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Time to recovery and its predictors among neonates undergone phototherapy at Comprehensive Specialized hospitals of the Northwest Ethiopia

Gezahagn Demsu Gedefaw[1✉], Abere Gebru Abuhay[2], Dawit Tesfaye Daka[3], Wubet Tazeb Wondie[4], Almaz Tefera Gonete[5], Fekadeselassie Belege Getaneh[6], Yaregal Semanew Endeshaw[6], Astewil Moges Bazezew[7], Bruck Tesfaye Legesse[3], Degalem Tilahun Worku[8], Mulugeta Endalamaw Ayenew[8] & Asnake Tadesse Abate[9]

Phototherapy is the preferred treatment for neonatal hyperbilirubinemia and has largely replaced exchange transfusions due to its effectiveness and safety. The primary aim of this study was to evaluate the time to recovery and its predictors among neonates undergoing phototherapy at the Neonatal Intensive Care Unit of the Northwest Comprehensive Specialized Hospital in Northwest Ethiopia. A multi-center institution-based retrospective follow-up study was conducted among 423 neonates admitted to the neonatal intensive care unit between September 2019 and December 2023, at Comprehensive Specialized Hospitals of Northwest Ethiopia. Simple random sampling techniques were used to select neonates. Data were entered into the EPI Data version 4.6.0.2 and exported to STATA 14 statistical software for analysis. The Kaplan–Meier failure curve was used to estimate the time to recovery from phototherapy. During follow-up, statistical differences between variables were compared using the log-rank test. After testing the goodness of fit of the final model, multi-variable Cox proportional hazard regression was used to identify predictors of recovery time from phototherapy. Variables with a p-value less than 0.05 were considered statistically significant. In total 423 neonates were included in this study. Of these, 68.79% (n = 291) achieved successful clinical recovery, with a median survival time of 4 days. Predictors affecting recovery time were Rh-setup (AHR: 0.63; 95% CI: (0.45–0.86) sepsis (AHR: 0.55; 95% CI: (0.33–0.91), ABO-setup (AHR: 0.59; 95%CI: (0.46–0.79), sex (AHR: 0.70; 95% CI (0.55–0.91), and inadequate feeding (AHR: 0.56; 95% CI: (0.33–0.92) which delayed recovery time. In the current study, the median time to recovery after phototherapy was prolonged compared to as a clinical recommendation. Rh setup, ABO setup, sepsis, poor feeding, and male sex were all predictive factors of delayed recovery time.

Keywords Jaundice, Time to recover, Neonate, Phototherapy, Predictors

[1]Department of Neonatal Health Nursing, School of Nursing, College of Medicine and Health Sciences, and Specialized Hospital, University of Gondar, Gondar, Ethiopia. [2]Department of Pediatrics and Child Health Nursing, College of Health Sciences, Debre Tabor University, Debre Tabor, Ethiopia. [3]Departments of Pediatric and Neonatal Nursing, School of Nursing and Midwifery, Institute of Health Science,, Wollega University, Nekemte, Ethiopia. [4]Department of Pediatrics and Child Health Nursing, College of Medicine and Health Sciences and Referral Hospital, Ambo University, Ambo, Ethiopia. [5]Department of Pediatrics and Child Health Nursing, School of Nursing, College of Medicine and Health Sciences, and Specialized Hospital, University of Gondar, Gondar, Ethiopia. [6]Department of Pediatric and Neonatal Nursing, School of Nursing and Midwifery, College of Medicine and Health Science, Wollo University, Dessie, Ethiopia. [7]Department of Surgical Nursing, School of Nursing, College of Medicine and Health Sciences, and Specialized Hospital, University of Gondar, Gondar, Ethiopia. [8]Department of Pediatrics and Child Health School of Medicine, College of Medicine and Health Sciences, University of Gondar, Gondar, Ethiopia. [9]Department of Pediatrics and Neonatal Health Nursing, College of Health and Medical Science, School of Nursing, Haremiya University, Harar, Ethiopia. ✉email: gezahagndemsu68@gmail.com

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Neonatal jaundice (NNJ) is common in neonatal period due to the physiological imbalance between increased bilirubin load and slower excretion[1,2]. Over 60% of newborns develop, a condition characterized by yellowish discoloration of the skin and conjunctiva from elevated serum bilirubin levels during the first week of life[3].

Phototherapy (PT) is the first-line treatment for jaundice leading to a very rare need for exchange transfusion[2]. All infant should be seen by a healthcare professional within 2–3 days post-discharge, regardless of total serum bilirubin levels or risk factors for severe hyperbilirubinemia[4].

Various factors contribute to neonatal jaundice, including G6PD deficiency, ABO blood group incompatibility, Rh blood group incompatibility, urinary tract infections, sepsis, cephalohematoma, polycythemia, and Crigler-Najjar syndrome[5,6].

The prevalence of neonatal jaundice is 60% of the full-term neonates and 80% of the pre-term newborns present with jaundice during the first 3 days of life severe neonatal jaundice is as high as 667.8 per 10,000 live births in Africa, but as low as 3.7 per 10,000 live births in Europe[7].

Factors for neonates after delivery many factors contribute to hyperbilirubinemia low birth weight, birth asphyxia, cephalohematoma, Rhesus (RH) incompatibility, and neonatal sepsis predictors for neonatal jaundice[8,9].

Healthcare facilities may lack the necessary equipment, expertise, or protocols for effective phototherapy administration and ineffective use can impact neonate recovery time. Inadequate treatment techniques, such as insufficient dose, treatment duration, or inconsistent monitoring, may lead to persistent jaundice and delayed healing, resulting in higher morbidity and potentially influencing long-term outcomes.

Addressing these gaps through targeted training initiatives can enhance the understanding and application of phototherapy techniques, leading to more effective treatments and shorter recovery times. Establishing systems for ongoing evaluation and feedback can help identify and rectify issues that contribute to ineffective phototherapy practices.

A multicenter study gather data from various health facilities located at different altitudes, allowing researchers to capture a diverse range of information on patient demographics, healthcare practices, and altitude-related environmental factors. By including multiple sites in the investigations, we able to obtain a large sample, thereby enhancing statistical power and improving the generalizability of the findings. Multicenter studies facilitate comparisons and evaluations of healthcare institutions with differing capacities and resources. Altitude significantly impact patient's health and outcomes. By conducting a multicenter study focused on both facility and altitude, researches can explore of altitude-related factors, such as hypoxia, climatic conditions, and geographical challenges, and their effect on patient care and recovery.

This study promotes knowledge exchange, sharing of best practices, and collaborative problem-solving, which in turn enhances the quality of research and fosters a culture of continuous improvement in healthcare delivery. The findings can inform healthcare policies, guidelines, and protocols tailored to different altitudes types of facilities, leading to the development of customized interventions, resource allocation strategies, and quality improvement initiatives aimed at optimizing patient care and outcomes.

However, our study identified a lack of evidence regarding the time to recovery and its predictors in neonates undergoing phototherapy. Therefore, this study specifically assessed the time to recovery and its predictors among neonates undergoing phototherapy admitted to the neonatal intensive care unit of northwest comprehensive specialized hospital, in Northwest Ethiopia in 2023.

Methods and materials
Study design, period and study area
This multi-center, institution-based retrospective follow-up study was conducted from September 2019 to December 2023 at the Northwest Amhara Region Comprehensive Specialized Hospitals in Northwest Ethiopia. Data were retrospectively extracted from January 1, 2024, to January 15, 2024.

The study took place in the Northwest Amhara region, which has five Comprehensive Specialized Hospitals (CSHs): Gondar, Tibebe Ghion, Felegehiwot, Debre Markos, and Debre Tabor. Each hospital is located at a distance from Addis Ababa: UoGCSH (727 km), Tibebe Ghion CSH (552 km), and Debre Tabor CSH (645 km). However, only three out of the five CSHs were selected for the study. While the number of neonatal admissions for jaundice varies among hospitals, the UoGCSH, TGCSH, and DTCSH reported 550, 480, and 380 admissions per half year, respectively. These hospitals serve as the ultimate referral option for other health facilities in the Northwest Amhara region. Each hospital has Neonatal Intensive Care Units (NICUs) staffed with neonatal and comprehensive nurses, general practitioners, pediatricians, and pediatric residents. Major services provided in the NICUs include general neonatal care, blood and exchange transfusions, phototherapy, and ventilation support such as continuous positive airway pressure.

Population of the study
Source population and study population
All neonates were admitted with jaundice to the NICU in the northwest Amhara Region comprehensive specialized hospitals were the source population. All neonates admitted with jaundice to the NICU in northwest Amhara Region comprehensive specialized hospitals between September 2019 and December 2023 were the study population.

Inclusion and exclusion criteria
The study included jaundiced neonates admitted to specialized hospitals' NICUs during the study period. However, neonates with cholestasis, those with a conjugated bilirubin level exceeding 15%, and those transferred from primary and general hospitals seeking exchange transfusion for jaundice management were not included in the study.

Sample size determination

The minimum required sample size was calculated using a single population proportion formula. by considering the following statistical assumptions, P = Proportion of time to recover among neonates admitted with jaundice 50%. $z_{a/2}$ = the corresponding Z score of 95% CI, and d margin of error (5%).

$$n = ((Z(a/2)2 * P * (1-P)))/d2 \quad n = ((1.96)2 * 0.5(1-0.5)))/((0.05)2) = 384$$

After adding a 10% non-response rate, a total of 423 participants were included in the study.

Sampling technique and procedure

This study was conducted in three specialized hospitals in the Northwest Amhara region. The average baseline data on neonate admissions over one year were collected from each hospital to consider the available data. The sample size for each hospital was determined based on the average number of newborn admissions each month. Although the neonatal admission numbers for jaundice vary by institution, the UoGCSH, TGCSH, and DTCSH reported 550, 480, and 380 admissions every half-year, respectively, from September 2019 to December 2023. The final sample size was 423, with each hospital receiving a proportional allocation. A sampling frame was created by collecting data from the registration books on the number of patients admitted. After identifying patients who met the inclusion criteria, study subjects were selected using a simple random sampling technique with lottery methods.

Variables of the study

Dependent variable

Time to recover from phototherapy.

Independent variables

Socio-demographic factors: Residence, maternal age, sex, Religion, Marital status, Occupation, and Educational status **Maternal medical factors** and **obstetric factors**: ANC follow-up, gravidity, parity, current of pregnancy, place of delivery, mode of delivery, and Rh.

Neonatal factors: birth weight and gestational age, perinatal asphyxia, time to breastfeeding, sepsis, polycythemia, MAS, jaundice, birth injury, medication, hypoglycemia, Incompatibility, ABO incompatibility, and blood group.

Operational definitions

Incomplete chart: Those charts do not provide clear information regarding medical diagnoses, admission or diagnostic timing, discharge details, or the duration of phototherapy.

Censored: Neonates who did not experience the desired outcome (time to recovery) by the end of the follow-up period, exchange transfusion done, were lost to follow-up, or were discharged against medical advice.

Time to recovery: The interval between the neonate starting phototherapy and his or her cessation of phototherapy while the neonate was recovering from phototherapy.

Follow-up time: the time between the start of phototherapy and the event of occurrence or censoring.

Failure status: If the outcome of the jaundice neonate is either death or censored.

Intensive phototherapy: The American Academy of Pediatrics defines it as a spectral irradiance of at least 30 W cm2 nm1 in the 430 to 490 nm wavelength range[10].

Data collection tool and procedures

The data collection tool was adapted by reviewing different relevant literature[11–13] on the problem under study including all possible variables that address the objectives of the study, and it contains Two-parts. Part One: maternal socio-demographic and Obstetric characteristics. Part Two: neonatal socio-demography and characteristics. Data were collected by reviewing a neonate's medical chart using a pre-tested checklist.

Neonates diagnosed with jaundice and admitted to the NICU were first identified. The required number of neonate medical charts and nurses were selected from the cases using a simple random sampling method. Finally, data were retrospectively collected by three experienced BSc nurses and supervised by one experienced MSc neonatal nurse.

Data quality control

The data quality was ensured by developing appropriate data abstraction tools. The data collection instrument was pretested on 5% of the sample size. To maintain the validity of the tool, its content was reviewed by senior pediatric and child health specialist nurses and MSc neonatal health nursing. Both data collectors and supervisors were neonatal nurses trained in Bsc and MSc respectively, on the data collection checklist and the data collection process. Supervisors and investigators performed strict monitoring and supervision during data collection.

Data processing and analysis

The data were cleaned for inconsistencies and missing values then the amendment was considered before analysis and then the data were entered into Epi-data 4.6.0.2 software. It was subsequently transformed into the statistical program STATA 14. Descriptive statistics (mean with standard deviation, median with interquartile range, frequency & percentage) were computed depending on the nature of the variables. Each participant was dichotomized into censored and event. The incidence density rate was calculated for the entire study period. Kaplan Meir was used to estimating median/ failure time and cumulative probability of failure and KM plots with log-rank tests were used to compare failure function curves between groups. Before performing the Cox-

proportional hazard regression, the model goodness-of-fit was checked by using the Schoenfeld residual test and the Cox-Snell residual.

Multicollinearity was also checked by using variance inflation factors. For each predictor variable, bi-variable Cox proportional Hazard regression was performed and the variable with p-vale < 0.25 was included in multivariable Cox proportional hazard regression. Adjusted hazard ratio with a 95% confidence interval and p-value < 0.05 were used to identify statistical significance. Finally, the result was presented in texts, graphs, figures, and tables.

Ethical approval and consent to participate

Ethical approval was obtained from the Institutional Review Board (IRB) of the School of Nursing, College of Medicine and Health Science, University of Gondar (Ref.no. SN/036/2015 E.C). In addition, due to the retrospective nature of the study, informed consent is waived by this Institutional Review Board (IRB). The information that was taken from medical records was kept private, though. Every procedure followed the appropriate norms and regulations as well as the Helsinki Declaration. This is also confirmed by the institutional review board. The patient names were replaced with the identification number to preserve anonymity. Additionally, all retrieved data were kept private.

Results
Socio-demographic and characteristics of mothers

A total of 423 jaundice neonate-mothers pairs were included in the study with a response rate of 100% of them met the inclusion criteria. In this study, approximately three-fourths of the mothers, 314, were age group 21–34 years old with a mean of 28.66 ± 6.32 SD years old. 337 (79.67%) of the total enrolled mothers had given birth via spontaneous vaginal delivery, and one-fourth of the 103 (24.35%) mothers had RH setups. The majority of mothers (n = 379, or 95.71%) in our study got ANC follow-ups at nearby health institutions (Table 1).

Neonatal socio-demography and Neonatal comorbidities

In this study, more than three-fourths of the neonates were admitted to the hospital for less than three days (80.38%), and more than half of the neonates had a normal birth weight of 228 (53.90%) and a median weight of 2800 g (IQR 1500). In addition, the majority of newborns (87.47%) were fed early. In this study, almost half of the neonates (n = 239, 56.50%) developed sepsis, ABO incompatibility (n = 147 (34.75), and (n = 121 (28.61); other comorbidities were disseminate intravascular coagulation (DIC), necrotizing enterocolites (NEC), polycythemia, early feeding, Cephalohematoma, and subgleal hemorrhage (Table 2).

The overall outcome of the neonate under phototherapy

In this follow-up study, from 423 neonates under phototherapy, 291 (68.79%) had recovered, 69 (16.31%) had exchanged transfusions, 52 (12.29%) left against, and 11 (2.60%) died (Fig. 1).

Time to recovery

291 (68.79%) of the 423 neonates admitted for jaundice experienced the event of interest (recovery), with an overall incidence rate of 20.65 per 100 person-days of observation (95% CI = 18.41–23.16).

Covariates	Category	Total Number (%)	Status Event	Status Censored
Age of the mother	< 20	50 (11.82)	30 (60.0)	20 (40.0)
	20–34	314 (74.23)	220 (70.06)	94 (29.94)
	> 35	59 (13.95)	41 (69.49)	18 (30.51)
Parity	Primi-para	182 (43.03)	129 (70.88)	53 (29.12)
	Multi para 182 241	241 (56.97)	162 (67.22)	79 (32.78)
Gravidity	Primi-garvida	190 (44.92)	130 (68.42)	60 (31.58)
	Multi gravida	233 (55.08)	161 (69.10)	72 (30.90)
Maternal RH negative	Yes	108 (25.53)	52 (48.15)	56 (51.85)
	No	315 (74.47)	239 (75.87)	76 (24.13)
ANC	Yes 379 17	397 (93.85)	23 (92.0)	2 (8.0)[a]
	No	26 (6.15)	267 (67.25)	130 (32.75)
Mode of delivery	SVD[a]	346 (81.80)	247 (71.39)	99 (28.61)
	C/S[a]	77 (18.20)	44 (57.14)	33 (42.86)

Table 1. Socio-demographic and obstetric characteristics of mothers at NICU in Northwest Amhara, Ethiopia, 2023. [a]ANC, Antenatal Care; SVD, spontaneous Vaginal Delivery; C/S, cesarean Section.

Variables	Category	Percent	Status	
			Event	Censored
Age of the neonate	< 3 days	322 (76.12)	216 (67.08)	106 (32.92)
	> 3 days	101 (23.88)	75 (74.26)	26 (25.74)
Sex	Male	273 (64.54)	179 (65.57)	94 (34.43)
	Female	150 (35.46)	112 (74.67)	38 (25.33)
GA	Term	227 (53.66)	159 (70.04)	68 (29.96)
	Preterm	173 (40.90)	114 (65.90)	59 (34.10)
	Post-term	23 (5.44)	18 (78.26)	5 (21.74)
Birth weight	NBW[a]	228 (53.90)	156 (68.42)	72 (31.58)
	LBW[a]	174 (41.13)	118 (67.82)	56 (32.18)
	Macrosomic	21 (4.96)	17 (80.95)	4 (19.05)
Sepsis	Yes	241 (56.97)	140 (58.09)	101 (41.91)
	No	182 (43.03)	151 (82.97)	31 (17.03)
NEC[a]	Yes	91 (21.51)	50 (54.95)	41 (45.05)
	No	332 (78.49)	241 (72.59)	91 (27.41)
MAS[a]	Yes	91 (21.51)	49 (53.85)	42 (46.15)
	No	332 (78.49)	242 (72.89)	90 (27.11)
PNA[a]	Yes	87 (20.57)	47 (54.02)	40 (45.98)
	No	336 (79.43)	244 (72.62)	92 (27.38)
Polycythemia	Yes	65 (15.37)	34 (52.31)	31 (47.69)
	No	358 (84.63)	257 (71.79)	101 (28.21)
DIC[a]	Yes	118 (27.90)	80 (67.80)	38 (32.20)
	No	305 (72.10)	211 (69.18)	94 (30.82)
Subgleal hemorrhage	Yes	28 (6.62)	15 (53.57)	13 (46.43)
	No	395 (93.38)	276 (69.87)	119 (30.13)
Cephalohematoma	Yes	42 (9.93)	24 (57.14)	18 (42.86)
	No	381 (90.07)	267 (70.08)	114 (29.92)
Breastfeed jaundice	Yes	66 (15.60)	39 (59.09)	27 (40.91)
	No	357 (84.40)	252 (70.59)	105 (29.41)
Early feeding	Yes	188 (44.44)	151 (80.32)	37 (19.68)
	No	235 (55.56)	140 (59.57)	95 (40.43)
ABO	Yes	147 (34.75)	88 (59.86)	59 (40.14)
	No	276 (65.25)	203 (73.55)	73 (26.45)

Table 2. Neonatal socio-demography and Characteristics who were admitted at NICU in Northwest Amhara, Ethiopia, 2023. [a]GA, gestational age; MAS, meconium aspiration syndrome; DIC, disseminated intravascular coagulation; PNA, perinatal asphyxia; NBW, normal birth weight; LBW, low birth weight; CHR, crude hazard ratio; AHR, adjusted hazard ratio.

Proportional hazard assumption
The Schoenfeld residual hazard assumption test for each independent variable and the overall global test were performed. The P-value of each independent variable was > 0.05, while the overall global test p-value was 0.1124.

Time to recovery of neonates with phototherapy admitted to NICU
The overall median time to recovery for neonates in the study was 4 days, which gave a total of 1409 neonatal days of observation. The minimum and maximum discharge dates of the neonate, respectively (Fig. 2).

Overall survival function
The overall Kaplan–Meier survival function revealed that the likelihood of newborns getting phototherapy and recovering faster rose during the follow-up period. The cumulative probabilities of recovery at the end of the first, second, and fourth days were 0.16, 0.75, 0.37, and 0.08, respectively. On the first day after admission, the probability of recovery wasn't observed (Table 3).

Log rank test result comparison on different categorical variables
In the bi-variable cox-Snell regression, Gender, MAS, Rh set up, polycythemia, DIC, Birth weight, sepsis, ABO, breast feeding jaundice, PNA, NEC, feeding, Gravida and, subgleal hemorrhage were associated with time to recovery among neonates under phototherapy (p-value < 0.25). However, in the multi-variable Cox-Snell regression analysis, only five variables were significant predictors of time to recovery among neonates under phototherapy (P-value < 0.05). This study revealed that neonates whose mothers had a history of Rh sensitization,
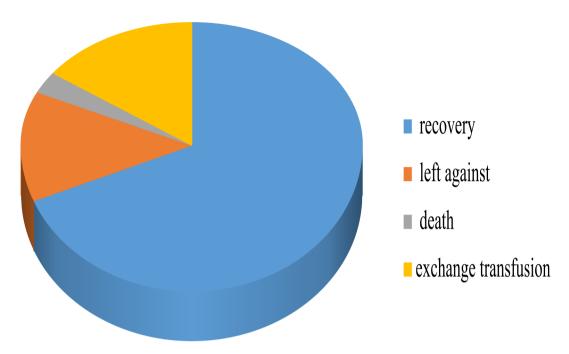
Fig. 1. Overall neonatal out-come among neonates admitted in Amhara region comprehensive and specialized hospitals.
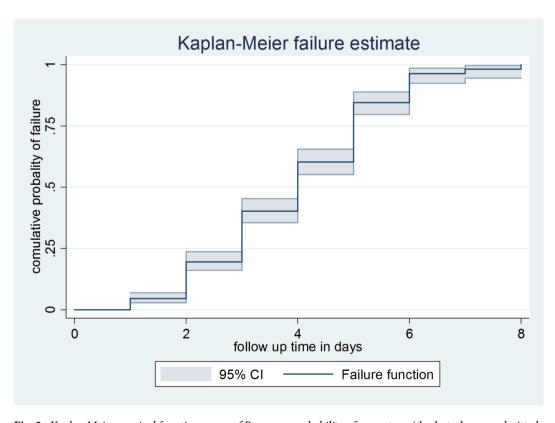

Fig. 2. Kaplan Meier survival function curve of Recovery probability of neonates with phototherapy admitted to NICU at the comprehensive specialized hospital from August 2023 to January 2024 (n = 423).

Time intervals	Person-in time	Recoveries	Rates	95CI%
0–1	423	19	0.05	0.03–0.07
1–2	394	62	0.16	0.12–0.20
2–3	295	76	0.26	0.21- 0.32
3–4	185	62	0.34	0.26- 0.43
>4	112	72	0.64	0.51–0.81
	1409	291	0.21	0.18- 0.23

Table 3. The cumulative probabilities of recovery time neonates undergoing phototherapy.
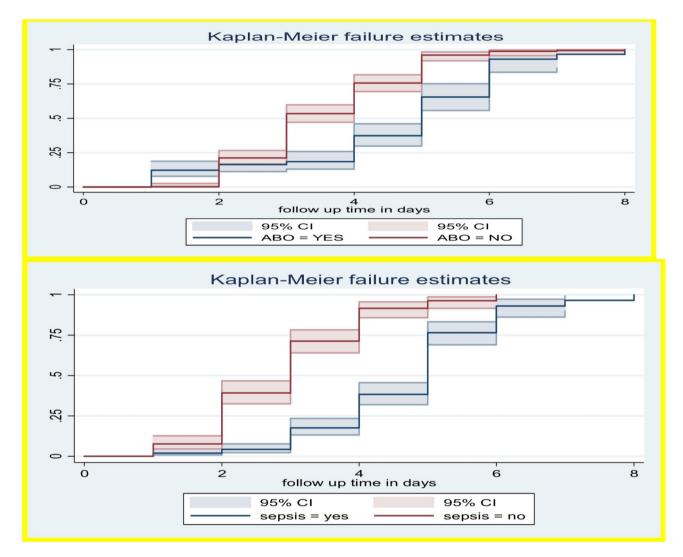
Fig. 3. Kaplan Meier survival function of the independent variable for time to recovery from neonates under phototherapy from August 2023 to January 2024 (N = 423).

ABO incompatibility, sepsis, sex and inadequate breastfeeding with a p-value of 0.05, these differences were statistically significant (Fig. 3).

The goodness of fit test
The goodness of fit for the fitted model was also performed using the Cox-Snell residual test and the model was adequate (Fig. 4).

Predictors of time to recovery neonates on phototherapy
In newborns born to mothers with Rh sensitization, the recovery was delayed by 37% compared to those born to mothers without Rh sensitization (AHR: 0.63; 95% CI: (0.45–0.86)). The analysis revealed that phototherapy
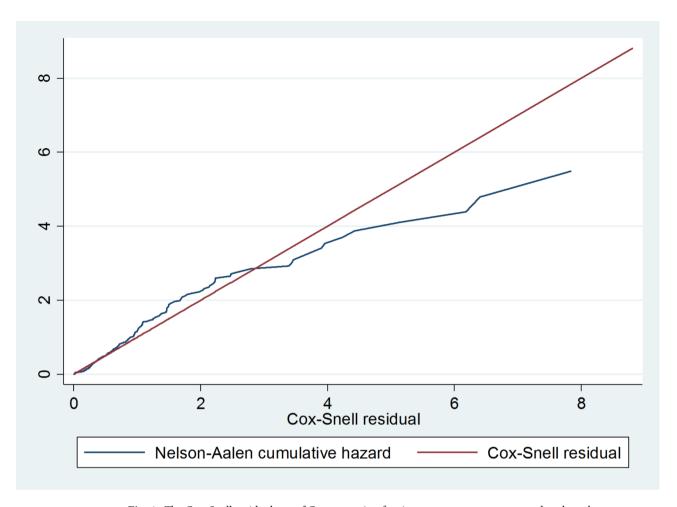
Fig. 4. The Cox-Snell residual test of Cox regression for time to recovery neonates under phototherapy.

recovery was affected by sepsis which delayed recovery by 45% compared to neonates who did not have sepsis (AHR: 0.55; 95% CI: (0.33–0.91)). Neonates born to mothers with ABO incompatibilities were 41% more likely to have delayed recovery from phototherapy than newborns who did not have ABO incompatibilities (AHR: 0.59; 95CI: (0.46–0.79). the nutritional status of neonates was analyzed. Neonates who received inadequate nutrition were 44% more likely to experience delayed recovery time after phototherapy compared to those neonates with adequate nutrition (AHR: 0.56; 95% CI: (0.33–0 92). Newborns male sex were 30% more likely to have delayed recovery from phototherapy than newborns who were female (AHR: 0.70; 95% CI (0 0.55–0 0.91) (Table 4).

Discussion

Of the 423 newborns admitted for phototherapy, 291 (68.79%) showed recovery, with an incidence rate of 20.65 per 100 person-days of observation (95% CI = 18.41–23.16).Overall median time to recovery was 4 days, totaling of 1409 neonatal days of observation. The minimum and maximum discharge dates of the neonate, respectively. The Kaplan–Meier survival function indicating that the chance of recovery for newborns receiving phototherapy increased over the follow-up period. The median recovery time was high because, in neonates with concomitant diseases or medical conditions, the intensity or duration of phototherapy was inadequate[10,14]. It may not efficiently reduce bilirubin levels, the existence of comorbidities, preterm, nutritional state, or the neonate's overall health condition[6,15,16].

In newborns born to mothers who had Rh sensitization, the recovery was 37% side compared to those born to mothers without Rh sensitization. This finding was supported by a study conducted in Ethiopia[17–20], India[21], Macedonia[22], and Turkey[23]. The possible reason for Rh incompatibility is that the mother's immune system may produce antibodies against the Rh antigen present in the neonate's blood. These antibodies can cross the placenta and attack the baby's red blood cells, leading to a condition called hemolytic disease of the newborn (HDN). HDN can cause increased breakdown of red blood cells, leading to bilirubin accumulation and jaundice in neonates. Recovery time for a neonate with Rh incompatibility undergoing phototherapy depends on several factors, including the severity of jaundice. In severe Rh-induced hemolytic disease, jaundice may be more pronounced, and recovery time may be prolonged.

Neonates born to mothers with ABO incompatibilities were 41% more likely to have delayed recovery from phototherapy than newborns without ABO incompatibilities. This finding was supported by a study conducted in Ethiopia[17,19,24], Iran[25,26], India[21,27], and Macedonia[22]. The possible justification for ABO incompatibilities

Variables	CHR(95%CI)	p-value	AHR (95%CI)	P-value
Gender				
Female	1		1	
Male	0.82 (0.65 1.044)	0.109	0.70(0.55—0 .91)	0.007
MAS				
Yes	1.21 (0.88 1.64)	0.235	1.01 (0.54 -1.88)	0.97
No	1		1	
RH—set up				
Yes	0.20 (0.52 .944)	0.020	0.63(0.45—0.86)	0.004
No	1		1	
Sepsis				
Yes	0.299 (0.23 0 .38)	0.020	0.55 (0.33 -0.91)	0.02
No	1		1	
Polycythemia				
Yes	0.79 (.56 1.14)	0.209	0.92 (0.64 -1.32)	0.66
No	1		1	
DIC				
Yes	0.84 (0.65 1.09)	0.193	0.81 (0.63 -1.06)	0.139
No	1		1	
NEC				
Yes	0.83 (0.61 1.12)	0.222	0.81 (0.43 -1.54)	0.52
No	1		1	
ABO set-up				
Yes	0.47 (0.36 0 .61)	0.000	0.59 (0.46 -0.79)	0.000
No	1		1	
PNA				
Yes	0 .82 (0.61 1.13)	0.233	0.88 (0.54 -1.43)	0.61
No	1		1	
Birth weight				
NBW	1	1		
LBW	0.84 (0.66 1.071)	0.162	0.95 (0.75 -1.25)	0.83
Macrosomic	1.43 (0.87 2.36)	0.163	1.33(0.69 -1.97)	0.55
Feeding				
Adequate	1	1	1	
Inadequate	0.30 (0.24 0 .39)	0.000	0.56 (0.33–0 .92)	0.023
Breastfeed jaundice				
Yes	0.75 (0.53 1.05)	0.097	0.85 (0.62 -1.27)	0.519
No	1	1	1	
Gravida				
Primi	0.83 (0.66 1.04)	0.114	0.89 (0.69 -1.44)	0.253
Multi	1	1	1	
Subgleal hemorrhage				
Yes	0.69 (0.41 1.15)	0.160	0.87(0.50 -1.49)	0.614
No	1		1	

Table 4. Bi-variable and multivariable Cox regression analysis for predictors of time to recovery neonates under phototherapy in Northwest Ethiopia Comprehensive Specialised Hospitals from August 2023 to January 2024 (n = 423). [a]MAS, meconium aspiration syndrome; DIC, disseminated intravascular coagulation; PNA, perinatal asphyxia; NBW, normal birth weight; LBW, low birth weight; CHR, crude hazard ratio; AHR, adjusted hazard ratio.

between the mother and neonate is the an increased risk of neonatal jaundice. However, ABO incompatibility does not necessarily affect the recovery time of neonates undergoing phototherapy; nonetheless, it can contribute to higher risk of developing significant jaundice in neonates[28,29].

Holding other variables constant, sepsis delayed recovery time 45% more than those who did not have sepsis. This finding was supported by a study conducted in Ethiopia[17,19], The possible reason neonates with sepsis may experience prolonged recovery time under phototherapy is due to several factors. Sepsis is a serious infection that can affect multiple organs, including the liver. When sepsis occurs, it can disrupt liver function, leading to

impaired bilirubin metabolism and clearance. However, the effectiveness of phototherapy in reducing bilirubin levels may be compromised in neonates with sepsis. Recovery time can vary depending on the severity of sepsis, effectiveness of the infection treatment, and the neonate's overall response to therapy[28,30].

Neonates who received inadequate nutrition were 44% more likely to have delayed recovery time after phototherapy than neonates with adequate nutrition. The possible reasons for Neonates who are adequately fed and receive appropriate nutrition generally have a better chance of recovering more efficiently under phototherapy. When a neonate is well-nourished and adequately hydrated, it can support liver function and optimize bilirubin metabolism. This, in turn, may enhance clearance of bilirubin from the bloodstream, leading to a potentially shorter recovery time. Breast milk is particularly beneficial for neonates due to its nutritional composition and immune-protective properties[31,32]. However, while adequate feeding can support the recovery process, it is just one aspect to consider in the overall management of neonatal jaundice.

Newborn male sex was 32% more likely to have delayed recovery from phototherapy than newborn sex with females. This study was supported by Debre markos[29], in Ethiopia[30]. The possible justification for this could be due to male newborn's undeveloped livers, which may not be able to process all of the bilirubin developed from red blood cells in a normal state. Male neonates often have higher hemoglobin levels at birth compared to females, leading to an increased breakdown of red blood cells, or hemolysis. In contrast, female neonates may benefit from maternal estrogen, which aids in the breakdown and excretion of bilirubin more effectively[1,29,30].

Limitation and strength

The study may provide valuable insights into the specific population of neonates receiving phototherapy in the NICU setting, which can help inform clinical practice and interventions. The findings of the study may have direct implications for optimizing the management of neonates undergoing phototherapy and improving outcomes in the NICU. Hospital service and health professionals were not assessed.

Conclusion

In the current study, the median time to recovery under phototherapy was prolonged compared to clinical recommendation according to American academy of pediatrician[33]. Rh setup, ABO setup, sepsis, poor feeding, and male sex were all predictive factors of delayed recovery time.

Data availability

The datasets generated and/or analyzed during the current study are not publicly available due to confidentiality but are available from the corresponding author on reasonable request.

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Declarations

Competing interests
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Additional information
Correspondence and requests for materials should be addressed to G.D.G.

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