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Correlation of the transcutaneous bilirubin and serum bilirubin levels measured before and after phototherapy in newborns: a prospective observational study

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ABSTRACT

Aim: The purpose of the present study was to show the reliability of the transcutaneous bilirubin (TcB) measurement as an alternative method to total serum bilirubin (TSB) when starting treatment with phototherapy (PT), which is one of the most important treatment methods of hyperbilirubinemia as a very common practice in the neonatal period and eliminates the disadvantages of blood collection.

Materyal and Method: Two measurements were made to evaluate whether there was a correlation between the total serum bilirubin and transcutaneous bilirubin level measurement for follow-up in newborns who were hospitalized and prospectively followed up in the Newborn Intensive Care Unit of Karabuk University Medical Faculty Training and Research Hospital between April 13 and June 30, 2022 (Level III Neonatal Center) who were scheduled for starting phototherapy. The primary result was the correlation between TcB and TSB at the first 24 hours and after, at the initiation of FT, termination of FT, and 12 hours after PT was discontinued.

Results: The TSB and TcB values of the newborns were measured at the beginning of PT, at the end of PT, and 12 hours after PT was ended. The first measurement values were 11.60±5.16 and 10.72±4.02, respectively; the second measurement values were 7.45±2.34 and 6.35±2.83, respectively; and the third measurement values were 8.03±2.45 and 7.35±2.63 mg/dL, respectively. A strong positive correlation was found among all measurement values. Also, when the newborns who received FT for the first 24 hours were evaluated by subgrouping, the high correlation between TcB and TSB levels continued.

Conclusion: The present study showed that there is a significant relationship between TcB taken from the covered skin and TSB at the start, end, and 12 hours after PT. Also, when the newborns who received PT for the first 24 hours were evaluated in a subgroup, it was found that TCB measurement predicted the TSB level at a high level before and after PT. Based on these findings, it was concluded that TcB measurement, including in the first 24 hours, is reliable in the follow-up of newborns receiving PT for the treatment of hyperbilirubinemia. However, we think that larger prospective controlled studies are required in this respect.

Keywords: Newborn, bilirubin, phototherapy

INTRODUCTION

Hyperbilirubinemia in newborns is very common (50-80%) in the first week of life (1). Although hyperbilirubinemia has a benign progression most of the time, it can result in serious neurological morbidities when it reaches high levels (2,3).

Phototherapy (PT) is considered a safe and effective treatment for the treatment of indirect hyperbilirubinemia in the neonatal period. The indication for starting treatment depends on the serum bilirubin levels, whether there are risk factors, pregnancy, and postnatal age.

Total serum bilirubin (TSB) measurement is considered the gold standard for monitoring bilirubin levels during and after PT. However, blood collection is painful, time-consuming, and increases the risk of infection (4). The transcutaneous bilirubinometry device works by directing light to the skin of the baby and measuring and analyzing the intensity of the returning wavelengths to predict TSB (5).

Transcutaneous bilirubin (TcB) measurement is recommended as a non-invasive test to predict bilirubin levels before the onset of PT in term and late-preterm newborns (6-8).

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Canadian Academy of Pediatrics recommends that the TcB and TSB and bilirubin levels of all newborns are measured at 24-72nd hours after birth (before the discharge from hospital) (9).

National Institute for Health and Care Excellence (NICE) Guidelines recommend TcB measurement in >35-week and >24-hour well-born newborns, or TSB measurement when this is not possible (10).

In some studies, although the use of TcB during and after PT was found to be beneficial in newborns, especially when measured on the covered skin, some studies report opposite results (11,12).

The present study was designed to examine the accuracy of TcB measured in the covered skin in estimating the TSB levels in newborns undergoing PT and starting PT within the first 24 hours, which are two controversial issues.

MATERIAL AND METHOD

The study was carried out with the permission of Karabük University Faculty of Medicine Noninvasive Clinical Researches Ethics Committee (Date: 13.04.2022, Decision No: 2022/859). The study was conducted in accordance with the Declaration of Helsinki and good clinical practice guidelines. Written informed consent was obtained from the parents.

The present study is a single-center, observational cohort study that was conducted on newborns who were prospectively hospitalized and followed up in the Neonatal Intensive Care Unit of Karabuk University Medical Faculty Training and Research Hospital (Level III Neonatal Center) between April 13, 2022, and June 30, 2022. All newborns who received PT treatment during the study and whose parents gave consent were enrolled in the study.

PT was initiated based on TSB levels according to the guidelines and by considering the gestational weeks, risk factors, and ages in hours of the infants.

In line with the recommendations of the Turkish Neonatology Association, the curves that included the gestational week (GW) and risk factors in newborns with a gestational age above 35 weeks and the tables that were prepared according to birth weights were used for newborns younger than 35 GW (13,14).

LED PT Units (Overhead PT light units capable of delivering 180 UW/cm2, Ertunç Özcan Medical Devices, Turkey) were used in the study. The eyes of the newborns who received PT were covered with PT glasses for protection. Disposable diapers were used to protect the genital area. When TSB fell below the relevant treatment threshold, PT was discontinued.

TcB was measured from the covered area right after the collection of the TSB samples (in 10 minutes). The measurements were made by an assistant physician who was trained and experienced in the use of MBJ20 (Beijing M&B Electronic Instrument Co. Ltd. [Beijing, China]). The TcB device was lightly touched to a covered area (forehead area covered by the eye patch) three times, and the average of the three values was taken. The instrument was calibrated regularly according to the manufacturer's instructions.

The Neonatology Specialist managed the frequency of TSB measurements. Total and direct bilirubin levels were measured and direct hyperbilirubinemia was discarded in addition to routine biochemistry parameters. For the next TSB measurement, blood was taken from the heel by puncturing with a needle. TSB levels were measured in the laboratory by using direct spectrophotometry (Abbott Architect C8000, Abbott, USA).

The primary result was the correlation between TcB and TSB in the first 24 hours and beyond, at the initiation of PT (1st measurement), at the termination of PT (2nd measurement), and 12 hours after PT was discontinued (3rd measurement).

Data Analysis

Statistical analyzes of the study results were performed by using the SPSS 20 (SPSS, Chicago, United States) program. Sociodemographic data were evaluated as mean and percentage. Since the kurtosis and skewness values of the data were at the +2;-2 limit, it showed a normal distribution (George, 2011). The difference between bilirubin values was analyzed with the Paired Sample T-test, bilirubin values in bivariate groups were analyzed with the Independent Sample T-test, and the relationship between bilirubin values was evaluated with the Pearson's correlation. The Bland-Altman graphs were used in the analysis of the bias against the mean to assess the presence of a proportional bias (15).

RESULTS

The mean delivery week of the 48 newborns that were included in the study was 36.10±2.47 weeks, the birth weight was 2855.21±618.194 grams, and the mean time to start phototherapy was 53.98±53.5 hours. The 1st-minute Apgar score of the newborns was calculated as a median of 8 points, and the 5th-minute Apgar score was calculated as 9 points. The TSB and TcB values of the newborns were evaluated in three rebound measurements at the beginning of PT, at the end of PT, and 12 hours after PT was ended. The first measurement values were 11.60±5.16; 10.72±4.02, respectively; the second measurement values were 7.45±2.34, 6.35±2.83 respectively; and the third measurement values were 8.03±2.45, 7.35±2.63 mg/dL, respectively (**Table 1**).

It was found that there was ABO incompatibility in 20.8% of newborns, Rh incompatibility in 10.4%, sepsis in 4.2%, perinatal asphyxia in 6.3%, cephalic hematoma in 2.1%, polycythemia 8.3%, and chorioamnionitis 4.2% (**Table 1**).

Table 1. Clinical characteristics of newborns

Characteristics	Mean±SD	Min-Max (Median)
Birth week	36.10±2.47	31-42 (36)
Birth weight	2855.21±618.194	1860-4510 (2830)
Phototherapy start time	53.98±53.5	3-222 (33.50)
Apgar score in the 1st minute		2-10 (8)
Apgar score in the 5th minute		4-10 (9)
Neonatal bilirubin 1	11.60±5.16	3.8-23.2 (11.3)
Transcutaneous bilirubin 1	10.72±4.02	3.10-19.80 (11.2)
Neonatal bilirubin 2	7.45±2.34	2.4-11.6 (7.4)
Transcutaneous bilirubin 2	6.35±2.83	1.3-13.6 (6.15)
Neonatal bilirubin 3	8.03±2.45	3-14 (7.9)
Transcutaneous bilirubin 3	7.35±2.63	3.4-24.5 (7.2)
	n	**%**
Presence of ABO incompatibility		
Yes	10	20.8
No	38	79.2
Presence of Rh incompatibility		
Yes	5	10.4
No	43	89.6
Presence of sepsis		
Yes	2	4.2
No	46	95.8
Presence of perinatal asphyxia		
Yes	3	6.3
No	45	93.8
Presence of cephalic hematoma		
Yes	1	2.1
No	47	97.9
Presence of polycythemia		
Yes	4	8.3
No	44	91.7
Presence of chorioamnionitis		
Yes	2	4.2
No	46	95.8
Total	48	100

The TSB and TcB values of the newborns at three different times are analyzed in **Table 2.** As a result of the analysis, significant differences were detected between TSB and TcB transcutaneous bilirubin values in each measurement ($p<0.001$). However, it was also found that there was a strong positive correlation among all measurement values.

To compare TSB and TcB values, firstly, the Bland-Altman method was applied to the related dataset by using the MedCalc program, and the graphs of the deviations of the observation values from the mean values were obtained as in **Figures 1-3.**

Table 2. Descriptive statistics of neonatal and transcutaneous bilirubin values of all newborns receiving PT

	TSB	TcB	Difference	p*	r**
1st measurement	11.60±5.16	10.72±4.02	0.88±2.14	0.000	0.921***
2nd measurement	7.45±2.34	6.35±2.83	1.1±1.98	0.000	0.724***
3rd measurement	8.03±2.45	7.35±2.63	0.67±1.51	0.000	0.837***

*Paired Samples T-test, **Pearson's correlation, ***Significant at 0.001.

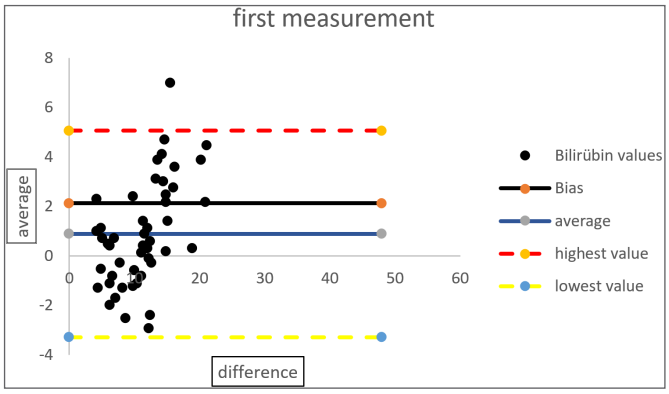

Figure 1. Paired graph of the difference between neonatal and transcutaneous bilirubin values in the first measurement (Bland-Altman plots graph).

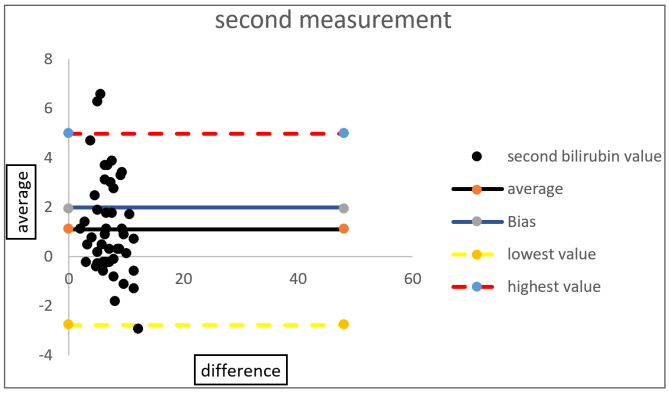

Figure 2. Paired graph of the difference between neonatal and transcutaneous bilirubin values in the second measurement (Bland-Altman plots graph).

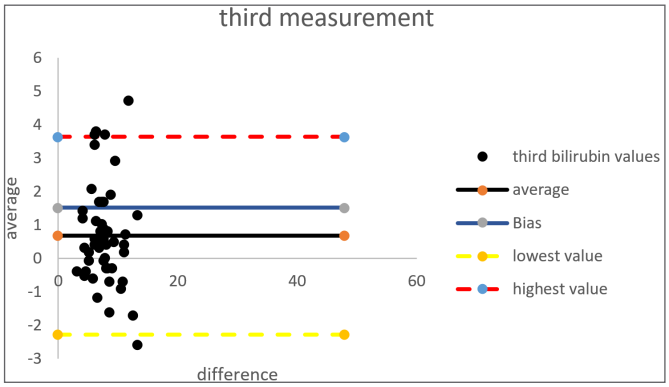

Figure 3. Paired graph of the difference between neonatal and transcutaneous bilirubin values in the third measurement (Bland-Altman plots graph).

When **Figures 1-3** are examined, it is seen that the averages of the differences in the measurement results obtained according to the two techniques show a normal distribution.

The values of the newborns receiving phototherapy before 24 hours

The TSB and TcB values of newborns who received phototherapy before 24 hours passed after birth are given in **Table 3**. The difference between TSB and TcB values was statistically insignificant (p=0.377).

Table 3. Descriptive statistics of neonatal and transcutaneous bilirubin values of newborns who received PT within the first 24 hours

	TSB	TcB	Difference	p*	r**
1st measurement	7.39±3.02	7.63±3.3	-0.24±1.12	0.377	0.941***
2nd measurement	6.64±2.35	5.99±2.42	0.64±1.3	0.050	0.853***
3rd measurement	7.32±1.98	6.78±2.42	0.54±1.61	0.175	0.749***

*Paired Samples T-test, **Pearson's correlation, *** Significant at 0.001.

DISCUSSION

The present study showed that there is a significant relationship between TcB taken from the covered skin and TSB at the beginning, during, and 12 hours after PT. TcB measurements taken from the uncovered skin were not evaluated. Also, when the newborns who received PT for the first 24 hours were evaluated in a subgroup in the study, it was found that TcB measurement predicted the TSB level at a high level before and after PT.

When the literature was reviewed, it was seen that there are parallel and opposite results to our results and there is no consensus.Contrary to the results of the present study, in their study comparing TcB and TSB by covering an area above the sternum in term and late preterm newborns who received PT between 34-41 GW, Murli et al.(16) found that there was a weak correlation between TcB and TSB measured at 0, 12, 24 hours after PT was discontinued, and concluded that the TcB measurement was not reliable in term and late preterm newborns who received PT.

Bhutani et al. (17) reported that up to 36-48 hours were required for bilirubin levels to rebalance after phototherapy to accurately evaluate TcB levels in uncoated skin areas. The findings of the present study showed that measuring TcB levels in the covered skin is safe at the beginning and immediately after PT, and that the disadvantages of waiting for 36-48 hours can be overcome in this way. This difference in results may be related to the device technology used in the study.

In a prospective study conducted in 2017 in the Haitian newborn population, in parallel with our findings, TcB and TSB levels were compared during phototherapy and 70 parallel TcB/TcB were measured in 35 term and preterm newborns, a good agreement was detected between TSB and TcB, and it was emphasized that TcB would show good compatibility with TSB in societies where serum bilirubin test is not widely available, and it could be used safely to guide the treatment of jaundice during phototherapy (18).

A study that was conducted in Iran partially supports the findings obtained in the present study. A total of 134 term and 36 preterm newborns who received FT were examined in this study and it was concluded that TcB measurement could be used safely in the evaluation of bilirubin levels in preterm and term newborns receiving FT, but it is slightly less reliable among preterm newborns (r: 0.921, P <0.001 in term newborns; r=0.887, P=0.001 in preterm newborns) (19).

In a meta-analysis that evaluated the reliability of TcB in premature newborns in 2019, it was concluded when 29 studies were evaluated that TcB values obtained from the forehead and sternum regions were well correlated with TSB and that it could be a reliable method to evaluate hyperbilirubinemia in premature newborns (20).

Again, in the study of Vasava et al. (21) conducted on 306 term and preterm newborns, it was concluded that the measurement of TcB strongly predicted the level of TSB at all gestational weeks and in different body regions.

In another study that had parallel results to the present study, Amneah et al. (22) conducted a study with 80 newborns who underwent PT by placing a patch on the skin and reported a strong correlation between TcB values from the patched skin and TSB levels.

In general, the significant correlation between TcB and TSB during PT is consistent with the findings of some previous studies conducted with preterm newborns.

Also, the results of the present showed the correlation between TcB and TSB after PT was discontinued.

The advantage of the present study was that it could show the high correlation between TcB and TSB in newborns who underwent PT in the first 24 hours when compared with previous studies.

Limitations of the present study; the sample size was small because of the single-center design and short study duration, the study included only the infant population in the neonatal intensive care unit, and the TcB-TSB correlation was evaluated only from the covered area.

CONCLUSION

TcB measurements were strongly correlated with TSB levels at 24 hours and beyond, at the start of PT, and after PT. However, we think that larger prospective studies are needed in this respect.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Karabük University Faculty of Medicine Noninvasive Clinical Researches Ethics Committee (Date: 13.04.2022, Decision No: 2022/859).

Informed Consent: Written informed consent was obtained from the parents. All parents signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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REFERENCES

1. Woodgate P, Jardine LA. Neonatal jaundice. BMJ Clin Evid 2011; 2011: 0319.
2. Johnson L, Bhutani VK. The clinical syndrome of bilirubin-induced neurologic dysfunction. Semin Perinatol 2011; 35: 101-13
3. Cashore WJ. The neurotoxicity of bilirubin. Clin Perinatol 1990; 17: 437–47.
4. Hassan Shabuj M, Hossain J, Dey S. Accuracy of transcutaneous bilirubinometry in the preterm infants: a comprehensive meta-analysis. J Matern Fetal Neonatal Med 2019; 32: 734-41.
5. Ahmed M, Mostafa S, Fisher G, Reynolds TM. Comparison between transcutaneous bilirubinometry and total serum bilirubin measurements in preterm infants <35 weeks gestation. Ann Clin Biochem 2010: 47: 72-7.
6. Özkan H, Ören H, Duman N, Duman M, Dermal bilirubin kinetics during phototherapy in term neonates. Acta Paediatr 2003; 92: 577-81.
7. Beck M, Kau N, Schlebusch H. Transcutaneous bilirubin measurement in newborn infants: evaluation of a new spectrophotometric method. Arch Dis Child Fetal Neonatal Ed 2003; 88: F350-1.
8. Nagar G, Vandermeer B, Campbell S, Kumar M. Effect of phototherapy on the reliability of transcutaneous bilirubin devices in term and near-term infants: a systematic review and meta-analysis. Neonatology 2016; 109: 203-12.
9. Newman J. Re: Guidelines for detection, management and prevention of hyperbilirubinemia in term and late preterm newborn infants (35 or more weeks' gestation) - Summary. Paediatr Child Health 2007; 12: 401-18.
10. Amos RC, Jacob H, Leith W. Jaundice in newborn babies under 28 days: NICE guideline 2016 (CG98). Arch Dis Child Educ Pract Ed 2017; 102: 207-9.
11. Tan KL, Dong F. Transcutaneous bilirubinometry during and after phototherapy. Acta Paediatr 2003; 92: 327–31.
12. Rylance S, Yan J, Molyneux E. Can transcutaneous bilirubinometry safely guide phototherapy treatment of neonatal jaundice in Malawi? Paediatr Int Child Health 2014; 34: 101-7.
13. Çoban A, Kaynak Türkmen M, Gürsoy T. Turkish Neonatal Society guideline to the approach, follow-up, and treatment of neonatal jaundice. Turk Pediatri Ars 2018; 53: 172-9.
14. American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics 2004; 114: 297-316.
15. George D. (2011). SPSS for windows step by step: A simple study guide and reference, 17.0 update, 10/e (4th ed.). Pearson Education India.
16. Murli L, Thukral A, Sankar MJ, et al. Reliability of transcutaneous bilirubinometry from shielded skin in neonates receiving phototherapy: a prospective cohort study. J Perinatol 2017; 37: 182-7.
17. Bhutani VK, Johnson LH, Gourley G. Measuring bilirubin through the skin?. Pediatrics 2003; 111: 919-20.
18. Johnson SM, Vasu V, Marseille C, et al. Validation of transcutaneous bilirubinometry during phototherapy for detection and monitoring of neonatal jaundice in a low-income setting. Paediatr Int Child Health 2020; 40: 25-9.
19. Radfar M, Hashemieh M, Shirvani F, Madani R. Transcutaneous Bilirubinometry in Preterm and Term Newborn Infants before and during Phototherapy. Arch Iran Med 2016; 19: 323-8.
20. 20.Hassan Shabuj M, Hossain J, Dey S. Accuracy of transcutaneous bilirubinometry in the preterm infants: a comprehensive meta-analysis. J Matern Fetal Neonatal Med 2019: 32: 734-41.
21. Vasava S, Dagli P. Transcutaneous bilirubinometry: Influence of gestational age and measurement site. Sri Lanka J Child Health 2018; 47: 27-32.
22. Amneenah A. Comparison of diagnostic accuracy of transcutaneous bilirubinometry during phototherapy by using skin patch. Int J Health Sci 2022; 6: 7276-88.