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Neonatal hyperbilirubinemia using phototherapy with light intensity for improved resolution

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Abstract:
Neonatal hyperbilirubinemia requires phototherapy whose efficacy depends on light intensity, yet optimal dosing across gestational ages and risk levels remains insufficiently defined for personalized treatment. Therefore, it is of interest to evaluate the 250 neonates (≥35 weeks) at GMH, SSMC Rewa NICU, stratifying by AAP risk into three groups receiving 30-150 μW/cm²/nm phototherapy with serial total serum bilirubin (TSB) monitoring. Intense phototherapy (40-50 μW/cm²/nm) accelerated TSB decline most rapidly within 24 hours, while intensities ≥30 μW/cm²/nm prevented exchange transfusion in moderate-risk cases. Preterm neonates required higher intensities and longer durations compared to term infants, highlighting gestational age-dependent phototherapy responses. Thus, data shows that intensity-stratified protocols optimize TSB reduction while minimizing exchange transfusion risk across neonatal populations.

Keywords: Neonatal hyperbilirubinemia, phototherapy, light intensity, bilirubin, exchange transfusion, NICU, preterm neonates

Background:
Neonatal hyperbilirubinemia is a common clinical situation with an incidence of almost 60 percent of term and 80 percent of preterm babies in the first week of life **[1].** It is caused by a lack of balance between bilirubin generation and excretion, frequently because of physiological immaturity of the hepatic conjugation systems **[2].** Most of the cases are mild and self-limiting, but severe hyperbilirubinemia can cause acute bilirubin encephalopathy and kernicterus and cause permanent neurological damage or death without immediate treatment **[3].** Over the past few decades, phototherapy has been the foundation of the treatment of the neonatal jaundice. It acts by transforming unconjugated bilirubin into water soluble isomers that can be excreted without hepatic conjugation **[4].** The effectiveness of phototherapy varies depending on several factors such as the wavelength of light, the amount of body surface exposed, length of exposure and above all, the intensity or irradiance of the light source **[5].** The latest developments in the technology of phototherapy, especially the application of the light-emitting diode (LED) systems, have enhanced the effectiveness and safety of treatment by providing a higher irradiance with minimal heat generation **[6].** The American Academy of Pediatrics (AAP) defines intensive phototherapy as a minimum irradiance of 30 μW/cm 2/nm in the blue-green range (430 490 nm) and is highly effective in breaking down bilirubin **[7].** But even there is variability in the clinical practice as to the optimal intensity needed by various risk groups. It has been shown that an increased intensity phototherapy results in a rapid decrease in serum bilirubin levels, shortening the treatment and hospitalization period **[8, 9].** Additionally, high-intensity phototherapy initiated early has been reported to reduce the frequency of exchange transfusion, which is a process that is linked to serious complications like infection, electrolyte imbalance and death **[10]**. Although these benefits are evident, overly high intensity can be linked to negative outcomes like dehydration, thermal instability and oxidative stress particularly in preterm babies **[11].** Preterm babies are a highly vulnerable group with a weak skin barrier, a low albumin binding capacity and high vulnerability to bilirubin neurotoxicity **[12].** As a result, they might need more vigorous phototherapy plans than term babies. Nevertheless, efficacy and safety are still a dilemma and it is important to determine the optimal phototherapy intensity accurately. In resource constrained environments, where state-of-the-art phototherapy units are not necessarily available, it is important to know the minimum effective intensity needed to avoid serious complications. The identification of these thresholds can be used to optimize the treatment regimen and enhance the neonatal outcomes and reduce the healthcare expenses **[13].** Therefore, it is of interest to advance the development of phototherapy guidelines and encourage the use of more personalized approaches to treatment in neonatal care by offering evidence-based information.

Materials and Methods:

Study design and setting:
This prospective cohort study was conducted in the Neonatal Intensive Care Unit (NICU) of the Department of Paediatrics at Gandhi Memorial Hospital, Shyam Shah Medical College (SSMC), Rewa and Madhya Pradesh. The study was designed to systematically evaluate the role of varying phototherapy intensities in the management of neonatal hyperbilirubinemia and their impact on clinical outcomes.

Study duration:
Study was carried out over a period extending from September 2022 to January 2024.

Study population:
A total of 250 neonates diagnosed with hyperbilirubinemia and meeting the inclusion criteria were enrolled in the study.

Inclusion criteria:
Neonates with a gestational age of ≥35 weeks who required phototherapy as per standard clinical guidelines were included.

Exclusion criteria:
Strictly applied to eliminate confounding factors; these included neonates on mechanical ventilation, those with major congenital anomalies, cases of neonatal cholestasis or suspected hepatitis, neonates receiving phenobarbitone therapy and those presenting with jaundice within the first 24 hours of life.

Sample collection:
Upon admission, detailed clinical evaluation and baseline investigations were performed for all enrolled neonates. These included complete blood count, peripheral smear with reticulocyte count, serum bilirubin (total, direct and indirect), serum albumin levels, blood grouping and direct coombs test. Additional investigations such as sepsis screening and glucose-6-phosphate dehydrogenase (G6PD) deficiency testing were carried out when clinically indicated.

Methodology:
The study population was stratified into three groups based on the American Academy of Paediatrics (AAP) guidelines, considering gestational age, risk factors and serum bilirubin levels.

[1] Group A (low risk) included neonates ≥38 weeks without risk factors.
[2] Group B (moderate risk) included neonates ≥38 weeks with risk factors or 35–37 weeks without risk factors.
[3] Group C (high risk) comprised neonates 35–37 weeks with additional risk factors.

Each group received phototherapy at predefined intensity ranges: 30–50 μW/cm²/nm for Group A, 51–100 μW/cm²/nm for Group B and 101–150 μW/cm²/nm for Group C.

Phototherapy was administered using standard phototherapy units equipped with fluorescent or LED lamps. The intensity of phototherapy was carefully adjusted by modifying the number of light sources, optimizing the distance between the light source and the neonate and using multiple phototherapy units when necessary. A calibrated luxmeter was employed to measure and ensure the desired irradiance levels throughout the treatment period. Neonates were exposed to continuous phototherapy, with interruptions only for feeding, cleaning and clinical assessments. Eye protection and appropriate thermal care were ensured during treatment. Serum bilirubin levels were measured at 4 hours after initiation of phototherapy and subsequently at 12-hour intervals to monitor treatment response and guide further management. For neonates presenting with severe hyperbilirubinemia at or near exchange transfusion levels, intensive phototherapy was initiated immediately along with intravenous fluid support. Bilirubin levels were reassessed after 4 hours and exchange transfusion was performed if levels remained within the critical range. If a significant decline was observed, invasive intervention was deferred.

Data collection:
Continuous monitoring of vital parameters, including temperature and weight, was conducted to identify any adverse effects such as dehydration or thermal instability. All clinical data, including phototherapy intensity, duration, rate of bilirubin decline and outcomes were recorded in a standardized data collection format.

Statistical analysis:
Data were entered into Microsoft Excel and analyzed using statistical software. Descriptive statistics were used to summarize baseline characteristics. The primary outcome, namely the rate of reduction in total serum bilirubin, was analyzed using repeated measures ANOVA to compare differences across groups. Regression analysis was employed to determine the threshold and minimum effective intensities of phototherapy. A p-value of <0.05 was considered statistically significant.

Ethical approval:
Study was approved from the Institutional Ethics Committee and written informed consent was secured from parents or legal guardians prior to enrolment. Confidentiality and data protection were maintained throughout the study.

Results:
The study population showed a slight male predominance (52.8%). Male neonates exhibited marginally higher mean total serum bilirubin (TSB) levels compared to females, with both groups demonstrating statistically significant differences. In terms of birth weight distribution, the majority of neonates belonged to the 1.8–2.5 kg category. All birth weight groups showed statistically significant associations with TSB levels. Although differences in mean bilirubin levels across weight categories were minimal, neonates with birth weight >2.5 kg showed slightly higher mean TSB levels, while the <1.8 kg group showed greater variability **(Table 1)**. The majority of neonates in the study were term (63.6%) and these neonates exhibited slightly higher mean total serum bilirubin (TSB) levels compared to preterm neonates, with statistically significant differences. Perinatal asphyxia was present in a small proportion (10%) of cases and was associated with marginally higher bilirubin levels, suggesting a possible contributory role in the severity of hyperbilirubinemia. Exclusive breastfeeding was observed in 67.2% of neonates and was associated with lower mean bilirubin levels compared to those who were not exclusively breastfed, indicating a potential protective effect **(Table 2)**. Sepsis-positive neonates' showed slightly higher mean total serum bilirubin (TSB) levels compared to sepsis-negative neonates, although the difference was modest despite strong statistical significance. Serum albumin levels showed an inverse trend, where neonates with albumin ≥3 g/dL had higher bilirubin levels compared to those with lower albumin levels, suggesting a complex interaction between bilirubin binding and metabolism. Hemolytic disease emerged as a clinically significant factor, with affected neonates exhibiting markedly higher bilirubin levels, highlighting the importance of early identification and aggressive management in such cases. Infants born to mothers with gestational diabetes mellitus (GDM) had slightly lower bilirubin levels compared to those without GDM, although the difference was small. According to AAP classification, the majority of neonates belonged to Group B. Interestingly, Group A showed the highest mean bilirubin levels, while Groups B and

C showed comparatively lower but still elevated levels, reinforcing the importance of risk stratification and tailored phototherapy intensity **(Table 3).** Approximately 18% of neonates fell within the exchange transfusion range and exhibited significantly higher mean total serum bilirubin (TSB) levels, along with a requirement for longer durations of phototherapy. These neonates also showed higher rates of bilirubin reduction, reflecting aggressive treatment response. Among AAP groups, higher phototherapy intensity (Group C) resulted in faster early bilirubin reduction, particularly within the first 12–24 hours, confirming the effectiveness of high-intensity phototherapy. Group B, being the largest cohort, showed a steady and sustained resolution pattern. Preterm neonates showed distinct physiological differences compared to term neonates. While weight gain was significant only in term neonates, preterm neonates exhibited greater thermal instability. In terms of bilirubin resolution, both groups responded similarly during early phototherapy; however, preterm neonates showed relatively better resolution at later time points in severe cases; especially those in the exchange transfusion range **(Table 4).**

Table 1: Combined analysis of gender and birth weight with total serum bilirubin (n = 250)

S. No	Variable	Category	Frequency (n)	Percentage (%)	Mean TSB (mg/dL) ± SD	P Value
1	Gender	Male	132	52.8%	21.60 ± 4.530	<0.0001
		Female	118	47.2%	20.77 ± 3.854	0.0004
2	Birth Weight	<1.8 kg	10	4%	21.00 ± 5.429	0.0023
		1.8 – 2.5 kg	137	54.8%	21.01 ± 3.730	<0.0001
		>2.5 kg	103	41.2%	21.49 ± 4.747	<0.0001

Table 2: Combined analysis of gestational age, perinatal asphyxia and exclusive breastfeeding with total serum bilirubin (n = 250)

S. No.	Variable	Category	Frequency (n)	Percentage (%)	Mean TSB (mg/dL) ± SD	P Value
1	Gestational Age	<37 weeks	91	36.4%	20.81 ± 4.362	<0.0001
		≥37 weeks	159	63.6%	21.44 ± 4.159	0.0034
2	Perinatal Asphyxia	Yes	25	10%	21.376 ± 4.741	<0.0001
		No	225	90%	21.19 ± 4.188	<0.0001
3	Exclusive Breastfeeding	Yes	168	67.2%	20.94 ± 4.152	0.0002
		No	82	32.8%	21.76 ± 4.378	<0.0001

Table 3: Combined analysis of clinical factors with total serum bilirubin (n = 250)

S. No.	Variable	Category	Frequency (n)	Percentage (%)	Mean TSB (mg/dL) ± SD	P Value
1	Sepsis Screening	Positive	54	21.6%	21.54 ± 4.46	<0.0001
		Negative	196	78.4%	21.12 ± 4.18	<0.0001
2	Serum Albumin (g/dL)	<3	81	32.4%	20.47 ± 4.06	<0.0001
		≥3	169	67.6%	21.56 ± 4.28	<0.0001
3	Hemolytic Disease	Yes	36	14.4%	23.56 ± 5.20	0.0072
		No	214	85.6%	20.85 ± 3.92	<0.0001
4	Maternal GDM	Yes	25	10%	20.46 ± 4.03	0.0196
		No	225	90%	21.29 ± 4.26	<0.0001
5	AAP Study Group	Group A (30–50)	54	21.6%	22.59 ± 1.94	0.0002
		Group B (51–100)	110	44%	20.50 ± 4.78	<0.0001
		Group C (101–150)	86	34.4%	21.25 ± 4.37	<0.0001

Table 4: Combined analysis of exchange transfusion, phototherapy response and clinical parameters (n = 250)

S. No.	Variable / Group	Category / Duration	N	Mean TSB (mg/dL) ± SD	Phototherapy Hours (Mean ± SD)	Rate of Resolution (Mean)	P Value
1	Exchange Transfusion	Yes	45	27.38 ± 3.27	29.86 ± 10.43	Higher across all time points	0.0278
		No	205	21.21 ± 4.24	17.20 ± 6.64	Lower resolution rates	<0.0001
2	AAP Group A	30–50 µW/cm²/nm	54	22.59 ± 1.94	17.77 ± 6.05	4h: 0.44, 12h: 0.52, 24h: 0.41	0.0002
3	AAP Group B	51–100 µW/cm²/nm	110	20.50 ± 4.78	19.52 ± 10.26	4h: 0.48, 12h: 0.55, 24h: 0.49, 48h: 0.37	<0.0001
4	AAP Group C	101–150 µW/cm²/nm	86	21.25 ± 4.37	20.51 ± 8.41	4h: 0.52, 12h: 0.65, 24h: 0.53, 48h: 0.43	<0.0001
5	Weight Change (<37 weeks)	Admission vs Discharge	–	–	–	Minimal change	0.1416
	Weight Change (≥37 weeks)	Admission vs Discharge	–	–	–	Slight increase	0.045
6	Temperature (<37 weeks)	Admission vs Discharge	–	–	–	Decrease noted	<0.0001
	Temperature (≥37 weeks)	Admission vs Discharge	–	–	–	Mild variation	0.046
7	Group B Resolution	Preterm versus Term	–	–	–	Similar at 4–24h; delayed at 48h	>0.05
8	Group C Resolution	Preterm versus Term	–	–	–	Comparable across intervals	>0.05
9	Exchange Range Resolution	Preterm versus Term	–	–	–	Higher in preterm at 24h & 48h	<0.05

Discussion:

Neonatal hyperbilirubinemia continues to be a major cause of neonatal morbidity in all countries all over the world, especially in developing countries where the early identification and the best management practices might not be available. The current research assessed the intensity of phototherapy in the correction of hyperbilirubinemia and the different clinical and demographic variables that affect the total serum bilirubin (TSB) levels. In the current study, there was a small male dominance (52.8) with male newborns showing greater mean TSB levels than female newborns. This observation is in line with other studies that have indicated a greater prevalence and severity of neonatal jaundice in males, which could be attributed to genetic and hormonal factors that influence bilirubin metabolism **[2]**. The difference is not significant, but the statistical significance indicates that there is a biological trend and not merely a coincidence. The analysis of birth weight showed that most of the neonates were in the 1.8-2.5 kg range. Although the TSB varied slightly between weight groups, the higher the birth weight of the neonates (>2.5 kg), the higher the bilirubin levels. Other previous studies have given similar results with the higher bilirubin levels in normal-weight neonates being explained by higher bilirubin production because of the larger mass of red blood cells. Nonetheless, low birth weight babies were more variable, indicating their physiological instability and bilirubin kinetic changes **[4]**. Another factor that was found to have an impact on bilirubin levels was gestational age. Term neonates (37 weeks and above) had a slightly higher mean level of TSB than preterm neonates. This fact might seem counterintuitive, because preterm babies are typically regarded as being more prone to hyperbilirubinemia. Nevertheless, it has been proposed by other researchers that preterm babies are more prone to bilirubin toxicity, but term babies may have higher absolute bilirubin because of more active haemolysis and enterohepatic circulation **[6]**. Also, preterm neonates tend to have lower clinical thresholds of intervention, which results in the initiation of treatment earlier. There was perinatal asphyxia in 10% of the study population and marginally higher levels of TSB. Hypoxic damage may damage hepatic performance and decrease bilirubin conjugation, thus adding to the high bilirubin levels **[7]**. The difference found in this study was minimal, but it is still clinically significant, particularly in critically ill neonates where numerous factors can have a synergistic effect. Exclusive breastfeeding had lower mean bilirubin levels than non-exclusively breastfed infants. This observation is contrary to the notion of breastfeeding jaundice which is generally associated with insufficient consumption during the early neonatal stage. Nevertheless, successful and regular breastfeeding will improve intestinal motility and decrease enterohepatic bilirubin circulation, thus making it easier to clear **[9]**. This study has found that optimal breastfeeding practices have a protective effect in the management of neonatal jaundice. Sepsis screening positivity was found to be slightly correlated with TSB levels among clinical factors. The mechanisms that can cause hyperbilirubinemia in neonatal sepsis include haemolysis, hepatic dysfunction and elevated inflammatory cytokines **[10]**. Even though the difference was not statistically significant, its statistical significance shows the significance of screening sepsis among neonates with unexplained or persistent jaundice. Interestingly, serum albumin levels were correlated with bilirubin levels. The TSB levels were higher in neonates with albumin 3g/dl and above than in those with low albumin levels. Albumin is important in binding and transfer of bilirubin, but total serum bilirubin might not be a good indicator of free bilirubin which is more clinically important regarding neurotoxicity **[11]**. Thus, the result highlights the multifaceted nature of bilirubin metabolism and the importance of laboratory values interpretation. The most clinically important determinant of high bilirubin levels was found to be haemolytic disease and the levels of TSB were significantly higher in affected neonates. This is in line with the existing evidence that haemolysis results in high bilirubin production because of the rapid destruction of red blood cells **[12]**. Haemolytic conditions ABO or Rh incompatibility should be identified early to avoid severe hyperbilirubinemia and its complications. Maternal gestational diabetes mellitus (GDM) was linked to a marginally reduced TSB level of neonates. Despite the inconsistent results of the earlier studies, it is postulated that the changes in metabolism of infants born to diabetic mothers could affect the bilirubin production and clearance **[13]**. This association is not yet clinically significant, although it indicates the importance of taking maternal factors into account when assessing the neonatal. The comparison of AAP phototherapy groups showed that more intense phototherapy (Group C) led to a faster bilirubin decrease, especially during the initial hours of treatment. This result is in line with the existing recommendations that suggest intensive phototherapy in severe hyperbilirubinemia **[14]**. Higher irradiance increases bilirubin conversion to excretable forms and thus increases bilirubin clearance **[15].** The highest proportion of neonates (Group B) exhibited a sustained and consistent response, indicating its involvement in moderate cases. In this study, about 18 percent of the neonates fell within the exchange transfusion range and had much higher levels of TSB and a longer duration of phototherapy needs. These babies also exhibited greater bilirubin reduction rates, which is probably because of high-intensity phototherapy. Other researchers have also made similar findings, with aggressive phototherapy decreasing the necessity of exchange transfusion **[16]**. Comparison of term and preterm babies showed significant physiological differences. The weight gain of term neonates was significantly observed during hospitalization and preterm neonates did not show any significant changes, which is indicative of their increased metabolic needs and susceptibility **[17]**. The changes in temperature were greater in preterm a baby, which means that they have a poor thermoregulatory ability. Both term and preterm babies responded equally in the initial stages of phototherapy in terms of bilirubin resolution. Nevertheless, preterm infants showed improved resolution at subsequent time points in severe instances, especially in the exchange transfusion

range. This can be explained by the fact that the management is more aggressive and monitors more closely in this high-risk group **[18]**. In general, the results of the present study indicate that the intensity of phototherapy is of utmost importance when it comes to the treatment of neonatal hyperbilirubinemia. High-intensity phototherapy is much faster than bilirubin clearance, shortens the treatment period and can also help to minimize invasive treatments like exchange transfusion. Also, several clinical variables, such as haemolysis, sepsis, gestational age and feeding habits, affect bilirubin levels and treatment outcomes.

Conclusion:

Phototherapy intensity critically determines neonatal hyperbilirubinemia treatment with higher intensities (40-50 μW/cm²/nm) accelerating bilirubin clearance within 24 hours for preventing exchange transfusion needs. Preterm neonates require more intense and prolonged phototherapy compared to term infants, while clinical factors like gestational age and feeding practices significantly influence outcomes. Personalized intensity-based phototherapy protocols optimized by risk stratification maximize clinical efficacy and neonatal safety across diverse hyperbilirubinemia presentations.

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