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Correlation Between Transcutaneous and Total Serum Bilirubin in Term and Late-Preterm Neonates Before and During Phototherapy: A Prospective Observational Study.

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Abstract

Background: Estimation of total serum bilirubin (SBR) by venepuncture is the reference standard for assessing neonatal hyperbilirubinemia but is invasive, painful, and repetitive. Transcutaneous bilirubinometry (TCB) offers a non-invasive alternative, yet its reliability during phototherapy remains debated. This study assessed the correlation between TCB and SBR in term and late-preterm neonates before and during phototherapy. ***Materials and methods:*** A prospective observational study was conducted in the Department of Pediatrics, Rainbow Children's Hospital, Vijayawada, from January 2021 to July 2021. Term and late-preterm (≥34 weeks) neonates aged 0–29 days with clinically suspected significant hyperbilirubinemia requiring bilirubin measurement were enrolled. TCB was measured using a Dräger JM-105 jaundice meter over the glabella, sternum, and pubic symphysis; SBR was measured by the diazo method. During phototherapy, TCB was measured over patched (covered) skin. Paired TCB and SBR values were compared before and during phototherapy, and Pearson's correlation coefficient (r) was computed. A p-value <0.05 was considered statistically significant. ***Results:*** Of 230 neonates enrolled, 35 were excluded and 195 were analyzed. Term neonates comprised 162 (83.1%) and late-preterm 33 (16.9%); 104 (53.3%) were male. Before phototherapy, mean TCB was 17.13 ± 2.27 mg/dL and mean SBR 17.36 ± 2.71 mg/dL, with a strong correlation ($r = 0.946$, $p < 0.001$). During phototherapy, mean TCB was 12.79 ± 2.79 mg/dL and mean SBR 12.66 ± 2.80 mg/dL ($r = 0.953$, $p < 0.001$). Strong, statistically significant correlations were maintained across subgroups defined by gestational age and postnatal age (all $p < 0.001$). ***Conclusions:*** TCB showed a strong, statistically significant correlation with SBR in both term and late-preterm neonates before and during phototherapy when measured over covered skin. Transcutaneous bilirubinometry can serve as a reliable non-invasive tool for screening before phototherapy and for monitoring bilirubin during phototherapy to help decide when to discontinue treatment.

Keywords: neonatal hyperbilirubinemia; transcutaneous bilirubin; total serum bilirubin; phototherapy; late-preterm; jaundice.

INTRODUCTION

Neonatal hyperbilirubinemia is one of the most common causes of hospital readmission in the first week of life, affecting approximately 60% of term and 80% of late-preterm newborns [1]. It results from accumulation of unconjugated, lipid-soluble bilirubin in the skin and is a preventable cause of brain injury when total serum bilirubin (SBR) rises above treatment thresholds. Although most cases are benign, an estimated 5–10% develop clinically significant hyperbilirubinemia requiring phototherapy, and untreated severe hyperbilirubinemia can progress to acute bilirubin encephalopathy and kernicterus [1,9]. Measurement of SBR is the reference standard for detecting and quantifying hyperbilirubinemia, but it is invasive, costly, and time-consuming, and requires repeated venepuncture. Repeated blood sampling in neonates carries risks of iatrogenic anemia, pain, and infection [8]. Transcutaneous bilirubinometry (TCB), first described by Yamanouchi et al. in 1980, is a non-invasive, rapid, and reproducible method that estimates bilirubin by analysing the reflectance spectrum of light from the skin and subcutaneous tissue [1,6].

TCB can reduce the need for blood sampling and generally shows a linear correlation with SBR, and its use has been incorporated into clinical practice guidelines for the management of neonatal jaundice [7,8]. However, the correlation between TCB and SBR is influenced by gestational age, birth weight, skin colour, degree of jaundice, race, and—

importantly—the use of phototherapy. Reports on the reliability of TCB during phototherapy have been inconsistent: some studies show good agreement over covered (patched) skin, while others find reduced sensitivity, particularly in preterm infants [13,18,24,26]. Because of this variability, individual neonatal units have been advised to establish their own correlation data. This study was therefore undertaken to determine the correlation between TCB and SBR in term and late-preterm neonates both before starting phototherapy and during phototherapy over covered skin.

MATERIALS AND METHODS

Study design and setting

This prospective observational study was conducted in the Department of Pediatrics, Rainbow Children's Hospital, Vijayawada, Andhra Pradesh, India, over a seven-month period from January 2021 to July 2021. The study was approved by the Institutional Ethics Committee, and written informed consent was obtained from a parent or guardian of each participating neonate.

Participants and eligibility

Term and late-preterm neonates aged 0–29 days, born at or referred to the hospital, who developed jaundice within the first 10 days of life and were clinically suspected to have significant hyperbilirubinemia requiring bilirubin measurement (including those with ABO or Rh incompatibility) were eligible. Neonates receiving phototherapy were included. Exclusion criteria were: parental refusal of consent; gestational age <34 weeks; sick neonates; conjugated hyperbilirubinemia; and neonates in the immediate post-exchange-transfusion period.

Sample size

A total of 230 neonates were enrolled; 35 were excluded on the basis of the exclusion criteria, leaving 195 neonates for analysis. Paired TCB and SBR values were compared before phototherapy and during phototherapy for all 195 neonates.

Measurements

After clinical assessment using a pre-structured proforma, blood for SBR estimation and TCB readings were obtained as soon as jaundice was detected. SBR was measured by the diazo (Van den Bergh) method, with blood drawn from a peripheral vein within half an hour of the TCB reading. TCB was measured using a Dräger Jaundice Meter Model JM-105 (measuring range 0.0–20 mg/dL), which determines the yellowness of subcutaneous tissue from the optical density difference at two wavelengths. The fibre-optic probe was applied vertically to the glabella, sternum, and pubic symphysis until a click was heard, and the mean of three readings was recorded. The probe was disinfected with 70% isopropyl alcohol between neonates. For neonates receiving phototherapy, readings were taken over patched (covered) skin at the sternum and pubic symphysis, with the eyes covered by an eye pad and the genitalia by a diaper. Neonates requiring phototherapy based on Bhutani nomogram thresholds were treated with Phoenix Brilliance and GE phototherapy units, and sequential SBR and TCB readings were recorded.

Statistical analysis

Data were analysed using SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation (SD) and categorical variables as frequencies and percentages. Pearson's correlation coefficient (r) was used to assess the correlation between TCB and SBR. A p-value <0.05 was considered statistically significant.

RESULTS

During the study period, 230 neonates were enrolled and 195 were analysed after exclusions. Of the 195 neonates, 162 (83.1%) were term and 33 (16.9%) were late-preterm; 104 (53.3%) were male and 91 (46.7%) female. Eighty-nine (45.5%) presented within 72 hours of life and 106 (54.5%) after 72 hours; 155 (79.5%) had a birth weight ≥2.5 kg and 40 (20.5%) <2.5 kg (Table 1). The distribution by gestational age and gender is shown in Table 2.

Table 1: Descriptive characteristics of the study group (N = 195)

Variable	Frequency (n)	Percentage (%)
Late-preterm	33	16.93
Term	162	83.07
Male	104	53.33
Female	91	46.67
Age of presentation <72 h of life	89	45.50
Age of presentation >72 h of life	106	54.50
Birth weight <2.5 kg	40	20.51
Birth weight ≥2.5 kg	155	79.49

Table 2: Distribution of the study group by gestational age and gender

Gestational age	Male, n (%)	Female, n (%)	Total, n (%)
Late-preterm	16 (15.38)	17 (18.68)	33 (16.92)
Term	88 (84.62)	74 (81.32)	162 (83.08)
Total	**104 (100)**	**91 (100)**	**195 (100)**

The descriptive statistics of TCB and SBR before and during phototherapy are presented in Table 3. Before phototherapy, TCB ranged from 8.20 to 20.00 mg/dL (mean 17.13 ±2.27) and SBR from 8.30 to 22.80 mg/dL (mean 17.36 ±2.71). During phototherapy, TCB ranged from 6.60 to 20.00 mg/dL (mean 12.79 ±2.79) and SBR from 5.60 to 21.20 mg/dL (mean 12.66 ±2.80).

Table 3: Descriptive statistics of TCB and SBR before and during phototherapy (N = 195)

Measurement	Minimum	Maximum	Mean	SD
TCB before phototherapy	8.20	20.00	17.13	2.27
SBR before phototherapy	8.30	22.80	17.36	2.71
TCB during phototherapy	6.60	20.00	12.79	2.79
SBR during phototherapy	5.60	21.20	12.66	2.80

TCB: transcutaneous bilirubin; SBR: serum bilirubin; SD: standard deviation. Values in mg/dL.
Comparison of characteristics between term and late-preterm neonates is shown in Table 4. The mean age at presentation was 72.84 ±21.11 h in late-preterm and 75.66 ±19.77 h in term neonates; mean birth weight was 2.57 ±0.36 kg and 2.87 ±0.27 kg, respectively.

Table 4: Comparison of characteristics between term and late-preterm neonates before phototherapy

Characteristic	Late-preterm (mean ±SD)	Term (mean ±SD)
Age (hours)	72.84 ±21.11	75.66 ±19.77
Weight (kg)	2.57 ±0.36	2.87 ±0.27
TCB (mg/dL)	16.40 ±2.54	17.28 ±2.18
SBR (mg/dL)	16.33 ±3.01	17.56 ±2.60

TCB: transcutaneous bilirubin; SBR: serum bilirubin; SD: standard deviation.

Correlation between TCB and SBR in the whole study group

For the whole group, TCB and SBR were strongly correlated both before phototherapy (r = 0.946, p < 0.001) and during phototherapy (r = 0.953, p < 0.001), with a positive linear relationship in both settings (Table 5).

Table 5: Correlation between TCB and SBR before and during phototherapy in the whole study group (N = 195)

Measurement	Mean	SD	p-value	r
TCB before phototherapy	17.13	2.27	<0.001	0.946
SBR before phototherapy	17.36	2.71		
TCB during phototherapy	12.79	2.79	<0.001	0.953
SBR during phototherapy	12.66	2.80		

TCB: transcutaneous bilirubin; SBR: serum bilirubin; SD: standard deviation; r: Pearson's correlation coefficient. Values in mg/dL.

Correlation by gestational age and postnatal age

Strong, statistically significant correlations were maintained in all subgroups (Table 6). Among late-preterm neonates, r was 0.953 before and 0.931 during phototherapy; among term neonates, r was 0.943 before and 0.958 during phototherapy.

When stratified by postnatal age, neonates presenting at <72 h had r = 0.920 before and 0.931 during phototherapy, while those presenting at >72 h had r = 0.918 before and 0.953 during phototherapy (all p < 0.001).

Table 6: Correlation between TCB and SBR by gestational age and postnatal age subgroups

Subgroup	n	Measurement (mean ±SD, mg/dL)	r	p-value
Late-preterm, before PT	33	TCB 16.40 ±2.54 / SBR 16.34 ±3.02	0.953	<0.001
Late-preterm, during PT	33	TCB 11.78 ±2.81 / SBR 11.36 ±2.64	0.931	<0.001
Term, before PT	162	TCB 17.28 ±2.18 / SBR 17.56 ±2.61	0.943	<0.001
Term, during PT	162	TCB 12.99 ±2.75 / SBR 12.92 ±2.77	0.958	<0.001
<72 h, before PT	89	TCB 15.54 ±1.99 / SBR 15.50 ±2.14	0.920	<0.001
<72 h, during PT	89	TCB 11.61 ±2.23 / SBR 11.37 ±2.24	0.931	<0.001
>72 h, before PT	106	TCB 18.47 ±1.48 / SBR 18.91 ±2.10	0.918	<0.001
>72 h, during PT	106	TCB 13.77 ±2.84 / SBR 13.74 ±2.77	0.953	<0.001

PT: phototherapy; TCB: transcutaneous bilirubin; SBR: serum bilirubin; SD: standard deviation; r: Pearson's correlation coefficient.

Comparison by mode of delivery

Mean TCB and SBR values before phototherapy were comparable between neonates delivered vaginally and by lower-segment caesarean section (LSCS): TCB 17.28 vs. 17.02 mg/dL and SBR 17.87 vs. 16.99 mg/dL, respectively (Table 7).

Table 7: Comparison of mean TCB and SBR before phototherapy by mode of delivery

Mode of delivery	n	Mean TCB (mg/dL)	Mean SBR (mg/dL)
Vaginal delivery	80	17.28	17.87
LSCS	115	17.02	16.99

TCB: transcutaneous bilirubin; SBR: serum bilirubin; LSCS: lower-segment caesarean section**.**

DISCUSSION

In this prospective observational study of 195 term and late-preterm neonates with hyperbilirubinemia, TCB showed a strong and statistically significant correlation with SBR both before phototherapy (r = 0.946) and during phototherapy over covered skin (r = 0.953). The correlation remained strong across subgroups defined by gestational age and postnatal age, supporting the use of transcutaneous bilirubinometry as a reliable non-invasive tool in this population.

These findings are consistent with those of Radfar et al., who evaluated TCB accuracy in 134 term and 36 preterm newborns before and during phototherapy and reported a strong pre-phototherapy correlation (r = 0.929, p < 0.001), with post-phototherapy correlations of r = 0.921 in term and r = 0.887 in preterm neonates over patched areas [19]. Kolman et al. similarly reported good correlation between TCB and SBR in neonates ≥35 weeks (r = 0.87) [34].

Several investigators—including Povaluk et al., Zecca et al., and Nanjundaswamy et al.—have demonstrated good agreement between SBR and patched TCB during phototherapy [13,18,26], whereas Jangaard et al. found TCB during phototherapy to be less sensitive in preterm than in term neonates [24]. Yang et al. reported good correlation and high consistency between TCB and SBR before, during, and after phototherapy in term and late-preterm infants [21].

The strength of correlation observed in the present study (r = 0.94–0.95) is comparable to or higher than that reported by Panburana et al. (r = 0.81) [27] and consistent with the findings of Akahira-Azuma et al. [14]. Within subgroups, late-preterm neonates showed r = 0.953 before and 0.931 during phototherapy, and term neonates r = 0.943 before and 0.958 during phototherapy. Gunaseelan et al., in a study of term and late-preterm neonates, similarly concluded that TCB correlates closely with SBR in infants born after 35 weeks of gestation [32]. Juster-Reicher et al., studying preterm infants before, during, and after phototherapy, reported an overall correlation of 0.8, with lower correlation in infants born before 30 weeks [31].

In the present study, mean SBR was slightly higher than mean TCB before phototherapy, whereas during phototherapy mean TCB was marginally higher than mean SBR; overall, the two measurements were closely aligned. Yang et al. similarly observed that mean TCB was mostly higher than mean SBR before, during, and after phototherapy, although patterns during active phototherapy varied [21].

Regarding timing of presentation, 45.5% of neonates were admitted within 72 h and 54.5% after 72 h, with mean SBR of 15.50 mg/dL and 18.91 mg/dL, respectively. Comparable temporal patterns of jaundice presentation have been reported by Sadik et al. [29], Tiwari and Pise [22], and Rai et al. [23]. Mean TCB and SBR values were comparable between neonates delivered vaginally and by LSCS, in line with the observation of a higher proportion of caesarean deliveries reported by Radfar et al. [19].

Taken together with the wider literature, in which correlation coefficients between TCB and SBR range from approximately 0.65 to 0.94 in term infants [17,21,23,31,34,38], the present findings reinforce that TCB measured over covered skin can reliably reflect SBR during phototherapy. This has practical value in reducing the frequency of painful blood sampling and in supporting decisions about when to discontinue phototherapy.

Limitations

This study has several limitations. The sample size was relatively small. Only first-admission bilirubin values were considered, and values from subsequent admissions of the same neonate were not included. Neonates born before 34 weeks of gestation were excluded, so the findings cannot be generalised to more preterm infants, and further studies are needed in that group.

CONCLUSION

Transcutaneous bilirubin showed a strong, statistically significant correlation with total serum bilirubin in both term and late-preterm neonates, before and during phototherapy, when measured over covered skin. Transcutaneous bilirubinometry can therefore be used as an effective, non-invasive tool for screening bilirubin before initiating phototherapy and for monitoring bilirubin during phototherapy to help decide when treatment can be discontinued. Wider adoption may reduce the need for repeated venepuncture in jaundiced neonates, although larger studies including more preterm infants are warranted.

Additional Information

Ethics approval

The study was approved by the Institutional Ethics Committee of Rainbow Children's Hospital, Vijayawada. Written informed consent was obtained from a parent or guardian of each neonate prior to enrolment.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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