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Evaluation of Jaundice meter in the assessment of jaundice among Nigerian preterm neonates

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Abstract: *Background:* The objective assessment of the severity of neonatal jaundice is Total Serum Bilirubin (TSB) determination, which requires multiple blood sampling. This has inherent problems, including risks of anaemia and infection. Transcutaneous Bilirubinometry (TcB) is a reliable, non-invasive alternative, however there is paucity of data on its performance in black preterm neonates.
Objectives: To evaluate the correlation between transcutaneous bilirubin (TcB) and total serum bilirubin (TSB) among Nigerian preterm neonates, and to determine the parameters affecting the relationship.
Method: Jaundiced preterm neonates delivered between 28 and 36 weeks of gestation admitted at the Irrua Specialist Teaching Hospital (ISTH), Nigeria were recruited . The TSB levels were determined by spectrophotometry while the corresponding TcB levels were obtained using Jaundice Meter (JM-103). The neonates were stratified into gestational age and birth weight groups.
Results: A total of 189 paired TcB and TSB levels were obtained from 60 neonates. The Mean (sd) TcB level of 11.4 (3.1) mg/dl was significantly higher than the mean TSB level of 10.2 (2.8)mg/dl (p= 0.028). The overall correlation coefficient between TcB and TSB was 0.98 and it was not significantly affected by the gestational age, birth weight and bilirubin levels.
Conclusion: Transcutneous bilirubin strongly correlates with total serum bilirubin levels among Nigerian preterm neonates, irrespective of gestational age, birth weight and the degree of jaundice.

Keywords: hyperbiliruinaemia, jaundice meter, Nigerian, preterm, neonates, transcutaneous bilirubinometry

Introduction

Neonatal Jaundice (NNJ) is a major cause of neonatal morbidity and mortality in developing countries, including Nigeria[1-3]. Jaundice is more prevalent, more severe and associated with a higher risk of bilirubin encephalopathy, and runs a more protracted course in preterm than term neonates[4-7].
Transcutaneous bilirubinometry, a non-invasive method of assessment of severity of neonatal jaundice (NNJ) has been extensively studied in term infants and shown to significantly reduce the need for blood sampling and the delay in intervention for NNJ in the Caucasians[8-15]. In contrast, less has been done on the reliability of transcutaneous bilirubinometry in preterm neonates, particularly in the Blacks. Transcutaneous bilirubinometry may be more beneficial to the Blacks in the gross resource-limited developing countries, particularly in Africa, because of the unfavourable conditions under which NNJ is managed. These conditions include poor access to healthcare facilities, erratic electricity, inadequate diagnostic and treatment facilities.
The Jaundice meter is portable and rechargeable. Moreover, gestational age and skin pigmentation have been speculated as potential limitations in the use of TcB[16]. Previous studies among term neonates in Nigeria suggested that skin pigmentation may not constitute a major limitation to the use of transcutaneous bilirubinometers[1,17]. There is however a dearth of data among preterm neonates, especially among Blacks in which transcutaneous bilirubinometry may be of particular benefit. This study set out to evaluate the correlation of the Jaundice Meter (JM-103) with TSB in assessing the severity of jaundice in Nigerian preterms and the factors affecting its correlation.

Subjects and Method

The study was carried out at the Special Care Baby Unit (SCBU) and Post Natal Ward (PNW) of Irrua Specialist Teaching Hospital (ISTH), Edo State, Nigeria. Approval was obtained from the Research and Ethics Committee of the hospital while written informed consent was obtained from the parents of the neonates involved. Subjects were consecutive jaundiced preterm neonates between the gestational ages of 28 and 36 weeks. They were recruited when the determination of serum bilirubin levels was indicated based on clinical assessment. Gestational age was assessed on admission using the results of antenatal ultrasonography, Naegele's rule and clinical assessment using the new Ballard Score[13]. Neonates who had undergone exchange blood transfusion, and those whose gestational ages could not be determined were excluded[8,10]. Neonates on phototherapy who were otherwise eligible for recruitment were included; an opaque plaster was applied to the site used for Tc Breadings, to prevent the bleaching effect of phototherapy on the skin[18,19].

The TcB readings were carried out using the Jaundice Meter-103 (JM-103). The JM-103 has been designed to overcome the limitations of older versions of Jaundice meters with respect to gestational age and skin pigmentation[10]. The readings were taken over the forehead and sternum[8,10]. Sampling for TSB was through venepuncture immediately after TcB reading and analysis for TSB was done at the Chemical Pathology Laboratory of the hospital, using an SM23A spectrophotometer (Malloy and Evelyn Method). Sampling was based on clinical indication; an average of three samples was obtained from each baby. The neonates were stratified into gestational age groups of 28-30 weeks, 31-33 weeks and 34-36weeks and into birth weight groups less than 1000gm, 1000-1499gm, 1500-2499gm and2500gm and above. Means of TcB readings and TSB levels were compared using paired Student's t-test while the correlation coefficient (r) between TcB readings and TSB levels was determined using linear regression analysis. The differences in means of TcB readings and TSB levels among the various categories of preterm neonates were compared. *P* values less than <0.05 were considered to be statistically significant.

Results

A total of 189 paired measurements of TcB readings and TSB levels were obtained from 60 neonates, comprising 35 (58.3%) males and 25 (41.7%)females. They were all born to Nigerian parents. The gestational age ranged from 28 to 36with mean (SD) of 31.5 (2.7) weeks while the birth weight ranged between 900 and 2600 with mean (SD) of 1624 (583) gm. Twenty-eight (46.6%) of the neonates were 28-30 weeks, and 16(26.7%) each in the 31-33 weeks and 34-36 weeks categories.

Overall relationship between TSB and TcB levels

There was no statistically significant difference between the mean of the sternal and forehead TcB readings (11.4 versus 11.3 mg/dl;95% CI of the difference = -0.51, 0.71, *p*= 0.746). The difference between the correlation coefficients of sternal and forehead TcB readings with TSB level was not statistically significant(0.98 versus 0.97, *p* = 0.76). The data obtained from sternal TcB readings in relation to TSB levels are subsequently presented below.

The mean (sd) TcB level of 11.4 (3.1)mg/dl was significantly higher than the mean TSB level of 10.2 (2.8)mg/dl (p= 0.028).Of the 189 pairs, the TcB readings were higher than the TSB levels in 181 (95.8%), lower in four (2.1%) and equal in four (2.1%) cases. The difference between TcB and TSB was less than 1 mg/dl in 134 (70.9%), 1 - 1.9 mg/dl in 40 (21.2%) and 2 - 2.8 mg/dl in 15 (7.9%) of the paired readings.

Fig 1 shows the linear regression of TcB readings on TSB levels. There was a strong positive relationship between TcB readings and TSB levels, with correlation coefficient (r) of 0.98 and coefficient of determination (R^2) of 96 ($p < 0.01$). The linear relationship between the two is described by the equation TSB = TcB x 0.93.

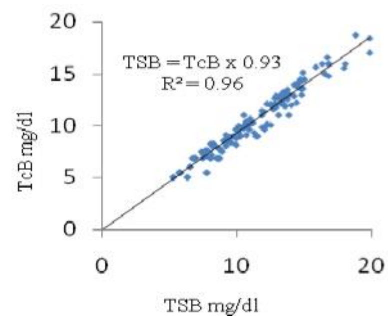

Fig 1: Linear regression of TcB on TSB for all the readings.

The effects of total serum bilirubin levels, gestational age (GA) and birth weight on the relationship between TcB readings and TSB levels.

Eleven neonates had TSB levels ≥15 mg/dl, the correlation coefficient between TcB and TSB in this TSB range was 0.78 while the correlation coefficient was 0.98 at TSB levels ≤ 14.9mg/dl. The difference clinically significant, although it did not attain statistically significance (p = 0.09) probably due to the small number (n=11) in that range. The mean (SD) of the difference between TcB readings and TSB levels of 1.16 (1.02) mg/dl at TSB levels ≥15 mg/dl was significantly higher than that of 0.76 (0.62)mg/dl at lower TSB levels ≤ 14.9mg/dl (p = 0.047).

The distribution of the means (SD) of TcB readings, TSB levels and differences in TcB-TSB in relation with GA are shown in Table 1. The means of TSB readings and TcB levels increased significantly with GA (p< 0.01). There was however no statistically significant difference in the means of TcB readings and TSB levels in any of the GA categories. The correlation coefficients 'r' among the GA of groups 28-30 weeks, 31-33 weeks and 34-36 weeks were (r =0.97, 0.98 and 0.98, respectively). There was no statistically significant difference in the correlation coefficient (r) within the three GA groups.

Table 1: Table showing the comparative statistics of TSB and TcB for different gestational age categories.

Gestational age category (weeks)	No of readings	Mean (SD) TSB(mg/dl)	Mean (SD) TcB(mg/dl)	Mean difference (95% CI)	t-value (*p*-value)
28-30	88	8.1 (1.8)	8.5 (1.8)	(-1.4, 0.6)	-0.83 (0.41)
31-33	49	11.1 (1.1)	11.8 (2.0)	(-1.9, 0.5)	-1.23 (0.23)
34-36	52	12.8 (2.3)	13.4 (2.4)	(-2.3, 1.1)	-0.72 (0.48)
All babies	189	10.2 (2.8)	11.4 (3.1)	(-2.3,0.2)	-1.79 (0.15)
P values		< 0.01	< 0.01	< 0.01	

Key: S.D = standard deviation; TSB = total serum bilirubin; TcB = transcutaneous bilirubin; CI = confidence interval

Table 2 shows distributions of means (SD) values of TcB and TSB, and the means (SD) of the differences between TcB and TSB levels in relation to birth weight categories. The Table shows the comparison between the means of TcB and TSB for each of the birth weight category. In each birth weight category, the mean of TcB was higher than that of TSB, though the difference was not statistically significant (p = 0.09 for < 1000gm, p = 0.51 for 1000-1499gm, p = 0.25 for 1500-2499gm and p = 0.42 for ≥ 2500gm. The means of both TSB and TcB increased significantly with birth weight (*p* <0.01). The correlation coefficients were r = 0.85 (p < 0.01); r = 0.98 (p < 0.01); r = 0.97 (p < 0.01); and r = 0.98 (p < 0.01) for the weight categories of <1000gm, 1000-1499gm, 1500-2499gm and ≥2500gm respectively. The weakest correlation coefficient between TcB and TSB was thus in the <1000gm weight category. However there was no statistically significant difference between the correlation coefficients (r) between the various birth weight categories (p = 0.08).

Table 2: Table showing the comparative statistics of TSB and TcB for different birth weight categories.

Birth weight category	No of readings	Mean (SD) TSB(mg/dl)*	Mean (SD) TcB(mg/dl)**	Mean difference (95% CI)	t-value (*p*-value)
ELBW	10	7.5 (1.0)	8.1 (0.7)	(-1.3, 0.1)	-1.77 (0.09)
VLBW	81	8.2 (1.9)	8.6 (2.0)	(-1.6, 0.8)	-0.66 (0.51)
LBW	66	11.5 (2.1)	12.2 (2.2)	(-1.9, 0.5)	-1.17 (0.25)
NBW	32	12.6 (2.5)	13.5 (2.4)	(-3.2, 1.4)	-0.82 (0.42)
All babies	198	10.2 (2.8)	11.4 (3.1)	(-2.3, 0.2)	-1.79 (0.15)
P values		< 0.01	< 0.01	< 0.01	

Discussion

The present study revealed a strong correlation between TcB readings and TSB levels in Black preterm neonates. The correlation was not significantly affected by the gestational age, Birth weight and, to a lesser extent, the TSB levels within the range of TSB obtained. The strength of the correlation was similar to that reported by Maisels *et al*,[8] Stillova *et al*[20] and Ahmed *et al*[21] in studies which involved term and preterm Caucasian neonates. The correlation coefficient was however higher than that reported by Owa *et al*[1], Slusher *et al*[17] in Black term neonates and Knupfer *et al*[22] in a study involving preterm Caucasian neonates. The greater correlation in the present study, relative to the correlation in the previous studies on African term neonates[1,17] and preterm Caucasian neonates may be due to the improved sensitivity of the study instrument, the JM-103, which was specifically designed to overcome the limitations of the older versions of jaundice meters with respect to gestational age and skin pigmentation.[8,10]

The tendency of higher TcB readings than TSB levels in the present study is consistent with the findings of other workers.[8,20,23] This tendency for the TcB readings to be higher than the TSB levels is not likely to result in major errors in the management of preterm neonates with jaundice. This is because at least one value of TSB is usually obtained before instituting treatment.

Moreover, the practical implication is a probable slight increase in the rate of interventions with phototherapy, if only the TcB readings were used for the assessment of the severity of the jaundice and in taking decision.

In agreement with the results of previous studies,[8,20] the correlation coefficient between TcB readings and TSB levels in the present study was higher with TcB measurements taken over the sternum than that taken over the forehead, although the difference was not statistically significant. The difference has been attributed to the probable bleaching effect of light on the forehead compared to the relatively less exposed sternum,[23] although precautions were taken to minimize this effect. The sternum is thus the preferred site for TcB measurements. The present study also revealed a lower correlation coefficient at higher TSB values as had been previously reported.[8,11,17]

The recommendation for the use of TcB as a screening device is based on the assumption that serum and tissue bilirubin levels are in constant equilibrium. This may not be totally true. It is possible that at higher serum bilirubin levels, the rate of equilibration between the serum bilirubin and tissue bilirubin is reduced and more bilirubin is retained in the tissues, including subcutaneous tissues. This may partly explain the increase in the differences between the TcB readings and TSB values at higher TSB levels. It is therefore important that due caution is exercised not to use TcB readings alone in decision-making at TcB readings above 15mg/dl. More studies are required in this respect. The GA of the preterm neonates in the present study did not significantly affect the relationship between TcB readings and TSB levels. The difference in the correlation coefficients between the various GA categories of preterm neonates (r = 0.97 versus r = 0.98) is too small to have any real impact on the clinical judgment. This conclusion is in agreement with the reports by Ahmed *et al*[21] and Schmidt *et al*[24] that TcB is as reliable in neonates with GA of 28 weeks as it is in late preterm neonates. Extremely preterm neonates have a more immature skin with paucity of subcutaneous tissue, which can affect the TcB readings. The use of transcutaneous bilirubinometry would appear more relevant in preterm neonates in whom the risks of anaemia and infection from repeated venepuncture are much higher.[25-27]

The difference between the means of TcB readings and

TSB values is similar to that reported by Maisels *et al.*[8] The maximum difference of 2.8mg/dl between TcB readings and TSB values is comparable to the inter-laboratory variations in TSB determination as reported by Vreman *et al*[28] and less than the difference reported between a Bilirubinometer and Malloy-Evelyn method of TSB determination by Owa.[29] Therefore, the differences observed between TcB readings and TSB values in the present study in the range of TSB of 5-18.7mg/dl studied may be comparable to differences observed in real clinical situations where different methods of TSB determination are used.

Limitations

The limitations of this study include the small number of ELBW neonates recruited and the very limited number of bilirubin levels in the range of 15mg/dl and above.

Conclusion

The correlation between TcB and TSB levels in the Nigerian preterm neonates is strong irrespective of the gestational age, birth weight and TSB level.
It is recommended that transcutaneous bilirubinometry be used routinely as a tool for the monitoring of severity of NNJ in Blacks. This will reduce the delay in intervention, minimize the problems of venepuncture and possibly reduce the burden of ABE.

Authors Contribution
BO: Study conceptualization, data collection and analysis, manuscript writing.
JA: Directed the study and manuscript writing.
GO: Manuscript writing and data analysis.
SO: Data analysis
Conflict of interest: None
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