Maternal & fetal risk factors for hypoxic-ischemic encephalopathy (HIE) in newborns: A case-control study from southern Odisha, India

Dr. Santosh Kumar Pradhan
Asst. Prof., Department of Pediatrics, MKCG Medical College, Berhampur

Dr. Ashok Kumar Nanda*
Asst. Prof., Department of Pediatrics, MKCG Medical College, Berhampur
*Corresponding author

Dr. Lal Mohan Alada
Senior Resident, Department of Pediatrics, FM Medical College, Balasore

Abstract---Introduction- Perinatal hypoxia leading to hypoxic-ischemic encephalopathy (HIE) is a leading cause of neonatal and under 5 mortality across the world and in India. There are wide regional and social variations in the risk factors associated with HIE and this study was conducted to assess the maternal & fetal risk factors in newborns with moderate to severe HIE. Methodology- This was a case-control study at the SNCU of MKCG Medical College and Hospital in southern Odisha where 100 cases of HIE and 100 matched controls were recruited over a period of 2 years. Data on maternal, antenatal, intrapartum, and post-delivery risk factors were collected from medical records and history taking using a pre-defined proforma. Comparative bivariate analysis was done to assess the strength of association of these risk factors between the two groups. Results- The incidence of HIE is more in 20-30 years age group, however, risk of HIE is significant in <20 years age group. Maternal anemia is a significant risk factor but Bad Obstetric History (BOH) has only clinical correlation. There is no statistical significance for antepartum hemorrhage (APH), pregnancy-induced hypertension (PIH) or gestational diabetes mellitus (GDM) in cases of HIE. Among intrapartum risk factors instrumental delivery & meconium-stained liquor occurrence were significant risk factors for HIE. Apgar score < 5 at 5 minutes is also significantly associated with a higher incidence of HIE.

Keywords---pediatrics, neonatology, perinatal asphyxia, HIE.
Introduction

In spite of major advances in monitoring technology and knowledge of foetal and perinatal medicine, perinatal asphyxia is one of the significant causes of mortality and long term morbidity. Perinatal asphyxia usually refers to an insult accompanied by decrease oxygen delivery to neonatal brain, when asphyxia followed by abnormal neonatal behaviour, a syndrome was been described as "hypoxic ischemic encephalopathy (HIE). (1) According to latest estimates by World Health Organization (WHO), approximately 4 million babies die each year before they reach the age of one month. Perinatal asphyxia and birth injuries together contribute to almost 29 % of these deaths. Out of the estimated 2-2.5 million annual neonatal deaths in the country, between 3000-35000 may be due to perinatal asphyxia. (2) In addition, 100000-150000 stillbirths each year are estimated to be due to intrapartum hypoxia and an unknown number of survivor may develop long-term neurological disability. (3,4)

The existence of certain highrisk factors during pregnancy and labour serve to forewarn and alert the labour room staff that they should be fully prepared to meet the challenge of an asphyxiated baby. Reviews over the subject shows the multiplicity of causes like age, parity, poor socioeconomic status, height, under nutrition, anemia, no or sub-optimal antenatal follow up, Pregnancy induced hypertension (PIH), gestational diabetes (GDM), multiple pregnancy, toxemia, other maternal diseases, Rh-isoimmunisation, antepartum hemorrhage (APH), hydramnios, congenital malformation, infection, prolonged labour, mode of delivery, prematurity, low birth weight, meconium aspiration, poor transportation facility and so many factors, which could directly or indirectly influence the asphyxia and its outcome. (5) These factors could vary in different geographic regions and community with different educational and socioeconomic background. There are no currently reported studies with sufficient power for comparisons between groups in eastern India. Therefore, with this background, the following study was planned to assess the maternal & fetal risk factors in newborns with moderate to severe HIE.

Methodology

This was a case control study conducted in HIE babies admitted into the SNCU Department of Paediatrics, M.K.C.G. Medical College Hospital, Berhampur, Ganjam, Odisha during the year 2017 to 2019. All the term babies with HIE II & HIE III, weighing over 2500 grams with or without other complication admitted in SNCU were included in the study. Those babies whose complete data were not available or who had gross congenital malformations were excluded from the study. We have enrolled a total of 200 Newborns in this study based on availability of eligible candidates during the study period.

Selection of cases

National neonatology forum of India has suggested that birth asphyxia should be diagnosed when "baby has gasping and inadequate breathing or no breathing at 1 minute". It is a simple and useful definition, which can be used in the community. It corresponds to 1 minute Apgar score of 3 or less, gasping or no
breathing at 1 minute is an acceptable definition for purpose of estimation of incidences of birth asphyxia. It also graded the degree of asphyxia upon the response to resuscitation and Apgar score at 5 and 10 minutes of age. NNF definition is simple, easy to apply can be used in the community and other hospitals with compromised facilities.

**Selection of controls**

For each case, the next live baby recorded in the labour ward delivery book with no features of perinatal asphyxia was selected as a control.

**Data collection**

Data from clinical examinations, labour room records and nursery records were recorded in a predesigned case record form keeping the primary objectives in mind. Information on the Age, Registration Number, Address, Socioeconomic status, order of birth, details of antenatal check up (ANC), details of previous illnesses, anemia, antepartum hemorrhage (APH), history of maternal diseases like preeclampsia, eclampsia, Premature rupture of membranes, prolonged labour, place of delivery and mode of delivery was collected. From the babies, data on Sex, birth weight, maturity, apgar score at 1 min and 5 min, history of cord around neck and congenital anomalies was collected. We used Levene staging for perinatal asphyxia and Sarnat classification for HIE in our study.

**Data analysis**

All the categorical variables were represented by percentages and Chi square is used to compare the percentages. We used bivariate analysis to compare cases and controls. All the statistical analysis are carried out at 5% level of significance & p value<0.05 considered as significant. Analysis is done by SPSS (Version 23) software.

**Results**

A total of 100 cases and 100 controls were included in the study. The mean age of the participants was 28.6 years. Most mothers in both cases and controls were between 20-30 years of age. Majority in both cases and controls belonged to middle socio-economic classes and had delivery at the same hospital. The descriptive characteristics of the included participants were similar across both cases and controls in the present study. Younger maternal age, primigravida status, anemia, PIH and GDM were related with higher odds of perinatal asphyxia (PA). The comparative analysis of the antepartum and intrapartum risk factors is given below table 1.

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Cases</th>
<th>Controls</th>
<th>ODDS RATIO (CI-95%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal Age (Years)</td>
<td>&lt;20</td>
<td>28</td>
<td>11</td>
<td>3.13(1.43-6.85)</td>
</tr>
</tbody>
</table>
Among the intrapartum risk factors assessed, meconium stained liquor presentation was highly correlated with an increased risk of PA. Among postpartum risk factors evaluated, only a better APGAR score at 5 minutes was highly significant as a risk factor with other factors being non-significant as shown in table-2 below.

Table-2. Analysis of Intrapartum and post-natal risk factors

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Cases</th>
<th>Controls</th>
<th>Odds Ratio (CI-95%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mode of delivery</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spontaneous vaginal</td>
<td>46</td>
<td>60</td>
<td>2.01</td>
<td>0.098</td>
</tr>
<tr>
<td>Instrumental</td>
<td>20</td>
<td>08</td>
<td>1.54(1.23-4.32)</td>
<td>0.015(p&lt;0.05)</td>
</tr>
<tr>
<td>Caeserean</td>
<td>34</td>
<td>32</td>
<td>0.9(1.26-3.45)</td>
<td>0.76</td>
</tr>
<tr>
<td>Meconium-stained liquor</td>
<td>33</td>
<td>08</td>
<td>5.664(2.46-13.04)</td>
<td>&lt;0.00(P&lt;0.05)</td>
</tr>
<tr>
<td>Induction of Labour</td>
<td>10</td>
<td>07</td>
<td>1.475(0.53-4.04)</td>
<td>0.447</td>
</tr>
<tr>
<td>General Anaesthesia</td>
<td>08</td>
<td>04</td>
<td>2.08(0.60-7.16)</td>
<td>0.234</td>
</tr>
<tr>
<td>General Anaesthesia</td>
<td>08</td>
<td>04</td>
<td>2.08(0.60-7.16)</td>
<td>0.234</td>
</tr>
<tr>
<td>--------------------</td>
<td>----</td>
<td>----</td>
<td>----------------</td>
<td>-------</td>
</tr>
<tr>
<td>APGAR Score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At 1 minute (&lt;5)</td>
<td>40</td>
<td>05</td>
<td>1.0</td>
<td>0.081</td>
</tr>
<tr>
<td>At 5 minute (&lt;5)</td>
<td>25</td>
<td>10</td>
<td>0.312(0.09-1.02)</td>
<td>0.047(P&lt;0.05)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>41</td>
<td>45</td>
<td>0.849(0.48-1.48)</td>
<td>0.568</td>
</tr>
<tr>
<td>Female</td>
<td>59</td>
<td>55</td>
<td>0.921</td>
<td></td>
</tr>
</tbody>
</table>

The absolute numbers of the cases and controls from each group of antenatal risk factors is shown below in figure-1.

![Figure 1. Frequency of antenatal risk factors in cases and controls](image)

**Discussion**

A total of 100 cases of Hypoxic ischemic encephalopathy and matched controls admitted to SNCU, Dept of Pediatrics, M.K.C.G. Medical College Hospital have been taken for the study. In our study, maternal age below 20 years, primigravida status, maternal anemia and sub-optimal antenatal care are significant risk factors for HIE. Similar findings have been reported in others settings. (6) Lower socioeconomic status was a significant risk factor in our study, as opposed to others who have found no significant association. (7). In another similar study Blume et. al. had reported a significant association. (6) This is possibly related to the differential distribution of economic status across India and Odisha, where this study was conducted is a relatively poor state with majority lower socioeconomic families.
Pregnancy induced hypertension [PIH] (10% Vs 4%) had an independent correlation towards HIE, similar to findings by Aslam et al. (8) In our study a history of PROM, APH, GDM, Bad Obstetric History were not significantly related to HIE. This, especially for PROM and APH, may possibly be due to improper history given by the mothers or due to absence of abruptio placenta in presence of APH. Another possibility is variations in definitions of PROM in different studies. (7,8) Others have reported bad obstetric history to have significant association to HIE. (9) In analysis of intrapartum risk factors association of HIE was seen with mode of delivery, meconium stained liquor, induction of labour & general anaesthesia. It has been well established that most perinatal asphyxia insults are strongly associated with pregnancy related complications such as hypertension and foetal growth retardation, and intrapartum problems such as prolonged labour, cord prolapse, vaginal breech and caesarean deliveries. (6,10,11)

Among post-natal factors, as expected, Low Apgar scores at 1 and 5 minutes and were associated with HIE. Occipitofrontal head circumference (OFHC) or simply head circumference has only clinical correlation (16% Vs 10%). But Hayes and Lee have reported significant statistical association with HIE. (9,12) These studies were not from India and further evaluation of this metric is warranted. Many studies have shown that the incidence of asphyxia is highest in term babies and with low Apgar score at 1 and 5 minutes. National Neonatology Forum of India has suggested that birth asphyxia should be diagnosed when "baby has gasping and inadequate breathing or no breathing at 1 minute". In our study APGAR score at 5 minute has significant statistical association with HIE as similar study by Ibrahim et al. (13)

Our study was limited by its narrow scope by being carried out in Southern part of Odisha (M.K.C.G medial college, Berhampur) where most patient from low or middle socioeconomic status which did not represent national picture. We did not follow random sampling due to the nature of case load and that also effects generalizations. We mostly relied on maternal history without consideration of how long the event occurred or how long the management period was.

Conclusion

Despite of major advances in monitoring technology and knowledge of fetal and neonatal conditions Hypoxic ischemic encephalopathy remains a serious condition that causes significant mortality and long-term morbidity. Improvement of socio-economic status in remote places may have beneficial effect. Strengthening antenatal screening, regular follow up, awareness regarding complicated pregnancies can reduce the incidence of HIE. Timely intervention, supportive care, close monitoring and prevention of complications are the main elements of managing HIE related mortality and morbidity.

References