Comparison of transcutaneous and total serum bilirubin measurement in Turkish newborns

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Severe neonatal hyperbilirubinemia can be prevented by screening for neonatal jaundice. Transcutaneous bilirubin (TcB) measurement is a noninvasive method for screening neonates.

The aim of this study was to examine the correlation between TcB measurement (using the JM-103 bilirubinometer) and total serum bilirubin (TSB) measurement. To our knowledge, this is the first study evaluating the usefulness of the JM-103 bilirubinometer in Turkish neonates. Two hundred and fifty healthy infants in our well-baby nurseries and follow-up clinic with a gestational age of ≥36 weeks who were ≤15 days old were enrolled in this study. TcB measurements were taken usinng the JM-103; almost simultaneously, TSB was checked using a spectrophotometric method. The mean±SD TSB level was 11.2±4.6 mg/dl (range, 0.9-27.0 mg/dl); 17.2% of cases had TSB>15 mg/dl. There was good correlation between transcutaneous bilirubin and total serum bilirubin measurements (Pearson's correlation coefficient 0.87 for TcB from the forehead, 0.88 for TcB from the sternum; p<0.001). The transcutaneous bilirubin measurement tended to underestimate the value with increasing discrepancy at higher TSB values. The mean difference between serum bilirubin and transcutaneous (from the sternum and forehead) bilirubin values was significantly lower in cases not requiring phototherapy than in those requiring phototherapy [2.6 mg/dl (sternum) vs 4.8 mg/dl, 2.9 mg/dl (forehead) vs. 5.2 mg/dl, respectively; p<0.001]

Although the JM-103 bilirubinometer tends to underestimate serum bilirubin, especially in patients with high bilirubin levels, it is a suitable screening tool to identify jaundiced infants that require a serum bilirubin check and may reduce the need for TSB measurements.

Key words: newborn, hyperbilirubinemia, transcutaneous bilirubin measurement.

Hyperbilirubinemia is the most common cause of readmission of healthy newborns after early hospital discharge[1]. Measurement of bilirubin concentration is essential for diagnosing severe hyperbilirubinemia and for timely management to prevent brain damage. Although the gold standard remains measurement of the serum bilirubin concentration, this method is invasive and painful and is usually very stressful for the parents. Transcutaneous bilirubin (TcB) measurement is a useful alternative to total serum bilirubin (TSB) measurement and has the potential to reduce serum bilirubin sampling.

Transcutaneous bilirubinometry was introduced into clinical practice in 1980 by Yamanouchi et al.[2] using a bilirubinometer developed by Minolta but has not been widely adopted due to issues with its accuracy. That instrument and the subsequent model, JM-102, gave the reading as a numerical index that required an initial correlation to TSB. It was also necessary to take into account gestational age and race, as both parameters affected the results[3]. The first transcutaneous bilirubinometry study in Turkish newborns was performed in 1998 by Kultursay et al.[4] using the Air Shields

Vickers JM-101 device. Neonatal skin colour and thickness represent important variables in TcB measurements. The variability between transcutaneous bilirubin and total serum bilirubin (TSB) measurements are related to other pigments in the skin, especially melanin and hemoglobin[5].

In recent years, a newer generation of transcutaneous bilirubinometer has been marketed. One of these newer transcutaneous devices, the Minolta JM-103 Jaundice Meter, was a refinement of the previous models (including the Minolta Air Shields Jaundice Meter JM-102). Its dual optical path system enables the machine to measure the bilirubin accumulated in deeper subcutaneous tissue, while reducing the influence of melanin pigment and skin maturity[6]. However, ethnicity and skin pigment influences are still reported[7]. The body site (forehead, sternum, back, knee, foot) used for TcB measurement has also been shown to have an effect on the accuracy of the results, with measurements made on the forehead and sternum having the best correlation with TSB[8]. The performance and correlation of the JM-103 when used for Turkish neonates could be different from that reported in studies based on other Caucasian populations.

The objective of the present study was to determine whether TcB measurements, as performed using the JM-103, correlate with TSB levels, and whether TcB measurements obtained from the forehead and sternum generate comparable performances. To our knowledge, this is the first study evaluating the usefulness of the JM-103 transcutaneous bilirubinometer in Turkish neonates.

Material and Methods

This propective study was performed beetween April 1, 2008, and September 1, 2008, in the well-baby nurseries and clinics at Umraniye Education and Research Hospital. Two hundred and fifty healthy infants in our well-baby nurseries and clinics with a gestational age of ≥36 weeks who were ≤15 days old were used for this study. The investigation protocol was approved by the local ethics committee and informed consent was obtained from the parents of each subject.

Infants undergoing postpartum discharge bilirubin measurement and infants who had a TSB ordered for clinical jaundice at follow-up were considered eligible. Patients with known skin disorders and those who had received phototherapy ± exchange transfusions were excluded from the study.

Samples were obtained from heelsticks in capillary tubes, protected from direct sunlight, centrifuged at 3000 rpm for five minutes and read by a neonatal bilirubin analyzer (Neo Bil Plus, Italy). Spectrophotometry was used as a reference, as it is the technique used in the daily routine and has better agreement with high-pressure liquid chromatography (HPLC) than any other technique[9]. Within 10 minutes prior to the TSB determinations, TcB was determined

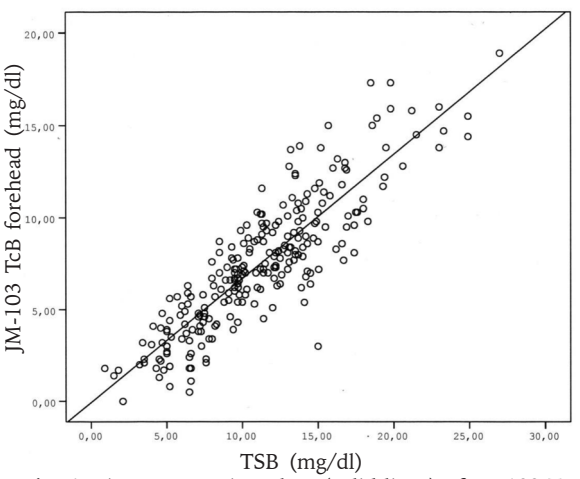

Fig. 1. Linear regression plots (solid lines) of JM-103 TcB measurements on the forehead versus TSB measurements for the cases studied.

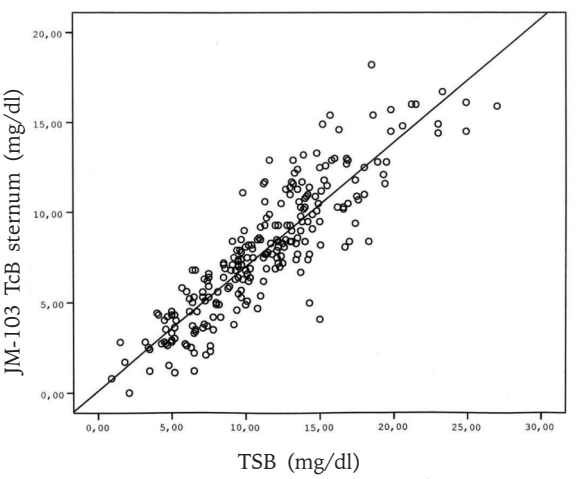

Fig. 2. Linear regression plots (solid lines) of JM-103 TcB measurements on the sternum versus TSB measurements for the cases studied.

Table I. Basic Characteristics and Clinical Variables of Infants (n=250)

Birth weight (g) (mean±SD) (range)	3277±417	2000-4500
Gestational age (weeks) (mean±SD) (range)	38.6±1.4	35-42
Delivery mode (n, %)		
Normal vaginal	172	69.2
Cesarean section	77	30.8
Male sex (n, %)	121	48.4
Female sex (n, %)	129	51.6
Well-baby nurseries (n, %)	105	42
Outpatients (n, %)	145	58
Postnatal age (n, %)		
24-48 hours	92	36.8
49-72 hours	57	22.8
73-96 hours	22	8.8
97-120 hours	21	8.4
> 120 hours	58	23.2
Readmission for phototherapy (n, %)	82	32.8
TSB (mg/dl) (mean±SD) (range)	11.2±4.6	0.9-27.0
TcB Forehead (mg/dl) (mean±SD) (range)	7.5±3.6	0.0-18.9
TcB Sternum (mg/dl) (mean±SD) (range)	8.8±3.6	0.0-18.2

TSB: Total serum bilirubin. TcB: Transcutaneous bilirubin.

using the Minolta JM-103 Jaundice Meter (Draeger Medical Systems Inc, Telford, US), which measures the yellowness of the subcutaneous tissue of newborns based on the difference between optical densities for light in the blue (450 nm) and green (550 nm) wavelength regions. All determinations were obtained from both the foreheads and sternums of the infants while they were in a quiet state. We obtained the transcutaneous measurements from both forehead and sternum because of the effect of natural phototherapy on the forehead, which typically is exposed to ambient light more than is the sternum[10]. Each measurement was calculated by averaging three readings.

The difference between bilirubinometer assay and transcutaneous measurement was calculated as TSB-TcB (mg/dl) for each patient. Mean difference represented the mean of the individual differences (TSB-TcB) (mg/dl).

Data were analyzed using NCSS 2007 & PASS 2008 Statistical Software (Utah, USA). Linear regression analysis and Pearson and Spearman's correlation coefficients were performed. Statistical significance was defined as a P value<0.05.

Results

A total of 250 determinations obtained from 250 Turkish infants were included in the study. The basic characteristics are shown in Table I. Out of the total studied population, 43 newborn babies (17.2%) had TSB >15 mg/dl, and 82 (32.8%) needed phototherapy.

Total serum bilirubin was determined over a wide concentration range (0.9-27 mg/dl) with a mean of 11.2 mg/dl. Related TcB values obtained using the JM-103 are reported in

Table II. Correlation Coefficients Between TcB and Total Serum Bilirubin

	Total Serum Bilirubin	
	r	p
TcB Forehead	0.873	0.001
TcB Sternum	0.885	0.001

TcB: Transcutaneous bilirubin.
r: Pearson's correlation coefficient.

Table III. Correlation Analysis Between TcB and Total Serum Bilirubin According to TcB Levels

		Total Serum Bilirubin (mg/dl)			
		Mean	SD	r	p
TcB Forehead (mg/dl)	<5	6.1	2.3	0.460	0.001
	5-10	11.4	2.6	0.582	0.001
	10-15	16.0	3.3	0.533	0.001
	≥15	21.6	3.0	0.360	0.382
TcB Sternum (mg/dl)	<5	6.2	2.5	0.561	0.001
	5-10	10.8	2.5	0.690	0.001
	10-15	15.5	3.0	0.517	0.001
	≥15	21.2	3.5	0.027	0.945

TcB: Transcutaneous bilirubin.
r: Pearson's correlation coefficient.

Table I. Figure 1 shows the linear regression analysis for TcB obtained from the forehead, and Figure 2 shows the linear regression analysis for TcB obtained from the sternum. Both TcB measurements strongly correlated with TSB (r=0.87 for TcB-forehead, and r=0.88 for TcB-sternum) (Table II). Correlation analysis showed that if TcB was ≥15 mg/dl, there was not a statistically significant correlation (Table III).

The study group was separated into two groups: one with patients who did not require phototherapy and another with patients who did require phototherapy. In both groups, TcB measurements were significantly correlated with TSB levels. However, at higher levels of TSB, where phototherapy and exchange transfusion might be considered, correlation was lower than for the group not requiring therapy (Table IV).

The difference between bilirubinometer assay and transcutaneous measurement (TSB-TcB) showed that TcB measurement with the JM-103 had a tendency to underestimate total serum bilirubin. The difference tended to increase with increasing bilirubin values (Table V). The mean difference of bilirubinometer assay and transcutaneous measurement was significantly higher in the group requiring phototherapy than in the group not requiring it (p<0.01) (Table VI).

Discussion

Kernicterus, which was thought to have almost completely disappeared, is now of greater concern for neonatologists and pediatricians. This is due to the earlier discharge of mothers and neonates, which can prevent adequate monitoring of jaundice. The possibility of using a noninvasive, painless and reliable method to determine neonatal bilirubin levels could be very important in the prevention of kernicterus[10]. Measurement of TcB in the nursery, in the office or in other outpatient settings, the including home, would provide a noninvasive, instantaneous estimate of TSB. TcB measurements may also help to avoid the potential errors associated with clinical estimation of bilirubin levels[11].

Table IV. Correlation Coefficients Between TcB and Total Serum Bilirubin of Patients Requiring and Not Requiring Phototherapy

	Total Serum Bilirubin			
	Patients Requiring Phototherapy		Patients Not Requiring Phototherapy	
	r	p	r	p
TcB Forehead	0.764	0.001	0.876	0.001
TcB Sternum	0.784	0.001	0.893	0.001

TcB: Transcutaneous bilirubin.
r: Pearson's correlation coefficient.

Table V. Mean Differences (TSB-TcB) According to TSB Levels

		TSB-TcB Forehead (mg/dl)		TSB-TcB Sternum (mg/dl)	
		Mean±SD	Median	Mean±SD	Median
TSB (mg/dl)	<5	1.4±1.1	1.3	1.1±1.1	1.1
	5-10	2.7±1.4	2.7	2.5±1.4	2.3
	10-15	4.1±2.1	4.2	3.6±1.9	3.7
	>15	6.0±2.5	7.0	5.7±2.6	5.9

TSB: Total serum bilirubin.
TcB: Transcutaneous bilirubin.

In this study, we showed a significant correlation between TcB (using the JM-103 bilirubinometer) and TSB measurements in Turkish newborns. The correlation coefficient (r=0.87 for TcB-forehead, r=0.88 for TcB-sternum) is comparable with that reported in the studies by Maisels et al.[3] and Ho et al.[12]. However, after calculation of the actual difference between TSB and TcB, the JM-103 bilirubinometer underestimated TSB by a mean of 2.6 mg/dl for the sternum and 2.9 mg/dl for the forehead in those of our newborns who did not require phototherapy. The magnitude of this underestimation was lower in the cases with mild hyperbilirubinemia, and higher in the cases with severe hyperbilirubinemia. In contrast, the study by Ho et al.[12] and the study by Maisels et al.[3] showed an overestimation of TSB in Chinese and black newborns, respectively. This may due to differences in race and skin pigmentation. Raimondi et al.[5] showed BiliCheck and the JM-103 but not BiliMed to be reliable and equally accurate screening tools for moderate neonatal hyperbilirubinemia. Türkmen et al.[13] reported that despite having good correlation with HPLC in Turkish newborns, transcutaneous measurement of bilirubin using BiliCheck showed poorer performance than bilirubinometer and diazo methods at various clinically relevant cutoff values. However, none of the neonates studied were tested within the first two days of life in this investigation.

The JM-103 represents an improvement of a previous device. In the study by Robertson et al.[14], the JM-102 was less accurate than Bilicheck and was influenced by skin color. In the present study, JM-103 performed well on Turkish newborns, required no disposables to calibrate and was quick to operate. Maisels et al.[3] showed that the average time needed to obtain a measurement was only 5.5 seconds. Sequential TcB monitoring over time should reduce the effect of random error from a single measurement and provide a good indication of the rate of bilirubin increase. Plotting

Table VI. Mean Differences (TSB-TcB) According to Whether Patients Required/Did Not Require Phototherapy

	Did Not Require Phototherapy (n=168)	Required Phototherapy (n=82)	p
TSB-TcB Forehead Mean±SD (median) (mg/dl)	2.9±1.8 (2.8)	5.2±2.5 (5.2)	0.001
TSB-TcB Sternum Mean±SD (median) (mg/dl)	2.6±1.6 (2.5)	4.8±2.5 (4.5)	0.001

TSB: Total serum bilirubin.
TcB: Transcutaneous bilirubin.

the TcB on a nomogram will soon show whether the jaundice is following an expected physiological course or rising and crossing centiles, necessitating close follow-up[12].

Our study was different from previous ones since 40.4% of our cases were over 72 hours of age and 17.2% of the cases had TSB >15 mg/dl and included cases with severe hyperbilirubinemia. High-performance liquid chromatography is the best method for TSB measurement. However, TSB was measured by the photometric method in our study, and this was a limitation of the study. In our laboratory, quality control of TSB measurement is done regularly. Nonchemical photometric devices can be compared with diazo methods for TSB measurement[15].

In conclusion, TcB measurements obtained from the forehead and sternum using the JM-103 generated comparable performances and correlated closely with moderately increased TSB levels. The device had a tendency to underestimate TSB with increasing discrepancies at higher TSB values, so in cases where the level approaches the high-risk zone or where the clinical assessment of jaundice differs from the TcB reading, the latter needs to be confirmed with TSB. Transcutaneous bilirubinometry is a suitable screening tool to identify jaundiced infants who require a serum bilirubin check, and may also reduce the need for TSB measurements.

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