Section: Pediatrics

Original Research Article

A CROSS SECTIONAL STUDY TO COMPARE THE TRANSCUTANEOUS BILIRUBINOMETER VALUES WITH SERUM BILIRUBIN MEASUREMENTS BEFORE AND AFTER INITIATION OF PHOTOTHERAPY IN PRETERM NEONATES WITH HYPERBILIRUBINEMIA ADMITTED IN NICU AT A TERTIARY CARE HOSPITAL

Nischal Puttaswamy[1], Keerthi Budnoor Jayaram[2], Vinay BS[3], Avinash Singraiah[4], Varsha[5]

[1]Junior Resident, Department of Pediatrics, Mandya Institute of Medical Sciences, Mandya, India.
[2]Associate Professor, Department of Pediatrics, Mandya Institute of Medical Sciences, Mandya, India.
[3]Assistant Professor, Department of Pediatrics, Mandya Institute of Medical Sciences, Mandya, India.
[4]Neonatologist, Department of Pediatrics, Mandya Institute of Medical Sciences, Mandya, India.

Received : 18/05/2023
Received in revised form : 24/06/2023
Accepted : 03/07/2023

Keywords:
Hyperbilirubinemia, Transcutaneous bilirubin, serum bilirubin, phototherapy.

Corresponding Author:
Dr. Avinash Singraiah,
Email: avinash.dhanu@gmail.com

DOI: 10.47009/jamp.2023.5.4.420

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (4); 2090-2094

Abstract

Background: Hyperbilirubinemia is a common problem in preterm neonates, which results in significant morbidity and mortality if not managed properly. Preterm neonates are at a higher risk of developing hyperbilirubinemia due to multiple factors. Serum bilirubin measurements are the gold standard for diagnosing hyperbilirubinemia, but they are invasive and time-consuming, requiring multiple blood samples. TCB measurements are non-invasive and provide a quick and easy method for measuring bilirubin levels in neonates. The accuracy of TCB measurements may be affected by several factors, such as skin pigmentation, gestational age, and the use of phototherapy. There is a need to validate the accuracy of TCB measurements before and after the initiation of phototherapy in preterm neonates with hyperbilirubinemia. Therefore our study was intended to compare TCB and serum bilirubin values before and after initiation of phototherapy among preterm neonates with hyperbilirubinemia. **Materials and Methods:** Hospital-based cross-sectional study was conducted at a tertiary care hospital in the neonatal intensive care unit (NICU) over a period of three months. A total of 50 preterm neonates fulfilling the criteria were included in the study. Serum bilirubin was estimated using the acid diazo method. Transcutaneous bilirubin (TCB) measurements were obtained using Dräger jaundice meter JM 105 on the sternum. Phototherapy using light-emitting diode units was instituted. Repeat serum bilirubin and TCB assessment were done as per clinical indication. The primary outcome was to compare TCB with serum bilirubin in preterm neonates before and after initiation of phototherapy. **Result:** Out of 50 study population, 48% constituted for gestational age of more than 32weeks. Male female ratio was 1:1.Very Low birth weight babies were 40%. The mean TCB before phototherapy was 13.94(±3.503) while mean serum bilirubin was 12.40(±3.743) and Pearson's value of 0.763 indicating strong positive correlation. The mean TCB after phototherapy was 9.62(±3.68) while mean serum bilirubin was 9.19(±3.25) and Pearson's value of 0.69 indicating strong positive correlation between TCB and serum bilirubin. Data also suggest strong correlation between TCB and serum bilirubin at lower serum bilirubin levels (r=0.7) and is highly statistically significant ($p<0.001$). These findings also suggest that TCB and serum bilirubin may be used interchangeably in clinical settings, although the systematic differences at lower levels should be taken into account. **Conclusion:** Our study contributes to the growing body of evidence supporting the positive correlation between transcutaneous bilirubin (TCB) and serum bilirubin (SBR) levels before and after phototherapy in preterm neonates with hyperbilirubinemia. The results align with previous research and emphasize the reliability and applicability of TCB measurements as a non-invasive tool for assessing the severity of hyperbilirubinemia in this population.

INTRODUCTION

Hyperbilirubinemia is a common problem in preterm neonates, which results in significant morbidity and mortality if not managed properly. Phototherapy is the primary intervention for treating hyperbilirubinemia in neonates.[1] The measurement of bilirubin levels in neonates is essential for the diagnosis and management of hyperbilirubinemia. The traditional method of measuring serum bilirubin levels is invasive, time-consuming, and requires multiple blood samples, which may cause discomfort to the neonate.[2] Transcutaneous bilirubinometry (TCB) is a non-invasive and reliable method for measuring bilirubin levels in neonates.[3]

TCB measures the bilirubin level by shining a light through the skin, and then measuring the amount of light absorbed by the bilirubin in the skin.[4] TCB has several advantages over serum bilirubin measurements, including its non-invasiveness, speed, and ease of use. However, TCB measurements may be affected by several factors, such as skin pigmentation, gestational age, and the presence of haemolytic disease.[5] Therefore, it is essential to validate TcB measurements before using them as a substitute for serum bilirubin measurements.

Several studies have compared TCB measurements with serum bilirubin measurements in neonates, but the results have been inconsistent.[6,7] Moreover, the accuracy of TCB measurements may be affected by the use of phototherapy, which can alter the skin's bilirubin content.[8] Therefore, there is a need for further research to validate the accuracy of TCB measurements in preterm neonates with hyperbilirubinemia, especially before and after the initiation of phototherapy.

Preterm neonates are at a higher risk of developing hyperbilirubinemia due to immature liver function and increased red blood cell turnover. The use of phototherapy is the primary intervention for treating hyperbilirubinemia in neonates. However, the effect of phototherapy on TCB measurements in preterm neonates with hyperbilirubinemia is not well established. Therefore, there is a need to validate the accuracy of TCB measurements before and after the initiation of phototherapy in preterm neonates with hyperbilirubinemia.

The results of this study will provide valuable information on the accuracy of TCB measurements in preterm neonates with hyperbilirubinemia, which will help in the management of hyperbilirubinemia in this vulnerable population. Moreover, this study will contribute to the existing literature on the use of TCB measurements in neonates and provide valuable information for healthcare providers in making informed decisions regarding the use of TCB measurements.

Aims and Objectives

To compare TCB and TSB values before and after initiation of phototherapy among preterm neonates with hyperbilirubinemia.

MATERIALS AND METHODS

Study Design: A hospital-based cross-sectional study was conducted at a tertiary care hospital in the neonatal intensive care unit (NICU) over a period of three months.

Sample Size Calculation: $N = [(Z\alpha + Z\beta)/C]2 + 3$

$\alpha = Z\alpha = 1.96$ (standard normal deviate)

$\beta = Z\beta = 0.84$ (power of the test)

$C = 0.5 * In[(1 + r)/(1 - r)] = 0.6328$

r = correlation coefficient

$N = [(1.96 + 0.84)/0.6328]2 + 3$

$N = 50$

Therefore, a total sample size of 50 preterm neonates is required for the study.

Sampling Method: A purposive sampling method was used to select preterm neonates admitted to the NICU during the study period who met the inclusion criteria.

Inclusion Criteria

- Preterm neonates born more than 28 and less than 35 weeks of gestation who appeared clinically icteric.
- Preterm neonates who were hemodynamically stable.
- Informed consent from parents.

Exclusion Criteria

- Babies who had received phototherapy before inclusion in the study.
- Babies who had undergone exchange transfusion.

Data Collection: Serum bilirubin was estimated using the acid diazo method (Vanden Bergh reaction), which is the gold standard method for measuring bilirubin levels. At the same time, transcutaneous bilirubin (TCB) measurements were obtained using Dräger jaundice meter JM 105 on the sternum. Three consecutive readings were taken, and the average was recorded in mg/dL. The device was calibrated before usage according to the manufacturer's recommendations.[9]

Phototherapy using light-emitting diode units with an irradiance of 20-30 μW/cm2/nm was instituted if the TSB fulfilled the criteria as per the sliding scale for preterm neonates.[10] A patch of skin over the sternum was shielded using an ECG electrode covered with aluminium foil.[11] A repeat TSB and TCB assessment were done as per clinical indication. The TSB and TCB were recorded within 15 minutes of each other. Other investigations were done as per need. The primary outcome was to compare TCB with TSB in preterm neonates before and after initiation of phototherapy.

Data Analysis: Data were entered into Microsoft Excel software. Descriptive statistics like mean, standard deviation, and proportions were used for analysis. A scatter plot was used to depict the relationship between TCB and TSB. Correlation coefficients were calculated using Pearson correlation (parametric test) or Spearman rank correlation (nonparametric test). A p-value of <0.05

ISSN (O): 2687-5365; ISSN (P): 2753-6556

at a 95% confidence interval was considered statistically significant. Bland-Altman analysis was used to visualize the agreement between TSB and TCB.

RESULTS

The [Table 1] shows that out of the total preterm neonates with hyperbilirubinemia, 38% were born to multiparous mothers, while 62% were born to primiparous mothers. Additionally, 54% of the neonates were delivered through a lower segment cesarean section (LSCS), while 46% were delivered vaginally.

Sex of the Baby

The table shows an equal distribution of sex among study population with ratio 1:1

Gestational Age

Among the preterm neonates, the majority had a gestational age of 32-35 weeks, accounting for 48.00% (24) of the cases. This was followed by 30-32 weeks, which constituted 32.00% (16) of the cases. The lowest proportion was observed in the 28-30 weeks gestational age category, with 20.00% (10) of the cases falling into this range.

Birthweight

Very low birth weight neonates accounted for 40% of study population

Time of Initial Screening for Clinical Jaundice

The table depicts the distribution of study population based on the time of initial screening for clinical jaundice. Among the cases, 32% (n-16) were screened within 24 hours of birth, 20% (n-10) were screened between 24-48 hours, 26% (n-13) were screened between 48-72 hours, and 22% (n-11) were screened after 72 hours of birth.

Table 1: Distribution of Parity and Mode of Delivery among Preterm Neonates with Hyperbilirubinemia

Parity		
Multi	19	38.00%
Primi	31	62.00%
Mode of Delivery		
LSCS	27	54.00%
NVD	23	46.00%

Table 2:

Sex of the Baby	**Frequency**	**Percentage**
Female	25	50.00%
Male	25	50.00%
Gestational Age		
28-30 Weeks	10	20.00%
30-32 Weeks	16	32.00%
32-35 Weeks	24	48.00%
Birthweight		
≥1.5 Kg	30	60.00%
<1.5 Kg	20	40.00%
Time of Initial Screening for clinical jaundice		
<24 Hours	16	32.00%
24-48 Hours	10	20.00%
48-72 Hours	13	26.00%
>72 Hours	11	22.00%

Table 3: Correlations between TCB and SBR values among study population before initiation of phototherapy

Pearson's Correlations		**Mean ± SD**	**Pearson's r**	**p**
TCB BEFORE PHOTOTHERAPY	-	13.94±3.503	0.763	< .001
SBR BEFORE PHOTOTHERPY	-	12.40±3.743		

Table 4: Correlations between TCB and SBR values among study population after initiation of phototherapy

Pearson's Correlations	**Mean ± SD**	**Pearson's r**	**p**
TCB AFER PHOTOTHERAPY	9.62±3.68	0.690	< .001
SBR AFTER PHOTOTHERPY	9.19±3.25		

Table 5: Agreement between SBR and TCB values across different SBR ranges before initiation of phototherapy.

	Mean	**SD**	**r value**	**p value**
SBR <10	8.2	1.6	0.70	<0.001
TCB	10.5	2.2		
SBR >10-15	12.4	1.2	0.33	<0.001
TCB	14.1	2.7		
SBR >15	17.6	2.2	0.37	<0.001
TCB	17.4	2.6		

[Table 3 and Figure 1] shows the mean TCB before phototherapy is 13.94 (with a standard deviation (SD) of ±3.503), while the mean SBR before phototherapy is 12.40 (with an SD of ±3.743). The Pearson's r value

ISSN (O): 2687-5365; ISSN (P): 2753-6556

of 0.763 indicates a strong positive correlation between the TCB and SBR measurements, suggesting that these two measures typically increase or decrease together.

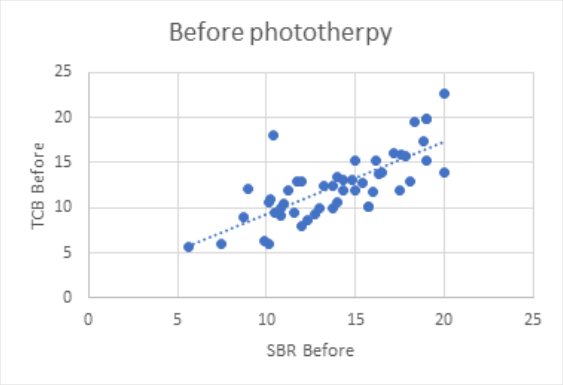

Figure 1: Pearson's Correlations between TCB and SBR (before phototherapy)

[Table 4 and Figure 2] shows the mean TCB after phototherapy is 9.62 (with a standard deviation (SD) of ±3.68), and the mean SBR after phototherapy is 9.19 (with an SD of ±3.25). The Pearson's correlation coefficient, (Pearson's r) is 0.690, indicating a strong positive correlation between TCB and SBR after phototherapy. This suggests that changes in TCB measurements align well with changes in SBR measurements after the treatment.

In practical terms, this strong correlation suggests that TCB measurements could be used as a non-invasive way to track the effectiveness of phototherapy in reducing bilirubin levels, with the understanding that TCB values tend to be slightly higher than SBR values.

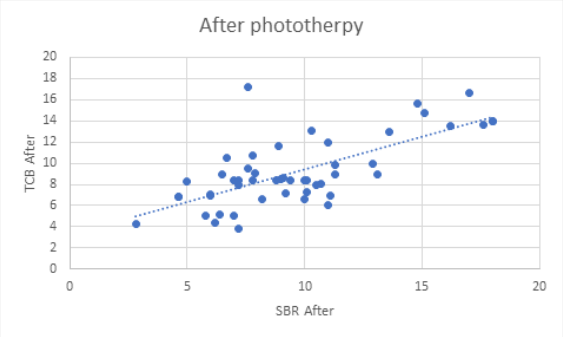

Figure 2: Pearson's Correlations between TCB and SBR (after phototherapy)

Overall the present study shows there was a strong positive correlation between TCB before phototherapy and SBR before phototherapy ($r = 0.763$, $p < .001$). There was also a strong positive correlation between TCB after phototherapy and SBR after phototherapy ($r = 0.690$, $p < .001$). The p-values indicate that both correlations were statistically significant at the $p < .001$ level.

In [Table 5] serum bilirubin was broken down into three ranges: less than 10mg/dl, between 10-15mg/dl, and greater than 15mg/dl and compared with TCB levels.

For each range, there is an associated mean and standard deviation (SD) for both the SBR and TCB measurements, as well as a correlation coefficient (r value) and p value for the relationship between the two measurements.

In the SBR <10 range, the SBR mean is 8.2 (SD 1.6) and the TCB mean is 10.5 (SD 2.2). The correlation between the two is strong (r=0.70), and is highly statistically significant (p<0.001). This suggests that the TCB and SBR measurements are closely aligned in this range, although the TCB values are systematically higher.

In the SBR 10-15 range, the SBR mean is 12.4 (SD 1.2) and the TCB mean is 14.1 (SD 2.7). Here, the correlation between the two is moderate (r=0.33), but is still statistically significant (p<0.001).

In the SBR >15 range, the SBR mean is 17.6 (SD 2.24) and the TCB mean is 17.4 (SD 2.6). The correlation is slightly higher than in the previous range (r=0.37), and again is highly statistically significant (p<0.001). In this range, the TCB and SBR means are almost identical, indicating a close alignment at high bilirubin levels.

In summary, the data suggest a strong correlation between TCB and SBR at lower bilirubin levels, with TCB readings tending to be higher. At higher bilirubin levels, the correlation is moderate but the mean values are closely aligned. These findings suggest that TCB and SBR may be used interchangeably in clinical settings, although the systematic differences at lower levels should be taken into account.

DISCUSSION

The current study sought to evaluate the effectiveness of transcutaneous bilirubin (TCB) measurements in comparison with serum bilirubin (SBR) measurements in preterm neonates with hyperbilirubinemia. Our results demonstrate a strong positive correlation between TCB and SBR both before and after the initiation of phototherapy, with Pearson's correlation coefficients of $r = 0.763$ and $r = 0.690$ respectively, both statistically significant at $p < .001$. This suggests that TCB measurements could be a reliable, noninvasive method for assessing bilirubin levels in preterm neonates.

Similar findings have been reported in the literature, strengthening the validity of our results. Mishra et al. in their study reported strong correlation coefficients of $r = 0.74$ pre-phototherapy and $r = 0.69$ post-phototherapy.[9] The slight differences in the correlation coefficients might be attributed to the variations in sample sizes, methodology, or the specific characteristics of the neonatal populations studied.

Interestingly, our study showed that the correlation between TCB and SBR was weakest in the subgroup of babies with SBR levels between 10-15 (r=0.33,

ISSN (O): 2687-5365; ISSN (P): 2753-6556

p<0.001). This contrasts with findings reported by Olusanya et al., who found that the correlation between TCB and SBR remained relatively consistent across different bilirubin ranges.[10] This discrepancy could potentially be due to differences in sample sizes, methodology, or the specific patient populations studied. Furthermore, the timing of TCB and SBR measurements relative to the initiation of phototherapy could also have influenced these results.

Despite the disparities between studies, there is a general consensus in the literature that TCB measurements can serve as a beneficial screening tool to determine which neonates require further SBR measurements and possible phototherapy.[11] However, it's important to note that the TCB measurement is not flawless. Several studies have pointed out that TCB readings can be influenced by numerous factors such as skin maturity, gestational age, and postnatal age.[12,13] These findings underscore the importance of considering these factors when interpreting TCB results and highlight that TCB should not be the sole determinant for phototherapy decision making.

In conclusion, while our study lends further support to the use of TCB measurements as an initial screening tool for hyperbilirubinemia in preterm neonates, it also emphasizes the need for careful interpretation of these readings. Further research is warranted, particularly large-scale, multi-centre studies, to corroborate these findings and help establish robust guidelines for TCB usage in neonatal intensive care units across diverse populations.

CONCLUSION

In conclusion, our study contributes to the growing body of evidence supporting the positive correlation between transcutaneous bilirubin (TCB) and serum bilirubin (SBR) levels before phototherapy in preterm neonates with hyperbilirubinemia. The results align with previous research and emphasize the reliability and applicability of TCB measurements as a non-invasive tool for assessing the severity of hyperbilirubinemia in this population.

However, it is important to note that further research is warranted to validate our findings and explore the long-term outcomes associated with TCB measurements in preterm neonates. Additionally, future studies should consider larger sample sizes and include diverse populations to ensure the generalizability of the results.

In summary, our study underscores the significance of TCB measurements as a reliable and non-invasive method for evaluating hyperbilirubinemia severity in preterm neonates. These findings have important implications for clinical practice, as they provide healthcare professionals with an additional tool for monitoring and managing hyperbilirubinemia in this vulnerable population.

REFERENCES

1. Maisels MJ, Bhutani VK, Bogen D, Newman TB, Stark AR, Watchko JF. Hyperbilirubinemia in the newborn infant ≥35 weeks' gestation: an update with clarifications. Pediatrics. 2009 Oct;124(4):1193.
2. Wong RJ, Bhutani VK, Stevenson DK. Understanding Newborn Jaundice: A Perspective on Genetics, Epidemiology, and Health Services Research. Pediatric Research. 2020;87(1):157-163.
3. 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 Aug;106(2):E17.
4. Socolovici C, Hagau N, Lazea C, Munteanu O, Florea M, Popescu R, et al. Transcutaneous bilirubinometry – the future in the diagnosis and management of neonatal hyperbilirubinemia? Journal of Medicine and Life. 2014;7(4):545-551.
5. Bhutani VK, Johnson L, Sivieri EM. Predictive ability of a predischarge hour-specific serum bilirubin for subsequent significant hyperbilirubinemia in healthy term and near-term newborns. Pediatrics. 1999 Sep;104(6):e60.
6. Ozkan H, Koklu E, Kahvecioglu D, Kurtoglu S, Yikilmaz A, Uras N, et al. Transcutaneous bilirubinometry in preterm infants receiving phototherapy. Acta Paediatr. 2008 Feb;97(2):147-150.
7. Wong V, Dalzell AM. Transcutaneous bilirubinometry during and after phototherapy. Arch Dis Child Fetal Neonatal Ed. 2005 Nov;90(6):F492-F494.
8. Rubaltelli FF, Gourley GR, Loskamp N, Modi N, Roth-Kleiner M, Sender A, et al. Transcutaneous bilirubin measurement: a multicenter evaluation of a new device. Pediatrics. 2001 May;107(5):1264-1271.
9. Mishra, S., Agarwal, R., Deorari, A. K., & Paul, V. K. (2009). Transcutaneous bilirubinometry reduces the need for blood sampling in neonates with visible jaundice. Acta paediatrica, 98(12), 1916-1919.
10. Olusanya, B. O., Imosemi, D. O., & Emokpae, A. A. (2016). Differences between transcutaneous and serum bilirubin measurements in black African neonates. Pediatrics, 138(3), e20160907.
11. De Luca, D., Zecca, E., Zuppa, A. A., & Romagnoli, C. (2008). The joint use of human and artificial intelligence in newborn medicine: a narrative review. Italian Journal of Pediatrics, 44(1), 88.
12. Knudsen, A. (1991). Prediction of the development of neonatal jaundice by increased umbilical cord blood bilirubin. Acta Paediatrica, 80(2), 219-223.
13. Briscoe, L., Clark, S., & Yoxall, C. W. (2002). Can transcutaneous bilirubinometry reduce the need for blood tests in jaundiced full term babies? Archives of Disease in Childhood - Fetal and Neonatal Edition, 86(3), F190–F192.

ISSN (O): 2687-5365; ISSN (P): 2753-6556