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Research Article

A Comparative Study between Transcutaneous Bilirubinometry and Total Serum Bilirubin Measurement in Jaundiced Newborns

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ABSTRACT

***Background*:** Drawing blood to measure total serum bilirubin is painful & time consuming. Transcutaneous bilirubinometer working by multiwavelength spectral reflectance from the skin surface on forehead or upper sternum is a quick & painless technique.

Objectives: to compare the effectiveness of transcutaneous (over the upper sternum and forehead) and serum bilirubin measurement of neonate with jaundice.

***Subjects and Methods*:** This is a cross sectional prospective study. It enrolled 175 jaundiced neonates & excluded those exposed to phototherapy. It was conducted at Child Central Teaching Hospital in Baghdad, Iraq from the 1st of August to the 30th of October 2018. Transcutaneous bilirubin measurement on forehead and upper sternum was done by JM 103 Minolta Air shields bilirubinometer. Total serum bilirubin was measured by APEL BR 501 BILIRUBIN METER. Data entered & analyzed using SPSS 20 computer software. Means, frequencies, cutoff values, sensitivity & specificity were calculated.

***Results*:** The mean age, gestational age & birth weight were (6.3±4.3 days), (36.9±2.1 weeks) and (2.7±0.6 Kg) respectively. Mean total serum bilirubin, transcutaneous chest & forehead bilirubin levels were 12.6±4.2 mg/dl, 11.8±3.8 mg/dl & 11.2±3.9 mg/dl respectively. Mean total serum bilirubin was significantly higher than transcutaneous chest and forehead bilirubin. Cutoff values of transcutaneous chest & forehead bilirubin levels were [(9 mg/dl) with sensitivity (95.4%) & specificity (86.4%)] and [(8.2 mg/dl) with sensitivity (94.7%) & specificity (86.4%)] respectively.

***Conclusions*:** Transcutaneous bilirubin measurements on chest and forehead have an acceptable validity in predicting hyperbilirubinemia with less accuracy on forehead.

Introduction

Jaundice is a term taken from the French word 'jaune' which means 'yellow'. So, a jaundiced baby means a baby whose skin became yellow. Jaundice often happens few days after birth. The yellow color is the result of bilirubin which is formed after break down of old red blood cells (RBCs) (1).

Approximately 60% of term infants and 80% of preterm infants become jaundiced in the 1st week after birth. The yellow color is due to unconjugated (indirect) and conjugated (direct) bilirubin. The

unconjugated bilirubin is the lipid-soluble bilirubin that accumulates in the skin and it results from catabolism of hemeprotein by a series of enzymatic reactions by heme oxygenase (HO) and biliverdin reductase and nonenzymatic reducing agents in the reticuloendothelial cells. The conjugated bilirubin results from indirect, unconjugated bilirubin that has underwent conjugation in the liver by the enzyme uridine diphosphoglucuronic acid (UDP)–glucuronyl transferase to form the polar, water-soluble glucuronide of bilirubin. Bilirubin may act as an antioxidant; however, elevation of unconjugated bilirubin is potentially neurotoxic. The conjugated form is not neurotoxic; however, direct hyperbilirubinemia indicates a potentially serious hepatic disorders or a systemic illness (2).

The need for total serum bilirubin (TSB) testing can be estimated through Kramer's rule which depends on the progression of yellow discoloration of the skin from cepahlocaudal progression. It is based on a study performed in 1969 on full term infants. It found that bilirubin concentrations correlated to 5 specific 'dermal zones' which are head and neck, upper trunk, lower trunk and thighs, arms and legs below the knees, hands and feet. Lowest TSB levels were associated with yellow discoloration of the head and neck only & highest levels with the discoloration extension to the hands and feet (3). If jaundice reaches the midabdomen, or there are signs or symptoms, or high-risk factors that suggest nonphysiologic jaundice, or hemolysis; further evaluation is needed (2). However, recent studies showed a poor correlation between visual assessment of TSB and measured TSB (4). Drawing blood sample to measure TSB is commonly requested in the neonatal units. It is often done by heel prick approach which is painful and have potential long-term consequences (5). The neonate nervous system is immature & undergoing major developmental changes; therefore, exposure of neonate to painful stimuli can cause many neurodevelopmental changes, such as neurosensory, cognition, behavior, pain processing, and health outcomes that persist into childhood and even adulthood (6).

Risk factors for hyperbilirubinemia can be due to maternal and/or neonatal causes, Table 1 (7).

Table (1):

Risk Factors for Hyperbilirubinemia in Newborns

Maternal factors	Neonatal factors
Blood type ABO or Rh incompatibility	Birth trauma: cephalohematoma, cutaneous bruising, instrumented delivery
Breastfeeding	Drugs: sulfisoxazole acetyl with erythromycin ethylsuccinate (Pediazole), chloramphenicol (Chloromycetin)
Drugs: diazepam (Valium), oxytocin (Pitocin)	Excessive weight loss after birth
Ethnicity: Asian, Native American	Infections: TORCH
Maternal illness: gestational diabetes	Infrequent feedings
	Male gender
	Polycythemia
	Prematurity
	Previous sibling with hyperbilirubinemia

TORCH = toxoplasmosis, other viruses, rubella, cytomegalovirus, herpes (simplex) viruses.

Kernicterus refers to the neurologic outcomes caused by unconjugated bilirubin deposition in the brain with damage of the basal ganglia and brainstem nuclei (7). Bilirubin role in kernicterus is not fully understood. When the level of unconjugated bilirubin exceeds the binding capacity of albumin, it crosses the blood-brain barrier. Albumin-bound bilirubin may also cross the blood-brain barrier in certain conditions such as asphyxia, acidosis and hypoxia (7, 8). The exact bilirubin level associated with kernicterus in the healthy term infant is unpredictable. Some factors cause variation of toxicity levels such as maturation of infant and the presence of hemolytic disease (7). The risk of bilirubin toxicity in a healthy term new born without hemolysis is probably negligible (7); however, the precise threshold above which indirect-reacting bilirubin or free bilirubin will bring harm in an infant is unpredictable, but in a large series, it was >20mg/dl. Ninety percent of the infants with kernicterus were previously healthy, predominantly breastfed term and near-term. It is unknown what is the duration of exposure to high bilirubin levels that lead to harmful effects.

Early signs of kernicterus are nonspecific, typically appearing 3 to 4 days after birth. However, hyperbilirubinemia may lead to kernicterus at any time during the neonatal period (7). After the 1st week of life, the affected newborn begins to demonstrate late effects of bilirubin toxicity. If the infant survives the initial severe neurologic insult, chronic bilirubin encephalopathy (evident by three years of age) leads to developmental and motor delays, sensorineural deafness, and mild mental retardation, table 2 (7).

Table (2): (7)

Effects of Bilirubin Toxicity in Newborns

Early	Late	Chronic
Lethargy	Irritability	Athetoid cerebral palsy
Poor feeding	Opisthotonos	High-frequency hearing loss
High-pitched cry	Seizures	Paralysis of upward gaze
Hypotonia	Apnea	Dental dysplasia
	Oculogyric crisis	Mild mental retardation
	Hypertonia	
	Fever	

When TSB reaches 85 micromoles per deciliter (5 mg/dl), jaundice becomes clinically visible. Physiological jaundice increases in severity until day 4–5 then gradually decreases and disappears by day 10 and does not usually require any treatment. It is diagnosed by exclusion, i.e., careful evaluation needed to exclude pathological causes. If the jaundice appears on the first day of life even in preterm babies, it is considered pathological and require intervention. The same applies if it persists beyond the usual period (7). The presence of jaundice can be demonstrated by examining the infant in a room with good lights and blanching the skin with pressure applied by digits to reveal the color of the skin and subcutaneous tissue (7). The visual estimation of TSB when dermal icterus is confined to above the nipple line can be reliable. In this situation, TSB is invariably below 12 mg per dL. When jaundice extends below the middle of the chest, the correlation between physical signs and measured TSB becomes increasingly unreliable. Predicting the TSB based on caudal progression alone can get difficult due to racial differences, delays in deposition of rapidly rising bilirubin levels in the dermis, interobserver variability, and other factors (7). The different methods

to measure bilirubin levels are biochemical, bilimeter and transcutaneous bilirubinometer.

Biochemical method for the total and conjugated bilirubin assessment is the gold standard one for TSB estimation and it is based on the van den Bergh reaction (9). Bilimeter method is based on spectrophotometry and it assesses TSB (9).

Transcutaneous Bilirubinometer (TcB) measurement devices do not require blood sampling. They use multiwavelength spectral reflectance from the skin surface and they estimate total serum or plasma bilirubin. It is a 'Point of Care' test (bed-side test) that can be performed by physicians, nurses or any other health caregiver within hospital or in community (10). It is very useful because it is a noninvasive quick technique (11). It was introduced for the first time in 1980 (12). One randomized controlled trial in the Netherlands found a significant reduction in the number of blood sampling in TcB group compared with non-TcB group (13). It is an inexpensive test that can be performed over forehead or mediastinum, but measurement over mediastinum is better (14). The wavelengths used vary depending on the device (15). The results of these devices have been shown to correlate well with TSB levels in term and near-term infants (16). Common TcB available in the market includes the Airsheilds- Minolta, Bilitest, BiliCheck. These can be divided into 2 categories which are the two-wavelength (460nm, 540nm) spectral reflectance meter (Bili-test, Minolta which include JM 101, JM 102, JM 103 and JM 105) and the multi wavelength spectral reflectance meters (17). In our study we used JM 103 Minolta Air shields bilirubinometer (figure 1).

Figure (1): JM 103 Minolta Air Shields Transcutaneous Bilirubinometer

It measures the difference in the optical densities of light reflected by neonate skin. With this method, two optical paths are incorporated into a measuring probe that minimizes the interference caused by melanin or skin maturity. When the light returns to the fiber, it is scattered from shallow area of subcutaneous tissue and passes through the inner core (short optical path) of the fiber, whereas the light scattered from deep areas of subcutaneous tissue pass through the outer core (long optical path). The reflected light is then collected by photodiodes (18).

The use of TcB devices for jaundice evaluation in infants>35 weeks of gestation is recommended by the American Academy of Pediatrics (19). In addition, recently, the use of TcB in infants 28 to 35 weeks of gestation was shown to be reliable (13). Using TcB for estimating jaundice is a valid method and is used in increasing frequency; however, its use is still not widespread worldwide (13). In 2016, a review among most Dutch hospitals with neonatal wards, revealed that TcB was used in only 27% of these wards. This could be due to a low confidence in TcB, based on earlier studies using older non valid techniques (13). One reason of not using TcB may be the assumption that blood sampling is often done for other indications in sick neonates and TSB measurement is simultaneously done. Furthermore, in low-income countries, TcB is not widely applied, although this may be of great value due to feasibility of TcB in community settings with low resources (13).

Treatment of jaundice depends on the gestational age and the postnatal age. In preterm babies, treatment should start at a lower bilirubin level than term baby. Several factors determine the threshold for treatment like general well-being of the baby, severity of hemolysis, and presence of sepsis. The mainstay of treatment are phototherapy and exchange transfusion (19). Some drugs can be used in treatment of jaundice including Phenobarbital, Metalloporphyrins, Albumin and IV immunoglobulin.

Subjects and Methods

This is a cross sectional prospective study. It was conducted at the neonatal care unit at Child Central Teaching Hospital in Baghdad, Iraq over a period of 3 months from the 1st of August to the 30th of October 2018. It enrolled 175 neonates with jaundice. It excluded those above the 28 days and those exposed to phototherapy. Permission to enroll neonates in this study was taken from their parents. Data were collected about gender, gestational age in weeks, age in days, and birth weight. TcB measurement was performed in all jaundiced neonates whether they were outpatients' clinic visitors or admitted to the ward before starting phototherapy. TcB was done by using JM-103 Minolta air shields bilirubinometer. The fiber optic probe was placed against forehead and upper sternum of the neonate in supine position. The device displays a calculated average of three measurement for each bilirubin estimation, then blood samples for TSB measurement were collected by laboratory worker using the heel-prick technique, the blood collected by capillary tube then centrifuged for 5 minutes and the measurements were obtained by APEL BR-501 BILIRUBIN METER, in the lab of Child Central Teaching Hospital. Data were entered & analyzed using Statistical Package for Social Sciences SPSS 20 computer software. Means of Tcb (chest and forehead) and TSB were compared frequencies, cutoff values, sensitivity & specificity were calculated.

A study limitation was that it is a single center study.

Descriptive statistics presented as mean ± standard deviation, and frequencies as percentages. Multiple contingency tables conducted and appropriate statistical tests performed, one-way ANOVA analysis was used to compare more than two means (Post HOC test which is a part of ANOVA analysis was used to compare the mean of TcB and TSB). The Receiver operating characteristic (ROC) curve test was used to predict the better cutoff values of TcB on chest and forehead in comparison to TSB with calculation of their

validity (sensitivity & specificity). As sensitivity and specificity of test increase, the ROC curve moves towards the upper left-hand corner of the plot, with a correspondingly higher area under curve (AUC). AUC values of 0.5 lack any diagnostic ability whereas AUC values of 1.0 correspond to a perfect screening test. In all statistical analyses, level of significance (p value) set at ≤ 0.05 and the result presented as tables and/or graphs.

Results

Total number of neonates was 175; 114 were term (above 36 weeks of gestation) and 61 were preterm (30-35 weeks). Neonatal age was distributed according to the peak of jaundice appearing in 4-6 days so the age groups were 1-3 days, 4-6 days and ≥7 days. Mean neonatal age was 6.3±4.3 days; 25.1% of them were in the age group 1-3 days, 36% of them were 4-6 days and 38.9% of them were ≥7 days. Male to female ratio was 1.2:1. Mean gestational age was 36.9±2.1 weeks; 34.9% of them were preterm and 65.1% were term. Mean birth weight was 2.7±0.6 Kg; 3.4% of them had birth weight <1.5 Kg, 20% had birth weight of 1.5-2.4 Kg and 76.6% had birth weight of ≥2.5 Kg. All these variables are shown in table 3.

Table (3): Neonatal age, gender, gestational age and birth weight of jaundiced neonates

Variable	No.	%
Neonatal age mean±SD (6.3±4.3 days)		
1-3 days	44	25.1
4-6 days	63	36.0
≥7 days	68	38.9
Total	175	100.0
Neonatal gender		
Male	98	56.0
Female	77	44.0
Total	175	100.0
Gestational age mean±SD (36.9±2.1 weeks)		
Preterm	61	34.9
Term	114	65.1
Total	175	100.0
Birth weight mean±SD (2.7±0.6 Kg)		
<1.5 Kg	6	3.4
1.5-2.4 Kg	35	20.0
≥2.5 Kg	134	76.6
Total	175	100.0

Mean TSB of jaundiced neonates was 12.6±4.2 mg/dl; 50 (28.6%) neonates had normal TSB (bilirubin value ≤10 mg/dl was considered normal, while value >10 was considered high). Mean TcB on chest was 11.8±3.8 mg/dl; 58 (33.1%) neonates had normal TcB. Mean TcB on forehead was 11.3±3.9 mg/dl; 70 (40%) neonates had normal TcB. All these findings are shown in table 4.

There was a statistically significant difference between bilirubin levels measured by TcB on chest, TcB on forehead and TSB ($p<0.001$). Post HOC test revealed that mean TcB on chest was significantly higher than TcB on forehead ($p<0.001$), TcB on chest was significantly lower than TSB ($p<0.001$), and TcB on forehead was significantly lower than TSB ($p<0.001$). All these results are shown in table 5 and figure 2.

Table (4): Total serum and transcutaneous bilirubin of jaundiced neonates

Variable	No.	%
Total serum bilirubin mean±SD (12.6±4.2 mg/dl)		
Normal (≤10 mg/dl)	50	28.6%
High (>10 mg/dl)	125	71.4%
Total	175	100.0
Chest transcutaneous bilirubin mean±SD (11.8±3.8 mg/dl)		
Normal (≤10 mg/dl)	58	33.1%
High (>10 mg/dl)	117	66.9%
Total	175	100.0
Forehead transcutaneous bilirubin mean±SD (11.3±3.9 mg/dl)		
Normal (≤10 mg/dl)	70	40%
High (>10 mg/dl)	105	60%
Total	175	100.0

Table (5): Distribution of bilirubin level according to different techniques.

Variable	TcB. Chest Mean±SD (mg/dl)	TcB. Forehead Mean±SD (mg/dl)	TSB Mean±SD (mg/dl)	P
Bilirubin	11.84±3.79	11.29±3.88	12.57±4.22	<0.001
		Post HOC test		
TcB. Chest vs. TcB. Forehead	11.84±3.79	11.29±3.88		<0.001
TcB chest vs. TSB	11.84±3.79		12.57±4.22	<0.001
TcB Forehead vs. TSB		11.29±3.88	12.57±4.22	<0.001

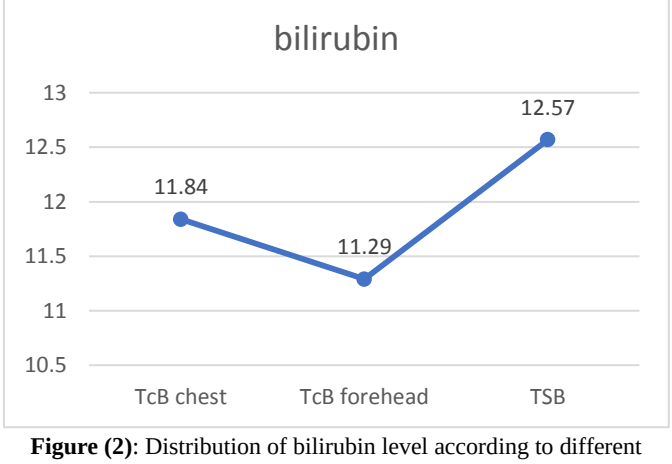

Figure (2): Distribution of bilirubin level according to different techniques

There was a significant positive correlation between TcB on chest, TcB on forehead and TSB as shown in table 6.

Table (6): correlation of bilirubin level among different techniques

	R (correlation coefficient)	P value
TcB. Chest vs. TcB. Forehead	0.973	<0.001

TcB chest vs. TSB	0.963	<0.001
TcB Forehead vs. TSB	0.946	<0.001

Table 7 demonstrates the distribution of bilirubin levels by technique for different age groups and gender. In all age groups, there was a significant difference between means of TcB on chest, TcB on forehead and TSB (p<0.001). TcB on chest was significantly higher than TcB on forehead in all age groups (p 0.006, p<0.001 and p<0.001 respectively), TcB on chest was significantly lower than TSB in the age groups 1-3 and ≥7 (P= 0.042 and P <0.001 respectively), while there was no significant difference in the age group 4-6 (P= 0.781). TcB on forehead was significantly lower than TSB in all age groups (p <0.001).

In both genders, there was a statistically significant difference between means of TcB on chest, TcB on forehead and TSB (p<0.001). TcB on chest was significantly higher than TcB on forehead in both genders (p<0.001), and was significantly lower than TSB in both genders (p<0.001), and TcB on forehead was significantly lower than TSB in both genders (p<0.001).

Table (7): Distribution of bilirubin levels according to technique for different age groups and gender

Variable	Tc. Chest	Tc. Forehead	TSB	P
	Mean±SD (mg/dl)	Mean±SD (mg/dl)	Mean±SD (mg/dl)	
1-3 days	10.70±3.56	10.28±3.84	11.13±3.90	<0.001
4-6 days	12.21±3.85	11.76±3.96	13.24±4.50	<0.001
≥7 days	12.24±3.78	11.53±3.79	12.89±4.00	<0.001
	TcB chest vs. TcB forehead	TcB chest vs. TSB	TcB forehead vs. TSB	
1-3 days	p 0.006	P 0.042	p <0.001	
4-6 days	P <0.001	P 0.781	P <0.001	
≥7 days	P <0.001	P <0.001	P <0.001	
Gender	Tc. Chest Mean±SD (mg/dl)	Tc. Forehead Mean±SD (mg/dl)	TSB Mean±SD (mg/dl)	P
Male	12.03±3.43	11.46±3.59	12.78±3.87	<0.001
Female	11.59±4.21	11.08±4.25	12.30±4.65	<0.001
	TcB chest vs. TcB forehead	TcB chest vs. TSB	TcB forehead vs. TSB	
Male	p<0.001	p<0.001	p<0.001	
Female	p<0.001	p<0.001	p<0.001	

Table 8 shows the distribution of bilirubin level according to technique for gestational age and birth weight. In both term and preterm neonates, there was a significant difference between means of TcB on chest, TcB on forehead and TSB (p<0.001). In both term and preterm neonates, TcB on chest was significantly higher than TcB on forehead and was significantly lower than TSB, while TcB on forehead was significantly lower than TSB (p<0.001).

In all birth weight groups, there was a statistically significant difference between means of TcB on chest, TcB on forehead and TSB (p 0.004, p <0.001 and p<0.001 respectively). TcB on chest was significantly higher than TcB on forehead in all age groups (p= 0.045, P 0.001 and p <0.001 respectively). TcB on chest was not significantly different from TSB in all weight groups except the group ≥2.5 Kg (P <0.001). TcB on forehead was significantly lower than TSB in all birth weight groups (p 0.003, p <0.001 and p <0.001 respectively).

Table (8): Distribution of bilirubin level according to technique for gestational age and birth weight

Variable	Tc. Chest	Tc. Forehead	TSB	P
	Mean±SD (mg/dl)	Mean±SD (mg/dl)	Mean±SD (mg/dl)	
Gestational age				
Preterm	11.36±4.06	10.74±4.11	12.02±4.37	<0.001
Term	12.10±3.63	11.59±3.75	12.87±4.14	<0.001
	TcB chest vs. TcB forehead	TcB chest vs. TSB	TcB forehead vs. TSB	
Preterm	p<0.001	p<0.001	p<0.001	
Term	p<0.001	p<0.001	p<0.001	
Birth weight				
<1.5 Kg	7.73±5.32	6.83±5.05	8.68±5.85	0.004
1.5-2.4 Kg	11.13± 3.59	10.57±3.59	11.58±3.66	<0.001
≥2.5 Kg	12.21± 3.66	11.68±3.79	13.01±4.18	<0.001
	TcB chest vs. TcB forehead	TcB chest vs. TSB	TcB forehead vs. TSB	
<1.5 Kg	p 0.045	p 0.146	p 0.003	
1.5-2.4 Kg	P 0.001	p 0.069	p <0.001	
≥2.5 Kg	p<0.001	P <0.001	p <0.001	

The appropriate cutoff points and the corresponding validity tests results (sensitivity & specificity) for TcB on chest in prediction of jaundice (TSB>10 mg/dl) were calculated by ROC test in SPSS which gives us ROC figure and two tables, first is area under the curve (AUC) table and second is coordinates of the curve table. ROC figure shows the cutoff values with relevant sensitivity and specificity in graphical way, while AUC table shows area under the curve value (the higher the AUC value, the higher the sensitivity and specificity), while coordinates of the curve table shows the individual values of TcB on chest with relevant sensitivity and specificity and by eye gaze we look at the individual values to choose a value that gives the highest possible sensitivity with the highest possible specificity. The value (9 mg/dl) met these conditions with acceptable validity results (96.2% sensitivity & 86.4% specificity). For the sake of briefing and space saving, we used figure 3 and included AUC value with its title, and we used table 9 showing only the chosen value (9 mg/dl) as a cutoff point and we omitted all other values.

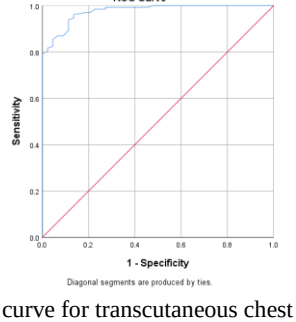

Figure (3): ROC curve for transcutaneous chest bilirubin values predicting TSB value >10mg/dl (area under the curve AUC=0.976)

Table (9): Coordinates of the Curve of transcutaneous chest bilirubin regarding jaundice.

Cutoff point	Sensitivity	Specificity
9 mg/dl	96.2 %	86.4%

The appropriate cut off points and the corresponding validity tests values (sensitivity & specificity) for TcB on forehead in prediction of jaundice (TSB>10 mg/dl) were calculated in the same way used to calculate the cutoff point of TcB on chest. Figure 4 and table 10 shows that AUC value was 0.973 and the cutoff TcB on forehead was 8 mg/dl and had acceptable validity results (96.2% sensitivity & 79.5% specificity).

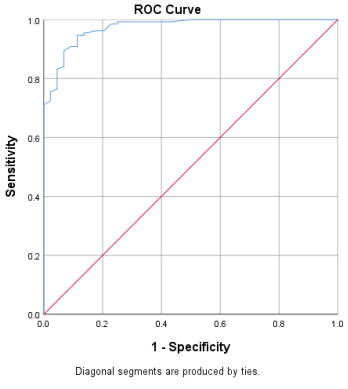

Figure (4): ROC curve for transcutaneous forehead bilirubin values predicting TSB value >10mg/dl (area under the curve AUC=0.973)

Table (10): Coordinates of the Curve of transcutaneous forehead bilirubin regarding jaundice.

Cutoff point	Sensitivity	Specificity
8 mg/dl	96.2%	79.5 %

Discussion

TcB measurement was introduced as a non-invasive method for measuring the bilirubin level of newborns and to minimize the blood loss from TSB measurement (21). In spite of the discrepancy between TcB measurement and TSB and between their different sites, the accuracy of bilirubin measurement has been proved (21).

The present study showed that the TSB of jaundiced neonates was significantly higher than TcB on chest and forehead ($p<0.001$) which is consistent with results of Taylor et al (11) study in USA which reviewed the medical records of newborns with jaundice comparing 8319 TcB measurements with matched 925 TSB measurements and found a significant difference in mean bilirubin measurement between TcB and TSB tests. In spite of this discrepancy, Taylor et al (11) stated that TcB measurement provided close estimates to TSB in newborns and this point is supported by the results of our study which revealed significant positive correlation of bilirubin level among TcB on chest, forehead and TSB. Another previous study in USA by Maisels et al (15) also detected difference in mean bilirubin measurement between TcB and TSB and this difference was affected by ethnicity. Our study revealed a significantly lower means of bilirubin assessed by TcB on chest in comparison to TSB ($p<0.001$). In contrast, Holland et al (22) documented overestimation of TcB on chest in comparison to TSB. However, in the present study, this underestimation did not affect the accuracy of TcB on chest as a screening device for referring neonates for further investigations including TSB. Present study showed also that mean TSB was significantly higher than TcB on forehead ($p<0.001$). This finding agrees with results of Şimşek et al (23) study in Turkey which compared the TcB (forehead & chest) with TSB for late term, preterm and term infants and found that TcB tended to be underestimated with increasing discrepancy from TSB for both forehead and chest. The current study revealed that TcB on chest was significantly higher than TcB on forehead ($p<0.001$) which is consistent with results of Conceição et al (24) study in Brazil that showed a significant correlation between TcB on chest and TSB but both of them significantly differ from TcB on forehead. The explanation of this difference between TcB on chest and forehead might be related to long period exposure to room light for forehead more than chest that was covered by clothes which in turn affect the readings of TcB (24). Many variable literatures found higher accuracy with strong correlation between TcB on chest and forehead and TSB (25-28).

Current study showed that accepted cutoff value in predicting TSB of >10 mg/dl using TcB on chest was 9 mg/dl with validity results of 96.2 % sensitivity & 86.4% specificity. These findings are close to results of Sarici et al (29) study in Turkey which reported cutoff value of TcB on chest for late preterm and term infants ranging from 9-11 mg/dl in predicting high TSB with sensitivity of 94% and specificity of 88%. The accepted cutoff value in predicting TSB of >10 mg/dl using TcB on forehead was 8 mg/dl with validity results of 96.2% sensitivity & 79.5% specificity. These findings are close to results of Mansouri et al (30) study in Iran which revealed that TcB on forehead of newborns was significantly correlated with TSB with validity results of TcB on forehead of 95.1% sensitivity and 68% specificity with cutoff value of 8 mg/dl. This lower cutoff value of TcB on forehead in comparison to TcB on chest is attributed to exposure of forehead to room light while the chest was covered by clothes leading to underestimation of TcB on forehead. This point is one of limitations for use of TcB (24).

In this study, the significant difference between TSB and both TcB on chest and forehead was more or less maintained in different neonatal age groups i.e. no changes in the significance of differences between techniques in different groups, except that in the age group 4-6 d. there was no significant difference between TcB on forehead and TSB. These findings are somewhat similar to results of El-Kabbany et al (31) study in Egypt which revealed that TcB is significantly correlated with TSB in different neonatal age groups but they reported that TcB on forehead for preterm newborns was less accurate than TcB on chest. Correlation between TcB (on chest or forehead) and TSB means that bilirubin values of all techniques tend to increase or decrease together in spite of the significant difference among them.

In this study, the significant difference between TSB and both TcB on chest and forehead was also maintained in in both genders ($p<0.001$). This finding agrees with results of Mandal et al (32) study in India which stated that there was an agreement between TcB and TSB with slight difference and this difference was not affected by neonatal age and gender. Regarding gestational age, the significant difference between TSB and both TcB on chest and forehead was also maintained in both preterm and term newborns and in all birth weight groups except that TcB on forehead was not significantly different from TSB in the birth weight groups 1.5-2.4 kg and ≥2.5 kg. This result is somewhat different from results of Maisels et al (33) study that found that mean difference between

TcB and TSB was significantly increased with decrease of gestational age or decrease of birth weight and this difference in the present study could be attributed to the fact that lower birth weight groups (<1.5 Kg and 1.5-2.4 kg) constitute 23.4 % of the sample i.e. it has a little impact on significance compared to the higher weight group (≥2.5 kg) which constitute the remaining 76.6 %. Maisels et al also recommended the use of TcB for newborns with gestational age of 28-35 weeks or less than 1.5 Kg birth weight before use of TSB.

Conclusions

TcB measurements in both chest and forehead have an acceptable validity (sensitivity and specificity) in predicting hyperbilirubinemia according to the device used in this study. TcB measurements are lower than TSB measurements. TcB on chest is more accurate than TcB on forehead.The difference between TSB total serum bilirubin and TcB is not much affected by neonatal age, gender, gestational age and weight.

Recommendations

TcB is a good choice for deciding which neonate needs referral for further TSB measurement. Rely on TcB on chest bilirubin measurement more than forehead site. Additionally, further national multi-center studies on TcB measurements are needed.

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Conflict of Interest

No conflict of interest

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