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Accuracy of Transcutaneous Bilirubin at Multiple Sites in Comparison to Serum Bilirubin in Neonatal Jaundice

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Abstract

Objective: To study accuracy of transcutaneous bilirubin at multiple sites in comparison to serum bilirubin in neonatal jaundice. Methods: Present cross sectional study included 361 neonates developing jaundice within 2 weeks of life. Transcutaneous bilirubinometer (model MBJ 20) was used to record TcB at following sites - forehead, sternum, upper thigh and sole (near heel). Corresponding serum bilirubin (SBR) level was obtained within 30 minutes of TcB reading. Results: Of 361 neonates, 6 were excluded due to insufficient data, there were 185 males, 170 females, 277 term, 78 preterm neonates and 103 low birth weight and 21 very low birth weight neonates. Majority (58.3%) were between 4-6 days of life. Though, all the sites correlated with SBR, forehead (FH) TcB best predicted SBR in both preterm and term neonates. Between FH TcB and SBR, correlation coefficient was 0.749 indicating a positive and significant correlation (p=0.000). We also found maximum agreement of 86.8% at 5mg/dl to 15mg/dl range between FH TCB and SBR values. The sensitivity of FH TcB was 81.40%, specificity 73.45%, positive predictive value 86.78% and negative predictive value was 64.84%. Conclusions: Forehead is the most ideal site for TcB measurement. The maximum agreement between FH TcB and SBR was in the 5mg/dl to 15 mg/dl range.

Key words: transcutaneous bilirubin, serum bilirubin, neonatal jaundice.

INTRODUCTION

Neonatal jaundice due to physiological immaturity of newborn babies is seen in nearly 60 percent of term and 80 percent of preterm neonates.[1] Hyperbilirubinemia, when excessive, can lead to potentially irreversible bilirubin-induced neurotoxicity called kernicterus. Kernicterus is associated with major neurological sequelae such as athetoid cerebral palsy, deafness, and intellectual deficits.[2] This can be prevented by early detection, prompt and timely management of jaundice.

Management of neonatal jaundice often requires measurement of total serum bilirubin. Total serum bilirubin is commonly determined by spectro-photometric methods by analyzing plasma or serum sample. Such techniques require drawing of blood causing pain, trauma, and discomfort to neonate.[3] The wait for the result may also unnecessarily delay discharge of both the mother and baby from the hospital.[4] In addition, there is wide range of intra and inter-laboratory variability in the performance of the bilirubin analyzers. Non-invasive assessments have included visual assessment of jaundice, blanched-skin color comparison with color strips that have previously demonstrated poor performance.[3-8] More objective methods, such as the icterometer, have attempted to standardize the subjective visual assessment with modest success.[9]

A large number of studies have demonstrated the possibility of prediction of serum bilirubin in neonates by measuring the yellowness of the skin in neonatal jaundice using transcutaneous bilirubinometers.[3,4,8-10] Transcutaneous bilirubinometry measures the intensity of yellow color in the skin and subcutaneous tissue and correlates with the serum bilirubin concentration in newborn infants.[9] These meters work by directing light into the skin of the neonate and measuring the intensity of specific wavelength that is returned. It is reported as safe, simple, objective, reproducible, cost effective, non-invasive modality in the screening and monitoring in neonatal jaundice.[11-16] The measurements are accurate for newborn of all races and ages.[3,4,9,11,12] It is optimized for measuring bilirubin in the venous plexus. The results are obtained in clinically appropriate units - mg/dl or micro mol/L.

Transcutaneous bilirubinometer values are found to vary at different sites. Hence, the present study was undertaken to find out the most ideal site for Transcutaneous bilirubin (TcB) measurement with an objective to study the correlation between TcB levels at multiple sites and serum bilirubin in neonatal jaundice. The present study was based on the hypothesis that there is no difference between TcB at multiple sites and serum bilirubin level in neonates (<2 weeks of age).

MATERIALS AND METHODS

The present study was a cross sectional study conducted from April 2011 to August 2011 in a tertiary care center in southern India after obtaining clearance from the institutional ethical committee. Newborns delivered at or referred to our hospital and fulfilling the criteria of jaundice, aged less than 2 weeks, were included in the study randomly by simple random sampling technique using random number tables. Neonates with any bruises, vascular malformations, or hyperemia at the sites of proposed measurement and neonates whose TcB values could not be confirmed by SBR within 30 minutes were excluded from the study. Also, neonates already on phototherapy were excluded from the study.

The primary objective of the study was to study correlation between transcutaneous bilirubin levels at multiple sites and serum bilirubin in neonatal jaundice. Sample size was calculated to be 340 using the formula {N= Z2 (1-α/2) × p × q /d2}and taking

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prevalence of jaundice in newborns as 66% with the absolute permissible error, d=5% at 95% confidence limit.[1]

Detailed history and examination of neonates admitted with jaundice was carried out, according to a predesigned proforma. After obtaining informed consent from parents and guardians, blood samples in all the admitted neonates were drawn from a peripheral vein for serum bilirubin (SBR) level estimation along with other investigations to evaluate the cause of jaundice. Serum bilirubin was estimated by diazo method of Pearlman and lee. Transcutaneous bilirubinometer (model: MBJ20, Beijing M&B electronic company limited) instrument was kept on the measuring site such that it completely touches the skin and no gap was seen between skin and Transcutaneous bilirubinometer. The readings were taken from multiple sites namely, forehead, sternum, upper part of thigh, and sole (near heel) and the probe was disinfected with 70% isopropyl alcohol after using it on each baby.[8] All the readings were taken by second author. Two readings were taken within a gap of 10 seconds at each site. Average of two readings was taken. Serum bilirubin value of the corresponding neonate was obtained within half an hour after the readings of Transcutaneous bilirubinometer.

Statistical analysis was performed using SPSS version 16.0 for MS-Windows. Pearson's correlation analyses and linear regression analyses were performed using the SPSS statistical software. 'p' value was calculated and p value <0.05 was taken as statistically significant. Usefulness of TcB as a diagnostic tool as compared to serum bilirubin was evaluated by sensitivity, specificity, positive predictive value and negative predictive values.

RESULTS

A total of 361 neonates fulfilling the inclusion criteria were included for the study. Out of 361 neonates, 6 neonates were excluded due to lack of confirmation of TcB values by serum bilirubin. A total of 355 neonates were finally selected for the present study. The baseline characteristics of these 355 neonates are shown in Table 1. Majority (58.3%) were aged between 4-6 days of life, mean age in days was 4.69±2.05 days and there were 185 males and 170 females with M:F ratio of 1.09:1. There were 103 low birth weight and 21 very low birth weight neonates. There were 78 preterm and 277 term neonates. Clinically, by visual assessment of jaundice, 109 neonates had jaundice till trunk and 159 had till lower limbs (but not palms and soles).

The correlation between serum bilirubin values and transcutaneous bilirubin values at various sites is shown in Table2. Of the four sites measured, forehead (FH) TcB and SBR had a significant association (p= 0.000), where in as the forehead TcB values increased, SBR values also increased linearly. This was further confirmed by Pearson's product moment correlation (r= 0.749,p=0.000) between FH TcB values and SBR values. We also found maximum agreement of 86.8% at 5mg/dl to 15mg/dl range (as shown in Figure 1). Though, there is significant association between TcB at other sites and serum bilirubin, the best correlation was between FH TcB values and SBR values as shown in [Table 2].

[Table 3] shows the accuracy of TcB values for serum bilirubin in the range 5mg/dl to 15mg/dl. This table shows that forehead is the most ideal site with sensitivity of 81.40%, specificity of 73.45% and positive predictive value of 86.78%. The second best site is thigh with sensitivity of 73.16%, specificity of 66.26% and positive predictive value of 87.66%..

When correlation was studied separately for preterm and term neonates there was statistically significant correlation of TcB with SBR in both the groups in any of the sites studied. FH TcB values showed significant association (p=0.000) in both the groups. This was further confirmed by Pearson's product moment correlation(r=0.750,p=0.000) for term neonates and for preterm neonates correlation was found to be (r=0.751,p=0.000) between FH TcB values and SBR values as shown in [Table 4].

DISCUSSION

The use of TcB reading as a screening device for neonatal jaundice is based on the assumption that serum and tissue bilirubins are in constant equilibrium. However, TcB and SBR measurements are evaluating different physiologic entities. TcB measures the blilrubin that has moved from the serum to tissue, similar to the movement of bilirubin across the blood brain barrier into the brain tissue, whereas serum bilirubin measures that which is circulating in the blood. Thus, TcB may in fact provide more information than SBR, although this hypothesis needs to be proved.[17] In the present study, TcB correlation with SBR was evaluated in neonates aged less than 2 weeks having jaundice and a good correlation was found between TcB at forehead and SBR.

Parameter		Frequency	Percent (%)
Age (days)	<4	103	29.0
	4-6	207	58.3
	>7	45	12.7
Sex	Male	185	52.11
	Female	170	47.89
Birth weight	>2.5kg	231	65.10
	1.5-2.5kg	103	29.0
	<1.5kg	21	5.9
Gestational age	Preterm	78	22.0
	Term	277	78.0
	Post-term	0	0
Visual jaundice	Face	3	0.8
	Trunk	109	30.7
	Lower limbs (not palms and soles)	159	44.8
	Palms and soles	84	23.7

Table 2 - Correlation of TcB at various sites with SBR

Sites	Trans-cutaneous Bilirubin	Serum Bilirubin Values				
		<5mg/dl N (%)	5-15mg/dl N (%)	15-20 mg/dl N (%)	>20mg/dl N (%)	Pearson's correlation
Forehead	<5mg/dl 5-15mg/dl 15-20mg/dl >20mg/dl	3 (50.0) 3 (50.0) 0 (0) 0 (0)	5 (2.2) 197 (86.8) 25 (11.0) 0 (0)	0 (0) 38 (40.9) 54 (58.1) 1 (1.1)	0 (0) 4 (13.8) 19 (65.5) 6 (20.7)	0.749 (p=0.000)
Sternum	<5mg/dl 5-15mg/dl 15-20mg/dl >20mg/dl	4 (66.7) 2 (33.3) 0 (0) 0 (0)	12 (5.3) 178 (78.4) 36 (15.9) 1 (0.4)	0 (0) 42 (45.2) 49 (53.3) 2 (2.2)	0 (0) 5 (17.2) 16 (55.2) 8 (27.6)	0.041 (p=0.436)
Upper 1/3rd of thigh	<5mg/dl 5-15mg/dl 15-20mg/dl >20mg/dl	3 (50.0) 2 (33.3) 0 (0) 1 (16.7)	15 (6.6) 199 (87.7) 13 (5.7) 0 (0)	0 (0) 67 (72.0) 26 (28.0) 0 (0)	0 (0) 4 (13.8) 22 (75.9) 3 (10.3)	0.599 (p=0.000)
Sole (near heel)	<5mg/dl 5-15mg/dl 15-20mg/dl >20mg/dl	6 (100) 0 (0) 0 (0) 0 (0)	184 (81.1) 43 (18.9) 0 (0) 0 (0)	43 (46.2) 50 (53.8) 0 (0) 0 (0)	6 (20.7) 23 (79.3) 0 (0) 0 (0)	0.552 (p=0.000)

Table 3 - Accuracy of TcB values at various sites in the range of 5-15mg/dl

	Sternum	Upper thigh	Sole (near heel)
Sensitivity	78.41	73.16	37.06
Specificity	61.71	66.26	23.01
Positive predictive value	78.41	87.66	18.94
Negative predictive value	61.71	42.96	42.96

Table 4 - Correlation of TcB at various sites with SBR in preterm and term neonates

TcB at various sites	Term	P value	Preterm	P value
Forehead	0.750	0.000	0.751	0.000
Sternum	0.029	0.626	0.302	0.007
Upper 1/3rd of thigh	0.587	0.000	0.638	0.000
Sole (near heel)	0.569	0.000	0.449	0.000

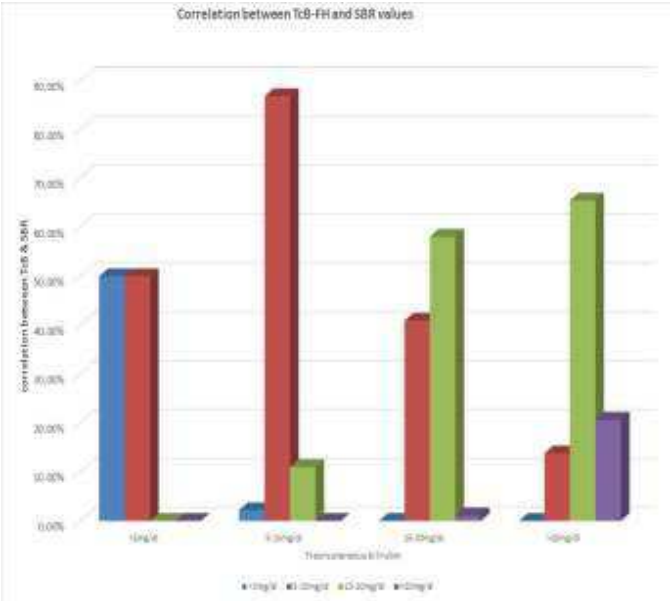

Figure 1 - Correlation between TcB-FH and SBR values

Similar results were obtained by Mahajan et al,[8] Arror et al and Sharma et al.[13,18] Maisels et al,[19] found that sternum TcB measurements correlate better with SBR than FH TcB measurement. They suggested that measurements from the sternum which is less likely to be exposed to sunlight or ambient light than forehead may be more desirable; especially after infants have been discharged from hospital. Randeberg et al,[20] found that TcB measurement on neonates taken from heel, back or thigh did not correlate as well with SBR as those taken from forehead. Skin thickness, vascularity of the skin, exposure to light and ease of measurement against a bony prominence in forehead and sternum may be some of the factors which explain the variability in value between the sites.[21]

In the present study maximum agreement between FH TcB values and SBR values were found in the range of 5-15mg/dl as shown in figure 1. However, for all the sites including forehead the agreement between SBR and TcB was reducing with values more than 15mg/dl. Similar results at SBR more than 15mg/dl were reported by Maisels et al.[19] El-Beshbishi et al,[22] also reported that TcB values more than 12-13mg/dl should be confirmed by SBR measurements. Hence, TcB values may not be reliable in higher levels of hyperbilirubinemia. Maisels et al,[19] also found in the black population, that the differences between the TcB and SBR measurement tend to increase with rising SBR levels. Hence, TcB may be used as a screening tool, but cannot be used directly to make decision on phototherapy and exchange transfusion. In the present study, there were about 94 cases with SBR between 15-20mg/dl and we had only 8 cases with SBR more than 20mg/dl. Hence, it is difficult to comment on this aspect in the present study.

Legend : correlation between transcutaneous bilirubin and serum bilirubin

X axis – Transcutaneous bilirubin, Y axis – correlation between TcB and SBR, Bars – Serum Bilirubin

For neonatal jaundice, screening test should have a high sensitivity, so that no neonate with the cut off level is missed, though few cases are falsely picked up. In the present study FH-TcB had sensitivity of 81.40% and specificity of 73.45%. This was closely followed by Sternum-TcB with sensitivity of 78.41% and specificity of 61.71%. Harish et al,[14] reported 97.3% sensitivity and 50.0% specificity of FH TcB at SBR of more than 13mg/dl. Rubaltelli et al,[17] found sensitivity of 90% and specificity of 87% for FH TcB at SBR of 17mg/dl.

As the thickness of skin varies between preterm and term neonates, we found a need to compare TcB correlation at different sites, separately for preterm and term neonates. We found statistically significant correlation in both the groups in any of the sites. Similar results were obtained by Mahajan et al and Harish et al,[8,14] who found statistically significant correlation in both the group. Limitation in the present study was that the present study included very few neonates with SBR less than 5mg/dl and more than 20mg/dl. Hence, correlation with SBR in these ranges is difficult to conclude.

CONCLUSION

Forehead is the most ideal site for TcB measurement with significant correlation with SBR.The maximum agreement between FH TcB and SBR was in the 5 to 15mg/dl range.

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