Case-Controlled Study

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Hypoxic-ischaemic encephalopathy based on clinical signs and symptoms and associated factors among neonates, Southern Ethiopian public hospitals: a case-control study

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Background: Hypoxic-ischaemic encephalopathy (HIE) is a severe condition that results from reduced oxygen supply and blood flow to the brain, leading to brain injury and potential long-term neurodevelopmental impairments. This study aimed to identify the maternal and neonatal factors associated with hypoxic-ischaemic encephalopathy among Neonates.

Methods: The authors conducted a case-control study in 15 public hospitals with 515 neonates and mothers (175 cases and 340 controls). The authors used a questionnaire and clinical records created and managed by Kobo software to collect data. The authors diagnosed hypoxic-ischaemic encephalopathy (HIE) by clinical signs and symptoms. The authors used logistic regression to identify HIE factors.

Results: Hypoxic-ischaemic encephalopathy (HIE) was associated with maternal education, ultrasound checkup, gestational age, delivery mode, and labour duration. Illiterate mothers [adjusted odds ratio (AOR) = 1.913, 95% CI: 1.177, 3.109], no ultrasound checkup (AOR = 1.859, 95% CI: 1.073, 3.221), preterm (AOR = 4.467, 95% CI: 1.993, 10.012) or post-term birth (AOR = 2.903, 95% CI: 1.325, 2.903), caesarean section (AOR = 7.569, 95% CI: 4.169, 13.741), and prolonged labour (AOR = 3.591, 95% CI: 2.067, 6.238) increased the incidence of HIE.

Conclusion: This study reveals the factors for hypoxic-ischaemic encephalopathy among neonates in Ethiopia. The authors found that neonates born to illiterate women, those who experienced prolonged labour, those whose mothers did not have ultrasound checkups during pregnancy, those delivered by caesarean section, and those born preterm, or post-term were more likely to develop hypoxic-ischaemic encephalopathy. These findings indicate that enhancing maternal education and healthcare services during pregnancy and delivery may positively reduce hypoxic-ischaemic encephalopathy among neonates.

Keywords: APGAR score, clinical signs and symptoms, hypoxic-ischaemic encephalopathy, neonates

Introduction

Hypoxic-ischaemic encephalopathy (HIE) is a type of brain dysfunction that occurs when the brain does not receive enough oxygen or blood flow for a while[1]. It can cause severe and permanent neurological impairments, such as cerebral palsy, epilepsy, developmental delay, and cognitive impairment which is a leading cause of death or severe disability among infants worldwide[2,3]. Clinical signs and physical exams are reliable signs and symptoms to detect hypoxic-ischaemic insult, a condition that affects neonates' brains which include low Apgar scores, neonatal seizures, and encephalopathy[4–6]. Moreover, a 5th min APGAR score of less than 7 or a 10th min APGAR score of less than 4 are clear indicators of hypoxic-ischaemic insult[4–7].

The incidence and factors of HIE may vary depending on the geographic region and the level of healthcare available. In high-income countries, the most common cause of HIE is perinatal asphyxia due to complications during labour and delivery, such as umbilical cord problems, placental abruption, or foetal distress

HIGHLIGHTS

- Maternal and neonatal factors associated with hypoxic-ischaemic encephalopathy (HIE) among neonates in Ethiopia were assessed.
- A case-control with 515 neonates from 15 public hospitals and diagnosed HIE by clinical signs and symptoms.
- Maternal education, ultrasound checkup, gestational age, delivery mode, and labour duration were significant factors for HIE.
- Improving maternal education and healthcare services during pregnancy and delivery can reduce the incidence of HIE among neonates.

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whereas in low- and middle-income countries, it may also result from maternal or foetal infections, anaemia, malnutrition, or lack of antenatal care[8,9]. HIE affects 1.5 out of every 1000 Neonates worldwide, but the prevalence varies by region and income. The condition is more common in low- and middle-income countries (1.8 per 1000) than in high-income countries (0.5 per 1000). Sub-Saharan Africa suffers the most from HIE, a condition that affects Neonates across the world[8,10]. It has the highest rate (3.1 per 1000) and the largest portion (30%) of the global HIE burden. High-income countries have much lower rates (0.3 to 2.6 per 1000) than low- and middle-income countries (1.6 to 7.9 per 1000)[11].

HIE is a condition that affects Neonates' brains and is predicted by factors related to pregnancy, delivery, and nutrition. Intrapartum factors, such as placental abruption, ruptured uterus, meconium in the amniotic fluid, and caesarean section delivery, account for 70.3% of the HIE cases[12–15]. Antenatal factors, such as being a first-time mother, having a previous foetal death/still birth, using antidepressants or illicit drugs, having Rh sensitization, and gaining more than 13.6 kg of weight during pregnancy, also contribute to HIE[14].

There is a lack of reliable data on the incidence of HIE in Ethiopia, but some studies have estimated it to be between 10.7 and 30.9 per 1000 live births[16]. The main causes of HIE in Ethiopia are infections in the mother or the baby, long labour, lack of oxygen at birth, and blood infection in the baby. The incidence of HIE in southern Ethiopia is also unclear, but one study found it to be 11.5 per 1000 live births at a tertiary hospital in Northern Tanzania, which may be like southern Ethiopia[10,16].

Ethiopia is a low-income country in Sub-Saharan Africa with a high neonatal mortality rate of 23 deaths per 1000 live births in which the prevalence and causes of HIE are not well documented, but some studies have suggested that maternal infections, prolonged labour, birth asphyxia, preterm birth, cord prolapse, post-term pregnancy, vacuum mode of delivery, male sex newborn, and neonatal sepsis are common factors[17,18]. In addition, there is a lack of standardized protocols and resources for the diagnosis and management of HIE in Ethiopian public hospitals[1,19–21].

Even though HIE is a serious condition that affects Neonates who experience oxygen deprivation and reduced blood flow to the brain which can cause brain damage, seizures, developmental delays, and cerebral palsy, the determinant factors are not well understood[22,23]. Therefore, this study aimed to identify factors based on clinical signs and symptoms associated with hypoxic-ischaemic encephalopathy (HIE) in neonates born at public hospitals in Southern Ethiopia.

Methods and materials

Study area, study aim, and design

An institution-based unmatched case-control study was conducted in public hospitals from June 2022 to March 2023 to identify associated factors based on clinical signs and symptoms associated with Hypoxic-Ischaemic Encephalopathy in Neonates in Neonates in which the work has been reported in line with the STROCSS criteria[24].

Operational definitions

Hypoxic-ischaemic encephalopathy (HIE): A type of brain dysfunction that occurs when a newborn does not receive enough oxygen and blood flow during or after birth[6,25]. Diagnosis of HIE: To diagnose HIE, the researcher used clinical signs and physical exams[25]. The clinical signs were low Apgar scores (below 7 at 5 min or below 4 at 10 min) and neonatal seizures. The physical exams evaluated consciousness, muscle tone, posture, reflexes, and autonomic function. Clinical Signs and Symptoms: The researcher used the following clinical signs and symptoms (sign and symptoms only) to indicate HIE: Apgar scores, neonatal seizures, level of consciousness, muscle tone, posture, reflexes, and autonomic function[5,6,25]. Cases: Neonates who were delivered and diagnosed with Hypoxic-ischaemic encephalopathy were considered as cases. Controls: Neonates who were delivered and did not have hypoxic-ischaemic encephalopathy (normal); Term neonates: neonates delivered between 38 and 42 weeks of gestational age; Preterm neonates: neonates born before 37 weeks of gestational age; Post-term neonates: Neonates delivered after 42 weeks of gestational age; Prolonged labour: labour duration greater than or equal to 12 h; Normal labour time: labour duration of less than or equal to 12 h. Maternal anaemia: Having a haemoglobin level of less than 10 mg/dl during pregnancy or the antepartum period, which was diagnosed, based on the laboratory results recorded on the mother's registration card during their antenatal care visits.

Study population and methods

The study population consisted of neonates born at public hospitals. Cases were neonates who had HIE diagnosed at public hospitals during the study period, while controls were neonates who did not have HIE diagnosed in the same area and period. Neonates that had any condition that made them unable to survive outside the womb were excluded from the study. These conditions included lethal congenital anomalies, chromosomal abnormalities, severe intrauterine growth restriction, and major birth defects. We included neonates that had evidence of HIE, which we diagnosed by using the following criteria: low Apgar scores (below 7 at 5 min or below 4 at 10 min) and neonatal seizures. We also performed physical exams to evaluate the level of consciousness, muscle tone, posture, reflexes, and autonomic function of the neonates.

We considered maternal anaemia, foetal presentation, the colour of amniotic fluid, and mode of delivery as exposure variables to calculate the sample size. We chose maternal anaemia as an independent variable because it yielded the largest sample size compared to other exposure variables. We used the Open Epi version 7 statistical software package and a formula for two population proportions to calculate the sample size. Based on a previous study in southern Ethiopia, we assumed that 6.74% of the controls who were exposed[26]. The assumptions for the sample size calculation are; 17.98% of the cases were exposed, a 95% CI, an 80% power of the study, and a 2:1 ratio of controls to cases with 3.87 odds ratio. This resulted in a sample size of 243 Neonates (81 cases and 162 controls). However, since the study was regional and had multiple stages, we applied a design effect and doubled the sample size to 486 Neonates (162 cases and 324 controls). We also accounted for a 10% nonresponse rate and aimed to study 535 neonates (178 cases and 357 controls). We conducted a multicenter case-control study in 15 government hospitals that were randomly selected from a total of 79 government hospitals in Ethiopia. We proportionally allocated the samples to each hospital based on the average case flow estimated by enrolment. We used well-designed data collection tools and trained data collectors on how to observe deliveries, APGAR scoring, clinical signs of HIE and fill data to ensure data quality. We created the instrument by reviewing various sources of literature. To ensure its accuracy and clarity, we translated it from English to Amharic and then back to English. We used a pretested structured questionnaire to collect data from the participants[16,27,28].

We used the Kobo toolbox, a free and open-source application, to design, manage, and collect data for our questionnaire. Kobo toolbox allows us to collect data online or offline using mobile devices, and to analyze and visualize data easily. We selected the Kobo toolbox because of its user-friendly, secure, and reliable interface. It also offers features that enhance data quality control, such as validation rules and skip logic. Our data collectors were professional midwives and nurses who worked at different hospitals from where they collected data.

Data processing and analysis

We used SPSS version 26 to enter and analyze the data. We ensured the data quality and performed descriptive and inferential statistics. We used cross-tabulation and logistic regression to assess the relationship between dependent and independent variables. We controlled confounding factors by using an adjusted odds ratio (AOR). We set the significance level at 0.05 and the confidence level at 95%.

Result

This study involved 175 neonates with HIE (cases) and their mothers, and 340 neonates without HIE (controls) and their mothers, with a response rate of 96.26%. The mothers' mean age was 26.57 years (+ SD = 4.317). The occupational status of the mothers showed that 48.6% of the case mothers and 30.6% of the control mothers were unemployed. Regarding the gestational age, most of the neonates (54.9% of cases and 52.1% of controls) were born at term. However, a considerable proportion of mothers (18.9% of cases and 17.1% of controls) had some illness during their pregnancy. This study explored antepartum, intrapartum, nutritional, and neonatal factors. During their pregnancy, 18.9% of case mothers and 17.1% of control mothers had some illness. Of these, 36.4% of cases and 32.2% of controls were anaemic during their antepartum period. Regarding the ANC visit status of the mothers, 59.9% of cases and 51.2% of controls did not complete their fourth ANC visit. Moreover, 89.5% of case mothers and 80.9% of control mothers had normal amniotic fluid volume.

We observed significant differences in the mode of delivery between neonates with HIE (cases) and without HIE (controls). Most of both groups had a cephalic presentation at delivery, but this was more common among controls (98.2%) than cases (86.9%). Cases were more likely to be delivered by C/S (40.0%) than controls (8.2%), and among those delivered vaginally, cases had less spontaneous labour (62.9%) than controls (92.6%). Moreover, cases had a higher proportion of emergency caesarean section (58.7%) than controls (27.0%), indicating the occurrence of complications during labour and delivery. We also found that 33.1% of cases and 26.4% of controls took some anti-pain or anaesthetic drug. More than half of the cases (53.1%) and more than a third of the controls (34.9%) had more than 12 h of labour and rupture of the membrane, respectively. Of all the participants, 41.1% of cases and 14.4% of controls had labour and delivery-related complications. The status of amniotic fluid was also important, with 50.3% of cases and 85.3% of controls having clear amniotic fluid status, which represented 73.4% of all mothers.

When it comes to nutrition, the pregnant mothers in this study favored meat and meat products over other foods. More than half of the cases (58.3%) and the controls (50.0%) selected this food group. Most mothers ate more than three times a day, but few knew the balanced diet for pregnancy in which many were ignorant of some foods to avoid. The newborns had an equal number of boys and girls. They had a good health status, with an average APGAR score of 7.06 (+ SD = 1.444). Their mean birth weight was 2873.2 grams (± SD = 480.171 grams), and most of them (66.3% of the cases and 80.0% of the controls) fell within the normal range of 2501–3999 grams. We also checked for intrauterine growth restriction (IUGR) right after delivery and found that only a few neonates (5.1% of the cases and 4.7% of the controls) had IUGR (Table 1).

Factors associated with the occurrence of neonatal hypoxic-ischaemic encephalopathy

We controlled confounders with multivariable analysis. We used predictors with *P* value less than 0.2: mother's occupation, education, gestational age, ANC, ultrasound, delivery mode, drug use, labour time, ROM time, food knowledge, and birth weight.

The multivariable logistic regression analysis revealed that these variables were statistically significant: mother's education level, gestational age at delivery, ultrasound status, delivery mode, and labour duration. Neonates with illiterate mothers had more than twice the odds (AOR = 1.913, 95% CI: 1.177, 3.109) of hypoxic-ischaemic encephalopathy than those with literate mothers. We found that preterm Neonates had 4.5 times the odds (AOR = 4.467, 95% CI: 1.993, 10.012), and post-term Neonates had 3 times the likelihood (AOR = 2.903, 95% CI: 1.325, 2.903) of hypoxic-ischaemic encephalopathy compared with term Neonates.

We also examined the effect of ultrasound examination during pregnancy and delivery method on hypoxic-ischaemic encephalopathy. We found that Neonates whose mothers did not have an ultrasound examination during pregnancy had twice the odds (AOR = 1.859, 95% CI: 1.073, 3.221) of developing HIE than those whose mothers did. Moreover, Neonates delivered by C/S had more than seven times the odds (AOR = 7.569, 95% CI: 4.169, 13.741) of suffering from HIE than those delivered vaginally. We also found that labour duration was linked to the occurrence of HIE. Neonates delivered after prolonged labour had 3.6 times the odds (AOR = 3.591, 95% CI: 2.067, 6.238) of HIE than those delivered after normal labour time (Table 2).

Discussion

This study found several factors in mothers and newborns that increased the incidence of hypoxic-ischaemic encephalopathy (HIE), a serious condition that causes brain injury and possible long-term problems due to low oxygen and blood flow to the brain, leading to brain injury and potential long-term neurodevelopmental impairments[29]. The findings of

Table 1

Sociodemographic and reproductive characteristics of mother, perinatal, intra-natal and post-natal factors of neonates delivered at public hospitals in Southern Ethiopia, 2023 ($n = 515$)

Variable	Category	Case $n = 175$, n (%)	Control $n = 340$, n (%)
Occupation of index mother	Unemployed	85 (48.6)	104 (30.6)
	Employed	90 (51.4)	236 (69.4)
Maternal educational status	Literate	99 (56.6)	252 (74.1)
	Illiterate	76 (43.4)	88 (25.9)
Pregnancy status	Singleton	94 (53.7)	196 (57.6)
	Multiple (> 2)	81 (46.3)	144 (42.4)
Parity	Primi	68 (38.9)	109 (32.1)
	Multi	107 (61.1)	231 (67.9)
Duration of current pregnancy	≤ 37 weeks	66 (37.7)	105 (30.9)
	38–42 weeks	96 (54.9)	177 (52.1)
	42 + weeks	13 (7.4)	58 (17.1)
History of bad pregnancy outcome	Miscarriage	58 (33.1)	129 (37.9)
	Still birth	87 (49.7)	119 (35.0)
	Child death	30 (17.1)	92 (27.1)
Illness during pregnancy?	Yes	33 (18.9)	58 (17.1)
	No	142 (81.1)	282 (82.9)
ANC visit during pregnancy	Yes	137 (78.3)	301 (88.5)
	No	38 (21.7)	39 (11.5)
Ultrasound checkup during your time of pregnancy	Yes	91 (52.0)	234 (68.8)
	No	84 (48.0)	106 (31.2)
Amniotic fluid status checkup during pregnancy time	Yes	76 (43.4)	236 (69.4)
	No	99 (56.6)	104 (30.6)
Mode of delivery	Vaginal	105 (60.0)	312 (91.8)
	C/S	70 (40.0)	28 (8.2)
Any drug used during labor[a]	Yes	127 (72.6)	216 (63.5)
	No	48 (27.4)	124 (36.5)
The duration of labour	> 12 h	93 (53.1)	79 (23.2)
	< 12 h	82 (46.9)	261 (76.8)
Duration of ROM	> 12 h	61 (34.9)	42 (12.4)
	< 12 h	114 (65.1)	298 (87.6)
Any complications during labor[b]	Yes	72 (41.1)	49 (14.4)
	No	103 (58.9)	291 (85.6)
Status of amniotic fluid (Colour)	Clear	88 (50.3)	290 (85.3)
	Meconium stained	77 (44.0)	33 (9.7)
	Bloody stained	10 (5.7)	17 (5.0)

ANC, antenatal care; C/S, caesarean section; ROM, rupture of membrane.
[a]Antipain/anaesthetics, uterotonics, anti-hypertensive, anti-convulsant, anti-microbial.
[b]Breech presentation, cord abnormality, foetal heart rate deprivation, sepsis/infection.

this study have important implications for the prevention and management of HIE.

One maternal factor significantly associated with HIE was the index mother's education level. Neonates born to illiterate mothers had two times the odds of developing HIE than those born to literate mothers. This result is in line with a study conducted in Northern and Southern Ethiopia[16,30]. This may mean that maternal literacy affects the knowledge and use of care services before and during birth, which are important for finding and avoiding problems that may lead to HIE. Maternal literacy may also affect the knowledge and practice of healthy behaviours during pregnancy, such as nutrition, hygiene, and infection prevention[31,32].

This study identified ultrasound checkup status during pregnancy and gestational age at delivery as maternal factors associated with HIE. Neonates whose mothers did not have an ultrasound checkup during pregnancy had higher odds of developing HIE than those whose mothers did, which is in line with previous studies done in Cameroon and Istanbul[32,33]. The reason may be that ultrasound helps to know the gestational age and the best time and way of delivery. Ultrasound checkup is a valuable tool for detecting and preventing conditions that may cause HIE, such as foetal anomalies, growth restriction, placental abnormalities, and abnormal foetal presentation. Ultrasound checkups may also help determine the gestational age and the optimal timing and mode of delivery, which are essential for avoiding preterm and post-term births. Both preterm and post-term births were found to increase the occurrence of HIE in this study, as well as in other studies done in Australia, Northern Ethiopia, and Addis Ababa[16,30,34,35].

Preterm Neonates had 4.5 times the odds of developing HIE, while post-term Neonates had 3 times the odds of developing HIE compared with term Neonates. These results are consistent with other studies done in Australia, Northern Ethiopia, and Addis Ababa[16,30,34–37]. This may be because they involve problems with the placenta, the foetus, the amniotic fluid, and the birth process, which may reduce the oxygen and blood flow to the brain as well as post-term birth may be associated with placental insufficiency, foetal distress, meconium aspiration, and birth trauma, which may compromise the oxygen supply and blood flow to the brain[36,37].

The mode of delivery was another factor that influenced the incidence of HIE. Neonates delivered by caesarean section (C/S) had more than 7 times the odds of developing HIE than those delivered vaginally. This is consistent with several studies conducted in Cameroon, Istanbul, and Northern Ethiopia[15,32,38]. This finding may reflect the fact that C/S is often performed as an emergency intervention when there is foetal distress or other complications that may compromise the oxygen supply to the foetus. However, C/S may also pose some negative consequences for the newborn, such as respiratory distress syndrome, transient tachypnea, and iatrogenic prematurity[39]. Therefore, C/S should be reserved for cases where there is a clear indication and benefit for the mother and the foetus and performed with adequate monitoring and care to minimize the occurrence of HIE.

The labour duration was another factor that affected the incidence of HIE. Neonates delivered after prolonged labour had 3.6 times the odds of developing HIE than those delivered after normal labour duration. This finding is consistent with previous studies conducted in developed and developing countries that have shown that prolonged labour is associated with an increased occurrence of foetal hypoxia, acidosis, meconium aspiration, infection, and birth trauma[16,40]. Therefore, timely detection and management of prolonged labour is essential for preventing HIE and its sequelae.

This study has some limitations that warrant further discussion. First, it relied on clinical biomarkers without laboratory or imaging investigation, which could introduce some subjectivity bias in the diagnosis. Second, it excluded private health institutions, health centres, and health posts that offer substantial maternal and child health-related services due to budget constraints, which could limit its applicability to other populations or contexts. Third, it did not evaluate the severity or outcome of HIE

Table 2

Bivariate and multivariable logistic regression among neonates delivered at public hospitals in Southern Ethiopia, 2023 ($n = 515$)

Variable	Category	Case $n = 175$, n (%)	Control $n = 340$, n (%)	COR (95% CI)	AOR (95% CI)	P
Occupation of index mother	Unemployed	85 (48.6)	104 (30.6)	2.143 (1.472, 3.120)	1.450 (0.911, 2.308)	0.118
	Employed	90 (51.4)	236 (69.4)	1	1	
Maternal educational status	Literate	99 (56.6)	252 (74.1)	1	1	
	Illiterate	76 (43.4)	88 (25.9)	2.198 (1.496, 3.231)	**1.913 (1.177, 3.109)**	**0.009***
Duration of current pregnancy	≤ 37 (Preterm)	66 (37.7)	105 (30.9)	2.804 (1.427, 5.512)	**4.467 (1.993, 10.012)**	**0.000***
	42 + (post-term)	13 (7.4)	58 (17.1)	2.420 (1.262, 4.639)	**2.903 (1.325, 2.903)**	**0.008***
	38–42 (Term)	96 (54.9)	177 (52.1)	1	1	
ANC visit during pregnancy	Yes	137 (78.3)	301 (88.5)	1	1	
	No	38 (21.7)	39 (11.5)	2.141 (1.311, 3.495)	0.974 (0.493, 1.926)	0.941
Ultrasound checkup during pregnancy	Yes	91 (52.0)	234 (68.8)	1	1	
	No	84 (48.0)	106 (31.2)	2.038 (1.401, 2.965)	**1.859 (1.073, 3.221)**	**0.027***
Mode of delivery	Vaginal	105 (60.0)	312 (91.8)	1	1	
	C/S	70 (40.0)	28 (8.2)	7.429 (4.547, 12.137)	**7.569 (4.169, 13.741)**	**0.000***
Any drug used during labour	Yes	127 (72.6)	216 (63.5)	1.519 (1.019, 2.263)	0.651 (0.393, 1.077)	0.095
	No	48 (27.4)	124 (36.5)	1	1	
The duration of labour	> 12 h	93 (53.1)	79 (23.2)	3.747 (2.539, 5.530)	**3.591 (2.067, 6.238)**	**0.000***
	< 12 h	82 (46.9)	261 (76.8)	1	1	
The duration of ROM	> 12 h	61 (34.9)	42 (12.4)	3.797 (2.425, 5.944)	1.076 (0.566, 2.047)	0.823
	< 12 hours	114 (65.1)	298 (87.6)	1	1	
Knowledge of mothers on the recommended foods during pregnancy	Yes	73 (41.7)	176 (51.8)	1	1	
	No	102 (58.3)	164 (48.2)	1.499 (1.038, 2.167)	1.144 (0.709, 1.848)	0.581
Wight of the newborn at birth	≤ 2500 g	42 (24.0)	57 (16.8)	1.728 (1.097, 2.720)	0.880 (0.511, 1.515)	0.644
	4000 + g	17 (9.7)	11 (3.2)	3.624 (1.646, 7.976)	2.679 (0.972, 7.382)	0.057
	2501–3999 grams	116 (66.3)	272 (80.0)	1		

Bold value is to show significantly associated variables.
*Denotes factors that were statistically significantly associated with hypoxic-ischaemic encephalopathy.
AOR, adjusted odds ratio; C/S, caesarean section; COR, crude odds ratio; ROM, rupture of membrane.

among newborns, which could vary depending on the extent and location of brain damage.

In addition, one of the limitations of this study is that we did not match the cases and controls based on any criteria, such as gestational age, parity, educational status, maternal age, etc. This may have introduced bias that could influence the association between HIE and its associated factors. Therefore, the results should be interpreted with caution, and further studies with matching techniques are recommended to validate our findings.

Despite these limitations, this study provides valuable insights into the associated factors for HIE among newborns in Ethiopia. It was regional and included most tertiary care hospitals that have a wide catchment population and used a large sample size. The findings suggest that improving maternal education and healthcare services during pregnancy and delivery may help reduce the incidence and severity of HIE. Future research should explore the mechanisms and pathways by which these factors influence the development of HIE, as well as the long-term outcomes and interventions for newborns with HIE.

Conclusion and recommendation

This study aimed to find the factors in mothers and newborns that affect the occurrence of HIE, a brain injury from low oxygen and blood flow. It found that the mother's education, ultrasound status, gestational age, delivery mode, and labour time were linked to HIE. Newborns with illiterate mothers, without ultrasound, born too early or late, delivered by C/S, and after long labour had more HIE than others had. These findings show that better maternal education and healthcare before and during birth may prevent and lessen HIE. This study suggests future research to use lab or imaging tests, include private health facilities and study the causes and outcomes of HIE.

Ethics approval and consent to participate

We conducted this research in accordance with the Declaration of Helsinki, which recommends considering the potential benefits for the participants. Since studying the risk factors of HIE involves ethical and methodological issues specific to human subject research, we followed the WHO's ethical and safety guidelines for human subject research. The Institutional Review Board (IRB) of Dilla University, College of Medicine and Health Sciences ethically approved this study (protocol unique number 010/18-06). We obtained written informed consent from the index mothers/legal guardians of the neonates who participated in the study after informing them about the study. The study participants were free to withdraw from the study at any time during data collection.

Consent for publication

Not applicable.

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Author contribution

All authors made substantial contributions to this work, including conception, design, data collection, cleaning, analysis, and interpretation. They also drafted and reviewed the manuscript; approved the final version for publication; chose the journal of submission; and accepted responsibility for all aspects of the work.

Conflicts of interest disclosure

There are no conflicts of interest.

Research registration unique identifying number (UIN)

1. Registry used: http://www.researchregistry.com
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Guarantor

Getnet Melaku.

Availability of data and materials

The data that support this study are not publicly available due to ethical and privacy concerns. However, the corresponding author will share the data upon reasonable request. The data include anonymized demographic and clinical data of the participants and questionnaires. The data will be accessible for 10 years after the publication of this paper. To request data access, please contact Getnet Melaku at getsen12@gmail.com.

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