

## Diagnostic Usefulness of Transcutaneous Bilirubinometry in Very Preterm Newborns

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### ABSTRACT

**Background:** This study was performed to find out whether transcutaneous bilirubinometry could be a valid screening method for hyperbilirubinemia in preterm infants, especially for those who needed mechanical ventilation.

**Methods:** We evaluated 63 preterm Iranian newborns who were managed in the neonatal intensive care unit of Shahidbeheshti University Hospital, Isfahan, Iran from April 2009 to April 2010. Transcutaneous bilirubin (TCB) measurements were obtained using BiliCheck™ shortly before or 10 minutes after taking blood for determination of the plasma bilirubin level in premature newborns, who did not receive phototherapy. We assessed the correlation between the transcutaneous bilirubin and plasma bilirubin level by linear regression analysis. We also analyzed the gestational age, birth weight, postnatal age, sex, and hematocrit, for determination of their effect on transcutaneous bilirubin accuracy.

**Results:** The overall bilirubin concentration ranged from 5.4 to 17 mg/dL and from 4.8 to 17.3 mg/dl for total serum bilirubin (TSB) and transcutaneous bilirubin, respectively. The mean values obtained by transcutaneous bilirubinometry were slightly higher than the total TSB values. The correlation coefficient between TSB and TCB was  $r=0.82$ ,  $P<0.001$ , and this was not influenced by gestational age, postnatal age or hematocrit, which were previously considered to be important. The correlation coefficient between TSB and TCB in mechanically ventilated preterm infants was  $r=0.75$ ,  $P<0.001$ .

**Conclusion:** Plasma bilirubin level can be accurately measured by BiliCheck™ in premature newborns, even in newborns who need mechanical ventilation.

**Keywords:** Neonatal jaundice, phototherapy, preterm newborn, transcutaneous bilirubinometry

### INTRODUCTION

Jaundice is a prevalent disorder that frequently requires

treatment with phototherapy and to a lesser extent exchange transfusion.<sup>[1]</sup> Indirect bilirubin could cross through the blood brain barrier especially in sick and premature babies.<sup>[2]</sup> Very high levels of indirect bilirubin are neurotoxic and may lead to hearing loss, gaze abnormality, athetoid cerebral palsy, and mental retardation.<sup>[3]</sup> Therefore, prevention of severe hyperbilirubinemia is very important, particularly in preterm infants. To determine those newborns at risk of bilirubin encephalopathy, an accurate measurement of serum bilirubin level is essential. Frequent blood sampling may cause anemia especially in premature newborns. In addition, blood sampling is a painful procedure and may increase the risk of infection and scar formation.<sup>[1]</sup> Accordingly, using other methods of plasma bilirubin determination could be very important for the prevention of these devastating complications. For screening of hyperbilirubinemia in well-term and near-term newborns, transcutaneous bilirubinometry is a safe and effective technique.<sup>[4,5]</sup> However, the accuracy of this screening device is not widely accepted in preterm newborns, especially those on mechanical ventilation.<sup>[5-7]</sup>

The present study was undertaken to measure the total serum bilirubin (TSB) concentrations and TCB concurrently, using BiliCheck™, to specify if the transcutaneous bilirubinometer could validate a screening device in premature infants and determine some factors that may affect the correlation between TCB and TSB in this population.

## METHODS

This prospective study comprised of 63 preterm Iranian premature infants managed in the neonatal intensive care unit (NICU) of the Shahidbeheshti University Hospital, Isfahan, Iran, from April 2009 to April 2010. Informed consent was obtained from the parents before participation and the study was approved by the Research Ethics Committee of the Isfahan University of Medical Sciences. The inclusion criteria were gestational age less than 34 weeks and an indication for the measurement of total serum bilirubin. The exclusion criteria were, receiving phototherapy 12 hours before measurement of serum bilirubin concentration, skin infection, and purpura or bruising at the site

of TCB measurement. The patients' characteristics, including birth weight, gestational age, postnatal age, sex, and hematocrit were recorded.

We measured TCB with the BiliCheck™ (Spect Rx, Norcross, GA, USA) shortly before or 10 minutes after blood sampling, for determination of the plasma bilirubin level. The BiliCheck™ apparatus was a fibrotic instrument assessing multiple wavelengths by spectral reflectance. It was calibrated before initiating the study. For each newborn we determined TCB over the forehead (glabella) thrice and the average was obtained. Two investigators, who did not have prior knowledge of the capillary blood bilirubin concentration, measured the TCB. Blood samples were drawn via heel puncture. Measurements of TSB were done within 60 minutes and without light exposure. The serum bilirubin level was determined in our laboratory using the method of spectrophotometry (Sanjesh, Iran).

All data were analyzed with SPSS 11 (SPSS Inc., Chicago, USA), and *P* values <0.05 were considered to indicate statistical significance. For comparing the means of TSB and TCB, we applied the Paired Student's *t*-test. Also we used Pearson's correlation coefficients (*r*) and linear regression analysis between TCB and SB. Factors potentially affecting the correlation between TSB and TCB were analyzed in a multiple linear regression model.

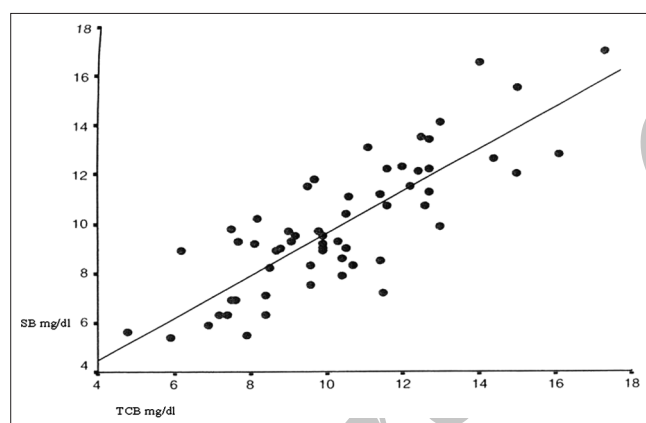
## RESULTS

Mean birth weight of newborns was  $1729 \pm 485$  g, ranging from 730 to 2500 g, and mean gestational age was  $31.3 \pm 2$  weeks, ranging from 25 to 33 weeks. There was little female prevalence (ratio female/male 32/31). The mean postnatal age was  $5.5 \pm 4.6$  days ranging from 1 to 24 days. Thirteen (20.6%) patients required mechanical ventilation due to respiratory distress syndrome. TSB values ranged from 5.4 to 17 mg/dl compared to 4.8 to 17.3 mg/dl for TCB values. There was no significant difference between the mean TSB levels and mean TCB levels ( $9.8 \pm 2.6$  mg/dl versus  $10.2 \pm 2.5$  mg/dl, *P*=0.8). Mean difference of the pairs (TCB – TSB) was  $0.43 \pm 1.5$  mg/dl (ranging from - 2.7 mg/dl to 4.3 mg/dl). There was a meaningful positive relationship between the TCB measures and plasma bilirubin levels (*r*=0.82, *P*<0.001) and the linear regression equation was:

$TSB=0.85 \text{ TCB}+1.075$ . A linear relationship was found between TSB and TCB, as shown in [Figure 1]. The influence of different parameters on the coherence between TSB and TCB are listed in Table 1. The TSB – TCB correlation coefficient increased with increasing gestational age, birth weigh and postnatal age. There was a meaningful positive relationship between the TCB and TSB in mechanically ventilated newborns ( $r=0.75$ ,  $P<0.001$ ), and the linear regression equation for these infants was:  $TSB=0.75 \text{ TCB}+1.726$ .

## DISCUSSION

The accuracy of transcutaneous bilirubinometry for bilirubin determination and its role in the prevention of frequent blood sampling in term infants have been established.<sup>[1,8]</sup> However, for the determination of hyperbilirubinemia in premature infants we still require invasive blood sampling. This study was performed to identify if TCB could



**Figure 1:** Correlation between TCB and TSB

**Table 1:** Influence of different parameters on the coherence between total serum bilirubin concentration and transcutaneous bilirubin values

Variable (n)	r	P
Gestational age $\leq 30$ weeks (18)	0.65	0.002
Gestational age $>30$ weeks (45)	0.85	$<0.001$
Male (31)	0.85	$<0.001$
Female (32)	0.79	$<0.001$
Birth weight $\leq 1500$ g (18)	0.70	0.001
Birth weight $>1500$ g (45)	0.82	$<0.001$
Postnatal age $\leq 7$ days (49)	0.84	$<0.001$
Postnatal age $>7$ days (14)	0.74	0.001
Hematocrit $\leq 35\%$ (11)	0.91	$<0.001$
Hematocrit $>35\%$ (52)	0.80	$<0.001$

be a reliable screening test in premature infants. Our results revealed a considerable positive correlation between the TCB measurements and TSB in premature infants, even those who needed mechanical ventilation. Therefore, this study confirmed the role of TCB in the prevention of blood sampling complications in premature and sick newborns.

In the previous studies, the reported range of the correlation coefficient between TCB and TSB in newborns was between 0.87 and 0.92.<sup>[1,4,8]</sup> The correlation coefficient of 0.82, which was obtained from premature infants in our study corresponded with that in the term infants.

There are a few studies evaluating the accuracy of transcutaneous bilirubinometers in preterm newborns. The study of Knupfer *et al.* on 145 preterm infants showed a correlation coefficient of 0.73 between TCB and TSB, in newborns who did not receive phototherapy.<sup>[6]</sup> Amanto and colleagues described a correlation coefficient of 0.7 between TCB and TSB in healthy low birth weight infants.<sup>[9]</sup> Schmidt and coworkers evaluated the accuracy of TCB in three groups of premature infants. The correlation between TCB and TSB was 0.79 to 0.92 in their study.<sup>[10]</sup> The study by Luca *et al.* on 340 premature infants, between 30 and 36 week gestational age, showed a correlation coefficient of 0.79 between TSB and TCB.<sup>[10]</sup> Numba and Kitajima reported a correlation coefficient of 0.69 between TCB and TSB in low birth weight infants. However, the correlation was closer in infants with a birth weight more of than 1000 g.<sup>[11]</sup> One possible explanation for these differences in correlation coefficient could be the employment of different bilirubinometers for TCB measurement. In addition the mean birth weight and gestational age were dissimilar in different studies.

The coefficient of determination  $r^2$  in our study was 0.67, which represented that about 67% of the variability of plasma bilirubin concentrations could be anticipated by the TCB measurements. This is very close to the 0.64 figure reported by Luca *et al.*<sup>2</sup>

Our data showed a meaningful positive correlation between TCB and TSB, even in newborns who needed mechanical ventilation, which was consistent to the finding of Knudsen *et al.*<sup>[12]</sup> On the contrary, Knupfer *et al.* found that the correlation between TCB and TSB decreased significantly with increasing breathing disturbances.<sup>[6]</sup> Luca and

co-workers excluded infants with asphyxia, RH or ABO isoimmunizations, conjugated bilirubin more than 1 mg/dl, liver disease, and congenital malformations, from their studies.<sup>[2]</sup>

This study demonstrates that the accuracy of TCB is not affected by sex, which supports studies published earlier.<sup>[2,4]</sup> Also our study demonstrates that the relationship between TCB and TSB is not influenced significantly by gestational age. Conversely, in the study by Knupfer *et al.*, the TCB – TSB correlation decreased with lowering gestational age.<sup>[6]</sup> On the other hand Willems and coworkers showed that the BiliCheck™ was a reliable screening device in very preterm infants (gestational age <30 weeks).<sup>[8]</sup> Similarly, Luca *et al.* showed no effect of gestational age, gender or PH on the TCB readings.<sup>[2]</sup>

A recently published study assessed the effect of hematocrit as an estimate of other skin pigmentations and found that hematocrit did not affect the TCB – TSB relationship.<sup>[2]</sup> Our results also showed the ineffectiveness of hematocrit on the TCB – TSB relationship.

Even as skin maturity increased with increasing postnatal age, we found that postnatal age did not affect the relationship between TSB and TCB, which was similar to the finding of Knupfer *et al.*<sup>[6]</sup> In contrast, Luca *et al.* stated that only postnatal age affected the relationship between TCB and TSB.<sup>[2]</sup>

We had some limitations to our study. First of all, we excluded newborns who were exposed to phototherapy. Therefore, our results could not be used for newborns who received phototherapy. Second, we measured TSB photometrically instead of using high pressure liquid chromatography, which was the typical method of TSB determination. Third, we assessed 63 patients and better results could be obtained by future studies with a larger sample size. On the other hand our study was unique because of the enrollment of not only healthy preterm infants, but also sick and ventilated premature newborns.

To sum up, the data from our study shows that transcutaneous bilirubin measurements using BiliCheck™ provide accurate results in premature infants without phototherapy, as also in newborns who need mechanical ventilation. This device is very helpful.

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