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Determinants of Neonatal Jaundice among Neonates Admitted to Neonatal Intensive Care Unit of Dessie Town Public Hospitals Amhara Region, Ethiopia 2020 Multi Center Cross-Sectional Study

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Abbreviations: AAU: Addis Ababa University, ANC: Antenatal, AOR: Adjusted Odd Ratio: APGAR scores Appearance, pulse, grimace, activity, respiration, score, BMH: Boru Meda Hospital; DRH: Dessie referral hospital; COR: crude odd ratio: EDHS: Ethiopian Demographic and Health Survey; G-6PD: Glucose-6-Phosphate Dehydrogenate: HMIS: Health Management Information System; LBW: Low Birth Weight; NICU: Neonatal Intensive Care Unit; NNJ: Neonatal Jaundice; Rh factors: Rhesus factor; SPSS is the Statistical Package for Social Science, and WHO is the World Health Organization.

Abstract

Background: Neonatal jaundice is a common condition that affects about 60–80% of newborns and, if severe, can lead to serious neurological squeals. Globally**,** every year about 1.1 million babies develop it, and the vast majority resides in sub-Saharan Africa and South Asia. It occurs frequently in newborn babies in the first week of life. It may be harmless but results in "Kernicterus" or "Bilirubin brain damage" when it becomes severe. The purpose of this study is to assess magnitude and determinants of neonatal jaundice among neonates admitted to the NICU

Methods: A hospital-based cross-sectional study was conducted from March 30 to April 30, 2020. In the neonatal intensive care unit of Dessie town public hospitals, a systematic random sampling technique was used to select study participants. Data was collected by interviewing mothers. Face to face Bivariate and multivariable binary logistic regression analyses were employed to identify determinates of neonatal jaundice.

Results: A total of 218 neonates and their mothers were included. The prevalence of neonatal jaundice was found to be 28.4%, and the major associated factors for neonatal jaundice were sepsis [AOR: 10.13, 95% CI=2.36, 43.56], prematurity 37 weeks [AOR: 6.03, 95% CI=1.41, 25.79] Low APGAR score 7 [AOR 7.34, 95% CI = 34.0, 39.65]; ABO incompatibility [AOR 24.55, 95% CI = 1.58,68.83]; prolonged labor [AOR 9.03, 95% CI = 1.67,48.33]; and Rh- incompatibility [AOR=30.40, 95%CI=2.01,66.20)] were found to be predictor of neonatal jaundice.

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Conclusion and recommendation: The magnitude of neonatal jaundice among neonates was found to be high. So, both the maternal and neonatal factors contributed a lot to the management of neonatal jaundice, and they also played a part in its management by phototherapy. Due consideration to these factors is essential while preventing and managing neonatal jaundice

Introduction

Neonatal jaundice (NNJ) is a very common condition affecting 60% of term and 80% of preterm newborns, to a variable degree, around the world [1]. If severe jaundice develops, it can lead to acute bilirubin encephalopathy or kernicterus with a significant risk of neonatal mortality and long-term neurodevelopmental symptoms such as cerebral palsy, sensori-neural hearing loss, intellectual difficulties, or gross developmental delays [2].

Neonatal jaundice is defined as a yellowish discoloration of the mucous membranes, skin, and sclera due to the accumulation of unconjugated, nonpolar, lipid-soluble bilirubin pigment in the skin [3]. Neonatal jaundice is the most common during the remaining weeks of neonatal age and an important condition needing medical attention; about 10% of breastfed neonates are still jaundiced within 1 month (NICE, 2014; Kliegman, 2016). It is a common disorder worldwide, and an estimated 75% of hospital readmissions [4]. Neonatal jaundice is primarily important because there is a relationship between the increase in unconjugated bilirubin levels and neurotoxic effects that can lead to long-term complications such as cerebral palsy, kernicterus, and hearing impairment [5].

Neonatal jaundice is an increased release of hemoglobin from the breakdown of red cells due to high hemoglobin at birth, as well as due to the reduced life span of newborn red blood cells (70–80 days) compared to that of adults (90–120 days), and reduced hepatic metabolism of bilirubin due to an immature liver and Most neonatal jaundice is a natural transition that resolves by the rest of the week with the maturing of the liver cells [6].

Neonatal jaundice may have severe side effects on the health of infants; consideration should be given to its associated factors in newborns, and kernicterus is one of the most important complications of the disease [7]. Neonatal jaundice is one of the most and nine dangerous signs of neonatal illness recognized by the World Health Organization [8]. According to a recent review, sub-Saharan Africa and South Asia were reported as the leading contributors to an estimated 1.1 million babies who would develop severe hyperbilirubinemia worldwide, so early identification of infants at risk of severe hyperbilirubinemia is more crucial for this potentially devastating condition [9].

So, it is clear that neonatal jaundice represents a heavy burden for healthcare services. Therefore, the purpose of this study is to determine the magnitude and determinants of neonatal jaundice among neonates admitted to the NICU at Dessie Town public hospitals. It is important to reduce the risk for future neonates to develop kernicterus through early intervention, prophylaxis, and treatment; improving prevention, early detection, and management of neonatal jaundice; and reducing neonatal deaths by strengthening newborn care and maternal health services. It may also help to create awareness among the community and mothers based on the results of the study, and health professionals will give health education to mothers about the different determinants of neonatal jaundice at the time of the antenatal clinic and postnatal care follow-up, which will help them be screened and treated early. Finally, it would also be a baseline for other researchers to do qualitative and other study designs in the future to assess the magnitude and determinants of neonatal jaundice.

Methods

Study design, area and setting

A health institution-based cross-sectional survey was conducted in public hospitals in Dessie Town from March 30 through April 30, 2020. The study was conducted at health facilities in Dessie Town, Ethiopia, which is located 401 kilometers from Addis Ababa, the capital city of Ethiopia, and 480 kilometers from Bahirdar, the capital city of Amhara regional state. Dessie town has a total population of 151,174, of whom 72,932 are men and 78,242 are women. The languages spoken include Amharic (94.89%), Tigrigna (3.79%), and other languages (0.67%) [10]. A total of two public hospitals have been offering the neonatal intensive care unit (NICU).

Source of population, sample size calculation and Sampling procedures

The source populations were all neonates with their mothers' who were admitted to the neonatal intensive care unit of those hospitals.

The sample size was calculated using a single population proportion formula with the assumption that the prevalence of neonatal jaundice was 44.6% [11], with a 95% confidence level and a 5% margin of error. With these assumptions, the minimum required sample size was 380, but according to the recent one-month health management information system registration data, the estimated total population in the study area was 414. This was less than 10,000. So, a correction formula was used: N=total estimated neonates with their mother in the study area during data collection time were 414. By considering the 10 percent none response rate of participants, 10 percent of the sample size, which was 20, was added. So the total sample size was 218 newborns.

A total sample size of 2,000 for the two hospitals was carried out according to the client patient load in each public institution. The individual cases of jaundice were investigated with reference to their charts.

Data collection

Data were collected using interviewer administered questionnaires and checklists. The data collection tools were adopted from previous similar studies [12] adapted to the local context. The data collection instrument was prepared in English and translated to the local language (Amharic) by a language expert who is fluent in both languages and back translated to English by another expert to ensure the language consistency and accuracy.

Data collectors were recruited based on their previous data collection experience, the relevance of their qualifications, and their ability to speak the local language. Training was given for three consecutive days in order to make the data collectors and supervisors familiar with the data collection tools and interview techniques. Emphasis was given to ethical considerations, the safety of participants, data collectors, and maintaining confidentiality. The data collection tools were pre-tested at Woldia

general hospital outside of the actual study site on 5% of the total sample size prior to actual data collection.

A field work manual was developed by the principal investigator and used by all research teams. To ensure the quality of the data and minimize inter-interviewer variation, about 5% of the respondents were re-interviewed at random by the principal investigator and supervisors and checked for consistency. In addition, daily checks and follow-up were done by the supervisors and investigators.

Operational definitions

Prevalence of neonatal jaundice: the number of neonates with neonatal jaundice as a percentage of the total admitted during the data collection period

Low birth weight: The neonatal birth weight is less than 2,500 grams.

Neonate: A neonate is from birth to 28 days of age.

Preterm: A newborn whose gestational age is less than 37 weeks.

Normal birth weight: The neonate's weight is greater than 2500 g and less than 4000 g.

Neonatal Jaundice: Neonates are diagnosed as jaundiced by physicians. Physiological Jaundice: Clinical jaundice appears after 24 hours of age, and clinical jaundice resolves by 1 week in term infants and 2 weeks in preterm infants. Breast Milk Jaundice: Late-onset jaundice begins after the fourth to seventh day of life and is caused by increased reabsorption of unconjugated bilirubin, perhaps due to an unidentified factor in human milk.

Breastfeeding jaundice: Occurs in the last 2–3 days of life and is related to decreased breast milk intake and decreased frequency of feeding, as well as a history of formula feeding that may indicate the occurrence of breastfeeding jaundice.

Pathological jaundice is evident on the 1st day of life, and clinical jaundice persists for more than 1 week in full-term infants or 2 weeks in preterm infants.

Data analysis

The data was cleaned manually, coded, and entered into Epi Data version 4.2 and analyzed by SPSS version 24 statistical software. The statistical analyses used were percentage, frequency, and bivariate and multivariate logistic regression analyses. Found to be significant at the bivariate level (P 0.05), they were selected and included in multivariate logistic regression models. Then multiple logistic regression analysis models were used to calculate the odds ratio with a 95% confidence interval to estimate the association and control confounding variables. Strength and Strength and direction of the association presented using odds ratios relative to the reference category and 95% confidence levels.

Results

Socio-demographic characteristics of the study participants

A total of 218 clients were approached; however, 209 newborn baby and mother pairs consented to participate in the study, constituting a response rate of 96%. The mean age of mothers was 28.68 years (SD = 5.4). More than half of the respondents (60.8%) were in the age group of 20–35, and the majority of the mothers (88.2%) were Amhara in ethnicity. More than three-quarters of the mothers, 188 (88.2%), were married, and 120 (54.85) were urban residents. Maternal educational status: 32 (14.8%) of the respondents were unable to read and write, and more than half of the mothers were housewives (Table1).

Table 1: Sociodemographic characteristics of pregnant women in Cotonou.

Variable	Category	Frequency	Percentage (%)
Age of the mother	< 20	15	6.9
	20-35	132	60.6
	36-50	71	32.5
Marital status	Single	30	13.8
	Married	188	86.2
Maternal educational status	Not read and write	32	14.8
	Read and write	29	13.4
	Primary education	108	49.5
	Secondary education	26	11.9
	Diploma and above	23	10.6
Residence	Urban	120	54.8
	Rural	98	45.2
Ethnicity	Amhara	192	88.2
	Tigre	8	3.7
	Oromo	15	6.8
	Others	3	1.3
Mother Occupation	Government employee	20	9.3
	Farmer	60	27.4
	Merchant	7	3.5
	Housewife	131	59.8

Maternal factors for jaundice

More than half (67.0%) of the respondents were Multi Para. Seventy-two (32.9%) of the respondents were prime Para. Regarding mode of delivery, 292 (92.2%) were spontaneous vaginal deliveries (SVD), whereas 11 (5.1%) were C-sections (C/S). About the place of delivery, one hundred eighteen (54%) were hospitalized, and six (2.8%) were home deliveries. One hundred ninety-two mothers (88%) had no previous sibling with jaundice. Two hundred and six (94.5%) of the mothers had an ANC follow-up. In the others, 91 (44.1%) had four or more ANC follow-ups. In the other, twenty-six (11.9%) women were taking substances during pregnancy. Of which alcohol consumption, harbor medication use, and tobacco chewing were (57.7%), (11.5%), and (30.8%) respectively, and regarding chronic medical illness, only (5.5%) mothers had medical chronic illness (**Table 2).**

Table 2: Maternal factor for neonatal jaundice in Dessie town public hospitals, Amhara region, Ethiopia, 2020. (n=218)

Variable(n=218)	Category	Frequency(n)	Percentage (%)
Parity	Primi Para	72	33
	Multi Para	146	67
Maternal BG and Rh- factor	A	59	26.9
	B	66	30.1
	AB	27	12.4
	O	57	26.6
	Unknown	9	4
Chronic Medical illness	Yes	12	5.5
	No	206	94.5
Mode of delivery	SVD	202	92.7
	C/S (C-section)	11	5
	Instrumental	5	2.3
Place of delivery	Home	6	2.8
	Health center	94	43.2
	Hospital	118	54
Timing of delivery	Day	43	19.7
	Night	175	80.3
Substance during pregnancy	Yes	26	11.9
	No	194	88.1
Types of substance abuse	Alcohol taking	15	57.7
	Herbal Medication	4	15.4
	Chat chewing	7	26.9
History prolonged PROM	Yes	23	10.6
	No	195	89.3
Infection during pregnancy	Yes	27	12.4
	No	194	87.6.
ANC follow up	Yes	206	94.5
	No	12	5.5
Prolonged labor	Yes	21	9.6
	No	198	90.4
Oxytocin during labor	Ye s	72	32.4
	No	147	67.6
Family/sibling history of jaundice	Yes	26	88.1
	No	192	11.9

Trimester of ANC

Noted:-ANC: Antenatal Care; SVD: Spontaneous vaginal Delivery and PROM: Premature rapture of membrane.

Neonatal factor for jaundice

More than fifty percent of neonates were male infants and the majority of the age group found between 1-7 days 164 (75.2%). The majority of neonates (68.8%) were LBW, and 146 (66.9% neonates were on breast feeding **(Table 3).**

Table 3: Neonatal factor for neonatal jaundice in Dessie town public hospitals Amhara region, Ethiopia 2020 (N=218).

Variables	Category	Frequency (N)	Percent (%)
Neonatal sex	Male	110	50.5
	Female	108	49.5
Neonatal age	1-7 days	164	75.2
	8-28 days	54	24.8
Birth weight	Less than 2.5kg	150	68.8
	More than 2.5kg	68	31.2
Gestational Age	< than 37 weeks	133	61
	> than 37weeks	85	39
Low APGAR score	Less than 7	108	49.5
	More than 7	110	50.5
Blood group and Rh-factor	A	52	23.9
	B	92	42.2
	AB	28	12.8
	O	46	21.1
Neonatal sepsis	Yes	55	25.3
	No	163	74.7
RH-incompatibility	Yes	12	5.5
	No	206	94.5
ABO incompatibility	Ye s	19	8.7
	No	207	91.3
Birth trauma	Yes	31	14.2
	No	187	86.8
Bilirubin encephalopathy	Yes	1	0.5
	No	217	99.5
Birth asphyxia	Yes	12	5.5
	No	206	94.5
Methods feeding	Breast feeding	146	66.9
	Formula feeding	25	11.5
	Mixed feeding	26	11.9
	Maintenance fluid	21	9.7

Neonatal age with onset neonatal jaundice indicated that less than 1 day, 1-7 days, 8-14 days, And more than 14 days were 28 (45.4%), 19(30.6%), 11 (17.5%) and 4 (6 5%) were respectively **(Figure 1)**

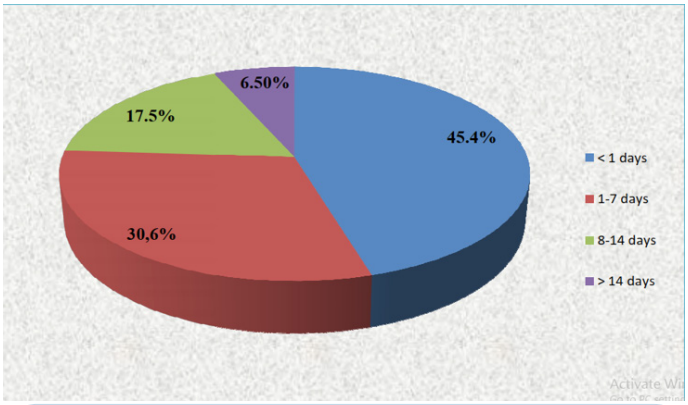

Figure 1: Neonatal age with the onset of neonatal jaundice in Dessie comprehensive specialized hospitals Amhara, Ethiopia 2020.

Prevalence of Neonatal jaundice

The prevalence of neonatal jaundice among neonates admitted to the neonatal intensive care unit (NICU) of Dessie Town public hospitals was found to be 62 (28.4%).

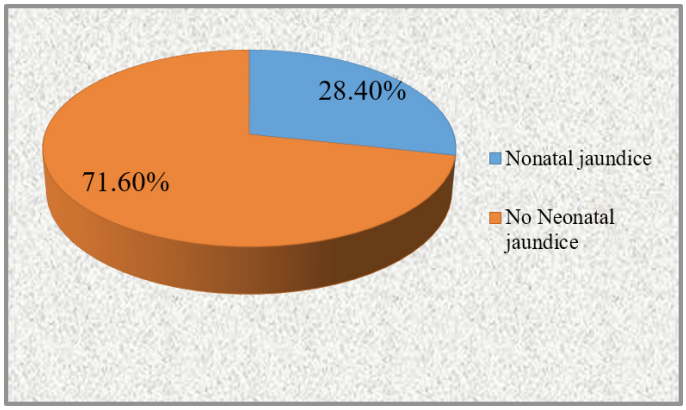

Figure 2: The prevalence of neonatal jaundice among neonates admitted to neonates (NICU) in Dessie comprehensive specialized hospitals, Amhara, Ethiopia 2020.

Determinant of neonatal jaundice

In multivariate logistic regression analysis Low APGAR score 7, ABO-incompatibility sepsis, breastfeeding, Rh-incompatibility, and gestational age 37 weeks were found to be independent predictors of neonatal jaundice. Rh-incompatibility was a variable for neonatal jaundiced neonates who had Rh-incompatibility were thirty times more likely to be affected by neonatal jaundice when compared to neonates who did not have RH-incompatibility [AOR = 30.40, 95% CI = 2.01, 66.20]. Similarly, this study showed that prolonged duration of labor had a significant effect on the development of neonatal jaundice. The odds of developing jaundice were about 9 times higher among neonates who were born with a long duration of labor compared with those neonates born in normal labor [AOR = 9.03 (95% CI = 1.67, 48.33)].

Newborn babies who were delivered before a gestational age of 37 weeks were six times more likely to develop neonatal jaundice when compared to babies born at a gestational age of 37 weeks or more (AOR = 6.03, 95% CI = 1.41, 25.79), and likewise Neonates with low APGAR scores were seven times more

Table 4: Bivariate and Multivariate logistic regression analysis of maternal and neonatal factors for neonatal jaundice Neonates were admitted to NICU in Dessie town Public hospitals, Amhara region, Ethiopia 2020 (N=218).

Variable	Category	NNJ		COR [95%CI]	AOR [95%CI]
		Yes	No		
Maternal parity	Prime Para	38	34	5.68[3.05,10.74]	5.58[1.66,18.82]
	Multi Para	24	122	1	1
Residence	Urban	28	92	1	1
	Rural	34	64	1.75[0.96,3.16]	1.84[0.99,3.38]
PROM	Yes	14	9	3.18[1.36,7.44]	1.38[0.22,8.78]
	No	48	147	1	1
Gestational Age	<37weeks	48	85	2.86[1.46,5.62]	**6.03[1.41,25.79]***
	>37weeks	14	71	1	1
Neonatal sex	Male	41	69	2.46[1.33,4.55]	5.42[1.37,21.49]
	Female	21	87	1	1
Birth asphyxia	Yes	8	4	5.63[1.63,19.45]	2.40[0.30,19.60]
	No	54	152	1	1
Sepsis	Yes	24	31	2.55[1.34,4.85]	**10.13[2.36.43.56)*** *
	No	38	125	1	1
Prolonged labor	Yes	12	9	3.52[1.38,8.99]	**9.03[1.67,48.33] ***
	No	50	147	1	1
Birth trauma	Yes	22	9	8.98[3.84,21.03]	22.65[3.64,74.82]
	No	40	147	1	1
Family/sibling history	Yes	19	7	10.83[4.06,28.81]	13.01[4.79,35.38
	No	43	149	1	1
ABO incompatibility	Yes	12	7	4.84[1.36,17.16]	**24.55[1.58,68.83)*** *
	No	47	152	1	1
LowAPGAR score	Less than 7	42	66	2.80[1.52,7.03]	**7.34[1.34,39.65]***
	More than 7	20	90	1	1
Rh-incompatibility	Yes	7	5	4.47[1.04,19.33]	**30.40[2.01,66.20]***
	No	55	151	1	1

=Statistically significant at p-value** <0.05 **with 95%CI and *: **Variable at p-value** <0.003

PROM: Premature Rapture of Membrane; AOR: Adjusted Odd Ratio; COR: Crude Odd Ration

likely to develop neonatal jaundice when compared to neonates with normal APGAR scores [AOR = 7.34 (95% CI = 1.34, 39.65)].

In this study, sepsis and blood type incompatibility had a significant association with the dependent variable. The odds of neonatal jaundice among neonates who had sepsis were ten times higher compared with those neonates who had no sepsis diagnosis [AOR = 10.13 (95% CI = 2.36, 43.56)]. In the same way, neonates with blood type incompatibility were 24 times more likely to be affected by neonatal jaundice compared with those neonates without blood type incompatibility [AOR = 24.55 (95% CI = 1.58, 68.8)].

Discussion

In the study, the prevalence of neonatal jaundice was found to be 62 (28.4%), and this was consistent with studies conducted in India and Pakistan [13,14]. But it was lower than the prevalence of retrospective studies conducted in Nigeria [11], Addis Ababa, Ethiopia [15], and Gondar, Ethiopia [16]. This inconsistency may be due to differences in the study area, time gaping, and methodology. This study is also lower than a study conducted in Nigeria(17). This discrepancy between the findings may be due to the time gap between the study periods, the different study areas, the study design, and the skills of the data collectors. Likewise, this finding was also lower when compared to the findings from the retrospective study conducted in Sub-Saharan Africa [18]. Inconsistency may be due `to a difference in the skills of data collectors, study areas, and study designs.

This study was also lower than a case-control study conducted at Bloemfontein [19]. The discrepancy of this finding might be due to the different study areas, study design, and skills of the data collectors. This study is also a little bit lower than the study conducted in Southeast Nigeria [20]. Besides the differences in methodology and time gaping, the study setting may be the reason behind this. This study also shows lower than the study that was conducted in Northern Ethiopia [21]. The discrepancy of this finding might be explained by the different study areas, time gaps, and skills of data collectors; also, this study was not a consistent case-control study conducted by Gondar University [16]. This difference could be due to the different study areas, study designs, and methodology reasons behind it.

The odds of jaundice were ten times higher among neonates who had no sepsis diagnosis compared with neonates who had no sepsis diagnosis. This finding was supported as a possible cause of neonatal jaundice in studies conducted in Nigeria [17], South Indian [13] and Israel-Aiwa [22]. This might be because hemolysis, hepatocellular damage, ileus, and/or acidosis may occur as a result of sepsis. These factors may increase bilirubin production (hemolysis), decrease bilirubin removal (liver cell damage), increase the reabsorption of bilirubin, or decrease liver function, which leads to the accumulation of serum bilirubin in the body [21].

Prematurity was six times more likely to affect neonatal jaundice than those neonates who had greater than or equal to 37 weeks of gestation. So, a significant association was found between gestational age and neonatal jaundice. This result is in line with studies done by Narayan in India and Nigeria [16,20]. So, gestational age plays an important role in determining neonatal jaundice. Infants who were delivered prematurely (less than 37 weeks) were at higher risk to develop jaundice due to the immaturity of their bilirubin conjugating system, a higher rate of hemolysis, increased enterohepatic circulation, and decreased caloric intake [23].

Another neonatal variable that was found to be significantly associated with neonatal jaundice was a low APGAR score of <7. Specifically, neonates who had a low APGAR score of 7 were around eight times more likely to be affected by neonatal jaundice compared to those who had an APGAR score of > 7. This finding was supported by studies conducted in Nigeria [24] South Indian [13] were revealed that Low APGAR score less than seven was an independent risk factor of neonatal jaundice. It is a fact that APGAR core is the overall indicator for the state of the newborn in the extra uterine environment, and neonates with a low APGAR score could be in a state of bradycardia, asphyxia, or sepsis, which could be precursors to neonatal jaundice [25].

This study also shows that the prolonged duration of labor had a significant effect on the development of neonatal jaundice. The odds of jaundice were about 9 times higher among neonates who were born with a long duration of labor compared with those born in normal labor. This finding was in line with those in Mekele [21] and Bloemfontein [19]. This might be attributed to bruising and swelling of the scalp of newborns due to the excessive pressure applied by birth attendants as a solution for prolonged labor, which, in turn, increases the risk of jaundice by increasing the bilirubin level in the blood.

Neonates who had ABO incompatibility were 24 times more likely to be affected by neonatal jaundice when compared to neonates who did not have ABO incompatibility. So, a significant association was found between jaundice and ABO incompatibility. This finding was supported by studies that were conducted in Nigeria [17] and south India [13].

Neonates who had Rh-incompatibility were 30 times more affected by neonatal jaundice compared to neonates who did not have Rh-incompatibility. This finding was supported by a study conducted by Troy Man et al. at the University Hospital of the West India [26]. The possible explanation would be the mother is Rh-negative and the fetus is Rh-positive and some fetal RBCs cross the placenta and enter the maternal circulation by minor tea or at the time of delivery and fetal red cells sensitize the mother to antigens on the surface of fetal red cells causing the synthesis of anti- D, IgM, and IgG antibodies so that it leads to neonatal jaundice [26].

Our finding suggests there is an association between neonatal jaundice and low Apgar scores (less than 7), prematurity (gestational age< 37weeks), blood type incompatibility, prolonged duration of labor, and neonatal sepsis. It is necessary that all women be tested for the mother's blood group as early as possible during antenatal follow-up, and if the woman's blood group O is detected during follow-up, it should be considered an ABO setup, making early prevention and detecting neonatal jaundice mandatory. It is also important for health care providers to adhere to aseptic techniques while carrying out and conducting neonatal invasive procedures and for policymakers to strengthen efforts to meet the needs of women through comprehensive care.

Ethical considerations

Ethical clearance was obtained from the institutional review board (IRB) of Addis Ababa University College of Health Sciences, School of Nursing and Midwifery. An official letter of permission was written to the respective hospitals. Consent was ob-

tained from medical directors and the respective unit heads at each health institution. Verbal consent was obtained from each participant. In order to make an informed decision, sufficient information was given to each participant. Confidentiality was strictly maintained for each piece of information, and the interview was conducted in a strictly private setting. At the end of the interview, general information, referral, and follow-up links were made for those who needed them.

Author's contribution

All authors contributed equally to the conception and design of the study. MT collected, analyzed, and interpreted the data. HM, TA, and YG monitored and evaluated the data. HM and TA critically revised and edited the article as well as the manuscript, participated as advisors, and helped with statistics. All authors read and approved the final content of the manuscript.

Availability of data and materials

The datasets were used for the study are available from the corresponding author upon needed.

Competing interests

We declare that no financial or non-financial competing interests related to this study.

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