Influence of skin colour on diagnostic accuracy of the jaundice meter JM 103 in newborns

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ABSTRACT

Aim To assess the diagnostic accuracy of the JM 103 as a screening tool for neonatal jaundice and explore differential effects based on skin colour.

Methods We prospectively compared the transcutaneous bilirubin (TcB) and serum bilirubin (TSB) measurements of newborns over a 3 month-period. Skin colour was assigned via reference colour swatches. Diagnostic measures of the TcB/TSB comparison were made and clinically relevant TcB cut-off values were determined for each skin colour group.

Results 451 infants (51 light, 326 medium and 74 dark skin colour) were recruited. The association between TcB and TSB was high for all skin colours (r_s>0.9). The Bland-Altman analysis showed an absolute mean difference between the two measures of 13.3±26.4 μmol/L with broad limits of agreement (−39.4–66.0 μmol/L), with TcB underestimating TSB in light and medium skin colours and overestimating in dark skin colour. Diagnostic measures were also consistently high across skin colours, with no clinically significant differences observed.

Conclusions The JM 103 is a useful screening tool to identify infants in need of serum bilirubin, regardless of skin colour. The effect of skin colour on the accuracy of this device at high levels of serum bilirubin could not be assessed fully due to small numbers in the light and dark groups.

What is already known on this topic

- Transcutaneous bilirubinometers can be used as a screening tool to determine when serum bilirubin is needed.
- Few reports are available on the influence of skin colour on the predictive ability of the devices.

What this study adds

- Applying predetermined cut-offs, JM 103 can be used as a reliable screening tool in infants of different skin colour at high risk for hyperbilirubinaemia.
- We were unable to confirm reliability at high levels of serum bilirubin in infants of light and dark skin.

BACKGROUND

Transcutaneous bilirubin (TcB) devices have been studied for over 30 years to assess their ability as a screening tool for neonatal jaundice and to subsequently reduce invasive blood sampling.[1–14] Several guidelines provide instructions on how to use TcB devices in a reliable and efficient manner while warning clinicians of the potential limitations of the device.[6 15 16] The uncertainty around the accuracy of TcB measures in newborns of different skin colours, particularly infants with darker skin has been of concern.[17] This has been the subject of few studies, which included a small number of dark-skinned babies.[1 12 17–19] We therefore aimed to evaluate the diagnostic accuracy of TcB measured by Konica Dräger Minolta/Air Shields JM 103 jaundice meter at predicting hyperbilirubinaemia among our multiethnic population with various skin colours.

PATIENTS AND METHODS

We prospectively recruited healthy newborns (≥35 weeks gestational age) admitted to the mother-baby unit of The Ottawa Hospital, General Campus, a large perinatal university-affiliated centre with >3500 deliveries per year, between 23 June 2011 and 14 September 2011. Total serum bilirubin (TSB) measurements were performed: (a) prior to discharge at the same time as the Ontario Newborn Screening sampling; (b) if the infant was visibly jaundiced; (c) by physician order or (d) during a return outpatient appointment, within the first 7–10 days of life. Infants were excluded if they were admitted to neonatal intensive care unit (NICU), had a TSB performed during or within 12 h of discontinuing phototherapy or if the corresponding TcB measurement was not performed.

Each infant was assigned a skin colour of light, medium or dark using a visual scale adapted from cosmetic references (available upon request). Skin colours were adapted from powder foundation (Clinique); the 'Very Fair' and 'Moderately Fair' colours were chosen as cut-offs. These colours were matched with custom made paints (Glidden Ultra Interior Latex Flat, 94500 Series), which were painted on a larger circle (8.5 cm diameter). These circles were placed near the infant's face and a skin colour designation was made by one of eight health practitioners. If the skin colour was lighter than Very Fair, the infant was labelled as light. Newborns with skin colour in between the two reference colours were labelled as medium while those with skin colour darker than Moderately Fair were considered dark.

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TSB measurements were performed on capillary samples and analysed by direct spectrophotometry using a Leica Unistat Bilirubinometer (Leica Microsystem). Analytical measuring range of the instrument is 35–510 μmol/L, with a day-to-day coefficient of variation of 2.6% @ 136 μmol/L and 2.5% @ 358 μmol/L.

A corresponding TcB measurement was obtained within 30 min of the TSB, with the Konica Dräger Minolta/Air Shields JM 103 jaundice meter (Dräger Medical Systems, Telford, Pennsylvania, USA) by the nurse responsible for the care of the mother-infant dyad. The day-to-day precision (coefficient of variation) of the meter (measured using the electronic 'checker' provided with the meter) was 8% for the 'L' and 14% for the 'S' checkers. We used the mid-sternum area, applying the device three times to obtain a calculated automated mean value, and performed quality assurance testing, as per manufacturer's recommendations.[20]

SAMPLE SIZE

We recruited all eligible newborns over a 3-month-period, when the TcB measurement device was available for the study, and anticipated that at least 400 newborns could be tested with minimum sample sizes of 50 for the light and dark skin tones. With a minimum sample of 50 newborns in both groups, it would be possible to produce estimates of TSB/TcB association within ±6.7% of the true value (α=0.05, estimated sensitivity=0.95, estimated prevalence=0.20), using the Buderer's equation.[21]

STATISTICAL ANALYSIS

General demographic characteristics of the study population were described with continuous variables being summarised using means, SDs and ranges and categorical variables summarised using frequencies and percentages. To assess the reliability of the JM 103 device, duplicate TcB measurements were performed on a subsample of patients (n=110) and the intraclass correlation coefficient was used. To evaluate the relationship between the TcB and TSB measurements, Spearman's correlation (as the distribution of bilirubin measurements is positively skewed) and Bland-Altman analyses were undertaken. From the Bland-Altman analysis, the bias (mean of the differences in two measures) and the limits of agreement were provided.

For infants with ongoing clinical concerns, more than one pair of TSB and TcB measurements was taken. Through a post hoc analysis we showed that these pairs of repeated measurements could not be treated as independent observations (see online supplementary appendix 1), and thus could not be included in the general analysis. However, random effects mixed models were used to control for the non-independence in creating the receiver operator characteristics (ROC) curves. Therefore, it was possible to use these repeated measurements to improve the power of the ROC analysis for the skin colours with smaller sample sizes.

ROC curves were then created for a moderately high risk of hyperbilirubinaemia according to the three TSB cut-offs corresponding to the high-intermediate risk line on the Bhutani Nomogram: 110 μmol/L at 24 h, 170 μmol/L at 48 h, and 230 μmol/L at 72 h[22] A binormal smoothing function was used to make the ROC curves more readable. TcB cut-offs were generated to obtain optimum sensitivity for prediction of the identified clinically important TSB levels in the three skin colour groups of infants. Standard sensitivity, specificity, positive and negative values were then calculated for each of the obtained cut-off values.

A p value <0.05 was considered statistically significant. Analyses were performed with the SAS software (SAS Institute, Cary, North Carolina, USA).

RESULTS

A total of 503 infants were recruited over the 12-week study period, with 52 with missing skin colour information, leaving a study population of 451 infants, corresponding to 598 pairs of measurements. We conducted a sensitivity analysis and showed that patients with missing skin tone information were not qualitatively different from those with complete information with respect to infant gender, gestational age and birth weight (see online supplementary appendix 2). Two trained individuals assigned 373 (82.7%) of the skin colour designations. Baseline characteristics of our population are included in table 1. Of all included infants, 292 (64.7%) had a TSB as part of routine predischarge screening, 39 (8.7%) were tested because of a clinical diagnosis of jaundice, 120 (26.6%) were outpatient measurements and 58 (12.9%) had a positive antiglobulin test.

There was very high reliability with the duplicate TcB measurements on the first 110 patients (intraclass correlation coefficient=0.98). Spearman's correlation between TcB and TSB was 0.93 in the total population and remained above 0.90 for all subgroups (0.95, 0.94 and 0.96 for light, medium and dark skin, respectively. Of the 451 paired measurements taken, the mean TSB and TcB were 144±67 μmol/L and 131±65 μmol/L, respectively. The mean difference between the two measures was 13.3±26.4 with limits of agreement of −39.4–66.0 μmol/L. There was a variation in agreement across the skin colours,

Table 1 Study population demographics

Demographics	Study population (n=451)	Light skin colour (n=51)	Medium skin colour (n=326)	Dark skin colour (n=74)
Sex (n, %)				
Female	208 (46.1)	28 (54.9)	145 (44.5)	35 (47.3)
Male	243 (53.9)	23 (45.1)	181 (55.5)	39 (52.7)
Gestational age (weeks) (mean±SD)	39.0±1.5	39.7±1.3	38.9±1.5	39.0±1.6
Preterm (<37 weeks) (n, %)	33 (7.3)	1 (2.0)	26 (8.0)	6 (8.1)
Birth weight (g) (mean±SD)	3381±539	3382±494	3414±545	3237±522
Age at time of study (hours) (mean±SD)	59.6±28.4	51.3±20.5	61.1±29.8	58.9±25.6
Total serum bilirubin in photo range (n, %)	24 (5.3)	0 (0.0)	20 (6.1)	4 (5.4)
High-intermediate zone or high-risk zone (n, %)	59 (13.1)	1 (2.0)	49 (15.0)	9 (12.2)
Number of total serum bilirubin measures (n)	598	59	445	94

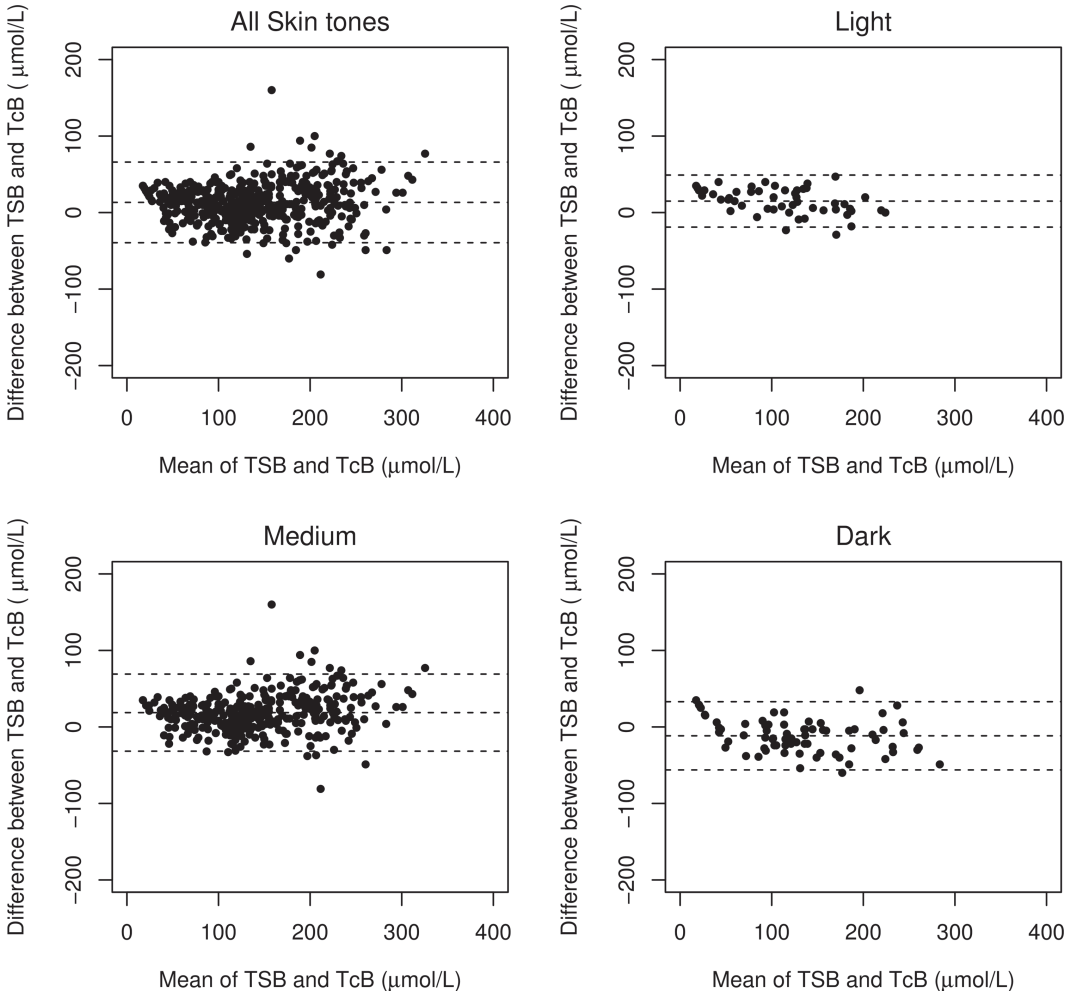

Figure 1 Bland Altman plot of agreement between total serum bilirubin (TSB) and transcutaneous bilirubin (TcB) by skin colour.

however this proved to be not statistically significant. It was however clinically significant as the TcB underestimated the TSB in light skin (mean difference 15.0±17.0; limits of agreement of −19–49 µmol/L) and medium skin (mean difference 18.7 ±25.2; limits of agreement of −31.7–69.1 µmol/L) colours while it overestimated the TSB in dark skin colour (mean difference 11.6±22.3; limits of agreement of −56.2–33 µmol/L) (figure 1).

ROC curves produced for each skin colour subgroup for each of the clinically relevant TSB cut-offs are presented in figure 2. Our study population included an insufficient number of light skin infants to create a ROC curve at a TSB level of 230 µmol/L. The area under the curve remained above 0.9 for all ROC curves across skin colours and all cut-offs, indicating excellent discrimination (figure 2). Although there was a statistically significant difference between light and medium, and medium and dark skin colours, these differences were not clinically meaningful.

TcB cut-offs with high sensitivity were determined for each TSB cut-off, for all skin colour groups, except light skin colour at TSB of 230 µmol/L (table 2).

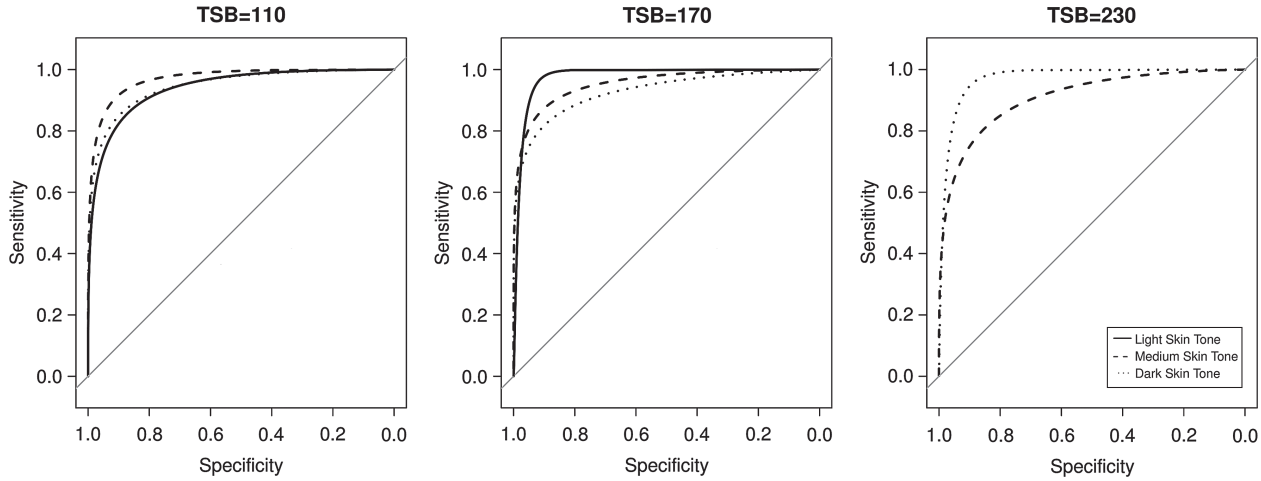

Figure 2 Receiver operator characteristic curves by skin colour at defined TSB concentrations. TSB=110 Light AUC: 0.96 (0.91, 1.0); Medium AUC: 0.98 (0.96, 0.99); Dark AUC: 0.99 (0.97, 1.0); all p>0.05. TSB=170 Light AUC: 1.0 (0.99, 1.0); Medium AUC: 0.97 (0.96, 0.99); Dark AUC: 0.96 (0.92, 1.0); Light vs medium: p<0.001. TSB =230 Light AUC: N/A; Medium AUC: 0.94 (0.91, 0.98); Dark AUC: 0.99 (0.98, 1.0); Medium versus dark: p=0.006. AUC, area under the curve; TSB, total serum bilirubin.

Table 2 Diagnostic measures corresponding to specific TSB cut-off values and optimal TcB cut-off values

Skin colour*	TSB cut-off (μmol/L)	Optimal† TcB cut-off (μmol/L)	Predictive indices			
			Sen.	Spec.	PPV	NPV
Light (n=51)	110	85	96.7	80.9	87.9	94.4
	170	145	100	95.0	84.6	100
	230	NA	NA	NA	NA	NA
Medium (n=326)	110	90	95.2	81.6	92.3	87.9
	170	130	95.9	75.1	69.5	96.9
	230	155	96.2	75.5	43.2	99.0
Dark (n=74)	110	110	95.3	80.6	87.2	92.6
	170	170	100	89.3	75.0	100
	230	210	100	91.0	53.8	100

*NB: No duplicate measurements.
†Optimal TcB cut-off value chosen to jointly maximise sensitivity (with a minimum value >95%) and specificity diagnostic measures.
NPV, negative predictive value; PPV, positive predictive value; Sen., sensitivity; spec., Specificity; TcB, transcutaneous bilirubin; TSB, total serum bilirubin.

DISCUSSION

Available evidence regarding the effect of skin colour is limited by either small sample size or the method of assigning the skin colour. A study of over 900 newborns by Wainer *et al*[17] found that more than half of the infants with declared black ethnicity were assigned a medium or light skin colour, emphasising that ethnicity may not be a valid surrogate for skin colour in the early neonatal period. We were able to recruit 72 infants with assigned dark skin colour, which is more than previous studies. We defined skin colour designations using a rigorous and objective approach, referencing colours that best matched our population's degree of skin colour. Our reference colours were noticeably lighter than those of Wainer *et al*. Consistent with their findings, we observed that TcB underestimated TSB in light and medium skin colour and overestimated it in dark skin colour with wide limits of agreement.[17] This reinforces the notion that transcutaneous devices should be used as a screening tool, in all infants, as opposed to being used at face value.[16 17 23 24]

For prespecified clinically important TSB cut-offs, we observed good discrimination for all skin colour subgroups. Our study shows that TcB cut-offs can be reliably generated in infants of different skin colour for prediction of clinically relevant TSB values. The cut-offs were fairly similar in light and medium skin colour and slightly higher for darker colour, for any given TSB value. This should be interpreted with the caveat that we did not have sufficient numbers to generate TcB cut-offs for TSB of 230 μmol/L in the light subgroup and had very few infants in the dark subgroup.

Evaluation of the diagnostic accuracy of TcB devices must be done in the context of analytical characteristics of the TSB comparator, both having improved substantially over the last 30 years. In 2008, Lo *et al*[25] reported considerable systematic error in bilirubin measurements across major instrument groups. Our laboratory monitors the performance of the Unistat Bilirubinometer through participation in the Ontario Quality Management Program Laboratory Services and the College of American Pathologists external quality assurance programmes. Quality Management Program Laboratory Services and College of American Pathologists surveys have shown an improvement in bilirubin assay performance across all methods in recent years, however systematic biases continue to exist and thus laboratories and neonatal care teams should work together to confirm the relationship between TcB and TSB measurements in their institution.

We acknowledge the following limitations: (1) our study is limited by the small number of dark and light skin colour infants with TSB >230 μmol/L; (2) the cut-offs proposed are for all infants ≥35 weeks, irrespective of other risk factors, therefore might not apply to higher risk infants; (3) we did not assess inter-rater reliability for skin colour assessment; despite trying to reduce subjectivity in skin colour assessment by having colour swatches, there remains a degree of subjectivity in assessment and (4) the colours chosen to determine skin pigmentation were noticeably lighter than those used by Wainer *et al*,[17] which may limit the generalisability of our findings.

CONCLUSION

Our study suggests that JM 103 is a reliable tool to identify infants in need for serum bilirubin testing, irrespective of skin colour. The effect of skin colour on the accuracy of this device at high levels of serum bilirubin could not be assessed fully due to insufficient numbers of infants in the light and dark colour groups.

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Contributors SS-Z collected data, contributed significantly to data interpretation, drafted the manuscript and approved the final version of the manuscript. JF participated in the conception and design of the study protocol, data collection and data interpretation. She critically revised the draft and approved the final version of the manuscript. KW analysed the data and contributed to data interpretation. She critically revised the draft and approved the final version of the manuscript. ASY analysed the data and contributed to data interpretation. He critically revised the draft and approved the final version of the manuscript. SLP participated in the conception and design of the study protocol, data collection and data interpretation. She critically revised the draft and approved the final version of the manuscript. BL participated in the conception and design of the study protocol, data collection and data interpretation. She critically revised the draft and approved the final version of the manuscript.

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Competing interests None.

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