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Maternal risk factors for the neonatal hypoxic-ischemic encephalopathy. Preliminary results

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Abstract

Due to the effect on the central nervous system, cerebral hypoxia-ischemia in the newborn is the major leading cause of death and invalidity. We conducted a case control study in order to find out the maternal risk factors associated with hypoxic ischemic encephalopathy (HIE) and its incidence. The study was conducted over a period of 4 years (January 2010 - December 2013). Included in the study were all the newborn babies without any major genetic or congenital malformations. For each newborn diagnosed with HIE, under the definition of Sarnat, we attributed a control case. There were 219 cases studied of newborn with HIE, giving an incidence of 8.5 cases per 1000 term births.
Keywords: *hypoxic ischemic encephalopathy, incidence, risk factors*

Introduction

Hypoxic ischemic encephalopathy (HIE), also known as intrapartum asphyxia is the leading cause of long-term morbidity, due to its chronic neurological disability and its high rates of mortality[1]. In the term infant, the most common mechanism of hypoxic injury is intrauterine asphyxia brought on by circulatory problems (clotting of placental arteries, placental abruption or inflammatory processes). These processes result in perinatal depression which leads to diminished exchange of oxygen and carbon dioxide and severe lactic acidosis[2]. Reduced cardiac output in the context of hypoxia is referred to as hypoxia ischemia (HI), but if an HI episode is severe enough to affect the brain, it leads within 12 to 36 hours to a neonatal HIE[3].

There is an estimated rate of 2-4% of term newborns that present hypoxia during delivery or shortly before birth[4], and even a much higher rate of preterm newborn presenting a serious risk of hypoxic ischemic injuries, due to the cardio-pulmonary instability, labile autoregulation of cerebral blood flow and metabolic disorders, leading to oxidative stress, inflammatory factors, and excitotoxicity. Postnatal insults account only for 10% of cases with HIE[5]. Numerous studies have shown that hypoxic-ischemic insult occur mostly antepartum and intrapartum and long term neurological damage such as cerebral palsy may be associated in a ratio of 10-15% with a hypoxic-ischemic insult.

Both clinical and experimental findings show that HIE is not a single "event", but it is the result of an evolving process. The clinical signs of HIE reflect the evolution of a delayed cascade of molecular events triggered by the initial result[6].

Methods

The study has a prospective observational character and was conducted between January 2010 to December 2013. From a total of 8641 births during this period, the target groups were the 274 of term babies aged between 36-40 weeks of gestation and with a birth weight between 2000 to 4900 grams. All the neonates were monitored in dynamic, evaluating the clinical biological parameters and the cerebral oxygenation. All of the 274 newborn babies presented aspects of HIE at birth. They were divided into 3 groups each belonging to a different stage of HIE, defined by Sarnat&Sarnat[7]. In the control group, we used a term singleton next to the index case for every affected newborn. Data for possible risk factors was collected, such as different disease related to pregnancy, maternal age, parity, social status, pregnancy control frequency; we also collected data regarding the type of delivery, type of fetal presentation and Apgar scores. We then compared the two groups.

Collection of data for statistical processing was performed with Microsoft Excel. The same program was also used for statistical analysis and descriptive statistics. We followed the parameters in terms of indicators of central tendency (mean, median, standard deviation) with a confidence interval of 95%. The statistical parameters from the descriptive analysis showed the centralization tendency or not; and also standard deviation showing the degree of dispersion of curve values around the mean value.

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Results

Out of 8641 births, 7905 were born between 36 weeks and 40 weeks. 274 of the term newborn babies were diagnosed with HIE fulfilling our inclusion criteria. The number of cases with mild HIE was 29 (10.6%), those with moderate HIE 154 (56.2%) and 91 (33.2%) babies had severe HIE (Figure 1).

A total of 274 cases were found in the studied period, giving an incidence of 3.17 per 1000 births, and 3.46 per term births. The incidence is higher, compared to many developing countries.

Maternal risk factors

Maternal vaginal bleeding in pregnancy was found to be a significant risk factor for neonatal encephalopathy. An association between antepartum haemorrhage and cerebral palsy has also been shown. The mean maternal age of 28.19 years did not differ much from the control group (27.93). This excludes the role of teenage pregnancy as a risk factor for HIE.

There is a statistical significant difference between the two groups in terms of numbers of pregnancies. When the mothers were grouped into prim gravidas, gravida 2-5 and gravida > 5 the differences in parity were evident. 58,45% from the study group were prim gravidas while in the control group there were 47.03%; for the rest of the 2 groups there were no significant differences (39.73% to 42.93% for 2-5 and 1.83% to 2.13% for the >5 gravidas groups).

Intrapartum period

In order to estimate the proportion of newborns who had been exposed to intrapartum hypoxia we used the following criteria (Table 1): maternal pyrexi, pregnancy induced hypertension, HELLP syndrome,breech presentation, presence of an abnormal intrapartum cardiotocogram (CTG) or abnormal fetal heart rate on auscultation or meconium in labour, or both, together with a 1 minute Apgar score.

Arterial hypertension, regardless of its form preexistent or with its debut during pregnancy or - represents a pathology quite frequently encountered with this category of patients.

The percentage of patients that had pregnancy-induced hypertension was also significantly high in the study group, compared to the control group. There were 22 cases in the study group (8.02 %) and 9 in the control group (3.28%, Figure 2).

We also found differences between the two groups, regarding the incidence of HELLP syndrome. There were 12 cases in the study group (4.37%) and only 4 cases in the control group (1.45%).

Subjects in the study group had breech presentation in a higher percentage than those in the control group 20.09% versus 13.24%.

The cardiotocography was abnormal in 58% of affected infants compared with 33% of control infants. Meconium was described more commonly in case infants than control infants (32% vs.13%). Among cases with moderate or severe neonatal encephalopathy, meconium was six times more frequent. Finally fetal distress during labour was recorded by the midwife more often in case infants than control infants (18% vs. 8%).

The mean Apgar score for the babies with mild HIE was 6.12, for babies with moderate HIE 6.09, while for those with severe HIE was 6.22 compared to 8.81 in the control group. In the group with mild HIE, the only ma-

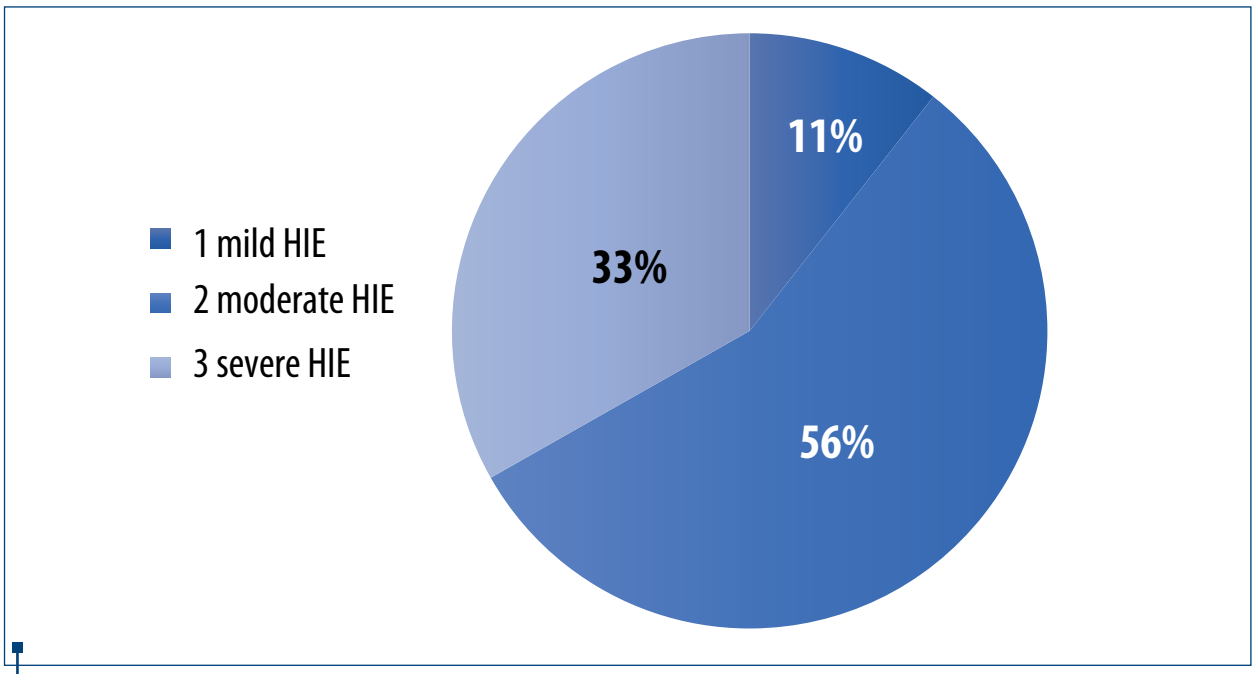

Figure 1. Type of HIE

Table 1 Intrapartum risk factors.

Risk factors	No (%) of cases (n=274)	No (%) of controls (n=274)
Maternal pyrexia		
No	263 (95.98%)	274 (100%)
Yes	11 (4.01%)	0
Pregnancy induced hypertension		
No	252 (91.98%)	265 (96.72%)
Yes	22 (8.02%)	9 (3.28%)
HELLP Syndrome		
No	262 (95.63%)	270 (98.55%)
Yes	12 (4.37%)	4 (1.45%)
Breech Presentation		
No	219 (79.91%)	238 (86.76%)
Yes	55 (20.09%)	36 (13.24%)
Abnormal Cardiotocography		
No	116 (42%)	184 (67%)
Yes	158(58%)	90 (33%)

ternal associated risk factor was hypertension induced by pregnancy, while for the other two groups we also noticed HELLP syndrome and preeclampsia.

Maternal pyrexia occurred in 11 of the cases and none of the controls. Regarding the distribution of cases by sex we observed a weigh almost equal in the two groups, although most of the cases in literature the male sex prevails.

Discussion

The causes of newborn HIE are heterogeneous and many of the causal pathways start before birth[8]. Pregnancy-induced hypertension is a common pathology that can lead to HIE in the newborn, and was present in 22 cases from the study group. We did not find significant differences between parity numbers between the study groups, as cited in other studies[9].

Prolonged interval between rupture of membranes and delivery, a risk factor for ascending infection, was more common in cases compared with controls but not significantly so. Chorioamnionitis is of current interest as a cause of cerebral palsy in both term and preterm newborn. The mechanisms of fetal damage, however, are not known but could include cerebral sepsis, hyperthermia, or action via inflammatory mediators[10].

Among the risk factors we found pregnancy-induced hypertension, pre eclampsia, maternal pyrexia and HELLP syndrome having the highest rates. Among the factors related to labor and delivery, breech presentation and preg-

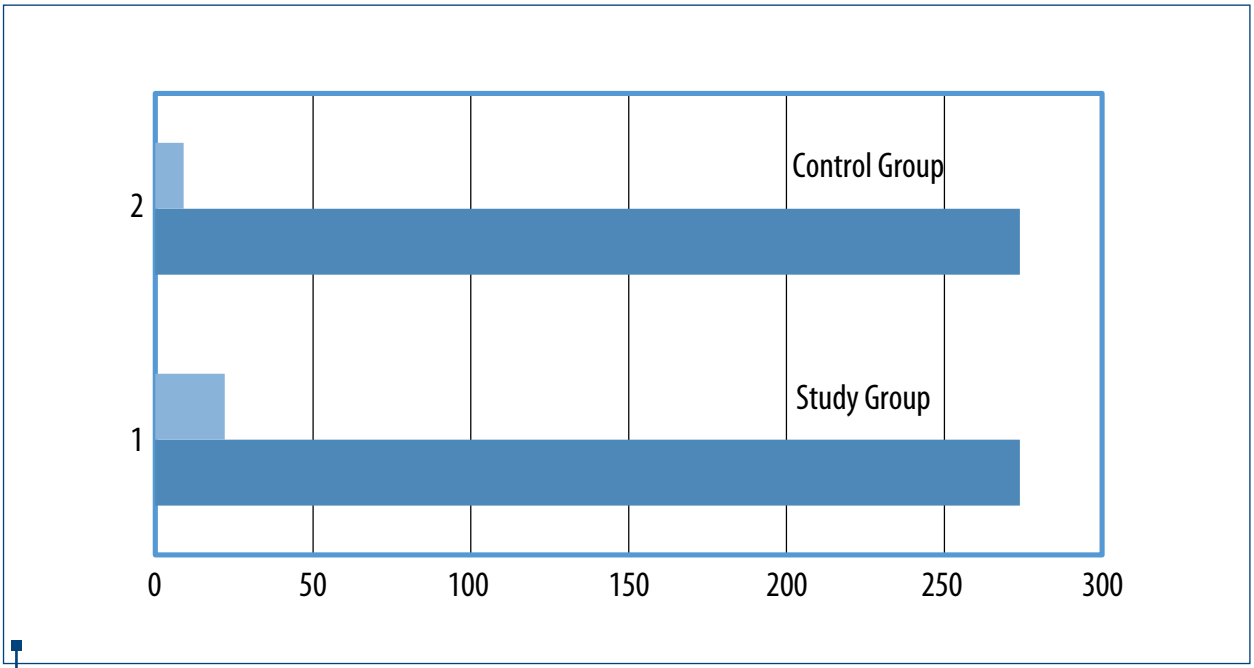

Figure 2. ***Patients with pregnancy induced hypertension***

nancy induced hypertension had the highest incidence.

Elective caesarean sections may avoid some of the intrapartum risk factors for encephalopathy. For example, elective c-sections prevent exposure to post-maturity, persistent occipito-posterior position, intrapartum maternal pyrexia, and unhappy events during labour. It may be the avoidance of these factors other than caesarean section per se which contributes to its apparent benefit[11].

Conclusions

In conclusion, HIE continues to be an important cause of morbidity and mortality in our country. The incidence is higher than in other developing countries. There is a need of future studies and a need to follow uniform criteria for diagnosis and prevention and identical terminology that can make comparison between different studies possible. ■

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