Perinatal Factors Preceding Neonatal Hypoxic-Ischemic Encephalopathy in El-Minia Locality

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Abstract

Objectives: We investigated the risk factors of birth asphyxia in neonates in EL-Minia University Hospital from January to 31 December 2015, in order to prevent it. Study design this was a retrospective case-control study.

Setting: Neonatal Intensive Care Unit (NICU) of Minia University Hospital. We studied 160 neonates. 80 neonates of them filled the criteria of hypoxic ischemic encephalopathy delivered at 28-41 weeks of gestation from 1 January to 31 December 2015 and admitted to Neonatal Intensive Care Unit (NICU) of El-Minia University Hospitals. In addition to the other 80, neurologically free neonates delivered in the same period included as a control group. Data collected include information about the prenatal period, peripartum period, demographic characteristics, admission and evolution during NICU stay.

Results: We found that antepartum, intrapartum and postpartum factors are important risks leading to neonatal encephalopathy. Intrapartum factors were highly associated with birth asphyxia as prolonged 2nd stage first then meconium-stained amniotic fluid and prenatal visits<4 show a statistical significance.

Conclusion: The identified risk factors may be useful indicators for defining children at risk of developing hypoxic ischemic encephalopathy, and helpful for targeting individuals for early intervention programmes.

Keywords: Hypoxic ischemic encephalopathy; Birth asphyxia; Antepartum factors; Intrapartum factors

Introduction

Perinatal hypoxic-ischemic encephalopathy (HIE) is a syndrome of disturbed neurological function in the early life characterized by clinical and laboratory proof of acute or subacute brain injury [1].

Perinatal asphyxia is the major cause of HIE in neonates. All pathological conditions that result in prenatal, perinatal, or postnatal hypoxia and tissue hypoperfusion are etiologic factors of HIE [2].

Birth asphyxia is a leading reason of neonatal mortality and morbidity in developing countries with an incidence of 100-250/1000 live births compared to 5-10/1000 live births in the developed world [3]. Infections, preterm births and birth asphyxia were the leading causes of neonatal deaths globally [4].

Several hazard elements associated with HIE. These include low birth weight, low Apgar score, low pH and hemoglobin level [5], as well as delivery by unskilled birth attendants, prolonged second stage of labor, delivery in nongovernmental hospitals, bad antenatal care [6], post-term gestation, vacuum extraction, male sex, and prolapsed cord [7].

Method

Study design

Authors performed a retrospective study of all new borns with HIE admitted at Neonatal intensive care unit (NICU) in El Minia University hospital. This unit is a tertiary centre. This study conducted from 1 January to 31 December 2015. We studied 160 neonates, 80 neonates of them included as a:

Group 1: Who delivered from 1 January to 31 December 2015 with low Apgar scores diagnosed as perinatal asphyxia and admitted to the Neonatal Intensive Care Unit (NICU) of El-Minia University Hospitals, fulfilling the following criteria:

• The first cry delayed for 5 minutes.
• Apgar scores at 5 minutes of age<5 and didn’t improve to more than 7/10 at 20 minutes of age.
• Post-asphyxial seizures (seizures identified by means of medical observation) within first 48 hours after birth (diagnosis of perinatal asphyxia in preterm neonates has similar criteria as full-term including suboptimal Apgar scores, a need for respiratory support, and an inability to suck-feed).

Exclusion criteria:

• Neonates with major congenital malformations.
• Intrauterine fetal death or stillbirth infants.
• Other causes of central nervous system encephalopathy (infectious, metabolic).

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The variable, and Fisher’s exact test for cases less than 5 in the variable. done for qualitative data using Chi-square test for cases more than 5 in cases of two groups with non-parametric. Analytical analyses were cases of two groups with parametric data and Mann-Whitney U in analytical analysis was done for quantitative variables using t-test in they were done for categorical data by number and percentage. The standard deviation, and minimum and maximum of the range, while software version 20.

In this study group 1 included 80 neonates with asphyxia or Apgar score ≤ 6 (case group) 57 male and 23 females compared to group 2, which included 80 neurologically free neonates (control group) 42 male and 38 female.

Table 1 showing the demographic data of the asphyxiated group is shown in Term babies represent a great percentage about 66.3%. Male gender occupies a large percentage about 71.3% (Table 1).

Comparison between asphyxiated group and control group as regarding the antepartum risk factors is shown in Table 2. We found that inappropriate antenatal care (ANC) was significantly higher in cases than a control group (p value<0.001). Bronchial asthma and anemia were significantly higher in mothers of cases than controls (p value=0.04), (p value=0.02) respectively. Also, hypertension in pregnancy was significantly higher in cases when compared with control (Table 2).

As regards polyhydramnios it was greater in mothers of cases than the control with a statistically significant difference. Place of delivery and anesthesia did not affect the outcome.

The significant risk factors of birth asphyxia were further analyzed by multiple logistic regression models as shown in Table 4 in which intrapartum factors associated with birth asphyxia as prolonged 2nd stage first then meconium-stained amniotic fluid and preeclampsia. Also, prenatal visits<4 show a statistical significance (Figures 1-4).

The level of significance at P value<0.050.

Results

Inappropriate ANC

Maternal age(year)

P

0.1

0.3

0.5

<0.001

0.1

0.04

0.1

0.001

Table 2: Comparison between asphyxiated group and control group as regarding the maternal factors (Antepartum factors).

Table 1: Demographic data of the asphyxiated group.

Discussion

Despite the important advances in perinatal care in the past decades, asphyxia remains a severe condition leading to significant mortality and morbidity. The term “asphyxia” is derived from the Greek and means “stopping of the pulse”. Perinatal asphyxia is a condition characterized by an impairment of exchange of the respiratory gasses (oxygen and carbon dioxide) resulting in hypoxemia and hypercapnia, accompanied by metabolic acidosis [8]. The asphyxial injury may involve body systems, but hypoxic-ischemic encephalopathy (HIE) remains the most studied serious sequelae.

HIE associated with many risk factors such as severe preeclampsia, peripartum fever, acute intrapartum event, meconium staining of amniotic fluid, nonsponstaneous vaginal delivery and male sex [9]. Actually, we found most of these risks in our locality so we aim in...
our study to discover the leading perinatal risk factors causing birth asphyxia.

Male sex represents a great proportion of cases than control (71.3%). This is in agreement with the results of Futrakul et al., [7] and Sithivudhi et al., [10] studies who mentioned that the male gender vulnerable to any threatening factors such as increasing the risk of sepsis, bronchial hyperresponsiveness, atopy, and mortality from RDS etc.

In contrast to Nayeri et al., [11] who found no enormous differences among male and female in their study.

HIE was reported more in males than females [12] and male sex associated with the risk of cerebral palsy, especially in very preterm infants. Although the biological basis of this increased risk of brain injury in male babies is not completely understood, several studies explain the mechanisms of cell death after HIE like:

### Table 3: Comparison between the asphyxiated and control groups as regarding the intrapartum factors.

<table>
<thead>
<tr>
<th>Model</th>
<th>Standardized Coefficients Beta</th>
<th>T</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>-1.247</td>
<td>0.214</td>
<td></td>
</tr>
<tr>
<td>Instrumental delivery</td>
<td>-0.094</td>
<td>-1.698</td>
<td>0.092</td>
</tr>
<tr>
<td>Prolonged 2nd stage</td>
<td>0.388</td>
<td>5.4</td>
<td>0</td>
</tr>
<tr>
<td>Prenatal visits&lt;4</td>
<td>0.074</td>
<td>-0.75</td>
<td>0.454</td>
</tr>
<tr>
<td>Polyhydraminos</td>
<td>-0.008</td>
<td>-0.326</td>
<td>0.745</td>
</tr>
<tr>
<td>PROM ≥ 12 h</td>
<td>0.093</td>
<td>1.617</td>
<td>0.108</td>
</tr>
<tr>
<td>Cord prolapsed</td>
<td>-0.009</td>
<td>-0.136</td>
<td>0.892</td>
</tr>
<tr>
<td>Bleeding</td>
<td>-0.044</td>
<td>-0.75</td>
<td>0.454</td>
</tr>
<tr>
<td>Chorioamnioticis</td>
<td>-0.003</td>
<td>-1</td>
<td>0.319</td>
</tr>
<tr>
<td>Meconium stain</td>
<td>0.027</td>
<td>1.454</td>
<td>0.148</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>0.15</td>
<td>2.317</td>
<td>0.022</td>
</tr>
<tr>
<td>Gest. Age</td>
<td>-0.155</td>
<td>-2.722</td>
<td>0.007</td>
</tr>
<tr>
<td>Birth weight</td>
<td>0.031</td>
<td>0.602</td>
<td>0.548</td>
</tr>
<tr>
<td>Outcome</td>
<td>0.165</td>
<td>2.374</td>
<td>0.019</td>
</tr>
<tr>
<td>Anemia</td>
<td>-0.054</td>
<td>-0.929</td>
<td>0.354</td>
</tr>
<tr>
<td>Bronchial asthma</td>
<td>0.007</td>
<td>0.141</td>
<td>0.888</td>
</tr>
</tbody>
</table>

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### Table 4: Multiple logistic regression analysis.
The nuclear enzyme poly (ADP-ribose) polymerase-1 (PARP), involved in DNA repair, is activated by HIE in both sexes, but contributes to neuronal injury, through depletion in NAD+ stores, only in males [13].

It was also shown that there is an increase in apoptosis-inducing factor (AIF) in the immature male brain, this is not observed in the female brain after HIE [14].

Similarly, under conditions of stress in vitro, male neurons die via an AIF-mediated pathway, while a more prominent cytchrome c release from the mitochondria occurs in female neurons, suggesting that intrinsic gender differences in the mechanisms of cell death may occur independently of circulating sex hormones [15].

The elevated circulating levels of dihydrotestosterone in males during the late embryonic period, persisting through the first year of life could be partially responsible for these differences as androgens increase the excitotoxic cell death induced by GABA activation in the developing hippocampus [16].

In our study, we found that the improper antenatal care (ANC) was significantly higher in asphyxiated than control groups. This is coinciding with Gane et al., [17] who found that mothers with antenatal visits less than three had a higher risk for perinatal asphyxia. This finding was a result of poor utilization of health care services in our locality so it is important to establish a safe motherhood policy recommendation based on the characteristics of the population of the locality. In the multiple logistic regression models, we found that the leading risks were risk screening, immunization, anemia prophylaxis, and treatment. Revealing that the leading risks were risk screening, immunization, anemia prophylaxis, and treatment.

Significant risk factors for birth asphyxia analyzed by multiple logistic regression models. Revealing that the leading risks were intrapartum factors which associated with birth asphyxia like prolonged 2nd stage, meconium-stained amniotic fluid.

Prolonged second stage of labor (>2 hours) remained the most important risk factor of birth asphyxia representing 78.8% of asphyxiated group. Similar finding in a study done by Kiyani et al. [18] who reported prolonged second stage of labor in (72%) cases, so early decision of cesarean section could eliminate the great proportion of asphyxiated group. Similar finding in a study done by Kiyani et al. [18] who reported prolonged second stage of labor in (72%) cases, so early decision of cesarean section could eliminate the great proportion of asphyxiated group. In our study, we found that the improper antenatal care (ANC) was significantly higher in asphyxiated than control groups. This is coinciding with Gane et al., [17] who found that mothers with antenatal visits less than three had a higher risk for perinatal asphyxia. This finding was a result of poor utilization of health care services in our locality so it is important to establish a safe motherhood policy recommendation based on the characteristics of the population of the locality. In the multiple logistic regression models, we found that the leading risks were risk screening, immunization, anemia prophylaxis, and treatment. Revealing that the leading risks were risk screening, immunization, anemia prophylaxis, and treatment.

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50% of asphyxiated group had meconium-stained amniotic fluid. Similarly, Pitsawong and Panichkul [19] study who found a higher number of asphyxiated group presented with thick meconium-stained amniotic fluid. It might be due to the fact that meconium aspiration syndrome was primarily associated with acute hypoxic events late in labor or related to acute events that occur late in labor or after birth and also depends on increasing consistency of meconium [20].

The major limitation of this study was its design. As it is a retrospective study, it mainly relies on information from medical records, with possible inaccuracies and loss of data. However, observations made in this study can help in planning larger population-based studies to confirm and target the risk factors of perinatal asphyxia to prevent birth asphyxia.


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