


Knowledge, Attitudes, and Behaviors of Pediatric Primary Care Providers on Management of Cholestasis

Global Pediatric Health
Volume 6: 1–7
© The Author(s) 2019
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/2333794X19829757
journals.sagepub.com/home/gph


Timothy Joseph Menz, MD^{1,2} , Michael Herzlinger, MD^{1,2},
Albert Ross, MD^{1,2}, and Mark R. Zonfrillo, MD, MSCE³

Abstract

Biliary atresia is a common cause of cholestasis in infants and is a time-sensitive diagnosis. A survey was distributed to pediatric primary care providers in order to assess variations in diagnosis and management of cholestasis. Participants were identified from physician parent groups on social media and regional pediatric residency programs. Information on knowledge and interpretation of screening tests, past experience/behavior, confidence, and comfort level managing cholestasis, as well as demographic information was collected. Out of 116 eligible respondents, 94.8% were confident in diagnosing hyperbilirubinemia but only 10.3% knew the biochemical definition of direct hyperbilirubinemia. Of the 56% of providers who had some knowledge of the guidelines, 18.5% stated the guidelines changed the way they evaluate cholestasis. These results demonstrate a gap in knowledge of diagnosing and evaluating cholestasis, which could provide the framework for standardized screening, leading to earlier identification of biliary atresia.

Keywords

biliary atresia, cholestasis, pediatric primary care, quality improvement

Received December 1, 2018. Received revised December 9, 2018. Accepted for publication December 20, 2018.

Introduction

Jaundice is a common clinical finding in the neonatal period (infants <28 days old) and is a normal finding in most newborns within the first 2 to 3 days of life. However, jaundice present at <24 hours or >14 days old, especially in a formula-fed infant, is concerning for pathologic causes and warrants further evaluation. Jaundice can be due to conjugated (direct) or unconjugated (indirect) hyperbilirubinemia. Conjugated hyperbilirubinemia is uncommon and usually caused by impaired bile acid flow and conjugated bilirubin excretion into bile, also known as cholestasis. Presence of cholestasis indicates hepatobiliary dysfunction and is diagnosed by elevated serum direct bilirubin levels. Hyperbilirubinemia in newborns >35 weeks' gestation is defined as total bilirubin level >95th percentile,^{1,2} whereas direct hyperbilirubinemia (a surrogate marker of cholestasis) is defined as a serum level >1.0 mg/dL (17 mmol/L) in the setting of an elevated serum total bilirubin level.^{3,4}

In a newborn with concern for cholestatic jaundice, urgent evaluation and/or referral is imperative as appropriate intervention can have an impact on clinical outcome. Biliary atresia (BA) is the most common identifiable cause of cholestatic jaundice and indication for liver transplant in children.⁵ The treatment for BA is Kasai portoenterostomy, and in the United States, most infants undergo this procedure after 60 days of life.^{5,6} This surgery performed in infants <60 days old results

¹Division of Pediatric Gastroenterology, Hasbro Children's Hospital, Providence/Rhode Island Hospital, RI, USA

²Department of Pediatrics, Alpert Medical School of Brown University, Providence, RI, USA

³Departments of Emergency Medicine and Pediatrics, Alpert Medical School of Brown University, Providence, RI, USA

Corresponding Author:

Timothy Joseph Menz, 758 Barossa Valley Dr NW, Concord, NC 28027, USA.

Email: tim.menz@gmail.com



in better outcomes, specifically improved survival with native liver.^{5,7}

In the continental United States, BA has a prevalence of 1/12,000 to 1/19,500 live births and an incidence of 6.5/100,000 to 7.5/100,000 live births.^{8,9} Diagnosing BA relies on persistently elevated serum direct bilirubin levels and a history of acholic stools. Although direct bilirubin levels are also elevated shortly after birth and remain elevated on subsequent laboratory draws,^{10,11} clinical presentation varies. Screening for BA is challenging as there are no screening guidelines that currently exist in the United States and results of previous scoring systems have been suboptimal.¹²⁻¹⁴ Stool cards have shown promising results in Taiwan and British Columbia^{15,16}; however, lack of standardized screening in the United States provides a challenge to pediatric primary care providers as to the best way to manage and diagnose cholestasis.

The North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) recently published updated guidelines on the evaluation of cholestatic jaundice in infants. Historically, clinical practice guidelines have not had a significant effect on changing how providers practice.^{17,18} It is important that community pediatric primary care providers are aware and familiar with these guidelines as a systematic approach when evaluating for cholestasis can help shed light on the cause of delay in the diagnosis of BA.

Methods

The study was designed as a cross-sectional electronic survey, approved by the Institutional Review Board at Rhode Island Hospital. Questions were developed based on the cholestatic jaundice guidelines published by members of NASPGHAN/ESPGHAN and reviewed by pediatric gastroenterologists at our institution for accuracy and functionality prior to distribution. Study participants were identified from regional pediatric residency programs in Rhode Island, Connecticut, and Massachusetts, as well as through the physician parent Facebook groups, Physician Moms' Group, and Physician Dads' Group (Figure 1). Requirements to join either group involves verification by a current member and he or she must hold a medical degree (MD/DO/MBBS). Further verification is also performed through other professional social media accounts (Doximity, LinkedIn). Physician Moms' Group also requires applicants to submit credentials (photo badge, medical school diploma, and residency training certificate). The electronic survey was designed using

REDCap software.¹⁹ Ethics approval was not required and consent for participation was implied by completion of the survey. After the initial email inviting providers to participate in the survey, there was 1 reminder email sent 2 weeks later. Participants were excluded if they were not a pediatric primary care provider taking care of infants <28 days old.

The survey contained 20 questions and required less than 5 minutes to complete. There was no incentive to participate (survey available online as Supplementary Material). The survey included multiple-choice and Likert-type scale questions. Information on knowledge and interpretation of appropriate screening tests, past experience/behavior, and confidence/comfort level managing cholestasis, as well as demographic information was collected. Providers were also asked their level of knowledge regarding the recently published guidelines on cholestatic jaundice by NASPGHAN and ESPGHAN. At the completion of the survey, providers were directed to a 1-page summary of the guidelines on cholestatic jaundice and a link to the full article (available online as Supplementary Material).

Data were compiled and analyzed through the REDCap software program to characterize the overall study population. No identifying information was connected to the surveys.

Ethics Approval and Informed Consent

This study was approved by the Institutional Review Board at Rhode Island Hospital. Ethics approval was not required and written consent was waived by the institutional review board as the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. All subject information was deidentified and subjects had the option to stop participation at any point if they found any questions offensive or disturbing. Knowledge, attitudes, and practice were not disclosed to departmental chairs or clinical supervisors. Completion of the survey served as consent to participate in the study.

Results

There were 128 total respondents, 12 who were ineligible to participate based on the initial survey question asking if the participating provider cared for infants younger than 28 days old, resulting in 116 eligible responses. Demographics of the 116 eligible participants is illustrated in Table 1. Providers participating in the survey were from varying practice settings with <2% from health maintenance organizations or representing

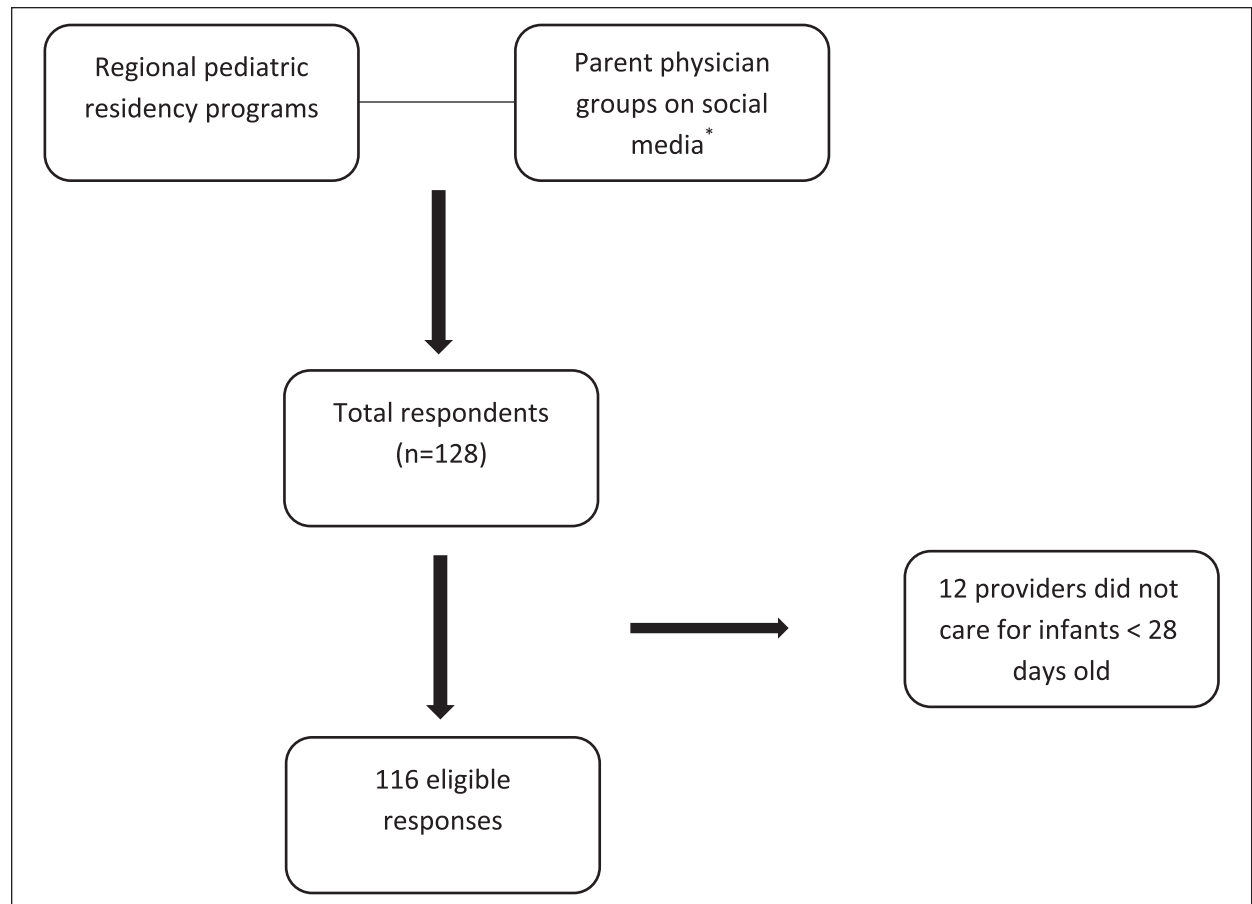


Figure 1. Survey participants.

*Facebook's Physician Moms' Group and Physician Dads' Group.

locum tenens. Most providers were from urban or suburban settings (78.4%). A majority of providers had been in practice for less than 5 years (48.7%) and were less than 45 years of age (84.4%).

Providers were asked 6 questions regarding past behaviors and patterns on diagnostic testing and medical knowledge regarding cholestasis (Table 2). A majority of providers felt that the most important condition to be ruled out in a newborn (<28 day old) with jaundice for >2 weeks duration is BA (80.2%). Most providers (73.3%) relied on a serum-fractionated bilirubin level when evaluating for possible cholestasis in a newborn, but not all agreed on the biochemical definition of direct hyperbilirubinemia (a surrogate marker of cholestasis). A total of 89.7% of providers were familiar with the biochemical definition of direct hyperbilirubinemia; however, 63.8% believed it to be defined as >20% of the serum total bilirubin and 25.9% defined it as a direct bilirubin >1.0 mg/dL. Most providers were appropriately concerned about jaundice if present at 1 to 2 weeks

of age regardless of diet (62.9%) and 44.3% of providers always saw infants for a 4-week follow-up while only 54.7% always or often saw infants for a 4-week follow-up. A majority of providers (63.8%) believed that surgery for BA improved outcomes if performed before 60 days of life; however, 30.2% of providers did not know at what age surgery should be performed once BA is diagnosed.

Providers were asked if they were confident/comfortable evaluating, diagnosing, and managing cholestasis using a Likert-type scale from 1 ("strongly disagree") to 5 ("strongly agree"; Table 3). A total of 94.8% of providers who participated in the survey were confident in diagnosing hyperbilirubinemia but only 70.7% were confident on what tests to order to assess for cholestasis. Of the survey respondents, 87.1% were comfortable interpreting the serum-fractionated bilirubin level but 28.5% and 17.8% of providers were not comfortable determining if stool is acholic or knowing when to refer to pediatric gastroenterology, respectively.

Table 1. Demographics.

Respondents (N = 116)	Percentage
Practice setting ^a	
Hospital-based practice	39.5
Community health center	15.8
Health maintenance organization	0.9
Multispecialty group	6.1
Single specialty group	19.3
Solo (private) practice	15.8
Locum tenens	1.7
Other ^b	0.9
Practice location	
Rural	12.1
Urban	37.9
Suburban	40.5
Underserved	7.8
Other ^c	1.7
Years in practice	
<5 years	48.7
5-9 years	21.7
10-20 years	23.5
Age, years	
>20	6.1
≤34	40.0
35-44	44.4
45-54	11.3
55-64	4.3
65-74	0
≥75 years	0

^a114 responses.^b1 Indian Health Service and 1 Military Health Clinic.^c1 academic center that serves both rural and small urban area and 1 Military Health Clinic.

Knowledge of the NASPGHAN/ESPGHAN guidelines on cholestatic jaundice was assessed using a Likert-type scale ranging from 1 (no knowledge at all) to 5 (very knowledgeable). Fifty-six percent of providers had some knowledge of the guidelines (Likert “2” or greater) and 44% had no knowledge at all (Figure 2). Of the providers who had some knowledge of the guidelines, only 18.5% stated the guidelines changed the way they workup cholestasis.

Discussion

Based on the responses, results demonstrate an overall gap in knowledge regarding the guidelines on cholestatic jaundice. Before completing the survey, only 56% of providers were familiar with the NASPGHAN/ESPGHAN guidelines on cholestatic jaundice. These results are suboptimal as pediatric primary care providers are responsible for the timeliness of workup and

Table 2. Provider Patterns Working up Cholestasis.

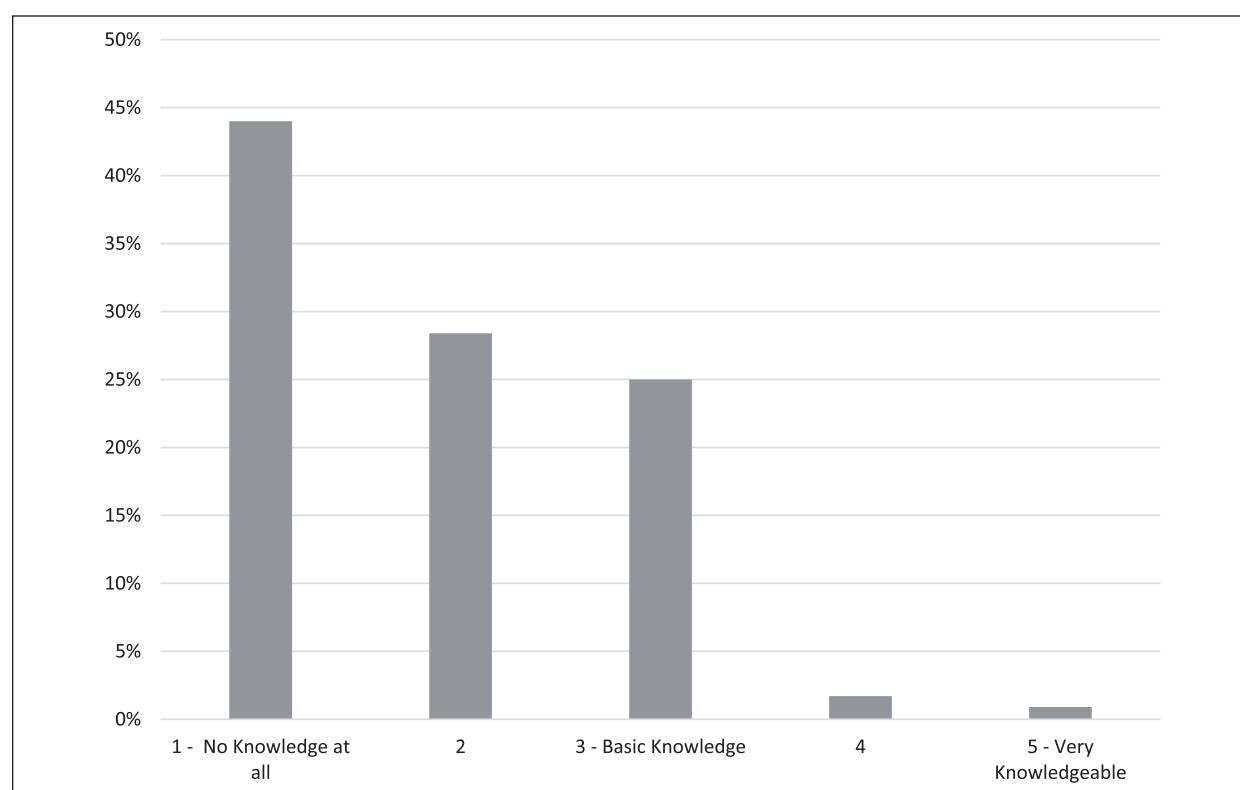
Provider Patterns	Percentage
What condition needs to be ruled out first in a newborn (<28 days old) with jaundice for >2 weeks duration?	
Bile acid synthetic defects	0.9
Biliary atresia	80.2
Breastfeeding jaundice	2.6
Breast milk jaundice	9.5
Choledochal cyst	0.9
Kernicterus	4.3
Obstructive gallstones	0.9
Other ^a	0.9
What screening tool do you rely on most when evaluating for possible direct hyperbilirubinemia (cholestasis) in a newborn (<28 days old)?	
Abdominal ultrasound	14.7
Hepatobiliary scintigraphy (HIDA)	10.3
Serum-fractionated bilirubin	73.3
Other ^b	1.7
What do you consider the best definition of direct hyperbilirubinemia (cholestasis)?	
Direct bilirubin >20% total bilirubin	63.8
Direct bilirubin >1.0 mg/dL	25.9
I am not familiar with the biochemical definition of direct hyperbilirubinemia (cholestasis)	8.6
Other ^c	1.7
After how many weeks of prolonged jaundice, starting on day 1, would you be concerned about a pathologic underlying cause?	
1 week	10.3
2 weeks	52.6
3 weeks	19.8
4 weeks	17.2
How often do you see newborns for a 4-week visit?	
Never	5.2
Rarely	17.4
Sometimes	22.6
Often	10.4
Always	44.3
Current evidence shows that outcomes for biliary atresia are improved if surgery is:	
Performed before 30 days of life	23.3
Performed before 45 days of life	12.9
Performed before 60 days of life	27.6
Performed before 90 days of life	6.0
I do not know what age surgery should be performed in a patient with biliary atresia	30.2

Abbreviation: HIDA, hepatobiliary iminodiacetic acid.

^aDid not have enough clinical information to answer question.^b2 respondents did not know.^c1 respondent wrote >2 mg/dL and 1 respondent left the field blank.

Table 3. Confidence Regarding Workup for Cholestasis.

Management Decision	% Selecting 4 or 5 (Confident or Comfortable in Management Decision) on a 5-Point Likert-Type Scale
Diagnosing neonatal hyperbilirubinemia	94.8
Managing neonatal hyperbilirubinemia	81.1
What tests to order to assess infants with jaundice for direct hyperbilirubinemia (cholestasis)	70.7
Interpreting the serum-fractionated bilirubin level	87.1
Determining if stool is acholic (pale or clay-colored)	71.5
When to refer to Pediatric Gastroenterology	82.2

**Figure 2.** Knowledge of NASPGHAN/ESPGHAN guidelines on cholestatic jaundice.

referral. For those providers who had some knowledge of the guidelines, a majority (>80%) did not report that the guidelines changed the way they evaluate cholestasis. This is problematic but is not an uncommon phenomenon. Petrova et al demonstrated that although the majority of a cohort of pediatricians in New Jersey were adherent to the 1994 guidelines on the management of neonatal hyperbilirubinemia developed by the American Academy of Pediatrics (AAP), there was variability in screening, follow-up, and treatment strategies.²⁰ Profit et al also discovered a wide variety in adherence to the 2004 AAP guidelines on management

of severe hyperbilirubinemia in healthy full-term infants, resulting in delayed follow-up.²¹

The variability of medical knowledge, diagnostic testing, and management of cholestasis, as illustrated in this study, can have a profound effect on the timing of diagnosing BA. Although the majority of providers felt that BA was the most important condition that needed to be ruled out after 2 weeks of prolonged jaundice, almost one third of providers did not know at what age surgery should be performed once BA is diagnosed. This lack of knowledge minimizes the sense of urgency, which can lead to a delay in BA diagnosis. A total of 87.1% of providers were

comfortable interpreting the serum-fractionated bilirubin level but only 70.7% of providers were confident on what tests to order, highlighting another gap in knowledge as serum-fractionated bilirubin level is the first screening test for a newborn with prolonged jaundice based on the NASPGHAN/ESPGHAN guidelines. Even in the cases with confident pediatricians as the survey results demonstrate, evaluation for cholestatic jaundice remains variable with areas of deficits that need improvement. The fact that 28.5% of providers were not comfortable determining if stool was acholic again reemphasizes the importance of increasing awareness of the guidelines as this is a key finding when investigating for cholestasis.

This study did have its limitations. First, the lack of monetary incentive or continuing medical education offered could have limited the respondents. Similarly, there could have been a selection bias favoring providers who are more, or less, interested and knowledgeable about hyperbilirubinemia and cholestasis. A majority of respondents were younger than 45 years of age suggesting an increased comfort level with technology, web-based surveys, and/or social media in this younger age group. Additionally, there is always potential for various interpretations regarding the language and terms used in each survey question, affecting providers' responses by not accurately reflecting their true thoughts or beliefs.

Screening for cholestasis is challenging but these results could potentially help identify areas of improvement to direct resources (distributing guidelines, identifying appropriate screening tools) in order to identify cholestasis earlier. Although our study did not evaluate patients with cholestasis or those diagnosed with BA, additional studies would be helpful comparing how knowledge of the guidelines on cholestatic jaundice affect the timing of testing, follow-up, and referrals. With increased awareness of the guidelines on cholestatic jaundice and appropriate timing of testing and referral, BA can be identified in a timely fashion, which can lead to improved outcomes including decreased morbidity, increased survival, and decrease in health care cost.

Author Contributions

TJM: Contributed to conception or design; contributed to acquisition, analysis, and interpretation of data; drafted the manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy

MH: Contributed to conception or design; contributed to acquisition, analysis, and interpretation of data; critically revised the manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

AR: Contributed to conception or design; contributed to acquisition of data; critically revised the manuscript; gave final

approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

MRZ: Contributed to conception or design; contributed to acquisition, analysis, or interpretation; critically revised the manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.


Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iD

Timothy Joseph Menz  <https://orcid.org/0000-0002-0239-3771>

Supplemental Material

Supplemental material for this article is available online.

References

1. 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.
2. 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.
3. Rosenthal P, Blanckaert N, Kabra PM, Thaler MM. Formation of bilirubin conjugates in human newborns. *Pediatr Res*. 1986;20:947-50.
4. Fawaz R, Baumann U, Ekong U, et al. Guideline for the evaluation of cholestatic jaundice in infants: joint recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition. *J Pediatr Gastroenterol Nutr*. 2017;64:154-168.
5. Superina R, Magee JC, Brandt ML, et al; Childhood Liver Disease Research and Education Network. The anatomic pattern of biliary atresia identified at time of Kasai hepatoportoenterostomy and early postoperative clearance of jaundice are significant predictors of transplant-free survival. *Ann Surg*. 2011;254:577-585.
6. Shneider BL, Brown MB, Haber B, et al; Biliary Atresia Research Consortium. A multicenter study of the outcome of biliary atresia in the United States, 1997 to 2000. *J Pediatr*. 2006;148:467-74.
7. Serinet MO, Wildhaber BE, Broué P, et al. Impact of age at Kasai operation on its results in late childhood and adolescence: a rational basis for biliary atresia screening. *Pediatrics*. 2009;123:1280-1286.

8. The NS, Honein MA, Caton AR, et al; National Birth Defects Prevention Study. Risk factors for isolated biliary atresia, National Birth Defects Prevention Study, 1997-2002. *Am J Med Genet A*. 2007;143A:2274-2284.
9. Wang KS; Section on Surgery; Committee on Fetus and Newborn; Childhood Liver Disease Research Network. Newborn screening for biliary atresia. *Pediatrics*. 2015; 136:e1663-e1669.
10. Harpavat S, Finegold MJ, Karpen SJ. Patients with biliary atresia have elevated direct/conjugated bilirubin levels shortly after birth. *Pediatrics*. 2011;128:e1428-e1433.
11. Harpavat S, Ramraj R, Finegold MJ, et al. Newborn direct or conjugated bilirubin measurements as a potential screen for biliary atresia. *J Pediatr Gastroenterol Nutr*. 2016;62:799-803.
12. El-Guindi MA, Sira MM, Sira AM, et al. Design and validation of a diagnostic score for biliary atresia. *J Hepatol*. 2014;61:116-123.
13. Sciveres M, Milazzo MP, Maggiore G. A scoring system for biliary atresia: is this the right one? *J Hepatol*. 2015;62:985-986.
14. Kim JR, Hwang JY, Yoon HM, et al. Risk estimation for biliary atresia in patients with neonatal cholestasis: development and validation of a risk score. *Radiology*. 2018;288:262-269.
15. Lien TH, Chang MH, Wu JF, et al; Taiwan Infant Stool Color Card Study Group. Effects of the infant stool color card screening program on 5-year outcome of biliary atresia in Taiwan. *Hepatology*. 2011;53:202-208.
16. Woolfson JP, Schreiber RA, Butler AE, et al. Province-wide biliary atresia home screening program in British Columbia: evaluation of first two years. *J Pediatr Gastroenterol Nutr*. 2018;66:845-849. doi:10.1097/MPG.0000000000001950
17. Cabana MD, Rand CS, Powe NR, et al. Why don't physicians follow clinical practice guidelines? A framework for improvement. *JAMA*. 1999;282:1458-1465.
18. Christakis DA, Rivara FP. Pediatricians' awareness of and attitudes about four clinical practice guidelines. *Pediatrics*. 1998;101:825-830.
19. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42:377-381.
20. Petrova A, Mehta R, Birchwood G, Ostfeld B, Hegyi T. Management of neonatal hyperbilirubinemia: pediatricians' practices and educational needs. *BMC Pediatr*. 2006;6:6.
21. Profit J, Cambric-Hargrove AJ, Tittle KO, Pietz K, Stark AR. Delayed pediatric office follow-up of newborns after birth hospitalization. *Pediatrics*. 2009;124: 548-554.