ORIGINAL RESEARCH

A COMPARATIVE STUDY OF TRANSCUTANEOUS BILIRUBIN WITH SERUM BILIRUBIN AT DIFFERENT SITES IN NEONATAL JAUNDICE

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ABSTRACT
Neonatal hyperbilirubinemia affects 50-80% of all neonates and higher percentage of preterm babies. To prevent complications arising from this, TSB is assessed. This method, though the gold standard has its own drawbacks. Hence, the need for a different modality of estimation and screening for hyperbilirubinemia like TcB.Of the 519 neonates included in the study, a slight male preponderance was seen, with a large number of neonates being of term gestation and a mean birth weight of 2.55 Kg. It was found in the study that TcB correlated well with TSB at moderate levels (10-15 mg/dl) , than at lower levels. Readings over sternum, interscapular regions gave better correlation with TSB levels than forehead. But as a screening tool, any of the three sites could be used.
Key words: Serum bilirubin, TcB, Jaundice

INTRODUCTION

The clinical condition of hyperbilirubinemia, the yellow discoloration of the skin and sclera is known as Jaundice [1]. Neonatal hyperbilirubinemia is extremely common condition affecting 50 to 80% of all neonates and higher percentage of preterm babies [2]. The burden is unacceptably high in LMICs and has prompted calls for intense scrutiny and attention [3]. Under the millennium development goals, the potential impact of adverse perinatal conditions such as preterm birth complications and birth asphyxia on thriving and wellbeing beyond survival rarely received attention [4] . With the current focus on inclusiveness for persons with disability under the SDGs, it is essential that we tackle SNJ as a key component of optimizing neurodevelopmental outcome.

Jaundice affects at least 60% of full-term and 80% of preterm neonates suggesting that about 84–112 million of the 140 million babies born yearly worldwide will develop this condition in the first 2 weeks of life. About one in ten newborn babies are likely to develop clinically significant jaundice or hyperbilirubinemia, requiring close monitoring and treatment.

It is a common and often harmless clinical condition in neonates. The bilirubin level above 95th percentile may lead to acute bilirubin encephalopathy and/or kernicterus which has long term morbidity in form of cerebral palsy, deafness etc.. Conventionally neonatal hyperbilirubinemia has been defined as Bilirubin

levels greater than 5 mg/dL on first day, 10 mg/dL on second day, and 12-13 mg/dL thereafter in term neonates[5] .

Any TSB value of 17 mg/dL or more should be regarded as pathologic and should be evaluated for the cause and possible intervention such as phototherapy is given.

Complications are preventable through early recognition, appropriate follow up and treatment such as phototherapy and exchange transfusion. The AAP guideline recommends assessment of jaundice in all newborns before hospital discharge [11]. It recommends the initiation of phototherapy to reduce excessive bilirubin for neonates falling in the severe hyperbilirubinemia[6].

The current gold standard to measure bilirubin levels is invasive blood sampling, commonly performed by venipuncture, followed by laboratory analysis of the blood sample. This method provides the total serum bilirubin concentration (TSB). Over the years this method has been proven to be successful in preventing kernicterus[7].

Invasive blood sampling is painful and stressful for the neonate, resulting in blood loss and an increased risk of developing sepsis, osteomyelitis and infections at the site of sampling [8]. In addition, the method is laborious and time consuming, an economic burden in the low income groups and lacking the possibility for immediate diagnosis or bed side monitoring of bilirubin levels.

METHODOLOGY

Study design: This is a comparative prospective cross sectional study**.**

Study period: 18 months

Inclusion Criteria:

All neonates with clinical jaundice both delivered in hospital and those delivered in other facilities and admitted with complaint of jaundice.

Exclusion Criteria:

1. Neonates already treated for hyperbilirubinemia (phototherapy or exchange transfusion)
2. Neonates with major congenital anomalies

All the patients fulfilling the inclusion criteria were enrolled for the study after obtaining informed consent. Purpose of the study was explained to the parents. Each day the patients were examined for any yellow discoloration indicating jaundice. Case record form with follow up chart i.e, proforma was used to record the findings. On day of appearance of jaundice transcutaneous bilirubin levels are measured at three different sites – forehead, sternum and interscapular region. Simultaneously, sample was drawn and sent for serum bilirubin.

Transcutaneous Bilirubinometry works by directing light into the skin of neonate and measures the intensity of specific wavelength that is returned. The number of wavelengths, used is variable in different transcutaneous bilirubinometers. The meter analyzes the spectrum of optical signal reflected from the neonate's subcutaneous tissues. These optical signals are converted to electrical signal by a photocell. These are analyzed by a microprocessor to generate a serum bilirubin value.

All transcutaneous bilirubinometers are spectrophotometric instruments that operate in the following manner:

Step 1: A pressure-sensitive probe is activated when pressed on the infant's skin. This illuminates a light-generating tube to produce a bright strobe light.

Step 2: This bright light travels for a short distance through the skin and trans illuminates the underlying subcutaneous tissue.

Step 3: The resultant scatter of light is then channeled through fiber optic filaments to a spectrophotometric module.

Step 4: In the spectrophotometric module, a dichromic mirror splits the reflected light into two component spectra that pass respectively through green (with maximum absorption at wavelength 550nm) and blue (with maximum absorption at wavelength 460nm) light filters. The difference between the optical densities of the beams traversing through the two filters indirectly indicates the intensity of yellow colour of the reflected beam and therefore, of the dermis of the infant.

Step 5: The instrument translates this yellow colour intensity to an arbitrary displayed number; the higher the number, the higher the intensity of yellow colour. The instrument is calibrated to read white light as zero. During regular use, the instrument is calibrated against glass standards/white sheets (with specific colour intensities) and the coefficient of variation for successive readings in a particular subject should not exceed 5% (manufacturer's recommendations).

Outcome measures:

Diagnostic accuracy of transcutaneous bilirubin readings when compared to serum bilirubin.

Diagnostic accuracy of transcutaneous bilirubin measured at different sites.

RESULTS

Table 1: Results of the TcB findings at different sites compared to TSB

TcB Site	Mean	SD*	SE#	MD@	t-test	P value
Forehead	10.43	3.503	0.154	0.154	1.718	0.086
Sternal	10.57	3.515	0.154	0.303	3.232	0.001
Inter-scapular	10.64	3.489	0.153	0.366	4.030	0.000
Mean TcB	10.51	3.439	0.151	0.236	2.724	0.007

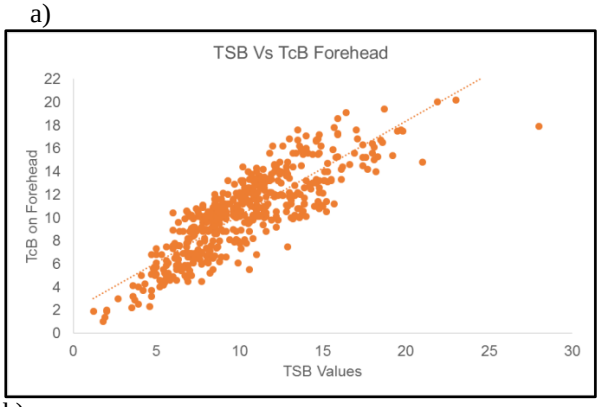
*Standard deviation, # Standard error, @Mean Difference

The mean, standard deviation and standard error of the bilirubin levels recorded using the device do not show much variation at the three different areas of the body. The correlation between the bilirubin levels on the forehead, sternum and inter scapular region with TSB levels was 0.086, 0.001 and 0.000 respectively. This shows that the TSB and the TcB levels at sternum and inter scapular region were significant but the TcB recorded on the forehead was not significant statistically.

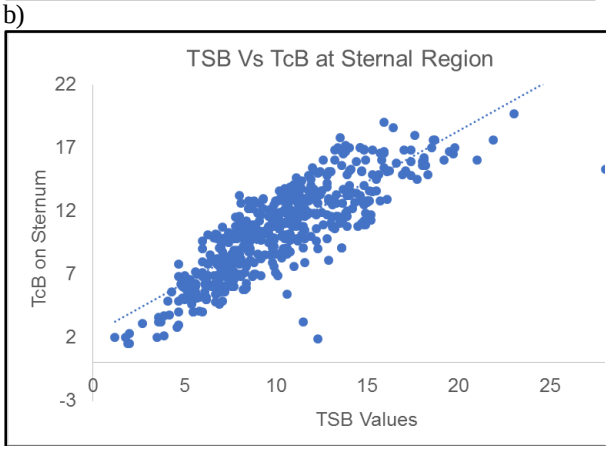
The scattering of the mean of TcB readings of these 3 sites is almost similar to that of TSB.This shows that the transcutaneous bilirubin levels are same as that of TSB. The mean TcB is 10.5 + 3.44 mg/dl while the range is 1.33 to 19.8 mg/dl.

It is seen that there is little difference in TcB and TSB readings when the bilirubin levels are low and moderate(10-15mg/dl) and the TcB variation is more when levels of serum bilirubin are higher.
The TSB levels was compared with the TcB readings at forehead, sternum and interscapular regions and the scatter plot drawn for these findings. The scatter plots had similar distribution in the forehead and sternal region and the values close to the trendline with very few observations lying away from the trendline. This shows the strong correlation between the TSB and the TcB readings at the different sites.

a)



b)



c)

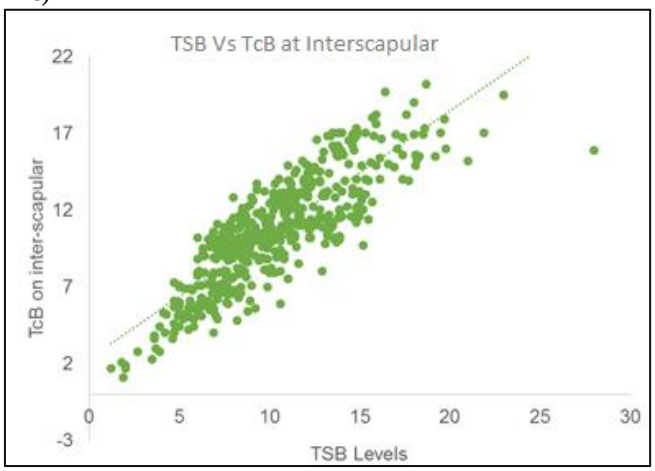


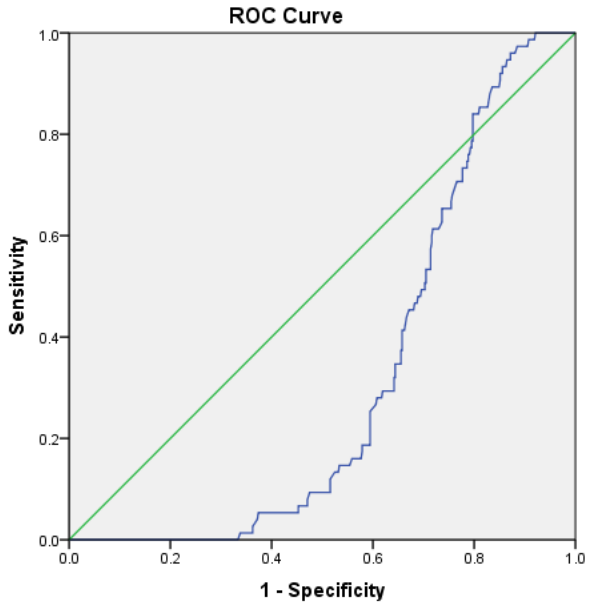
Fig 1: TSB VsTcB at Different sites comparison – a) Forehead b) Sternum c) Interscapular

Table 2: Sensitivity and specificity for TcB (Test variable) Vs TSB (State variable)

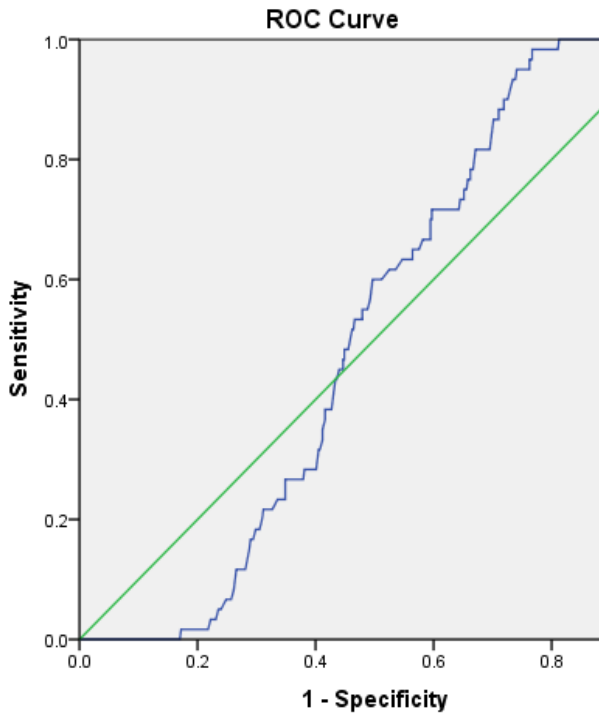
TSB (mg/dl)	Sensitivity	1-Specificity
8	70.7%	77.5%
10	66.7%	58.6%
12	54.5%	29.1%
15	73.9%	85.2%
18	90.3%	96.2%

Receiver Operating Curve (ROC)

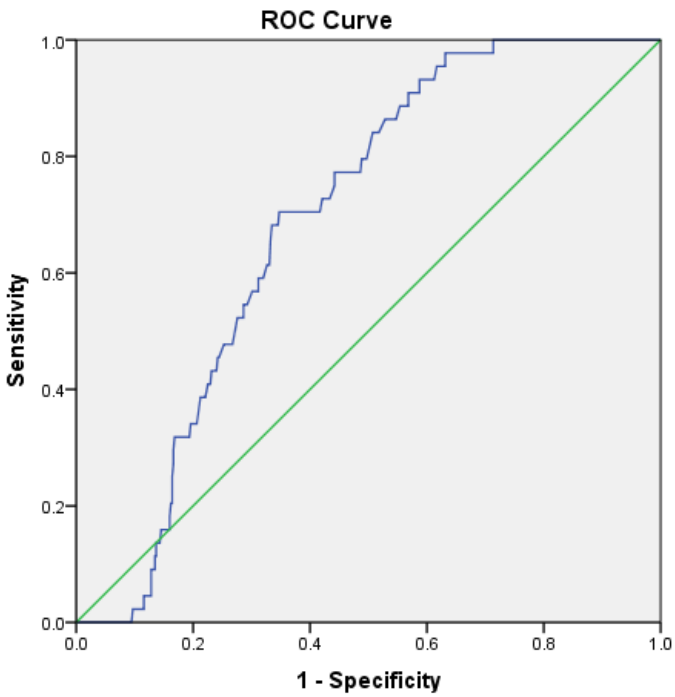
The receiver operating curve was obtained to assess the reliability of TcB at various readings of the TSB. When cut off for TSB is taken as 8 mg/dl the ROC for TcB showed AUC as 0.317. When TSB 10 mg/dl AUC for TcB is 0.512. These values indicate that the testing tool is not reliable and has poor sensitivity and specificity. But when the TSB was 12 mg/dl the AUC in ROC for TcB is 0.689 which is valid. As TSB cut off was increased to 15 mg/dl and 18 mg/dl the AUC improved to 0.795 and 0.933 respectively. Thus the TcB test is more reliable and valid at higher levels of serum bilirubin. The sensitivity increased as the TSB cut off level is increased as shown in Table 2. When the cut off of TSB was taken as 8 mg/dl the sensitivity is 70.7%, at 10 mg/dl it is 66.7%, at 12 mg/dl sensitivity is 54.5%, at 15 mg/dl is 73.9% and at 18 mg/dl it is 90.3%.



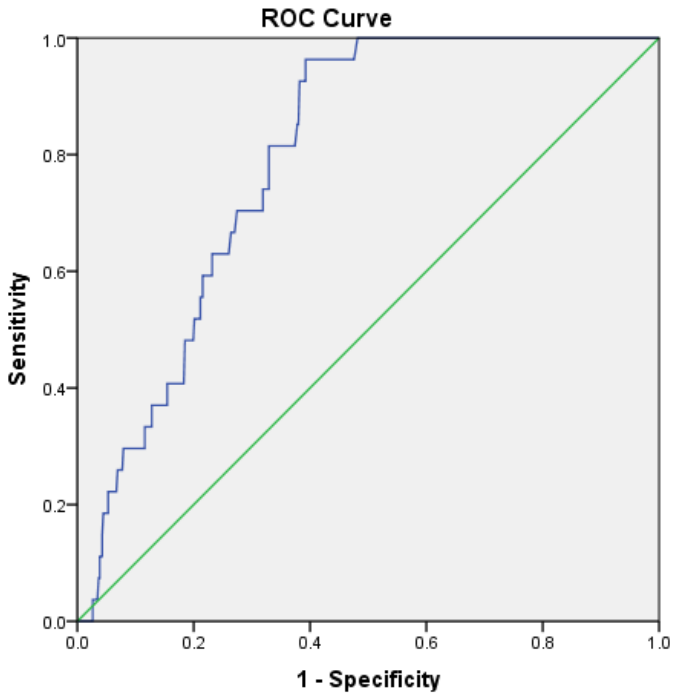
(a) Cut off TSB is 8 mg/dl : AUC = 0.317



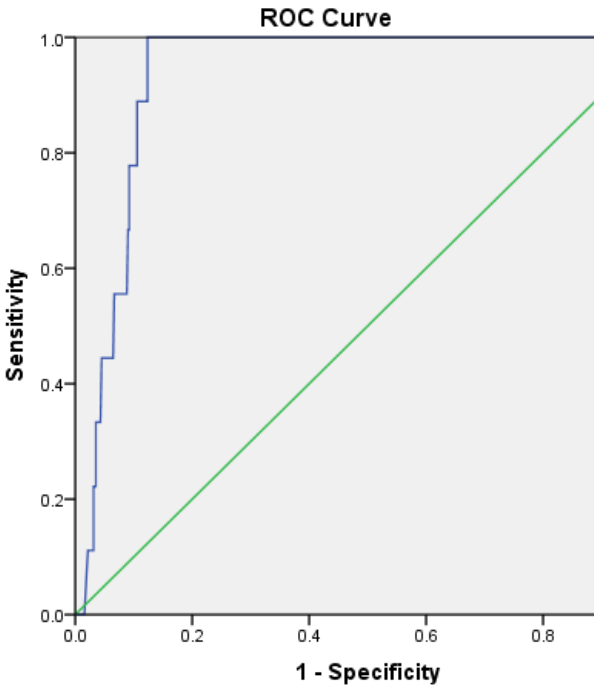
(b) Cut off TSB is 10 mg/dl : AUC = 0.512



(c) Cut off TSB is 12 mg/dl: AUC = 0.689



(d) Cut off TSB is 15 mg/dl : AUC = 0.795



(e) Cut off TSB 18 mg/dl :AUC = .933

Fig 2: ROC curve for the different TSB values

DISCUSSION

The correlation between the bilirubin levels on the forehead, sternum and inter scapular region and TSB levels was 0.086, 0.001 and 0.000 respectively in our study. This shows that the TSB and the TcB levels at sternum and inter scapular region were significant but the TcB recorded on the forehead was not significant statistically. Though the forehead is highly vascular and has lower amounts of subcutaneous fat, the nonsignificance of readings obtained from forehead area could probably be attributed to difference in pigmentation of the skin and the cultural practice of applying "kajal" on the forehead of infants, followed alike by most communities in India.

In the Mongolian study, the p-value for the comparison between TSB and TcB on forehead was 0.315 and TcB on midsternum was 0.073. This comparison between TcB (forehead) and TcB (midsternum) was 0.247. This study demonstrated a strong correlation between TcB and TSB measured at both the forehead and midsternum of ethnic Mongolian neonates [9]. This study validates the use of TcB as an alternative, quick and convenient measure of TSB in ethnic Mongolian neonates.

In another study the measurement of TcB with and without phototherapy was assessed for the forehead and sternum sites. The linear regression analysis in both conditions on forehead and sternum TcB values well matched to the corresponding TSB value; however, the correlation coefficients were lower than those obtained without phototherapy. In this study the forehead TcB was better matched to the corresponding TSB value than the sternum TcB. This study confirmed that TcB assessment in NICUs is accurate, more so in infants without phototherapy than in babies who receives phototherapy [10], which was contrary to our study as described above.

The accuracy of interscapular area as a site for measuring TcB in neonates has not been studied as extensively as the other sites (forehead, sternum), which was one of the aims of our study. But a similar study like ours comparing the three sites was done in a hospital based prospective comparative study in Jaipur on early preterm infants with gestational age ≤ 34 weeks. Transcutaneous bilirubin was measured from three sites: forehead, sternum and interscapular region. Correlation coefficients of transcutaneous bilirubin measured from forehead, sternum and interscapular sites were 0.82, 0.84 and 0.86 respectively. TcB measured from all the three sites correlated significantly with serum bilirubin ($p < 0.001$), but the correlation was best at interscapular site. Interscapular site had the highest sensitivity and lowest false negative rate (87.6 and 12.4% respectively) as compared to forehead (79.2 and 20.8% respectively) and sternum (87.1 and 12.9% respectively)[11]. Therefore, recommending interscapular region as a reliable site in infants for measuring transcutaneous bilirubin. Similar results were obtained in our study. The skin thickness and the subcutaneous fat in the interscapular region is less with good number of capillaries, which could attribute to the superiority of interscapular site in measuring TcB.

Though in comparison to the above study, our study included neonates belonging to late preterm and term gestation with most of them being in the weight range of 2.1-3 kgs. Good co-relation was found in all the serum bilirubin and TcB at all three sites but the, the co-relation was significant over the sternum and interscapular regions.

In a cross-sectional study done at Groote Schuur neonatal unit TcBs were measured over the forehead, sternum and interscapular area in neonates. Pearson's correlation coefficients and differences between TSB and TcBs were computed. This study documented the correlation coefficients for TcBs ranged from 0.859 to 0.929 (P=0.001). With respect to initiating phototherapy, the interscapular site had the highest sensitivity of 94% and lowest false negative rate of 6%, thus concluding using transcutaneous bilirubinometry, the interscapular site is superior and safer for screening preterm neonates [12].

The Amigo MBJ20 meter used in our study had good validity. It is the first handheld bilirubinometer of designed in India. This tool is non-invasive and easy to use, gives prompt measurements, and is minimally influenced by skin pigmentation. Therefore this can be used for screening jaundice in hospitals, NICUs and home visit setting too, reducing the time and labour and the economic burden in detecting hyperbilirubinemia in neonates. The TcB jaundice

meter would be suitable for the early detection of subsequent hyperbilirubinemia especially when postnatal discharges are done early these days.
It can be used at various sites against any bony prominence, on the forehead, sternum and interscapular regions, with either site being used for co-relation with serum bilirubin levels, but with slightly more accurate levels in sternal and interscapular region.

CONCLUSION

The risk of unmonitored neonatal jaundice is uncertain. Total bilirubin is measured via blood obtained from venipuncute. Though this is the gold standard, it has its own drawbacks like- requirement of skill to draw blood in a neonate, pain, stress and risk of infection in the neonate, time lag in obtaining results causing delay in interventions, economic burden on the parent, etc.Hence the need for an alternate method to assess bilirubin levels. As it is a simple and feasible non-invasive tool, requiring less skill and time of medical personnel to estimate hyperbilirubinemia at bedside in neonates, Transcutaneous Bilirubin screening can be used to prevent many complications due to hyperbilirubinemia.
The Amigo MBJ-20 jaundice meter is a valuable screening tool for assessing jaundice in neonates. All the three sites – forehead, inter scapular and sternal regions, are suitable for performing transcutaneous estimations to screen neonates initially for hyperbilirubinemia, with better correlation at higher level of jaundice, and the sternal and interscapular areas showing a slight edge over the forehead region.

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