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Medical Education Content Required for Kernicterus Risk Recognition

Gláucia Macedo de Lima*, MD; Maria Amélia Sayeg Campos Porto, MD, and Antônio Ledo Alves da Cunha, MD

Institute of Pediatrics and Child Care Martagão Gesteira, Faculty of Medicine, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil

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Abstract

Objective: The objective of this study was to define the minimum academic content required for pediatricians to recognize the risk of kernicterus.

Methods: A questionnaire was developed on the basis of American Academy of Pediatrics guidelines seeking to develop a consensus for pediatricians in training on the theoretical content about neonatal hyperbilirubinemia. To validate the instrument, we used the Delphi consensus method. The 14 invited experts interviewed, eminent Brazilian researchers of neonatal hyperbilirubinemia, analyzed the questions posed in accordance with the literature and validated the instrument

Findings: An assessment instrument, the Student Questionnaire (SQ), was developed on the basis of indicators of risk of neonatal hyperbilirubinemia obtained from the literature. A panel of academic experts, composed of the leading researchers of neonatal hyperbilirubinemia in Brazil according to research rankings of the Brazilian government's Lattes Platform, was assembled for consensus validation of the assessment instrument. Validation of the SQ was achieved after two rounds of the Delphi technique. Finally, the SQ itself was validated with the medical education content required for recognition of kernicterus risk.

Conclusion: The consensus among experts stressed the need to identify the primary epidemiologic risk factors for significant hyperbilirubinemia associated with neonatal jaundice and to characterize risk of bilirubin encephalopathy according to the literature. The minimum capacity required of physicians in training is that they have the insight to consult the reference material specific to each clinical situation in which hyperbilirubinemia may be involved. The present study emphasized the need for knowledge of the four variables related to management of neonatal jaundice: gestational age, birth weight, infant age, and total serum bilirubin. This validated questionnaire can be a useful tool to prepare pediatricians to recognize the possibility of bilirubin encephalopathy in neonates and prescribe intervention as necessary.

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Key Words: Neonatal jaundice; Neonatal hyperbilirubinemia; Kernicterus; Delphi technique; Practice guideline

Introduction

Although the subject of neonatal hyperbilirubinemia is part of the curricular content of medical schools and graduate Pediatrics programs in Brazil, the current literature provides no clear proposals on how to practically teach physicians in training to manage the icteric newborn [4-6]. In 2004, a specialized Committee of the American Academy of Pediatrics (AAP) published a guideline reviewing the matter [1-3].

Due to the metabolic peculiarities of the newborn child, hyperbilirubinemia is universally found in the first days of life. It can be difficult to

*** Corresponding Author;**
Address: Avenida Prefeito Dulcídio Cardoso, 1400, apt. 2203, block 1. Postcode: 22620-311. Barra da Tijuca. Rio de Janeiro RJ. Brazil
E-mail: lglaucia@globo.com

manage and, if not identified early and treated adequately, can carry a grim prognosis [3,4].

Given the current practice of discharging infants from maternity care at the 48th hour of life and the increased frequency of breastfeeding in response to breastfeeding encouragement strategies, physiological hyperbilirubinemia– which generally arises after the 72nd hour of life, - and may be exacerbated by breastfeeding – has come to present more intensely, and become a frequent reason for hospital readmission after maternity discharge [3,4-6].

The AAP stresses the particular importance of looking for risk factors for hyperbilirubinemia or kernicterus in full-term or near-term neonates about to be discharged [3,7,8]

This study seeks to define specific theoretical content geared at guiding practical management of neonatal jaundice by producing a theoretical assessment instrument composed of practical items on the theme of neonatal indirect hyperbilirubinemia, with the following research question: "What is the minimal theoretical content required to give future pediatricians the capacity to recognize the risk of kernicterus in jaundiced neonates?"

Subjects and Methods

This study was structured as a descriptive survey leading to the development of an instrument that could answer its research question. The Delphi consensus method for expert-based questionnaire validation was used. In designing the questionnaire, we used the current literature to define key points for practice in the management of neonatal jaundice before discharge. These indicators were also tied in with the 2004 AAP guidelines [3,8,12].

One of the limitations of this method as used in our study is that experts were not included in the primary definition of these questions, only in their later discussion. We believed it would have been inappropriate to burden these busy experts with such an arduous and time-consuming task. They did, however, take part in assessing the form, content, and detail of each of the items presented.

Advantages of the Delphi method included the fact that isolated responses minimized the tendency for experts to influence one another, while maximizing our ability to discern distinctive opinions. Furthermore, the possibility of conducting the Delphi rounds via email made this a cost-effective and efficient method, saving time and money on data input and output [8].

Ten vignettes on the topic of neonatal hyperbilirubinemia were grouped and the questionnaire items prepared were validated by means of the Delphi method.

Information was sent to each expert separately. Each item was recorded on a report, which was resent to each expert for approval or rejection until a final consensus was obtained.

Delphi principles and corresponding methodological adaptation:

a) "Which indicators were selected for the questions to be formulated to explore the matter?" – questionnaire items
b) "Who are the experts, and where are they?" – selected experts
c) "Which technique will be applied?" – systematic Delphi stages
d) "What are the expected results?" – instrument validation.

Findings

The ten items of the Student Questionnaire (SQ) were as follows:

1) Epidemiological indicators of worsening hyperbilirubinemia; 2) predictors of risk of bilirubin encephalopathy; 3) visual clinical recognition of jaundice and its hazards; 4) correlation between clinical indicators of encephalopathy and progression to kernicterus; 5) laboratory assessment of pathological neonatal jaundice; 6) management of indirect hyper-bilirubinemia; 8) management of neonatal jaundice detected before the 48th hour of life; 9) diagnostic definition of neonatal jaundice at review (after discharge); 10) minimum systematic approach for recognition of kernicterus.

The Experts

Our pool of experts was composed of National Council for Scientific and Technological Development (CNPq) fellows conducting research on neonatal indirect hyperbilirubinemia who agreed to take part in the study. The criteria for expert selection used the Lattes Platform, an online database maintained by the Brazilian government and containing information on researchers and research institutions working in science, technology, and innovation in the country. The database was searched for medical school professors who had authored articles with the descriptors "neonatal jaundice", "newborn hyperbilirubinemia", or "neonatal indirect hyperbilirubinemia", published in indexed journals between 2002 and 2006. We invited the top 30 such authors (as of 2007) to take part in the study.

Of these, the first 15 to agree were selected to make up the expert panel; 14 remained on the panel until the end of the study.

Delphi Stages

The stages of SQ development, from concept to validation, were:

1) Production of questionnaire (target audience: pediatricians in training); 2) questionnaire sent to experts who agreed to take part; 3) consensus analysis of the first expert responses received; 4) modification of SQ and pilot study to assess item clarity; 5) second (modified) SQ sent to experts; 6) consensus report, concluding that the SQ was validated by the expert panel.

Instrument Validation

The target demographic of the measurement instrument comprised future pediatricians who were finishing medical school or had graduated from medical school no more than 6 months before responding to the questionnaire.

The SQ sent to the 14 selected experts for validation comprised ten items, or questions, of theoretical and practical relevance to "neonatal hyperbilirubinemia in the first days of life". All 12 items of the Expert Questionnaire or EQ (with item 8 subdivided into two, for a total of 13 questions) were designed to enable validation of the 10-item SQ. Experts were asked to measure the relevance and importance of proposed content; give their opinion as to whether content should be kept or changed, suggesting improvements as necessary; and give their opinion on whether additional relevant items should be included, or redundant items removed.

Expert validation of each SQ question focused on reviewing

1) instructions; 2) clarity; 3) subjectivity; 4) bias; 5) redundancy; 6) omission; 7) success (i.e., the potential for successful responses); 8) comprehensiveness in terms of a) hyperbilirubinemia and b) kernicterus; 9) overall comprehensiveness; 10) item weights; 11) relevance of content; 12) format/presentation (Fig. 1). The validated consensus on content, presentation, and qualification was pooled to become the overall consensus [2], obtained by means of the EQ (Table 1), which was used to define each SQ item as indispensable, important, or expendable and (based on presentation) whether each SQ item should be kept, modified, or removed.

On the basis of overall qualification of means and standard deviations of Likert-type assessments, each SQ item was defined as complete/perfect, fair, poor, or unacceptable. All comments made by experts during epidemiological assessment and validation of the SQ were taken into account. The literature framework for the 10 SQ items was combined with the comments made by the 14 experts to validate the instrument. Analysis enabled description of the mean (±standard deviation) as the likelihood of the statistical outcome. The consensus for final validation was thus defined.

Student Questionnaire (SQ)

The Delphi method proved effective in constructing a consensus expert opinion on the SQ after two rounds of study.

Discussion

Overall, the structure of the pilot version of the SQ was modified on the basis of the consensus expert decision that, when faced with difficulties in

Table 1: Consensus of expert questions (EQ) for validation of the Student Questionnaire (SQ)

CONSENSUS VALIDITY	1	2	3	4	5	6	7
Formative content* mean Q11- EQ	expendable/ no importance	very little importance	little importance	important	very important	extremely important	indispensable / of greatest importance
Formulation or presentation † mean Q12- EQ	remove	modify nearly everything	modify consi-derably	modify	modify little	modify very little	Keep
Qualification‡ MoM, 12/13 SQ Qs	unacceptable	very poor	Poor	not very adequate	good	very good	complete/ perfect
Overall mean for the 3 consensuses	unacceptable	very poor	Poor	not very adequate	good	very good	complete/ perfect
Adequacy‡ QMoM+MF>60%	not feasible	very poor	Poor	not very adequate	good	very good	complete/ perfect
Rtg. Variation # FM var. EQ Q. Rtg.	complete/ perfect	very good	Good	not very adequate	poor	very poor	Nonexistent

*mean of 14 experts' opinions regarding content, 10 SQ items/11 EQ items;
†mean of 14 experts' opinions regarding format, 10 SQ items/12 EQ items;
‡mean of means (MoM) for 14 experts' opinions regarding the 10 SQ items in the 12/13 EQ items;
‡final mean for numbers corresponding to the cumulative percentage >60% in the 10 SQ questions for each of the 12/13 EQ questions;
+ mean of means (MoM) for all opinions of all 14 experts regarding the 10 SQ items per response to the 12/13 EQ items.
#final mean or rating variation in EQ expert rating for the 10 SQ items. Here, the scale is inversely proportional: the fewer points (denoting less variation), the better the consensus.

management of neonatal jaundice, physicians should consult the relevant literature. This is particularly important in the study sample, which consisted of inexperienced young physicians or medical students, who still lack the expertise and discernment required to carry out risk assessment on the basis of clinical observation alone.

The present study took on a more instructional nature through the addition of reference material for assessment of hyperbilirubinemia risk, including hour-specific nomograms for hyper-

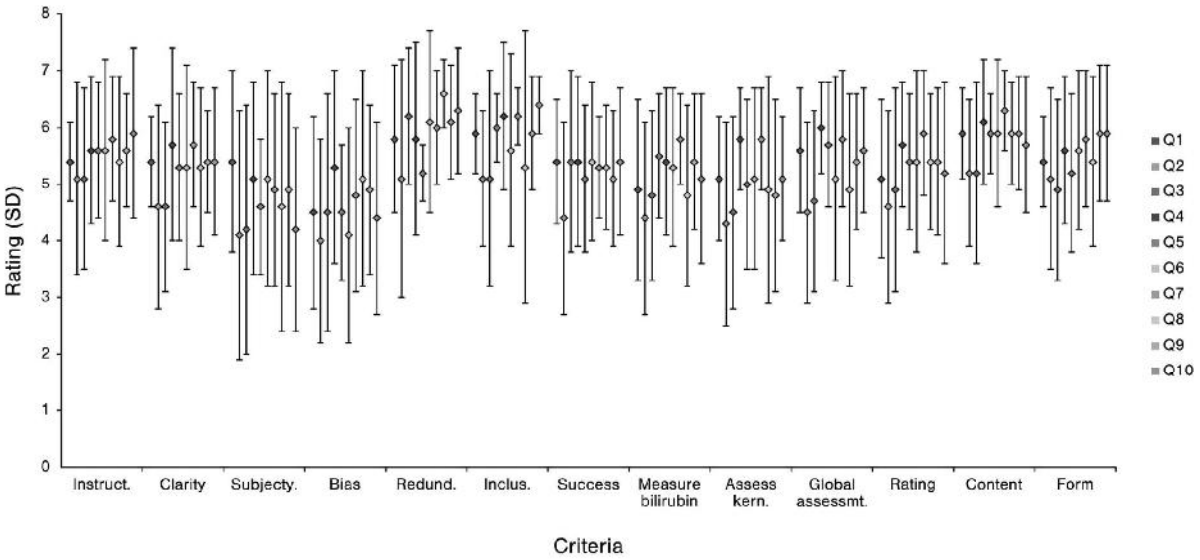

Fig.1: Expert validation of the 10-item Student Questionnaire (SQ); means and standard deviations of the 12/13-item Expert Questionnaire (EQ)

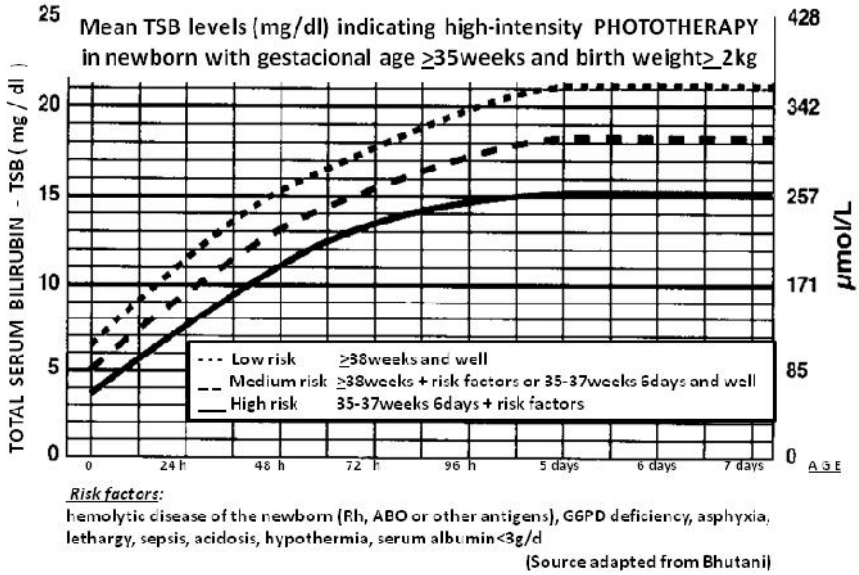

Fig. 2: Hour-specific nomogram of mean TSB levels (mg/dL) indicating high-intensity phototherapy in newborns with a gestational age ≥35 weeks and birth weight ≥2 kg

bilirubinemia, to the questionnaire. Of note, TSB, gestational age (GA), birth weight (BW), and age must always be recorded and presented for nomogram analysis.

Some unanimous expert suggestions were used to enrich the vignettes used in the questionnaire, but the material provided as background for contextualization of answers (Fig 2, 3 and Box 1) was based exclusively on AAP guidelines, which were, in turn, based on robust epidemiological data [15].

An example of risk characterization based on the SQ items and not on the references used to build the SQ was the mention of Kramer's rule. Although the caudal progression of clinical jaundice is not a proven prognostic indicator of severity, it was suggested during the expert validation process. Greater emphasis was afforded to the relevance of the difficulty of clinically observing jaundice during phototherapy, particularly in patients with darker skin and/or in the absence of natural lighting [16].

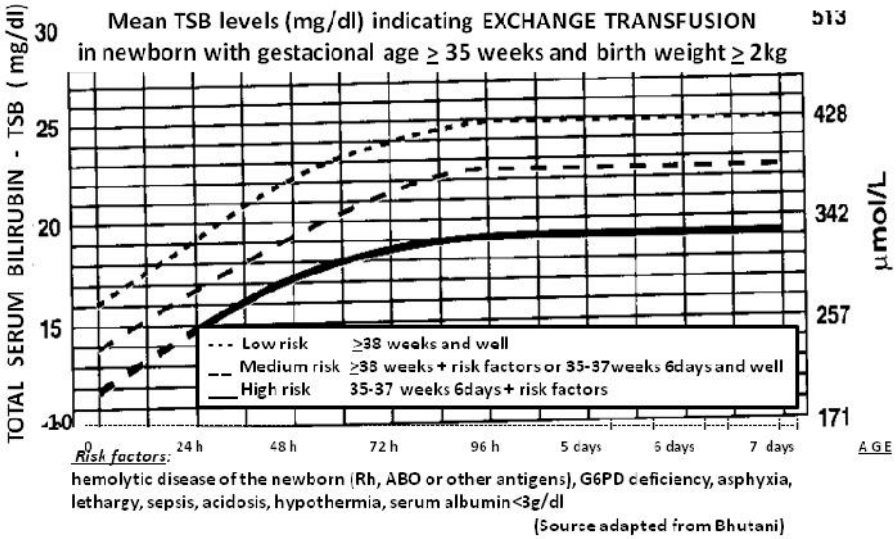

Fig. 3: Hour-specific nomogram of mean TSB levels (mg/dL) indicating exchange transfusion in newborns with a gestational age ≥35 weeks and birth weight ≥2 kg.

BOX 1: Epidemiological risk factors for worsening of significant hyperbilirubinemia in neonates with gestational age ≥35 weeks and birth weight ≥2 kg

GREATER RISK:	Total serum bilirubin (TSB) level in the high risk area of the hour-specific nomogram prior to discharge; gestational age between 35 and 36 weeks; jaundice in the first 24 hours of life; Rh incompatibility, positive Coombs test and other hemolytic disorders, such as ABO incompatibility and reduced glucose-6-phosphate dehydrogenase levels; siblings who required phototherapy at birth; cephalohematoma or ecchymosis; exclusive breastfeeding with supraphysiological weight loss, in excess of 10% in the first week of life; Asian ethnicity.
INTERMEDIATE RISK:	TSB level in the intermediate risk area of the hour-specific nomogram prior to discharge; gestational age between 37 and 38 weeks; macrosomic child born to diabetic mother; maternal age ≥25 years; male gender.
MINIMAL RISK:	TSB level in the low risk area of the hour-specific nomogram prior to discharge; gestational age >40 weeks; exclusively formula-fed; discharged after 72nd hour of life.

Experts noted the difficulty of assessing the risk of hyperbilirubinemia by visual observation of jaundice even when carried out by experienced neonatologists. In addition to the factors described in the AAP material, experts mentioned the need for careful assessment of the following neurotoxic factors for kernicterus: administration of drugs that compete with albumin binding of bilirubin (vitamin K, sulfas, ceftriaxone); and intracranial bleeding with increased cerebral blood flow. We note that the potential for adverse effects of high-dose synthetic vitamin K therapy was addressed years ago, and no longer poses any risk, as long as appropriate dosages are used [17,18].

The experts also stressed the importance of quantitating glucose-6-phosphate dehydrogenase (G6PD) whenever prolonged exposure to adequate phototherapy is unable to effect a reduction in hyperbilirubinemia, regardless of ethnicity or family history of G6PD deficiency [3,7,13].

Another point of emphasis was that "intensive phototherapy", defined as the use of high levels of irradiance – in the 430 to 490 nm range, 30μW/cm2/nm or higher – should be measured directly at the bassinet by a radiometer whenever indicated [3,14].

Expert suggestions were used to expand and adapt the SQ vignettes to the Brazilian reality.

For instance, in adapting the AAP guidelines to the Brazilian reality, we removed the need for notification of kernicterus to the CDC, as Brazil has no equivalent organization to receive this information. We also disregarded the possibility of transcutaneous bilirubin measurement, which would only be possible with bilirubinemia below 15 mg/dL [19]. The necessary equipment is ususlly not available in Brazilian care facilities.

Furthermore, the device mentioned in the AAP guidelines for measurement of ETCOC as it relates to hyperbilirubinemia is extremely costly, and used only in clinical research, thus making it a low

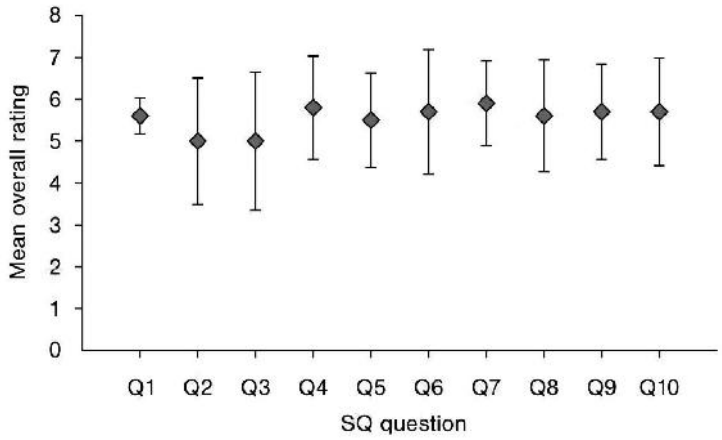

Fig. 4: Mean of means, consensus opinions of the 14 experts on the 10 SQ items

priority for acquisition in Brazil.

Another consensus comment was that, in the etiologic diagnosis of jaundice, one must stress that variations from birth weight upon follow-up exam generally coincide with a physiological weight reduction, which may be confused with low or inadequate infant feeding.

The last validated SQ question recommended a minimum response standard, focusing on diagnostic and therapeutic strategies applicable to healthcare professionals and to the caregivers of newborn infants, meant to address the repercussions of jaundice as early as the first days of life, using data from prenatal care and including intervention whenever necessary [18,20,21].

Our decision to recruit experts with teaching experience and applying their suggestions to a questionnaire administered to a sample of young physicians and medical students appears to have reached its primary objective: to develop an accurate, validated instrument for determination of the minimum theoretical content required to teach kernicterus risk assessment to physicians in training.

We humbly thank the 14 investigators who assisted in the construction of this instrument in their capacity as Brazil's foremost experts in neonatal hyperbilirubinemia.

Conclusion

In conclusion, the minimum theoretical content that must be part of medical education programs if pediatricians are to identify and address neonatal jaundice in an appropriate manner is mostly tied to building awareness of the epidemiological risk factors for indirect hyperbilirubinemia and of the potential risk characteristics for bilirubin encephalopathy, in light of the specific literature guidelines for clinical conduct analysis of each case.

The guidelines and rules for reference are those found in the literature, and must be made available in services that provide neonatal care. The minimum primary care capacity physicians must have is the discernment to consult reference materials specific to each clinical situation where hyperbilirubinemia may be involved.

This study places particular emphasis on knowledge of the four variables that should guide management of neonatal jaundice: gestational age at birth, birth weight, extrauterine age, and total serum bilirubin.

This validated questionnaire should prove a useful instrument, preparing pediatricians to recognize the possibility of bilirubin encephalopathy in susceptible neonates and to provide timely intervention whenever necessary.

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Conflict of Interest: None

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