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Original Research Article

Accuracy and correlation of transcutaneous bilirubin with total serum bilirubin in preterm neonates born at 28-34 weeks of gestation during the first week of life

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ABSTRACT

Background: Transcutaneous bilirubin (TcB) measurement is a non-invasive method for screening neonatal hyperbilirubinemia and may reduce the need for repeated blood sampling. Although its accuracy has been well established in term and late preterm neonates, evidence in preterm infants remains limited. This study aimed to evaluate the correlation between TcB and total serum bilirubin (TSB) levels in preterm neonates born between 28 and 34 weeks of gestation during the first seven days of life.
Methods: This prospective observational study included 100 preterm neonates (28-34 weeks' gestation) admitted to the neonatal intensive care unit of a tertiary care hospital over a two-year period. TcB was measured using the BiliCare™ device on the helix of the ear immediately before or within five minutes of blood sampling for TSB estimation. The correlation between TcB and TSB values was evaluated by using Spearman's and Pearson's correlation coefficients.
Results: The mean gestational age was 31.4±1.97 weeks, and the mean birth weight was 1.56±0.35 kg. TcB and TSB mean values were 10.74±2.77 mg/dl and 10.16±3.59 mg/dl, respectively. It showed positive correlation between TcB and TSB (Spearman's rho=0.794, $p<0.05$; Pearson's correlation=0.870, $p<0.05$). The linear regression analysis showed the equation: TSB=1.6667×TcB-8.3333. This shows good predictive ability of TcB for serum bilirubin levels estimation.
Conclusions: TcB measurement showed positive correlation with TSB in preterm neonates of 28-34 weeks' gestation before initiation of phototherapy. TcB is a reliable, non-invasive screening tool that may avoid the need for invasive blood sampling in neonates, while TSB estimation should continue to guide therapeutic decisions.

Keywords: Transcutaneous bilirubin, Neonatal hyperbilirubinemia, Bilirubinometer

INTRODUCTION

Neonatal hyperbilirubinemia is one of the common conditions encountered during the first week of life, affecting nearly 60% of term and 80% of preterm neonates.[1] Although physiological jaundice is usually benign and self-limiting, severe unconjugated hyperbilirubinemia may result in acute bilirubin encephalopathy and kernicterus, leading to cerebral palsy, sensorineural hearing loss, gaze abnormalities, and developmental delay, which are irreversible neurological sequelae.[2]

Preterm neonates are high risk groups more prone to develop bilirubin-induced neurotoxicity (BIND) due to immaturity of the liver, increased bilirubin production, reduced serum albumin-binding capacity, enhanced enterohepatic circulation, and frequent links to sepsis, hypoxia, and acidosis.[3] Early recognition is a cornerstone

in the management of hyperbilirubinemia to minimize bilirubin-related morbidity and mortality.[1,3]

TSB estimation remains the gold standard in neonatal jaundice assessment and treatment. However, it is invasive, painful, and may contribute to anemia, especially in preterm infants. Infection chances increase if there is repeated blood sampling.[2,4]

TcB measurement is a newer, faster, non-invasive screening technique for bilirubin level measurement involving the analysis of optical parameters of the skin and subcutaneous tissue. Numerous studies have shown that TcB and TSB measurements are very similar in term and late preterm neonates. TcB measurement reduces unnecessary blood tests, which helps the patients.[5,6]

TcB has been extensively validated in infants of ≥35 weeks' gestation. However, evidence regarding its accuracy in preterm infants remains limited. Variations in skin thickness, dermal maturation, tissue perfusion, and the effects of phototherapy may influence TcB measurements in premature neonates, resulting in inconsistent findings across different studies.[7] Recent systematic reviews and observational studies have nevertheless reported encouraging correlations between TcB and TSB in preterm neonates before phototherapy, supporting its use as a screening tool in neonatal intensive care units.[8,9]

Despite increasing evidence from international studies, published data on the accuracy of TcB among Indian preterm neonates born before 35 weeks' gestation remain limited. The present study was therefore undertaken to evaluate the correlation between TcB and TSB values in preterm neonates born between 28 and 34 weeks of gestation during the first seven days of life. Establishing a correlation between TcB and TSB may help in early identification of hyperbilirubinemia while reducing the need for repeated invasive blood withdrawals in a high-risk population.[10]

METHODS

Study design and setting

This prospective observational study was conducted in the Neonatal Intensive Care Unit (NICU), Department of Pediatrics, Cheluvamba Hospital, Mysore, Karnataka, India, for a duration of 24 months from September 2020 to till September 2022, after obtaining approval from the Institutional Ethics Committee.

Study participants

Preterm neonates born between 28 and 34 weeks of gestation and aged less than 7 days who required TSB estimation as part of routine clinical care were enrolled consecutively after obtaining written informed consent from their parents or legal guardians.

Preterm neonates born between 28 and 34 weeks of gestation, postnatal age less than 7 days, requiring TSB estimation as part of routine clinical management, parents willing to provide written informed consent were included in our study.

Neonates with major congenital anomalies, significant skin lesions or edema interfering with TcB measurement, previous exchange transfusion, clinical conditions likely to interfere with accurate bilirubin estimation were excluded from our study.

Sample size

A total of 100 preterm neonates fulfilling the eligibility criteria were enrolled by consecutive sampling during the study period.[12]

Study procedure

Baseline demographic and clinical characteristics, including gestational age, birth weight, sex, mode of delivery, postnatal age, and relevant maternal and neonatal details, were recorded using a structured case record form.

TcB was measured using BiliCare™ transcutaneous bilirubinometer. Measurements were obtained from helix of ear immediately before/within 5 min of venous blood sampling to minimize temporal variation in bilirubin levels. Three consecutive TcB readings were obtained for each neonate and average value was recorded.[12]

Venous blood samples were collected under aseptic precautions as part of routine clinical care for estimation of TSB using the hospital laboratory's standard biochemical method.

Outcome measures

The primary outcome was the correlation between TcB and TSB values in preterm neonates born between 28 and 34 weeks of gestation during the first seven days of life. Secondary outcomes included evaluation of the agreement between TcB and TSB values and derivation of a regression equation for prediction of TSB from TcB.

Statistical analysis

Data were entered into MS excel and analyzed using statistical package for the social sciences (SPSS) version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean±SD, while categorical variables were summarized as frequencies and percentages. Pearson's and Spearman's rank correlation coefficients were used to determine correlation between TcB and TSB values. Linear regression analysis was performed to derive predictive equation to estimate TSB from TcB. Statistically significance was defined as a $p<0.05$.[12]

RESULTS

A total of 100 preterm neonates born between 28 and 34 weeks of gestation and aged less than seven days were enrolled in the study. All enrolled neonates completed the study and were included in the final analysis.

Baseline characteristics

The mean gestational age of the study population was 31.4±1.97 weeks, with the majority of neonates belonging to the 30-32week gestational age group.60 (60%) were males and 40 (40%) were females. The mean birth weight was 1.56±0.35 kg. The average time of blood sampling was, a mean±SD of 66.04±22.44 hours. Phototherapy was required for 67% of the newborn and was not needed in 33% (Table 1).

The mean TcB value was 10.74±2.77 mg/dL, while the mean TSB value was 10.16±3.59 mg/dL (Table 2).

Correlation between transcutaneous bilirubin and TSB

The scatter plot of TCB versus SBR showed strong positive correlation. (Figure 1) Spearman's rank correlation analysis showed a statistically significant correlation coefficient (ρ) of 0.794 ($p<0.001$). Similarly, there was a significant positive linear correlation found between TcB and TSB values with Pearson's correlation coefficient ($r=0.870$, $p<0.001$).

Regression analysis (linear)

Linear regression analysis showed significant linear relationship between TcB and TSB values. The regression equation generated from the study was:

TSB (mg/dL)=1.6667×TcB (mg/dL)-8.3333

The regression model indicated that TcB values were a significant predictor of serum bilirubin levels in preterm neonates.

Overall findings

The study showed excellent agreement between transcutaneous bilirubin and TSB measurements in preterm neonates before starting phototherapy.

The strong positive correlation suggests that TcB could be a reliable, rapid, and non-invasive screening method for neonatal hyperbilirubinemia in preterm infants born between 28 and 34 weeks of gestation. However, TSB estimation should still be used for therapeutic decisions.

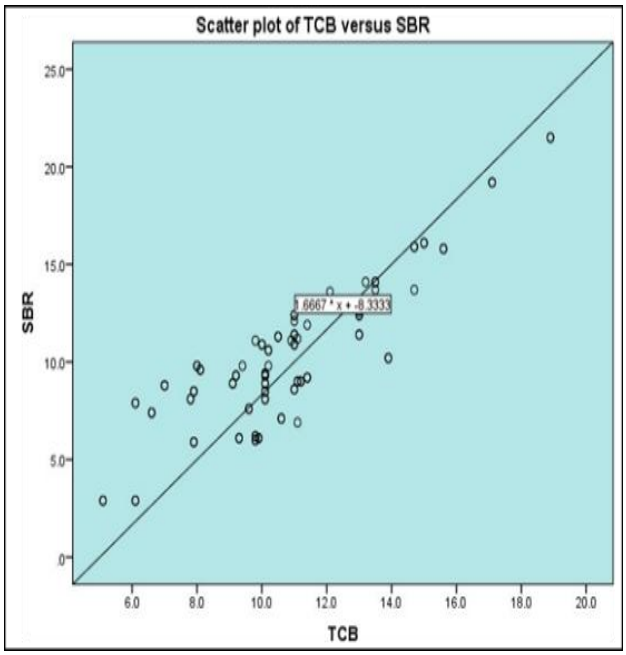

Figure 1: Scatter plot of TCB vs SBR of newborns.

Table 1: Demographic data of the study participants, (n=100).

Variables		Percent (%)
Gestational age (in weeks)	28-30	17
	30-32	35
	32-34	48
Gender	Female	40
	Male	60
Birth weight (kg)	<1	2
	1-1.5	40
	>1.5	58
Age at the time of blood sampling	≤24	2
	>24 to ≤48	40
	>48 to ≤72	45
	>72	13
Phototherapy required	Yes	67
	No	33

Table 2: Descriptive statistics and correlation TcB and SBR in the newborns.

Study variables	Min.	Max.	Mean	SD	Median	Mode	Q1	Q3
TCB (mg/dL)	5.1	18.9	10.74	2.77	10.2	10.1	9.3	12.8
SBR (mg/dL)	2.9	21.5	10.16	3.59	9.4	2.9	8.1	12.1
Correlation	**Sample size (n)**		**Correlation coefficient**				**P value**	
TCB vs SBR	100		Spearman's RHO=0.794				<0.05	
			Pearson correlation=0.870				<0.05	

*SBR-Serum bilirubin levels, TCB-Transcutaneous bilirubin levels

DISCUSSION

The present study demonstrated a strong positive correlation between TcB and TSB measurements in preterm neonates born between 28 and 34 weeks of gestation during the first seven days of life. The Pearson's correlation coefficient (r=0.870) and Spearman's rank correlation coefficient (ρ=0.794) indicated excellent agreement between the two methods, suggesting that TcB is a reliable non-invasive screening tool for estimating bilirubin levels in preterm infants before initiation of phototherapy.[14]

Preterm neonates are at greater risk of bilirubin-induced neurological dysfunction because of immature hepatic conjugation, reduced albumin-binding capacity, increased enterohepatic circulation, and associated comorbidities such as hypoxia, acidosis, and sepsis.[14-16] Even relatively low concentrations of bilirubin may cause bilirubin neurotoxicity in preterm infants compared with term neonates, highlighting the importance of early recognition and close surveillance.[17-18]

While visual assessment of jaundice is commonly performed, it has poor diagnostic accuracy and cannot reliably identify significant hyperbilirubinemia, particularly in preterm infants and those with variable skin pigmentation.[20-22] Hence, objective methods for estimation of bilirubin are recommended for accurate diagnosis and timely intervention.

In the present study, TcB measurements correlated well with TSB values, supporting the use of TcB as a bedside screening test. Maisels et al also reported similar findings, indicating the newer generation transcutaneous bilirinometers accurately estimate bilirubin concentrations and markedly diminish the need for repeated serum bilirubin measurements.[5,23] Bhutani et al also demonstrated that screening for bilirubin enables early identification of neonates at risk for significant hyperbilirubinemia, allowing timely intervention and reducing the risk of bilirubin-induced neurological injury.[24,25]

The derived regression equation (TSB=1.6667×TcB-8.3333) indicates that TcB measurements can reasonably predict serum bilirubin concentrations in preterm neonates. Although TcB should not replace laboratory estimation when treatment decisions are required, it serves as an effective screening modality that minimizes painful blood sampling and decreases iatrogenic blood loss, particularly in very low birth weight infants.[26,27]

Several previous studies evaluating TcB in preterm neonates have reported findings comparable with the present study. Lodha et al demonstrated good agreement between TcB and TSB measurements in Indian neonates using multi-wavelength spectral reflectance technology.[28] Schmidt et al observed a strong correlation between TcB and TSB in preterm neonates admitted to neonatal intensive care units and concluded that TcB is a dependable screening tool before phototherapy.[29] Willems et al similarly reported satisfactory agreement between Bilicheck® measurements and serum bilirubin levels in very premature newborns.[30]

Nanjundaswamy et al demonstrated high accuracy of TcB measurements across different bilirubin concentrations and suggested that TcB may reduce unnecessary venepunctures in neonatal practice.[31] More recently, Panda et al reported excellent agreement between TcB and TSB using Bland-Altman analysis in preterm neonates, supporting the clinical utility of TcB for routine bilirubin screening.[32] Furthermore, the systematic review by Nagar et al concluded that currently available transcutaneous bilirubin devices have acceptable diagnostic accuracy in preterm infants, although serum bilirubin estimation remains necessary for confirmation before therapeutic interventions.[33] Similar observations have been reported by Ahmed et al, Arman et al and Rubio et al all of whom demonstrated good correlation between TcB and TSB in infants born before 35 weeks of gestation while emphasizing the influence of gestational age, skin maturity, and phototherapy on measurement accuracy.[34-36]

The strengths of the present study include its prospective design, inclusion of exclusively preterm neonates between 28 and 34 weeks of gestation, and measurement of TcB immediately before serum bilirubin estimation, thereby minimizing temporal variation. These methodological strengths enhance the validity of the observed correlation.

The study has some limitations. It was single center study and the relatively small sample size, might limit the generalizability of the findings. TcB values post-phototherapy initiation was not assessed and long-term neurodevelopmental outcomes were beyond the scope of the study. Large sample size multicentric studies are needed to validate these findings and to develop gestational age-specific TcB nomograms for Indian preterm neonates.

CONCLUSION

To conclude, the findings of this study support the use of transcutaneous bilirubinometry as a fast, reliable, and non-invasive screening tool for the assessment of neonatal hyperbilirubinemia in preterm infants prior to phototherapy. While TcB cannot substitute the measurements of TSB in making treatment decisions, its routine use may decrease unnecessary invasive blood sampling and enable early detection of significant hyperbilirubinemia in neonatal intensive care unit.

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