Section: DVL

Original Research Article

CLINICAL PROFILE OF PHOTOTHERAPY-RELATED SKIN CHANGES IN NEONATAL HYPERBILIRUBINEMIA: CORRELATION WITH SERUM BILIRUBIN LEVELS

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Received : 10/06/2026
Received in revised form : 23/07/2026
Accepted : 07/08/2026

Keywords:
Neonatal hyperbilirubinemia; Phototherapy; Cutaneous manifestations.

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DOI: 10.47009/jamp.2026.8.4.249

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2026; 8 (4); 1489-1498

ABSTRACT

Background: Phototherapy is the principal treatment for significant neonatal unconjugated hyperbilirubinemia. Although it is generally safe, it may produce transient or clinically important skin changes. Evidence regarding the clinical spectrum of these manifestations and their relationship with serum bilirubin levels remains limited. Aim: To evaluate the clinical profile of phototherapy-related skin changes in neonates with hyperbilirubinemia and determine their correlation with serum bilirubin levels. **Materials and Methods:** This hospital-based descriptive observational study included 100 neonates receiving blue-light phototherapy for hyperbilirubinemia in the neonatal intensive-care units of Chigateri General Hospital and Bapuji Hospital, Davangere, from March 2021 to January 2023. Clinical and neonatal characteristics, pre-existing dermatoses and newly developed skin changes were documented using a structured proforma. A detailed dermatological examination was performed before and during phototherapy. Serum bilirubin levels were recorded serially on days 1, 2 and 3. Quantitative variables were expressed as mean and standard deviation, while categorical variables were presented as frequencies and percentages. Chi-square, Fisher's exact and repeated-measures tests were applied as appropriate, with $P<0.05$ considered statistically significant. **Results:** The most frequent age at phototherapy was 4–6 days (41%). Males constituted 59%, while 55% were term and 43% were preterm. Pre-existing or transient neonatal dermatoses were documented in 66%, and phototherapy-related special skin changes occurred in 48%. Miliaria was the most common transient dermatosis (28%), followed by cutis marmorata (13%) and erythema toxicum neonatorum (11%). Purpura was the most common special lesion (19%), followed by petechiae (12%) and bronze baby syndrome (10%). The chest was the most frequently involved site. Bronze baby syndrome had the highest day-1 mean bilirubin level at 22.04 (9.03) mg/dL. However, no lesion category demonstrated a significant serial change in bilirubin. In the overall special-lesion group, mean bilirubin levels were 14.05 (7.15), 13.86 (5.49) and 13.93 (5.14) mg/dL on days 1, 2 and 3, respectively ($P=0.979$). Preterm neonates had significantly higher odds of special skin changes than term or post-term neonates (OR=2.89; 95% CI: 1.27–6.56; $P=0.010$). Skin changes also differed significantly across birth-weight categories ($P=0.001$). Of the pre-existing dermatoses, 57.6% remained unchanged, 30.3% became more prominent and 12.1% improved. **Conclusion**: Cutaneous manifestations were common among neonates receiving phototherapy. Purpura, petechiae and bronze baby syndrome were the principal special skin changes. Bronze baby syndrome was associated with comparatively higher bilirubin levels, but serial bilirubin changes were not significant in any lesion category. Prematurity and lower birth weight were important correlates of phototherapy-related skin changes. Careful dermatological monitoring is therefore warranted, particularly among preterm and very-low-birth-weight neonates.

INTRODUCTION

Neonatal hyperbilirubinemia is one of the most frequently encountered conditions during the neonatal period, affecting approximately 60% of term and up to 80% of preterm neonates. It results from increased bilirubin production, immature hepatic conjugation and enhanced enterohepatic circulation. Although most cases are physiological and self-limiting, excessive unconjugated bilirubin can cross the blood–brain barrier and cause acute bilirubin encephalopathy, kernicterus and permanent neurodevelopmental impairment. Therefore, timely assessment of serum bilirubin and initiation of appropriate treatment are essential [1,2]. Phototherapy is the mainstay of treatment for significant unconjugated hyperbilirubinemia. Blue-green light converts bilirubin in the skin into water-soluble photoisomers that can be excreted without hepatic conjugation. Its effectiveness depends on the wavelength and irradiance of the light source, the exposed body-surface area, duration of exposure, baseline serum bilirubin concentration, gestational age and underlying cause of jaundice.[1,3]

Although phototherapy is generally considered safe, it is not entirely free from adverse effects. Common short-term effects include temperature instability, increased transepidermal water loss, dehydration, loose stools, feeding disturbance, erythematous skin rash and interference with maternal–neonatal bonding. Cutaneous manifestations may include transient erythema, tanning, petechiae, purpura, bullous eruptions, thermal burns and, rarely, bronze baby syndrome.[3,4] Bronze baby syndrome is characterised by greyish-brown discoloration of the skin, mucous membranes and urine and is more frequently observed in neonates with conjugated hyperbilirubinemia or cholestasis. Preterm and low-birth-weight neonates may be particularly susceptible to phototherapy-related skin injury because of their immature epidermal barrier, reduced thermoregulatory capacity and increased transepidermal water loss.[3,5]

Neonates may also have physiological or pathological skin conditions before phototherapy, including erythema toxicum neonatorum, transient neonatal pustular melanosis, miliaria and cutis marmorata. Phototherapy may alter the appearance or clinical course of these lesions, making differentiation between pre-existing dermatoses and treatment-related changes difficult. Systematic dermatological examination before, during and after phototherapy is therefore necessary. Correlating individual skin changes with serial serum bilirubin levels may help determine whether particular manifestations are related to the severity of hyperbilirubinemia, the response to treatment or phototherapy exposure itself. Because clinical evidence describing the spectrum of phototherapy-associated cutaneous changes remains limited, especially in Indian neonatal intensive-care settings, the present study was conducted to document these manifestations and examine their relationship with serum bilirubin levels.

Aim

To evaluate the clinical profile of phototherapy-related skin changes in neonates with hyperbilirubinemia and determine their correlation with serum bilirubin levels.

Objectives

1. To identify and describe the pattern, frequency and distribution of skin changes occurring among neonates receiving phototherapy for hyperbilirubinemia.
2. To compare serial serum bilirubin levels in neonates with different phototherapy-related cutaneous manifestations.
3. To assess the effect of phototherapy on pre-existing neonatal dermatoses and examine the association of skin changes with relevant neonatal characteristics.

MATERIALS AND METHODS

Source of Data

The study population consisted of neonates with hyperbilirubinemia who received phototherapy in the Neonatal Intensive Care Units of Chigateri General Hospital and Bapuji Hospital, teaching hospitals attached to J.J.M. Medical College, Davangere, Karnataka. Eligible neonates were recruited after obtaining written informed consent from their parents or legally authorised guardians.

Study Design

The study was conducted as a hospital-based, descriptive cross-sectional observational study with prospective clinical assessment and serial measurement of serum bilirubin levels during phototherapy.

Study Location

The study was undertaken in the Neonatal Intensive Care Units of Chigateri General Hospital and Bapuji Hospital, attached to J.J.M. Medical College, Davangere, Karnataka. Dermatological evaluation was performed in coordination with the Departments of Dermatology and Neonatology.

Study Duration

The study was conducted from March 2021 to January 2023.

Sample Size

A total of 100 neonates who satisfied the eligibility criteria were included. The sample size was estimated using the formula:

where at the 95% confidence level, represented the expected proportion of phototherapy-related cutaneous changes, and represented the permissible absolute error. Based on the calculated requirement and feasibility during the study period, a minimum sample of 100 neonates was selected.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Sampling Technique

Eligible neonates receiving phototherapy during the study period were enrolled consecutively until the required sample size of 100 was achieved.

Inclusion Criteria

- Neonates admitted to the NICU with hyperbilirubinemia for whom phototherapy was initiated according to the treating neonatologist's clinical and serum bilirubin-based criteria.
- Term, preterm and post-term neonates receiving blue-light phototherapy.
- Neonates whose parents or legally authorised guardians provided written informed consent.
- Neonates in whom baseline dermatological examination and serum bilirubin assessment could be performed.

Exclusion Criteria

- Neonates whose parents or guardians declined consent.
- Neonates who were critically unstable and could not undergo the required dermatological examination.
- Neonates transferred, discharged or deceased before adequate clinical assessment could be completed.
- Neonates with incomplete clinical or serial serum bilirubin data required for correlation analysis.
- Neonates receiving phototherapy before admission when reliable baseline skin findings were unavailable.

Procedure and Methodology

Ethical clearance was obtained from the Institutional Ethics Committee before commencement of the study. Written informed consent was obtained from a parent or legally authorised guardian before enrolment. Each neonate was evaluated using a predesigned and pretested study proforma.

Information was recorded regarding postnatal age, sex, gestational age, birth weight, birth order, mode of delivery, maternal illnesses, drug exposure, consanguinity, blood-group incompatibility, indication for NICU admission and associated neonatal disorders. Relevant clinical details, including the indication for phototherapy and baseline serum bilirubin level, were obtained from the hospital records.

A detailed general and systemic examination was performed. A complete dermatological examination was undertaken before or at the initiation of phototherapy to document pre-existing neonatal dermatoses. The morphology, colour, number, distribution, symmetry and anatomical sites of all lesions were recorded. Skin appendages, umbilicus, vernix, lanugo hair, icterus and cyanosis were also assessed.

Blue-light phototherapy was administered according to the NICU protocol. During treatment, neonates were periodically examined for newly developed or changing skin lesions. Phototherapy-related changes such as transient erythema, bronze discoloration, petechiae, purpura, bullous eruption, thermal injury and other clinically significant lesions were recorded. Pre-existing lesions, including erythema toxicum neonatorum, transient neonatal pustular melanosis, miliaria and cutis marmorata, were followed to determine whether their morphology, distribution or clinical course changed during phototherapy.

Serum bilirubin values were recorded on the first, second and third days of phototherapy, wherever available. The occurrence and clinical pattern of each cutaneous manifestation were correlated with the corresponding serial bilirubin concentrations. Relevant lesions were photographed after parental consent while maintaining confidentiality and avoiding disclosure of identifying information.

Sample Processing

Blood samples were collected using aseptic precautions by trained NICU personnel as part of routine clinical management. The required quantity of venous or capillary blood was collected in an appropriate plain or serum-separator tube. Samples were allowed to clot and were centrifuged to separate the serum. Total serum bilirubin and, wherever clinically indicated, direct and indirect bilirubin fractions were measured in the hospital laboratory using the routinely validated biochemical method and calibrated analyser. Samples showing significant haemolysis or inadequate volume were not used and were recollected when clinically appropriate. Serum bilirubin results were expressed in mg/dL and entered according to the day and timing of phototherapy.

Data Collection

Data were collected prospectively using a structured case-record form. The form included maternal and birth history, neonatal characteristics, reason for NICU admission, associated systemic conditions, baseline dermatological findings, type and distribution of lesions, duration of phototherapy and serial serum bilirubin measurements. Each participant was assigned a unique study number. Completed forms were checked for completeness and consistency before the data were entered into a Microsoft Excel spreadsheet. Confidentiality was maintained by excluding personal identifiers from the analytical dataset.

Statistical Methods

Data were entered in Microsoft Excel and analysed using an appropriate statistical software package. Continuous variables such as age, birth weight and serum bilirubin levels were summarised using mean, standard deviation, median and range, as appropriate. Categorical variables such as sex, gestational-age category and type of skin lesion were expressed as frequencies and percentages.

Serial serum bilirubin measurements obtained on days 1, 2 and 3 were compared using repeated-measures analysis of variance when assumptions of normality and sphericity were satisfied. When these assumptions were not fulfilled, an appropriate non-parametric alternative such as the Friedman test was considered. Independent-samples *t* test or one-way ANOVA was used to compare mean bilirubin levels

ISSN (O): 2687-5365; ISSN (P): 2753-6556

across two or more independent groups, respectively. The Mann–Whitney *U* test or Kruskal–Wallis test was used for non-normally distributed data.

Associations between categorical variables were assessed using the chi-square test or Fisher's exact test. Correlation between serum bilirubin concentration and the number or severity of skin changes was evaluated using Pearson's or Spearman's correlation coefficient, depending on data distribution. Effect estimates were reported with 95% confidence intervals wherever applicable. All tests were two-tailed, and a *P* value <0.05 was considered statistically significant.

RESULTS

Table 1: Overall clinical profile, skin changes and serum bilirubin levels among neonates receiving phototherapy (N=100)

Parameter	n (%) or Mean (SD)	95% CI	Test of significance	P value
Postnatal age 1–3 days	24 (24.0)	16.7%–33.2%		
Postnatal age 4–6 days	41 (41.0)	31.9%–50.8%	χ^2=31.70†	<0.001*
Postnatal age 7–9 days	20 (20.0)	13.3%–28.9%		
Postnatal age 10–12 days	9 (9.0)	4.8%–16.2%		
Postnatal age >12 days	6 (6.0)	2.8%–12.5%		
Male sex	59 (59.0)	49.2%–68.1%	χ^2=3.24‡	0.072
Female sex	41 (41.0)	31.9%–50.8%		
Preterm	43 (43.0)	33.7%–52.8%		
Term	55 (55.0)	45.2%–64.4%	χ^2=42.14†	<0.001*
Post-term	2 (2.0)	0.6%–7.0%		
Very low birth weight	31 (31.0)	22.8%–40.6%		
Low birth weight	22 (22.0)	15.0%–31.1%	χ^2=9.62†	0.008*
Normal birth weight	47 (47.0)	37.5%–56.7%		
Pre-existing/transient neonatal dermatosis	66 (66.0)	56.3%–74.5%	χ^2=10.24‡	0.001*
Phototherapy-related/special skin change	48 (48.0)	38.5%–57.7%	χ^2=0.16‡	0.689
No phototherapy-related special skin change	52 (52.0)	42.3%–61.5%		
Day-1 serum bilirubin among neonates with special lesions, mg/dL§	14.05 (7.15)	11.97–16.13		
Day-2 serum bilirubin among neonates with special lesions, mg/dL§	13.86 (5.49)	12.26–15.45	F=0.02¶	0.979
Day-3 serum bilirubin among neonates with special lesions, mg/dL§	13.93 (5.14)	12.44–15.42		

**Statistically significant.*
†Chi-square goodness-of-fit test across categories.
‡One-sample chi-square test against an equal proportion.
§Calculated from the lesion-specific summary statistics for 48 neonates.

Approximate repeated-measures comparison based on aggregated summary data.

Table 1 presents the overall clinical profile, skin manifestations and serial serum bilirubin levels of 100 neonates receiving phototherapy. The largest proportion of neonates, 41 (41.0%; 95% CI: 31.9%–50.8%), received phototherapy at 4–6 days of life, followed by 24 (24.0%) at 1–3 days and 20 (20.0%) at 7–9 days. Only 9 (9.0%) were aged 10–12 days and 6 (6.0%) were older than 12 days. The age distribution differed significantly across categories (χ^2=31.70, P<0.001). Males constituted 59 (59.0%) participants and females 41 (41.0%); however, the sex distribution did not differ significantly from an equal distribution (χ^2=3.24, P=0.072). Regarding gestational maturity, 55 (55.0%) neonates were term, 43 (43.0%) were preterm and 2 (2.0%) were post-term, with a significant difference across the gestational categories (χ^2=42.14, P<0.001). Normal-birth-weight neonates accounted for 47 (47.0%), whereas 31 (31.0%) had very low birth weight and 22 (22.0%) had low birth weight. The difference among birth-weight categories was statistically significant (χ^2=9.62, P=0.008). Pre-existing or transient neonatal dermatoses were identified in 66 (66.0%; 95% CI: 56.3%–74.5%) neonates, representing a significantly greater proportion than those without such dermatoses (χ^2=10.24, P=0.001). Phototherapy-related special skin changes occurred in 48 (48.0%; 95% CI: 38.5%–57.7%) neonates, while 52 (52.0%) had no special skin changes; this difference was not statistically significant (χ^2=0.16, P=0.689). Among

ISSN (O): 2687-5365; ISSN (P): 2753-6556

the 48 neonates with special lesions, mean serum bilirubin levels were 14.05 (7.15) mg/dL on day 1, 13.86 (5.49) mg/dL on day 2 and 13.93 (5.14) mg/dL on day 3. There was no significant change in mean bilirubin levels over the three days (F=0.02, P=0.979), indicating that the overall bilirubin concentration remained close to 14 mg/dL during the observation period.

Table 2: Pattern, frequency and distribution of skin changes among neonates receiving phototherapy (N=100)

Skin change or distribution	n (%)	95% CI	Test of significance	P value
Pre-existing/transient neonatal dermatoses				
Miliaria	28 (28.0)	20.1%–37.5%		
Cutis marmorata	13 (13.0)	7.8%–21.0%		
Erythema toxicum neonatorum	11 (11.0)	6.3%–18.6%		
Physiological desquamation	4 (4.0)	1.6%–9.8%	χ^2=87.33†	<0.001*
Milia	3 (3.0)	1.0%–8.5%		
Sebaceous hyperplasia	2 (2.0)	0.6%–7.0%		
Transient neonatal pustular melanosis	2 (2.0)	0.6%–7.0%		
Acne neonatorum	1 (1.0)	0.2%–5.4%		
Dyssebacia	1 (1.0)	0.2%–5.4%		
Suckling blister	1 (1.0)	0.2%–5.4%		
Phototherapy-related/special skin changes				
Purpura	19 (19.0)	12.5%–27.8%		
Petechiae	12 (12.0)	7.0%–19.8%		
Bronze baby syndrome	10 (10.0)	5.5%–17.4%	χ^2=30.25‡	<0.001*
Transient erythema	4 (4.0)	1.6%–9.8%		
Bullous eruption	2 (2.0)	0.6%–7.0%		
Sclerema neonatorum	1 (1.0)	0.2%–5.4%		
Distribution of transient lesions§				
Chest	59 (59.0)	49.2%–68.1%		
Flexures	46 (46.0)	36.6%–55.7%		
Face	40 (40.0)	30.9%–49.8%	—	—
Upper limbs	39 (39.0)	30.0%–48.8%		
Abdomen	33 (33.0)	24.6%–42.7%		
Lower limbs	32 (32.0)	23.7%–41.7%		
Distribution of special lesions§				
Chest	45 (45.0)	35.6%–54.8%		
Upper limbs	40 (40.0)	30.9%–49.8%		
Lower limbs	25 (25.0)	17.5%–34.3%	—	—
Abdomen	23 (23.0)	15.8%–32.2%		
Generalised	9 (9.0)	4.8%–16.2%		

**Statistically significant.*

†Goodness-of-fit test comparing the frequencies of the ten transient dermatoses.

‡Goodness-of-fit test comparing the frequencies of the six special lesions among 48 affected neonates.

§An individual neonate could have lesions at more than one site; therefore, percentages were not mutually exclusive and an omnibus chi-square test was not appropriate.

Table 2 describes the pattern, frequency and anatomical distribution of skin changes among neonates receiving phototherapy. Among the pre-existing or transient neonatal dermatoses, miliaria was the most frequent condition, occurring in 28 (28.0%; 95% CI: 20.1%–37.5%) neonates. This was followed by cutis marmorata in 13 (13.0%), erythema toxicum neonatorum in 11 (11.0%), physiological desquamation in 4 (4.0%) and milia in 3 (3.0%). Sebaceous hyperplasia and transient neonatal pustular melanosis were each observed in 2 (2.0%) neonates, whereas acne neonatorum, dyssebacia and suckling blister were each found in 1 (1.0%) neonate. The distribution of transient dermatoses was significantly non-uniform (χ^2=87.33, P<0.001), reflecting the predominance of miliaria. Among phototherapy-related special skin changes, purpura was most common, affecting 19 (19.0%; 95% CI: 12.5%–27.8%) neonates. Petechiae occurred in 12 (12.0%), bronze baby syndrome in 10 (10.0%), transient erythema in 4 (4.0%), bullous eruption in 2 (2.0%) and sclerema neonatorum in 1 (1.0%). The frequencies of these special lesions also differed significantly (χ^2=30.25, P<0.001). Transient lesions most frequently involved the chest in 59 (59.0%) neonates, followed by the flexures in 46 (46.0%), face in 40 (40.0%), upper limbs in 39 (39.0%), abdomen in 33 (33.0%) and lower limbs in 32 (32.0%). Similarly, special lesions most commonly affected the chest in 45 (45.0%) neonates and upper limbs in 40 (40.0%), followed by the lower limbs in 25 (25.0%) and abdomen in 23 (23.0%); generalised involvement was observed in 9 (9.0%). Because an individual neonate could have lesions involving multiple anatomical sites, the site-specific percentages were overlapping and were not suitable for an omnibus chi-square comparison.

Table 3: Serial serum bilirubin levels according to phototherapy-related cutaneous manifestation

Cutaneous manifestation	Day 1, Mean (SD), mg/dL	Day 2, Mean (SD), mg/dL	Day 3, Mean (SD), mg/dL	95% CI of Day-1 mean	Repeated-measures test	P value
Bronze baby syndrome (n=10)	22.04 (9.03)	21.24 (6.81)	19.90 (7.67)	15.58–28.50	F=0.575	0.573
Bullous eruption (n=2)	11.25 (1.63)	13.00 (2.26)	8.80 (0.14)	−3.40–25.90†	F=7.512	0.223

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Petechiae (n=12)	12.77 (5.27)	11.64 (3.51)	12.83 (2.83)	9.42–16.12	F=0.492	0.574
Purpura (n=19)	12.33 (5.01)	12.15 (2.80)	12.79 (2.44)	9.91–14.75	F=0.246	0.729
Sclerema neonatorum (n=1)	3.90 (NA)	8.20 (NA)	10.10 (NA)	Not estimable	Not applicable	Not applicable
Transient erythema (n=4)	10.05 (2.03)	12.03 (2.07)	11.25 (2.83)	6.82–13.28	F=1.946	0.246
Overall special-lesion group (n=48)	**14.05 (7.15)**	**13.86 (5.49)**	**13.93 (5.14)**	**11.97–16.13**	**F=0.02‡**	**0.979**

†The extremely wide confidence interval resulted from the sample size of only two neonates and should not be interpreted clinically.
‡Approximate test based on aggregated lesion-specific summary statistics.

Table 3 compares serial serum bilirubin levels across different phototherapy-related cutaneous manifestations. Neonates with bronze baby syndrome had the highest mean bilirubin levels throughout the study period. In this group, mean bilirubin decreased from 22.04 (9.03) mg/dL on day 1 to 21.24 (6.81) mg/dL on day 2 and 19.90 (7.67) mg/dL on day 3. The day-1 mean had a 95% CI of 15.58–28.50 mg/dL. Although a declining trend was observed, the serial difference was not statistically significant (F=0.575, P=0.573). Among neonates with bullous eruption, mean bilirubin levels were 11.25 (1.63), 13.00 (2.26) and 8.80 (0.14) mg/dL on days 1, 2 and 3, respectively, without a significant serial difference (F=7.512, P=0.223). The extremely wide day-1 confidence interval of −3.40 to 25.90 mg/dL reflected the very small sample of two neonates and was not clinically informative. In neonates with petechiae, mean bilirubin levels were 12.77 (5.27), 11.64 (3.51) and 12.83 (2.83) mg/dL across the three days, with no significant temporal change (F=0.492, P=0.574). Similarly, neonates with purpura had mean levels of 12.33 (5.01), 12.15 (2.80) and 12.79 (2.44) mg/dL, respectively (F=0.246, P=0.729). The single neonate with sclerema neonatorum showed an increase from 3.90 mg/dL on day 1 to 8.20 mg/dL on day 2 and 10.10 mg/dL on day 3, but statistical analysis was not possible. Among neonates with transient erythema, bilirubin levels were 10.05 (2.03), 12.03 (2.07) and 11.25 (2.83) mg/dL, with no significant difference (F=1.946, P=0.246). For the overall special-lesion group, mean levels remained almost unchanged at 14.05, 13.86 and 13.93 mg/dL (F=0.02, P=0.979).

Table 4: Effect on pre-existing dermatoses and association of phototherapy-related skin changes with neonatal characteristics (N=100)

Variable	Total	Phototherapy-related skin change, n (%)	No special skin change, n (%)	Effect estimate (95% CI)	Test of significance	P value
Pre-existing dermatosis						
Present	66	36 (54.5)	30 (45.5)	OR=2.20 (0.93–5.21)	χ^2=3.25	0.071
Absent	34	12 (35.3)	22 (64.7)	Reference		
Sex						
Male	59	30 (50.8)	29 (49.2)	OR=1.32 (0.59–2.97)	χ^2=0.46	0.499
Female	41	18 (43.9)	23 (56.1)	Reference		
Gestational maturity						
Preterm	43	27 (62.8)	16 (37.2)	OR=2.89 (1.27–6.56)	χ^2=6.61	0.010*
Term/post-term	57	21 (36.8)	36 (63.2)	Reference		
Birth-weight category						
Very low birth weight	31	22 (71.0)	9 (29.0)			
Low birth weight	22	12 (54.5)	10 (45.5)	—	χ^2=13.18†	0.001*
Normal birth weight	47	14 (29.8)	33 (70.2)			
Postnatal age						
≤6 days	65	35 (53.8)	30 (46.2)	OR=1.97 (0.83–4.70)	χ^2=2.37	0.124
>6 days	35	13 (37.1)	22 (62.9)	Reference		
Course of pre-existing dermatoses (n=66)		n (%)	95% CI			
Remained clinically unchanged	66	38 (57.6)	45.5%–68.8%			
Became more prominent/exacerbated	66	20 (30.3)	20.5%–42.2%	—	χ^2=20.73‡	<0.001*
Improved during observation	66	8 (12.1)	6.2%–22.1%			

**Statistically significant.*
†Chi-square test comparing all three birth-weight categories.
‡Goodness-of-fit test comparing the three possible clinical courses.

Table 4 demonstrates the effects of phototherapy on pre-existing dermatoses and the association of special skin changes with neonatal characteristics. Among 66 neonates with a pre-existing dermatosis, 36 (54.5%) developed a phototherapy-related skin change compared with 12 of 34 (35.3%) without a pre-existing dermatosis. The presence of a pre-existing dermatosis was associated with 2.20 times higher

ISSN (O): 2687-5365; ISSN (P): 2753-6556

odds of developing a special skin change, although the association did not attain statistical significance (OR=2.20; 95% CI: 0.93–5.21; χ^2=3.25, P=0.071). Special skin changes occurred in 30 of 59 (50.8%) males and 18 of 41 (43.9%) females. Sex was not significantly associated with skin changes (OR=1.32; 95% CI: 0.59–2.97; P=0.499). A significant association was observed with gestational maturity: 27 of 43 (62.8%) preterm neonates developed special skin changes compared with 21 of 57 (36.8%) term or post-term neonates. Preterm neonates had approximately 2.9 times higher odds of developing these manifestations (OR=2.89; 95% CI: 1.27–6.56; χ^2=6.61, P=0.010). Skin changes were also significantly associated with birth weight (χ^2=13.18, P=0.001). They occurred in 22 of 31 (71.0%) very-low-birth-weight neonates, 12 of 22 (54.5%) low-birth-weight neonates and 14 of 47 (29.8%) normal-birth-weight neonates, demonstrating a progressively greater occurrence with decreasing birth weight. Phototherapy-related changes were identified in 35 of 65 (53.8%) neonates aged ≤6 days and 13 of 35 (37.1%) aged >6 days. Although younger neonates had higher odds of developing skin changes, this association was not statistically significant (OR=1.97; 95% CI: 0.83–4.70; P=0.124). Of the 66 neonates with pre-existing dermatoses, the lesions remained clinically unchanged in 38 (57.6%), became more prominent or exacerbated in 20 (30.3%) and improved in 8 (12.1%). The distribution of these clinical courses was statistically significant (χ^2=20.73, P<0.001), indicating that most pre-existing dermatoses remained stable, although nearly one-third became more prominent during phototherapy.

DISCUSSION

Table 1: Clinical profile, skin changes and serum bilirubin levels

In the present study, the largest proportion of neonates received phototherapy between 4 and 6 days of life (41.0%), followed by 1–3 days (24.0%), and the distribution across postnatal-age categories was statistically significant (P<0.001). This clustering during the first postnatal week corresponds to the physiological rise in unconjugated bilirubin caused by increased bilirubin production, immature hepatic conjugation and enhanced enterohepatic circulation. The 2022 American Academy of Pediatrics guideline similarly emphasised that treatment decisions during this period should be based on postnatal age in hours, gestational age, serum bilirubin concentration and neurotoxicity risk factors rather than a single fixed bilirubin threshold, as reported by Kemper et al. (2022).[1] NICE (2023),[2] also recommended age- and gestation-specific treatment thresholds and serial serum bilirubin monitoring during phototherapy.

Males constituted 59.0% of the cohort, although the difference from an equal sex distribution was not statistically significant (P=0.072). Quazi et al. (2023),[3] also reported slight male predominance among neonates with dermatoses, with males accounting for 53.8% of their study population. The small male predominance in the present study may reflect the admission pattern rather than an independent biological susceptibility because sex was not subsequently associated with special skin changes. Term neonates comprised 55.0%, while 43.0% were preterm. The relatively high proportion of preterm neonates was clinically important because hepatic immaturity, reduced albumin binding, concurrent illness and increased vulnerability to bilirubin neurotoxicity frequently result in earlier treatment at lower bilirubin concentrations among preterm infants. Visscher and Narendran (2015),[4] further explained that neonatal skin-barrier structure and function vary considerably with gestational maturity, potentially modifying the skin's response to heat, light exposure, moisture and intensive-care procedures.

Very-low-birth-weight and low-birth-weight neonates together accounted for 53.0% of the sample, and the difference among birth-weight categories was significant (P=0.008). This finding indicated that the study represented a clinically vulnerable NICU population rather than only healthy term neonates with physiological jaundice. Pre-existing or transient neonatal dermatoses were documented in 66.0% of the neonates. This was lower than the 94.1% prevalence reported by Dash et al. (2018),[5] and the 87.3% reported by Kamatham et al. (2024),[6] but direct comparison is limited because those studies evaluated broad cutaneous findings among newborn populations, while the present study was restricted to neonates receiving phototherapy in the NICU.

Phototherapy-related special skin changes occurred in 48.0% of neonates, although the proportion did not differ significantly from that without special changes (P=0.689). Wang et al. (2021),[7] described phototherapy as generally safe but recognised transient rashes, petechiae, purpura, bullous eruptions and bronze baby syndrome among its cutaneous complications. The observed frequency in the present study was comparatively high, possibly because repeated specialist dermatological examinations detected mild and transient changes that may be missed during routine neonatal care. Among the 48 affected neonates, the mean serum bilirubin remained near 14 mg/dL from day 1 to day 3, with no significant overall temporal change (P=0.979). This contrasts with Gutta et al. (2019),[8] who reported a significant fall in serum bilirubin during phototherapy and a greater decline with LED than conventional phototherapy. The difference may be explained by the present analysis being restricted to neonates with special lesions, heterogeneity in gestational age and underlying disease, variations in phototherapy intensity or duration, and aggregation of lesion-specific summary data.

Table 2: Pattern and distribution of skin changes

Miliaria was the most common transient dermatosis, affecting 28.0% of neonates, followed by cutis

ISSN (O): 2687-5365; ISSN (P): 2753-6556

marmorata (13.0%) and erythema toxicum neonatorum (11.0%). The distribution of transient dermatoses was significantly non-uniform (P<0.001). Patel et al. (2017),[9] similarly identified transient physiological skin manifestations as the predominant neonatal cutaneous findings and reported miliaria in 38.1% of neonates, moderately higher than the 28.0% observed in the present study. In contrast, Quazi et al. (2023),[3] reported miliaria in 4.6%, erythema toxicum neonatorum in 8.4% and physiological desquamation in 5.3%. Differences between studies may be related to climate, ambient temperature, gestational-age composition, NICU humidity, wrapping practices and timing of examination. The relatively high frequency of miliaria in the present study may have been promoted by thermal exposure, occlusion and sweating during phototherapy.

Cutis marmorata was observed in 13.0% and could reflect the immature vasomotor response of neonates, particularly preterm and low-birth-weight infants. Erythema toxicum neonatorum was detected in 11.0%, which was lower than the 51.6% reported by Patel et al. (2017).[9] The greater proportion of preterm and medically ill neonates in the present study may partly explain this difference because erythema toxicum is generally more frequent in healthy term neonates. Physiological desquamation, milia, sebaceous hyperplasia, transient neonatal pustular melanosis, acne neonatorum, dyssebacia and suckling blisters occurred less frequently.

Purpura was the most common special lesion at 19.0%, followed by petechiae at 12.0% and bronze baby syndrome at 10.0%. The variation among special-lesion categories was statistically significant (P<0.001). LaRusso et al. (2015),[10] described phototherapy-induced purpura as an uncommon but recognisable eruption, particularly in susceptible or transfused neonates, and noted that purpura, bullous lesions and bronze discoloration had been reported following phototherapy. Wang et al. (2021),[7] proposed that phototherapy-related petechiae could be associated with light-induced thrombocytopenia, while purpuric and bullous eruptions might occur in neonates with cholestasis or elevated circulating porphyrins. Consequently, petechiae and purpura during phototherapy should prompt evaluation for platelet abnormalities, coagulation disorders, sepsis, cholestasis and other systemic causes before attributing them exclusively to light exposure.

Bronze baby syndrome was recorded in 10.0%, which is higher than generally expected for this rare complication. Prasad et al. (2017),[11] described bronze baby syndrome as an infrequent, usually reversible greyish-brown discoloration of the skin, plasma and urine during phototherapy, commonly associated with conjugated hyperbilirubinemia or hepatobiliary dysfunction. Therefore, the comparatively high frequency in the present cohort could indicate a higher prevalence of conjugated hyperbilirubinemia, cholestasis or severe systemic illness and supports assessment of direct bilirubin and liver function in affected neonates.

The chest was the most frequent site of transient lesions (59.0%), followed by flexures (46.0%) and face (40.0%). Special lesions also commonly involved the chest (45.0%) and upper limbs (40.0%). This distribution was clinically plausible because the trunk and limbs represented large areas exposed to the phototherapy source, while flexural occlusion and moisture could favour miliaria. As individual neonates had involvement at more than one site, the site-specific percentages were overlapping and should be interpreted as patterns of anatomical involvement rather than mutually exclusive distributions.

Table 3: Serial bilirubin according to cutaneous manifestation

Bronze baby syndrome was associated with the highest serum bilirubin levels, with mean values of 22.04 mg/dL on day 1, 21.24 mg/dL on day 2 and 19.90 mg/dL on day 3. Although a downward trend was observed, it was not statistically significant (P=0.573). This observation was consistent with the association of bronze baby syndrome with more marked or complicated hyperbilirubinemia described by Prasad et al. (2017).[11] However, bronze discoloration is believed to be more closely related to conjugated bilirubin, cholestasis and the accumulation of bilirubin photo-products or porphyrins than to total bilirubin alone. Thus, the higher total bilirubin observed in this group suggested greater disease severity but did not establish a direct causal relationship.

Mean bilirubin levels among neonates with petechiae and purpura remained approximately 12–13 mg/dL throughout the observation period, and neither group demonstrated a significant serial change. This supported the possibility that these manifestations were not determined solely by the total bilirubin concentration. LaRusso et al. (2015),[10] similarly reported phototherapy-induced purpura as a distinct cutaneous reaction and emphasised its association with clinical factors beyond bilirubin concentration itself. Wang et al. (2021),[7] also highlighted possible roles for thrombocytopenia, porphyrin accumulation and cholestatic disease.

The bullous-eruption group showed a decline to 8.80 mg/dL on day 3, but the result was based on only two neonates and was not statistically significant (P=0.223). Likewise, statistical inference was impossible for the single neonate with sclerema neonatorum. The wide confidence interval for bullous eruption demonstrated the imprecision caused by the very small sample. Transient erythema was associated with mean bilirubin levels of approximately 10–12 mg/dL and showed no significant temporal variation (P=0.246). Overall, no cutaneous category demonstrated a statistically significant serial bilirubin change.

The absence of a significant overall decline differed from Gutta et al. (2019),[8] who found that LED phototherapy produced a mean bilirubin reduction rate of 5.3±2.91 μmol/L/hour compared with 3.76±2.39 μmol/L/hour under conventional

ISSN (O): 2687-5365; ISSN (P): 2753-6556

phototherapy (P<0.001). Gottimukkala et al. (2021),[12] also found intermittent phototherapy to be clinically comparable with continuous therapy for eligible neonates, demonstrating that bilirubin response depends on irradiance, exposure schedule and baseline clinical profile. In the present study, aggregation across heterogeneous lesion groups, small subgroup sizes and the absence of adjustment for gestational age, phototherapy dose, conjugated bilirubin and underlying disease may have obscured temporal changes. The non-significant results should therefore not be interpreted as evidence that phototherapy was ineffective.

Table 4: Associated neonatal characteristics and course of dermatoses

Phototherapy-related skin changes occurred in 54.5% of neonates with a pre-existing dermatosis compared with 35.3% of those without one. Although the odds were approximately doubled, the association did not reach statistical significance (OR=2.20, 95% CI: 0.93–5.21; P=0.071). The direction of this association suggested that an already altered or inflamed skin barrier might increase susceptibility to heat, moisture, friction and photic exposure. Nevertheless, the confidence interval included unity, and a larger sample would be required to confirm this relationship. Mendelson (2023),[13] similarly emphasised that separating the adverse effects of phototherapy from the effects of hyperbilirubinemia, prematurity and concurrent illness remains methodologically challenging.

There was no significant association between sex and special skin changes (P=0.499), consistent with the modest and statistically non-significant male predominance in the overall cohort. Postnatal age ≤6 days was associated with higher odds of skin changes, but the result was also non-significant (OR=1.97, P=0.124). In contrast, gestational maturity was significantly associated with the outcome. Preterm neonates had a 62.8% frequency of special changes compared with 36.8% among term or post-term neonates and had nearly threefold higher odds of developing these manifestations (OR=2.89, 95% CI: 1.27–6.56; P=0.010). Visscher and Narendran (2015),[4] described the structural and functional immaturity of preterm skin, including reduced barrier competence at earlier gestations and vulnerability to environmental and treatment-related stressors, providing biological support for this association.

A clear birth-weight gradient was also observed: special changes occurred in 71.0% of very-low-birth-weight, 54.5% of low-birth-weight and 29.8% of normal-birth-weight neonates (P=0.001). This gradient was consistent with the strong relationship between lower birth weight, prematurity, skin immaturity and the intensity of NICU care. It also suggested that gestational age and birth weight may be interrelated predictors; multivariable analysis would be required to determine their independent effects.

Among the 66 neonates with pre-existing dermatoses, 57.6% remained unchanged, 30.3% became more prominent or exacerbated and 12.1% improved. The difference among these clinical courses was significant (P<0.001). The predominance of unchanged lesions indicated that phototherapy did not adversely alter most benign neonatal dermatoses. Nevertheless, exacerbation in almost one-third supports careful baseline and serial skin examination, particularly among preterm and very-low-birth-weight neonates. The findings collectively suggest that phototherapy-related skin manifestations may be influenced more by neonatal maturity, birth weight, skin-barrier status and associated systemic illness than by total serum bilirubin alone.

CONCLUSION

The present study demonstrated that cutaneous findings were common among neonates receiving phototherapy for hyperbilirubinemia. Pre-existing or transient neonatal dermatoses were observed in 66% of neonates, while 48% developed phototherapy-related special skin changes. Miliaria was the most frequent transient dermatosis, followed by cutis marmorata and erythema toxicum neonatorum. Among special manifestations, purpura was most common, followed by petechiae and bronze baby syndrome. The chest was the most frequently involved anatomical site for both transient and special lesions.

Bronze baby syndrome was associated with the highest serum bilirubin concentrations, with a day-1 mean of 22.04 mg/dL. However, none of the individual cutaneous manifestations showed a statistically significant change in bilirubin levels over the three observation days. In the overall special-lesion group, mean bilirubin levels remained approximately 14 mg/dL, with no significant temporal change. These findings suggested that the occurrence of most skin changes was not determined by total serum bilirubin concentration alone and could also be influenced by phototherapy exposure, gestational maturity, birth weight, skin-barrier integrity and associated systemic illness.

Preterm neonates had significantly higher odds of developing special skin changes than term or post-term neonates. A significant birth-weight gradient was also observed, with the highest frequency among very-low-birth-weight neonates. Most pre-existing dermatoses remained clinically unchanged during phototherapy, although almost one-third became more prominent or exacerbated. Phototherapy remained an effective and generally safe treatment for neonatal hyperbilirubinemia, but systematic skin examination before and during treatment was important, particularly in preterm and very-low-birth-weight neonates. The occurrence of purpura, petechiae, bullous lesions or bronze discoloration should prompt evaluation for thrombocytopenia, coagulopathy, cholestasis, porphyrin abnormalities and other underlying systemic disorders.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Limitations of Study

1. The study was conducted in two teaching hospitals attached to a single medical college; therefore, its findings might not be generalisable to neonates treated in other settings.
2. The sample size was limited to 100 neonates, and several cutaneous subgroups, particularly bullous eruption, transient erythema and sclerema neonatorum, contained very few cases.
3. The small subgroup sizes produced wide confidence intervals and limited the statistical power to detect meaningful changes in serial serum bilirubin levels.
4. The descriptive observational design could identify associations but could not establish a causal relationship between phototherapy and the observed skin changes.
5. There was no separate comparison group of hyperbilirubinaemic neonates who did not receive phototherapy. Consequently, it was difficult to distinguish changes caused by phototherapy from those caused by hyperbilirubinemia or concurrent neonatal illness.
6. Total serum bilirubin was the principal biochemical parameter. Direct and indirect bilirubin fractions, serum bile acids and porphyrin concentrations were not systematically analysed, limiting interpretation of bronze baby syndrome and phototherapy-induced purpura.
7. Phototherapy-related variables such as light source, wavelength, irradiance, distance from the neonate, duration of daily exposure and cumulative phototherapy dose were not included in the analysis.
8. The diagnosis and assessment of cutaneous lesions were primarily clinical. Histopathological examination, dermoscopy, microbiological testing and other confirmatory investigations were not routinely performed.
9. The severity of skin changes was not measured using a validated neonatal dermatological scoring system.
10. Potential confounders such as sepsis, thrombocytopenia, coagulopathy, cholestasis, blood transfusion, medication exposure, humidity and thermal instability were not uniformly controlled.
11. Gestational age and birth weight are closely related variables, but multivariable regression was not performed to establish whether they were independent predictors of skin changes.
12. Serial bilirubin analysis was based partly on aggregated lesion-specific data, which limited detailed paired analysis and adjustment for differences in baseline bilirubin levels.
13. Follow-up was restricted to the phototherapy and immediate hospitalisation periods. The time required for complete resolution, recurrence of lesions and possible long-term dermatological consequences were not assessed.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556