Diagnosing Jaundice by Eye—Outpatient Assessment of Conjunctival Icterus in the Newborn

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In pediatric office practices, we compared transcutaneous bilirubin levels in 689 newborns, age 3-10 days, with and without conjunctival icterus. In this age range, and in the absence of other clinical or laboratory indications, the presence of conjunctival icterus does not imply the need to measure the transcutaneous bilirubin or serum bilirubin level, but the absence of conjunctival icterus helps to rule out significant hyperbilirubinemia. *(J Pediatr 2016;172:212-4).*

Visual inspection of the jaundiced newborn frequently does not provide a sufficiently accurate assessment of the bilirubin level to determine the need for additional measurement or intervention.[1] Some jaundiced infants also have yellow eyes. For many years, with one exception,[1] the deposition of bilirubin in the eye has been referred to in textbooks and journals as "scleral icterus," but, contrary to popular belief, this eye color is primarily the result of bilirubin deposition in the conjunctiva.[2,3] In a recent study of infants aged 7 days or less and hospitalized in the neonatal intensive care unit, Azzuqa and Watchko[4] found that >85% of infants with conjunctival icterus had a total serum bilirubin (TSB) ≥15 mg/dL and recommended that a TSB should be measured in these infants. As many, if not most, US hospitals routinely measure the transcutaneous bilirubin (TcB) or TSB on all newborns prior to discharge, the presence or absence of conjunctival icterus as a physical sign should now be most relevant for newborns seen in the outpatient setting. We compared TcB levels in newborns aged 3-10 days, with and without conjunctival icterus who are seen in office practices.

Methods

Between March and October 2014, we identified a convenience sample of 689 infants ≥35 weeks' gestation seen during 901 visits to 5 pediatric office practices and a hospital-based pediatric clinic.

Investigators were asked to include all healthy newborns returning for a routine follow-up office visit between ages 3 and 10 days. No patients were selected based on the presence or absence of jaundice. Demographic data (estimated gestational age, age at visit, sex, race) were recorded prospectively at each visit by the nurse on a data collection form. The study was approved by the hospital's Institutional Review Board with a waiver of consent because of the noninvasive nature of the assessments.

TcB	Transcutaneous bilirubin
TSB	Total serum bilirubin

Each office practice owned a Konica Minolta Draeger AirShields JM-103 transcutaneous jaundice meter (Draeger Medical, Telford, Pennsylvania) and performed the manufacturer's recommended electronic calibration daily. TcB measurements were routinely performed on all newborns less than 2 weeks old in each practice. At each visit, 3 midsternum TcB measurements were obtained by a nurse, and the infant was then examined by a physician, blinded to the TcB, for the presence or absence of conjunctival icterus. The TcB screening protocol called for 3 independent TcB measurements, and the highest of the 3 was used to determine whether or not to obtain a TSB.[5] Although some infants had several visits, only the highest TcB measurement and corresponding conjunctival icterus assessment were analyzed for each infant.

Statistical Analyses

Simultaneous 95% CI for the proportion of infants with measured maximum TcB in specified nonoverlapping intervals were obtained separately for infants with and without conjunctival icterus using Goodman's Bonferroni based procedure for multinomial proportions based on Blyth-Still-Casella CIs (Cytel Inc, Cambridge, Massachusetts). The SAS System for Windows v 9.3 (SAS Institute, Cary, North Carolina) was used for other statistical analysis and Minitab (Minitab Inc, State College, Pennsylvania) was used for the **Figure**.

Results

The study population was 76% white, 14% black, 6% Asian, and 4% other. Conjunctival icterus was present in 308 (45%) and absent in 381 (55%). There was a statistically significant

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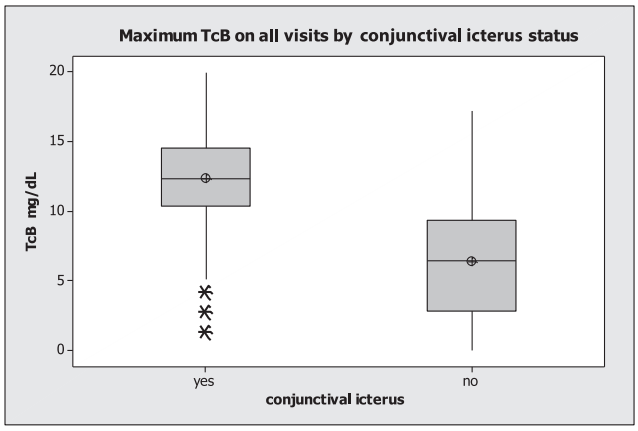

Figure. Box plot showing the median, 25th and 75th percentiles of the TcB by conjunctival icterus status. xxx = outliers.

but clinically unimportant difference in mean gestational age and age at visit between the groups (**Table I**; available at www.jpeds.com). Conjunctival icterus was seen more often in Asian infants (69%) than in white (44%) and black (36%) infants (P = .001), but Asian infants also had higher TcB levels (11.4 ± 3.7 mg/dL) compared with white infants (8.6 ± 4.7) and black infants (9.3 ± 5.2). Infants with conjunctival icterus tended to have higher TcB values than those without conjunctival icterus (**Figure**). **Table II** provides the frequency of various nonoverlapping TcB ranges in the presence or absence of conjunctival icterus: 41.2% (95% CI 35.8%-46.9%) of infants with conjunctival icterus had a TcB ≥13 mg/dL, and 19.8% (95% CI 15.7%-24.5%) a TcB ≥15 mg/dL, but 20.4% (95% CI 16.0-25.2) had a TcB <10 mg/dL. In infants with no conjunctival icterus, only 4.5% (95% CI 2.6-6.9) had a TcB ≥13 mg/dL, and 1.8% (95% CI 0.9-3.7) had a TcB ≥15 mg/dL.

Table III (available at www.jpeds.com) gives the frequency of conjunctival icterus in the specified TcB intervals. Conjunctival icterus was observed for some infants with a TcB value <10, although a majority of these infants do not have conjunctival icterus. In all of the specified TcB ranges ≥10 mg/dL, a majority of the infants have conjunctival icterus.

Table II. Distribution of maximum TcB levels based on presence or absence of conjunctival icterus (all races)

TcB mg/dL	Conjunctival icterus present % (95% CI)*, n = 308	Conjunctival icterus absent % (95% CI)*, n = 381
<5	1.0 (0.1, 3.5)	37.8 (31.3, 44.6)
5-9.9	19.5 (14.0, 25.9)	42.8 (36.1, 49.6)
10-12.9	38.3 (31.2, 45.9)	15.0 (10.5, 20.3)
13-14.9	21.4 (15.6, 28.0)	2.6 (1.1, 5.5)
15-16.9	13.3 (8.8, 19.1)	1.3 (0.3, 3.7)
≥17	6.5 (3.5, 11.0)	0.5 (0.03, 2.3)

*Goodman simultaneous CIs.

Discussion

Although previously commonly referred to as scleral icterus (with the exception of the study by Moyer et al[1]), Kuiper,[2] and Tripathi and Sidrys[3] have documented that the yellow color seen in the eyes of jaundiced adults is the result of bilirubin deposition in the conjunctiva and not in the avascular sclera.[3] In an unselected population of infants, aged 3-10 days, seen in office practices, we saw conjunctival icterus in 45%, and found that most (59%) infants with conjunctival icterus had a TcB <13 mg/dL. Thus, although infants with conjunctival icterus tend to have higher TcB values than those without conjunctival icterus (**Figure**), the presence of conjunctival icterus in infants of this age does not appear to be a reliable indicator of significant hyperbilirubinemia. On the other hand, in the absence of conjunctival icterus, only 0.5% (0.03-2.3) have a TcB ≥17 mg/dL and 1.8% (0.9-3.7) a TcB ≥15 mg/dL. Thus, the absence of conjunctival icterus is a relatively informative sign that can help to rule out significant hyperbilirubinemia, particularly when the measurement of TSB or TcB is not readily available.

Our results differ from the observations of Azzuqa and Watchko.[4] They studied 2 cohorts of 120 term and late preterm infants no more than a week old admitted to their neonatal intensive care unit with TSB levels ≥10 mg/dL. In the first cohort, in which the examiners were not blinded to the TSB levels, no infant with a TSB 10-14.9 mg/dL had conjunctival icterus. In the second cohort, when the examiner was blinded to the TSB, only 5/76 (7%) infants with a TSB 10-14.9 mg/dL had conjunctival icterus and 31/36 (86%) of those with conjunctival icterus had TSBs ≥15 mg/dL. In our population, 184/251 (73%) infants with TcBs 10-14.9 mg/dL had conjunctival icterus as did 63/370 (17%) of those with TcBs <10 mg/dL. We do not have a ready explanation for the lack of agreement in these observations except for the difference in the study populations, the reason for assessing the presence or absence of conjunctival icterus, and the difference in the type of bilirubin measurement. Azzuqa and Watchko[4] studied a relatively small, selected, infant population, some of whom were readmitted for hyperbilirubinemia. All their examiners looking for conjunctival icterus, including those blinded to the TSB, knew that every infant had a TSB of at least 10 mg/dL. The infants in our study were not seen because they were jaundiced. They were part of a large and unselected population of healthy newborn infants, seen for routine follow-up following hospital discharge, in 5 pediatric office practices and a hospital-based clinic. They were assessed for the presence or absence of conjunctival icterus by pediatricians or, in the case of the hospital-based clinic, by residents, all of whom were blinded to the TcB level. Surprisingly, only 32% of the infants in the Azzuqa and Watchko[4] study were diagnosed with conjunctival icterus compared with 45% of our population. Because of the patient selection, as noted above, this is the opposite of what would be expected in these 2 studies, but might be explained by interobserver variability. Although Azzuqa and