RESEARCH
O&G Forum 2024; 34-3s: 2745-2749

CORRELATION BETWEEN VALUES OF BILIRUBIN MEASUREMENT BY TRANSCUTANEOUS AND SERUM LEVELS IN TERM NEONATES

Dr. Tahera Tabassum[1], Dr. Hepsiba Katuri[2], Dr. G. Santosh Kumar Reddy[3], *Dr. Naila Mazher[4], Dr. Shafa Tayyaba[5]

[1,5]Post Graduate, Department of Pediatrics, Apollo Institute of Medical Sciences and Research, JubleeHills, Hyderabad, Telangana.
[2,3,4]Assistant Professor, Department of Pediatrics, Apollo Institute of Medical Sciences and Research, JubleeHills, Hyderabad, Telangana.

Abstract
Background: One of the most prevalent reasons for hospitalization within the first week following birth is neonatal jaundice. Neonatal hyperbilirubinemia is a very prevalent illness, affecting 25 to 50% of all newborns and 80% of preterm babies. In India, around 5% of newborns have pathological jaundice1.
OBJECTIVES:
1. To estimate bilirubin levels in neonates using a non-invasive method.
2. To assess the difference between Transcutaneous Bilirubin and Total Serum Bilirubin paired values.
MATERIAL & METHODS: Study Design: Hospital-based, cross sectional study. Study area: The study was conducted in the Department of paediatrics, Apollo Institute of Medical Sciences and Research, JubleeHills, Hyderabad, Telangana. Sample size: Study consisted a total of 192 subjects. Sampling Technique: Simple Random technique. Study tools and Data collection procedure: An informed written consent was obtained from all the parents of the newborns who were enrolled in the study. From all the newborns, information such as demographic data, day of life, bilirubin values were recorded. Neonates who seem icteric visually were examined by a pediatric resident. If they had the inclusion criteria for the study, their bilirubin levels were measured three times on the sternum for avoiding any bias induced by the bilirubinometer.
Results: The TcB – TSB difference for the paired measurements when the TSB was <15 mg/dL was 1.03 to 1.83 mg/dL. The difference became progressively less positive as the TSB level increased, with TcB – TSB difference of - 5 to 3 mg/dL for the paired measurements when the TSB level was ≥15 mg/dL.
CONCLUSION: The findings in this study suggest that TcB measurements can be used effectively to screen newborn infants for significant hyperbilirubinemia, with TSB measurements reserved for those newborns whose TcB level is above a certain cutoff value (15 mg/dl). We recommend that transcutaneous bilirubinometer can be effectively used as a screening tool to predict bilirubin levels in term babies and can be used to dictate management guidelines.
Keywords: neonatal jaundice, Total serum bilirubin, bilirubinometer

Introduction
One of the most prevalent reasons for hospitalization within the first week following birth is neonatal jaundice. Neonatal hyperbilirubinemia is a very prevalent illness, affecting 25 to 50% of all newborns and 80% of preterm babies. In India, around 5% of newborns have pathological jaundice[1].
Bilirubin-induced neurologic dysfunction (BIND) can arise in these infants due to severe hyperbilirubinemia1. The young brain is sensitive to toxicity from unconjugated bilirubin, which results in kernicterus[2]. Kernicterus is linked with a high death rate, and survivors frequently experience sequelae such as athetoid cerebral palsy, high-frequency hearing loss, and intellectual disability[3]. Severe neonatal hyperbilirubinemia and its complications can be avoided with proper serum bilirubin monitoring and prompt treatment with phototherapy or an exchange blood transfusion.
Visual estimations of jaundice and serum bilirubin levels might be deceiving. Recent investigations and safety data evaluations have shown that visual assessment of jaundice is an unreliable and risky indicator of severe hyperbilirubinemia[4]. In most situations, jaundice is minor and temporary; nonetheless, in some children, it is one of the most prevalent reasons for readmission to the hospital within the first week of life. Jaundice affects 60-70 percent of term neonates and around 80% of preterm infants. Serum bilirubin levels more than 15mg/dl are observed in 3% of normal term neonates 4. Various pre-discharge screening procedures were implemented to identify patients at risk of severe hyperbilirubinemia. They include total serum bilirubin, transcutaneous bilirubin, and clinical risk factor scoring[1].
As a result, serum bilirubin levels must frequently be measured in the lab. Total serum bilirubin (TSB) measurement by a biochemical laboratory is still considered the gold standard for determining bilirubin levels, but it is invasive, requiring needle pricks that pose the risk of infection and cause discomfort and stress to neonates [5]. The time it takes to receive bilirubin test results may cause the start of neonatal hyperbilirubinemia therapy to be delayed. In recent years, the transcutaneous

bilirubinometer, which detects bilirubin levels by photometry, has been utilized as an alternative to estimating bilirubin levels. The first electronic transcutaneous bilirubinometry (TcB) equipment proved beneficial as a screening approach for identifying neonates who need serum bilirubin testing. Noninvasive transcutaneous bilirubin (TcB) monitoring is an appealing alternative for newborns, however, perspectives on its utility differ between studies[6]. The transcutaneous bilirubinometer measures bilirubin's spectral reflectance. This is done based on the difference in optical densities for light in the blue (450 nm) and green (550 nm) wavelengths. Pigments on the skin, such as melanin and haemoglobin, should be reduced due to bilirubin accumulation in the deeper subcutaneous tissue. The gadget provides a direct TcB measurement in mmol/l or mg/dl, allowing straightforward interpretation.

A transcutaneous bilirubinometer is a portable, painless, and non-invasive tool. The bilirubin level is measured by putting a probe to the infant forehead or sternum. It provides a rapid response, allowing for the beginning of therapy and lowering the burden on health care providers. This study used a transcutaneous bilirubinometer to assess bilirubin levels in the midsternum (TCBS), which is one of the approved sites. The correlation between serum bilirubin (TSB) and jaundice estimated by this instrument could aid in the early detection of neonatal hyperbilirubinemia, allowing for timely intervention and a better outcome in newborns with hyperbilirubinemia, as well as the prevention of complications involving the central nervous system.

OBJECTIVES:

1. To estimate bilirubin levels in neonates using a non-invasive method.
2. To assess the difference between Transcutaneous Bilirubin and Total Serum Bilirubin paired values.
3. To assess the demographic distribution – age wise, gender wise, mothers and babies blood group distribution, type of feeding among the study population.
4. To correlate the values of bilirubin measurements by transcutaneous and total serum levels in term neonates.

MATERIAL & METHODS:

Study Design: Hospital-based, cross sectional study.

Study area: The study was conducted in the Department of paediatrics, Apollo Institute of Medical Sciences and Research, Jublee Hills, Hyderabad, Telangana.

Sample size: Study consisted a total of 192 subjects.

Sampling Technique: Simple Random technique.

Inclusion Criteria: All full term neonates admitted in postnatal ward, weighing >2500gm with clinical jaundice.

Exclusion criteria:

1. Newborns with birth asphyxia.
2. Newborns with major congenital malformations
3. Newborns who have received phototherapy or blood transfusion.

Study tools and Data collection procedure: An informed written consent was obtained from all the parents of the newborns who were enrolled in the study. From all the newborns, information such as demographic data, day of life, bilirubin values were recorded. Neonates who seem icteric visually were examined by a pediatric resident. If they had the inclusion criteria for the study, their bilirubin levels were measured three times on the sternum for avoiding any bias induced by the bilirubinometer. BM-100C model by DAVID brand transcutaneous bilirubinometer was used for this study**.** The mean levels were recorded and blood samples were obtained within 30 minutes and sent to the laboratory for determining TSB. Measurements obtained from the two methods were then compared.

Statistical analysis:

Data entry and analysis were performed using the SPSS software version 24. Demographic data among the neonates were grouped and analysed using descriptive analysis. Normally distributed numerical data were presented as mean and standard deviation (SD), while categorical data were presented as frequency (n) and percentage (%). Pearson correlation between study variables is performed to find the degree of relationship. The direction and strength of linear relationship were shown by the correlation coefficient (r) and the coefficient of determination (R2).

OBSERVATIONS & RESULTS:

Table 1: Age wise distribution of babies (n=192)

Age of baby (in days)	No. of babies	Percentage
1-2 days	13	6.8
3-5 days	175	91.1
6-10 days	4	2.1
Total	192	100

In the present study, the babies included were from day 1 to day 10 of life, majority (91%) of the babies were included on day 3 to day 5 of life.

Table 2: Gender wise distribution of babies (n=192)

Gender	No. of babies	Percentage
Males	109	56.8
Females	83	43.2
Total	192	100

Out of the 192 babies included in the study, 56.8% (n=109) were males and 43.2% (n=83) were females.

Table 3. Distribution of birth weight among babies (n=192)

Birth weight(Kg)	No. of babies	Percentage
2.5 – 3	170	88.5
3 -4	22	11.5
>4	0	0
Total	192	100

Among the study group, majority (88.5%) of babies weighed between 2.5 to 3 kg at birth. Among babies included in this study, 88.7% (170/192) weighed between 2.5 and 3 kgs, 11.5% (22/192) weighed 3-4 kg.

A majority of mothers (38 %) had a O positive blood group, whereas a least (0.5%) had AB negative blood group. Among the babies, 35.9% had O positive blood group, 37.5% had B positive blood group. A majority (98 %) of babies were breastfed, 2% were on both breast and formula feeding.

Table 4. Total serum bilirubin distribution of babies (n=192)

TSB	No. of babies	Percentage	Mean TSB
<12	103	53.6	8.7542
12-18	82	42.7	14.6341
>18	7	3.6	21.0129

Among the 192babies included in the study, 53.6 % had a total bilirubin of 12 – 18 mg/dl, 42.7% had < 12 mg/dl.

Table 5. Transcutaneous bilirubin values distribution in babies (n=192)

TCB	No. of babies	Percentage	Mean TcB
<12	83	43.2	9.1831
12-18	102	53.1	14.9324
>18	7	3.6	19.3571

Among the babies studied, predominating TCBS value of 12 to 18 was noticed among 43.2 % in mid sternum.

Table 6. Age of baby and transcutaneous bilirubin values

Age of baby (in days)	No. of babies	Mean	SD
1	0	-	-
2	13	8.2077	4.17402
3	125	12.4552	3.35700
4	45	13.6356	3.47178
5	5	16.0600	5.41923
6	3	15.1000	6.82862
7	1	18.0000	.

In the present study, 91.1% of the babies were in the 3rd to 5 th day of life.

Table 7. Comparison between difference of TCB and TSB paired values

TB	No. of babies	TCB		TSB		Difference between TcBand TSB paired values
		Mean	SD	Mean	SD	
<15	143	11.0615	3.05646	10.1269	3.20859	1.03 -1.08 mg/dl
>15	49	17.1224	1.36782	16.3392	2.46131	-5 to 3 mg/dl
P value		<0.000*		<0.000*		

The TcB – TSB difference for the paired measurements when the TSB was <15 mg/dL was 1.03 to 1.83 mg/dL. The difference became progressively less positive as the TSB level increased, with TcB – TSB difference of - 5 to 3 mg/dL for the paired measurements when the TSB level was ≥15 mg/dL.

Table 8: Pearson correlation between total serum bilirubin and transcutaneous bilirubin

Persons correlation	r value	P value
TCB vs. TSB	0.951	<0.000**

Pearson correlation between study variables is performed to find the degree of relationship. The correlation coefficient between total serum bilirubin and transcutaneous bilirubin values (mid sternum) was found to be 0.951with a statistically significant p value.

Table 9: Regression analysis

Regression equation	R^2	Beta	P value
-1.127=1.018*TcB	95.1	0.951	<0.000*

Regression equation: TSB= -1.127=1.018*TcB

DISCUSSION:

Neonatal hyperbilirubinemia is a complex metabolic condition caused by a combination of physiological and pathological mechanisms throughout the neonatal era. It is concerning because it is a frequent and preventable illness affecting approximately 25-50% of neonates. These newborns may suffer from serious problems such as cerebral palsy, encephalopathy, and mental impairment. However, neurological signs accompanying newborn hyperbilirubinemia are not present in approximately 15% of babies with kernicterus.

Due to financial restrictions and medical-social concerns, an increasing number of newborn newborns are released from the hospital within 48 hours of birth. As a result, hyperbilirubinemia is identified less frequently prior to discharge. Given these life-threatening problems, it is critical to predict jaundice in all neonates using a non-invasive and sensitive approach. This will assist in implementing effective preventative measures and early treatment to reduce mortality and morbidity. All 192 infants with clinical jaundice who met the inclusion criteria were included.

In the present study, 91.1% of the babies were in the 3rd to 5th day of life. A total serum bilirubin value of more than 18 mg/dl was observed in 3.6% of babies included in the present study. Male babies constituted 56.8% of the study population and female babies were 43.2%. A similar study done by Mazrah Mohamed et al[7] showed 56% as females and 43.8% males. Whereas in a study conducted by Pushpendra Kumar et al[8] in 2018 on 100 neonates males constituted 62% and 38% were females. In a similar study conducted by Romagnoli et al[9] in 2013 on 298 neonates 52% were male and 47.9% were females. In this study majority 88.5% of babies were of the weight 2500gms -3000gms and the remaining 11.5% were 3500-4000 gms. A similar study done by Mazrah Mohamed et al[7] majority of the babies (86.9%) were between 2500 -3000gms. In the present study, 98% of the babies were exclusively breastfed and 2% had mixed feeding.These findings were consistent with a previous study by Pushpendra Kumar et al[8] where 99% of the babies were exclusively breastfed and 1% were formula fed.

In the present study, 91.1% of the babies were in the 3rd to 5th day of life and a mean ± SD of transcutaneous bilirubin value on DAY 6 of life was 15.1 ± 6.8. In a similar study conducted by Majid Mansouri et al[10] 121 babies were more than day 4 of life and the mean mean ± SD cutaneous bilirubin values were 19.8±3.53. TSB values in study newborns ranged from 0.17mg/dL to 23 mg/dL; TSB values (25%) were ≥15 mg/dL. Overall, the mean ± SD TcB – TSB difference for the 192 paired measurements was 0.89 ± 1.25 mg/dL, with differences ranging from – 5 mg/dL to 3 mg/dL. The correlation between paired measurements was 0.95. The TcB – TSB difference varied based on the TSB level.

The TcB – TSB difference for the paired measurements when the TSB was <15 mg/dL was 1.03 to 1.83 mg/dL. The difference became progressively less positive as the TSB level increased, with TcB – TSB difference of -5 to 3 mg/dL for the paired measurements when the TSB level was ≥15 mg/dL. The findings were consistent in a similar study done by Taylor et al38 where TSB values in study newborns ranged from 1.8

mg/dL to 16.6 mg/dL; 20 TSB values (2.2%) were ≥15 mg/dL. Overall, the mean ± SD TcB – TSB difference for the 925 paired measurements was 0.84 ± 1.78 mg/dL, with differences ranging from –6.9 mg/dL to 8.8 mg/dL. The correlation between paired measurements was 0.78. the TcB – TSB difference varied based on the TSB level. The mean TcB – TSB difference for the 31 paired measurements when the TSB was <5 mg/dL was 1.3 ± 2.3 mg/dL. The difference became progressively less positive as the TSB level increased, with a mean TcB – TSB difference of –1.4 ± 2.4 mg/dL for the 20 paired measurements when the TSB level was ≥15 mg/dL.

There were 52 TcB values (5.6% [95% CI: 4.2–7.3]) that were ≥2 mg/dL lower than the matching TSB level, and 20 TcB values (2.2% [95% CI: 1.3–3.3]) that were ≥3 mg/dL lower than the corresponding TSB level. Conversely, there were 215 TcB values (23.2% [95% CI: 20.6–26.1]) that were 2 mg/dL higher than the TSB level, and 92 TcB values (10.0% [95% CI: 8.1–12.1]) that were ≥3 mg/dL higher than the TSB level. Overall, TcB readings differed from the matched TSB value by a clinically relevant difference in 28.8% (95% CI: 25.9–31.8) or 12.1% (95% CI: 10.1–14.4) of measurements, respectively, defined as a discrepancy (ie, absolute value of difference) of ≥2 mg/dL or ≥3 mg/dL between a TcB and TSB measurement.

The correlation coefficient between total serum bilirubin and transcutaneous bilirubin values (mid sternum) was found to be 0.951. This study found a strong linear relationship between TSB and TcB with a r value of 0.95 and a statistically significant p value of<0.001. This observation is similar to a study by Taylor et al[11] where data were obtained from 27 nursery sites involving 925 matched TcB and TSB level from both the chest and forehead. They used two brands of the TcB device (BiliCheck and JM-103) and found a good correlation between TSB and TcB values. Majid Mansouri et al[10] reported a good positive linear relationship between TSB and TcB, of the 200 neonates with a r value of 0.89.

A positive linear relationship was observed between TSB with TcB forehead (r = 0.82) and TcB sternum (r = 0.80) in a similar study conducted by Mazrah Mohamed et al[7] on130 neonates. In other similar studies by Mandal et al[12] and Panda et al[13], similar observations were made wherein, there was a significant correlation between transcutaneous bilirubin and total serum bilirubin. Regression equation derived from our study is TSB= -1.127=1.018*TcB. Pearson correlation coefficient of 0.951. This value is significant as p value was <0.001.

The results of our study indicate that TcB measurement provides an effective estimate of TSB values in healthy newborn infants during their nursery stay. A potentially significant issue with the use of TcB screening is that TcB levels provide less accurate estimates of TSB values at higher serum bilirubin levels. As opposed to lower levels in which TcB tended to overestimate TSB levels, we found that at TSB levels ≥15 mg/dL. Other investigators have reported similar findings. In a study comparing TcB and TSB values among a largely Hispanic population of newborns, Engle et al41 also found that TcB measurements tended to underestimate TSB at higher levels. Similarly, in one of the few assessments of TcB use in newborns after discharge from the nursery, the overall correlation between TcB and TSB levels was 0.77, with increasing variability at higher TSB values; 40% of the 121 newborns in this study had TSB levels ≥15 mg/dL.

Overall, our results and the results of other studies suggest that TcB screening might be most effective at an age when most TSB levels would be expected to be <15 mg/dL. Overall, the findings in this study suggest that TcB measurements can be used effectively to screen newborn infants for significant hyperbilirubinemia, with TSB measurements reserved for those newborns whose TcB level is above a certain cutoff value.

CONCLUSION:

The findings in this study suggest that TcB measurements can be used effectively to screen newborn infants for significant hyperbilirubinemia, with TSB measurements reserved for those newborns whose TcB level is above a certain cutoff value (15 mg/dl). We recommend that transcutaneous bilirubinometer can be effectively used as a screening tool to predict bilirubin levels in term babies and can be used to dictate management guidelines.

References

1. *Bhutani VK, Johnson LH, Keren R. Diagnosis and management of hyperbilirubinemia in the term neonate; for a safer first week. Pediatr Clin N Am 2004; 51: 843-861.*
2. *Ministry of Health Malaysia. Clinical practice guidelines: management of neonatal jaundice. 2nd ed. Kuala Lumpur, Malaysia: Ministry of Health; 2014.*
3. *Johnson LH,Bhutani VK,Brown AK.system-based approach to management of neonatal jaundice and prevention of kernicterus. J pediatr 2002; 140:396-403*
4. *Ratnavel N, Ives NK. Investigation of prolonged neonatal jaundice. Curr Paediatr. 2005; 15 (2) : 85 – 91*
5. *Taylor JA, Burgos AE, Flaherman V, Chung EK, Simpson EA, Goyal NK, et al. Discrepancies between transcutaneous and serum bilirubin measurements. Pediatrics. 2015;135(2):224–231.*
6. *Ho HT, Ng T K , Tsui KC and Lo YC. Evaluation of a new transcutaneous bilirubinometer in Chinese newborns. Arch Dis Child Fetal Neonatal Ed 2006; 91: F434– F438.*
7. *Mohamed M, Ibrahim NR, Ramli N, Abdul Majid N, Yacob NM, Nasir A. Comparison between the Transcutaneous and Total Serum Bilirubin Measurement in Malay Neonates with Neonatal Jaundice. Malays J Med Sci. 2022 Feb;29(1):43-54.*
8. *Kumar, P. (2019). A Comparison between Transcutaneous Bilirubin (TcB) and Total Serum Bilirubin (TSB) Measurements in Term Neonates. Asian Journal of Clinical Pediatrics and Neonatology, 6(4), 13-16.*
9. *Romagnoli C, Tiberi E, Barone G, De Curtis M, Regoli D, Paolillo P et al. Validation of transcutaneous bilirubin nomogram in identifying neonates not at risk of hyperbilirubinemia: A prospective, observational, multicenter study. Early human development .2012;88(1):51-55.*
10. *Mansouri M, Mahmoodnejad A, Sarvestani RT, Gharibi F. A comparison between transcutaneous bilirubin (TcB) and total serum bilirubin (TSB) measurements in term neonates. Int J Pediatr. 2015;3(3):633–641. doi: 10.22038/ijp.2015.4352*
11. *Taylor JA, Burgos AE, Flaherman V, Chung EK, Simpson EA, Goyal NK, Von Kohorn I, Dhepyasuwan N; Better Outcomes through Research for Newborns Network. Discrepancies between transcutaneous and serum bilirubin measurements. Pediatrics. 2015 Feb;135(2):224-31.*

12. Mandal A, Bannerji R, Ray J, Mitra M, Azad SM, Basu S. Correlation between transcutaneous bilirubin estimation and total serum bilirubin estimation in neonatal hyperbilirubinemia. BLDE Univ J Health Sci 2018; 3:36-42.

13. Panda SK, Gaurav A, Das P, Swain N, Rath S. A Comparison Between Transcutaneous Bilirubin and Total Serum Bilirubin Levels for the Management of Jaundice in Preterm Neonates by Bland-Altman Plot. Cureus. 2021 Oct 2;13(10):e18442.