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# Diagnostic accuracy of transcutaneous bilirubinometer as non invasive method to measure bilirubin in neonates

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**Abstract:** *Background:* The use of non-invasive, transcutaneous bilirubin monitoring (QTcB) as a jaundice screening in full-term infants is a well-established practice; however, there is a paucity of research in evaluating the use of QTcB in comparison with serum total bilirubin (TSB). The aim of the study is to assess the concordance between transcutaneous bilirubin and serum bilirubin in neonates with physiological jaundice and determine the utility of transcutaneous bilirubinometry in the management of physiological jaundice. *Method:* It is a cross-sectional observational study conducted at the Biochemistry department of tertiary care hospital, Mangalore over a period of 6 months with approval of the institutional ethics committee. All the newborn delivered by normal vaginal delivery were included for the study after obtaining the written informed consent from the parents. They were assessed for the hyperbilirubinemia by quantification of the serum bilirubin (Diazo method) and also transcutaneous bilirubinometer (BILIPROBE, MBJ20 at 450nm & 550nm wavelenght) testing on the forehead and sternum within the 10mins of blood collection for the serum bilirubin estimation. This was done at around 72hrs of birth as a pre-discharge screening of neonates. *Results:* Overall, 620 neonates were screened in the study of which 498 babies were assessed for eligibility, a total of 299 neonates were finally enrolled. QTcB and TSB measurements were taken and were correlating significantly with good strength of association ($p<.001$) with the sternum and forehead location. ROC curve for prediction of TSB and QTcB with cut-off index was 93.67% serum bilirubin, 89.6% at the sternum and 82.25% at the forehead. *Conclusion:* QTcB correlates closely with TSB concentration in neonates with full-term gestational age. The rate of rising in TcB may help in identification of neonates at risk and minimizing invasive blood investigations.

**Keywords:** Hyperbilirubinemia, Jaundice, Newborn, Transcutaneous Bilirubin (QTcB), Total Serum Bilirubin (TSB).

## Introduction

Neonatal jaundice remains an important issue occurring in upto 60% of term and 80% of preterm babies in the first week of life [1-2]. Some of the most common causes includes physiological jaundice, breastfeeding or non-breast feeding jaundice, breast milk jaundice, prematurity leading to jaundice in neonates and various pathological type of jaundice such as haemolytic disease, liver dysfunction, sepsis, G6PD enzyme deficiency, hypothyroidism or rare conditions such as Gilbert's syndrome etc [3-4]. The potential toxicity of bilirubin is acute bilirubin encephalopathy or kernicterus, which is associated with significant morbidity and mortality. Unconjugated bilirubin has been noted to cross the blood-brain barrier, causing encephalopathy in the immediate period, and potential for causing long term choreo-athetoid cerebral palsy and other complications.

Managing bilirubin encephalopathy with the use of phototherapy and exchange transfusion are the mainstay in prevention which have been subjects of rigorous investigation over the last 60-70 year. The visual judgment of jaundice is not objective. Estimation of total

serum bilirubin levels in the clinical laboratory necessitates the collection of multiple blood samples from the healthy neonates. This collection of blood samples is traumatic and painful for the neonates and parents. Suboptimal collection technique may result in specimen hemolysis that interferes with serum bilirubin measurement, also there is significant inter-laboratory and intra-laboratory variability [5]. In an effort to reduce the agony due to blood sampling, transcutaneous bilirubin meter can be used judiciously.

The transcutaneous bilirubin meter readings are immediate and non-invasive. Transcutaneous bilirubin meter depends upon a number of factor such as gestational age, skin, color, race, ethnicity, phototherapy and degree of jaundice [6]. Despite a lot of advancement in transcutaneous technology, a lot of debate persists regarding its efficacy in detecting neonatal jaundice. The aim of the study is to correlate transcutaneous bilirubin levels to serum bilirubin in neonates with physiological jaundice and determine the utility of transcutaneous bilirubinometry in the management of physiological jaundice.

## Material and Methods

It is a cross-sectional observational study conducted at Biochemistry department central laboratory of Father Muller Medical College & Hospital, Mangalore over a period of 6 months with approval of institutional ethics committee. All the newborn delivered by normal vaginal delivery were included for the study after obtaining the written informed consent from the parents. Inclusion criteria: all term neonates with physiological jaundice, defined as yellowish discoloration of the skin according to the Krammer scale [7]; Breastfed only neonates were enrolled for the study; Physiological jaundice at 72hrs was checked and documented. A very sick newborn (sepsis, congenital malformation, pathological jaundice, conjugated hyperbilirubinemia); newborn < 37 completed weeks; Newborn with birth weight < 1800 grams; or Newborn receiving / received phototherapy/ exchange transfusion were excluded from the current study.

All the newborn included in the study were assessed for the hyperbilirubinemia by quantification of the serum bilirubin (Diazo method) and also transcutaneous bilirubinometer (BILIPROBE, MBJ20 which uses dual wavelengths 450nm and 550nm which reach different layers of the skin) testing on the forehead and sternum within the 10mins of blood collection for the serum bilirubin estimation. This was done at around 72hrs of birth as a pre-discharge screening of neonates. The baseline characteristics of the included study subjects such as gestational age, birth weight, gender were collected from the datasheet or hospital case records. The Transcutaneous bilirubinometer equipment was calibrated daily and used according to the manufacturer's instruction manual. It was ensured that QTcB (transcutaneous bilirubin) measurements were done within 10mins of blood collection for TSB (total serum bilirubin)

*Statistical Analysis:* Collected data were represented as mean, standard deviation and frequency distribution. The Pearson correlation coefficient was calculated to find the relationship between the sternum with the forehead, forehead to serum bilirubin and serum bilirubin with the sternum. $P<0.05$ was considered statistically significant. Receiver Operating curve was drawn for serum bilirubin levels, sternum and forehead score to predict the phototherapy required or not and find the best cut-off, sensitivity, specificity, and positive predictive value and negative predictive value. The statistical analysis was done using SPSS version 23 operating on windows 10.

## Results

Overall, 620 neonates were screened in the study of which 498 babies were assessed for eligibility, a total of 299 neonates were finally enrolled for the above study based on the inclusion criteria. 180 neonates were excluded from the study based on the exclusion criteria (birth weight <1800gram, sepsis, sick newborn, Rh incompatibility, phototherapy, congenital malformation, etc.). Another 19 neonate report was not followed up. All the babies enrolled were breastfed. The distribution of subjects according to the gestational age, gender and growth percentile curve is given in table 1.

| Table-1: Showing the distribution of gestational weeks, Gender and growth percentile curve in the included neonates. | | | |
|---|---|---|---|
| | | **Number (N)** | **Percentage (%)** |
| Gestational age in weeks | 37 | 91 | 30.43% |
| | 38 | 133 | 44.48% |
| | 39 | 50 | 16.72% |
| | 40 | 16 | 5.35% |
| | 41 | 1 | 0.33% |
| | 42 | 8 | 2.68% |
| Gender | Male | 177 | 59% |
| | Female | 122 | 41% |
| Growth percentile curve | AGA | 273 | 91.3% |
| | LGA | 7 | 2.34% |
| | SGA | 19 | 6.35% |

| Table-2: Showing the Mean ± SD of the birth weight and transcutaneous bilirubin level and serum total bilirubin | | |
|---|---|---|
| | **Mean ± SD** | **Min – Max** |
| Birth weight | 2.91 ± 0.49 | 1.9 – 4.5 |
| Forehead (QTcB) | 10.33 ± 3.34 | 0.5 – 16.8 |
| Sternum (QTcB) | 12.4 ± 3.44 | 3.1 – 22.0 |
| Serum bilirubin mg/dL | 12.19 ± 3.52 | 3.19 – 25.0 |

The Mean ± SD for transcutaneous bilirubin for forehead and sternum was 10.33 ± 3.34, and 12.40 ± 3.44 respectively and serum bilirubin levels is 12.19 ± 3.52. (Table 2)

| Table-3: Showing the Pearson's correlation between the forehead, sternum, and serum total bilirubin. | | | |
|---|---|---|---|
| | | Pearson's correlation | |
| Serum bilirubin | Forehead | r<br>p | 0.71 (<.001) |
| | Sternum | r<br>p | 0.90 (<.001) |
| Forehead | Sternum | r<br>p | 0.78 (<.001) |
| p-value <.05 is statistically significant; p-value<.001 is statistically highly significant (HS) | | | |

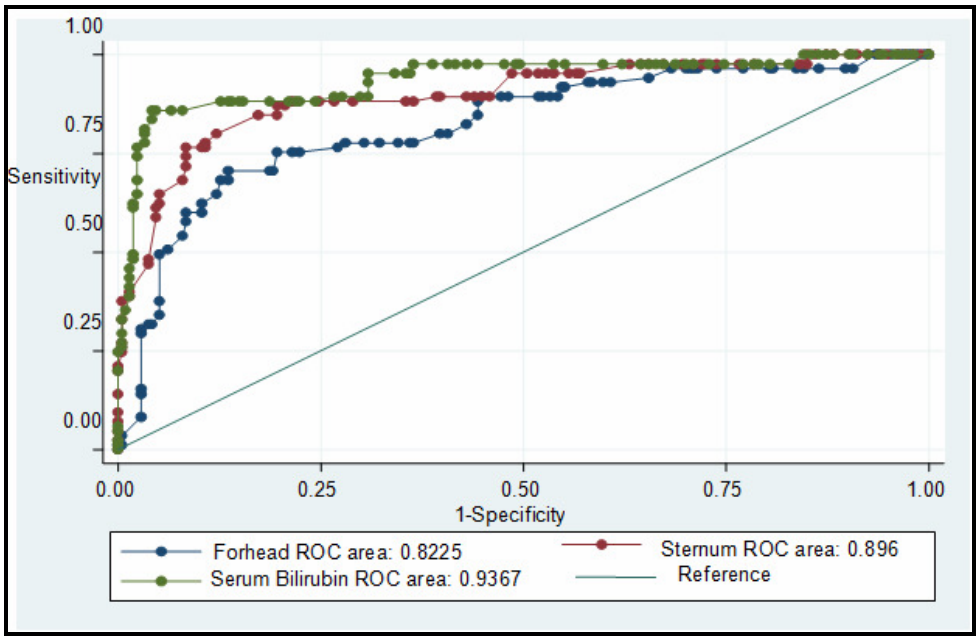
The correlation of coefficient of the sternum as a site of measurement in this study has the highest correlation of 0.90 ($p<0.001$) compared to the forehead with the serum bilirubin levels. We also assessed the sensitivity and specificity of QTcB measurements in correlation to forehead and sternum to the serum bilirubin levels along with the positive predictive value and negative predictive value (Table 3).

| Table-4: Showing the sensitivity and specificity, positive predictive value and negative predictive value for the bilirubin. | | | |
|---|---|---|---|
| | **Forehead** | **Sternum** | **Serum Bilirubin** |
| Sensitivity (%) | 77.65 | 88.24 | 88.25 |
| Specificity (%) | 64.02 | 71.03 | 84.58 |
| Positive predicted value (%) | 45.83 | 54.74 | 69.44 |
| Negative predicted value (%) | 87.74 | 93.83 | 94.76 |
| Cut off | 10.60 | 12.53 | 12.81 |

With the Receiver Operative Curve, the area under the curve for both sites forehead and sternum with serum bilirubin were comparable. The cut-off values for sternum and forehead and serum bilirubin respectively is 10.60, 12.53, and 12.81, with the sensitivity of 77.65%, 88.24%, and 88.25% respectively. The specificity for the above was 64.02%, 71.03%, and 84.5% for the forehead, sternum and serum bilirubin respectively (Table 4, 5 and fig 1)

| Table-5: Receiver operating characteristic (ROC) curves for prediction of serum bilirubin and transcutaneous bilirubin with cut off index | | |
|---|---|---|
| | **ROC** | **95%. C.I** |
| Forehead | 82.25% | 76.17% - 87.78% |
| Sternum | 89.60% | 85.30% - 93.89% |
| Serum Bilirubin | 93.67% | 90.21% - 97.12% |

**Fig-1:** Receiver operating curve for the prediction of sensitivity and specificity for transcutaneous bilirubinometer




Among the included subjects, 85(28%) neonates required phototherapy whereas 214(72%) discharged with no indication for phototherapy.

## Discussion

Kernicterus and bilirubin encephalopathy which of greater concern for neonatologists and pediatricians because of the earlier discharge of the mother and the baby from the hospital prevents adequate monitoring of jaundice. The possibility of using a noninvasive, painless, and reliable method to determine the bilirubin level and its increment in the first 72hrs hours after birth could be very important in the prevention of kernicterus. The primary outcome of the study is to assess the

correlation between the paired samples of transcutaneous bilirubin levels to serum bilirubin level in newborn at 72hrs of life.

The correlation coefficient of forehead QTcB of forehead is 0.71 ($p<0.001$) found in this study was higher than that described by other studies [8-10] while the correlation coefficient of chest (sternum) QTcB of 0.90($p<0.001$) is comparable to the finding of Schmidt et al over the sternum 0.79 to 0.92 ($p<0.001$) [11].

The discrepancy in the correlation of forehead and total serum bilirubin may be due to the fact that the forehead is continuously exposed to ambient light hence results varying from infant to infant. Similar to findings from this study, other studies using different transcutaneous bilirubin meters have also reported wide differences between TSB and QTcB's measured over forehead and chest [8-10] with an overall tendency of forehead and chest QTcB to underestimate the TSB. The reason for this is not clear but it might have to do with light exposure to the forehead and scarcity of subcutaneous fat in the sternal area.

Several studies done in the past has shown a good correlation between QTcB and TSB levels using various instruments available in the united states [12-13] and pre-discharge QTcB measurement are recommended by the American Academy of Pediatrics (AAP) as one of the methods of accessing the risk of subsequently developing or not developing hyperbilirubinemia [5].

Another study conducted by Keren et.al, [14] in a prospective cohort concluded that the combination of QTcB with the gestational age improved the accuracy of the prediction of subsequent rising serum bilirubin level, requiring the phototherapy treatment threshold recommended by the AAP [5]. The demographic data for our cases are typical of neonatal physiological jaundice with the preponderance of the neonate within the range of above 37 completed weeks and are only breastfed.
Similar to the finding of Keren et.al [14], and Newman et.al, [15] we found that simply combining the pre-discharge QTcB measurement with the infant's gestational age it does provides a good prediction of the risk of developing hyperbilirubinemia. When only exclusive breast neonates were included the prediction was slightly superior although not significantly better outcomes. It is possible that predischarge screening will definitely reduce the need for additional and unnecessary testing and inappropriate use of phototherapy and there is evidence that this has occurred in the past [16-17].

More testing and more treatment do have a negative effect on the bonding between the mother and the baby and affect breastfeeding [18]. As most of the infants had two reading of QTcB in the hospital pre-discharge, the calculated risk for hyperbilirubinemia and the need to start phototherapy was very decisive and quick.

The limitation of the study has been that we chose the peak pre-discharge QTcB as one of the predictors which have been used in the earlier studies. If the pre-discharge QTcB was low, some infants might not have been followed closely and probably subsequent hyperbilirubinemia must have been missed. The neonates who were readmitted for rebound hyperbilirubinemia after discharge was not followed up.

## Conclusion

All of the 299 breast fed babies who were screened for serum bilirubin and QTcB levels at 72hrs of life as per the study protocol, it was found that, transcutaneous bilirubinometry is an efficient method for screening babies for physiological jaundice, it a non-invasive and rapid way to access the bilirubin, reducing the prolonged stay of the babies in the hospital. It was also observed that based on the QTcB a quick decision can be made whether the baby requiring phototherapy/not or the baby ready for discharge.

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