European Journal of Biotechnology and Bioscience
Online ISSN: 2321-9122, Impact Factor: RJIF 5.44
www.biosciencejournals.com
Volume 4; Issue 11, November 2016; Page No. 34-37

The correlation study of transcutaneous bilirubin measurements in neonates

[1] Andra Kurnianto, [2] Herman Bermawi, [3] Erial Bahar, [4] Afifa Ramadanti, [5] Indrayadi

[1, 2, 4, 5] Departement of Child Health, Sriwijaya University Medical School, Mohammad Hoesin Hospital, Palembang, Indonesia
[3] Departement of Public Health, Sriwijaya University Medical School, Mohammad Hoesin Hospital, Palembang, Indonesia

Abstract
The use of TcB screening reduces the number of blood tests for bilirubin determination. Our aim was to evaluate the correlation of TSB and TcB measurement in neonates. This prospective study was done in Mohammad Hoesin Hospital Palembang from February 2016 through July 2016. Transcutaneous bilirubin measurements were performed on the infant's forehead and sternum. TSB/TcB measurements were performed in 150 Asian origin infant's age $\leq$ 28 days (3.77$\pm$3.46 days). The correlation coefficients (r) for TSB and TcB measurements over forehead and sternum were 0.897 and 0.891 ($p<0.001$). Transcutaneous bilirubin assessment by JM-105 at forehead and sternum has demonstrated high and significant correlation when compared to total serum bilirubin measured by chemical laboratory method. It can be favorably used as a screening test to identify the need for serum bilirubin measurement, but it cannot substitute for total serum bilirubin estimation.

Keywords: neonates; transcutaneous bilirubin; total bilirubin serum

1. Introduction
In recent years, lot of efforts have gone in to predict babies likely to develop neonatal hyperbilirubinemia. The incidence of neonatal hyperbilirubinemia has been reported 60% in full-term newborns and nearly 80% in premature infants [1]. The accurate measurement of bilirubin concentrations is essential for the diagnosis of hyperbilirubinemia and for guiding the clinician with regard to treatment. Although flawed by some imprecision, the gold standard remains the measurement of total serum bilirubin (TSB). This method however is invasive, painful and costly in terms of workload, time and money. Moreover, repeated blood samplings may lead to significant blood loss, which may be of particular concern in preterm infants. Trying to overcome these drawbacks, non-invasive methods of bilirubin measurements have been proposed. Transcutaneous bilirubinometry has been shown to correlate with serum bilirubin concentration in term infants [2-6].
Transcutaneous bilirubin (TcB) measurement devices use multiwavelength spectral reflectance from the skin surface and can be used to estimate TSB, and, thus, avoid blood sampling. However, TcB measurements are not reliable in infants undergoing phototherapy [7, 8]. In addition, controversy still exists as to whether TcB testing is affected by skin pigmentation [9, 10]. As a result, TcB measurements may be limited in these neonates (i.e. infants treated with phototherapy), as the magnitude of hyperbilirubinemia cannot be accurately ascertained.
In several reports of racially and ethnically diverse groups of term and late preterm newborns, a close correlation between TcB and TB measurements was demonstrated [9].
The new JM-105 Jaundice Meter uses 2 wavelengths and a dual optical path system. The principle of operation has been described in detail by Yasuda *et al* using JM-103 (predecessor to the JM-105) [11]. This includes the formation of 2 beams, 1 of which reaches only the shallow areas of the subcutaneous tissue while the other penetrates the deeper layers. The differences between the optical densities are detected by blue and green photocells. The measurement of bilirubin accumulated primarily in the deeper subcutaneous tissue should decrease the in- fluence of other pigments in the skin such as melanin and hemoglobin. In a study of 77 Japanese infants, measurements of TcB with the JM-103 correlated well with TSB measurements and better than the JM-102 [11].
There are significant variations among different instruments for TcB measurement. When TcB is used clinically as a substitute for TSB, values of new instruments should always be compared to TSB performed by the laboratory to ensure good correlation [12].
The use of TcB screening reduces the number of blood tests for bilirubin determination compared to visual assessment without compromising detection of infants with significant TSB values [13, 14]. The aim of this work is to evaluate a non-invasive new transcautaneous jaundice meter JM-105 as screening test and decrease unnecessary blood sampling in follow up of jaundice in neonatal period.

2. Patients and Methods
A prospective study was performed in Mohammad Hoesin Hospital Palembang, South Sumatera, Indonesia. We intended to include 150 neonates presenting for jaundice during the period from February 1, 2016 through July 31, 2016 (maternity ward, intermediate care and NICU). No infant had been treated with phototherapy until enrolment. The study was approved by the local ethics committee, and parental consent was obtained.
Transcutaneous bilirubin (TcB) and capillary bilirubin assays were performed for each patient, with a maximum interval of 15 min between them. Infants who were receiving phototherapy or who had exchange transfusion were excluded.
All TcB measurements were performed by one investigator, using the bilirubinometer (jaundice meter Minolta JM-105, Drager). The measurements were obtained from the forehead dan sternum of the infants, while lying in a supine position. Gentle pressure was applied, while the fiber optic probe was

placed against the forehead to exert even contact by the probe with the forehead and sternum skin.

The TSB assay was performed using diazo-based methods in the clinical chemistry laboratory of Mohammad Hoesin Hospital Palembang. Both devices were calibrated before use daily, in accordance with the manufacturer's instructions Demographic data, TcB and TSB values were analyzed using SPSS (Statistical Product and Service Solutions) software. The correlation coefficient between TcB and TSB was performed using Pearson Linear Regression Analysis.

3. Results

A total of 150 Asian origin infants were included in the study. TSB/TcB measurements were performed in infant's age ≤ 28 days (mean 3.77 ± 3.46 days). Most of the infants had a birth weight between 2500 and 4000 g (n=94, 62.7%); 55 neonates (36.6%) were less than 2500 g, and only 1 neonates (0.7%) were greater than 4000 g. (Table 1)

The relationship between TSB and TcB forehead was y=0.9+0.87*x and relationship between TSB and TcB sternum was 1.06+0.81*x. (Figure 1 and 2)

The correlations between TSB and TcB were found to be significant and close when measured at any of the two sites. The Pearson's correlation coefficients (r) for TSB and TcB measurements over forehead and sternum were 0.897 and 0.891 (p<0.001).

Table 1: Demographic Characteristics

Characteristics		n	(%)
Gender:	Male	68	45.3
	Female	82	54.7
Age (day)	<7	139	92.7
	7-14	6	4
	15-28	5	3.3
Gestational Age: (week)	<38	41	27.3
	38-42	105	70
	> 42	4	2.7
Birth Weight: (gram)	1000-1500 g	5	3.3
	1500-2500 g	50	33.3
	2500-4000 g	94	62.7
	>4000 g	1	0.7

Table 2: TSB and TcB Characteristics

	Minimum (mg/dL)	Maximum (mg/dL)	Mean ± SD
TSB	4.15	21.66	12.32 ± 3.4
TcB forehead	4.03	19.50	13.05 ± 3.5
TcB Sternum	4.30	19.83	11.67 ± 3.7

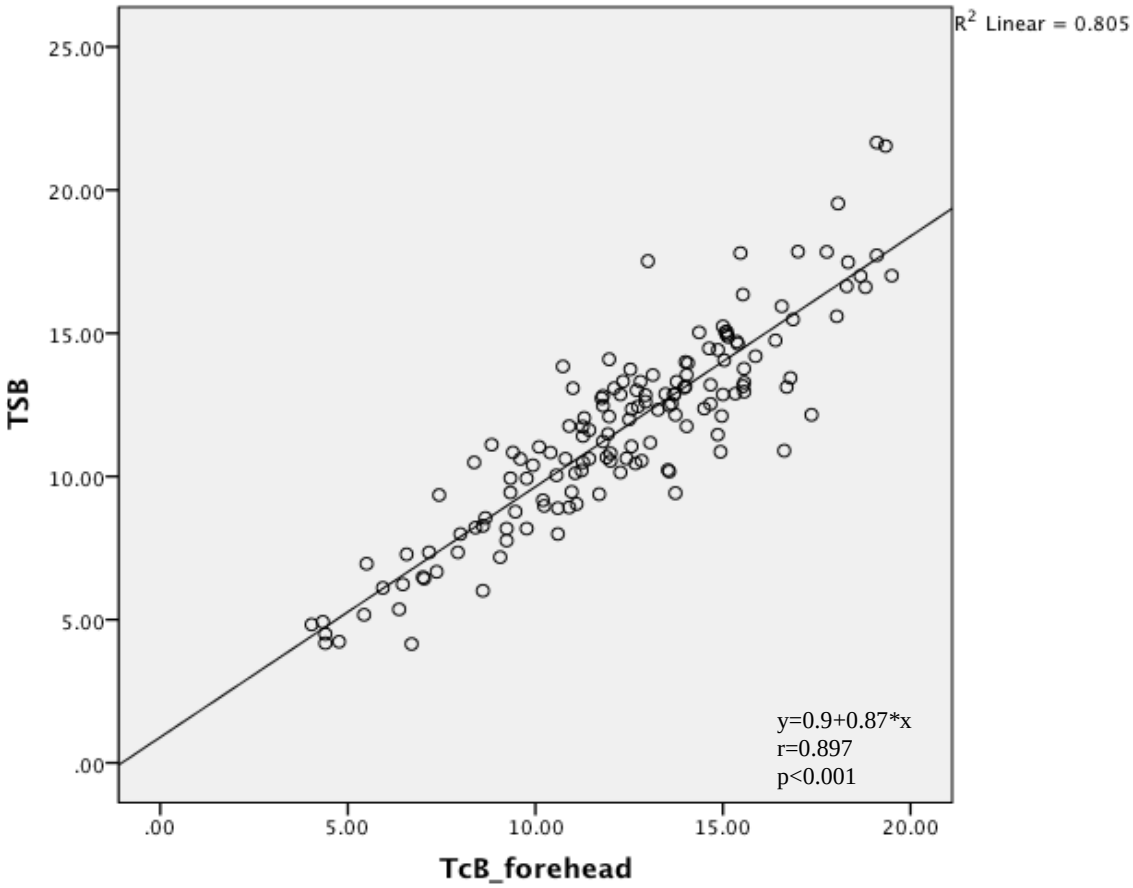

Fig 1: Correlation between TSB and TcB Forehead measurements

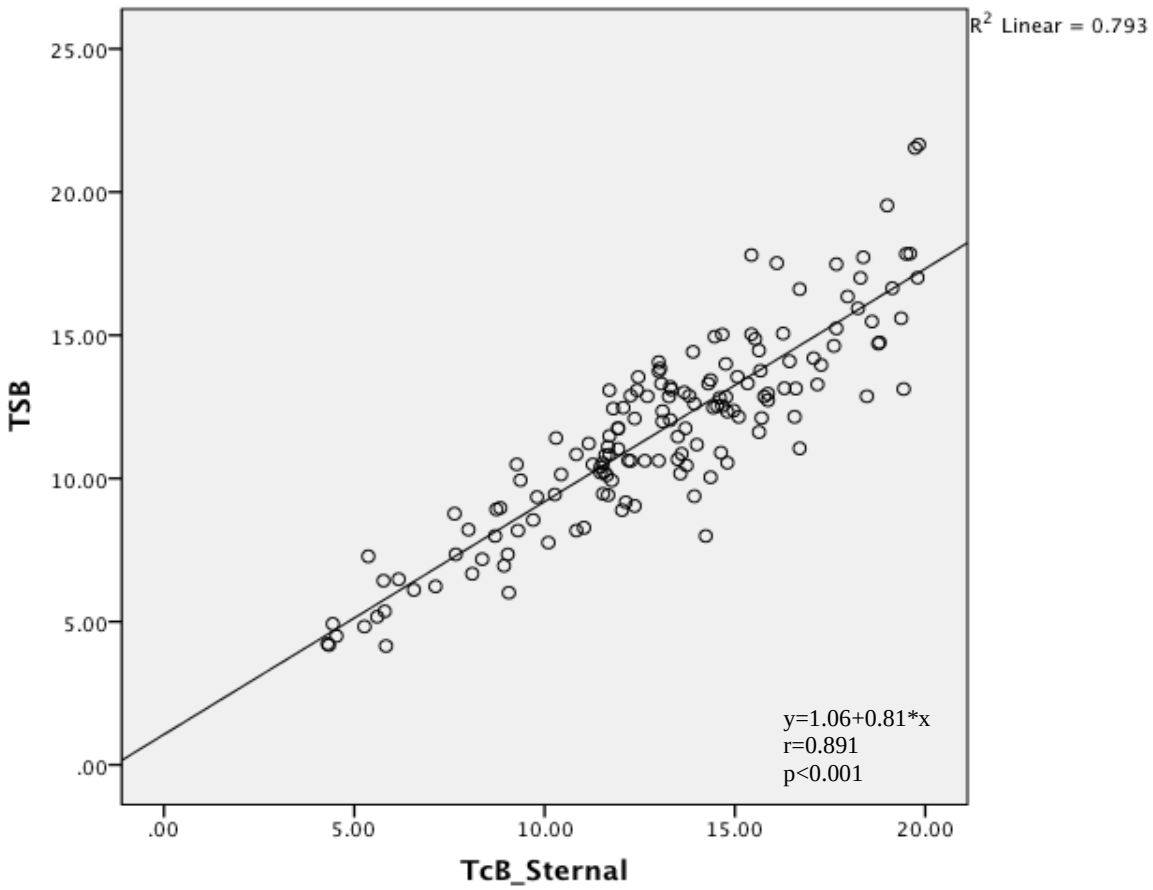

Fig 2: Correlation between TSB and TcB Sternum measurements

4. Discussion

A number of studies have demonstrated the possibility of prediction of serum bilirubin in neonates by analysis of the spectral reflectance from the skin [15, 16]. However, the accuracy of these techniques has been complicated by the variability introduced by skin pigmentation and the dermal maturity; hence the results of studies in white infants may not be applicable to heterogeneous Indonesian population. A handled Transcutaneous bilirubinometer (JM-105) has been designed to correct for these interfering factors; being based on recent studies on light scattering charactristics of the human skin. The overall correlation between JM-103 measurements and total serum bilirubin estimation is linear (r = 0.89). The measure-ments were independent of gestation, race and ethnicity [10].

In our study the correlation coefficient between TSB and TcB (JM 105) at the two sites were both high and significant (r = 0.897 and 0.891, $p < 0.01$), in agreement with study done by Maisels MJ in China (r=0.83), Tommy SK Lam (r=0.83) but Ho EY *et al* found that TSB had higher correlations with TcB at the sternum than at the forehead (0.81 and 0.71) [17-19].

The correlation coefficient does not provide information about clinical significance of diagnostic test, it was found that when TSB level increase the difference between values of TcB and TSB increase as well. However, a lower level of TSB upon which treatment begins can cause frequent monitoring of blood sampling, a painful procedure with possible complications. TcB can be used as a screening test to determine the need for TSB measurement [20].

When comparing TcB and TSB measurements, it is also important to remember that the 2 methods of measurement may be evaluating different physiologic entities. Rubaltelli suggested that TcB methods measure the amount of bilirubin that has moved from the serum into the tissue, possibly mimicking the movement of bilirubin across the blood– brain barrier and into brain issue, whereas laboratory-based methods measure only bilirubin that is circulating in the blood. Thus, TcB may actually offer additional information not provided by TSB measurements, although this hypothesis remains to be proven [21].

5. Conclusions

Noninvasive transcutaneous bilirubin assessment by JM-105 at forehead and sternum has demonstrated high and significant correlation when compared to total serum bilirubin measured by chemical laboratory method. It can be favorably used as a screening test to identify the need for serum bilirubin measurement, but it cannot substitute for total serum bilirubin estimation.

6. Acknowledgments

The authors thank pediatricians, nurses and technicians working in the Baby Nursery of Mohammad Hoesin Hospital Palembang

7. Disclosure Statement

The authors declare that they have no conflicts of interest and no financial relationships relevant to this article to disclose.

8. References

1. Narang A, Gathwala G, Kumar P. Neonatal Jaundice: An analysis of 551 cases. Indian Pediatr, 1997; 34:429-432.
2. Donzelli G, Pratesi S. Transcutaneous Bilirubinometry in Healthy Preterm Newborns. Clinical Biochemistry. 2000; 33(6):505-508.
3. Carbonell X, Botet F, Figueras J, Riu-Godo A. Prediction of hyper-bilirubinaemia in the healthy term newborn. Acta Paediatr. 2001; 90:166-170.
4. Engle WD, Jackson GL, Sendelbach DM, Manning DM, Frawley WH. Assessment of a transcutaneous device in the evaluation of neonatal hyperbilirubinemia in a primarily Hispanic popula- tion. Pediatrics, 2002; 110:61-67.
5. Szabo P, Wolf M, Bucher HU, Fauchère JC, Haensse D, Arlettaz R. Detection of hyperbilirubinemia in jaundiced-full-term neonates by eye or by bilirubinometer. Eur J Pediatr. 2004; 163:722-727.
6. Knudsen A, Ebbesen R. Transcutaneous bilirubinometry in neo- natal intensive care units. Arch Dis Child Fetal Neonatal Ed. 1996; 75:F53-56.
7. Fay DL, Schellhase KG, Suresh GK. Bilirubin screening for normal newborns: a critique of the hour- specific bilirubin nomogram. Pediatrics, 2009; 124:1203-1205.
8. 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.
9. Wainer S, Rabi Y, Parmar SM, Allegro D, Lyon M. Impact of skin tone on the performance of a transcutaneous jaundice meter. Acta Paediatr. 2009; 98(12):1909.
10. 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.
11. Yasuda S, Itoh S, Isobe K, *et al*. New transcutaneous jaundice device with two optical paths. J Perinat Med. 2003; 31:81-88.
12. Maisels MJ, Bhutani VK, Bogen D, *et al*. Hyperbilirubinemia in the newborn infant > or =35 weeks' gestation: an update with clarifications. Pediatrics, 2009; 124:1193.
13. Kaplan M, Shchors I, Algur N, Bromiker R, Schimmel MS, Hammerman C. Visual screening versus transcutaneous bilirubinometry for predischarge jaundice assessment. Acta Paediatr. 2008; 97(6):759.
14. Mishra S, Chawla D, Agarwal R, Deorari AK, Paul VK, Bhutani VK. Transcutaneous bilirubinometry reduces the need for blood sampling in neonates with visible jaundice. Acta Paediatr. 2009; 98(12):1916.
15. Tan KL. Transcutaneous bilirubinometry in full term Chinese and Malay infants. Acta Pediatr Scand. 1982; 71:593-596.
16. Jacques S, Saidi I, Ladner A, Oerlberg D. Developing an optical fiber refelectance spectrometer to monitor bilirubinemia in neonates. SPIE Proceedings 2975, Laser Tissue Interactions, San Jose CA, February, 1997; p7.
17. Maisels MJ, Ostrea EM Jr, Touch S, *et al*. Evaluation of a new transcutaneous bilirubinometer. Pediatrics, 2004; 113:1628-35.
18. Tommy SK Lam, KL Tsui, CW Kam. Evaluation of a point-of-care transcutaneous bilirubinometer in Chinese neonates at an accident and emergency department. Hong Kong Med J. 2008; 14(3):56-60.
19. Ho EY, Lee SY, Chow CB, *et al*. BiliCheck transcutaneous bilirubinometer: a screening tool for neonatal jaundice in the Chinese population. Hong Kong Med J. 2006; 12(2):99-102.
20. Briscoe L, Clark S, Yoxall CW. Can transcutaneous bilirubinometry reduce the need for blood tests in jaundiced full term babies? Arch Dis Child Fetal Neonatal Ed 2002; 86:F190-2.
21. Rubaltelli FF, Gourley GR, Loskamp N, Modi N, Roth-Kleiner AM, Sender A, Vert P. Transcutaneous bilirubin measurement: a multicenter evaluation of a new device. Pediatrics. 2001; 1264:71-107.