ORIGINAL RESEARCH

Comparison of Transcutaneous Bilirubin with Total Serum Bilirubin Levels Before, During, and Post-phototherapy in Preterm and Term Newborns in Uttarakhand, India

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Abstract

Background: Neonatal jaundice, although generally benign, can pose a significant threat to a select number of newborns, potentially resulting in severe brain damage or even death.

Objectives: To compare the transcutaneous bilirubin (TCB) with total serum bilirubin (TSB) levels before, during the phototherapy on a covered definite spot of skin and after 2 days of post-phototherapy in preterm and term newborns.

Materials and methods: A total of 272 babies, who had jaundice, admitted to NICU of Sahota Superspeciality Hospital, Kashipur, Uttarakhand, India, were enrolled in the study during the period March 2018 to February 2020. Transcutaneous bilirubin and TSB were done in all the babies and compared before starting phototherapy, during phototherapy, and after 48 hours of stopping the phototherapy.

Results: Before phototherapy (PT)-TCB showed statistically significant positive correlation with before PT-TSB. During PT-TCB showed statistically significant positive correlation with PT-TSB. After PT-TCB showed statistically significant positive correlation. Bilirubin level measured by TCB and TSB method was statistically significantly comparable before, during, and after PT ($p > 0.05$).

Conclusion: There is a significant positive correlation between TCB and TSB in preterm and term newborns who required phototherapy for hyperbilirubinemia, before starting the phototherapy, during phototherapy, and after 48 hours of its stoppage.

Clinical significance: Transcutaneous bilirubin is a good tool to do screening for hyperbilirubinemia. TCB can be used as a noninvasive tool to assess bilirubin during and after phototherapy.

Keywords: Bilirubin, Newborn, Phototherapy, Transcutaneous bilirubin, Total serum bilirubin.

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Introduction

Hyperbilirubinemia is a common occurrence in both full-term and premature newborns, affecting approximately 60% of all newborns.[1] It is primarily a result of their increased bilirubin production and limited capacity to excrete it.[2] The majority of cases of newborn jaundice are mild and typically resolve on their own. However, in rare instances, infants may develop extremely high bilirubin levels, which can lead to a condition known as bilirubin encephalopathy and kernicterus which can result in high mortality and long-term complications, such as athetoid cerebral palsy, high-frequency hearing loss, and intellectual disability.[3,4] Early detection and appropriate management are crucial to prevent such complications. Estimating serum bilirubin levels through visual inspection of the skin is a quick and cost-effective method, but it is prone to errors, even when performed by experienced clinicians.[5]

Neonatal jaundice is a frequently-seen reason for hospital admission during the first week after birth and is primarily caused by hyperbilirubinemia.[6,7] Prompt monitoring of serum bilirubin levels and early intervention through methods like phototherapy or exchange blood transfusion can effectively prevent severe neonatal hyperbilirubinemia and its associated complications.[8]

Traditionally, total serum bilirubin (TSB) measured by a biochemical laboratory has been considered the gold standard for bilirubin level measurement. However, this method is invasive, involving needle pricks that carry infection risks and cause discomfort to neonates.[6] Additionally, the time required to obtain TSB results can delay the initiation of hyperbilirubinemia therapy.

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In recent years, transcutaneous bilirubinometers have emerged as a non-invasive alternative for estimating bilirubin levels. These portable devices use photometry to measure bilirubin levels by gently pressing a probe against the neonate's forehead or sternum. They provide immediate results, enabling swift treatment initiation and reducing the burden on healthcare providers.[9]

Current research regarding the accuracy of transcutaneous bilirubinometer measurements based on different skin locations

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and time intervals after phototherapy is inconclusive.[10,11] Previous studies focused on various locations or time points separately and did not offer comprehensive results within a single study. Long waiting times may lead to inadequate phototherapy and treatment delays.[12] Therefore, the present study was conducted with aim to compare the transcutaneous bilirubin (TCB) with TSB levels before, during the phototherapy on a covered definite spot of skin and after 2 days of post-phototherapy in preterm and term newborns.

Materials and Methods

We performed a prospective observational study of all babies admitted to NICU of Sahota Superspeciality Hospital Kashipur, Uttarakhand, India during the period March 2018 to February 2020. During this study period, the 272 infants were divided in two groups: group A: Preterm babies ($n = 136$) and group B: term babies ($n = 136$).

The study included all preterm and term neonates with hyperbilirubinemia, who were admitted in the NICU satisfying the inclusion and exclusion criteria during the study period. The informed consent of the parents/relatives were taken before enrolling them in the study. The clinical profile of babies like demographic data, antenatal history, including relevant maternal diseases or complications during pregnancy, detailed history with feeding details, examination, and diagnosis was noted in a preformed pro forma. The discretion to use phototherapy for each case was taken by the attending neonatologist based on the hospital criteria. All babies were kept naked with diaper alone, to allow maximum skin exposure to phototherapy. Eye protection was used during the treatment. Phototherapy was given using ZEAL LED standard phototherapy units. Phototherapy was interrupted only for feedings breaks. It was stopped only once the TSB levels goes below the threshold of treatment. Total duration required for completion of phototherapy was documented in the information sheet of each patient.

Percentage was used to analyze data. The data were recorded in an Excel sheet and descriptive analysis was performed by Epi.Info. Sotware 7.2. Data were presented in the tables.

Material Used and Location Chosen

A circular photo-opaque patch around 2.5 cm in diameter, made from Maxicor electrode which was covered on one side with aluminum foil and the other side with an adhesive was used for covering the lower part of sternum.

Phototherapy Unit Used

Phototherapy unit was used in the treatment was zeal—LED continuous special neo blue light which emits a wavelength of 400–550 nm. Dominant wavelength range was 450–465 nm at peak irradiance of 45 μw/cm^2/nm.

TSB and TCB Estimation Techniques and Devices

All TSB values were obtained from intravenous samples of blood through fully automated spectrophotometer. TCB values were obtained using the latest version of Drager JM-105 which was the instrument used for it. This device was calibrated before usage according to manufacturer's recommendation.

Inclusion Criteria

All term and preterm newborn with hyperbilirubinemia. The exclusion criteria include parents or relatives who were not willing to give consent for research and neonates who received the exchange blood transfusion.

Table 1: Sociodemographic characteristic of study participants ($N = 272$)

Variable	*Number*	*%*
Gestational age (in week)		
<28	11	4.1
28.0–31.6	33	12.0
32.0–36.6	104	38.4
≥37.0	124	45.6
Mode of delivery		
Normal	129	47.4
LSCS	143	52.6
Gender		
Male	156	57.4
Female	116	42.6
Birth weight (in kg)		
<1.00	11	3.9
1.00–1.49	30	11.2
1.50–2.49	127	46.7
≥2.50	104	38.2
Time of passage of first stool (in hour)		
0–6	0	0.0
6–12	0	0.0
13–18	124	45.7
19–24	148	54.3
Duration of phototherapy (in hour)		
48	90	33.0
72	114	42.0
96	68	25.0

Results

Table 1 depicts that 4.1, 12.0, 38.4, and 45.6% of participants were noted with gestational age <28, 28–31, 32–36, and ≥37 weeks, respectively. Almost 47.4% of babies were delivered by normal vaginal delivery and 52.6% of babies were by LSCS. Around 57.4% of babies were male and 42.6% were female. Almost 3.9, 11.2, 46.7, and 38.2% participants noted with birth weight <1, 1–1.49, 1.50–2.49, ≥2.50 kg, respectively. Almost 0, 0, 45.7, and 54.3% of babies passed the first stool at 0–6, 6–12, 13–18, 19–24 hours after birth, respectively. Around 33, 42, and 25% of babies received phototherapy for 48, 72, and 96 hours, respectively.

Table 2 presents that the mean duration of phototherapy was 53.3 minutes with 12.9 SD and 79.2 minutes with 17.1 SD in babies who passed the first stool after birth at 13–18 and 19–24 hours, respectively. The difference in the meantime of phototherapy according to the time of passage of first stool was statistically significant ($p < 0.05$). The mean duration of phototherapy was 59.1 minutes with 18.1 SD and 70.3 minutes with 18.4 SD in babies whose weight loss after birth <5% and >5%, respectively. The difference in the meantime of phototherapy according to the weight loss was statistically significant ($p < 0.05$). The mean duration of phototherapy was 67.7 minutes with 18.9 SD and 69.9 minutes with 18 SD in babies delivered by normal and LSCS method, respectively. The difference in the meantime of phototherapy

Table 2: Association between 'Mean duration of PT' with different clinical parameters (*N* = 272)

Parameters	*PT (mean ± SD)*	*p-value*
Time of passage of first stool (in hour)		
13–18	53.3 ± 12.9	**0.001***
19–24	79.2 ± 17.1	
Weight loss (%)		
<5%	59.1 ± 18.1	**0.017***
>5%	70.3 ± 18.4	
Mode of delivery		
Normal	61.7 ± 18.9	0.248*
LSCS	69.9 ± 18.0	
Type of feeding		
Total parenteral nutrition (TPN)	74.4 ± 15.9	0.098**
Nasogastric tube (NGT)	63.3 ± 15.8	
Orogastric tube (OGT)	77.1 ± 21.0	
Breastfeeding (BF)	61.9 ± 14.9	

*Student's *t*-test, **One way ANNOVA test. *p*-values < 0.05 will be taken as significant

Table 3: Comparison of "mean bilirubin level" measured by TCB and TSB method at before, during, and after PT (*N* = 272)

	Bilirubin levels (mg/dL)		
PT	*TCB*	*TSB*	*p-value**
Before PT	14.62 ± 2.98	14.71 ± 3.0	**0.01**
During PT	7.49 ± 1.94	7.29 ± 1.91	**0.03**
After PT	11.52 ± 4.36	11.43 ± 4.39	**0.001**

*Student's *t*-test. *p*-values < 0.05 will be taken as significant

according to the mode of delivery was statistically not significantly different ($p > 0.05$). The mean duration of phototherapy was 74.4 minutes with 15.9 SD, 63.3 minutes with 15.8 SD, 77.1 minutes with 21.0 SD and 61.9 minutes with 14.9 SD in babies fed by TPN, NGT, OGT, and BF method, respectively. The difference in the meantime of phototherapy according to the type of feeding was statistically not significant ($p > 0.05$).

Table 3 depicts that the mean value of TCB was 14.62 mg/dL with 3.2 SD, 7.49 mg/dL with 1.94 SD, and 11.52 mg/dL with 4.36 SD and the mean value of TSB was 14.71 mg/dL with 3.0 SD, 7.29 mg/dL with 1.94 SD, and 11.43 mg/dL with 4.39 SD at before PT, during PT, and after PT, respectively. The difference in the mean value of TCB and TSB at before PT, during PT, and after PT was statistically significant ($p < 0.05$).

Table 4 illustrates that the mean value of TCB in preterm babies was 14.86 mg/dL with 3.2 SD, 6.85 mg/dL with 1.67 SD, and 10.13 mg/dL with 4.01 SD; and in term babies, it was14.29 mg/dL with 2.47 SD, 8.42 mg/dL with 1.94 SD, and 13.55 mg/dL with 4.08 SD at before PT, during PT, and after PT, respectively. The mean TSB values did not differ prior to initiation of phototherapy but were significantly different during and after phototherapy. The mean value of TSB in preterm babies was 14.96 mg/dL with 3.32 SD, 6.6 mg/dL with 1.59 SD, and 10.09 mg/dL with 3.31 SD; and in term babies, it was14.34 mg/dL with 2.47 SD, 8.28 mg/dL with 1.92 SD, and 13.45 mg/dL with 4.14 SD at before PT, during PT, and after PT, respectively. The difference in the mean value of TSB of preterm and term babies at during PT and after PT was statistically significant ($p < 0.05$) and statistically not significant at before PT ($p > 0.05$).

Table 4: Comparison of "mean bilirubin level according to gestational term" measured by TCB and TSB method at before, during, and after PT (*N* = 272)

	Bilirubin levels (mg/dL)		
PT	*Preterm*	*Term*	*p-value**
TCB			
Before PT	14.86 ± 3.2	14.29 ± 2.47	0.327
During PT	6.85 ± 1.67	8.42 ± 1.94	**0.001**
After PT	10.13 ± 4.01	13.55 ± 4.08	**0.001**
TSB			
Before PT	14.96 ± 3.32	14.34 ± 2.47	0.287
During PT	6.60 ± 1.59	8.28 ± 1.92	**0.001**
After PT	10.09 ± 3.32	13.45 ± 4.14	**0.001**

*Student's *t*-test. *p*-values < 0.05 will be taken as significant

Figure 1 shows that before PT-TCB showed statistically significant positive correlation with before PT-TSB with very high Pearson's *r*- value of 0.999 ($p < 0.05$). During PT-TCB showed statistically significant positive correlation with during PT-TSB with very high Pearson's *r*-value of 0.973 ($p < 0.05$). The after PT-TCB showed statistically significant positive correlation with after PT-TSB with very high Pearson's *r*-value of 0.999 ($p < 0.05$).

Discussion

In the present study, more than half of all cases (54%) were born prior to 37 weeks of gestational age. Fifty-two percent were delivered by lower segment cesarean section (LSCS). Because our center was a tertiary care referral center for mostly high-risk pregnancies, the incidence of LSCS births was significant in our study. Of the 272 cases studied, 57.4% were male and 42.6% were female. The birth weights of 46.7% of the 272 newborns tested ranged from 1.5 to 2.49 kg.

Fifty-four percent of infants in our study passed their first stool in the 18–24 hour period after birth. The overall duration of phototherapy was longer when stool transit was delayed. We discovered that the mean duration of phototherapy in these babies was 79 hours, compared to 59 hours in those who passed their first stool before 18 hours after birth. Meconium includes a high concentration of bilirubin, and its retention causes an increase in enterohepatic circulation, which contributes to neonatal hyperbilirubinemia.

The present study found that bilirubin level measured by TCB and TSB method was significantly comparable before, during, and after PT ($p > 0.05$). We found satisfactory results on the utility of TCB as a screening tool in our work, similar to those previously described. Our study further added that TCB is a reliable noninvasive tool in measurement of bilirubin during and after phototherapy when used to measure bilirubin in a covered site.

In this study, we discovered that the overall duration of phototherapy increased when the percentage of weight loss was more than 5%; the mean duration of phototherapy required in these babies was 70 hours as compared with those babies who had weight loss <5% requiring phototherapy for 59 hours of duration. These findings showed a statistically significant positive correlation. But we did not compare this with babies who had similar weight loss and had not developed hyperbilirubinemia. In the present study, there was no significant association between the mode of delivery and the type of feeding with the duration of phototherapy.

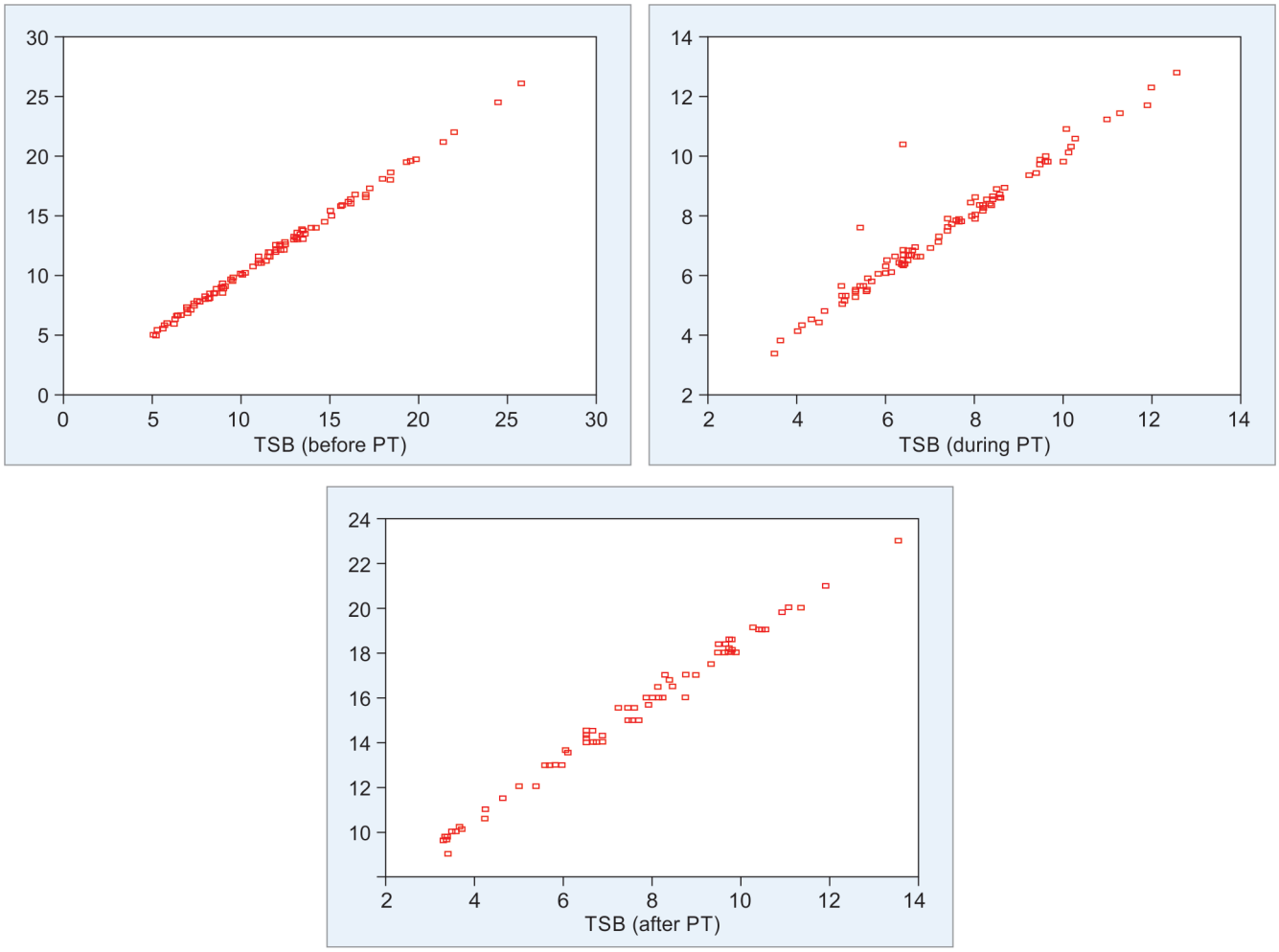

Fig. 1: Correlation between TCB and TSB method according to 'mean bilirubin level' at before, during and after PT ($N = 111$)

The present study revealed that the bilirubin level was significantly lower in preterm babies after starting of phototherapy and also after completion of phototherapy in both the TCB and TSB groups.

A 2017 prospective study conducted in the Haitian newborn population, in alignment with our findings, compared TCB and TSB levels during phototherapy. In this study, a good agreement was observed between the two methods. Transcutaneous bilirubin measurements could be a viable option for guiding jaundice treatment in regions where serum bilirubin tests are not widely available.[13]

Another study conducted in Iran partially supported our study's findings. It involved 134 full-term and 36 preterm newborns who received phototherapy and concluded that TCB measurements could be safely used to evaluate bilirubin levels in both preterm and full-term newborns receiving phototherapy, with slightly lower reliability in preterm newborns.[14] A meta-analysis in 2019 assessed the reliability of TCB measurements in premature newborns. It included 29 studies and concluded that TCB values obtained from the forehead and sternum regions were well correlated with TSB levels, making it a reliable method for assessing hyperbilirubinemia in premature newborns.[15] Furthermore, in a study by Vasava S and Dagli.[16] involving 306 full-term and preterm newborns, TCB measurements strongly predicted TSB levels across different gestational weeks and body regions. Similarly, Amneah A.[17] conducted a study with 80 newborns who received phototherapy by placing a patch on their skin. They reported a strong correlation between TCB values from the patched skin and TSB levels.

Conclusion

We noted a significant positive correlation between TCB and TSB in preterm and term newborns who required phototherapy for hyperbilirubinemia. Hence, in future, TSB measurements can be replaced by TCB measurements for monitoring bilirubin levels in neonates suffering from hyperbilirubinemia, as TCB measurement is a reliable, noninvasive method.

The overall duration of phototherapy increased when stool transit was delayed and percentage of weight loss was more than 5% but there is no significant correlation between other risk factors like mode of the delivery, type of feeding, and change in the color of the stool. All clinical parameters were assessed in babies already having hyperbilirubinemia. But these clinical parameters were not assessed and compared with healthy newborn.

Clinical Significance

Transcutaneous bilirubin is a good tool to do screening for hyperbilirubinemia. Transcutaneous bilirubin can be used as a noninvasive tool to assess bilirubin during and after phototherapy.

Ethical Approval

The study was approved by the Institutional Ethics Committee.

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