Original Research Article

A study to evaluate the levels of Transcutaneous Bilirubin (TcB) and Total Serum Bilirubin (TSB) Measurements in TermNeonates: A comparative study

Rakesh Kumar[1], Sujit Kumar[2*], Priyanka Prasad[3]

[1,2]Associate Professor, Department of Pediatrics, Nalanda Medical College and Hospital, Patna, Bihar, India

[3]Assistant Professor, Department of Biochemistry, Nalanda Medical College and Hospital, Patna, Bihar, India

Received: 20-06-2020 / Revised: 30-07-2020 / Accepted: 05-08-2020

Abstract

Introduction: Transcutaneous Bilirubinometry (TcB) is a simple method for estimating bilirubin levels in neonates. This method is non-invasive, quick, and painless. We aimed to compare serum and cutaneous bilirubin measurements in term neonates.**Materials and Methods:**In this descriptive cross-sectional study, 230 neonates with icterus and birth weights of at least 2,500 grams or more were studied. TcB was measured using a bilirubinometer three times on the forehead and mean levels were calculated. Then, during the subsequent 30 minutes blood samples were obtained and sent to the laboratory for determining the Total Serum Bilirubin (TSB) levels.**Results:**Of the 230 neonates, 124 (62%) were boys and 76 (38%) were girls, with aMean± SD (Standard Deviation) age of 5.3±4.5 to 5.1+3.5 days (range: 1-22 days). 99% of the neonates were breastfed and 49(21.30%) neonates had a history of icterus. Most of the neonates were the first child (53.90%). Moreover, 32.60% were the second child, and 13.50% were the third child and the next. 12.17%,13.91%, 13.91%,60.43% of the neonates became icteric on days 1, 2, 3, and 4 or more of birth respectively. Most neonates with hyperbilirubinemia have B+ blood(53.90) group and then A+ blood group(34.78%) have the highest frequency in the study. O+ blood group in mothers of newborns with jaundice was the most common (53.04 %), and then B+ blood group have the highest frequency in the mothers (25.65%). The mean ± SD serum and cutaneous bilirubin levels were 18.70±5.33 and 17.75±4.26 mg/dl, respectively. A high correlation (0.84) was observed between TSB and TcB.**Conclusion:**There was a strong correlation between serum and transcutaneous bilirubin levels. As transcutaneous bilirubin estimation is non-invasive, it gives quick and reproducible results. So, this method has potential screening value especially in the high-risk neonates for early intervention.

Keywords: Neonatal icterus, Serum bilirubin, Transcutaneous bilirubin

Introduction

Neonatal hyperbilirubinemia is a common problem with incidence of around 60% in term babies and nearly 80- 100% in preterm babies. The bilirubin level above 95th percentile may lead to acute bilirubin encephalopathy and or kernicterus which also has long term morbidity in form of cerebral palsy.[1,2]This complication is preventable through early recognition, appropriate follow up and treatment such as phototherapy and exchange transfusion.[2-6]

**Correspondence*

Dr. Sujit Kumar

Associate Professor, Department of Pediatrics,

Nalanda Medical College and Hospital, Patna, Bihar India.

The AAP guideline recommends assessment of jaundice in all newborns before hospital discharge. However, the method by which jaundice must be assessed is not specified. Both transcutaneous bilirubin (TcB) and total serum bilirubin (TSB) measurements are cited as acceptable method.[5] TSB measurement is still considered the gold standard. But it is invasive, painful and costly in terms of workload, time and money. Moreover, there is a concern of significant blood loss due to repeated sampling especially in preterms. TcB being a noninvasive method can overcome these problems.[7,8] Studies have shown good correlation between TSB and TcB in various ethnic groups by various authors. However, correlation was affected by various factors like race, gestational age, birth weight, skin color, type of TcB instrument.[9-13]Considering the importance of this issue and the inconsistencies betweenprevious studies regarding the accuracy of TcB, we aimed to compare

the relationship between TcB and TSB measurements in term neonates. Moreover, we also studied the sensitivity and specificity of TcB based on the age of the neonates and bilirubin levels.

Materials and Methods

This was an observational cross-sectional study to compare serum and transcutaneous bilirubin measurements in newborns by measuring serum bilirubin level and transcutaneous bilirubinometer level who was admitted at neonatal intensive care unit of Nalanda Medical College and Hospital, Patna, Bihar India.The study was carried out for the period of 1 year.

Inclusion criteria

Hyperbilirubinemia
Those willing to participate

Exclusion criteria

Neonate with sepsis,
Direct hyperbilirubinemia,
Major congenital anomaly,
Hemangioma or ecchymosis on the forehead,
Previous phototherapy, birth asphyxia, skin diseases

Data collection -Data was collected using pre-tested semi structured proforma. Neonatal data collected including age, sex, birth weight, current weight, length, onset of jaundice, birth order in the family, history of jaundice in the family, type of feeding, history of hospitalization, neonatal and maternal blood group, history of phototherapy. Previous measurements in serum and skin bilirubin, history of blood transfusion in new-born, and maternal prenatal care. Sample for both bilirubin levels reading serum and transcutaneous were taken simultaneously. Blood samples were obtained from neonates collected from venous sample into plainbulb.The samples were immediately sent to the hospital laboratory where the serum was separated and then immediately assayed for bilirubin by a DIAZO method which involves reacting serum with diazo reagent and then through spectrophotometry the levels of direct and indirect bilirubin were determined. Transcutaneous bilirubin level measurement was done by a single transcutaneous bilirubinometer used throughout the study period. The optic head of the meter is gently pressed against the neonate's skin (usually forehead or upper part of the sternum). For correct measurement, the optic head should make full contact with the skin and there should be no gaps between the head and the skin. This should be achieved by gentle pressure. The reading from forehead and sternum were measured and an average reading taken for comparison. After taking first reading babies were kept on phototherapy and patch cover of an area approximately 1.5 cm2were applied over forehead and sternum and a second reading was taken after 24 hour and third reading thereafter by the same way.

Results

Of the 230 neonates, 124 (62%) were boys and 76 (38%) were girls, with aMean±SD (Standard Deviation) age of 5.3±4.5 5.1+3.5 days (range: 1-22 days). 99% of the neonates were breastfed and 49(21.30%) neonates had a history of icterus. The mean±SDweights of the neonates were 3001±339 grams. Most of the neonates were the first child (53.90%). Moreover, 32.60% were the second child, and 13.50% were the third child and the next. 12.17%, 13.91%, 13.91%, 60.43% of the neonates became icteric on days 1, 2, 3, and 4 or more of birth respectively (Table.1).No significant relationship was observed between serum and cutaneous bilirubin and history of jaundice in the family. Moreover, no significant relationship was found between type of delivery and hyperbilirubinemia. In this study, no significant relationship was observed between history of hospitalization and serum and cutaneous bilirubin. Moreover, no significant relationship was found between nutrition and serum and cutaneousbilirubin. Most neonates with hyperbilirubinemia have B+ blood(53.90%) group and then A+ blood group(34.78%) have the highest frequency in the study. O + blood group in mothers of newborns with jaundice was the most common (53.04 %), and then B+ blood group have the highest frequency in the mothers (25.65%).(table 2,3) We also assessed the sensitivity and specificity of different TcB measurements. Table.4 shows the sensitivity and specificity of this method for different bilirubin levels. As shown, the highest specificity and sensitivity was related to bilirubin levels between 12-15 mg/dl. The mean ± SD serum and cutaneous bilirubin levels were 18.70±5.33 and 17.75±4.26 mg/dl, respectively. A high correlation (0.84) was observed between TSB and TcB. Table.5 shows the frequency and percentage of serum bilirubin as compared with cutaneous bilirubin in normal and abnormal states for calculating positive and negative predictive values of cutaneous bilirubin based on serum bilirubin. In this table bilirubin levels below 12 are considered normal. In this study the positive and negative predictive values of TcB were 92.63%and 70%. We also calculated the sensitivity and specificity

Table 1: **Frequency distribution of different study variables**

Variables	N	% age
Gender		
Male	144	62.60
Female	86	37.39
Weight (grams)		
2500-3000	137	59.56
3001-3500	71	30.86
≥3500	22	9.56
History of icter		
Yes	49	21.30
No	181	78.69
Birth Order		
First	124	53.91
Second	75	32.60
Third or more	31	13.47

Table 2: Blood groups of the mothers

Mother blood group	No. of mothers	% age
A^+ve	31	13.47
B^+ve	59	25.65
AB^+ve	9	3.91
O^+ve	122	53.04
A^-ve	3	1.30
B^-ve	1	0.43
O^-ve	5	2.17

Table 3: Blood groups of the patients/new-borns

Newborn blood group	No. of mothers	% age
A^+ve	80	34.78
B^+ve	124	53.91
AB^+ve	6	2.60
O^+ve	16	6.9
A^-ve	4	1.73

Table 4: **Specificity and sensitivity of cutaneous bilirubin measurement based on bilirubin levels**

Bilirubin Levels (mg/dl)	Specificity (%)	Sensitivity (%)
<8	25	100
8-12	25	94.5
12-15	100	96.2
≤15	80	96

Table 5: **Frequency and percentage of Serum bilirubin versus cutaneous bilirubin**

Cutaneous bilirubin	Serumbilirubin		Total
	Abnormal	Normal	
Abnormal*	176 (92.63%)	14 (7.37%)	190 (100.0%)
Normal	12 (30%)	28 (70%)	40 (100.0%)
Total	188 (81.74%)	42 (18.26%)	230 (100.0%)

* Bilirubin levels above 12 (mg/dl) are considered abnormal

Table 6: **Sensitivity and Specificity of TcB measurements with respect to age**

Age	Bilirubin	Mean±SD(mg/dl)	Specificity(%)	Sensitivity (%)
One day	Cutaneous	10.5±2.33	25	100
	Serum	10.5±2.48		
Two days	Cutaneous	15.42±3.29	25	95
	Serum	15.11±3.43		
Three days	Cutaneous	17.11±2.49	100	92
	Serum	18.71±3.99		
Four or More days	Cutaneous	19.2±3.33	80	96
	Serum	18.71±4.10		

Discussion

We found a high correlation between TcB and TSB measurements in neonates (r=0.84). Consistently, in another study on 490 neonates over 2.5 kg a high correlation (r=0.91) was observed between TcB and TSB[14]. Several studies have been done in this regard[15-18].One study on 388 healthy term neonates showed a correlation coefficient of 0.8; which is very similar to our study[18]. In another study on 490 neonates with a gestational age of more than 35 weeks, a correlation coefficient of 0.91 was observed[14].Briscoe and colleagues also found a correlation coefficient of 0.76 by studying 285 neonates[19]. Minor differences between the mentioned studies could be attributed to differences in the type of bilirubinometers, skin color, ethnicity, laboratory methods and kits, etc.We found that TcB had a high specificity for bilirubin levels over 12 mg/dl, especially for levels between 12-17 mg/dl. For levels lower than 12 mg/dl, its specificity decreased while its sensitivity increased; therefore, increasing the number of false positives. Also, for levels higher than 17 mg/dl, false negative cases would increase. In a study on 200 Brazilian neonates, higher correlations between TSB and TcB measurements were observed for bilirubin levels lower than 14 mg/dl. The researchers concluded that for levels over 14 mg/dl, serum measurements should be done[20]. Few studies have been done on specificity and sensitivity based on birth age, and most studies have calculated the sensitivity and specificity of TcB based on gestational age, sex, ethnicity, and weight. However, we also evaluated the former variable in our study.Day one and day two TcB yielded low specificity and high sensitivity. Therefore, during these days, false positive cases would increase and the accuracy of TCB would decrease. From day three onward false positive cases would decrease considering its higher specificity and accuracy would rise. Therefore, TcB measurements are closer to TSB measurements on days three and four.Our results are relatively comparable with another recent study in Italy that showed a significant increase in the specificity of bilicheck 61-96 hours after birth compared with 0-60 hours (P=0.074). However, the mentioned study did not assess the sensitivity of bilicheck as well as its specificity after 96 hours from

birth[21].In a study on 560 neonates, a good correlation was found between TcBand TSB after 24 hours from birth. However, the mentioned study did not evaluate the association between TcB and TSB on the first day of birth. The specificity and sensitivity of bilicheck was also not assessed[22]. The highest levels of bilirubin are seen on the fifth and sixth days of birth. This is while most neonates are discharged 48 hours after birth. Therefore, they should be followed accurately with respect to icterafterdischarge. However, because of its relatively low specificity, in this study we emphasize that in neonates with progressive jaundice, those with risk factors such as hemolysis or infection, or those with higher than normal bilirubin levels detected by TcB, serum bilirubin levels must be checked. With respect to the effect of gestational age on the correlation between TcB and TSB, De Luca and colleagues reported a correlation coefficient of 0.79 and confirmed a lower correlation coefficient in term neonates as compared with premature ones[23]. On the other hand, other researchers found that the correlation coefficient between TcB and TSB increase as the gestational age increases (from 0.43 for 23-28 weeks to o.72 for 35036 weeks)[24]. Douville et al., also found an excellent correlation between TcBand TSB in term neonates as compared with premature ones[25]. Further research is needed in this regard. In our study, we did not consider gestational age since all neonates wereterm

Conclusion

We found a high correlation between TcB and TSB measurements in term neonates. Due to its simplicity and painlessness, serial cutaneous bilirubin measurements would be helpful in following neonatal icterus. Although TcB has a high sensitivity in detecting icter, it should not replace TSB due to its relatively low specificity. Therefore, in high risk neonates, measuring TSB alongside TcB isnecessary.

References

1. Singh M. Jaundice. In: Singh M. Care of the newborn. 8th ed. 2016:323-48.
2. Karyn BK, Kathleen MM and Carlos F. A comparison of transcutaneous and total serum bilirubin in newborn hispanic infants at 35 or more weeks of gestation. J Am Board Family Med. 2007;20(3):266-71.
3. Johnson LH, Bhutani VK. System based approach to management of neonatal jaundice and prevention of kernicterus. J Pediatr. 2002;140(4):393-403.
4. American Academy of Pediatrics, Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics. 2004;114:297-16.
5. Ip S, Chung M, Kulig J, O'Brien R, Sege R, Glicken S, et al. An evidence based review of important issues concerning neonatal hyperbilirubinemia. Pediatrics. 2004;114(1):130-53.
6. Tayaba R, Gribetz D, Gribetz I, Holzman IR. Noninvasive estimation of serum bilirubin. Pediatrics. 1998;102:e28.
7. Tanja K, Hans Ulrich B, Jean- Claude F. Comparison of a new transcutaneous bilirubinometer (Bilimed) with serum bilirubin measurements in preterm and full-term infants. BMC Pediatrics. 2009;9:70.
8. Mahajan G, Kaushal RK, Sankhyan N, Sharma RL, Nakra M. Transcutaneous bilirubinometer in assessment of neonatal jaundice in Northern India. Indian Pediatr. 2005;42:41-5.
9. Yamanouchi I, Yamauchi I, Igarash I. Transcutaneous bilirubinometry: Preliminary studies of noninvasive Transcutaneous bili-rubinometer in Okayama National Hospital. Pediatrics 1980;65(2):195-202.
10. Tan KL. Transcutaneous bilirubinometry in full term Chienese and Malay infants. Acta Pediatric Scand. 1982;71:593-6.
11. Aroor AR, Christo GG, Kamath S, Venketesh A. Transcutaneous bilirubinometry in newborns. Indian Pediatr. 1988;25:1073-7.
12. Harish R, Sharma DB. Transcutaneous bilirubinometry in neonates: Evaluation of Minolta Airshields Jaundicemeter. Indian Pediatr. 1998;35:264-7.
13. Narang A, Buche VB. Evaluation of Minolta Jaundicemeter as a screening device in Indian infants. Indian Pediatr. 1983;20:583-5
14. Bhutani VK, Gourley GR, Adler S, Kreamer B, Dalin C, Johnson LH. Noninvasive measurement of total serum bilirubin in a multiracial predischarge newborn population to assess the risk of severe hyperbilirubinemia. Pediatrics 2000; 106(2):17-26.
15. Ho HT, Ng TK, Tsui KC, LoYC.Evaluation of a new transcutaneous bilirubinometer in Chinese newborns. Arch Dis Child Fetal Neonatal 2006; 91(6):434-8.
16. Lam TS, Tsui KL, Kam CW. Evaluation of a point of care transcutaneous bilirubinometer in Chinese neonates at an accident and emergency department. Hong Kong Med J 2008; 14(5): 356-60.

17. Bhat YR, Rao A. Transcutaneous bilirubin in predicting hyperbilirubinemia in term neonates. Indian Journal of Pediatrics 2008; 75(2):119-23.
18. Sanpavant S, Nuchprayoon I. Comparison of two transcutaneous bilirubinometers, Minolta Airshields Jaundice Meter JM103 and SpectrxBilicheck I Thai neonates. Southeast Asian J Trop Med Public Health 2005; 36(6): 1533-7.
19. Briscoe L, Clark S, Yoxall C. Can transcutaneousebilirubinometry reduce the need for blood tests in jaundiced full term babies? Arch Dis Child Fetal Neonatal Ed 2002;86(3) :190-2
20. Leite MG GranatoVde A, Facchini FP, Marba ST. Comparison of transcutaneous and plasma bilirubin measurement. J Pediatr 2007; 83(3) :283-6.
21. Romangoli C, Catenazzi P, Barone G, Giordano L, Riccardo R, Zuppa AA, et al. BiliCheck vs JM-103 in identifying neonates not at risk of hyperbilirubinemia. Italian Journal of Pediatrics 2013; 39(46):1-6.
22. Hemmati F, Kiyani Rad NA. The Value of Bilicheck as a Screening Tool for Neonatal Jaundice in the Sourth of Iran. Iran J Med Sci 2013;38(2):122-8.
23. Boo NY, Ishak S. Prediction of severe hyperbilirubinemia using the Bilicheck transcutaneous bilirubinometer. J Pediatr Child Health 2007;43(4):297-302.
24. De Luca D, Zecca E, De Turris P, Barbato G, Marras M, Romangnoli C. Using Bilicheck for preterm neonates in a sub intensive unit: diagnostic usefulness and suitability. Early Hum Dev 2007; 83(5):313-7.
25. Douville P, Masson M, Forest JC. Diagnostic value of sequential readings with the Minolta Transcutaneous Bilirubinometer in normal andlow-birthweight infants. Clinical Chemistry 1983; 29(4):740-1.

Source of Support:Nil
Conflict of Interest: Nil