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# Determinants of neonatal jaundice among neonates admitted to five referral hospitals in Amhara region, Northern Ethiopia: an unmatched case-control study

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## ABSTRACT

**Background** Neonatal jaundice is associated with a significant risk of neonatal morbidity and mortality. It is a major cause of hospital neonatal intensive care unit admission and readmissions during the neonatal period. Hence, the study aimed to identify the determinant factors of neonatal jaundice among neonates admitted at five referral hospitals in Amhara region, Northern Ethiopia.

**Method** A hospital-based unmatched case-control study design was employed, on 447 neonates (149 cases and 298 controls) at referral hospitals in Amhara region, Northern Ethiopia, from 1 March to 30 July 2019. Consecutive sampling method was used to select both the cases and controls. The collected data were entered into Epi data V.4.2 and then exported into SPSS window V.24 for analysis. Bivariable and multivariable analysis were carried out by using binary logistic regression. A p value of <0.05 was considered as significant difference between cases and controls for the exposure variable of interest.

**Results** The median (±IQR) age of neonate at the time of admission and gestational age were 3±2 days and 38 (±3) weeks, respectively. Prolonged duration of labour (adjusted OR (AOR)=2.45, 95% CI 1.34 to 4.47), being male sex (AOR=3.54, 95% CI 1.99 to 6.29), low birth weight (AOR=5.06, 95% CI 2.61 to 9.82), birth asphyxia (AOR=2.88, 95% CI 1.38 to 5.99), sepsis (AOR=2.49, 95% CI 1.22 to 5.11) and hypothermia (AOR=2.88, 95% CI 2.63 to 14.02) were the determinant factors for neonatal jaundice.

**Conclusions** Prolonged duration of labour, hypothermia, sepsis, birth asphyxia, low birth weight and sex of neonate were independent determinants of neonatal jaundice. Early recognition and management of identified modifiable determinants are the recommended interventions.

### What is known about the subject?

- Jaundice is a common clinical problem in neonates that occur due to bilirubin disposition.
- Previous studies done on the determinant of neonatal jaundice in Ethiopia were done using chart review identified the prevalence of neonatal jaundice using cross-sectional study design.
- Research data on the determinant of neonatal jaundice in the prospective study are not done in Ethiopia.

### What this study adds?

- Prolonged duration of labour, hypothermia, sepsis, birth asphyxia, low birth weight and sex of neonate were the identified determinant factors for neonatal jaundice in Ethiopia.
- Prevention, early recognition and treatment of those identified modifiable risk factors should be considered to reduce neonatal jaundice.

## BACKGROUND

Neonatal jaundice (NNJ) is a yellow-orange discolouration of the skin and sclera of neonates because of excessive bilirubin in the skin and mucous membranes.[1] In newborns, jaundice appears when total bilirubin (TB) is more than 120 µmol/L.[2 3] Hyperbilirubinaemia with a TB 428–513 µmol/L is associated with an increased risk for bilirubin-induced neurological dysfunction with a significant risk of neonatal mortality and long-term neurodevelopmental sequelae.[4–7] Around three-fourth, of affected neonates, reside in sub-Saharan Africa and South Asia[8–10] and surviving infants after severe NNJ may acquire long-term neurodevelopmental sequelae such as cerebral palsy, sensorineural hearing loss, intellectual difficulties, upward gaze palsy, seizure, gross dental dysplasia and developmental delays in the survivors and death.[7 11 12] Hyperbilirubinaemia can be described in the form of pathological, physiological, jaundice secondary to breast milk or breastfeeding failure, and haemolytic jaundice due to glucose-6-phosphate dehydrogenase deficiency, ABO and Rh incompatibility.[12–14]

Jaundice can be severe when it is seen anywhere on the body on the first day or the

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hands and feet in addition to the arms and legs on the next day. It can be managed by therapeutic interventions which include phototherapy, exchange transfusion and improving the frequency and efficacy of breast feeding or supplementing inadequate formula breast feeding.[2 14 15]

Globally, 2.6 million newborns died in 2016, out of this half of all these deaths occurred in India, Pakistan, Nigeria, the Democratic Republic of Congo and Ethiopia. More than 22% of neonatal deaths were associated with Rh disease and bilirubin encephalopathy in which sub-Saharan Africa and South Asia account for 35%, and 39% of the deaths.[8 16] Severe NNJ accounted for 2.8% of neonatal deaths in the UK, 30.8% in India, 34% in Nigeria, 14% in Kenya and 6.7% in Egypt.[17] NNJ is a major cause of hospital neonatal intensive care unit (NICU) admission and accounts for 75% of hospital readmissions in the first week of life, and is associated with significant mortality.[18–20] It is a common condition worldwide occurring in up to 50%–60% of full-term newborn babies and 80% of preterm newborn babies in the first week of life and it has been recognised as a condition which deserves more global health attention.[21 22] Different studies done reported that in developed countries fetomaternal blood group incompatibilities are the leading cause of NNJ, but in developing countries, the case is different as it is mostly prematurity, low birth weight, birth trauma, ABO incompatibility, sepsis as well as effects of herbal medications in pregnancy and application of dusting powder on the baby may result in G6PD deficiency which is one of the most important causes of NNJ in Africa and Asia.[23 24] In studies conducted in Tikur Anbessa Specialized Hospital and Mekelle, Ethiopia showed that prolonged labour, maternal 'O' blood group, and sepsis were identified determinant factors for NNJs.[25 26] Despite a remarkable reduction in the under-5 mortality in the past few years following important interventions like immunisation, early detection and treatment of infections and diarrhoea control programmes, the neonatal mortality in sub-Saharan Africa including Ethiopia is still alarmingly high which is 30/1000.[27]

The early identification of neonates who are at a greater risk of developing severe NNJ is of paramount importance to prevent brain damage.[28] Therefore, this study aimed to identify the determinants of NNJ among neonates admitted at referral hospitals in Amhara region Northern Ethiopia, 2019.

## METHODS

### Study setting, design and period

A hospital-based unmatched case-control study design was conducted from 1 March to 30 July at Amhara regional state referral hospitals. According to 2019 Amhara region, health bureau reports the region has a total of six referral hospitals. Namely: Felegehiwot referral hospital, University of Gondar referral hospital, Debre Markos referral hospital, Debre Birhan referral hospital, Dessie referral hospital and Tibebe Gion referral hospital. Of the total six hospitals, five of them except Tibebe Gion referral hospital (newly opened referral hospital) have had level-III (subspecialty) NICU rendering services with continuously available personnel (paediatricians and/or neonatologists, general practitioners and neonatal nurses) and equipment to provide life support for as long as needed. All referral hospitals provide general and specialised treatment, known to be open 24 hours for emergency services and each of them assumed to serve more than 5 million peoples.

#### Inclusion criteria

All neonates who were present to the NICU ward of the hospital with NNJ (pathological) were included as cases and neonates without NNJ, healthy babies not on any medication, except nevirapine for the prevention of mother-to-child transmission with volunteer mothers were included as controls in the study.

#### Exclusion criteria

Babies with or without NNJ, abandoned neonates, critically ill and mentally incompetent mothers were excluded from the study. Additionally, neonates with incomplete chart were excluded from the study.

### Operational definitions

Neonatal jaundice: neonates diagnosed as jaundiced through history, clinical signs and symptoms and/or laboratory investigations (TB value more than 205 µmol/L in term babies and more than 257 µmol/L in preterm babies) by physicians (general practitioners, paediatricians and neonatologists).[29]

Physiological jaundice: neonates in the presence of one more of the established Integrated Management of Newborn and Childhood Illness (IMNCI) criteria (only skin on the face or eyes yellow and infant aged 2–13 days old) along with TB value under 205 µmol/L in term babies and under 257 µmol/L in preterm babies.

Hyperthermia: an axillary temperature of >37.5°C.

Hypothermia: an axillary temperature of less than 36.5°C.

Hyperglycaemia: blood glucose level greater than 125 mg/dL.

Hypoglycaemia: blood glucose level less than 40 mg/dL.

Neonatal sepsis: a clinical syndrome of bacteraemia with systemic signs and symptoms of infection in the first 4 weeks of life.

Meconium aspiration syndrome: is a breathing problem that a newborn baby may have due to the aspiration of stained amniotic fluid, which can occur before, during or immediately after birth.

Traditional medicine: taking any herbal traditional medicine during pregnancy to treat nausea and vomiting, reduce the risk of preeclampsia, shorten labour and treat the common cold and urinary tract infections.

### Sample size determination and sampling procedures

The sample size was calculated using Open EPI INFO V.7 software with double population formula by assuming; CI: 95%, power: 80%, case to control ratio: 1:2, P1: per cent of outcome with an exposed group (neonates with jaundice)=80.6%, P2: per cent of outcome in the unexposed

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group (neonates without jaundice)=14.5%.[26] In consideration of 10% of the non-response rate, the final sample was adjusted to 453 (151 cases and 302 controls).

### Data collection tool and procedures

The data were collected after admission by diploma nurses and midwives working in the labour ward and NICU ward under the supervision of BSc holder neonatal nurses. Data were collected by interview with the mothers and review of case records of neonates in the hospital. A checklist consisting of demographic, neonatal, and maternal information were used for data collection. The questions are both open and close ended. The questionnaire addressed the women's sociodemographic characteristics, obstetrics and health-related characteristics and neonatal related characteristics.

### Data quality control

Two days training was given for data collectors and supervisors on how to ask and fill the questions, and how to approach the respondents. The questionnaires were pretested in 5% of the total sample size at Woldia general hospital before the actual data collection time to see the accuracy of responses, language clarity and appropriateness of the tools. The necessary amendment was done based on the findings of the pretest and the amended tool was used for actual data collection at the selected public health facilities. Double data entry was done by two data clerks and compared with the original data to check the consistency.

### Data processing and analysis

The data were coded, cleaned, edited and entered into Epi data V.4.2.0 to minimise logical errors and design skipping patterns. Then, the data were exported to SPSS window V.24 for analysis. The bivariable analysis was used to see the association between each determinant and the outcome variable by using binary logistic regression. All variables with $p \leq 0.25$ in the bivariable analysis was included in the final model of multivariable analysis. Adjusted OR (AOR) along with 95% CI was estimated and $p<0.05$ was set as a cut-off point for the significant determinants of NNJ.

### Patient and public involvement

In this study, neither patient nor public was involved in study proposal development, design and analysis of the study.

## RESULTS

### Sociodemographic characteristics

In this study, a total of 447 neonates with their mother (149 cases and 298 controls) were included making the overall response rate of 98.68%. The median ((±IQR) age of the mother was 26±7 years which ranged from 18 to

**Table 1** Sociodemographic characteristics of mothers in five referral hospitals of Amhara region, Northern Ethiopia, 2019 (cases=149, controls=298)

| | | Neonatal jaundice | |
|---|---|---|---|
| **Characteristics** | **Category** | **Yes (%)** | **No (%)** |
| Mothers age (years) | <20 | 14 (9.4) | 39 (13.1) |
| | 20–35 | 127 (85.2) | 244 (81.9) |
| | >35 | 8 (5.4) | 15 (5.0) |
| Marital status | Married | 142 (95.3) | 281 (94.3) |
| | Divorced | 4 (2.7) | 14 (4.7) |
| | Others* | 3 (2.0) | 3 (1.0) |
| Mothers education | No formal education | 41 (27.5) | 48 (16.1) |
| | Read and write | 23 (15.4) | 39 (13.1) |
| | Primary education | 35 (23.5) | 68 (22.8) |
| | Secondary education | 29 (19.5) | 77 (25.8) |
| | College and above | 21 (14.1) | 66 (22.1) |
| Occupation of the mother | Government employee | 19 (12.8) | 57 (19.1) |
| | Housewife | 96 (64.4) | 137 (46.0) |
| | Merchant | 10 (6.7) | 21 (7.0) |
| | Student | 2 (1.3) | 31 (10.4) |
| | Farmer | 13 (8.7) | 22 (7.4) |
| | Daily workers | 3 (2.0) | 20 (6.7) |
| | Others† | 6 (4.0) | 10 (3.4) |
| Residence | Urban | 98 (65.8) | 215 (72.1) |
| | Rural | 51 (34.2) | 83 (27.9) |

*Divorced. Single.
†Private employee.



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**Table 2** Obstetrics characteristics of mothers in five referral hospitals of Amhara region Northern Ethiopia, 2019 (cases=149, controls=298)

| Characteristics | Category | Neonatal jaundice | |
|---|---|---|---|
| | | Yes (%) | No (%) |
| Health institutions | University of Gondar referral hospital | 31 (20.8) | 71 (23.8) |
| | Debre Markos referral hospital | 14 (9.4) | 31 (10.4) |
| | Felege Hiwot referral hospital | 53 (35.6) | 67 (22.5) |
| | Debre Birhan referral hospital | 28 (18.8) | 65 (21.8) |
| | Dessie referral hospital | 23 (15.4) | 64 (21.5) |
| Number of delivery (parity) | Primiparous | 100 (67.1) | 244 (81.9) |
| | Multiparous | 49 (32.9) | 54 (18.1) |
| Previous child Hx of neonatal jaundice | Yes | 21 (14.1) | 19 (6.4) |
| | No | 128 (85.9) | 279 (93.6) |
| Antenatal care follow-up | Yes | 145 (97.3) | 272 (91.3) |
| | No | 4 (2.7) | 26 (8.7) |
| Number of antenatal care visit(n=417) | 1 | 10 (6.7) | 31 (10.4) |
| | 2–4 | 116 (77.9) | 204 (68.5) |
| | >4 | 23 (15.4) | 63 (21.1) |
| Hx of using traditional medicine | Yes | 3 (2.0) | 11 (3.7) |
| | No | 146 (98.0) | 287 (96.3) |
| Obstetrics complication during pregnancy | Yes | 56 (37.6) | 83 (27.9) |
| | No | 93 (62.4) | 215 (72.1) |
| Type of obstetrics complication | HTN | 24 (46.2) | 28 (53.8) |
| | Obstructed labour | 3 (37.5) | 5 (62.5) |
| | Antepartum haemorrhage | 12 (36.4) | 21 (63.6) |
| | Anaemia | 8 (47.1) | 9 (52.9) |
| | Multiple pregnancy | 6 (54.5) | 5 (45.5) |
| | Gestational DM | 3 (60.0) | 2 (40.0) |
| | Intrauterine growth restriction | 3 (50.0) | 3 (50.0) |
| | Oligohaydraminous | 7 (36.8) | 12 (63.2) |
| Rh status | Positive | 128 (85.9) | 250 (83.9) |
| | Negative | 21 (14.1) | 48 (16.1) |
| Blood group | A | 35 (23.5) | 60 (20.1) |
| | B | 33 (22.1) | 61 (20.5) |
| | AB | 19 (12.8) | 44 (14.8) |
| | O | 62 (41.6) | 133 (44.6) |
| Gestational age at birth (in weeks) | Preterm | 57 (38.3) | 64 (21.5) |
| | Term | 72 (48.3) | 177 (59.4) |
| | Post term | 9 (6.0) | 19 (6.4) |
| | Unknown | 11 (7.4) | 38 (12.8) |
| Onset of labour | Spontaneous | 132 (88.6) | 240 (80.5) |
| | Induced | 15 (10.1) | 40 (13.4) |
| | Not in labour | 2 (1.3) | 18 (6.0) |
| Method of induction (n=55) | Oxytocin | 13 (86.7) | 40(100) |
| | Others | 2 (13.3) | – |
| Presentation | Normal presentation | 136 (91.3) | 282 (94.6) |
| | Malpresentation | 13 (8.7) | 16 (5.4) |
| Premature rupture of membrane | Yes | 53 (35.6) | 54 (18.1) |
| | No | 96 (64.4) | 244 (81.9) |

Continued



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Table 2 Continued

| Characteristics | Category | Neonatal jaundice | |
|---|---|---|---|
| | | Yes (%) | No (%) |
| Meconium stained amniotic fluid (n=107) | Yes | 15 (28.3) | 17 (31.5) |
| | No | 38 (71.7) | 37 (68.5) |
| Meconium stained amniotic fluid Grade (n=32) | Grade I | 4 (26.7) | 7 (41.2) |
| | Grade II | 8 (53.3) | 8 (47.1) |
| | Grade III | 3 (20.0) | 2 (11.8) |
| Duration of labour | Normal | 96 (64.4) | 214 (71.8) |
| | Prolonged | 53 (35.6) | 84 (28.2) |
| Mode of delivery | Spontaneous vaginal delivery | 99 (66.4) | 207 (69.5) |
| | Caesarean section | 39 (26.2) | 63 (21.1) |
| | Instrumental delivery | 11 (7.4) | 28 (9.4) |

DM, Diabetes Mellitus; HTN, Hypertension.

43 years. About 85% of mothers who have neonates with jaundice and more than four-fifths (81.9%) of mothers with neonates without jaundice were between the age group of 20–35 years (table 1).

### Obstetric characteristics

The median (±IQR) gestational age of the baby at birth was 38 (±3) weeks. Regarding parity, 100 (67.1%) of cases and 244 (81.9%) controls were primiparous. Regarding utilisation of antenatal care, almost all 145 (97.3%) of cases and 272 (91.3%) of controls had ANC follow-up, of them 116 (77.9%) of cases and 204 (68.5%) controls had 2–4 ANC visit during their recent pregnancy. One hundred forty-six (98.0%) of cases and 287 (96.3%) of controls have no history of using traditional medicine. Concerning the mode of delivery, 99 (66.4%) of cases and 207 (69.5%) of controls were delivered through spontaneous vaginal delivery. A total of 39 (11 cases and 28 controls) were delivered through instrumental deliveries. Of these 4 cases and 8 controls were through forceps whereas 7 cases and 20 controls were delivered via vacuum (table 2).

### Neonatal related characteristics

In this study, 87 (58.4%) of cases and 170 (57.0%) of controls were males. The median (±IQR) age of neonate at the time of admission were 3±2 days ranging from less than 1 day to 24 days of whom 100 (67.1%) of cases and 199 (66.8%) of controls of neonates age lies within 2–7 days. Fifty-eight (38.9%) of cases and 8 (2.7%) of controls were hypothermic whereas 27 (18.1%) of cases and 4 (1.3%) of controls were hypoglycaemic (table 3).

### Determinants of NNJ

In bivariable binary logistic regression, the covariates mothers education level, duration of labour, sex of neonates, birth weight, neonatal sepsis, APGAR score, gestational age, premature rupture of membrane (PROM), birth asphyxia, parity, hypothermia, feed breast milk, Meconium stained amniotic fluid (MSAF, obstetrics

Table 3 Neonatal characteristics distribution among neonates in five referral Hospitals of Amhara region, Northern Ethiopia, 2019 (cases=149, controls=298)

| Characteristics | Category | Neonatal jaundice | |
|---|---|---|---|
| | | Yes (%) | No (%) |
| Sex of neonates | Male | 87 (58.4) | 170 (57.0) |
| | Female | 62 (41.6) | 128 (43.0) |
| Age of neonates at admission (in days) | <2 days | 30 (20.1) | 83 (27.9) |
| | 2–7 days | 100 (67.1) | 199 (66.8) |
| | >7 days | 19 (12.8) | 16 (5.4) |
| Birth weight (g) | <2500 | 59 (39.6) | 46 (15.4) |
| | 2500–4000 | 88 (59.1) | 246 (82.6) |
| | ≥4000 | 2 (1.3) | 6 (2.0) |
| Five minute APGAR score | ≤6 | 13 (8.7) | 10 (3.4) |
| | 7–10 | 136 (91.3) | 288 (96.6) |
| Birth asphyxia | Yes | 42 (28.2) | 33 (11.1) |
| | No | 107 (71.8) | 265 (88.9) |
| Feed breast milk | Yes | 138 (92.6) | 283 (94.9) |
| | No | 11 (7.4) | 15 (5.1) |
| Use formula feeding | Yes | 14 (9.4) | 12 (4.0) |
| | No | 135 (90.6) | 286 (96.0) |
| MAS | Yes | 20 (13.4) | 16 (5.4) |
| | No | 129 (86.6) | 282 (94.6) |
| Hypothermia | Yes | 58 (38.9) | 8 (2.7) |
| | No | 91 (61.1) | 290 (97.3) |
| Hypoglycaemia | Yes | 27 (18.1) | 4 (1.3) |
| | No | 122 (81.9) | 294 (98.7) |
| Neonatal sepsis/ infections | Yes | 81 (54.4) | 10 (3.4) |
| | No | 68 (45.6) | 288 (96.6) |
| Birth trauma | Yes | 13 (8.7) | 4 (1.3) |
| | No | 136 (91.3) | 294 (98.7) |

APGAR, Appearance, Pulse, Grimace, Activity, and Respiration; MAS, Meconium aspiration syndrome.

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complication and history of jaundice were candidates for the multivariable binary logistic regression model. Multivariable binary logistic regression analysis was done by taking variables showing significant association on bivariable analysis at a p value of ≤0.25 to control (adjust) the possible confounding factors.

Prolonged duration of labour, hypothermia, sex of neonate, sepsis, birth asphyxia and birth weight had a significant association with NNJ at p<0.05 in multivariate analysis.

The odds of NNJ were 2.45 times higher among neonates born from mothers whose labour was prolonged than neonates delivered from mothers whose labour was normal (AOR=2.45, 95% CI 1.34 to 4.47, p=0.004). The chance of developing NNJ among male neonates was 3.54 times higher than female neonates (AOR=3.54, 95% CI 1.99 to 6.29, p<0.001). The odds of NNJ were 5.06 times more likely among neonates with birth weight less than 2500 g than neonates with normal birth weight (AOR=5.06, 95% CI 2.61 to 9.82; p<0.001).

The odds of NNJ were 2.88 times more likely among neonates with birth asphyxia than neonates without birth asphyxia (AOR=2.88, 95% CI 1.38 to 5.99, p=0.012). Similarly, the odds of NNJ were 2.49 times more likely among neonates with neonatal sepsis than neonates without neonatal sepsis (AOR=2.49, 95% CI 1.22 to 5.11, p=0.005). The odds of NNJ were 6.07 times higher among neonates with hypothermia than neonates without hypothermia (AOR=2.88, 95% CI 2.63 to 14.02, p<0.001; table 4).

## DISCUSSION

This study was employed using institution-based unmatched case-control study design among neonates in Amhara region referral hospitals, Northern Ethiopia to investigate the main determinants of NNJ. Thus, from the adjusted analysis, we found that prolonged duration of labour, hypothermia, parity, sex of neonate, birth asphyxia, sepsis and birth weight were independent determinants of NNJ.

This study revealed that prolonged duration of labour was found to be a determinant factor for NNJ. This finding was consistent with studies conducted in the USA,[30] Tehran Iran,[31] Nepal,[32] Ghana[33] and Mekelle Ethiopia.[25] This might be attributed to bruising and swelling of the scalp of newborns due to the excessive pressure applied by birth attendants as management for prolonged labour which in turn increases the risk of jaundice by increasing bilirubin level in the blood. It may also be due to the clinical relationship between longer labour with cephalohaematoma and subgaleal haemorrhage which is a known determinant factor for NNJ and/or severe hyperbilirubinaemia.

This study shows the sex of neonate was an important determinant factor for NNJ. Male sex was a determinant factor for NNJ. This finding is consistent with a study conducted in Nepal,[32] Iran,[24] Pasir Malaysia,[34] Addis Ababa Ethiopia[26] and Mekelle Ethiopia.[25] This might be due to male newborns have relatively immature liver which may not be able to process all the bilirubin formed from red blood cells in normal condition. Besides, a male has a higher concentration of bilirubin and hige risk of acute bilirubin encephalopathy as compared with females.[12 35]

This study revealed that the birth weight of newborns was a determinant factor for NNJ. The odds of NNJ were 5.06 times more likely among neonates with birth weight less than 2500 g than neonates with normal birth weight. This finding was in line with studies conducted in Tehran Iran,[31] Kerala India,[36] North India,[37] Nepal,[32] South Nigeria[38] and Ghana.[33] This might be due to the fact that most of the time low birth weight is common in newborns with prematurity the presents with immature organs particularly immature liver which fails to conjugate normally produced bilirubin from red blood cell which results in jaundices.[35 39]

Birth asphyxia was also an important determinant of NNJ. The odds of NNJ were 2.88 times more likely among neonates with birth asphyxia than neonates without birth asphyxia. Different studies conducted in Kerala India,[36] Southern Nigeria[38] and Southeastern Nigeria[40] supported that NNJs are influenced by birth asphyxia. This might be due to the fact that asphyxia is an insult to the newborn due to lack of oxygen, lack of perfusion to various organs which results in multiorgan system dysfunction due to hypoxic damage mainly on brain, lung, liver and intraventricular haemorrhage which affect the bilirubin conjugation ability of the liver that results in jaundice.[41] Also, perinatal asphyxia with hypoxic-ischaemic encephalopathy can lead to disruption of the blood-brain barrier, thereby allowing free entry of the unconjugated bilirubin to the neurons resulting in acute bilirubin encephalopathy. Besides, kidney damage from PNA can lead to less excretion of the conjugated bilirubin, thereby causing conjugated hyperbilirubinaemia and jaundice.[42]

This study revealed that neonatal sepsis was another determinant factor for NNJ. The odds of NNJ were 2.49 times more likely among neonates with neonatal sepsis than neonates without neonatal sepsis. This finding is in line with a study conducted in North India,[37] Kerala India,[36] Southeastern Nigeria,[40] Addis Ababa Ethiopia[26] and Mekelle Ethiopia.[25] This might be due to the fact that sepsis might cause haemolysis of red blood cells and hepatic dysfunction that leads to accumulation of serum bilirubin in the body.[43]

This study revealed that hypothermia was an important determinant of NNJ. The odds of NNJ were 6.07 times more likely among neonates with hypothermia than neonates without hypothermia. This might be due to the fact that prolonged cold injury mainly moderate and severe hypothermia leads to oedema, general haemorrhage (especially pulmonary haemorrhage) which produces excess bilirubin that increases unconjugated serum bilirubin level.[29]

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**Table 4** Association of sociodemographic, obstetric and neonatal risk factors with neonatal jaundice in referral hospitals of Amhara region Northern Ethiopia, 2019 (cases=149, controls=298)

| Characteristics | Neonatal jaundice | | COR (95% CI) | AOR (95% CI) |
|---|---|---|---|---|
| | Yes (%) | No (%) | | |
| Mothers education | | | | |
| No formal education | 41 (27.5) | 48 (16.1) | 2.68 (1.41 to 5.11) | 0.83 (0.35 to 1.97) |
| Read and write | 23 (15.4) | 39 (13.1) | 1.85 (0.91 to 3.77) | 1.05 (0.41 to 2.67) |
| Primary education | 35 (23.5) | 68 (22.8) | 1.61 (0.85 to 3.06) | 1.22 (0.53 to 2.80) |
| Secondary education | 29 (19.5) | 77 (25.8) | 1.18 (0.61 to 2.26) | 0.72 (0.31 to 1.66) |
| College and above | 21 (14.1) | 66 (22.1) | 1 | 1 |
| Parity | | | | |
| Primiparous | 100 (67.1) | 244 (81.9) | 1 | 1 |
| Multiparous | 49 (32.9) | 54 (18.1) | 2.21 (1.41 to 3.47) | 2.89 (0.86 to 5.59) |
| Hx of neonatal jaundice | | | | |
| Yes | 21 (14.1) | 19 (6.4) | 2.29 (1.18 to 4.44) | 2.06 (0.84 to 5.06) |
| No | 128 (85.9) | 279 (93.6) | 1 | 1 |
| Obstetrics complication | | | | |
| Yes | 56 (37.6) | 83 (27.9) | 1.56 (1.03 to 2.36) | 0.79 (0.44 to 1.44) |
| No | 93 (62.4) | 215 (72.1) | 1 | 1 |
| Gestational age at birth | | | | |
| Preterm | 57 (38.3) | 64 (21.5) | 2.19 (1.39 to 3.43) | 1.08 (0.54 to 2.13) |
| Term | 72 (48.3) | 177 (59.4) | 1 | 1 |
| Post-term | 9 (6.0) | 19 (6.4) | 1.16 (0.50 to 2.69) | 1.07 (0.35 to 3.22) |
| Unknown | 11 (7.4) | 38 (12.8) | 0.712 (0.34 to 1.46) | 0.98 (0.41 to 2.34) |
| PROM | | | | |
| Yes | 53 (35.6) | 54 (18.1) | 2.49 (1.59 to 3.89) | 1.43 (0.73 to 2.77) |
| No | 96 (64.4) | 244 (81.9) | 1 | 1 |
| Duration of labour | | | | |
| ≤24 hours | 96 (64.4) | 214 (71.8) | 1 | 1 |
| >24 hours | 53 (35.6) | 84 (28.2) | 1.96 (1.29 to 2.99) | **2.45 (1.34 to 4.47)*** |
| Sex of neonates | | | | |
| Male | 87 (58.4) | 170 (57.0) | 2.4 (1.57 to 3.65) | **3.54 (1.99 to 6.29)**** |
| Female | 62 (41.6) | 128 (43.0) | 1 | 1 |
| Birth weight (g) | | | | |
| <2500 | 59 (39.6) | 46 (15.4) | 6.67 (4.13 to 10.77) | **5.06 (2.61 to 9.82)**** |
| 2500–4000 | 88 (59.1) | 246 (82.6) | 1 | 1 |
| ≥4000 | 2 (1.3) | 6 (2.0) | 1.11 (0.22 to 5.62) | 1.69 (0.25 to 11.30) |
| Five minute APGAR score | | | | |
| ≤6 | 13 (8.7) | 10 (3.4) | 2.75 (1.17 to 6.43) | 1.48 (0.41 to 5.28) |
| 7–10 | 136 (91.3) | 288 (96.6) | 1 | 1 |
| Birth asphyxia | | | | |
| Yes | 42 (28.2) | 33 (11.1) | 4.14 (2.47 to 6.95) | **2.88 (1.38 to 5.99)***** |
| No | 107 (71.8) | 265 (88.9) | 1 | 1 |
| Feed breast milk | | | | |
| Yes | 138 (92.6) | 283 (94.9) | 1 | 1 |
| No | 11 (7.4) | 15 (5.1) | 3.09 (1.94 to 4.92) | 1.46 (0.73 to 2.89) |
| Neonatal sepsis | | | | |
| Yes | 81 (54.4) | 10 (3.4) | 8.09 (4.83 to 13.56) | **2.49 (1.22 to 5.11)****** |

Continued



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Table 4 Continued

| Characteristics | Neonatal jaundice | | COR (95% CI) | AOR (95% CI) |
|---|---|---|---|---|
| | Yes (%) | No (%) | | |
| No | 68 (45.6) | 288 (96.6) | 1 | 1 |
| MAS | | | | |
| Yes | 20 (13.4) | 16 (5.4) | 2.73 (1.37 to 5.44) | 2.39 (0.88 to 6.48) |
| No | 129 (86.6) | 282 (94.6) | 1 | 1 |
| Hypothermia | | | | |
| Yes | 58 (38.9) | 8 (2.7) | 6.76 (3.79 to 12.07) | **6.07 (2.63 to 14.02)**** |
| No | 91 (61.1) | 290 (97.3) | 1 | 1 |

Significant at: *p=004, **p<0.001, ***p=012, ****p=0.005, 1=constant.

## CONCLUSION

This study showed that maternal/obstetrics and neonatal characteristics were risk factors for NNJs in the study area. Prolonged duration of labour, hypothermia, low birth weight sepsis, birth asphyxia and sex of neonate were independent determinants of NNJ. Therefore, health providers should provide client-centred and meticulous antenatal care for high-risk pregnancies and intrapartum and postpartum care which help to identify high-risk newborns before discharge during routine postnatal care that would reduce the short-term and long-term complication that arise from late diagnosis. Furthermore, the ministry of health should formulate and evolve strategies to identify high-risk cases and optimise early recognition and management strategies for the identified modifiable determinants to reduce the incidence of NNJ.

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**Patient consent for publication** Not required.

**Ethics approval** The ethical clearance was obtained from Woldia University, College of Health Sciences, institutional health research ethics review committee (IHRERC) with Ref No. (Wdu/rcs/aca/fhs/34/2019). A formal letter for permission and support from Woldia University wrote to Amhara regional health bureau (ARHB) and finally to selected health facilities. All the study participants were informed about the purpose of the study, their right to refuse. Written and signed voluntary consent was obtained from mothers before distributing the questionnaire. The respondents were also be told that the information obtained from them was treated with complete confidentiality and do not cause any harm to them.

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**Data availability statement** Data are available upon reasonable request. All data relevant to the study are included in the article or uploaded as supplementary information. All data relevant to the study are included in the article.

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