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Original Articles

Transcutaneous Billirubinometry: A Useful Screening Tool for Neonatal Jaundice in Term and Near Term Babies - A Hospital Based Study

NARGIS ARA BEGUM[1], KHORSHED ALAM[2], ANAMIKA SHAHA[3], MD. SOHEL SHOWMIK[4], RUNA LAILA[5], SHAHNAZ PARVIN[6], ABDUR RAHMAN[7], MIZANUR RAHMAN[8]

Abstract

Background*: Hyperbilirubinemia is a common problem in newborn. Most of the cases are benign but severe hyperbilirubinemia can lead to kernicterus and brain damage which is preventable. The gold standard to asses neonatal hyperbilirubinaemia is serum bilirubin measurement. Unfortunately, this procedure is invasive, painful and time consuming. As the consequence of missing severe hyperbilirubinemia is serious, there is a constant search to find out a safe method to detect jaundice. Transcutaneous bilirubinometry offers objective method of assessing degree of jaundice reducing subjectivity of clinical assessment.*

Objective*: To evaluate the relationship between transcutaneous bilirubin (TcB) and total serum bilirubin (TSB) and assess whether transcutaneous bilirubinometry can be used as a valid screening method for detecting jaundice in term and late preterm babies.*

Method*: A prospective cross-sectional study was performed in well baby nursery of United Hospital Limited, Dhaka from January 2013 to December 2013. Healthy term and late pre term newborn of ≥ 35 wk gestation with clinical evidence of jaundice were included in the study. Total serum bilirubin was measured by Dichlorophenyl Diazonin method and transcutaneous bilirubinometer (JM-103) was used to measure transcutaneous bilirubin (TcB) level.*

Result*: A total of 116 paired samples were analyzed and found strong correlation between TcB and TSB (correlation coefficient 0.8, mean difference 0.83, SD± 1.96 and 95% CI 0.6 to 1.06). Post natal age has significant association with TcB (p value 0.01) and TSB (p value 0.031). Requirement of phototherapy in both group were also significant (p value <0.001). TcB value of 11 mg/dl was chosen as cut off point corresponding TSB level 13 mg/dl with sensitivity 90% and specificity 71%. Above this level indicate need for blood sampling to take appropriate therapeutic measure.*

Conclusion: *Transcutaneous billirubinometry is a non-invasive and valid screening tool for assessing jaundice in newborn.*

Key words: *Neonatal jaundice, Transcutaneous billirubinometry, Total serum bilirubin*

1. Consultant, Department of Neonatology, United Hospital Ltd. Dhaka.
2. Specialist, Department of Neonatology and Paediatrics, United Hospital Ltd. Dhaka.
3. Medical Officer, Upazilla Health Complex, Ghatail, Tangail.
4. Research Investigator, ICDDRB, Dhaka, Bangladesh.
5. Specialist, Department of Neonatology and Paediatrics, United Hospital Ltd. Dhaka.
6. Junior consultant, Department of Neonatology and Paediatrics, United Hospital Ltd. Dhaka.
7. Specialist, Department of Neonatology and Paediatrics, United Hospital Ltd. Dhaka.
8. Specialist, Department of Neonatology and Paediatrics, United Hospital Ltd. Dhaka.

Correspondence: Dr. Nargis Ara Begum, Email: nargisdr@yahoo.com

Introduction

Jaundice is a common problem occurring in 60% term babies during 1st few days of life.[1] Most cases are benign, resolve spontaneously requiring medical intervention in 20% cases to treat significant jaundice.[2] Significant jaundice is found in 10.5% of term and 25.3% of late preterm infants.[3,4] Therefore each case must be evaluated to detect at risk babies and follow up should be continued even after discharge from hospital as bilirubin level may vary over time and may not peak until 5th day of life or later to prevent significant morbidity.[2]

The gold standard for measurement of billirubin level in newborn is total serum billirubin estimation (TSB).[5,6] In most postnatal ward the decision to perform TSB depends on postnatal age and visual assessment of jaundice using "Kramer Rule".[7] But poor correlation between visual assessment and total serum bilirubin was found in various study.[8,9] Depending on visual assessment unnecessary blood tests are being practiced in newborn babies who do not have significant jaundice. Moreover, blood test is a painful, time-consuming and also stressful procedure for neonates and their parents. There was a constant search to find out comfortable and valid tool for detecting jaundice level in newborn.

Transcutaneous Billirubinometry offers a more objective method of assessing the degree of jaundice, reducing the subjectivity of clinical assessment.[9] It is also a safe, noninvasive, painless, technically easy, instantaneous reporting tool.[10] It is also an important 'Point of Care' test (bed side test) can be performed by doctor, nurse even others health staff in hospital as well as in community.[11]

A number of previous studies showed a good correlation between transcutaneous and total serum billirubin measurement in term babies.[12-14] Accuracy of transcutanuous bilirubinometry is not widely accepted in preterm newborn.[15,16] In preterm infant transcutaneous bilirubinometry is less accurate than in term infant as result are affected by immature skin and by different albumin to bilirubin binding.[16-18] In our country transcutaneous bilirubinometry has not been widely adopted due to concern of its validity and accuracy. In this context this study was performed with the objectives of estimating the relationship between transcutaneous bilirubin (TcB) and TSB and to evaluate whether transcutaneous billirubinometry could be a valid screening method for detecting jaundice in term and near term newborn.

Materials and Methods

A prospective cross-sectional study was conducted at well baby nursery of United Hospital in Dhaka from January to December, 2013. Total 116 healthy term and late preterm (>35 to <37 weeks) babies were enrolled. Jaundice was assessed in the newborn babies from 25 hours to 168 hours of postnatal life (due to most of the physiological jaundice appears 2nd day onwards persists up to 5 to 7 days). We excluded sick baby requiring intensive care and who had major congenital anomalies and prior administration of phototherapy and Rh incompatibility. TCB and TSB correlation was done as primary outcome. Birth weight, gestational age, sex, postnatal age requirement of phototherapy and ABO incompatibility (initial inclusion of O+ve mother and A/B+ve baby was selected as normal physiological jaundice) were compared as secondary measures. Informed consent was taken from parents before enrollment.

A database was maintained to record birth details and to identify neonates born ≥35 wks of gestation. Gestation was determined by 1st trimester USG (when available) or date of last menstrual period confirmed by Expanded New Ballard score within 24 hr. The identified neonates were assessed every 12 hrly for onset and progression of jaundice by an experienced pediatrician according to" Kramer's description" and decision for blood sampling was done according to clinical judgment and AAP guide line.[7,15] The serum sample (1ml) was collected by venepuncture and serum bilirubin estimation in laboratory was done by Dichlorophenyl Diazonium method (cbas integra 700; hert ford shire, UK).[19] Phototherapy was started on TSB value according to AAP guideline2004.[15]

This study performed TcB measurement using JM-103 within 30 min of serum sampling. For each newborn TcB readings was obtained by placing the device over forehead and sternum by trained nurses. A total of 3 readings were obtained from each infant and were averaged to obtain a single TcB value that was used in subsequent analysis. Only one device, JM-103 transcutaneous bilirubinometer was used for the whole study. JM-103 determines the yellowness (bilirubin) of the subcutaneous tissue of a neonate by measuring the difference in the optical densities of reflected light at 450 and 550 nm by the newborn skin. With this method, 2 optical paths are incorporated into a measuring probe that minimizes the interference due to melanin or skin maturity. When the light returns to the fiber, it is scattered from shallow areas of subcutaneous tissue and passes through the inner core (short optical path) of the fiber, where as the light scattered from deep areas of subcutaneous tissue pass through the outer core (long optical path). The reflected light is then collected by photodiodes.[3,17] Based on the reflected wave specification, the cutaneous bilirubin is calculated. Data were entered and analyzed using SPSS (version 15). Relationship between TcB and TSB was determined using Pearson correlation coefficient. In order to assess agreement a Bland-Altman graph was constructed. Paired t test was performed for continuous variables and ANOVA test for repeated measures. P value of <0.05 was taken as statistically significant. Sensitivity and Specificity

of our study cohort were calculated to find out the accuracy of TcB in place of TSB. The study protocol was approved by the hospital ethics committee.

Result

A total of 116 neonates were enrolled in study who meet the inclusion criteria. Among them 8 data were excluded due to technical error. Finally 108 data were analyzed and found strong correlation of TcB with TSB correlation coefficient 0.8, mean difference 0.83 and 95% CI 0.6 to 1.06.

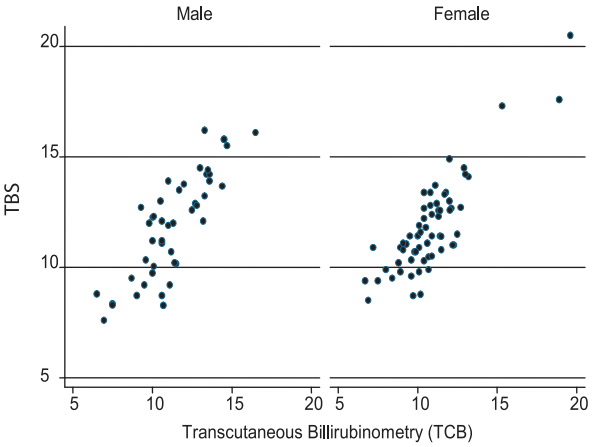

Fig.-1: *This scatter plot revealed corelation and coefficient of TcB &TSB 0.8, No significant difference between male and female.*

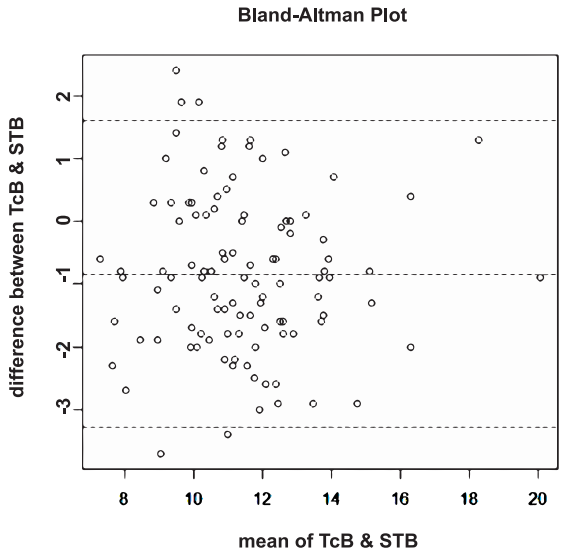

Fig.-2: *The graph displays a scatter diagram of the differences plotted against the averages of the two measurements. Horizontal lines are drawn at the mean difference, and at the limits of agreement, which are defined as the mean difference plus and minus 1.96 times the standard deviation of the differences.*

Fig.-3: *Transcutaneous bilirubinometer (JM-103).*

Table-I

Basic characteristics and clinical variable of study population

Character	n (%)	Range	Mean
Sex			
Male	46(42.6)		
Female	62(57.4)		
Birth weight	108(100)	2400-4000gm	3067.13(±358.23)
Gestational age			
Late preterm	15(13.8)	36- 40 weeks	37.58(±1.14)
Term	93(86.2)		
Post natal age			
< 3 days	37(34.3)	2 -6 days	2.88(±0.89)
≥3 days	71(65.7)		
Phototherapy			
Yes	34(31.5)		
No	74(68.5)		
ABO incompatibility			
Yes	18(16.7)		
No	90(83.3)		
TCB	108(100)	6.5-19.6mg/dl	11.03(±2.21)
TSB	108(100)	7.6-0.5mg/dl	11.87(±2.23)

Regarding demographic variables (table-I), 57% were female, 43% were male. Term babies were 86% and 14% were late preterm. Gestational age varied 36 weeks to 40 weeks and mean gestational age 37.6±1.14. Weight of babies ranged from 2400 gm to 4000 gm and mean BW 3067±358 gm. Jaundice was

detected in 66% neonates at ≥ 3 days of post natal age. Total serum billirubin ranged 7.6-20.5 (mean 11.87±2.23) mg/dl and transcutaneous bilirubin were 6.5-19.6 (mean 11.03±2.21) mg/dl. Overall 32% neonates ultimately required phototherapy and ABO incompatibility was present in 17%.

All the study variables were compared with TcB and TSB value (table-II) and both value showed significant association with phototherapy (p value<0.001) but postnatal age showed significant association with TcB only (p value-<0.05).

Sensitivity and specificity analysis of TcB and TSB were calculated (table-III) in our study showing TcB value of 9 to 10 mg/dl with corresponding TSB value 10.5 to 12 mg/dl having high sensitivity (96 to 98)% and low specificity (34 to 45)%. Similarly to detect TSB value of 13mg/dl, a TcB value of 11mg/dl would provide sensitivity 90% specificity 71% (best sensitivity and desired specificity). Again at TcB 14 mg/dl, it detected TSB value of 16mg/dl with a sensitivity of 85% and specificity 90%. So TcB cut off value11mg/dl can detect most of jaundiced newborn for intervention.

Table – II

Comparison of TcB & TSB by study variables

Variables	N	TcB	P value	STB	P value
Assays	108	11.02 ± 2.21		11.87 ± 2.23	<0.001
Postnatal age					
< 3 days of life	37	10.28 ± 1.89	0.01	11.23 ± 1.86	0.031
≥ 3 days of life	71	11.42 ± 2.27		12.2 ± 2.34	
Gestational age					
< 37 weeks	15	11.1 ± 2.34	0.887	12.21 ± 2.67	0.524
≥ 37 weeks	93	11.01 ± 2.2		11.81 ± 2.16	
Phototherapy					
Yes	34	12.96 ± 2.24	<0.001	14.23 ± 1.87	<0.001
No	74	10.14 ± 1.53		10.78 ± 1.38	
ABO incompatibility					
Yes	18	12.23 ± 2.9	0.011	12.71 ± 3.02	0.079
No	90	10.79 ± 1.98		11.7 ± 2.01	
Sex					
Male	46	11.3 ± 2.19	0.265	11.93 ± 2.37	0.805
Female	62	10.82 ± 2.22		11.82 ± 2.13	

Table- III

Sensitivity & Specificity of TcB & TSB

TcB	TSB	Sensitivity	Specificity
9.0	10.5	97%	40%
9.5	11	96%	41%
9.5	11.5	98%	34%
10	12	96%	45%
11	12.5	85%	79%
11	13	90%	71%
14	16	85%	90%

Discussion

Detection of neonatal jaundice is a challenge for pediatrician for it neurotoxic sequelae. Non invasive evaluation of jaundice is highly desirable to predict bilirubin status. Transcutaneous billirubinometry demand the criteria.

This study demonstrated significant correlation between TcB and TSB (correlation coefficient 0.8, mean difference 0.83 and 95% CI 0.6 to 1.06). The correlation coefficient in our study is comparable to those obtained by Rubal telli et al (r- 0.89),R Ebbsen (r-0.88) R, Robertson et al (r-0.93) R and Janjiondamai

et al (r- 0.95).[17,18,20.21] The mean difference between the two measurements was statistically significant which prevent the use of TcB as a replacement for TSB. Ebbeson et al also found similar finding in their study.[18]

The factors that interfere were accuracy of TcB are sex, gestational age, postnatal age, birth weight, haematocrit value, requirements of phototherapy .[22]

This study result showed TcB is not affected by birth weight, gestational age, and sex. Similar finding is observed in Rubal et al[17]. Hossenie et al[23], Luca et al[24], Badiee et al.[25] Sotitrios et al[26] found 2 fold greater risk related to male sex. TCB value of male babies were detected significantly than the female in study of Laeeq et al[27], possibly due to the selection bias for better medical care for male in their social set up. On the other hand Ebbeson et al[18] reported greater TCB level in the female than their male counterpart. (P value 0.003). Study by Knupfr et al[28] found that TCB TSB correlation decrease with lower gestation. On the other hand William and co worker show TCB is reliable screening tools in vary preterm infant less than 30 weeks.[28,29]

As we know skin maturation increases with post natal age, we found post natal age of our studied babies had significant relationship with TCB value. Similar findings was observed in Maria el al[14] and Luca et al[24] in contrast, Knupfer et al[25] and Baiee et al[28] did not find any relation of post natal age with TCB and TSB. The potential effect of post natal age is attributed to maturation and thickening skin and changed in the amount of albumin binding. These factors are exaggerated in preterm newborn, data from Ebbeson et al[18] support this. Karen et al[30], Steven et al[31] found a direct linear relationship with greater birth weight and significant jaundice, which is in contrast to our study. Karen & Steven explained the relationship of higher birth weight to hyperbilirubinemia might be due to maternal diabetes, neonatal polycyhtemia, bruise and cephal hematoma of their babies.[30,31]

Overall 30% of our studies babies required phototherapy and phototherapy had significant relationship with TCB & STB (p value <.0001). So optimum TCB cut of value is applicable to capture significant jaundiced newborn who required phototherapy. The relationship of TCB and requirement of phototherapy was not found in the study done by Mansouri et al.[32] But Tan and Dong et al[33] found a relationship of TCB and requirement of phototherapy.[33]

To identify as an effective screening tool TCB must have a high sensitivity and a desirable specificity. This study assessed sensitivity and specificity of TCB at different TCB cut-off values. it was found that at TCB cut-off 11mg/dl can detect TSB 13mg/dl with a sensitivity of 90% and specificity of 71%. Above this level blood test would be necessary to take appropriate therapeutic measures for starting phototherapy. This cut off value was lower than that of Maria et al[5] (cut-off value 14mg/dl, Nem-yun boo et al[14] (14.6mg/dl) and Hemmati (15mg/dl). The cut of value were different probably they used different device.

This study had some limitations. High pressure liquid chromatography (HPLC) is a gold standard of billirubin estimation but we used DIAZO method in our study. Finally, we assessed only 116 babies and better result could be obtained by future studies with larger sample size.

Conclusion

Transcutaneous billirubinometry is a non-invasive and valid screening tool for assessing jaundice in newborn.

Recommendation

Though the device is expensive, it is long lasting, portable and provides instant result. It can be used in community level where blood sampling is difficult. So, it is very time to think about cost-benefit ratio of this tool.

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