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Original Article

Neonatal Jaundice: Frequency of Rh-Incompatibility Among Neonates with Jaundice and Role Intensive Phototherapy in Reducing the Need for Exchange Transfusion in HDN

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ABSTRACT

Background: Neonatal jaundice is common during early life, but pathological hyperbilirubinemia associated with Rh incompatibility may progress rapidly and increase the need for intensive treatment. Intensive phototherapy may accelerate bilirubin reduction and reduce exchange transfusion requirement compared with conventional phototherapy. Objective: To determine the frequency of Rh incompatibility among term neonates with pathological jaundice and compare bilirubin decline, phototherapy duration, and exchange transfusion requirement between intensive and conventional phototherapy. Methods: This retrospective comparative cohort study included 350 term neonates with pathological jaundice at a tertiary care hospital in Lahore, Pakistan. The intensive phototherapy group included 175 neonates admitted from January 2024 to March 2026, while 175 historical controls admitted in 2015 received conventional phototherapy. Demographic, maternal, laboratory, and treatment outcomes were analyzed using chi-square, t-test, Mann–Whitney U test, and repeated-measures analysis where applicable. Results: Rh incompatibility was identified in 17/175 neonates (9.7%) in the intensive phototherapy cohort. Rh-incompatible neonates had higher median total serum bilirubin than Rh-compatible neonates, 23.21 versus 18.87 mg/dL ($p<0.001$). Exchange transfusion was required in 5/175 neonates receiving intensive phototherapy and 39/175 receiving conventional phototherapy, corresponding to 2.9% versus 22.3% ($p<0.001$). Intensive phototherapy also produced greater reported bilirubin decrement and shorter treatment duration. Conclusion: Rh incompatibility remained an important marker of bilirubin severity, while intensive phototherapy was associated with improved bilirubin control and reduced exchange transfusion requirement. Keywords: Neonatal jaundice; Rh incompatibility; hyperbilirubinemia; intensive phototherapy; exchange transfusion; hemolytic disease of the newborn.

INTRODUCTION

Neonatal jaundice is among the most common clinical conditions encountered during the early neonatal period and is characterized by yellow discoloration of the skin, sclera, and mucous membranes due to elevated serum bilirubin concentration. Although most neonatal jaundice is physiological, transient, and self-limiting, jaundice that appears within the first 24 hours of life, progresses rapidly, reaches treatment thresholds, or occurs in association with hemolysis is considered pathological and requires prompt clinical evaluation. The distinction between physiological and pathological jaundice is clinically important because severe unconjugated hyperbilirubinemia may progress to acute bilirubin

encephalopathy and kernicterus, resulting in long-term neurological sequelae such as hearing impairment, cerebral palsy, developmental delay, and permanent neurodisability (1, 2).

The pathophysiology of neonatal hyperbilirubinemia reflects the balance between bilirubin production, hepatic conjugation, and bilirubin elimination. Newborns are particularly vulnerable because of increased erythrocyte turnover, immature hepatic glucuronidation, and enhanced enterohepatic circulation during early postnatal life. Unconjugated bilirubin is transported in plasma bound to albumin and is subsequently conjugated in the liver before biliary excretion. In physiological jaundice, bilirubin levels usually rise after the first day of life and decline without invasive intervention, whereas pathological jaundice is more frequently associated with hemolysis, infection, enzyme deficiency, prematurity, or blood group incompatibility. Hemolytic disease of the newborn remains one of the most important causes of severe unconjugated hyperbilirubinemia, particularly when maternal antibodies target fetal erythrocytes and accelerate bilirubin production (3-5).

Rh incompatibility is a clinically important form of hemolytic disease of the newborn that occurs when an Rh-negative mother carries an Rh-positive fetus and develops anti-D immunoglobulin G antibodies capable of crossing the placenta. These antibodies bind fetal red blood cells and may cause immune-mediated hemolysis, anemia, reticulocytosis, and rapid postnatal bilirubin elevation. Although anti-D immunoglobulin prophylaxis has substantially reduced the burden of Rh-mediated hemolytic disease in many settings, Rh incompatibility remains relevant in developing healthcare systems because of delayed antenatal booking, inconsistent screening, incomplete prophylaxis, missed postpartum prophylaxis, previous alloimmunization, and variable access to specialized neonatal care (6-9).

The reported frequency of Rh incompatibility among jaundiced neonates varies across hospital-based studies, reflecting differences in maternal Rh-negative prevalence, case definitions, referral patterns, prophylaxis coverage, and neonatal admission thresholds. This variation is clinically meaningful because Rh-incompatible neonates may develop higher bilirubin levels, present earlier in life, require more frequent monitoring, and carry a greater risk of severe hyperbilirubinemia than neonates with non-hemolytic jaundice. In settings where standardized bilirubin surveillance and timely escalation of treatment are not uniformly available, local data on Rh incompatibility are necessary to guide risk stratification and early treatment decisions (10-17).

Phototherapy is the standard first-line treatment for significant unconjugated neonatal hyperbilirubinemia because light exposure converts bilirubin into water-soluble photoisomers that can be excreted without hepatic conjugation. Conventional phototherapy is widely used; however, intensive phototherapy is designed to provide greater irradiance and wider body-surface exposure, thereby producing a faster decline in total serum bilirubin. This effect is particularly relevant in neonates at risk of bilirubin neurotoxicity, including those with hemolytic jaundice. When phototherapy fails to adequately reduce bilirubin or when bilirubin reaches critical treatment thresholds, exchange transfusion may be required, but this procedure is invasive and associated with important risks, including hemodynamic instability, electrolyte imbalance, infection, thrombocytopenia, and procedure-related morbidity (18-23).

Despite the established role of phototherapy, there remains a need for locally applicable evidence on whether intensive phototherapy reduces bilirubin burden, treatment duration, and exchange transfusion requirement compared with conventional phototherapy among term neonates with pathological jaundice. This question is especially important in tertiary neonatal units where resource constraints, late presentation, and hemolytic jaundice may increase the likelihood of severe hyperbilirubinemia. The present study was therefore conducted to determine the frequency of Rh incompatibility among term neonates admitted with pathological jaundice and to compare bilirubin decline, duration of phototherapy, and exchange transfusion requirement between neonates treated with intensive phototherapy and historical controls treated with conventional phototherapy. The study hypothesized that Rh incompatibility would be associated with higher total serum bilirubin levels and that intensive

phototherapy would achieve greater bilirubin reduction with shorter treatment duration and fewer exchange transfusions than conventional phototherapy.

MATERIAL AND METHODS

This retrospective comparative cohort study was conducted in the Department of Pediatrics at a tertiary care hospital in Lahore, Pakistan. The study was designed to evaluate two related clinical questions: the frequency of Rh incompatibility among term neonates admitted with pathological jaundice and the comparative effectiveness of intensive phototherapy versus conventional phototherapy in reducing total serum bilirubin, duration of phototherapy, and exchange transfusion requirement. The study included two treatment cohorts selected from different time periods. Neonates admitted from January 2024 to March 2026 and managed with intensive phototherapy were included in the intensive phototherapy group, whereas neonates admitted from January to December 2015 and managed with conventional phototherapy were included as historical controls. The historical comparison was used to assess treatment outcomes before and after the use of intensive phototherapy in the same clinical context, while applying the same core eligibility criteria across both cohorts.

The study population comprised 350 term neonates with pathological jaundice who required phototherapy, including 175 neonates in the intensive phototherapy group and 175 neonates in the conventional phototherapy group. Term neonates of either sex were eligible if they had gestational age greater than 37 completed weeks, clinical jaundice, and serum bilirubin levels requiring phototherapy according to the unit's treatment practice. Neonates were excluded if they were premature, had gestational age less than 37 weeks, had congenital abnormalities, hypothyroidism, or direct hyperbilirubinemia. Pathological jaundice was considered in neonates with clinically significant hyperbilirubinemia requiring phototherapy, particularly when jaundice was early, progressive, or associated with laboratory evidence suggesting hemolysis. Rh incompatibility was operationally defined as maternal-neonatal Rh discordance consistent with risk of hemolytic disease of the newborn, specifically an Rh-negative mother with an Rh-positive neonate, assessed using recorded maternal Rh status, neonatal blood group and Rh type, and relevant hematological or immunohematological findings available in the medical record.

Eligible records were identified from hospital documentation for the specified study periods. Data were extracted using a predesigned structured data collection form to ensure uniform capture of demographic, clinical, maternal, laboratory, and treatment-related variables. Neonatal variables included sex, gestational age, birth weight, mode of delivery, age at admission, onset of jaundice, neonatal blood group, Rh status, baseline total serum bilirubin, hemoglobin, hematocrit, white blood cell count, platelet count, reticulocyte count, direct Coombs test status when documented, intravenous immunoglobulin therapy when documented, duration of phototherapy, and exchange transfusion requirement. Maternal variables included age, blood group, Rh status, history of anti-D administration, and history of miscarriage or stillbirth. Total serum bilirubin was recorded at admission and after initiation of phototherapy at the documented follow-up time points, including 6 hours and 12 hours, with continued treatment duration recorded according to clinical course up to 24, 36, or 48 hours where applicable.

Phototherapy exposure was classified according to treatment modality during the relevant study period. Neonates in the intensive phototherapy group received intensive phototherapy with maximum feasible skin exposure, while wearing only diapers and eye protection; interruptions were limited to feeding, nursing care, and blood sampling. Neonates in the conventional phototherapy group received conventional phototherapy according to the unit practice during the historical control period. The main comparative exposure was treatment group, categorized as intensive phototherapy or conventional phototherapy. The principal outcomes were absolute and percentage reduction in total serum bilirubin after initiation of phototherapy, total duration of phototherapy, and requirement for exchange transfusion. The secondary analytic exposure was Rh-incompatibility status, and its association was

assessed with neonatal demographic characteristics, maternal characteristics, and laboratory parameters.

Several steps were incorporated to strengthen internal validity and reduce bias. The same gestational age threshold and exclusion criteria were applied to both treatment cohorts to improve comparability. Data were collected using a structured extraction form, and variables were coded using uniform operational definitions before analysis. Baseline characteristics were compared between intensive and conventional phototherapy groups to identify potential imbalance. Because the control group was historical, interpretation of comparative treatment effects considered possible temporal confounding due to changes in neonatal admission practices, bilirubin monitoring, treatment thresholds, documentation quality, and supportive care between the two study periods. Clinically relevant baseline variables, including gestational age, birth weight, sex, age at admission, onset of jaundice, baseline total serum bilirubin, hemoglobin, hematocrit, reticulocyte count, white blood cell count, platelet count, maternal Rh status, and anti-D history, were considered during interpretation of treatment outcomes. Records with missing values for individual variables were analyzed using available-case analysis for that specific variable, and denominators were reported clearly for each analysis.

The total sample size was 350 neonates, with equal allocation of 175 neonates in each treatment group. The sample size was calculated using a 95% confidence level and 5% margin of error through a web-based EPI sample size calculator, and equal group sizes were maintained to support comparative analysis of bilirubin reduction, treatment duration, and exchange transfusion requirement. Data were entered and analyzed using the Statistical Package for Social Sciences. Continuous variables were assessed for distribution and summarized as mean with standard deviation for normally distributed variables or median with interquartile range for non-normally distributed variables. Categorical variables were summarized as frequencies and percentages. The chi-square test was used for comparison of categorical variables, Student's t-test was used for normally distributed continuous variables, and the Mann–Whitney U test was used for non-normally distributed continuous variables. Repeated bilirubin measurements were analyzed using repeated-measures analysis of variance to assess the effect of time, treatment group, and time-by-group change in total serum bilirubin after initiation of phototherapy. Two-sided p-values were used, and a p-value less than 0.05 was considered statistically significant.

Ethical approval for the study was obtained from the relevant hospital administration before data extraction. The study was conducted according to institutional ethical standards, and confidentiality of neonatal and maternal information was maintained throughout data collection, analysis, and reporting. Data were extracted and analyzed in aggregate form without disclosure of personal identifiers. The dataset was used solely for research purposes. Data integrity was supported through structured data extraction, verification of group allocation, checking of denominators, comparison of table values against statistical output, and consistency review of all reported frequencies, percentages, medians, means, p-values, and outcome definitions before final manuscript preparation.

RESULTS

A total of 350 term neonates with pathological jaundice were included in the study, comprising 175 neonates in the intensive phototherapy group and 175 neonates in the conventional phototherapy group. The overall cohort included 197 male neonates and 153 female neonates, representing 56.3% and 43.7% of the sample, respectively. The median gestational age was 38 weeks, with an interquartile range of 38–40 weeks, and the median birth weight was 2950 g, with an interquartile range of 2700–3400 g. Cesarean delivery was recorded in 179 neonates, accounting for 51.1% of the cohort, while 171 neonates, representing 48.9%, were delivered vaginally. The baseline descriptive characteristics of the study cohort are presented in Table 1.

Rh incompatibility was assessed in the intensive phototherapy cohort of 175 neonates. Overall, 17 neonates were Rh-incompatible, giving a frequency of 9.7%, while 158 neonates, representing 90.3%,

were Rh-compatible. Male neonates accounted for 10 of 17 Rh-incompatible cases and 85 of 158 Rh-compatible cases, with no statistically significant association between neonatal sex and Rh incompatibility. Gestational age category, mode of delivery, birth weight category, and neonatal blood group also showed no statistically significant association with Rh incompatibility. However, day of admission differed significantly between Rh-incompatible and Rh-compatible neonates. All Rh-incompatible neonates were admitted within the first two days of life, whereas Rh-compatible neonates were admitted between day 1 and day 4, producing a statistically significant association between earlier admission and Rh-incompatibility status (p=0.023). The association between Rh incompatibility and neonatal characteristics is shown in Table 2.

Table 1. Baseline Demographic Characteristics of Neonates Included in the Study

Characteristic	Total Cohort (N=350)
Male sex, n (%)	197 (56.3)
Female sex, n (%)	153 (43.7)
Vaginal delivery, n (%)	171 (48.9)
Cesarean delivery, n (%)	179 (51.1)
Birth weight, median (IQR), g	2950 (2700–3400)
Gestational age, median (IQR), weeks	38 (38–40)

Table 2. Association of Rh Incompatibility With Neonatal Characteristics in the Intensive Phototherapy Group

Characteristic	Total (N=175), n (%)	Rh-Incompatible (n=17), n (%)	Rh-Compatible (n=158), n (%)	p-value
Sex				0.693
Male	95 (54.3)	10 (58.8)	85 (53.8)	
Female	80 (45.7)	7 (41.2)	73 (46.2)	
Gestational age				0.110
37–39 weeks	148 (84.6)	12 (70.6)	136 (86.1)	
40–42 weeks	27 (15.4)	5 (29.4)	22 (13.9)	
Mode of delivery				0.170
Vaginal	79 (45.1)	5 (29.4)	74 (46.8)	
Cesarean	96 (54.9)	12 (70.6)	84 (53.2)	
Birth weight				0.211
2.5–3.0 kg	103 (58.9)	13 (76.5)	90 (57.0)	
>3.0 kg	72 (41.1)	4 (23.5)	68 (43.0)	
Day of admission				0.023
Day 1	85 (48.6)	9 (52.9)	76 (48.1)	
Day 2	52 (29.7)	8 (47.1)	44 (27.8)	
Day 3	37 (21.1)	0 (0.0)	37 (23.4)	
Day 4	1 (0.6)	0 (0.0)	1 (0.6)	
Neonatal blood group				0.603
A	32 (18.3)	4 (23.5)	28 (17.7)	
B	55 (31.4)	6 (35.3)	49 (31.0)	
AB	12 (6.9)	2 (11.8)	10 (6.3)	
O	76 (43.4)	5 (29.4)	71 (44.9)	

Maternal Rh status showed the strongest association with neonatal Rh incompatibility. Among 175 mothers in the intensive phototherapy cohort, 24 were Rh-negative and 151 were Rh-positive. All 17 Rh-incompatible neonates were born to Rh-negative mothers, whereas only 7 of 158 Rh-compatible neonates were born to Rh-negative mothers. This produced a highly significant association between maternal Rh-negative status and neonatal Rh incompatibility ($p<0.001$). Anti-D administration was also significantly associated with Rh-incompatibility status, being recorded in 10 of 17 mothers of Rh-incompatible neonates compared with 5 of 158 mothers of Rh-compatible neonates ($p<0.001$). Maternal age group, maternal ABO blood group, and history of miscarriage or stillbirth were not significantly associated with neonatal Rh incompatibility. These findings are presented in Table 3.

Laboratory comparison demonstrated that Rh-incompatible neonates had significantly higher total serum bilirubin levels than Rh-compatible neonates. The median total serum bilirubin level was 23.21 mg/dL in Rh-incompatible neonates compared with 18.87 mg/dL in Rh-compatible neonates, with a

statistically significant difference between groups (p<0.001). Hemoglobin, hematocrit, and reticulocyte count did not differ significantly between Rh-incompatible and Rh-compatible neonates. Although the median reticulocyte count was numerically higher in Rh-incompatible neonates, 12.1% compared with 9.8% in Rh-compatible neonates, this difference did not reach statistical significance (p=0.133). The laboratory profile according to Rh-incompatibility status is shown in Table 4.

Table 3. Association of Rh Incompatibility With Maternal Characteristics in the Intensive Phototherapy Group

Maternal Characteristic	Total (N=175), n (%)	Rh-Incompatible Neonate (n=17), n (%)	Rh-Compatible Neonate (n=158), n (%)	p-value
Maternal age				0.324
20–30 years	104 (59.4)	12 (70.6)	92 (58.2)	
31–40 years	71 (40.6)	5 (29.4)	66 (41.8)	
Maternal blood group				0.439
A	31 (17.7)	5 (29.4)	26 (16.5)	
B	57 (32.6)	6 (35.3)	51 (32.3)	
AB	18 (10.3)	2 (11.8)	16 (10.1)	
O	69 (39.4)	4 (23.5)	65 (41.1)	
Maternal Rh status				<0.001
Rh-positive	151 (86.3)	0 (0.0)	151 (95.6)	
Rh-negative	24 (13.7)	17 (100.0)	7 (4.4)	
History of Anti-D administration	15 (8.6)	10 (58.8)	5 (3.2)	<0.001
History of miscarriage or stillbirth	65 (37.1)	8 (47.1)	57 (36.1)	0.373

Table 4. Association of Rh Incompatibility With Laboratory Parameters in the Intensive Phototherapy Group

Laboratory Parameter	Total Median (IQR)	Rh-Incompatible Median (IQR)	Rh-Compatible Median (IQR)	p-value
Total serum bilirubin, mg/dL	18.87 (17.54–21.65)	23.21 (21.39–24.12)	18.87 (17.92–21.65)	<0.001
Hemoglobin, g/dL	13.9 (12.9–16.7)	14.4 (12.45–16.95)	13.8 (12.87–16.70)	0.892
Hematocrit, %	43.7 (35.67–48.9)	44.7 (38.34–51.3)	43.16 (35.62–48.66)	0.606
Reticulocyte count, %	9.8 (6.09–14.2)	12.1 (6.9–17.65)	9.8 (5.94–13.95)	0.133

The intensive and conventional phototherapy groups were then compared to evaluate treatment outcomes. Both groups included 175 neonates. Baseline gestational age, birth weight, onset of jaundice, total serum bilirubin, hemoglobin, hematocrit, platelet count, and reticulocyte count were statistically comparable between groups. Age at admission was statistically different between groups, with both groups having a median admission age of 2 days but different interquartile distributions (p=0.014). White blood cell count was also significantly higher in the intensive phototherapy group, with a median of 15.19 compared with 14.15 in the conventional phototherapy group (p=0.005). These baseline differences should be considered when interpreting treatment comparisons, especially because the conventional phototherapy cohort was historical. Intensive phototherapy was associated with a markedly shorter phototherapy duration and a lower frequency of exchange transfusion. The median phototherapy duration was 1.4 days in the intensive group compared with 5.3 days in the conventional group (p<0.001). Exchange transfusion was required in 5 neonates in the intensive group compared with 39 neonates in the conventional group, corresponding to 2.9% versus 22.3%, respectively (p<0.001). This represented an absolute risk reduction of 19.4 percentage points and a relative risk of 0.13 for exchange transfusion among neonates treated with intensive phototherapy. The comparative treatment outcomes are shown in Table 5.

Bilirubin reduction after initiation of phototherapy was greater in the intensive phototherapy group than in the conventional phototherapy group at each reported post-treatment assessment. After 6 hours of phototherapy, the intensive group showed a total serum bilirubin decline of 3.2 mg/dL, corresponding to a 16.7% reduction, compared with 2.8 mg/dL, corresponding to a 14.5% reduction, in the conventional group (p<0.001). At the later reported assessment interval, bilirubin reduction remained greater in the intensive group, with a decline of 6.1 mg/dL, corresponding to 38.9%, compared with 3.05 mg/dL, corresponding to 18.6%, in the conventional group (p<0.001). The overall reported percentage decrement was also greater with intensive phototherapy than with conventional phototherapy, 48.9% versus 30.4%, respectively (p<0.001). These findings indicate a faster and larger bilirubin decline among neonates

treated with intensive phototherapy, although exact timepoint labelling should be standardized across the final manuscript before submission. The bilirubin-decline outcomes are summarized in Table 6.

Table 5. Comparison of Baseline Clinical Characteristics, Laboratory Parameters, Phototherapy Duration, and Exchange Transfusion Between Treatment Groups

Variable	Intensive Phototherapy Group (N=175)	Conventional Phototherapy Group (N=175)	p-value
Gestational age, median (IQR), weeks	38 (38–39)	38 (37–39)	0.394
Birth weight, median (IQR), kg	3.1 (2.8–3.32)	2.96 (2.9–3.23)	0.334
Onset of jaundice, median (IQR), days	2 (1–3)	2 (2–3)	0.798
Age at admission, median (IQR), days	2 (1–2)	2 (1–2)	0.014
Total serum bilirubin, median (IQR), mg/dL	18.87 (17.54–21.65)	18.87 (17.54–21.98)	0.371
Hemoglobin, median (IQR), g/dL	13.9 (12.9–16.7)	13.67 (12.8–15.8)	0.899
Hematocrit, median (IQR), %	43.76 (35.67–48.94)	42.17 (34.9–47.8)	0.577
Platelet count, median (IQR)	309.0 (232.0–376.0)	309.0 (232.0–377.0)	0.951
White blood cell count, median (IQR)	15.19 (13.04–17.61)	14.15 (11.23–16.23)	0.005
Reticulocyte count, median (IQR), %	9.8 (6.09–14.2)	10.8 (6.80–14.7)	0.314
Duration of phototherapy, median (IQR	1.4 (0.72)	5.3 (1.05)	<0.001
Exchange transfusion, n (%)	5 (2.9)	39 (22.3)	<0.001

Table 6. Reported Bilirubin Decline After Phototherapy Initiation According to Treatment Group

Bilirubin Outcome	Intensive Phototherapy Group	Conventional Phototherapy Group	p-value
TSB decline after 6 hours, mg/dL (%)	3.2 (16.7%)	2.8 (14.5%)	<0.001
Reported later TSB decline, mg/dL (%)	6.1 (38.9%)	3.05 (18.6%)	<0.001
Overall reported bilirubin decrement, %	48.9%	30.4%	<0.001

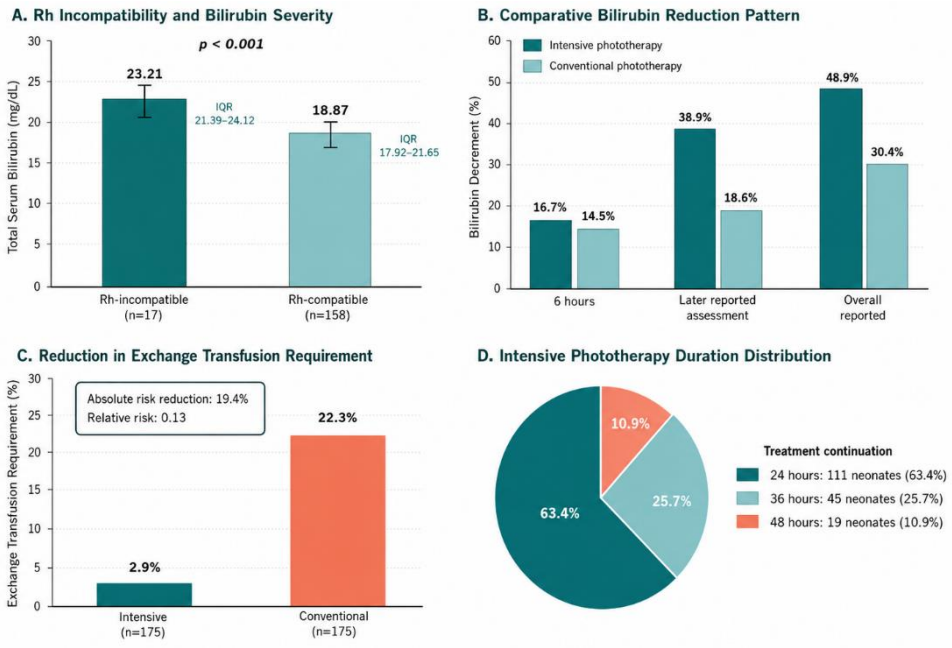

Figure 1 Clinical Response Profile in Term Neonates With Pathological Jaundice.

Rh-incompatible neonates demonstrated a substantially higher median total serum bilirubin level than Rh-compatible neonates, with median values of 23.21 mg/dL and 18.87 mg/dL, respectively (p<0.001). Intensive phototherapy showed consistently greater bilirubin decrement than conventional phototherapy at the reported post-treatment assessments, including 16.7% versus 14.5% after 6 hours, 38.9% versus 18.6% at the later reported assessment, and 48.9% versus 30.4% overall. Exchange transfusion requirement was markedly lower in the intensive phototherapy group than in the conventional phototherapy group, 2.9% versus 22.3%, corresponding to an absolute risk reduction of 19.4 percentage points and a relative risk of 0.13. Within the intensive phototherapy group, most neonates completed treatment by 24 hours, 111/175 (63.4%), while 45/175 (25.7%) and 19/175 (10.9%) required

continuation to 36 and 48 hours, respectively, indicating a clinically meaningful pattern of early bilirubin control with reduced escalation to exchange transfusion.

Among neonates receiving intensive phototherapy, treatment continuation varied according to clinical course. A total of 111 neonates, representing 63.4% of the intensive phototherapy group, continued treatment until 24 hours; 45 neonates, representing 25.7%, continued until 36 hours; and 19 neonates, representing 10.9%, continued until 48 hours. These findings suggest that most neonates treated with intensive phototherapy completed the intensive treatment phase within the first 24 hours, while a smaller proportion required prolonged exposure up to 36 or 48 hours. The distribution of intensive phototherapy duration is presented in Table 7.

Table 7. Duration Pattern Within the Intensive Phototherapy Group

Duration of Intensive Phototherapy	Intensive Phototherapy Group (N=175), n (%)
Continued until 24 hours	111 (63.4)
Continued until 36 hours	45 (25.7)
Continued until 48 hours	19 (10.9)

Overall, the results demonstrate that Rh incompatibility was present in 9.7% of term neonates with pathological jaundice in the intensive phototherapy cohort and was associated with significantly higher total serum bilirubin levels. Intensive phototherapy and conventional phototherapy groups were broadly comparable in most baseline clinical and laboratory parameters, although differences in age-at-admission distribution and white blood cell count were observed. Intensive phototherapy was associated with greater bilirubin decline, substantially shorter phototherapy duration, and a markedly lower requirement for exchange transfusion compared with conventional phototherapy.

DISCUSSION

This retrospective comparative cohort study found that Rh incompatibility was present in 17 of 175 term neonates with pathological jaundice assessed in the intensive phototherapy cohort, corresponding to a frequency of 9.7%. Rh-incompatible neonates had substantially higher total serum bilirubin levels than Rh-compatible neonates, with median values of 23.21 mg/dL and 18.87 mg/dL, respectively, indicating that Rh discordance remained an important marker of bilirubin severity in this neonatal population. Although sex, gestational age category, mode of delivery, birth weight category, and neonatal ABO blood group were not significantly associated with Rh incompatibility, all Rh-incompatible neonates were admitted within the first two days of life, and the association between Rh-incompatibility status and earlier day of admission was statistically significant. This pattern is clinically plausible because immune-mediated hemolysis may produce earlier bilirubin rise and earlier clinical presentation than non-hemolytic causes of jaundice.

The observed frequency of Rh incompatibility is broadly consistent with hospital-based studies from similar clinical contexts, although published estimates vary considerably across regions and study designs. Previous reports have documented Rh incompatibility frequencies ranging from low single-digit values to approximately one-tenth of jaundiced neonatal admissions, with variation likely explained by differences in maternal Rh-negative prevalence, antenatal screening coverage, prophylaxis practices, referral patterns, and criteria used to define pathological jaundice (2, 24-26). In the present study, maternal Rh-negative status showed the strongest association with neonatal Rh incompatibility, as all Rh-incompatible neonates were born to Rh-negative mothers. This finding reinforces the continuing importance of maternal blood grouping, neonatal Rh typing, and structured postnatal bilirubin surveillance, particularly in settings where antenatal prophylaxis pathways may be inconsistently implemented.

The significantly higher bilirubin burden among Rh-incompatible neonates supports the established biological mechanism of Rh-mediated hemolytic disease of the newborn. Maternal anti-D immunoglobulin G antibodies can cross the placenta and bind fetal Rh-positive erythrocytes, leading to

immune hemolysis, increased bilirubin production, and risk of severe unconjugated hyperbilirubinemia after birth (16, 28, 29). In this study, the median reticulocyte count was numerically higher among Rh-incompatible neonates than among Rh-compatible neonates, although the difference was not statistically significant. Hemoglobin and hematocrit were also comparable between groups. These findings suggest that bilirubin elevation may be a more sensitive clinical signal than single admission hemoglobin values in this dataset, but interpretation should remain cautious because direct Coombs test results, antibody titers, timing of hemolysis, and prior intrauterine or early postnatal interventions were not comprehensively analyzed.

Anti-D administration was significantly more frequent among mothers of Rh-incompatible neonates than among mothers of Rh-compatible neonates. This should not be interpreted as evidence that prophylaxis was ineffective, because the available data do not establish timing, dose adequacy, completeness of antenatal and postpartum prophylaxis, maternal sensitization status before prophylaxis, or adherence to recommended protocols. Persistent Rh-related neonatal jaundice despite recorded anti-D exposure may reflect delayed prophylaxis, incomplete documentation, previous alloimmunization, suboptimal dose timing, or prophylaxis given after sensitization had already occurred. Therefore, the finding is best interpreted as a signal that Rh-negative pregnancies require careful documentation of prophylaxis timing and follow-up rather than as proof of prophylaxis failure (13, 15, 16).

The comparative treatment analysis showed that intensive phototherapy was associated with faster bilirubin reduction, shorter phototherapy duration, and lower exchange transfusion requirement than conventional phototherapy. Baseline total serum bilirubin was similar in the two treatment cohorts, with both groups having a median value of 18.87 mg/dL, supporting comparability for the principal biochemical outcome. The reported bilirubin decrement was greater in the intensive phototherapy group than in the conventional phototherapy group after 6 hours, at the later reported assessment, and overall. Clinically, this suggests that intensive phototherapy may provide earlier bilirubin control, which is particularly important for neonates at risk of bilirubin neurotoxicity or escalation to exchange transfusion. These findings are consistent with prior evidence that higher irradiance, greater exposed body surface area, and optimized phototherapy delivery can accelerate bilirubin photoisomerization and clearance (10, 31-34).

The reduction in exchange transfusion requirement is the most clinically important treatment finding. Exchange transfusion was required in 5 of 175 neonates in the intensive phototherapy group compared with 39 of 175 neonates in the conventional phototherapy group, corresponding to 2.9% versus 22.3%. This represents an absolute risk reduction of 19.4 percentage points and a relative risk of 0.13, suggesting a large reduction in escalation to invasive therapy among neonates managed with intensive phototherapy. This finding is clinically relevant because exchange transfusion, although effective, is associated with important procedural risks, including hemodynamic instability, electrolyte imbalance, thrombocytopenia, infection, vascular complications, and procedure-related morbidity (22, 23). By reducing the need for exchange transfusion, intensive phototherapy may reduce procedural risk, improve neonatal safety, decrease treatment burden, and support more efficient use of neonatal unit resources.

The shorter phototherapy duration observed with intensive phototherapy further supports its clinical utility. In the corrected table-based analysis, the reported duration of phototherapy was markedly shorter in the intensive group than in the conventional group, and most neonates receiving intensive phototherapy completed treatment within 24 hours. Shorter treatment duration may reduce hospital stay, mother–infant separation, interruption of feeding, nursing workload, and overall care costs. However, these outcomes were not directly measured in the present study, and therefore should be interpreted as potential clinical implications rather than confirmed study outcomes. Future studies should evaluate hospital stay, feeding outcomes, rebound hyperbilirubinemia, readmission, and cost-effectiveness alongside bilirubin reduction and exchange transfusion frequency.

Several limitations should be considered when interpreting these findings. First, the study used a retrospective design with a historical control group, which introduces potential temporal bias. Changes in neonatal admission thresholds, phototherapy devices, bilirubin monitoring practices, exchange transfusion criteria, supportive care, documentation quality, and clinician decision-making between 2015 and 2024–2026 may have influenced the observed differences. Second, the study was conducted at a single tertiary care hospital, which may limit generalizability to primary or secondary care settings and to regions with different maternal Rh-negative prevalence or neonatal referral patterns. Third, some potentially important confounders were not fully controlled, including feeding pattern, hydration status, weight loss, sepsis evaluation, glucose-6-phosphate dehydrogenase deficiency, direct Coombs test status, antibody titers, IVIG timing, and exact phototherapy irradiance. Fourth, although baseline bilirubin was comparable between treatment groups, age-at-admission distribution and white blood cell count differed significantly, and adjusted modelling was not reported. Finally, the study did not include long-term neurodevelopmental follow-up, rebound bilirubin assessment, or post-discharge outcomes.

Despite these limitations, the study provides clinically useful local evidence that Rh incompatibility remains an important contributor to bilirubin severity among term neonates with pathological jaundice and that intensive phototherapy may reduce bilirubin burden and exchange transfusion requirement compared with conventional phototherapy. The findings support routine maternal and neonatal blood group assessment, early identification of Rh-incompatible neonates, close bilirubin monitoring during the first days of life, and timely use of intensive phototherapy when treatment thresholds are reached. Larger multicenter prospective studies using standardized phototherapy irradiance measurement, uniform exchange transfusion criteria, adjusted statistical modelling, and post-discharge follow-up are needed to confirm these findings and define the most effective treatment pathways for neonates with hemolytic and non-hemolytic hyperbilirubinemia.

CONCLUSION

Rh incompatibility was identified in 9.7% of term neonates with pathological jaundice assessed in the intensive phototherapy cohort and was associated with significantly higher total serum bilirubin levels, supporting its continued clinical importance as a marker of severe neonatal hyperbilirubinemia. Intensive phototherapy was associated with greater bilirubin reduction, shorter treatment duration, and a substantially lower exchange transfusion requirement than conventional phototherapy, with exchange transfusion needed in 2.9% of neonates receiving intensive phototherapy compared with 22.3% of those receiving conventional phototherapy. These findings support early Rh-risk identification, careful bilirubin surveillance, and timely use of intensive phototherapy in term neonates with clinically significant jaundice, while larger prospective studies with standardized treatment thresholds, adjusted analyses, and follow-up outcomes are needed to confirm effectiveness and safety across broader neonatal populations.

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