ORIGINAL RESEARCH

Treatment Outcome of Jaundice and Its Associated Factors Among Neonates Treated in Neonatal Intensive Care Unit of Comprehensive and Specialized Hospitals of Southern Nations Nationalities and Peoples Region, Ethiopia 2022

Christian Kebede [1], Beletech Fentie[2], Bethelihem Tigabu [2]

[1]Department of Pediatrics and Neonatology Nursing, School of Nursing, College of Health Science and Medicine, Wolaita Sodo University, Wolaita Sodo, Ethiopia; [2]Department of Pediatrics and Child Health Nursing, School of Nursing, College of Health science and Medicine, University of Gondar, Gondar, Ethiopia

Correspondence: Christian Kebede, Department of Pediatrics and Neonatology Nursing, School of Nursing, College of Health science and Medicine, Wolaita Sodo University, P.O. Box 138, Wolaita Sodo, Ethiopia, Tel +251924741458, Email kebedechristian@gmail.com

Introduction: Jaundice is a common problem that affects up to 50–60% of full-term babies and 80% of preterm babies. It is a benign condition, but sometimes it can cause profound complications and eventually death. Identifying the treatment outcome of jaundice and the factors affecting it is crucial to preventing the death associated with it.

Objective: To determine the treatment outcome of jaundice and its associated factors among neonates treated in neonatal intensive care unit of comprehensive and specialized hospitals of SNNPR, Ethiopia, 2022.

Methods: An institution-based retrospective follow up study was conducted from April 2018 to April 2022. The data was checked for completeness and then entered into Epi-data version 4.6 and exported to STATA version 17. The results were presented in frequencies and percentages for categorical variables as well as mean and median for continuous variables. A binary logistic regression model was used to estimate the effect of an independent variable and the outcome variable.

Results: A total of 423 charts were reviewed, and 416 (98%) were included in the final analysis. Almost 91.3% (95% CI: 88.2, 93.7) of neonates had improved. Factors significantly associated with the treatment outcome were: residence (AOR = 0.36, 95% CI: 0.2, 0.8); origin of admission (AOR = 0.35, 95% CI: 0.2, 0.8); gestational age (AOR = 0.26, 95% CI: 0.1, 0.8); and total serum bilirubin level (AOR = 0.40, 95% CI: 0.2, 0.9).

Conclusion and Recommendation: Improvement was lower compared to other low and middle-income countries; more emphasis should be given to improving treatment outcomes in hospitals.

Keywords: hyperbilirubinemia, jaundice, neonate, treatment outcome

Introduction

Neonatal jaundice refers to when an infant's skin, mucous membranes, and whites of eyes become yellow within the early neonatal period due to a rise of bilirubin in the blood and a then accumulation of it on the skin and mucous membranes.[1–3] Bilirubin is produced from the breakdown of senescent red blood cells during the early neonatal period.[4,5] Jaundice is a frequent disorder that affects up to 50–60% of full-term and 80% of preterm newborn babies in their first week of life. It is a benign condition in most cases, but sometimes it results in profound complications such as bilirubin-induced neurologic dysfunction and death.[6]

Neonatal jaundice has been identified as a problem that requires increased global health attention, particularly in sub-Saharan Africa and Southeast Asia.[7–10] In high-income countries, mortality due to neonatal jaundice is reported as 1 in 100,000 live births.

In these countries, infants are routinely screened during their birth hospitalization, and monitored for the risk of subsequent severe hyperbilirubinemia and treatment is initiated early. So, this system facilitated timely referral for treatment and significantly improved treatment outcomes, resulting in low mortality due to jaundice.[11,12] Since the 1990s, the number of cases of severe hyperbilirubinemia and associated morbidity and mortality has decreased in high-income countries due to advances in diagnosis and treatment.[13]

When compared to developed countries, the treatment outcome of jaundice is poor in developing countries, with mortality rate of 119 in 100,000 live births.[14,15] Sub-Saharan Africa and Southeast Asia account for 70% of all cases of severe neonatal jaundice occurring worldwide each year, with a death rate of 16–35%.[16] This was due to a failure to initiate appropriate treatment early due to constrained resources, such as devices for measuring bilirubin as well as effective phototherapy (PT).[16] However, the true dimension of the problem was unknown in Ethiopia, where there was high neonatal mortality and a high prevalence of neonatal jaundice.[17,18]

During the period between the 3rd and 6th postnatal days, the risk of severe neonatal jaundice is highest and the serum bilirubin level reaches its peak, so timely detection and initiation of treatment within this critical period is important in improving the treatment outcome of jaundice.[19,20] Nowadays, most parts of the world use various types of effective phototherapies and adjunctive treatment as well as exchange blood transfusion (EBT) severe cases to reduce jaundice-related morbidity and mortality.[21] In developing countries factors such as socio-economic, delayed seeking of health care, health facility-related factors, home deliveries, and late presentation to the hospital led to severe jaundice and resulted in higher death rates among neonates as compared to affluent countries.[6,12,14,22–24] Neonatal mortality due to jaundice can be reduced by determining magnitude of mortality due to jaundice and factors that affects treatment outcome. The principal investigator used different searching techniques to find studies on the treatment outcome of jaundice among neonates treated in the NICU. But in Ethiopia, no study has been found on this topic area. So, this study aims to identify the treatment outcome of jaundice and factors associated with it among neonates admitted to neonatal intensive care units. It is important for healthcare professionals and other stakeholders to give special emphasis to developing action plans and strategies for improving the treatment outcome.

Methods
Study Design, Area, and Period
An institution-based retrospective follow-up study was conducted in two University comprehensive and specialized hospitals of the SNNPR, Ethiopia, namely, Wolaita Sodo University comprehensive and specialized hospital (WSUCSH) and Wachamo University comprehensive and specialized hospital (WCSH) from April to May 2022.

Wolaita Sodo University Comprehensive and Specialized Hospital (WSUCSH) is found in the Wolaita zone, Sodo town, and is about 300 kilometers away to the south of Addis Ababa. It serves people in a catchment area of about 3.5–5 million, including the neighboring Dawuro Zone, Gamo Zone, Gofa Zone, and Kambata Tambaro Zone. There are three senior physicians, five neonatology nurses, eleven BSc nurses, two general practitioners, and four interns working in the neonatal intensive care unit. There are 22 beds in the ward, which has three phototherapy units and is an exchange transfusion referral center for the Wolaita zone and surrounding neighborhoods. The second one was Wachamo University comprehensive and specialized hospital (WCSH), which is found in Hadiya Zone, Hosaena town. It is located 230.9 kilometers to the south of Addis Ababa. There are two senior physicians, two general practitioners, three neonatal nurses, and fifteen BSc nurses working in the neonatal intensive care unit. The hospital also has a total of 19 beds in the ward, three phototherapy units, and a referral center for exchange transfusions in Hadiya Zone and surrounding neighborhoods. The region has no standardized guidelines for the treatment of neonatal jaundice, but hospitals use their own guidelines depending on the availability of healthcare professionals and diagnostic and treatment tools.

Population
Neonatal clinical charts and registries were reviewed for neonates treated for jaundice in the neonatal intensive care unit. The study population consisted of neonates treated for jaundice in a neonatal intensive care unit from April 2018 to April 2022 in two University comprehensive and specialized hospitals in SNNPR, Ethiopia.

Inclusion Criteria and Exclusion Criteria

All neonates treated for jaundice in the neonatal intensive care unit from April 2018 to April 2022 were included in the study, and neonates who left the hospital against medical orders by family wish, were referred to another center, or had physician-confirmed conjugated hyperbilirubinemia were excluded.

Sample Size and Sampling Procedure

The sample size was calculated using the assumption of a single population proportion formula using a 50% proportion because no similar previous study was found in the study area. The lists of neonates treated for neonatal jaundice in the neonatal intensive care unit from April 2018 to April 2022 were extracted from the patients' registration books in each hospital. Then a proportionate number of study participants was allocated to each hospital. Finally, a simple random sampling method was used to choose participants by using a computer-generated random number from the extracted cases using the medical registration number as a sampling frame.

Variables of the Study

The treatment outcome of neonatal jaundice was defined based on the patient's status during discharge from the hospital: either improved or dead. Neonates were said to be improved when an improvement report was recorded on the patient's registration book. Independent variables of the study were socio-demographic factors of mothers and neonates, maternal factors, neonatal factors, and treatment-related factors.

Data Collection Tool and Procedure

Data was collected by using a data extraction tool. It has four components, such as socio-demographic, maternal, neonatal, and treatment-related factors, which were adapted from reviewing different literature.[25–28] Since data collectors were nurses working in the hospital, an English-version data extraction tool was used. After obtaining permission, four BSc nurses working in the adult surgical ward and two NICU ward heads were assigned for data collection and supervision, respectively. To conduct sampling, a medical registration number was obtained from the patient's registration book. Then a total of 423 sampled charts were extracted from the patients' chart store according to inclusion and exclusion criteria. Then, incomplete charts were excluded, and if the neonate died, a death summary for the neonate was extracted from the codes in the patient's registration book. If the cause of death was not due to neonatal jaundice, the charts were excluded and replaced with the next jaundice case chart.

To maintain confidentiality and privacy, only the patient chart room coordinator extracted the patient chart from the store, and the names of the participants were not mentioned during data collection.

Data Quality Control

The data extraction tool was pretested with 5%[20] of the total sample size at the WSU comprehensive and specialized hospital to check for the clarity and consistency of the information. Tool face validation was performed by a senior physician working in the NICU at WSU's comprehensive and specialized hospital and an assistant professor in pediatrics and child health nursing working at WSU. A one-day data collection training was given for data collectors and supervisors, emphasizing the objectives of the study and the data collection procedure. During data collection, close supervision was carried out by the supervisor and the principal investigator. The supervisor and principal investigator checked the data for completeness and consistency regularly until data collection was completed.

Data Processing and Analysis

The collected data was checked for completeness manually. Then it was entered into EP-data version 4.6 and exported to STATA version 17 for further cleaning, recoding, and analysis. Results were presented in frequency tables and charts, descriptively. Categorical variables were computed for their frequencies and percentages. Continuous variables were compiled as mean, median, standard deviation (SD), and interquartile range (IQR). The chi-square assumption test was checked for categorical variables. Multicollinearity was checked for categorical variables (rho = 1.15), and for continuous variables using

a variation inflation factor (VIF =1.25). A binary logistic regression model was used to estimate the strength of the association of an independent variable with an outcome variable. Variables that were statistically significant with p<0.25 in the bivariable analysis were included in the multivariable analysis to control confounders. Model fitness was checked with the Hosmer-Lemeshow goodness-of-fit test for logistic regression (X^2 = 8.6 and p = 0.51). The results were interpreted in terms of an adjusted odds ratio (AOR) with 95% confidence intervals, and a p-value less than 0.05 is considered statistically significant.

Results

Socio-Demographic Characteristics

A total of 423 neonatal charts were reviewed; 416 (98%) were used in the final analysis. More than half of the neonates, 233 (56%) were male, and nearly half, 215 (51.7%) were urban residents. The median post-natal age of the neonates at admission was 2 (IQR ±3) days (Table 1).

Maternal and Neonatal Characteristics

Overall, 347 (83.4%) of mothers were under 35 years old, with a mean age of 29 (SD±4.5) years. Almost 240 (57.7%) of neonates were gestational ages of 37 weeks or more, and the median gestational age was 37 (IQR ± 4) weeks. The median neonatal birth weight was 2.7 (IQR±1.2) kg (Table 2).

Table 1 Socio-Demographic Characteristics of Neonates Treated for Neonatal Jaundice in the Neonatal Intensive Care Unit of in Two Comprehensive and Specialized Hospitals of SNNPR, Ethiopia April, 2022

Variables	Characteristics	Frequency	Percent
Sex	Male	233	56.0
	Female	183	44.0
Residence	Rural	201	48.3
	Urban	215	51.7
Post-natal age at admission	Within 24hrs	122	29.3
	2–7 days	234	56.2
	>7 days	60	14.4
Origin of admission	Inborn	280	67.3
	Out born	126	32.7
Length of Hospital stay	<7 days	206	49.5
	≥7 days	210	50.5

Table 2 Maternal and Neonatal Characteristics Among Neonates Treated in Neonatal Intensive Care Unit in University Comprehensive Specialized Hospitals of SNNPR Ethiopia, 2022

Variables	Characteristics	Frequency	Percent
Maternal age in years	<35 years	347	83.4
	≥35 years	69	16.6
Antenatal follow up	No	61	14.7
	Irregular	66	15.9
	Regular	289	69.4
Mode of Delivery	Spontaneous vaginal delivery	249	59.9
	Caesarean section	108	25.9
	Assisted delivery	59	14.2

(*Continued*)

Table 2 (Continued).

| Variables	Characteristics	Frequency	Percent
Place of delivery	Home	24	5.8
	Health institution	392	94.2
Premature rupture of membrane	Yes	71	17.1
	No	345	82.9
Duration of labor	Normal	318	76.4
	Prolonged	98	23.6
Maternal intrapartum fever	Yes	66	15.9
	No	350	84.1
Gestational age	<37 weeks	176	42.3
	≥37 weeks	240	57.7
Birth weight	<2.5kgs	164	39.4
	≥2.5kgs	252	60.6
1st minute Apgar score	<7	138	33.2
	≥7	278	66.8
5th minute Apgar score	<7	60	14.4
	≥7	356	85.6
ABO incompatibility	Yes	147	35.3
	No	269	64.7
Rh incompatibility	Yes	55	14.7
	No	361	85.3
Neonatal sepsis	Yes	260	62.5
	No	156	37.5
Birth Injury	Yes	92	22.1
	No	324	77.9
Total serum bilirubin	<20mg/dl	272	65.4
	≥20 mg/dl	144	34.6
Perinatal asphyxia	Yes	60	14.4
	No	356	85.6
Infant Feeding	Breast milk feeding	168	40.4
	Bottle feeding	44	10.6
	Mixed feeding	90	21.6
	Parenteral feeding	114	27.4

Treatment and Outcome

In the current study, 316 (76%) neonates were treated with phototherapy, and 100 (24%) neonates needed exchange transfusions. In addition to phototherapy and exchange transfusions, 30 (7.2%) neonates were treated with phenobarbitone.

Overall, 91.3% (95% CI: 88.2%, 93.7%) neonates were discharged home with improvement, and 8.7%, (95% CI CI: 6%, 12%) were dead (Figure 1).

Factors Associated with Treatment Outcome of Jaundice

In bi-variable analysis, residence, origin of admission, length of hospital stay, gestational age, birth weight, first minute Apgar score, fifth minute Apgar score, treatment type, and total serum bilirubin level at admission were significantly associated with the treatment outcome of jaundice. In multivariable analysis, residence, origin of admission, gestational age, and total serum bilirubin level at admission were significantly associated with the treatment outcome of neonatal jaundice.

Treatment outcome of jaundice
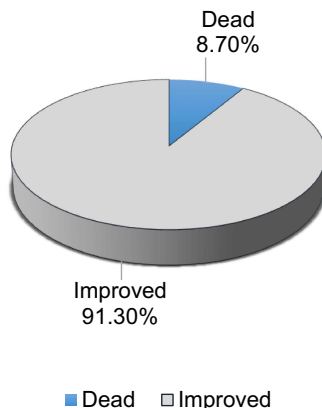
Figure 1 Treatment outcome of jaundice among neonates treated in neonatal intensive care unit of university comprehensive and specialized hospitals of SNNPR, Ethiopia 2022.

In terms of residence, neonates who came from rural areas were 64% (AOR = 0.36, 95% CI: 0.2, 0.8) less likely to improve than their urban counterparts. Meanwhile, neonates who were admitted from outside (out born) were almost 65% (OR = 0.35, 95% CI: 0.2, 0.8) less likely to improve as compared to those who were born inside.

Compared to treatment outcome in terms of gestational age, babies who were born <37 weeks of gestation were 74% (AOR = 0.26, 95% CI: 0.1, 0.8) less likely to improve than those who were born ≥37 weeks of gestation, keeping other variables constant. When compared to neonates with a TSB level of <20 mg/dl at admission, those with a TSB level of ≥20 mg/dl were 60% (AOR = 0.4, 95% CI: 0.2, 0.9) less likely to improve (Table 3).

Table 3 Factors Associated with the Treatment Outcome of Jaundice Among Neonates Treated in Neonatal Intensive Care Unit in Two University Comprehensive Specialized Hospitals of SNNPR Ethiopia, April 2022

Variables	Treatment Outcome		COR(95% CI)	AOR(95% CI)	p-value
	Improved	Dead			
Residence					
Urban	209	10	1.00	1.00	1.00
Rural	171	26	0.32 (0.2, 0.7)*	0.36 (0.2, 0.8)	0.01
Origin of admission					
In born	264	16	1.00	1.00	1.00
Out born	116	20	0.35 (0.2, 0.7)*	0.35 (0.2, 0.8)	0.00
Length of stay					
<7 days	184	22	1.00	1.00	1.00
≥7 days	196	14	1.7 (0.8, 3.3)	0.56 (0.3, 1.2)	0.15
Rh incompatibility					
No	334	27	1.00	1.00	1.00
Yes	46	9	0.3 (0.2, 0.7)*	0.50 (0.2, 1.3)	0.16
Gestational age					
≥37 weeks	232	8	1.00	1.00	1.00
<37 weeks	148	28	0.2 (0.1, 0.4)*	0.26 (0.1, 0.8)	0.01
Birth weight					
≥2.5Kgs	240	12	1.00	1.00	1.00
<2.5Kgs	140	24	0.3 (0.1, 0.6)*	0.73 (0.3, 1.9)	0.53
1st Apgar score					
≥7	263	15	1.00	1.00	1.00
<7	117	21	0.31 (0.2, 0.6)*	0.99 (0.4, 2.6)	0.98

(Continued)

Table 3 (Continued).

Variables	Treatment Outcome		COR(95% CI)	AOR(95% CI)	p-value
	Improved	Dead			
5th Apgar score					
≥7	333	23	1.00	1.00	1.00
<7	47	13	0.25 (0.1, 0.5)*	0.53 (0.2, 1.4)	0.20
Total serum bilirubin					
<20	260	12	1.00	1.00	1.00
≥20	120	24	0.23 (0.1, 0.5)*	0.40 (0.2, 0.9)	0.02
Treatments type					
Phototherapy only	297	19	1.00	1.00	1.00
EBT and PT	59	11	0.34 (0.2, 0.7)*	0.63 (0.2, 1.7)	0.36
EBT, PT and Phenobarbital.	24	6	0.25 (0.1, 0.7)*	0.68 (0.2, 1.7)	0.27

Note: *Significant association.

Discussion

This study aimed to identify the magnitude and factors associated with the treatment outcome of neonatal jaundice. Treatment outcomes were assessed in terms of improvement and mortality in the hospital.

Overall, 91.3% (95% CI: 88.2%, 93.7%) of neonates treated for jaundice were discharged home with improvement. This finding was in line with studies conducted in Bangladesh,[29] north India,[26] and Nigeria[30] that revealed that 91.7%, 91.7%, and 91% of neonates were discharged home with improvement, respectively.

The treatment outcome of the current study was higher than studies conducted in western Nepal,[25] South-east Nigeria[31] and Benin City[32] which revealed 86.2%, 83.3%, and 78.6% of neonates admitted to NICU were discharged home with improvement, respectively. The possible reason might be the variation in the definition of treatment outcome in the study. In the previous studies neonates discharged against medical orders were included under those who were not improved, which accounted for a large proportion in study. In the current study, those who left the hospital against a medical order were excluded because treatment outcome was not well determined for those who left the hospital without completing treatment.

In addition, as compared with the previous study conducted in western Nepal,[25] neonates in the current study were admitted earlier, on the 2nd day of median postnatal age. But in the previous study conducted in western Nepal, the neonates were admitted on the 6th day of postnatal age. Early admission and treatment are important for good outcomes in every case. So in the current study, earlier admission might have helped to have a comparatively good outcome as compared to a study conducted in western Nepal.

In the current study, the number of neonates discharged home with improvement was lower as compared with reports in Baghdad,[33] Egypt,[34] India,[35] and south-west Iran.[27] In studies conducted in those countries, 99.3%, 99.6%, 96%, and 99.6% of neonates were discharged home with improvement, respectively. This difference might be due to the differences in standards of the neonatal intensive care unit in the setting and the difference in management protocols for neonatal jaundice.

In the current study setting, advanced diagnostic tools and treatments, such as advanced phototherapy units and other standard neonatal care equipment's are less consolidated[36] as compared to those study setting. So, standards of diagnostic tools and treatment might affect treatment outcomes in the neonatal intensive care unit.

Also, the number of neonates discharged home with improvement was lower as compared with outcomes reported in south-west Nigeria[37] and Uganda,[38] which revealed 96% and 97% of neonates discharged home with improvement, respectively. The possible reason might be due to a difference in the selection of study participants. In the previous studies, all cases of jaundice, regardless of severity, were selected, whereas in the current study, mild cases that were not candidates for phototherapy were not included in the study participants.

Among factors, residence was significantly associated with the treatment outcome of neonatal jaundice. Neonates who came from rural areas were 64% (AOR = 0.36, 95% CI: 0.2, 0.8) less likely to improve as compared to their urban

counterparts. This finding was consistent with a study conducted in western Nepal.[25] The possible reason might be that rural mothers have less knowledge of neonatal jaundice, its danger signs, consequences, and treatment modalities, so they might not seek care immediately when the condition occurs.[39] In general, rural mothers have lower health-seeking behavior[40,41] and have less access to appropriate health institutions and transportation nearby to seek care early so that neonates might be admitted and treated late.

In regard to origin of admission, out-born neonates (who were born in other health facilities and referred to this site) were 65% (AOR = 0.35, 95% CI: 0.2, 0.8) less likely to improve as compared to neonates born inside the hospital. This finding was consistent with studies conducted in South East Nigeria,[42] Western Nepal,[43] and Benin City.[32] This might be due to out-born babies presented with severe illness and a higher total serum bilirubin level than in-born babies. They were also presented later than inborn babies because they might be referred from a longer distance, so jaundice was detected later after it reached a severe stage. But in-born babies were diagnosed and treated earlier due to the available equipment and health professionals in those hospitals, so that they were less severely ill and eventually more likely to improve.

In the case of gestational age, neonates with a gestational age of <37 weeks were 74% (AOR = 0.26, 95% CI: 0.1, 0.8) less likely to improve as compared to those with a gestational age of ≥37 completed weeks. A study conducted on the outcome of phototherapy among neonates treated for jaundice in India[44] and a similar study on the efficacy of intensive phototherapy in the treatment of hyperbilirubinemia conducted in Egypt[45] supports this finding, where premature babies were less responsive to treatment and less likely to improve than mature babies. And other studies conducted in south eastern Nigeria and Benin City[32] revealed decreased improvement of neonates who had sepsis and prematurity.

This may be due to the fact that preterm neonates are prone to severe neurotoxicity of free bilirubin due to an immature blood-brain barrier and the liver as compared to mature neonates.[46,47] For that reason, they have a decreased response to treatment and are less likely to improve than mature neonates. They are also prone to different phototherapy[48] and exchange transfusion related complication,[49] such as electrolyte imbalance, thrombocytopenia, dehydration, and even death, which further influence the treatment outcome of jaundice.

In the case of TSB level at admission, neonates with TSB level ≥20mg/dl were 60% (AOR = 0.40, 95% CI: 0.2, 0.9) less likely to improve as compared to neonates with TSB level <20mg/dl. This finding was consistent with studies conducted in China.[50] The possible reason might be due to the fact that unconjugated bilirubin is neurotoxic at a high level that can lead to ABE and eventually death.[51]

Limitation

Since this study was built upon secondary data, some important variables, such as family income and the educational level of mothers, were not included in the study.

The long-term outcome was not considered in the current study.

This finding might not be representative for neonates treated in lower level health facilities, such as general and primary hospitals.

Conclusion and Recommendation

This study aimed to assess the treatment outcome of jaundice and its associated factors among neonates treated in the neonatal intensive care unit. Improvement upon treatment is still low because if neonates are admitted and treated early, jaundice will have good improvement. So, health professionals and other stakeholders need to emphasize improving the treatment outcome of neonatal jaundice. Special care needs to be given to low-gestational-age babies with jaundice. Priority needs to be given to those babies who come from rural areas and who have elevated serum bilirubin levels.

Abbreviations

AAP, American Academy of Pediatrics; ABE, Acute Bilirubin Encephalopathy; AOR, Adjusted Odds Ratio; BSc, Bachelor of Science; COR, Crude Odds Ratio; EBT, Exchange Blood Transfusion; G6PD, Glucose-6-Phosphate Dehydrogenase; IQR, Interquartile Range; LED, Light Emitting Diode; LMICs, Low and Middle Income Countries; MSc, Master of Science; NICE, National Institute for Health and Care Excellence; NICU, Neonatal Intensive Care

Unit; PCHN, Pediatrics and Child Health Nursing; PDA, Patent Ductus Arteriosus; P.O, Post Office; PT, Phototherapy; SD, Standard Deviation; SNJ, Severe Neonatal Jaundice; SNNPR, Southern Nations Nationalities and Peoples Region; TcB, Transcutaneous Bilirubin; TSB, Total serum Bilirubin; UK, United Kingdom; WCUSH, Wachamo University Comprehensive Specialized Hospital; WSUCSH, Wolaita Sodo University Comprehensive Specialized Hospital.

Data Sharing Statement
Data that supports the study's findings is available upon reasonable request of the corresponding author.

Ethical Consideration and Patient Privacy
The study was carried out after getting ethical clearance from the ethical clearance committee of the school of nursing on behalf of the Ethical Review Board of the University of Gondar (PCHN/720). After reviewing the ethical clearance, the chief clinical director of each hospital ordered to contact with the NICU head. Data collection began after getting permission from the neonatal intensive care unit head.

By removing names and other identifiers from the data extraction tool, patients' information was kept private. So this work complied with the Declaration of the Helsinki.

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Disclosure
The authors report no conflicts of interest in this work.

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