Determinants of Neonatal Jaundice among Neonates Admitted to Neonatal Intensive Care Unit in Public General Hospitals of Central Zone, Tigray, Northern Ethiopia, 2019: a Case-Control Study

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Background. Neonatal jaundice is common a clinical problem worldwide. Globally, every year, about 1.1 million babies develop severe hyperbilirubinemia with or without bilirubin encephalopathy and the vast majority reside in sub-Saharan Africa and South Asia. Strategies and information on determinants of neonatal jaundice in sub-Saharan Africa are limited. So, investigating determinant factors of neonatal jaundice has paramount importance in mitigating jaundice-related neonatal morbidity and mortality.

Methodology. Hospital-based unmatched case-control study was conducted by reviewing medical charts of 272 neonates in public general hospitals of the central zone of Tigray, northern Ethiopia. The sample size was calculated using Epi Info version 7.2.2.12, and participants were selected using a simple random sampling technique. One year medical record documents were included in the study. Data were collected through a data extraction format looking on the cards. Data were entered to the EpiData Manager version 4.4.2.1 and exported to SPSS version 20 for analysis. Descriptive and multivariate analysis was performed. Binary logistic regression was used to test the association between independent and dependent variables. Variables at p value less than 0.25 in bivariate analysis were entered to a multivariable analysis to identify the determinant factors of jaundice. The level of significance was declared at p value <0.05. Results. A total of 272 neonatal medical charts were included. Obstetric complication (AOR: 5.77; 95% CI: 1.85-17.98), low birth weight (AOR: 4.27; 95% CI:1.58-11.56), birth asphyxia (AOR: 4.83; 95% CI: 1.617-14.4), RH-incompatibility (AOR: 5.45; 95% CI: 1.58-18.74), breastfeeding (AOR: 6.11; 95% CI: 1.71-21.90) and polycythemia (AOR: 7.32; 95% CI: 2.51-21.311) were the determinants of neonatal jaundice. Conclusion. Obstetric complication, low birth weight, birth asphyxia, RH-incompatibility, breastfeeding, and polycythemia were among the determinants of neonatal jaundice. Hence, early prevention and timely treatment of neonatal jaundice are important since it was a cause of long-term complication and death in neonates.
1. Introduction

Jaundice is derived from the French word *juan* which means yellow [1]. Neonatal jaundice (NNJ) is the yellow discoloration of the skin, sclera, and mucosa caused by excess accumulation of bilirubin in the tissue and plasma (serum bilirubin level should be in excess 7 mg/dl). It occurs in up to 60-80% of preterm and term as well as 10% of breastfeeding neonates [2]. The bilirubin level in neonates is much higher than in adults because the life span of the erythrocytes is relatively short and the capacity for bilirubin elimination is lower than in adults; however, hyperbilirubinemia, or jaundice, is a life-threatening disorder in newborns [3, 4].

Neonatal jaundice is a common clinical problem worldwide. Globally, every year, about 1.1 million babies would develop severe hyperbilirubinemia with or without bilirubin encephalopathy, and the majority resides in sub-Saharan Africa and South Asia. In Nigeria, it is 100 times more than in developed countries [5, 6]. The burden was highest in low and middle income countries of subsaharan Africa and South Asia [7]. The global burden of neonatal jaundice reported that the African region has the highest incidence of severe neonatal jaundice per 1000 live births (667.8 to 738.5) followed by the Southeast Asian (251.3 to 473.2) and Americas and European regions 4.4 and 3.7 respectively [8]. Ethiopia is one of the top ten countries with jaundice-related neonatal mortality [9]. A study done at Gonder University showed that jaundice was among the causes of neonatal admission and deaths [10].

Severe neonatal jaundice leads to acute bilirubin encephalopathy or kernicterus with a significant risk of neonatal mortality and long-term neurologic damage such as cerebral palsy, sensory neural hearing loss, intellectual difficulties, or gross developmental delays [11]. It is estimated for 75% hospitalization which needs medical concern and hospital readmission in newborns [11]. It results in brain encephalopathy which requires close attention, evaulation and treatment. It also increases the economic and social burden on the patient's families and societies. There are well-developed systems to identify, investigate, and manage the problem in developed countries, but studies and development are still required to address the problem in poor countries [8].

A study in developed countries reveals that blood incompatibilities are the main causes of neonatal jaundice, whereas prematurity, low birth weight, G6PD deficiency, infection, and traditional practice such as herbal consumption and application of dusting powder were causes of NNJ in developing countries [12].

Understanding of determinant factors of jaundice is crucial to prevent and control the problem. Investigating the factors among the cases is also important to prevent the devastating morbidity and mortality. An evidence-based strategy is needed for prevention, early detection, and treatment. As far as our knowledge is concerned, information on determinants of neonatal jaundice, preventive programs, and uniform practice guidelines, including developmental assessment and surveillance of neonates with jaundice were not available at the health care delivery of the study area. Therefore, identifying the determinant factors of neonatal jaundice has paramount importance in mitigating jaundice-related neonatal morbidity and mortality. The result of this study would help in formulating measures of improving prevention, early detection, and management of neonatal jaundice. Adequate study on factors responsible for the occurrence of NNJ is still lacking in the study area. Therefore, preventing and controlling jaundice desires an understanding of the determinant factors in decisive manner.

2. Materials and Methods

2.1. Aim of the Study. The objective of this study is to identify the determinants of neonatal jaundice among neonates admitted to NICU in the public general hospitals of the central zone of Tigray, Ethiopia.

2.2. Study Design. In this study, a hospital-based unmatched case-control study design was used.

2.3. Study Setting and Period. The study was conducted in public general hospitals of the central zone of Tigray. The central zone had an estimated total population of 1,283,388 according to the Ethiopian Central Statistics report of 2007. The zone has three public general hospitals, one referral hospital, eight district hospitals, and fifty-seven health centers. The public general hospitals are Saint Marry Axum, Adwa, and Abyi Adi hospitals. The study was carried out from August 20 to September 20, 2019.

2.4. Population

2.4.1. Source Population. Cases. All medical record documents of jaundiced neonates admitted to NICU in the public general hospitals of the central zone.

Control. All medical record documents of neonates' without jaundice admitted to NICU in the public general hospitals of the central zone.

2.4.2. Study Population. Cases. All medical record documents of jaundiced neonates who were admitted to NICU in the public general hospitals of the central zone within the last one year.

Control. All medical record documents of neonates without jaundice who were admitted to NICU in the public general hospitals of the central zone within the last one year.

2.5. Sample Size Determination. The required sample size was determined using Epi Info version 7.2.2.12 from the previous study conducted in southern India on maternal and neonatal determinants of jaundice with the assumptions and parameters of power 80%, 95% level of certainty, percent of cases with prim parity of 67.8%, percent of control with prim parity of 49.2%, and OR 2.17 and 2 : 1 ratio with regard to prim parity [13]. The estimated sample size was cases = 91 and controls = 181. Hereby, the actual sample for this study was 272.

2.6. Sampling Technique and Procedure. The study was conducted in the central zone, and all the public general hospitals of the central zone, Adwa, ST Marry Axum, and Abyi Adi hospitals, were included. Medical record documents of cases
and controls were used for data collection. Cases and controls were selected by simple random sampling method. The sample size was allocated to each hospital proportionally.

2.7 Data Collection Tool and Procedures. The data were collected using extraction format and review of medical record documents. One year medical record documents were included in the study. The extract formats were developed by reviewing previous similar studies that consist of all the variables that can meet the objective of the study. It includes sociodemographic, obstetric, maternal, and neonatal factors. Pretest was done on 5% of the sample on both cases and controls.
controls in Suhul Shire General Hospital before ten days of actual data collection. Necessary corrections were done based on the information obtained from the pretest result.

2.8. Data Quality Control. Three data collectors (midwifery professionals) and three supervisors were involved in the data collection. The principal investigator and coordinators have attended the activities on a daily base to give clarification and support for data collectors. Training was given for the data collectors and supervisors. In the training session, the data collectors have been oriented on the objective of the study and how to collect data. The supervisor had assessed the performance of data collectors and correct any problem encountered together with the principal investigator. The collected data were reviewed and checked for completeness by the principal investigator.

2.9. Data Processing and Analysis. Data was entered using the EpiData Manager and exported to SPSS version 20. Further cleaning and recoding were done before the analysis. Bivariate and multivariable logistic regression analysis was used at a 95% confidence interval for the existence of the association. All variables with p value <0.25 in bivariate analysis were entered in the multivariable logistic regression. The strength of the association between dependent and independent variables was measured using odds ratio at 95% confidence interval (CI), and p value <0.05 was used to determine the level of statistical significance. Model fitness was checked by the Hosmer and Lemeshow test. Multicollinearity was checked by S.E, tolerance, and VIF. The result was presented using numerical value, texts, percentages, tables and frequencies, mean, median, and standard deviation.

2.10. Operational Definition. Low APGAR score. A neonate was classified in the APGAR score if it scored ≤4.

Polycythemia. A neonate whose RBC was ≥65 mg/dl was categorized under polycythemia.

3. Results

3.1. Sociodemographic Characteristics of the Neonates and Their Mother. A total of 272 with 91 cases and 181 controls were included in the study. The median age of the neonates (controls) at admission was 2 (±2) days with a maximum of 19 days and a minimum of two hours, whereas for the cases was 2 (±2) days with a maximum of 20 days and a minimum of 6 hours. The mean age of the mothers of the controls and cases was 28.91 (±6.497) and 29.25 (±6.764), respectively (see Table 1).

3.2. Obstetric Characteristics of the Last Pregnancy. One hundred thirteen (62.4%) of the control and 51 (56%) of the cases were born from multipara mothers. More than 3/4 (79.1%) of the controls and more than 2/3 (69%) of the cases were RH positive. One hundred two (56.4%) of the controls and 60 (65.9%) of the cases were delivered at the hospital, whereas fifteen (8.3%) of the controls and six (6.6%) of the cases were delivered at home. Fifty-eight (32%) of the controls and 20 (22%) of the cases were delivered at a health center. The remaining neonates were delivered on the vehicle transporting to a health institution. (see Table 2).

3.3. Neonatal Characteristics. The mean amount of hemoglobin for the controls was 16 (±3.428), and those of cases were 17.84 (4.0 ± 19). The mean amount of total bilirubin level of controls was 10.66 (±5.98), and the median amount of direct bilirubin level of cases was 1.22 (±2).

According to the type of treatment given to cases of jaundice, 2/3 of the cases were treated with phototherapy, exchange transfusion, and drug therapy together (see Figure 1).

Nearly 3/4 of the cases had a bilirubin level of <15 mg/dl (see Table 3).

Regarding the ABO compatibility between mothers and babies, 60.9% of the cases and 53.9% of the controls encountered ABO incompatibility (see Figure 2).

Looking at the chi-square test, there is no significant statistical difference in the odds of developing jaundice between the cases and controls. At a 5% level of significance, from the data, there is sufficient evidence to conclude that the distribution of ABO incompatibility was the same on cases and controls of jaundice (p value = 0.272).

3.4. Determinants of Neonatal Jaundice. The bivariate logistic regression analysis showed that maternal blood group, obstetric complication, mode of delivery, neonatal birth weight, breastfeeding, neonatal sepsis, birth asphyxia, cephalohematoma, neonatal blood group, RH incompatibility, polycythemia, and hepatitis B status had a positive. One hundred two (56.4%) of the controls and 60 (65.9%) of the cases were delivered at the hospital, whereas fifteen (8.3%) of the controls and six (6.6%) of the cases were delivered at home. Fifty-eight (32%) of the controls and 20 (22%) of the cases were delivered at a health center. The remaining neonates were delivered on the vehicle transporting to a health institution. (see Table 2).

3.5. Determinants of Neonatal Jaundice. The bivariate logistic regression analysis showed that maternal blood group, obstetric complication, mode of delivery, neonatal birth weight, breastfeeding, neonatal sepsis, birth asphyxia, cephalohematoma, neonatal blood group, RH incompatibility, polycythemia, and hepatitis B status had a p value <0.25 and were eligible for multiple logistic regression. However, the statistically significant determinants of neonatal jaundice in the multivariable analysis were obstetric complication, low birth weight, birth asphyxia, “B” blood type of the neonate, RH incompatibility, polycythemia, breastfeeding and maternal “O” blood group with p < 0.05.

The odds ratio of obstetric complication was 5.8 times higher among jaundiced neonates as compared to the controls (AOR: 5.77 at 95% CI: 1.85–17.98). The odds of maternal blood group "O" mother was 90% less to develop jaundice compared to blood type A among the cases (AOR: 0.10 at 95% CI: 0.022–0.38). The odds of low birth weight was 4.3 times more among jaundiced neonates compared to...
the controls (AOR: 4.27 at 95% CI: 1.579-11.555). The odds of birth asphyxia was 4.8 times among jaundiced compared to the controls (AOR: 4.83 at 95% CI: 1.617-14.395). Neonates with RH incompatibility were 5.5 times at high risk for jaundice compared to the controls (AOR: 5.45 at 95% CI: 1.583-18.737). The odds of breastfeeding was 6 times higher among the cases compared to the controls (AOR: 6.11 at 95% CI: 1.707-21.886). Polycythemia (hematocrit > 65%) was more frequent in neonates with jaundice as compared to neonates without jaundice (AOR: 7.32 (2.51-21.31)). Neonatal “B” blood type had a negative association with neonatal jaundice (AOR: 0.22 at 95% CI: 0.076-0.602). The odds of cephalohematoma was 4.9 times more among the cases compared to the controls (AOR: 4.86 at 95% CI: 1.173-20.131) (see Table 4).

4. Discussion

This study was aimed at assessing the determinants of neonatal jaundice among neonates admitted to the neonatal intensive care unit in public general hospitals of the central zone Tigray, Ethiopia.

The finding of this study showed that RH incompatibility, low birth weight, breastfeeding, polycythemia, obstetric complication, birth asphyxia, B blood type of the neonate, and maternal O blood group were the determinants of neonatal jaundice among the neonates who were admitted to the NICU at public general hospitals of the central zone.

![Figure 2: ABO compatibility between mothers and babies.](image-url)
Neonatal jaundice was positively associated with RH incompatibility compared to those without incompatibility. The finding of this study was similar to a study conducted in the Mekelle public hospitals and TASH (Addis Ababa) [14, 15]. It was also consistent with the findings in Effutu (Ghana) and Canada [16, 17]. Low birth weight was positively associated with the development of neonatal jaundice. This was in agreement with the study conducted in Effutu Municipality of Ghana, Central Hospital of Nigeria, Government Medical Colleges of South India [13, 16, 18, 19]. This might be due to similarity in gestational age among study populations.

The result of this study revealed that neonatal jaundice was positively associated with breastfeeding. This was consistent with the study done in Addis Ababa [15], Southeast Nigeria [20], India [18], and Southern Nepal [21]. This association is due to the fact that breastfeeding leads to substantial elevation of bilirubin levels during the first few days of life by inhibiting conjugation of bilirubin due to the existence of nonesterified free fatty acid called pregnanediol [22]. However, it was contradicting with the study result in India [13]. The disparity may be related to the sample size difference.

In this study, jaundice was positively associated to obstetric complication. This was correspondent with the study report of Mekelle [15], Harare [23], and India [18]. Birth asphyxia was higher in the jaundiced neonates compared to

<table>
<thead>
<tr>
<th>Variables</th>
<th>Category</th>
<th>Case (n=91)</th>
<th>Control (n=181)</th>
<th>COR (95% CI)</th>
<th>AOR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obstetric complication</td>
<td>Yes</td>
<td>20 (22%)</td>
<td>17 (9.4%)</td>
<td>2.72 (1.34-5.49)</td>
<td>5.77 (1.85-17.98) * p = 0.002</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>71 (78%)</td>
<td>164 (90.6%)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Birth weight</td>
<td>Normal</td>
<td>60 (65.9%)</td>
<td>144 (79.6%)</td>
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<td>1</td>
</tr>
<tr>
<td></td>
<td>Macrocosmic</td>
<td>8 (8.8%)</td>
<td>10 (5.5%)</td>
<td>1.4 (0.61-2)</td>
<td>4.56 (0.396-52.14)</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>20 (22%)</td>
<td>40 (22.1%)</td>
<td>1.26 (0.67-2.39)</td>
<td>4.83 (1.62-14.4) * p = 0.005</td>
</tr>
<tr>
<td>Birth asphyxia</td>
<td>Unknown</td>
<td>27 (29.7%)</td>
<td>30 (16.6%)</td>
<td>2.27 (1.21-4.25)</td>
<td>2.36 (0.86-6.48)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>44 (48.4%)</td>
<td>111 (61.3%)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Cephalohematoma</td>
<td>Yes</td>
<td>16 (17.6%)</td>
<td>12 (6.6)</td>
<td>3.0 (1.36-6.66)</td>
<td>4.86 (1.173-20.131)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>75 (82.4%)</td>
<td>169 (93.4%)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>RH incompatibility</td>
<td>Yes</td>
<td>16 (17.6%)</td>
<td>7 (5.1%)</td>
<td>3.96 (1.56-10.07)</td>
<td>5.45 (1.58-18.174) * p = 0.007</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>75 (82.4%)</td>
<td>130 (94.9%)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Breastfeeding</td>
<td>Breast feed</td>
<td>74 (81.3%)</td>
<td>126 (69.6%)</td>
<td>3.03 (1.21-7.62)</td>
<td>6.11 (1.71-21.89) * p = 0.005</td>
</tr>
<tr>
<td></td>
<td>Formula</td>
<td>6 (6.6%)</td>
<td>31 (17.1%)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Polycythemia</td>
<td>Yes</td>
<td>21 (23.1%)</td>
<td>13 (7.2%)</td>
<td>3.88 (1.84-8.17)</td>
<td>7.32 (2.51-21.31) * p = 0.000</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>70 (76.9%)</td>
<td>168 (92.8%)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Hepatitis B status</td>
<td>Reactive</td>
<td>7 (7.7%)</td>
<td>15 (8.3%)</td>
<td>0.59 (0.23-1.54)</td>
<td>0.35 (0.03-1.47)</td>
</tr>
<tr>
<td></td>
<td>Nonreactive</td>
<td>60 (65.9%)</td>
<td>76 (42%)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Neonatal sepsis</td>
<td>Yes</td>
<td>43 (47.3%)</td>
<td>58 (32%)</td>
<td>1.9 (1.1-3.18)</td>
<td>1.74 (0.79-3.82)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>48 (52.7%)</td>
<td>123 (68%)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Mode of delivery</td>
<td>c/s</td>
<td>17 (18.7%)</td>
<td>19 (10.5%)</td>
<td>2.13 (1.04-4.38)</td>
<td>0.75 (0.25-2.25)</td>
</tr>
<tr>
<td></td>
<td>SVD</td>
<td>60 (65.9%)</td>
<td>143 (79%)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Maternal blood</td>
<td>AB</td>
<td>9 (9.9%)</td>
<td>20 (11%)</td>
<td>4.7 (1.3-17.9)</td>
<td>0.47 (0.07-3.05)</td>
</tr>
<tr>
<td></td>
<td>O</td>
<td>5 (5.5%)</td>
<td>42 (23.2%)</td>
<td>0.21 (0.08-0.57)</td>
<td>0.10 (0.02-0.38)</td>
</tr>
<tr>
<td></td>
<td>A</td>
<td>36 (39.6%)</td>
<td>63 (34.8%)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Blood group neonate</td>
<td>AB</td>
<td>9 (9.9%)</td>
<td>10 (5.5%)</td>
<td>0.3 (0.15-0.61)</td>
<td>0.57 (0.14-2.28)</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>15 (16.5%)</td>
<td>57 (31.5%)</td>
<td>0.3 (0.15-0.61)</td>
<td>0.22 (0.08-0.61) * p = 0.000</td>
</tr>
<tr>
<td></td>
<td>A</td>
<td>38 (41.8%)</td>
<td>43 (23.8%)</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

N.B * indicates the determinant of neonatal jaundice at p value <0.05. LBW: low birth weight, c/s: cesarean section, SVD: spontaneous vaginal delivery.
the controls. This was supported by the case-control study conducted in India [13, 18]. Neonates with polycythemia were high risk to develop jaundice compared to normal hematocrit. This was similar to a study conducted in Nehru Hospital (India) and Share Medical Center of Jerusalem [24–26]. Maternal blood group O was associated with neonatal jaundice. This was supported by the study in Mekelle [15] and Jerusalem [26]. ABO incompatibility occurs when the mother is O type while the neonates are type A, B, and AB. Maternal blood group O with anti-A and anti-B crosses the placenta might hurt neonates with blood group A, B and AB.

In fact, this study reported LBW was positively associated with jaundice (p value = 0.004). This might be due to many (68.4%) of LBW neonates in this study were male babies. So, this may be associated with G6PD as this disease affects males lonely.

4.1. Limitation. The diagnosis of jaundice by health care providers widely varies and depends both on observer attention and on infants’ characteristics.

5. Conclusion

Neonatal jaundice was a common cause of neonatal morbidity and mortality. The major determinants of neonatal jaundice in this study were RH incompatibility, obstetric complication, asphyxia, low birth weight, polycythemia, and breastfeeding. Therefore, identifying the determinants will enable to develop the preventive measures and to identify the high-risk cases. So, early prevention and timely treatment of neonatal jaundice are important to prevent long-term complications and death in neonates.

Abbreviations

AOR: Adjusted odds ratio
C/D: Cesarean delivery
EBF: Exclusive breastfeeding
EDHS: Ethiopian Demographic and Health Survey
LBW: Low birth weighs
LMICs: Low- and middle-income countries
mg/dl: Milligram per deciliter
NNJ: Neonatal jaundice
NICU: Neonatal intensive care unit
PROM: Premature rapture of membrane
SPSS: Stastically Package software for Social Science.

Data Availability

The dataset analyzed in the current study is available from the corresponding author on reasonable request.

Ethical Approval

Ethical clearance was obtained from the institutional ethical review board of the Mekelle University College of Health Sciences. Permission was obtained from Tigray Regional Health Bureau, and a formal letter was submitted to all the concerned bodies in the study area (public general hospital of the central zone) to obtain their cooperation in facilitating the study.

Conflicts of Interest

The authors declare that they have no conflict of interests.

Authors’ Contributions

HN and GG proposed and designed the study and developed the manuscript. MW and MB supervised, advised and helped the author in developing of this study. FT conceptualized the importance of this study. TG and BH assisted in the interpretation of the result and preparation of the draft of the manuscript. AG and KZ assisted on the proposal development and the final write up of the data collection tool. SA, AH, and TM performed the statistical analysis of the study. Eventually, it has been done to read the last version of this manuscript by all contributors for possible modifications they want to make. The manuscript is then amended and gets approved by every author before it is being sent to publication. All authors read and approved the final manuscript.

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