492; p=0.044). Kurinczuk *et al.,* [15] supported this findings (OR=3.16, 95% CI= 1.50 to 6.66).

This study revealed that primiparity by 1.8 times increased the risk of development of HIE (OR=1.850; 95% of CI=1.029-3.325; p=0.039). Primiparity was a risk factors of development of HIE reported in several other studies [12- 15]. Since the first delivery is more difficult than the subsequent one. This points to the importance of intrapartum factors in the causation of HIE.

In the present study the mean gestational age did not differ significantly between HIE group and control group (37.93 ± 0.93 weeks versus 38.16 ± 1.01 weeks; p=0.104). This result was consistent with several other studies [4, 11- 12].

In this study incomplete or absent antenatal care during pregnancy 1.9 times increased risk of development of HIE (OR=1.905; 95% of CI=1.044-3.476; p=0.035). This result was supported by Elliss *et al.,* [10] that absent antenatal care during pregnancy increased the risk of developing HIE [OR=2.05 (95% CI 1.16-3.66)]. Several other studies also revealed that no or irregular antenatal care is a risk factor for development of HIE [4, 10-15].

In this study presence of pregnancy induced hypertension increased the risk of development of HIE by 2.2 times than that of mother without pregnancy induced hypertension (OR=2.204; 95% of CI=1.777-4.128; p=0.013). Itoo *et al.,* [14] found that pregnancy induced hypertension was 13 (19%) cases of HIE and 5 (7%) cases of control group; difference was statistically significant (p=0.025). Several other studies also supported this finding [10-15].

CONCLUSION

From the findings of the present study it may be concluded that maternal risk factors of development of hypoxic ischemic encephalopathy in neonates include maternal age (<20 years), maternal height (<145 cm), primigravida mother, absence or irregular antenatal care, pregnancy induced hypertension were significantly linked with HIE development.

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