Discrepancy between Transcutaneous and Serum Bilirubin Measurement in Healthy Chinese Newborns in a Baby-friendly Hospital in Hong Kong

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Objective: To characterise the discrepancy between transcutaneous bilirubin (TcB) and total serum bilirubin (TSB) levels and to evaluate the use of TcB measurements in detection of severe hyperbilirubinaemia requiring phototherapy among healthy Chinese newborns.
Methods: Medical records were reviewed to collect data on paired TcB-TSB measurements. The paired TSB level was obtained within 2 hours of the TcB measurement in healthy Chinese neonates admitted to one of our postnatal wards over a 1-year period, from January to December 2015. Demographic information and outcome for individual newborns were also recorded. TcB-TSB differences were calculated and analysed in order to obtain their correlations. Multivariate regression analysis was used to identify characteristics independently associated with TcB-TSB difference of ≥20 and ≥30 μmol/L. The clinical application of TcB, together with Bhutani nomogram in the prediction of severe hyperbilirubinaemia in medium- and higher-risk thresholds for phototherapy was also analysed.
Results: A total of 220 TSB levels were matched with a TcB value. The correlation between paired measurements was 0.75. The mean TcB-TSB difference was 28.76±23.83 μmol/L. TcB measurements in general tended to overestimate TSB, although the TcB-TSB difference varied with different TSB values and TcB measurements tended to be underestimated as TSB levels increased. Using the 75th centile tract of Bhutani nomogram as threshold, TcB measurements could predict all cases in the high-risk zone with a sensitivity and negative predictive value of 100% each. At medium-risk and higher-risk thresholds for phototherapy, using the 75th centile as the cut-off level, the sensitivity was 93.2% and 73.1%, respectively.
Conclusions: TcB measurement provided a reasonable estimate of TSB in healthy newborns with a high breastfeeding rate. As TcB-TSB difference varied with different TSB levels, caution should be taken especially in cases with severe hyperbilirubinaemia in which TcB measurements tended to be underestimated with higher TSB level. Combining the use of TcB measurements and the 75th centile tract of Bhutani nomogram as the cut-off level can detect all high-risk cases of severe hyperbilirubinaemia.
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Keywords: Bilirubin/blood; Hyperbilirubinemia; Jaundice, neonatal; Neonatal screening

Introduction

Neonatal jaundice (NNJ) is one of the most common diseases encountered during the early neonatal period and is more prevalent in the Asian population compared with Caucasians. A study in Hong Kong showed that 87% of full-term Chinese newborns had clinical jaundice, of whom 23.9% had a peak total serum bilirubin (TSB) of >204 μmol/L[1]. Severe unconjugated hyperbilirubinaemia can lead to irreversible brain damage, namely kernicterus. Prevention of kernicterus in neonates is a primary focus of neonatal care in the postnatal nursery unit. Visual estimates of the degree of jaundice and the serum bilirubin level can be misleading[2-4]. To promote early detection of significant hyperbilirubinaemia, the Subcommittee on Hyperbilirubinemia of the American Academy of Pediatrics recommended that all newborns be screened before discharge with transcutaneous bilirubin (TcB) or TSB measurement[5]. TcB measurement is a quick and non-invasive alternative to invasive blood taking to screen for NNJ. Studies have shown that TcB is highly correlated with TSB, with a correlation coefficient of around 0.8 in both international and local studies[6-8]. Differences between TcB and TSB (TcB-TSB difference) are associated with different ethnic origin, age (in hours) of when TcB measurement was taken, and different TSB levels[6].

Our hospital is one of the major public hospitals in Hong Kong that serves a mostly Chinese population. There is evidence of a good correlation between TcB and

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TSB in Chinese infants[7,8]. A study in the US showed that the TcB-TSB difference becomes larger with each hour of advancing age, even after adjusting for TSB level[6]. Local studies suggested that the mean TcB-TSB difference was 21.7 μmol/L when TcB measurements were taken in the first 3 days of life[7], compared with 14 μmol/L when taken at 3 to 7 days of life[8]. Whether there is any association between the TcB-TSB difference and the hours of age in Chinese infants remains unknown.

Both Chinese ethnicity and breastfeeding are associated with a higher maximum TSB level in newborns[9]. With the promotion of breastfeeding and recent baby-friendly hospital initiative in our hospital, the rate of exclusive breastfeeding in our department has almost doubled from 22.8% in 2013 to 41.2% in 2015 (personal communication from our breastfeeding consultant). One may expect to see more newborns with a higher TSB level in our department. Since September 2014, our hospital had started to use a higher cut-off TSB threshold for phototherapy, modified from the American Academy of Pediatrics (AAP) guideline published in 2004[10]. According to this guideline, East Asian race is one of the major risk factors for babies to develop severe hyperbilirubinaemia. Therefore, in our hospital, we adopted the higher-risk threshold in infants who were 35-0/7 to 37-6/7 weeks at birth and well or ≥38 weeks with risks. In those who were ≥38 weeks and well, we adopted the medium-risk threshold instead of the medium-risk and lower-risk thresholds, respectively for phototherapy according to the AAP. This change was supported by a subsequent consensus guideline issued by the Hospital Authority hospitals[11]. If a TcB level is within the threshold for phototherapy (20-35 μmol/L) then TSB measurement is recommended. Although TcB measurements are an overestimation and cause unnecessary blood taking, they provide a safety margin for confirmation and further monitoring. On the contrary, TcB underestimation can be potentially dangerous when infants do not have TSB level checked and can lead to potential missed diagnosis and delayed treatment of severe hyperbilirubinaemia. A study in the US in which the majority of subjects were white showed that at higher serum bilirubin levels, TcB tended to underestimate the TSB level with substantial variability when TSB level was ≥256.5 μmol/L[6]. Studies have suggested that the use of TcB measurements together with the Bhutani nomogram could improve the identification of cases with significant hyperbilirubinaemia[7,12,13].

The present study aimed to characterise the discrepancies between TcB measurements and TSB levels at different TSB levels and with different newborn variables among term or near-term healthy Chinese newborns. The clinical application of TcB measurements, together with the Bhutani nomogram in the prediction of severe hyperbilirubinaemia in medium-risk and higher-risk thresholds for phototherapy, were also analysed in order to facilitate NNJ screening and avoid unnecessary blood tests.

Methods

A retrospective study was carried out on healthy term neonates admitted to a postnatal ward in a regional hospital in Hong Kong. According to our departmental protocol, all newborns discharged from our postnatal ward are screened by TcB measurement before discharge using JM-103 Minolta (Dräger Medical Systems Inc., Telford [PA], US). Two readings were measured from the sternum by a nurse and the higher reading was recorded. If a TcB level is within the threshold for phototherapy of 20 to 35 μmol/L, a TSB measurement by a direct spectrophotometric method in the laboratory will be done. Medical records were reviewed on all healthy Chinese newborns admitted to the postnatal nursery between January and December 2015. Healthy neonates with no evidence of birth trauma, neonatal infection, asphyxia, Chinese descendants, near-term and term infants of ≥35 weeks of gestation, and no evidence of rhesus isoimmunisation were included. Non-Chinese infants, preterm infants of <35 weeks of gestation, sick newborns who required admission to the special care baby unit (SCBU) or neonatal intensive care units (NICU), and newborns who had received phototherapy were excluded. For each eligible newborn, demographic data and outcome were retrieved from the medical records, including gestational age, sex, birth weight, type of feeding (exclusive breast milk, mixed breast milk and formula, only formula), glucose-6-phosphate dehydrogenase (G6PD) status, type of delivery, maternal blood group, readmission for NNJ, and whether phototherapy or exchange transfusion were given. The results of all TcB tests for each enrolled newborn were abstracted along with the infant's age (in hours) and time when the measurement was made. In addition, data on TSB measurement performed within 2 hours of a TcB measurement were obtained. TcB and TSB measurements that were obtained within 2 hours of each other were considered paired.

Outcome and Statistical Analyses

The Statistical Package for the Social Sciences (SPSS V.21; IBM, US) was used for statistical analysis. The primary study outcome was the TcB-TSB difference between paired values, such that a positive difference indicated that the TcB value was greater than the

corresponding TSB level and a negative difference indicated that the TcB measurement was less. Only the first paired TcB-TSB values of each eligible infant were used in the analyses. In addition to descriptive statistics, the correlation between paired TcB and TSB level was determined by Pearson product-moment correlation coefficient. The association of different patient characteristics with the TcB-TSB difference, including gestational age at birth, birth weight, gender, type of feeding, G6PD status, maternal blood group, type of delivery, hours of age when TcB was measured, TSB level and neonatal outcome, were individually assessed using regression analyses. Because the magnitude of the TcB-TSB difference might vary based on the TSB level, TSB levels were included in all regression models. Patient variables statistically associated with a TcB-TSB difference ($p<0.05$) in bivariate analyses were included in a full model to identify characteristics independently associated with the difference.

Proportions of clinically relevant underestimations and overestimations for ≥20 and ≥30 μmol/L between paired TcB-TSB samples were determined. Logistic regression was used to identify characteristics associated with clinically relevant underestimations of TSB by TcB (i.e. TcB levels ≥20 μmol/L or ≥30 μmol/L lower than the corresponding TSB value). Those variables statistically associated with the outcome in bivariate analyses were included in a multivariate model. For all analyses, TSB levels were included. A similar analytic strategy was used to identify characteristics associated with clinically relevant overestimations of TSB by TcB measurement.

The ability of various TcB cut-off values to predict elevated TSB value was analysed using standard 2 x 2 table analysis. Sensitivity, specificity, as well as positive and negative predictive values were calculated. The Bhutani nomogram[12] was used to identify risk zones for bilirubin values. The percentage of blood taking avoided was calculated ([false negatives + true negatives] / total No. of comparisons). The clinical value of TcB level for prediction of severe hyperbilirubinaemia above the medium-risk and higher-risk thresholds for phototherapy according to the AAP guidelines[10] was also determined. The sensitivity and specificity of TcB level in different hour-specific risk zones of Bhutani nomogram (40th, 75th and 95th centiles) for medium- and higher-risk thresholds for phototherapy was then calculated.

The study was approved by the Hospital Authority Research Ethics Committee (Kowloon Central/ Kowloon East).

Results

A total of 1266 newborns were admitted to the postnatal ward during the 1-year study period. Newborns with at least one blood sample taken for TSB measurement were identified through the Clinical Data Analysis and Reporting System and 559 records were reviewed. After excluding non-Chinese newborns, newborns who became sick and required transfer to SCBU/NICU, and non-paired TcB-TSB samples (i.e. TSB taken >2 hours apart from TcB measurement), a total of 220 healthy term Chinese newborns contributed to the study. Their characteristics and outcome are summarised in Table 1. All were term infants of ≥37 weeks of gestation. All women with Rhesus D–positive status showed no risk of rhesus isoimmunisation. The majority (95.0%) of neonates were either exclusively or partially breastfed.

The TSB value in study newborns ranged from 76 μmol/L to 293 μmol/L; 12 (5.45%) of whom being ≥250 μmol/L. Overall, the mean (±standard deviation) TcB-TSB difference for the 220 paired measurements was 28.76±23.83 μmol/L, with differences ranging from -30 μmol/L to 94 μmol/L, following a normal distribution verified by Shapiro-Wilk test ($p=0.53$). The majority (94.5%) of the paired TcB-TSB samples were obtained on days 2 and 3. The correlation coefficient between paired measurements was significant ($r=0.75$; $p<0.001$).

The TcB-TSB difference varied with the TSB level (Figure 1). The mean TcB-TSB difference for the five paired measurements, when TSB level was ≤125 μmol/L, was 35.4 μmol/L (95% confidence interval [CI], 0.18-70.62 μmol/L). The mean TcB-TSB difference became progressively less positive as the TSB level increased, with a mean TcB-TSB difference of 18.8 μmol/L (95% CI, 2.9-34.7 μmol/L) for the 10 paired measurements when TSB level was ≥251 μmol/L. The regression coefficient was -0.382 (95% CI, –0.353 to –0.180; $p<0.001$). A Bland-Altman plot of all 220 comparisons showed that TcB measurement overestimated TSB level in the majority of comparisons, and the bias was +28.8 μmol/L (Figure 2). After controlling for TSB level, no neonatal characteristic was significantly associated with TcB-TSB difference (Table 2).

There were seven (3.2%) neonates with a TcB level ≥20 μmol/L lower than the corresponding TSB level, and 150 (68.2%) neonates with a TcB level ≥20 μmol/L higher than the corresponding TSB level. Overall, TcB reading differed from the matched TSB value by a ≥20 μmol/L difference in 71% (95% CI, 65-77%) of cases. The analysis of the association of individual newborn characteristics

Table 1. Characteristics of newborns and their outcome with at least one paired TcB-TSB level (n=220)*

Characteristics	Data
Gestational age (weeks)	39.1 ± 1.0
Birth weight (g)	3208 ± 323
Gender	
Male	120 (54.5)
Female	100 (45.5)
Mean (range) hours of age	52.6 (8.0-124.6)
Vaginal delivery	150 (68.2)
Feeding	
Exclusive breast	150 (68.2)
Breast and formula	59 (26.8)
Formula only	11 (5.0)
G6PD deficiency	12 (5.5)
Maternal blood group	
A	50 (22.7)
B	47 (21.4)
AB	14 (6.4)
O	109 (49.5)
Excessive weight loss >7% on day 2/3	138 (62.7)
Excessive weight loss >10% on day 2/3	20 (9.1)
Outcomes	
Readmission for NNJ†	106 (48.2)
Phototherapy given‡	85 (38.6)
Exchange transfusion given‡	1 (0.5)

Abbreviations: G6PD = glucose-6-phosphate dehydrogenase; NNJ = neonatal jaundice; SCBU = special care baby unit; TcB-TSB level = transcutaneous bilirubin–total serum bilirubin level

* Data are shown as mean ± standard deviation or No. (%) of subjects, unless otherwise specified

† Readmission for NNJ was defined as newborns who were already discharged home from postnatal ward and were readmitted to SCBU for NNJ

‡ Phototherapy / exchange transfusion received either before discharge or during readmission for NNJ

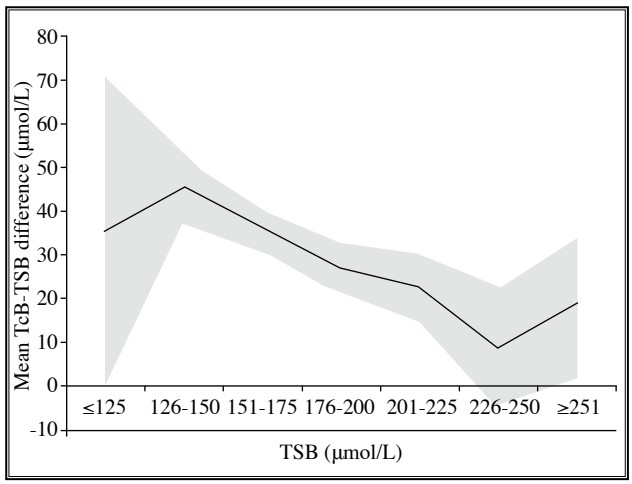

Figure 1. Mean TcB-TSB difference at different ranges of TSB levels

The shaded area represents the 95% confidence intervals around the means

Abbreviations: TcB = transcutaneous bilirubin; TSB = total serum bilirubin

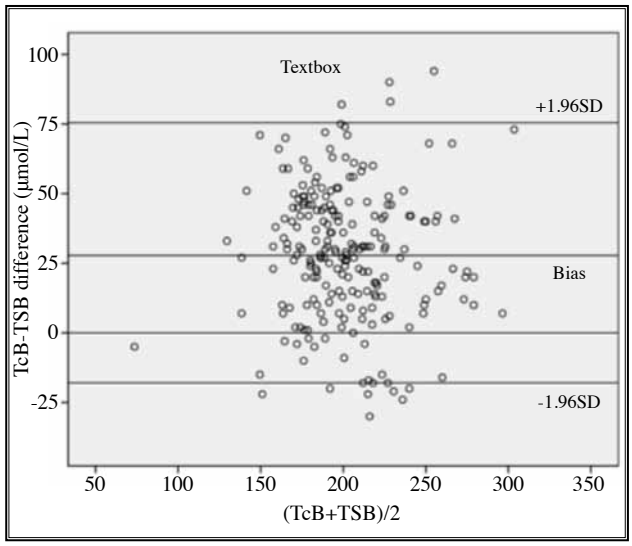

Figure 2. Bland-Altman plot comparing TSB and TcB

Abbreviations: SD = standard deviation; TcB = transcutaneous bilirubin; TSB = total serum bilirubin

with a TcB level ≥20 or ≤20 μmol/L than the corresponding TSB level is summarised in Table 2. The TSB level was significantly associated with an overestimation of TcB ≥20 μmol/L with the matched TSB level, with an odds ratio of 0.976 (95% CI, 0.966-0.985). Both TSB level and hours of age when TcB measurement was taken were significantly associated with an underestimation of TcB ≥20 μmol/L with the matched TSB level, with an odds ratio of 1.029 (95% CI, 1.008-1.051) and 0.920 (95% CI, 0.856-0.988), respectively (Table 2).

One (0.45%) neonate had a TcB level ≥30 μmol/L lower than the corresponding TSB level, and 111 (50.4%) neonates with a TcB level ≥30 μmol/L higher than the corresponding TSB level. Overall, TcB reading differed from the matched TSB value by a ≥30 μmol/L difference in 50.9% (95% CI, 44-58%) of cases. The analysis of the association of individual newborn characteristics with a TcB

level ≥30 μmol/L higher than the corresponding TSB level is summarised in Table 2. Both gestational age and TSB level were significantly associated with overestimation of TcB ≥30 μmol/L with the matched TSB level, with an odds ratio of 1.363 (95% CI, 1.030-1.805) and 0.976 (95% CI, 0.966-0.985), respectively. Similar analysis could not be done for the single newborn with a TcB level 30 μmol/L lower than the corresponding TSB level because of the low frequency of the outcome (n=1, 0.45%).

Regarding the AAP risk zone distribution of TSB values, 27 (12%) were in low-risk zone, 105 (48%) in low-intermediate risk zone, 71 (32%) in high-intermediate risk zone, and 17 (8%) in high-risk zone. For those in the high-risk zone, the corresponding distribution of TcB measurements was two (12%) in the high-intermediate risk zone and 15 (88%) in high-risk zone. Results of data analysis using hour-specific risk zones are shown in Table 3. A TSB value in the high-risk zone could be predicted by a TcB measurement in or above the high-intermediate risk zone, with a sensitivity and negative predictive value of 100% each. The application of 75th centile tract could reduce 25% of blood tests. Among the 17 TSB values in the high-risk zone, 16 (94.1%) subsequently required phototherapy. If the medium-risk (≥38 weeks and well) threshold for severe hyperbilirubinaemia was used for prediction, the sensitivity of using the 40th, 75th, and 95th centile tracts was 100%, 93.2% and 40.7%, respectively. If the higher-risk (35-0/7 to 37-6/7 weeks and well or ≥38 weeks with risks) thresholds for severe hyperbilirubinaemia was used for prediction, the sensitivity of using the 40th, 75th, and 95th centile tracts was 100%, 73.1% and 26.9%, respectively. On the contrary, the specificity for the 95th centile tract was 100% (Table 4).

Table 2. Association between individual patient characteristics and TcB-TSB difference, and TcB values that were ≥20 or ≤20, or ≥30 μmol/L than the corresponding TSB level

Variable	Coefficient*	p Value*	Outcome (odds ratio [95% confidence interval])		
			TcB ≥20 μmol/L higher than TSB	TcB ≥20 μmol/L lower than TSB	TcB ≥30 μmol/L higher than TSB
Hours of age	-0.30	0.660	1.002 (0.976-1.028)	0.920 (0.856-0.988)	0.987 (0.964-1.01)
Gestational age	0.116	0.065	1.167 (0.863-1.579)	0.362 (0.122-1.074)	1.363 (1.030-1.805)
Birth weight	-0.02	0.754	1.000 (0.999-1.001)	0.998 (0.995-1.001)	1.000 (0.999-1.001)
Gender	-0.017	0.785	0.861 (0.467-1.587)	0.166 (0.019-1.488)	0.712 (0.402-1.263)
G6PD deficiency	-0.041	0.519	1.763 (0.473-6.499)	0.496 (0.050-4.928)	1.109 (0.293-4.205)
Feeding (exclusive breastfeeding)	-0.043	0.495	1.045 (0.542-2.014)	0.294 (0.034-2.580)	0.968 (0.523-1.79)
Excessive weight loss >7%	-0.063	0.328	1.339 (0.695-2.579)	1.027 (0.182-5.789)	1.528 (0.841-2.776)
TSB level	-	-	0.976 (0.966-0.985)	1.029 (1.008-1.051)	0.976 (0.966-0.985)
Mode of delivery	-0.004	0.946	-	-	-
Maternal blood group	0.004	0.952	-	-	-

Abbreviations: G6PD = glucose-6-phosphate dehydrogenase; TcB = transcutaneous bilirubin; TSB = total serum bilirubin
* Coefficients and p values determined with regression analysis after controlling for TSB level

Table 3. TSB levels and TcB cut-off values related to AAP risk zones[7]

TSB zone*	TcB zone*	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Blood tests avoided† (%)
4	4	0.88	0.78	0.25	0.99	72.7
4	≥3	1.0	0.28	0.10	1.0	25.5
≥3	≥3	0.93	0.38	0.50	0.89	25.5
≥3	≥2	1.0	0.008	0.40	1.0	0.5

Abbreviations: AAP = American Academy of Pediatrics; TcB = transcutaneous bilirubin; TSB = total serum bilirubin
* Classification of zones: zone 2 = low-intermediate risk; zone 3 = high-intermediate risk; zone 4 = high risk
† Calculated by: (false negatives + true negatives) / total No. of comparisons

Table 4. Statistical analysis for phototherapy with medium-risk and higher-risk thresholds

Transcutaneous bilirubin category	Phototherapy		Sensitivity (95% confidence interval)	Specificity (95% confidence interval)
	Yes	No		
Medium-risk threshold (n=185)				
>40%	58	127	100% (93.8-100%)	0 (0-2.94%)
≤40%	0	0		
>75%	55	88	93.2% (83.8-97.3%)	30.2 (22.8-38.7%)
≤75%	4	38		
>95%	24	29	40.7% (29.1-53.4%)	77.0% (68.9-83.5%)
≤95%	35	97		
Higher-risk threshold (n=35)				
>40%	26	8	100% (87.1-100%)	11.1% (1.99-43.5%)
≤40%	0	1		
>75%	19	2	73.1% (53.9-86.3%)	77.8% (45.3-93.7%)
≤75%	7	7		
>95%	7	0	26.9% (13.7-46.1%)	100% (70.1-100%)
≤95%	19	9		

Discussion

This study has shown a significant strong, positive correlation between TcB and TSB measurements in our local Chinese newborns. The correlation coefficient (r=0.75) was comparable to that reported in a recent study by Taylor et al[6] that involved mainly white or black races (r=0.78), and to a Chinese population in another study (r=0.83)[7].

The TcB measurements overestimated TSB by a mean of 28.76±23.83 μmol/L in our study population. The magnitude of this overestimation was similar to another local study by Ho et al[7] in 2006 (21.7±21.2 μmol/L), but was much larger than that in the study by Taylor et al[6] (14.36±30.44 μmol/L). Nonetheless, a study done on mainly Hispanic neonates showed an underestimation of TSB[13]. This may be due to the difference in race and skin pigmentation. JM-103 Minolta determines the yellowish colour of the subcutaneous tissue and uses a dual optical path system designed to minimise the influence of melanin pigment[14]. It has been suggested that significant differences existed in TcB measurements across populations[15], with a tendency for TcB to underestimate TSB in the lighter skin tone group and to overestimate it in the darker skin tone group[16].

The TcB-TSB difference was associated with the hours of age in some studies in a non-Asian population, but the association was weak[6,13]. TcB-TSB difference did not reveal a significant association with the hours of age in our study. Our study nonetheless demonstrated a significant association between TcB measurements and underestimation of TSB level by ≥20 μmol/L with the hours of age, even though the association was also weak with a regression coefficient of -0.083. The mechanism was not exactly known but changes in haemoglobin concentration in the first days of life were postulated to account for this phenomenon[17].

The use of TcB measurements together with the 75th centile tract of Bhutani nomogram was shown to predict all study cases in the high-risk zone for severe hyperbilirubinaemia (sensitivity=100%) in this cohort. In another study of a Hispanic population in 2004, use of the 75th centile had a lower sensitivity of 71%[13]. Therefore, use of the 75th centile tract of Bhutani nomogram should be able to reduce 25% of unnecessary blood taking, and is associated with less patient suffering and reduced costs. The majority (94.1%) of these newborns in the high-risk zone subsequently required phototherapy. Nonetheless, use of the 75th centile gave a lower sensitivity for predicting the need for phototherapy, especially in higher-risk infants (≥38 weeks with risks or 35-0/7 to 37-6/7 weeks and well Chinese infants) compared with medium-risk infants (≥38 weeks and well), with a sensitivity of 73.1% and 93.2%, respectively. The sensitivity results were lower than in a similar study of Chinese infants by Ho et al[7], in which

the predictive sensitivity for use of the 75th centile was 100% for medium-risk infants and 86.7% for higher-risk infants. Nonetheless, this comparison may not be directly comparable as the study done by Ho et al[7] did not take into consideration Chinese ethnicity as a major risk factor when defining the infant risk level. The advantage of our study is that the thresholds used for phototherapy complied with the latest suggestions by the consensus guideline of the Hospital Authority[11].

There were several limitations of this study. Firstly, most of the paired TcB and TSB levels were taken within the first 3 days of life, as most of the normal newborns in our hospital were discharged by day 3. A higher physiological TSB level would be expected in the later part of the first week of life, especially in our Chinese breastfed newborns. Here we only evaluated the clinical use of TcB measurement in the postnatal ward setting and our finding may not be generalisable to the use of TcB in outpatient newborns. None of our paired samples had TSB levels of >300 μmol/L. The magnitude of TcB measurement overestimation decreases as the TSB level increases with a regression coefficient of -0.382. Further, the TcB measurements tend to be associated with clinically significant underestimation instead of overestimation with increasing TSB level. This finding is consistent with the studies of Taylor et al[6]. Although TcB overestimation provides a safety margin for confirmation and further monitoring, TcB underestimation can potentially result in missing neonates with severe hyperbilirubinaemia. This can cause catastrophic permanent neurological damage as in the case of kernicterus. More caution should be taken and more studies are needed to investigate the accuracy of TcB measurements in babies with more severe jaundice. In addition, although we used the same JM-103 Minolta to take TcB measurements, they were obtained by different operators and this might have introduced error. Third, our neonates were mostly term, healthy, and in the first 3 days of life. The results, conclusions, or recommendations from this study may not be applicable to preterm infants, infants after discharge, or sick infants in SCBU/NICU.

Overall, the TcB value had a high sensitivity and negative predictive value in detecting NNJ in healthy Chinese newborns before discharge from the postnatal ward. Nonetheless, it cannot be considered a substitute for TSB, but rather an effective non-invasive and convenient tool to screen newborns at high risk of significant jaundice. As TcB-TSB differences varied with different TSB levels, caution should be taken especially in cases with severe hyperbilirubinaemia in which TcB measurement tended to underestimate with higher TSB level. The TSB measurements can be reserved for those newborns with TcB level above the 75th centile tract of Bhutani nomogram. Further studies are needed to address the reliability of TcB measurement at high TSB levels that usually occur after discharge. Studies are also needed to evaluate the impact of routine TcB measurement combined with the use of Bhutani nomogram before home discharge on the hospital readmission rate due to high bilirubin level.

Declaration

All authors have disclosed no conflicts of interest.

References

1. Fok TF, Lau SP, Hui CW. Neonatal jaundice: its prevalence in Chinese babies and associating factors. *Aust Paediatr J* 1986; 22:215-9.
2. Davidson LT, Merritt KK, Weech AA. Hyperbilirubinemia in the newborn. *Am J Dis Child* 1941; 61:958-80.
3. Moyer VA, Ahn C, Sneed S. Accuracy of clinical judgment in neonatal jaundice. *Arch Pediatr Adolesc Med* 2000; 154:391-4.
4. Tayaba R, Gribetz D, Gribetz I, Holzman IR. Noninvasive estimation of serum bilirubin. *Pediatrics* 1998; 102:E28.
5. Maisels MJ, Bhutani VK, Bogen D, Newman TB, Stark AR, Watchko JF. Hyperbilirubinemia in the newborn infant ≥35 weeks' gestation: an update with clarifications. *Pediatrics* 2009; 124:1193-8.
6. Taylor JA, Burgos AE, Flaherman V, et al. Discrepancies between transcutaneous and serum bilirubin measurements. *Pediatrics* 2015; 135:224-31.
7. Ho HT, Ng TK, Tsui KC, Lo YC. Evaluation of a new transcutaneous bilirubinometer in Chinese newborns. *Arch Dis Child Fetal Neonatal Ed* 2006; 91:F434-8.
8. Lam TS, Tsui KL, Kam CW. Evaluation of a point-of-care transcutaneous bilirubinometer in Chinese neonates at an accident and emergency department. *Hong Kong Med J* 2008; 14:356-60.
9. Bertini G, Dani C, Tronchin M, Rubaltelli FF. Is breastfeeding really favoring early neonatal jaundice? *Pediatrics* 2001; 107:E41.
10. 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. Erratum in: *Pediatrics* 2004; 114:1138.
11. Consensus guideline on management of unconjugated hyperbilirubinemia in Hong Kong HA hospitals in newborn infants 35 or more weeks of gestation. *Hong Kong: Hospital Authority*; June 2015.
12. Bhutani VK, Johnson L, Sivieri EM. Predictive ability of a predischarge hour-specific serum bilirubin for subsequent significant hyperbilirubinemia in healthy term and near-term newborns. *Pediatrics* 1999; 103:6-14.
13. Engle WD, Jackson GL, Stehel EK, Sendelbach DM, Manning MD. Evaluation of a transcutaneous jaundice meter following hospital discharge in term and near-term neonates. *J Perinatol* 2005; 25:486-90.
14. Yasuda S, Itoh S, Isobe K, et al. New transcutaneous jaundice device with two optical paths. *J Perinat Med* 2003; 31:81-8.
15. De Luca D, Jackson GL, Tridente A, Carnielli VP, Engle WD. Transcutaneous bilirubin nomograms: a systematic review of population differences and analysis of bilirubin kinetics. *Arch Pediatr Adolesc Med* 2009; 163:1054-9.
16. 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; 98:1909-15.
17. Jopling J, Henry E, Wiedmeier SE, Christensen RD. Reference ranges for hematocrit and blood hemoglobin concentration during the neonatal period: data from a multihospital health care system. *Pediatrics* 2009; 123:e333-7.