Simplifying Hyperbilirubinemia Risk Estimation

Laura R. Kair, MD, MAS, Carrie A. Phillipi, MD, PhD

Jaundice impacts more than half of term and late preterm newborns in the first week of life. Although in most cases, jaundice is benign, the consequences of severe hyperbilirubinemia are debilitating; thus, identification of newborns likely to exceed bilirubin treatment thresholds is needed. The American Academy of Pediatrics (AAP) recommends stratification of predischarge total serum bilirubin (TSB) levels by using the Bhutani Nomogram to help determine the appropriate timing of newborn follow-up. A separate nomogram is then used to determine if an infant meets criteria for phototherapy.

Kuzniewicz et al2 aim to simplify the process and more precisely determine when a newborn requires outpatient follow-up for jaundice with a simple equation. Starting with a retrospective cohort study of a diverse sample of 148,162 newborns born at ≥35 weeks’ gestation at 11 Kaiser Permanente Northern California facilities from 2012 to 2017, the researchers identified newborns whose TSB measurements did not exceed phototherapy levels and did not receive phototherapy during the birth hospitalization. Using the newborn’s last TSB value before hospital discharge (predischarge TSB), the authors calculated the difference between the predischarge total serum bilirubin and the corresponding American Academy of Pediatrics phototherapy threshold (in milligrams/deciliter) (Δ-TSB). Newborns who required phototherapy after discharge were identified. The authors compared the ability of the Δ-TSB model to predict postdischarge TSB above phototherapy thresholds to the Bhutani Nomogram. Examining additional variables, they also compared a more complicated Δ-TSB-Plus model. Although all 3 models performed well for those at highest and lowest risk of subsequent severe hyperbilirubinemia, both Δ-TSB and Δ-TSB-Plus models differentiated newborns in the intermediate zones better than the Bhutani Nomogram. Forty-four percent of newborns in Bhutani’s high-intermediate risk zone (who would have follow-up recommended within 48 hours) had a Δ-TSB between −4 and −5 mg/dL. In these newborns, the risk of ever having a subsequent TSB measurement greater than the AAP threshold was only 1.6%, suggesting follow-up within 48 hours might not be indicated.

The Δ-TSB measurements used in this study relied on clinician discretion in follow-up; therefore, the predictive accuracy of the Δ-TSB models may be inflated because of differential verification bias as the authors mention. Only TSB measurements were included, but many hospitals and clinics use transcutaneous bilirubinometry.3 Although one can extrapolate the Δ-TSB for low bilirubin levels, the additional uncertainty involved when transcutaneous bilirubin measurements are used to approximate TSB levels has the potential to impact effective implementation of the Δ-TSB risk prediction approach.4 The 2004 AAP bilirubin thresholds were used in this study, but some clinicians caring

"Department of Pediatrics, University of California, Davis, Sacramento, California; and "Department of Pediatrics, Oregon Health & Science University, Portland, Oregon

Opinions expressed in these commentaries are those of the authors and not necessarily those of the American Academy of Pediatrics or its Committees.

DOI: https://doi.org/10.1542/peds.2020-046284

Accepted for publication Feb 17, 2021

Address correspondence to Laura R. Kair, MD, MAS, Department of Pediatrics, University of California, Davis, 2516 Stockton Blvd, Ticon II, Room 341, Sacramento, CA 95817. E-mail: lrkair@ucdavis.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1089-4275).

Copyright © 2021 by the American Academy of Pediatrics

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: Dr Kair’s effort was supported by a Building Interdisciplinary Research Careers in Women’s Health award (2K12HD051958) awarded to principal investigator Nancy Lane, MD, funded by the National Institute of Child Health and Human Development, Office of Research on Women’s Health, Office of Dietary Supplements, and the National Institute of Aging. This work was also supported by the Center for Advancing Translational Sciences and the National Institutes of Health through grant UL1 TR001860. The contents of this publication are solely the responsibility of the authors and do not represent the official views of the National Institutes of Health, the National Institutes of Health, or the National Institutes of Health, or the National Institutes of Health. Funded by the National Institutes of Health (NIH).

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

COMPANION PAPER: A companion to this article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-019778.
for the patients studied may have followed other recommendations. For example, if the Northern California Neonatal Consortium criteria were used, some newborns may not have received a TSB assessment. Because nearly half of treated newborns were provided home phototherapy, we suspect their bilirubin levels were close to AAP thresholds. Clinicians may want to understand which newborns returned with bilirubin levels nearing or exceeding exchange thresholds and if they were predictable; these data were not provided. Given the wide range of gestational ages in the AAP phototherapy risk strata (35–38 weeks; >38 weeks), a more delineated approach by gestational age and sex would be helpful because we know lower gestational age and male sex contribute to a higher risk of hyperbilirubinemia. An implementation study across different health systems will improve the generalizability of the Δ-TSB strategy.

Despite any limitations, this study could have significant impact on the experience of care for new families and curb health care overuse. Currently, the AAP Bright Futures Guidelines recommend timing the initial newborn posthospitalization continuing care visit within 3 to 5 days after birth and 48 to 72 hours after discharge. This recommendation is based primarily on concern for jaundice and feeding problems leading to excessive weight loss. Select newborns could be discharged at 24 hours rather than 48 hours given this new evidence supporting an enhanced understanding of bilirubin trajectories. Some newborns with intermediate risk could safely defer in-person follow-up through weekends, holidays, and inclement weather days, whereas others may avoid daily outpatient bilirubin sampling with more optimally timed follow-up. This research also highlights, with large numbers, how truly low risk some newborns are for developing significant hyperbilirubinemia. With increasing adoption of telemedicine, those newborns who are also at low risk of feeding problems could be safely cared for in their homes.

ACKNOWLEDGMENT
We thank Arthur Jaffe, MD, for reviewing and editing this commentary.

ABBREVIATIONS
AAP: American Academy of Pediatrics
TSB: total serum bilirubin
Δ-TSB: difference between the predischarge total serum bilirubin and the corresponding AAP phototherapy threshold (in milligrams/deciliter)

REFERENCES
Simplifying Hyperbilirubinemia Risk Estimation
Laura R. Kair and Carrie A. Phillipi
Pediatrics 2021;147;
DOI: 10.1542/peds.2020-046284 originally published online April 26, 2021;

Updated Information & Services
including high resolution figures, can be found at:
http://pediatrics.aappublications.org/content/147/5/e2020046284

References
This article cites 8 articles, 5 of which you can access for free at:
http://pediatrics.aappublications.org/content/147/5/e2020046284#BIBL

Subspecialty Collections
This article, along with others on similar topics, appears in the following collection(s):
Fetus/Newborn Infant
http://www.aappublications.org/cgi/collection/fetus:newborn_infant_sub
Hyperbilirubinemia
http://www.aappublications.org/cgi/collection/hyperbilirubinemia_sub

Permissions & Licensing
Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
http://www.aappublications.org/site/misc/Permissions.xhtml

Reprints
Information about ordering reprints can be found online:
http://www.aappublications.org/site/misc/reprints.xhtml
Simplifying Hyperbilirubinemia Risk Estimation
Laura R. Kair and Carrie A. Phillipi
Pediatrics 2021;147;
DOI: 10.1542/peds.2020-046284 originally published online April 26, 2021;

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://pediatrics.aappublications.org/content/147/5/e2020046284