

## Comparison of Transcutaneous Bilirubin Measurement With Total Serum Bilirubin Levels in Preterm Neonates Receiving Phototherapy

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**Objective:** To compare transcutaneous bilirubin with total serum bilirubin in preterm neonates after initiation of phototherapy. **Methods:** Jaundice was assessed in 30 preterm neonates with transcutaneous bilirubin and total serum bilirubin before initiation of phototherapy and at 12 hr after initiation of phototherapy. A photo-occlusive patch was applied over the sternum. **Results:** Transcutaneous bilirubin has a good correlation with total serum bilirubin after initiation of phototherapy. ( $r=0.918$ ,  $P<0.001$ ). Transcutaneous bilirubin at 28-32 weeks of gestation ( $r = 0.97$ ) was better correlated with total serum bilirubin than those at 32-37 weeks ( $r=0.88$ ). The correlation was better for neonates <72 hours old ( $r = 0.96$ ) than those >72 hours of age ( $r = 0.82$ ). **Conclusion:** Transcutaneous bilirubin correlates significantly with total serum bilirubin at the patched sternal site after initiation of phototherapy in preterm neonates.

**Keywords:** Assessment, Diagnosis, Hyperbilirubinemia, Jaundice.

Preterm neonates are susceptible to higher risk of kernicterus at lower bilirubin values. Transcutaneous bilirubin (TcB) testing has the advantages of instantaneous results and avoidance of repeated blood sampling [1]. However, its use after the initiation of phototherapy (PT) has not been reliably studied in preterm neonates [2-4]. We planned to compare TcB with total serum bilirubin (TSB) in preterm neonates after initiation of PT over a patched sternal area.

### METHODS

The study was conducted in a level III neonatal intensive care unit from September 2014 to February 2015. The study protocol was approved by the institutional ethics committee. Written informed consent was obtained from either of the parents or guardian prior to enrollment in the study.

Preterm neonates >28 and <37 weeks gestation having clinically detectable jaundice were included and neonates with conjugated hyperbilirubinemia, evidence of hemolysis or poor perfusion were excluded.

TSB was estimated using acid diazo method (Vanden Bergh reaction). Simultaneously, the TcB was measured on sternum using Drager jaundice meter JM 105. Average of three consecutive readings was recorded in mg/dL. The device was calibrated before usage according to the manufacturer's recommendations [5].

PT (compact fluorescent light or light emitting diode units with an irradiance of 20-30  $\mu\text{W}/\text{cm}^2/\text{nm}$ ) was instituted if the TSB fulfilled the criteria as per sliding scale for preterm neonates [6]. A patch of skin over the sternum was shielded using a maxicor electrode covered with aluminium foil [7]. A repeat TSB and TcB assessment was done 12 hours after the initiation of PT on the shielded skin area. The TSB and TCB were recorded within 15 minutes of each other. No additional blood investigations were done for the purpose of the study. The skin integrity was assessed with the Neonatal skin condition score (NSCS) before and after the application of the skin patch [8].

The primary outcome was comparison of TcB with TSB in preterm neonates after initiation of phototherapy. Secondary outcome was to compare TcB with TSB after initiation of phototherapy according to gestational age (28-32 vs 32-37 weeks) and postnatal age (<72 vs >72 hours).

**Statistical analysis:** Sample size was calculated by using formula for correlation coefficient using z transformation. From previous studies the correlation coefficient between TcB and TSB measurement varies between  $r = 0.5$  to  $0.9$ . Assuming alpha error of  $0.05$ , beta error of  $0.2$  and  $r$  value of  $0.5$ , estimated sample size was 29. A scatter plot was used to depict the relationship between TcB and TSB. Correlation coefficients were

calculated using Pearson correlation (parametric test) or Spearman rank correlation (nonparametric test). A *P* value of <0.05 was considered as statistically significant. Bland-Altman analysis was used to visualize the agreement between TSB and TcB.

**RESULTS**

The study included 30 (12, 28-32 wks; 18, 32-37 wks) preterm neonates. The baseline characteristics are shown in **Table 1**. TcB estimated at sternum correlated significantly with TSB prior to initiation of phototherapy ( $r=0.903$ ,  $P<0.001$ ) and after phototherapy over the patched sternal area ( $r=0.918$ ,  $P<0.001$ ) (**Fig. 1a**). The mean difference between TcB and TSB after initiation of PT was 0.87 mg/dL. TcB overestimated TSB in majority of the readings (76.7%) more so for higher levels of TSB (>10 mg/dL). Using the Bland Altman analysis (**Fig. 1b**), 90% of the data points were in the 95% confidence interval which are the limits of agreement. By regression analysis, the mean differences between TcB and TSB were not statistically significant ( $P=0.512$ ).

TcB in babies 28-32 weeks of gestation ( $r=0.97$ ;  $P<0.001$ ) were better correlated with TSB than in 32-37 weeks ( $r=0.88$ ;  $P<0.001$ ). The correlation coefficient was better for neonates <72 hours ( $r=0.96$ ;  $P<0.001$ ) than those >72 hours of age ( $r=0.82$ ;  $P<0.001$ ). None of the neonates had evidence of loss of skin integrity as assessed by NSCS.

**DISCUSSION**

This study showed a positive correlation between TSB and patched TcB in preterm neonates after starting PT.

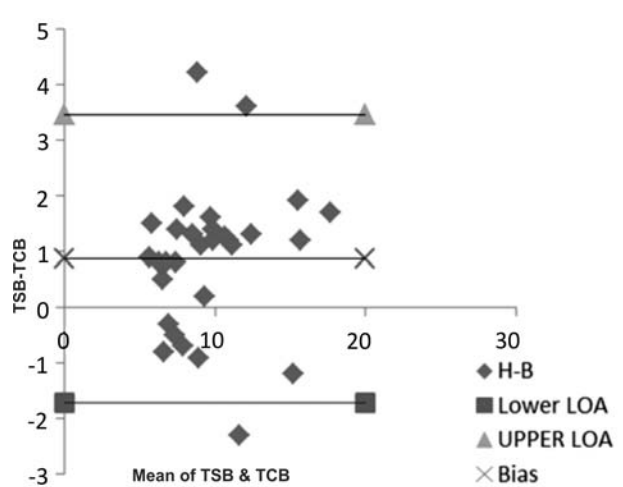
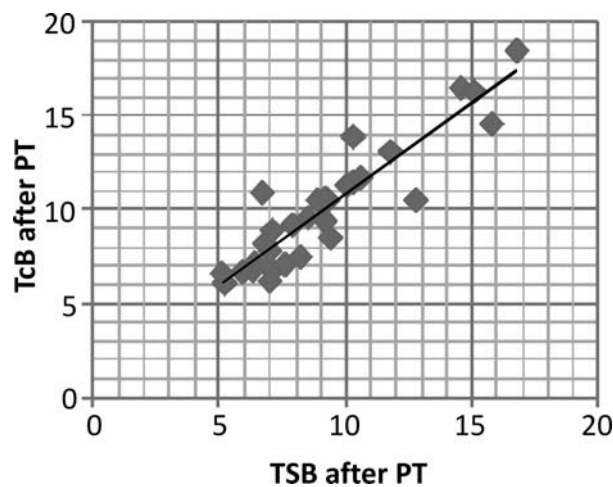
**TABLE 1** BASELINE CHARACTERISTICS OF STUDY POPULATION

Characteristic	
*Birth weight (g)	1680 (633.6)
*Gestational Age (wks)	32.9 (2.6)
#APGAR at 1 min	8 (7-9)
#APGAR at 5 min	9 (8-9)
Cesarean Section, <i>n</i> (%)	14 (46.7)
Small for gestation at age, <i>n</i> (%)	9 (30)
Male, <i>n</i> (%)	13 (43.3)
*Age at estimation of bilirubin before PT (h)	70.4 (24.9)
Average time (h) of taking TcB after initiation of PT	12.58
*TSB before PT (mg/dL)	12.05 (3.49)
*TcB before PT (mg/dL)	13.03 (3.83)

*\*Values are expressed in Mean (Standard Deviation) or #median (interquartile range); TcB: Transcutaneous bilirubin measurement; PT: Phototherapy; TSB: Total serum bilirubin level.*

Previous studies have demonstrated a good agreement between TSB and patched TcB during PT in preterm neonates [7,9,10]. However, in a study by Jangaard, *et al.* [11], TcB measurement during PT was not found to be as sensitive in preterm compared to term neonates.

The difference noted between 32-37 week and 28-32 weeks gestation groups could be explained by the skin immaturity of very preterm neonates. There are no studies till date which have evaluated this difference. The correlation coefficient was better for neonates <72 hours than those >72 hours of age. We hypothesize that as the skin pigmentation increases with age, correlation begins to decline.



**FIG. 1** (a) Scatter plot depicting correlation; (b) Bland altman analysis.

Limitations of the present study are lack of comparison with other sites like forehead and inter-scapular area [12]. Also, serial TcB measurements from the patched site after starting PT could have been a better guide to evaluate the trends in correlation during the course of PT.

This study has major implications for developing countries where the rate of prematurity is high, necessitating prolonged NICU admissions, phlebotomy losses and unavailability of micro-methods for bilirubin estimation in most laboratories.

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