

Transcutaneous Bilirubin Measurement as a Predictor of Significant Neonatal Hyperbilirubinemia in Low Birth Weight Neonates

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Abstract

Introduction: Early recognition of neonatal hyperbilirubinemia is essential to prevent bilirubin encephalopathy. Transcutaneous bilirubin (TCB) measurement is a simple and easy method to predict neonatal hyperbilirubinemia. We aimed to study the efficacy of TCB as a predictor of subsequent significant neonatal hyperbilirubinemia in low birth neonates and compared the forehead and sternal sites for TCB measurement.

Methods: A prospective study was conducted from August to October 2018 at a teaching hospital in South India including term and late preterm neonates weighing < 2.5 kg. The TCB values were obtained from the forehead (TCB-FH) and sternum (TCB-S) by a non-Invasive Bilirubin Analyser. The average of TCB (TCB- AV) was determined for each baby with TCB-FH and TCB -S values. Neonates were followed up subsequently till discharge for the development of significant hyperbilirubinemia. Receiver operating characteristic (ROC) curve was generated and the best cut-off value for 24-hour TCB as a predictor of significant hyperbilirubinemia was established.

Results: The study included 88 neonates, of which 39 (44.3%) were late preterm and 49 (55.7%) term small for gestation age. Mean values of TCB -AV 6.25 ± 1.58 , TCB - FH 6.24 ± 1.57391 , and TCB - S 6.27 ± 1.56 were noted. The cut off value for TCB - AV was found to be 6.85 as a predictor for subsequent neonatal hyperbilirubinemia. TCB - AV was a better predictor than TCB - FH or TCB - S.

Conclusions: TCB measurement is an easy and reliable predictor for subsequent significant hyperbilirubinemia in low birth weight neonates. The average of TCB forehead and sternum was a better predictor of significant hyperbilirubinemia.

Introduction

Jaundice in a neonate is a common disorder, with more than half of babies getting affected in the early postnatal period. Hyperbilirubinemia in the preterm neonate is more exaggerated than the term neonate.¹ Severe hyperbilirubinemia can lead to irreversible neurological damage, hence early identification of newborn with high risk for hyperbilirubinemia is essential.² Increased prevalence, more severity, and protracted course of hyperbilirubinemia are seen in preterm neonates than term neonates.³ Low birth weight (LBW) neonates are more prone to bilirubin-induced brain damage at lesser bilirubin levels compared to term neonates.^{4,5} The incidence of kernicterus has drastically decreased with routine screening and early initiation of phototherapy.⁶ The American Academy of Pediatrics (AAP) recommends every neonate to be screened at 24 hours of life and subsequently based on 24-hour values.⁷

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Total serum bilirubin (TSB) is the gold standard for diagnosing hyperbilirubinemia. Transcutaneous bilirubin (TCB) measurement is an easy, non-invasive measure of predicting hyperbilirubinemia.⁸ Previous studies have proved the efficacy of TCB as a predictor of TSB.^{2,9} In preterm neonates, immaturity of skin and different albumin to bilirubin binding makes TCB less accurate than term neonates.¹⁰

Prior studies have compared the diagnostic accuracy of forehead, sternum, interscapular areas for TCB measurements and have shown varying results.¹¹ Hence, we aimed to study the efficacy of TCB as a predictor of subsequent significant neonatal hyperbilirubinemia in LBW neonates and we compared the accuracy of the forehead and sternal TCB measurement.

Methods

A prospective study was conducted from August to October 2018, at Government Lady Goschen Maternity Hospital, Mangalore, India, affiliated to Kasturba Medical College Mangalore, Manipal Academy of Higher Education. Institutional ethics committee approval was obtained. Inborn term newborn infants and late preterm infants between gestational age of 35 to 37 weeks, weighing below 2.5 kg were included after informed consent. Neonates with jaundice < 24 hrs, neonatal septicemia, major congenital anomalies, resuscitation performed at birth, surfactant administration, intravenous antibiotics therapy, requiring oxygen support, mechanical ventilation and evidence of hemolysis were excluded. Maternal and neonatal details from medical records were entered in a proforma. Parents were explained about the procedure of measuring TCB. The TCB values were obtained from the forehead (TCB - FH) and sternum (TCB - S) by non-Invasive Bilirubin Analyzer, Drager JM - 103 at 24 ± 4 hours. The same device was used all the way through the study to eradicate inter-device variability. The device was calibrated regularly as per the manufacturer's instructions. Eyes were covered while performing the TCB measurement at the forehead and the probe was disinfected after using it on each baby. The average of TCB (TCB - AV) was determined for each baby with TCB - FH and TCB - S values. Neonates were followed up subsequently by daily examination for development of clinical jaundice and invasive bilirubin monitoring was done in neonates with clinical jaundice. Significant hyperbilirubinemia was defined as a requirement of phototherapy or exchange transfusion as per age - specific TSB value nomogram. AAP chart was used to determine significant hyperbilirubinemia and phototherapy was given as per AAP guidelines.⁷ Neonates were followed up until their discharge. With a 95% confidence interval, 80 % power, and 5% level of significance and using data from Varvarigou et al, a sample size of 88 was calculated.⁹ The collected data was coded and entered in the statistical Package for IBM (SPSS) statistics for windows version 17.0. Armonk, NY: IBM Corp. Descriptive statistics were used for baseline characteristics. Independent variables were compared using one-way analysis of variance. Chi-square test was used to compare the categories. A p-value of less than

0.05 was considered for statistical significance. (ROC) curve was created and optimal 24-hour TCB values as a predictor of 'significant hyperbilirubinemia' derived.

Results

The study enrolled 90 neonates as per eligibility criteria. Two babies were excluded subsequently as they developed features of neonatal sepsis and received intravenous antibiotic therapy. Of 88 neonates, 39 (44.3%) belonged to the late preterm category and 49 (55.7%) were term small for gestation babies. Forty two (47.7%) neonates were males and 47 (52.3%) were females. Mean gestational age in weeks was 37.21 ± 1.80 weeks and mean birth weight was 2.26 ± 0.25 kg. Mean TCB - AV 6.25 ± 1.58 , mean TCB - FH 6.24 ± 1.57391 , and TCB - S 6.27 ± 1.56 were noted. Baseline line characteristics and mean value of TCB - AV in each category are depicted in Table 1. There was no statistical difference among the categories.

Table 1. Baseline characteristics and comparison of mean TCB - AV values

Baseline characteristic	N (%)	Mean TCB - AV	Std. Deviation	95% Confidence interval for mean	
				Lower Bound	Upper Bound
Gender					
Male	42 (47.7)	6.1179	1.54706	5.6358	6.6000
Female	46 (52.3)	6.3652	1.60585	5.8883	6.8421
Gestation					
Preterm	39 (44.3)	6.1333	1.61136	5.6110	6.6557
Term	49 (55.7)	6.3378	1.55418	5.8913	6.7842
Mode of delivery					
Vaginal delivery	53 (60.2)	6.3226	1.57219	5.8893	6.7560
LSCS	33 (37.5)	6.1197	1.64012	5.5381	6.7013
Instrumental	2 (2.3)	6.3500	.21213	4.4441	8.2559
Blood group					
A	29 (33)	6.1793	1.63081	5.5590	6.7996
B	26 (29.5)	6.2269	1.54209	5.6041	6.8498
O	12 (13.6)	6.1250	1.47101	5.1904	7.0596
AB	21 (23.9)	6.4357	1.68413	5.6691	7.2023

During the hospital stay, 17 (19.3%) neonates developed significant hyperbilirubinemia requiring phototherapy as per the AAP chart.⁷ Mean age of institution of phototherapy was 73.81 ± 26.65 hours. Mean Total bilirubin at the time of institution of phototherapy was 14.92 ± 2.74 mg / dl. The number of neonates developing hyperbilirubinemia in various subgroups based on the TCB -AV value is depicted in Table 2.

Table 2. TCB - AV values and neonates with subsequent significant hyperbilirubinemia

TCB-AV	Subsequent significant hyperbilirubinemia n (%)	No subsequent significant hyperbilirubinemia n (%)
< 5	0	22 (100)
5 - 6	2 (9.5)	19 (19.5)
6 - 7	2 (10.5)	17 (89.5)
	6 (35.3)	11 (64.7)
> 8	7 (77.8%)	2 (22.2)
Total	17 (19.3)	71 (80.7)

ROC curves in Figure 1 compare the predictive accuracy of TCB -AV, TCB-FH, and TCB-S measured at 24 hours.

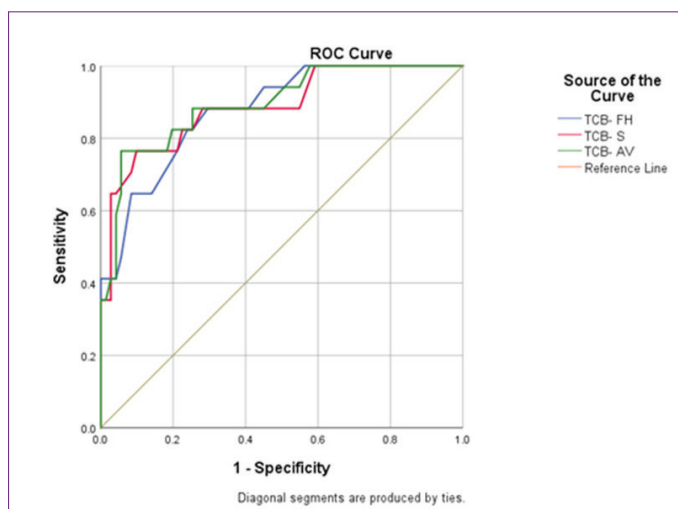


Fig.1 ROC curve of transcutaneous bilirubin measurements at the forehead (TCB - FH), sternum (TCB - S), and an average of forehead and sternum values (TCB - AV) as a predictor of subsequent significant hyperbilirubinemia

The area under the ROC curve for TCB - AV, TCB - S, and TCB - FH were 0.894, 0.887 and 0.878 respectively (Table 3). The cut off value for TCB - AV was found to be 6.85 as a predictor for subsequent neonatal hyperbilirubinemia.

Table 3. TCB values and area under the curve of receiving operator characteristic for different sites of TCB

TCB	Area	95% Confidence Interval for Mean	
		Lower Bound	Upper Bound
TCB-FH	0.878	0.792	0.963
TCB-S	0.887	0.794	0.980
TCB-AV	0.894	0.808	0.981

Discussion

Early detection of hyperbilirubinemia is important to prevent bilirubin encephalopathy. The incidence of significant hyperbilirubinemia is dissimilar in various populations. The extent of hyperbilirubinemia is more severe in late preterm neonates compared to the term infants. A study of hyperbilirubinemia in normal and LBW babies by Ravishankar et al in South India concluded that significant hyperbilirubinemia developed earlier and persisted requiring phototherapy for a longer duration.⁴ Significant jaundice was found in as high as 57 % of late preterm neonates in a study by Lavanya et al.¹² A prospective study including term and near term infants reported the occurrence of significant hyperbilirubinemia in 25.3% of the babies.¹³ In the present study, significant jaundice was found 19.3% of LBW neonates which is much lower than the previous studies.^{12,13}

A study by Bhutani et al concluded that neonates who developed significant hyperbilirubinemia subsequently had higher bilirubin values in early days.¹⁴ TCB in the first 6 to 24 hours has been found to correlate well with the TSB and decreases the need for blood sampling.⁸ A study by Rahmawati et al which included preterm neonates 35 weeks concluded that TCB cut-off value of 4.5 mg / dl in neonates weighing 1000 - 1500 gm and TCB cut-off value of 5.8 mg / dl predicted subsequent hyperbilirubinemia at 48 hours.¹⁵ A study by Lavanya et al, which included late preterm neonates indicated that TCB value greater than 5.9 mg / dl predicted subsequent hyperbilirubinemia in late preterm neonates.¹² In the present study which included late preterm and term small for gestational age neonates, the cut-off value for TCB -AV was found to be 6.85 as a predictor for subsequent neonatal hyperbilirubinemia. Inclusion of term small for gestational age neonates probably has led to higher TCB cut off values in our study compared to the previous studies.^{12,15}

Studies have compared various sites for TCB measurement in late preterm infants and the results are contradicting.^{11,16-18} Agrawal G et al studied the diagnostic accuracy of TCB at three different sites (Forehead, sternum, and interscapular area) in early preterm infants opined that the interscapular region as a reliable area to measure TCB in infants 34 weeks.¹¹ They reported a correlation coefficient of 0.82, 0.84 and 0.86 for the forehead, sternum,

and interscapular region respectively. In a study from Japan, five different areas of the body were compared for TCB measurement accuracy. It was found that the forehead and upper back were reliable sites to predict hyperbilirubinemia compared to the lower abdomen, or waist.¹⁶ A prospective cohort study of Canadian neonates, born preterm at 24 to 36 weeks concluded that TCB correlated acceptably with TSB before phototherapy in neonates born preterm at 33 to 36 weeks.¹⁷ Forehead and sternum had the similar predictive ability before the start of phototherapy, whereas in neonates who received phototherapy, the forehead was a better anatomical site for TCB measurement.¹⁷

A study by Weber et al to evaluate the validity of TCB in preterm neonates born at 23 to 34 weeks of gestation, inferred that TCB measurement was reliable in preterm babies when TSB was > 5 mg / dl. Interscapular was preferred site in neonates born at 23 to 34 weeks, sternal TCB was more sensitive and specific in babies born at 29 to 35 weeks.¹⁸ In the present study, the average of the forehead and sternal value was a better predictor of neonatal hyperbilirubinemia. The area under the ROC curve for TCB measurements, TCB-AV, TCB - S and TCB-FH were 0.894, 0.887 and 0.878 respectively. Although our study is a prospective observational study, there are certain limitations. As TSB values at 24 hours were not available, correlation of TSB and TCB as a predictor of subsequent significant hyperbilirubinemia could not be determined. In this regards, we recommend that a larger study comparing late preterm and LBW neonates would yield better predictive accuracy in both groups of neonates.

Conclusions

TCB measurement is an easy and reliable predictor for subsequent significant hyperbilirubinemia in low birth weight neonates. The average of TCB forehead and sternum was a better predictor of significant hyperbilirubinemia.

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