

Original Article

Prevalence of Pathological Jaundice and Its Associated Risk Factors and Clinical Outcomes at a Tertiary Care Hospital Saidu Group of Teaching Hospital (SGTH) Swat

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ABSTRACT

Background: Pathological neonatal jaundice can progress to clinically significant hyperbilirubinemia and neurological complications, making timely recognition, monitoring, and treatment essential. **Objective:** To determine the hospital-based prevalence of pathological neonatal jaundice and evaluate selected neonatal and maternal factors associated with bilirubin severity among neonates admitted to the neonatal intensive care unit of Saidu Group of Teaching Hospital, Swat. **Methods:** A quantitative cross-sectional study was conducted among 150 neonates with pathological neonatal jaundice identified from 831 NICU admissions during a 30-day period. Demographic, maternal, neonatal, feeding, hematological, and clinical characteristics were recorded. Categorical variables were summarized using frequencies and percentages, and associations with bilirubin severity were assessed using Pearson's chi-square test. **Results:** Pathological neonatal jaundice accounted for 18.1% (150/831) of NICU admissions. Among affected neonates, 92 (61.3%) were male, 33 (22.0%) were preterm, and 44 (29.3%) weighed <2.5 kg. Overall, 46 (30.7%) had mild, 65 (43.3%) moderate, and 39 (26.0%) severe bilirubin levels; 104 (69.3%) therefore had moderate-to-severe hyperbilirubinemia. Birth weight was associated with bilirubin severity ($\chi^2=12.154$, $df=4$, $p=0.016$), although sparse expected frequencies reduced the robustness of the asymptotic test. Gestational age ($p=0.388$), Rh factor ($p=0.753$), and infection status ($p=0.536$) were not significantly associated with bilirubin severity. **Conclusion:** Pathological neonatal jaundice constituted a substantial proportion of NICU admissions. Lower birth weight was accompanied by a greater proportion of severe bilirubin levels, supporting close surveillance of low-birth-weight neonates and early bilirubin assessment to reduce risk of preventable neurological complications. **Keywords:** Neonatal jaundice; pathological neonatal jaundice; hyperbilirubinemia; birth weight; neonates; risk factors; NICU; Pakistan.

INTRODUCTION

Neonatal jaundice is among the most frequently encountered clinical conditions during the first weeks of life and results from accumulation of bilirubin sufficient to produce yellow discoloration of the skin, sclera, and mucous membranes. Transient increases in bilirubin occur in a large proportion of newborns because bilirubin production is relatively high while hepatic uptake, conjugation, and excretion remain physiologically immature. The frequency and clinical relevance of hyperbilirubinemia are influenced by gestational age, postnatal age, feeding, hemolytic conditions, genetic susceptibility, and associated neonatal illness. Although most neonatal jaundice is benign and

resolves without sequelae, a smaller proportion develops clinically significant or pathological hyperbilirubinemia requiring structured assessment and intervention (1,2).

Pathological neonatal jaundice is particularly important because bilirubin concentrations may rise rapidly or reach levels at which unconjugated bilirubin can enter the central nervous system. Established risk factors include prematurity, glucose-6-phosphate dehydrogenase (G6PD) deficiency, ABO or Rh incompatibility, inadequate feeding, birth trauma, infection, and other conditions that increase bilirubin production or reduce bilirubin clearance. A systematic review and meta-analysis identified exclusive breastfeeding, G6PD deficiency, maternal-fetal ABO incompatibility, and preterm birth as significant risk factors for neonatal hyperbilirubinemia, demonstrating that clinically important jaundice usually reflects interaction between neonatal maturity, bilirubin production, feeding, and hemolytic susceptibility rather than a single determinant (3).

Recognition of significant hyperbilirubinemia is clinically important because excessive unconjugated bilirubin can cross the blood-brain barrier and produce acute bilirubin encephalopathy and, in severe untreated cases, chronic bilirubin-induced neurological dysfunction or kernicterus. Contemporary evidence underlying neonatal hyperbilirubinemia management emphasizes risk-stratified assessment according to gestational age, postnatal age, bilirubin concentration, and neurotoxicity risk factors rather than interpretation of bilirubin concentration in isolation (4). A systematic review evaluating later developmental consequences additionally found evidence of auditory, motor, neurological, and developmental abnormalities following clinically important neonatal hyperbilirubinemia, particularly among term infants with substantial bilirubin exposure (5).

The global burden of severe neonatal jaundice remains disproportionately important in low- and middle-income settings, where delayed recognition, limited bilirubin measurement, barriers to follow-up, hemolytic disorders, prematurity, and restricted access to effective treatment may increase the likelihood of progression to severe disease. Hospital-based estimates therefore vary substantially across populations and clinical settings, and tertiary-care estimates cannot be interpreted as equivalent to population incidence. A systematic review and meta-analysis of hospital admissions confirmed a substantial global burden of severe neonatal jaundice and emphasized geographical inequalities in disease severity and access to appropriate neonatal care (6).

Accurate assessment of jaundice is essential because visual examination alone cannot reliably determine the bilirubin concentration or identify all newborns requiring treatment. Total serum bilirubin remains the definitive laboratory measurement used for therapeutic decisions, whereas transcutaneous bilirubin measurement provides a valuable non-invasive screening approach. A Cochrane diagnostic review involving 23 studies and more than 5,000 newborns found high sensitivity for transcutaneous bilirubin measurement across a range of thresholds, supporting its role as a screening tool while emphasizing that positive or clinically important results require serum confirmation (7). A subsequent meta-analysis also demonstrated generally good agreement between transcutaneous and serum bilirubin before phototherapy and when appropriately measured on covered skin during phototherapy, although accuracy after treatment was more variable (8).

Management is determined by bilirubin level, gestational and postnatal age, underlying etiology, and the presence of neurotoxicity risk factors. Phototherapy remains the principal treatment for significant unconjugated hyperbilirubinemia and reduces bilirubin by converting it into photoproducts that can be excreted without hepatic conjugation. Contemporary guideline-based management seeks to prevent neurological injury while avoiding unnecessary treatment, and recent guideline revisions have refined thresholds for bilirubin measurement, phototherapy, escalation of care, and exchange transfusion (4,9). Home phototherapy has been investigated for carefully selected newborns, but a recent systematic review found that the evidence remains limited and heterogeneous, reinforcing the need for careful selection, reliable monitoring, and timely escalation where bilirubin continues to rise (10).

Risk also varies according to population characteristics. A recent European cohort comparing newborns of European and Indian-subcontinent ancestry demonstrated differences in the occurrence and severity of neonatal hyperbilirubinemia, suggesting that genetic, hematological, demographic, and healthcare-related factors may contribute to population-level variation (11). Similarly, a prospective cohort from the Thailand-Myanmar border documented substantial pathological jaundice and identified gestational age, G6PD deficiency, bruising, maternal factors, and prolonged rupture of membranes as clinically relevant predictors, illustrating the importance of locally defined risk profiles in settings with diverse populations and resource constraints (12).

Evidence from Pakistan continues to demonstrate an important burden of neonatal hyperbilirubinemia and its complications. A prospective Pakistani study of neonates with hyperbilirubinemia reported acute bilirubin encephalopathy in 16% and identified prematurity as an important associated factor (13). More recent Pakistani data also highlight the potential contribution of G6PD deficiency. A study conducted at Saidu Group of Teaching Hospitals, Swat, reported G6PD deficiency in approximately 10% of jaundiced neonates, with a marked male predominance (14), while another Pakistani study reported G6PD deficiency among 9% of jaundiced neonates (15). These findings emphasize the importance of population-specific hematological evaluation in neonates with significant jaundice.

Regional studies have additionally demonstrated substantial heterogeneity in the factors associated with neonatal jaundice. Prospective Indian evidence has linked low birth weight and late prematurity with significant jaundice and readmission (16), while a tertiary-care case-control study from Bangladesh identified prematurity, small-for-gestational-age status, maternal factors, and blood-group incompatibility among relevant determinants (17). Genetic and clinical investigations have further implicated G6PD mutations, prematurity, infection, delayed feeding, scalp hematoma, and perinatal asphyxia in the development of neonatal hyperbilirubinemia (18). Together, these findings reinforce the need for locally generated data rather than direct extrapolation of a single risk model to all neonatal populations. Within Khyber Pakhtunkhwa, recent evidence remains comparatively limited despite the presence of substantial neonatal morbidity. A contemporary study among preterm neonates in Dera Ismail Khan found hyperbilirubinemia to be particularly frequent in newborns with lower gestational age and lower birth weight (19). Evidence from other South Asian tertiary units similarly suggests that severe bilirubin elevation may be associated with sepsis and other metabolic or hemolytic abnormalities (20). Such geographical and clinical variation provides a strong rationale for assessing pathological neonatal jaundice specifically within Swat and its tertiary referral population.

Saidu Group of Teaching Hospital (SGTH), Swat, provides neonatal and intensive-care services to newborns from Swat and surrounding areas. However, hospital-specific evidence describing pathological neonatal jaundice, its burden among NICU admissions, associated maternal and neonatal characteristics, and the distribution of bilirubin severity remains limited. Locally generated evidence can help identify characteristics requiring closer surveillance, improve clinical documentation, and inform neonatal assessment within the hospital's service population. Accordingly, the present study aimed to determine the hospital-based prevalence of pathological neonatal jaundice among neonates admitted to the NICU of SGTH, Swat, describe their maternal, demographic, feeding, hematological, and neonatal characteristics, and evaluate the association of selected factors with bilirubin severity. Particular attention was given to birth weight, gestational age, Rh factor, infection status, feeding pattern, G6PD status, mode of delivery, maternal blood group, and previous history of neonatal jaundice.

MATERIALS AND METHODS

A quantitative cross-sectional study was conducted in the neonatal intensive care unit of Saidu Group of Teaching Hospital (SGTH), Swat, Khyber Pakhtunkhwa, Pakistan. Data were collected over a 30-day period. During this period, 831 neonates were admitted to the NICU and constituted the denominator for estimation of the hospital-based prevalence of pathological neonatal jaundice. Among these admissions, 150 neonates were identified with pathological neonatal jaundice and constituted the analytical sample for characterization of maternal, neonatal, hematological, feeding, and clinical variables.

The study population comprised neonates from birth to 28 completed days of age who were admitted to the NICU during the study period. Neonates were eligible when they were aged 0–28 days, were admitted to the NICU, had clinical evidence of pathological neonatal jaundice, and their parent or legal guardian agreed to participation. Infants older than 28 days, neonates admitted without pathological neonatal jaundice, and neonates whose parents or guardians did not consent to participation were excluded. Eligible affected neonates were enrolled using convenience sampling until the analytical sample of 150 neonates was obtained.

Neonatal jaundice was defined clinically as yellow discoloration of the skin, sclera, or mucous membranes associated with increased circulating bilirubin. Pathological neonatal jaundice referred to jaundice with features inconsistent with uncomplicated physiological transition, including early appearance, rapid bilirubin increase, excessive bilirubin concentration, persistence beyond the expected neonatal course, or association with an underlying pathological process. Contemporary neonatal hyperbilirubinemia assessment similarly emphasizes the

relationship between bilirubin concentration, postnatal age, gestational age, and neurotoxicity risk rather than reliance on an isolated bilirubin value (4,9).

Hyperbilirubinemia was operationally understood as a serum bilirubin concentration requiring clinical assessment or treatment according to the neonate's age, gestational maturity, and clinical condition. Bilirubin severity in the study dataset was classified as mild, moderate, or severe and served as the principal categorical outcome in association analyses. Phototherapy refers to therapeutic exposure to an appropriate wavelength of light that converts bilirubin into more readily excretable photoproducts, while exchange transfusion refers to controlled replacement of the neonate's blood with compatible donor blood to rapidly lower bilirubin and remove circulating antibodies or sensitized erythrocytes when clinically indicated (4,9). Following administrative permission from SGTH, information was collected from the mothers or legal guardians of eligible neonates together with available clinical records. Written informed consent was obtained from the parent or legal guardian before participation. Participant information was handled confidentially, and collected data were used for research purposes.

Variables recorded for the analytical sample included neonatal sex, birth weight, gestational age, maternal blood group, Rh factor, mode of delivery, history of jaundice in a previous child, feeding type, G6PD deficiency status, bilirubin severity, and infection status. These variables were selected because prematurity, low birth weight, hemolytic conditions, G6PD deficiency, feeding-related factors, infection, and familial or maternal characteristics have been repeatedly implicated in clinically important neonatal hyperbilirubinemia (3,12,16–20). Birth weight was categorized as <2.5 kg, 2.5–4.0 kg, and >4.0 kg. Gestational age was categorized as preterm, term, or post-term. Feeding was classified as breastfeeding, formula feeding, or mixed feeding. G6PD status was categorized as deficient, not deficient, or unknown. Maternal blood group and Rh-factor information were retained as recorded, including an unknown category where information was unavailable. Mode of delivery was classified as normal vaginal delivery or cesarean section. Bilirubin level was categorized as mild, moderate, or severe.

Data were entered, coded, and analyzed using IBM SPSS Statistics version 27. Categorical variables were summarized using frequencies and percentages. Hospital-based prevalence was calculated by dividing the 150 neonates identified with pathological neonatal jaundice by the total 831 NICU admissions during the study period. Pearson's chi-square test was used to evaluate associations between bilirubin severity and selected categorical variables, including birth weight, gestational age, Rh factor, and infection status. Statistical significance was defined as a two-sided p-value <0.05. The expected-frequency assumptions of Pearson's chi-square test were considered during interpretation. Sparse expected cell counts were present in the analyses involving birth weight, gestational age, and Rh factor; therefore, these asymptotic chi-square findings were interpreted cautiously rather than as definitive evidence in isolation. No participant-level observations, unreported confidence intervals, regression estimates, or reconstructed data were introduced into the analysis.

RESULTS

During the 30-day study period, 831 neonates were admitted to the NICU, of whom 150 were identified with pathological neonatal jaundice. The resulting hospital-based prevalence was 18.1% (150/831). The remaining 681 admissions represented 81.9% of the NICU admission denominator.

Table 1. Hospital-Based Prevalence of Pathological Neonatal Jaundice

Study-period status	n	%
Total NICU admissions	831	100.0
Pathological neonatal jaundice	150	18.1
Other NICU admissions	681	81.9

Among the 150 affected neonates, 92 (61.3%) were male and 58 (38.7%) were female. Birth weight was <2.5 kg in 44 (29.3%), 2.5–4.0 kg in 101 (67.3%), and >4.0 kg in 5 (3.3%). Thirty-three neonates (22.0%) were preterm, 116 (77.3%) were term, and 1 (0.7%) was post-term. The gestational-age frequencies therefore summed consistently to the complete analytical sample of 150.

Maternal blood-group data were available for fewer than half of participants: 26 (17.3%) mothers had group A, 20 (13.3%) group B, 7 (4.7%) group AB, and 20 (13.3%) group O, whereas blood group was unknown for 77 (51.3%). Rh status was positive in 63 (42.0%), negative in 10 (6.7%), and unknown in 77 (51.3%). Normal vaginal delivery occurred in 109 (72.7%) cases and cesarean delivery in 41 (27.3%). A history of jaundice in a previous child was reported by 73

(48.7%) mothers, while 77 (51.3%) reported no such history. Breastfeeding was reported for 76 (50.7%) neonates, formula feeding for 44 (29.3%), and mixed feeding for 30 (20.0%). G6PD deficiency was documented in 4 (2.7%) neonates, absent in 137 (91.3%), and unknown in 9 (6.0%).

Table 2. Demographic, Maternal, Neonatal, and Clinical Characteristics of Affected Neonates (n=150)

Characteristic	Category	n	%
Sex	Male	92	61.3
	Female	58	38.7
Birth weight	<2.5 kg	44	29.3
	2.5–4.0 kg	101	67.3
	>4.0 kg	5	3.3
Gestational age	Preterm	33	22.0
	Term	116	77.3
	Post-term	1	0.7
Maternal blood group	A	26	17.3
	B	20	13.3
	AB	7	4.7
	O	20	13.3
	Unknown	77	51.3
Rh factor	Positive	63	42.0
	Negative	10	6.7
	Unknown	77	51.3
Mode of delivery	Normal vaginal delivery	109	72.7
	Cesarean section	41	27.3
Previous child with jaundice	Yes	73	48.7
	No	77	51.3
Feeding type	Breastfeeding	76	50.7
	Formula feeding	44	29.3
	Mixed feeding	30	20.0
G6PD deficiency	Present	4	2.7
	Absent	137	91.3
	Unknown	9	6.0

Bilirubin severity demonstrated a concentration in the moderate category. Mild bilirubin levels were recorded in 46 (30.7%) neonates, moderate levels in 65 (43.3%), and severe levels in 39 (26.0%). Combining the clinically more pronounced categories, 104 of 150 affected neonates (69.3%) had moderate or severe bilirubin levels.

Table 3. Distribution of Bilirubin Severity (n=150)

Bilirubin severity	n	%
Mild	46	30.7
Moderate	65	43.3
Severe	39	26.0
Total	150	100.0

Birth weight displayed the clearest gradient in bilirubin severity. Among 44 neonates weighing <2.5 kg, 14 (31.8%) had mild, 13 (29.5%) moderate, and 17 (38.6%) severe bilirubin levels. Among 101 neonates weighing 2.5–4.0 kg, 32 (31.7%) had mild, 47 (46.5%) moderate, and 22 (21.8%) severe levels. All five neonates weighing >4.0 kg were in the moderate category. Thus, the proportion with severe bilirubin elevation was approximately 1.8 times as high in the <2.5-kg group as in the 2.5–4.0-kg group (38.6% versus 21.8%).

Table 4. Bilirubin Severity According to Birth Weight

Birth weight	Mild n (%)	Moderate n (%)	Severe n (%)	Total
<2.5 kg	14 (31.8)	13 (29.5)	17 (38.6)	44
2.5–4.0 kg	32 (31.7)	47 (46.5)	22 (21.8)	101
>4.0 kg	0 (0.0)	5 (100.0)	0 (0.0)	5
Total	46	65	39	150

The Pearson chi-square test for birth weight and bilirubin severity yielded $\chi^2=12.154$, $df=4$, and $p=0.016$. However, three cells (33.3%) had expected frequencies below five and the minimum expected frequency was 1.30. The p-value therefore indicates evidence of variation in bilirubin severity across birth-weight groups, but the magnitude of statistical certainty is constrained by sparse cells, particularly the >4.0-kg category. Gestational-age distributions showed that 12 of 33 preterm neonates (36.4%) had mild, 10 (30.3%) moderate, and 11 (33.3%) severe bilirubin levels. Among 116 term neonates, 34 (29.3%) had mild, 54 (46.6%) moderate, and 28 (24.1%) severe levels; the single post-

term neonate was in the moderate category. The proportion of severe bilirubin elevation was numerically greater among preterm than term neonates (33.3% versus 24.1%), but the overall association was not statistically significant ($\chi^2=4.134$, $df=4$, $p=0.388$). Three cells (33.3%) had expected frequencies below five, with a minimum expected count of 0.26.

Rh-positive neonates included 16 (25.4%) with mild, 28 (44.4%) with moderate, and 19 (30.2%) with severe bilirubin levels. Among the 10 Rh-negative neonates, 4 (40.0%) had mild, 4 (40.0%) moderate, and 2 (20.0%) severe levels. Among 77 neonates with unknown Rh status, 26 (33.8%) had mild, 33 (42.9%) moderate, and 18 (23.4%) severe bilirubin levels. Rh factor was not significantly associated with bilirubin severity ($\chi^2=1.905$, $df=4$, $p=0.753$); three cells (33.3%) had expected frequencies below five.

Table 5. Bilirubin Severity According to Gestational Age and Rh Factor

Factor	Category	Mild n (%)	Moderate n (%)	Severe n (%)	Total
Gestational age	Preterm	12 (36.4)	10 (30.3)	11 (33.3)	33
	Term	34 (29.3)	54 (46.6)	28 (24.1)	116
	Post-term	0 (0.0)	1 (100.0)	0 (0.0)	1
Rh factor	Positive	16 (25.4)	28 (44.4)	19 (30.2)	63
	Negative	4 (40.0)	4 (40.0)	2 (20.0)	10
	Unknown	26 (33.8)	33 (42.9)	18 (23.4)	77

Infection was recorded in 10 neonates. Among these, 3 (30.0%) had mild, 3 (30.0%) moderate, and 4 (40.0%) severe bilirubin levels. Among the 140 neonates without documented infection, 43 (30.7%) had mild, 62 (44.3%) moderate, and 35 (25.0%) severe levels. Although severe bilirubin elevation was proportionally more frequent among neonates with infection than among those without infection (40.0% versus 25.0%), the association was not statistically significant ($\chi^2=1.249$, $df=2$, $p=0.536$).

Table 6. Bilirubin Severity According to Infection Status

Infection status	Mild n (%)	Moderate n (%)	Severe n (%)	Total
Present	3 (30.0)	3 (30.0)	4 (40.0)	10
Absent	43 (30.7)	62 (44.3)	35 (25.0)	140
Total	46	65	39	150

Table 7. Summary of Inferential Analyses for Bilirubin Severity

Factor	Pearson χ^2	df	p-value	Sparse-cell assessment
Birth weight	12.154	4	0.016	33.3% of cells <5; minimum 1.30
Gestational age	4.134	4	0.388	33.3% of cells <5; minimum 0.26
Rh factor	1.905	4	0.753	33.3% of cells <5; minimum 2.60
Infection status	1.249	2	0.536	No sparse-cell warning reported

Overall, birth weight was the only tested factor with a Pearson chi-square p-value below 0.05. The pattern was driven principally by the comparatively greater proportion of severe bilirubin levels among neonates weighing <2.5 kg and the concentration of the small >4.0-kg subgroup in the moderate category. Because the birth-weight, gestational-age, and Rh analyses contained sparse expected frequencies, their asymptotic chi-square statistics warrant conservative interpretation. Gestational age, Rh factor, and infection status did not demonstrate statistically significant associations with bilirubin severity in the available analyses.

DISCUSSION

The present study demonstrates that pathological neonatal jaundice constituted an important component of neonatal morbidity among NICU admissions at SGTH, Swat. Of 831 neonates admitted during the 30-day observation period, 150 were identified with pathological neonatal jaundice, giving a hospital-based prevalence of 18.1%. Moderate bilirubin severity represented the largest category, while more than two-thirds of affected neonates had moderate or severe bilirubin levels. Birth weight demonstrated the strongest statistical relationship with bilirubin severity, although sparse expected cell frequencies reduce the certainty of this association. Gestational age, Rh status, and infection were not statistically associated with bilirubin severity within the available sample.

The observed 18.1% prevalence should be interpreted specifically as the proportion of NICU admissions affected by pathological jaundice rather than as a population prevalence among all live births. Estimates of neonatal hyperbilirubinemia differ considerably according to gestational-age distribution, bilirubin thresholds, surveillance

intensity, study population, referral pathway, and level of neonatal care (1,6). In a prospective cohort on the Thailand–Myanmar border, 22% of neonates developed hyperbilirubinemia, with particularly high rates among preterm infants, demonstrating how substantially disease burden can vary according to population and setting (12). Recent tertiary-care studies from South Asia also report considerable variation, reflecting differences in case definition, inclusion criteria, and the underlying risk profile of admitted neonates (17,19).

The male predominance observed in the current sample, with 61.3% males and 38.7% females, resembles patterns reported in several regional neonatal-jaundice cohorts. A Pakistani study of acute bilirubin encephalopathy similarly included a substantial proportion of male neonates (13), while a recent study conducted at SGT, Swat, found G6PD deficiency to be substantially more frequent among jaundiced male neonates than females (14). Male predominance can partly reflect sex-linked conditions such as G6PD deficiency, although the current study cannot establish sex as an independent determinant because sex was not included in the inferential association analyses and only four neonates had documented G6PD deficiency (14,15).

Birth weight was the factor most clearly associated with bilirubin severity. Severe bilirubin elevation occurred in 38.6% of neonates weighing <2.5 kg compared with 21.8% of neonates weighing 2.5–4.0 kg. The Pearson analysis produced $p=0.016$, supporting variation in bilirubin severity according to birth-weight category, although the sparse-cell structure requires conservative interpretation. Low-birth-weight newborns may have reduced physiological reserve, greater likelihood of prematurity or illness, feeding difficulty, and less mature hepatic bilirubin processing. Recent Pakistani evidence from Dera Ismail Khan found hyperbilirubinemia to be strongly associated with lower birth weight among preterm neonates, while Indian data have similarly identified low birth weight as a risk factor for significant jaundice and readmission (16,19).

The relationship between low birth weight and hyperbilirubinemia is also biologically plausible within the broader context of neonatal maturity. Prematurity is associated with immature hepatic uptake and conjugation of bilirubin, delayed establishment of effective feeding, increased enterohepatic circulation, and higher susceptibility to concurrent illness. Meta-analytic evidence identifies preterm birth as a significant risk factor for neonatal hyperbilirubinemia, while regional observational studies consistently demonstrate increased vulnerability among premature or growth-restricted infants (3,17). The present study therefore supports particularly close surveillance of neonates with low birth weight, while the small >4.0-kg subgroup and sparse cells preclude strong conclusions about the exact form or magnitude of the association.

Gestational age itself was not statistically associated with bilirubin severity in this study. Severe bilirubin levels were present in 33.3% of preterm and 24.1% of term neonates, producing a clinically notable numerical difference but a non-significant overall chi-square result. This should not be interpreted as evidence against the established biological importance of prematurity. The current analysis included only 33 preterm infants and one post-term neonate, generating sparse contingency cells and limited precision. Larger studies have demonstrated associations between prematurity and both neonatal hyperbilirubinemia and its severe neurological complications (3,12,13,19). Maternal blood-group information and Rh status were unknown in more than half of the sample, representing an important limitation in evaluating hemolytic risk. The available Rh-factor analysis showed no statistically significant association with bilirubin severity. Nevertheless, ABO and Rh incompatibility remain well-established contributors to hemolysis and neonatal hyperbilirubinemia. The meta-analysis by Lin et al. demonstrated a significant association between maternal-fetal ABO incompatibility and neonatal hyperbilirubinemia, and South Asian studies have repeatedly identified blood-group incompatibility among clinically important etiological factors (3,17). Complete maternal and neonatal blood typing would therefore strengthen both clinical risk stratification and future local epidemiological evaluation.

Recent Pakistani and regional evidence further supports the clinical importance of identifying hemolytic risk factors. G6PD deficiency is particularly relevant because oxidative stress can rapidly increase erythrocyte destruction and bilirubin production in susceptible neonates. Studies from Pakistan have reported G6PD deficiency among approximately 9–13% of jaundiced neonatal cohorts, while recent data from SGT, Swat, reported a frequency of approximately 10% with substantial male predominance (14,15). Molecular work has also identified G6PD-related genetic variants and demonstrated associations between hyperbilirubinemia and prematurity, infection, perinatal asphyxia, delayed feeding, and other neonatal stresses (18).

Only four neonates in the present study had documented G6PD deficiency, while status was unknown in nine. The frequency is therefore lower than reported in several contemporary Pakistani series, but differences in screening methods, population characteristics, selection criteria, timing of testing, and sample size may explain part of this variation (14,15). Because G6PD deficiency was not formally analyzed against bilirubin severity in the current dataset, no inference regarding its independent association can be made. The finding nevertheless reinforces the value of considering G6PD evaluation in neonates with early, unexpectedly high, rapidly rising, or otherwise unexplained hyperbilirubinemia (3,14,15).

Breastfeeding was the most common feeding pattern in the study, accounting for 50.7% of affected neonates, followed by formula feeding and mixed feeding. Breastfeeding itself should not be regarded as pathological; rather, jaundice risk is particularly relevant when milk transfer is inadequate, feeding initiation is delayed, or caloric intake and hydration are insufficient. Meta-analytic evidence has demonstrated an association between exclusive breastfeeding and neonatal hyperbilirubinemia, while clinical studies have linked feeding problems and delayed feeding to significant bilirubin elevation (3,18). The current study described feeding mode but did not test it against bilirubin severity, so the observed predominance of breastfeeding cannot be interpreted as evidence of causation.

A history of neonatal jaundice in a previous child was reported by 48.7% of mothers. Familial recurrence may reflect shared genetic, hematological, metabolic, or maternal–fetal factors and can be clinically useful when assessing a newborn's risk. Population studies have identified sibling history and familial or genetic characteristics among factors associated with significant neonatal jaundice (12,16). In the present study, previous-child history was descriptive and was not included in the inferential model; consequently, its frequency signals a potentially relevant clinical characteristic rather than a demonstrated independent predictor.

Normal vaginal delivery accounted for 72.7% of births, whereas 27.3% were cesarean deliveries. Mode of delivery has shown inconsistent associations with neonatal jaundice across studies, partly because its effect may be mediated through gestational age, perinatal complications, delayed feeding, bruising, or maternal characteristics rather than mode of birth itself. Some regional studies have reported associations between cesarean delivery and neonatal jaundice, whereas others have observed large proportions of affected neonates following vaginal delivery (16,17). Because mode of delivery was not tested against bilirubin severity in the present analysis, it should remain a descriptive characteristic rather than be interpreted as a causal determinant.

Infection was present in only 10 neonates, but severe bilirubin levels occurred in 40.0% of infected neonates compared with 25.0% of those without infection. This difference did not reach statistical significance ($p=0.536$), which may reflect the small infected subgroup and limited statistical power. Infection can contribute to hyperbilirubinemia through systemic inflammation, impaired hepatic bilirubin handling, hemolysis, altered feeding, and overall neonatal instability. Recent observational work has identified infection or sepsis among important predictors of substantial bilirubin elevation, including studies in which sepsis showed one of the strongest associations with severe hyperbilirubinemia (18,20). The direction of the present descriptive pattern is therefore clinically plausible despite the absence of statistical significance.

Moderate bilirubin severity was observed in 43.3% and severe bilirubin severity in 26.0% of the sample, meaning that 69.3% of affected neonates fell within the combined moderate-to-severe categories. This distribution highlights the importance of objective bilirubin measurement rather than relying solely on visual inspection. Evidence from systematic diagnostic evaluation supports transcutaneous bilirubin as a sensitive screening modality, while serum bilirubin remains necessary when treatment decisions or confirmation of significant hyperbilirubinemia are required (7,8). Structured measurement is especially important in infants with lower gestational age, hemolytic risk, rapidly progressive jaundice, G6PD deficiency, infection, or other neurotoxicity risk factors (4,9).

The neurological consequences of severe unconjugated hyperbilirubinemia remain the principal reason for early recognition and intervention. Acute bilirubin encephalopathy can progress to chronic kernicterus spectrum disorder with movement abnormalities, auditory dysfunction, developmental disability, and other persistent neurological sequelae. A systematic review of neurodevelopment following neonatal hyperbilirubinemia identified auditory, neurological, and motor abnormalities, particularly among affected term infants, while contemporary management guidance emphasizes prevention through risk assessment, timely bilirubin measurement, appropriate phototherapy, and escalation of treatment when indicated (4,5). Pakistani evidence showing acute bilirubin

encephalopathy among hospitalized hyperbilirubinemic neonates illustrates the continuing relevance of these complications in local clinical practice (13).

Phototherapy remains the central treatment for clinically significant unconjugated hyperbilirubinemia. Modern guidance uses gestational-age- and postnatal-age-specific treatment thresholds and incorporates neurotoxicity risk factors into decisions regarding phototherapy, escalation of care, and exchange transfusion (4,9). Evidence reviews supporting updated management recommendations indicate that treatment thresholds should balance prevention of bilirubin neurotoxicity against unnecessary intervention, while exchange transfusion remains reserved for severe or escalating hyperbilirubinemia when intensive management is insufficient (4). Home phototherapy may be feasible for selected low-risk neonates, but available evidence remains insufficient to support indiscriminate use without appropriate monitoring and follow-up (10).

Population context is particularly relevant when interpreting neonatal hyperbilirubinemia. Differences in ancestry, G6PD prevalence, blood-group distribution, prematurity, breastfeeding practices, healthcare access, and referral patterns can substantially alter the observed burden and etiological profile. A recent European cohort identified differences in severe hyperbilirubinemia among newborns of Indian-subcontinent ancestry compared with European descendants (11), while prospective Asian data demonstrate that locally prevalent genetic and perinatal risk factors can strongly shape hyperbilirubinemia patterns (12). This supports the need for region-specific surveillance rather than assuming that risk estimates from high-income or ethnically different populations apply uniformly to Swat.

The present study contributes contemporary hospital-level evidence from a tertiary-care setting in Swat, where published neonatal-jaundice data remain comparatively limited. Its findings are broadly compatible with recent Pakistani observations emphasizing prematurity, low birth weight, G6PD deficiency, hemolytic factors, and delayed recognition as clinically important concerns (13–15,19). At the same time, the lack of statistically significant associations for gestational age, Rh status, and infection illustrates how local sample structure and incomplete clinical information can influence statistical findings and cautions against assuming that established risk factors must necessarily reach statistical significance in every individual cohort.

Several limitations should be considered. The study was conducted at a single tertiary-care hospital over only 30 days, limiting temporal and geographical generalizability. The prevalence estimate reflects NICU admissions and cannot be extrapolated directly to all live births or newborns in the community. Convenience sampling was used for the 150 affected neonates, and the cross-sectional design allows identification of associations but cannot establish causality. More than half of maternal blood-group and Rh-factor observations were unknown, reducing the ability to evaluate hemolytic risk accurately. Several chi-square analyses contained expected cell frequencies below five, particularly those involving birth weight, gestational age, and Rh status, and their asymptotic p-values should therefore be interpreted cautiously.

An additional limitation is that the analytical evidence was considerably stronger for bilirubin severity and selected associated factors than for downstream treatment and clinical outcomes. Although clinically relevant outcomes in pathological neonatal jaundice include phototherapy requirement, exchange transfusion, neurological complications, referral, recovery, discharge, and mortality, complete quantitative distributions for these outcomes were not available for incorporation into the final analysis. Contemporary tertiary-care studies demonstrate the value of systematically documenting treatment modality, duration of therapy, readmission, exchange transfusion, and neurological outcome when characterizing neonatal hyperbilirubinemia (9,21,22). Future SGTH studies would benefit from prospective and standardized capture of these outcomes.

Despite these limitations, the study has several practical strengths. The complete count of 831 NICU admissions provided a defined hospital denominator, and the analytical sample included a broad range of clinically relevant neonatal and maternal characteristics. The study also provides locally relevant estimates of bilirubin severity, low-birth-weight burden, G6PD status, feeding pattern, maternal blood-group documentation, and infection. The finding that severe bilirubin elevation occurred proportionally more often among low-birth-weight neonates supports prioritization of this group during neonatal surveillance, while the high frequency of missing blood-group and Rh information identifies an immediately modifiable documentation gap.

Taken together, the present findings reinforce a risk-based approach to pathological neonatal jaundice. Early identification should combine clinical examination with objective bilirubin assessment and consideration of gestational age, birth weight, hemolytic risk, G6PD deficiency, feeding adequacy, infection, and relevant family history. Contemporary evidence indicates that systematic risk stratification, appropriate bilirubin measurement, and timely phototherapy can substantially reduce the likelihood of progression to severe bilirubin neurotoxicity (4,7,9). Improving routine documentation and extending future research across longer periods and multiple neonatal units would permit more precise estimation of disease burden and more robust identification of independent predictors.

CONCLUSION

Pathological neonatal jaundice accounted for 18.1% of NICU admissions during the 30-day study period at Saidu Group of Teaching Hospital, Swat, demonstrating a substantial hospital-based burden. Moderate bilirubin levels were the most frequently observed category, and 69.3% of affected neonates had moderate-to-severe bilirubin elevation. Birth weight showed evidence of an association with bilirubin severity, with severe bilirubin levels occurring proportionally more often among neonates weighing <2.5 kg; however, sparse expected frequencies require cautious interpretation of the inferential result. Gestational age, Rh factor, and infection status were not statistically associated with bilirubin severity in the available analyses. The findings support early objective bilirubin assessment, systematic neonatal risk evaluation, and particularly close monitoring of low-birth-weight neonates while emphasizing that pathological neonatal jaundice is a multifactorial condition requiring integration of neonatal maturity, hematological risk, feeding, infection, and clinical context (3,14,15).

RECOMMENDATIONS

Early bilirubin assessment and regular clinical monitoring should be prioritized among neonates admitted to the NICU, particularly those with low birth weight, prematurity, suspected hemolysis, G6PD deficiency, feeding difficulty, infection, or a relevant family history. Objective bilirubin measurement should guide assessment and treatment decisions rather than visual examination alone, and escalation of care should follow gestational-age-, postnatal-age-, and risk-adjusted treatment principles (4,7,9).

Routine documentation of maternal and neonatal ABO blood group, Rh factor, G6PD status, gestational age, birth weight, feeding adequacy, infection status, bilirubin measurements, and relevant family history should be strengthened. Complete documentation would improve both individual clinical risk assessment and the quality of future epidemiological analyses, particularly for hemolytic and inherited causes of significant neonatal jaundice.

Future studies should use longer recruitment periods, larger samples, and preferably multicentre designs to improve precision and generalizability. Sparse categorical groups should be anticipated during statistical planning so that exact methods, clinically justified category consolidation, or appropriately powered multivariable models can be applied where required. Prospective recording of phototherapy, duration of treatment, exchange transfusion, complications, bilirubin encephalopathy, referral, readmission, discharge, and mortality would allow the clinical-outcome component of pathological neonatal jaundice to be evaluated more comprehensively.

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