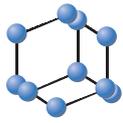


REVIEW ARTICLE


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SCIENCE**

Maternal Empowerment – An Underutilized Strategy to Prevent Kernicterus?

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Abstract: Background: Kernicterus is a common cause of death and morbidity in many Low-Middle-income Countries (LMICs) and still occurs in affluent nations. In either case, the immediate cause is delayed treatment of severe hyperbilirubinemia. In the West, a provider driven “systems approach” has been widely adopted to identify babies at risk prior to discharge from birthing centers with follow up monitoring based on the serum bilirubin level at time of discharge. The situation is more complicated in regions of the world where kernicterus is endemic, especially in LMICs where Glucose-6-phosphate Dehydrogenase Deficiency (G6PDd) is common and the system of jaundice management is often fragmented.

Objective: To examine reasons for errors in jaundice management leading to kernicterus and the potential beneficial role of enlisting more parental participation in management decisions.

Method: We searched world literature related to pitfalls in jaundice management including deficiencies in providers' and parents' knowledge and behavior. Perspectives from mothers of children with kernicterus supplemented the literature review.

Result: System failures contributing to kernicterus in affluent countries include a lack of follow up planning, bad advice by providers, and a delay in care seeking by parents. In many LMICs, the majority of births occur at home with unskilled attendants. Traditional practices potentiate hemolysis in G6PDd babies. The danger of severe jaundice is frequently underestimated both by parents and care providers, and cultural and economic barriers as well as ineffective therapies delay care seeking. The failure to provide parents information about identifying severe jaundice and knowledge about the risks and treatment of hyperbilirubinemia has contributed to delayed treatment in both affluent and low-middle-income countries. A recent non-randomized clinical trial, supports teaching all parents skills to monitor jaundice, signs of early neurotoxicity, the importance of breast feeding, avoidance of ineffective or dangerous practices, and when/where to seek help.

Conclusion: Empowering parents allow them to participate more fully in care decisions and to confront obstacles to care when provider services fail.

Keywords: Maternal empowerment, education, acute bilirubin encephalopathy, kernicterus, glucose-6-phosphate dehydrogenase deficiency.

1. INTRODUCTION

Kernicterus remains a major cause of neonatal death, cerebral palsy and hearing loss in Low-middle Income Countries (LMICs) [1-4], especially in regions with a high prevalence of glucose-6-phosphate dehydrogenase deficiency (G6PDd) [5-18] and out of hospital births [19-22]. In affluent nations, treatment with anti-D immunoglobulin has nearly eliminated Rh isoimmune hemolytic disease and close monitoring has led to early use of phototherapy, but kernicterus still occurs [23, 24].

In both LMICs and affluent countries the majority of babies with irreversible bilirubin encephalopathy are already affected at time of admission to institutions capable of treating severe hyperbilirubinemia [1, 25, 26]. A small number of babies develop irreversible encephalopathy post-admission because of delayed or inadequate treatment (ineffective phototherapy, inability to perform exchange transfusion). In all cases, timely care seeking, accurate assessment, and appropriate treatment are critical to favor a good outcome. This review explores whether providing instructions to mothers about diagnosing jaundice, avoiding dangerous ‘traditional’ and ineffective therapies, and recognizing signs of early bilirubin neurotoxicity will empower them to seek early care when jaun-

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dice is observed and, if needed, to challenge barriers to timely treatment.

2. A SYSTEMS APPROACH TO PREVENT SEVERE HYPERBILIRUBINEMIA

In 2002, Johnson *et al.* [27] promoted a “systems approach” to prevent kernicterus that has been adopted in most high resource countries to facilitate timely intervention of newborns with hyperbilirubinemia. Most newborn services now mandate pre-discharge screening for jaundice (visual documentation and/or transcutaneous or laboratory Total Serum Bilirubin (TSB) determinations) and recommend a follow up appointment based on clinical risks, age at discharge, the presence of jaundice before 24 hours of age, and projection of bilirubin levels using an hour specific nomogram [28-32]. These recommendations have been incorporated into management of jaundice consensus guidelines developed by medical societies in at least seven countries, most commonly by the American Academy of Pediatrics (AAP) in 2004 updated 2009 [33, 34] the National Institute for Health and Care Excellence (NICE), 2010 updated 2016, (<https://www.nice.org.uk/guidance/cg98>), and the Canadian Pediatric Society (2007) [35].

For the system to work, several conditions must be met. For hospital deliveries, risks for hyperbilirubinemia must be correctly determined prior to discharge and follow up appointments made at an appropriate post-discharge age. Care givers at follow up, be they visiting nurse, family physician, pediatrician, or physician extenders, must be aware that jaundice is not always benign, hyperbilirubinemia not always easy to estimate by physical findings, have a low threshold for measuring TSB either by clinical laboratory assay or transcutaneous monitoring, recognize early signs of acute bilirubin encephalopathy (ABE), and know when to refer for treatment. For home deliveries, early post-natal monitoring for jaundice and successful breastfeeding are critical, either in clinics or by home visits from health care providers. Successful management of patients with signs of severe hyperbilirubinemia or incipient ABE requires an efficient referral and transport network (including weekends), especially in rural or LMIC settings. Unfortunately, effective post-partum follow up infrastructures in many LMICs are either fragmented or nonexistent [3].

This system is primarily provider driven and managed. It works well when conducted according to plan, quite successful in health maintenance organizations [36, 37], but requires the coordination of all providers in the chain of care, skill, sound advice, as well as participation of parents. Waldrop *et al.* [38] found that educational intervention with medical providers in combination with a medical tool to facilitate clinical guidelines resulted in fewer infants discharged with bilirubin values in the high-risk zone and a 50% reduction of readmissions for hyperbilirubinemia during the first week. Notwithstanding the efforts to reinforce coordination of pre-discharge assessment and appropriate follow up in the West, the report card is not very reassuring [39-41]. Systematic pre-discharge evaluation and organized follow up is even

more fragmented in LMICs; a high percentage of home births, very early post-delivery discharge, and limited resources further challenge implementation of a systems approach.

At the receiving end, parents must have transportation resources and incentive to comply with follow-up appointments. Ontario, Canada introduced universal bilirubin screening in 2003, but compliance with scheduled follow up to assess jaundice, although free of charge, improved only slightly following TSB screening (from 32% to 37%). A recent population study used medical billings and residential distribution to evaluate the effect of social economic status on follow-up service utilization. Between 2003 and 2011, significant differences in follow-up attendance were observed depending on social economic index of their neighborhood. The improved attendance, though still meager, was confined to patients with higher socioeconomic status (40% compliance compared with 32%) [41]. The report did not describe discharge information provided parents about jaundice and its risks or discuss how the message parents received might have influenced compliance.

3. PROVIDER KNOWLEDGE AND BEHAVIOR

In LMICs, community health extension workers (CHEWs) are often the only medical resource in rural clinics. They provide the critical functions of screening and referring cases in need of further care, attend many deliveries in clinics and at homes, and are a major provider of health information. Forty to 60% of mothers receive their information about neonatal jaundice from CHEWs [42, 43]. A 2006 survey of 66 CHEWs’ knowledge about jaundice in Nigeria by Ogunfowora and Daniel [42] revealed fairly adequate knowledge by most; 74% could identify jaundice and refer immediately to a hospital for care, but 26% would treat with drugs, herbal medicine or exposure to sun. In 2014, WHO initiated an “Every newborn actions plan to end preventable deaths” that emphasizes increasing the capacity of community health workers and groups to implement essential newborn care. Kirkwood *et al.* [44] provided evidence that community focused care delivery improves early breast feeding, delayed bathing, and early referral of serious disease, but the impact on neonatal mortality rates was negligible.

In Egypt, Iskander *et al.* [45] identified multiple deficiencies in health provision leading to delayed admission (>6 days) and ABE. She interviewed 130 mothers of babies admitted to Cairo University Children’s Hospital with severe hyperbilirubinemia using a pretested questionnaire. Major systemic failures contributing to delayed admissions of 125 babies born in health care facilities were no discharge physical in 99/125, no parent given instructions about jaundice, and no follow up appointment scheduled. Parents of 109 infants sought medical advice. All were examined by physicians, TSB was measured in only 28 infants, 87/109 were advised to place the baby under a fluorescent lamp at home, 75 advised to supplement feeds, and 15 were prescribed medicines including vitamins. 14/125 had signs of advanced ABE on admission.

In the United States, a volunteer Pilot Kernicterus Registry was established in 1992 to gather information about known cases occurring in the USA. In 2009, Johnson *et al.* [46] summarized and analyzed data from 125 term/near term infants with ABE or kernicterus occurring between 1992 and 2004. As in Egypt, cases frequently demonstrated multiple breakdowns in health care delivery including inadequate planning, poor provider judgment, and bad advice to parents. Common provider driven barriers to care resulting in kernicterus are listed in Table 1. To this list we could add failure to provide mothers with verbal/written information about risks of jaundice and signs of early encephalopathy.

The international Parents of Infants and Children with Kernicterus (PICK) support group (pic-k.org) recently conducted a survey of 18 mothers of affected children (shared with permission). Proper treatment of neonatal jaundice during the birth hospitalization was delayed or inappropriate in 3 cases. Of the 15 newborns readmitted after discharge, 5 did not have bilirubin screening at discharge, 5 had follow up intervals exceeding AAP recommendations, providers failed to recognize a connection between signs of ABE (decreased feeding, lethargy, fussy) and jaundice in 7, and 6 received recommendations to place their infants in the sun without measuring TSB. Vomiting/reflux was a prominent sign in 5 infants. Transfers to tertiary care hospitals further delayed treatment in 3 cases. In total, the “system” failed for one or more reasons in 14/15 cases discharged from the birthing hospital.

4. PARENT KNOWLEDGE AND BEHAVIOR

At least 16 surveys evaluating mothers’ knowledge and attitude about jaundice conducted in various regions of the world have been published in the English language (Table 2) [43, 47-60]. All surveys involved interviews or self-administered questionnaires. Three studies were conducted at antenatal clinics, 8 occurred 1 to 28 days after delivery, 4 surveyed mothers of babies readmitted to hospitals with jaundice, and one was a community based

household study. Questionnaires were structured differently, and some provided only scaled results (*e.g.*, excellent, good, poor knowledge) without providing details of survey questions or responses [47, 51, 55, 58, 60]. Only one randomized controlled study compared antenatal training with knowledge tested at 28 days post-partum [54]. Mothers’ knowledge and intent to seek care varied between countries and between regions within a country, but there were many similarities.

Most mothers were aware of jaundice, ranging 86-100% in 9 of 10 antenatal and post-partum surveys. Awareness was lower in mothers of babies re-admitted with jaundice and in a community survey. Knowledge about the risks of severe jaundice varied widely, ranging 6% to 95% (median 54%) of mothers interviewed, and only a few knew signs of incipient neurotoxicity.

Forty-seven to 90% (median 67%) stated they would seek medical care immediately if jaundice appears, but compliance was much lower in the few instances recorded. In LMICs the intent to seek medical care would sometimes succumb to family or social pressures for a trial of traditional home remedies such as sunning or herbal medicine [48, 52, 55]. Exposing newborns with jaundice to unfiltered sunlight is a common practice in high-income countries as well as LMIC’s, imbedded in various cultures and often recommended by physicians and health care workers [47-50, 52, 53, 55-57, 61, 62]. These practices are major contributors to delayed care seeking resulting in ABE [56].

Eight of 12 studies identified greater knowledge about jaundice and, usually, better attitude and behavior (timely care seeking, less likely to use traditional medicines and sunning) among mothers with tertiary or higher education. Four of eight studies found better knowledge and behavior in mothers having had a previous baby with jaundice. Social economic standing did not influence knowledge level or attitude in most perinatal studies, but was identified as a risk factor for ABE among patients admitted with jaundice [47, 52, 55, 56, 60].

Table 1. Barriers to care created by providers that led to kernicterus.

<ul style="list-style-type: none"> • Not recognizing the severity of jaundice, especially in darkly pigmented newborns; not ordering a TSB.
<ul style="list-style-type: none"> • Not recognizing the connection between signs of ABE and jaundice (<i>e.g.</i>, focusing solely on feeding technique in a jaundiced baby who will not suck).
<ul style="list-style-type: none"> • Inappropriate treatment (drugs, herbs, lamp or sun exposure).
<ul style="list-style-type: none"> • Not believing the bilirubin level reported from the laboratory and delaying phototherapy and preparation for exchange transfusion while it is repeated.
<ul style="list-style-type: none"> • Delaying treatment or interrupting phototherapy for diagnostic testing (<i>e.g.</i>, lumbar puncture, echocardiogram, auditory evoked response).
<ul style="list-style-type: none"> • Using the indirect (or unconjugated) bilirubin level instead of the total bilirubin level to make treatment decisions.
<ul style="list-style-type: none"> • Measuring the bilirubin and not comparing it to hour-specific norms.
<ul style="list-style-type: none"> • Not recognizing the significance of jaundice appearing before 24 h of age.
<ul style="list-style-type: none"> • Failure to ensure timely post-discharge follow-up based on the pre-discharge TSB or TcB.
<ul style="list-style-type: none"> • Not monitoring and aggressively treating severe hyperbilirubinemia with intensive phototherapy

¹Adapted from Johnson *et al.* [44] and Shapiro (www.kernicterus.org).

Table 2. Surveys of mothers' knowledge/skills/attitude about neonatal jaundice.

Year	Country	Survey Site	N	Education % ≥12 Yrs or Median Years	Correlation Education/ Knowledge	Aware Jaundice	Can Identify Jaundice +	Aware of Risks +	Aware of Treatment+	Seek Care <24h +	Treat with Sun Exposure
2013	Nigeria [45]	1	389	61%	YES	86%	97%	67%	72%	86%	12%
2014	Nigeria [42]	1	488	61%	YES	88%	63%	60%	72%	NI	9%
2011	Malaysia [46]	1,2	400	10.1-11.6 yrs	YES	94%	86%	71%	NI	58%	83%
2008	Iran [47]	2	400	>21%	YES	91%	91%	45-80%	48%	52%	2%
2009	Nigeria [48]	2	255	54%	NI	88%	NI	22%	NI	NI	51%
2012	Turkey [49]	2	161	32%	YES	91%	NI	52%	18%	47%	NI
2012	Egypt [50]	2	400	24%	NO	86%	NI	51%	NI	88%	67%
2011	Sri Lanka [58]	2	396	NI	YES	NI	43%	6%	44%	90%	NI
2014	Viet Nam [51]	2	979	47%	NI	56%	21%	27%	NI	<60%	27%
2015	China ^a [52]	1	465	14.7 yrs	NO	100%	93%	95%	54%	89%	0%
2015	China ^b [52]	1	452	13.5 yrs	NO	88%	54%	38%	41%	67%	10%
2008	Iran [53]	2,3	1666	46%	YES	77%	96%	72%	NI	96% ^c	40%
2012	Nigeria [54]	3	182	58%	YES	>70%	70%	64%	NI	29%	29%
2014	Malaysia [55]	3	198	NI	NO	NI	95% ^d	71%	94%	83%	11%
2015	Nigeria [56]	3	98	43%	YES	57%	47%	64%	15%	58%	NI
2014	Nigeria [43]	1	488	61%	YES	88%	63%	23-37%	NI	70%	12-30%
2015	Nigeria [57]	4	358	36%	NO	75%	91%	46%	NI	44%	58%

+ Percent limited to those aware of jaundice NI = No information, or not asked.

a. Antenatal instruction 518 recruited, 465 completed questionnaire 28 days post-partum

b. No antenatal instruction 518 recruited, 452 completed questionnaire

c. 96% said they should see physician immediately; 33% did.

d. 95% claimed to recognize jaundice; Only 8% were first to recognize jaundice in their baby.

e. Range = current plans (n=431) versus previous action with a jaundiced baby (n=128).

Survey Site

1 Antenatal clinic

2 Postpartum or <30 day follow up

3 When admitted for jaundice

4. Randomized community survey

The only population study surveyed mostly non-pregnant mothers of all ages in randomly selected households in a community of Lagos, Nigeria [59]. Only 36% of mothers had a tertiary level education (36%). 32% of mothers identified death and 34% brain damage as risks of severe hyperbilirubinemia. They found no relationship between mothers' education and knowledge about jaundice. Among those aware of jaundice, only 44% believed they should seek care when jaundice is seen, and 58% would treat or have treated jaundice with sun exposure. In contrast, a multi-center survey conducted at antenatal care clinics in Nigeria [43] found a positive relationship between mothers' education and knowledge; a higher percentage of participants had tertiary education (61%), and 52% understood that severe jaundice could kill their baby. Only 4% of mothers with previous jaundice experience had exposed their infants to sun.

The largest study, consisted of 1666 babies admitted for jaundice in Iran [55]. Three quarters of the mothers were aware of jaundice, and 77% of these mothers were considered to have good knowledge/attitude about jaundice (although questions testing knowledge were limited).

Knowledge, while greater in educated mothers, was not always translated into action; 96% of mothers agreed that it is "necessary to consult a physician immediately" if jaundice is observed, but only a third of mothers did so. Forty percent believed traditional remedies were helpful leading to delays in effective care seeking. Mean TSB on admission was 21.6 mg/dL (range 8-53 mg/dL); the incidence of ABE and the relationship of knowledge to maternal behavior were not documented.

The only randomized controlled study testing the impact and retention of antenatal education was performed in China [54]. 1036 primiparous women were randomly assigned to receive informational pamphlets in antenatal clinics and tested for knowledge about jaundice 28 days post-partum. The pamphlet was based on a Canadian Family Practice 1999 information sheet [63]. Twenty-eight days following delivery, both instructed and control subjects were quizzed using a 16 yes/no questionnaire covering basic jaundice information. The level of maternal education was high – mean years of education were 13.5 in both groups. Visible jaundice developed in 83-84% babies in both groups. Mothers who had received infor-

mation were more likely to be the first to recognize jaundice in their infants, 71% of the time compared with 41% for controls where 37% were identified by visiting nurses. Control infants were more likely to sun their infants and use traditional medicines, and slightly less likely to seek care immediately when jaundice was recognized. Ninety-five percent of intervention mothers knew that jaundice can cause brain damage compared with 38% of controls, and 93% of intervention mothers agreed that more fluids and increased breast feeding is encouraged for jaundiced newborns compared with only 23% of controls. The report did not document TSB levels, number of babies receiving phototherapy or signs of ABE in each group.

Although largely limited to observational studies and surveys, the data in aggregate strongly suggest that lack of knowledge about jaundice and its risks is a major contributor to delayed care of babies with severe hyperbilirubinemia. However, even with high levels of knowledge and/or intent to seek care if their baby develops jaundice, many mothers still faced significant barriers to timely evaluation and treatment. These barriers included cultural, religious, and family pressures to remain at home, use of traditional herbal medicines, sunlight exposure, and bad advice from physicians or health care workers. Practical barriers included limited finances, child care responsibilities, transportation problems, and distance to care facilities [1, 3].

There is limited information on population knowledge and behavior with respect to neonatal jaundice in affluent countries. Even many highly educated mothers in the West are unaware of the risks of jaundice or management guidelines, and this is reflected in the PICK pilot survey. Ten of 15 babies readmitted with kernicterus had bilirubin screening prior to discharge (age 5 hours to 58 hours of age, median 36 hours). Yet, only 5 mothers received verbal and three written information about neonatal jaundice. Two mothers were given verbal instruction about dangers of hyperbilirubinemia, but no mother received written information about signs of neurotoxicity. All stated they would have been more proactive in their babies' care had they known what they now know about clinical assessment of increasing jaundice, risks of hyperbilirubinemia and signs of ABE.

5. WHAT SHOULD MOTHERS BE TAUGHT?

AAP and NICE guidelines both recommend giving parents verbal and written advice about jaundice prior to discharge. The AAP 2004 guidelines recommend that parents be given "explicit educational materials ... (a key component of all AAP guidelines) concerning the identification of newborns with jaundice," but recommended content of educational materials is not detailed [33]. The NICE guidelines (2016) advise that parents be provided information "that is tailored to the their needs and expressed concerns... Care should be taken to avoid causing unnecessary anxiety ... Information should include [the fact that] neonatal jaundice is common and is usually transient and harmless" (<https://www.nice.org.uk/guidance/cg98>). Information for parents explaining specific risks

of severe hyperbilirubinemia or how to recognize signs of bilirubin-induced neurotoxicity is not specified in either guideline. Since the primary reason to monitor and treat neonatal jaundice is to prevent brain damage, excluding information about bilirubin neurotoxicity lays the burden of prevention exclusively on the shoulders of providers.

Identifying jaundice and recognizing danger signs of early neurotoxicity are critical to early care seeking and are more likely to be first identified by mothers if they know what to look for. In promoting community-based triage of sick children, the World Health Organization produced a list of danger signs that require referral by local providers for further evaluation (WHO recommendations on postnatal care of the mother and new born, 2013). These signs include fever, listlessness, decrease in feeding well, convulsions, not moving, and respiratory distress. Most of these signs are common to both sepsis and advanced ABE. Danger signs specifically assigned to neonatal jaundice are 1) jaundice appearing in the first 24 hours of age and 2) jaundice extending to palms and soles at any age (a sign of severe hyperbilirubinemia). The guidelines were established from an evidence based review of generic signs predicting neonatal death, but fail to discriminate clinical signs associated with *early* (reversible) and advanced (irreversible) ABE [46]. Waiting for most of these signs to appear in a jaundiced infant will likely be waiting too long.

The accuracy of visual assessment using cephalocaudal progression of jaundice in predicting TSB [64] has received mixed reviews [30, 65, 66]. Jaundice is more difficult to assess in darkly pigmented newborns; waiting for yellow staining of soles to appear is waiting for a crisis to happen. Bilirubin staining of the conjunctiva, on the other hand, is not affected by skin color. The relationship between yellow conjunctiva and TSB was recently documented in 240 jaundice newborns by Azzuqa and Watchko [67]. The appearance of conjunctiva icterus (76 babies) was indicative of a TSB >14.9 mg/dL; only a small number of patients with yellow conjunctiva had TSBs in the range 10-14.9 mg/dL (171-255 μ mol/L). The appearance of icteric conjunctiva should demand immediate attention and TSB determination.

Several examples of teaching materials can be found in the literature and the Internet. Some list signs of ABE that should prompt a "call to your pediatrician" but understate the emergent need for care when they appear. Similarly, the AAP (healthchildren.org) lists several AAP web pages for mothers; One advises newborn follow up at age 2-5 days, another recommends breast feeding 8 to 12 times a day for the first few days, not treating jaundice with sunlight, and calling your pediatrician if jaundice increases and involves abdomen, extremities, or if your jaundiced baby is hard to wake, fussy, not nursing well. Perhaps not to alarm, mothers are not advised that the latter signs represent a possible emergency requiring immediate evaluation and intensive intervention. Information focusing on appropriate actions to be taken by parents according to severity of jaundice and signs of toxicity can be found on the Center for Disease Control website, but

this site is not commonly visited by parents. (www.cdc.gov/ncbddd/jaundice/documents/kernicterus_fs.pdf).

Effective messaging requires alerting mothers to the danger (threat = kernicterus) but reassures them with an effective and easy to enact plan of action (seek care if jaundice appears; rush if signs of disease appear) to prevent it (phototherapy is simple and effective). Without a threat, follow up may be viewed as an inconvenience, and this may have contributed to the low compliance rate for post-discharge follow up reported in Ontario, Canada [41]. However, a threat with no clear solution may result in denial. Knowing the threat (ABE), knowing an easy solution (timely phototherapy), mothers are more likely to engage in the recommended response (early care-seeking or monitoring) [68].

Suggested message content to facilitate mothers' participation in management decisions is listed in Table 3. In the absence of specific risk factors requiring special attention (e.g., G6PDd), maternal instruction need not dwell on physiology or medical causes of jaundice other than explaining that jaundice is a transient benign newborn

phenomenon unless excessive bilirubin is produced. The critical parental behavior required to prevent ABE is timely care-seeking when babies have significant jaundice. In environments where postpartum monitoring depends on a mother's skill to complement care by community providers, this might be facilitated by specific antenatal instructions on how to identify identify jaundice, avoid dangerous practices, seek early evaluation, and recognize danger signs that require emergent medical care. Verbal instruction followed by simple written instruction (graphics in areas with low maternal literacy rates) presented in antenatal clinics or by community workers with reinforced written material following birth is likely to be most effective [54]. Initiating jaundice instruction only after birth is compromised by a high rate of very early hospital discharge and home births with uncertain follow up.

6. THE SPECIAL CASE OF G6PD DEFICIENCY

In the volunteer kernicterus registry of 125 babies with ABE or kernicterus in the United States, 26 had labora-

Table 3. Suggested content for parent instruction¹.

Things you should know.
<ul style="list-style-type: none"> • Jaundice (yellow skin color) occurs in 40-60% of all newborns during the first week of life. It is caused by elevated levels of bilirubin, a normal substance in blood resulting from the breakdown of red blood cells. The mother's liver excretes the baby's bilirubin before birth and it takes 5-10 days for the newborn liver to take over the job. Bilirubin levels usually reach peak values by day 3-4 of life and then slowly decrease. Most of the time no treatment is necessary.
<ul style="list-style-type: none"> • Severe jaundice can occasionally occur when bilirubin production is excessive and can cause brain damage resulting in cerebral palsy, hearing loss, and learning disabilities.
<ul style="list-style-type: none"> • Severe jaundice is easy to prevent by treating moderate jaundice with blue light exposure (phototherapy). About 10-15% of babies will require phototherapy.
Things you can do.
<ul style="list-style-type: none"> • Examine your baby for jaundice at least twice a day during the first 5-7 days and seek care if jaundice is observed anytime. Be aware that jaundice appearing before 24 hours of age requires immediate attention and bilirubin measured. Be sure your health care provider checks your baby for jaundice before hospital discharge, preferably with a pre-discharge bilirubin measurement.; for home births, attendants must also check for early jaundice and ensure timely evaluation within 2 days.²
<ul style="list-style-type: none"> • Seek medical care if you observe jaundice anytime, and be sure to keep your baby's follow up appointment (normally 2-3 days later if discharged before 36 hours of age).
<ul style="list-style-type: none"> • Breast feed 8-12 times a day for the first week. Jaundice increases with low fluid intake. Should have 5 or more wet or dirty diapers every 24 hours.
<ul style="list-style-type: none"> • ³ Avoid eating fava beans if breast feeding; do not use baby clothes stored in moth balls; do not use triple dye or menthol containing salves for skin or cord care; henna must not be applied to baby's skin. All of these activities can produce severe jaundice in some babies.
Danger signs
<ul style="list-style-type: none"> • Increasing jaundice: Call your doctor and ask to see your baby the same day if the whites of the eye become yellow, or you see jaundice below the nipple lines, or if he/she has decreased feeding or voiding.
<ul style="list-style-type: none"> • Seek emergency help from your doctor or emergency room if jaundice extends to hands and feet and/or if your baby becomes very fussy, sleepy, stops sucking well, cries inconsolably or stiffens when held (or alternatively is limp and lethargic). These are signs of brain poisoning from bilirubin and require immediate treatment.

Additional information can be found at the Center for Disease Control website (www.CDC.gov)

¹Adapted from the Centers for Disease Control and Prevention website (www.cdc.gov) and Kaplan *et al.* [70].

²When attended by unskilled individuals, have baby check at clinic within 48 hours.

³Instructions for patients with proven G6PDd or population at risk when G6PD screening is not available. May need adaptation for unique regional demographics.

tory confirmed G6PDd, and many with unexplained hyperbilirubinemia were not tested [46]. High rates of kernicterus in LMICs are concentrated in regions with high rates of G6PDd [4, 8] and, despite the absence of available anti-Rh globulin in most regions, far surpass Rh immunization as a cause of severe hyperbilirubinemia [4, 10, 16, 25, 69-72].

WHO consensus guidelines established in 1989, recommend screening all newborns in regions where G6PD deficiency affects >3-5% of male population accompanied by education of parents for babies proven to be deficient [73], but implementation has been sporadic. In order to effectively target maternal instruction, identification of babies at risk must be immediate, since hospital births are commonly discharged within 24 hours. Even with a low cost point of care test, timely screening and instruction is further compromised by the large percentage of out of hospital births in LMICs. In many LMICs, parents must bear the cost of screening, creating an additional barrier to enactment of WHO guidelines. Thus, in regions where G6PDd is endemic and rapid G6PD screening is not available, educational efforts must assume that all newborns have G6PDd and should avoid exposure to substances known to trigger hemolysis.

7. DOES EDUCATING MOTHERS ACTUALLY MAKE A DIFFERENCE?

The major untested question is whether empowering mothers with knowledge and skills to participate more fully in care and management decisions will actually decrease the incidence of severe hyperbilirubinemia and, more importantly, ABE and kernicterus. If mothers know that severe jaundice can cause brain damage; if they know how to recognize jaundice and severe jaundice; if they know the early signs of ABE; if they know that treatment is available, will they seek care more quickly and be more assertive advocates for their infants? Armed with this information, will parents be able to successfully confront family, social and provider barriers to care? Some studies suggest that maternal education will improve early care seeking for babies with jaundice and decrease ABE [43, 54, 57], but there are no randomized studies to confirm that.

Kaplan and colleagues [54, 74] recently reviewed evidence whether educating mothers of G6PD deficient newborns decreases the incidence of hyperbilirubinemia or kernicterus. Four studies identified patients with G6PDd and provided information prior to discharge [75-78]. The content of maternal information and methods of delivery varied, and analysis was based on historic experience or parallel comparisons with hospitals not screening or educating patients. In one study, at risk babies were observed for 1-3 weeks until jaundice subsided before discharge [75]. All studies provided evidence that the risk of kernicterus was greatly reduced or completely eliminated when compared to historic controls when a combined screening and education program was offered. The data, while largely observational, support the view that G6PDd screening must be combined with parental empowerment to be effective [73, 79]. In Nigeria, and likely in other

LMICs with a high prevalence of hyperbilirubinemia and kernicterus, the dominant medical causes are G6PDd, followed by ABO incompatibility, sepsis, prematurity, and Rh hemolytic disease [16, 25, 26]. Pending universal G6PDd screening and an effective community-based newborn monitoring system, it may be argued that the best protective strategy is to assume all babies are deficient, and empower parents, the most invested stakeholders, with the knowledge and skills needed to care for a baby with that condition.

A prospective non-randomized multi-centered effort to decrease the incidence of ABE in Nigeria through maternal education was presented at the Pediatric Academic Society annual meeting (Baltimore, April 26-May 2, 2016) [78]. Training was provided in antenatal clinics, and included posters, verbal and written information about risks of severe jaundice, how to detect jaundice and early signs of brain injury, with instructions to avoid traditional practices that trigger G6PDd crises, avoid sunning and herbal medicines and seek immediate care if jaundice is recognized. They reported a decrease in cases of ABE from 15% to 11% of jaundice admissions after introducing antenatal maternal and health provider education (not all mothers received instruction). A cross sectional analysis comparing outcomes in patients whose mothers received instruction with mothers who failed to receive instruction (opportunistic controls) revealed incidences of ABE per jaundice admission of 6.1% and 23.2% respectively. The presenter acknowledged a potential selection bias since receipt of maternal instruction was not randomized. Although instruction was not offered in many antenatal clinics, a greater number of controls who did not receive instruction were "high risk" (e.g., out of hospital births with little or no antenatal care). While acknowledging these limitations, the relationship of jaundice instruction to timely care seeking and a decrease in ABE among infants admitted with jaundice was striking.

Universal programmed education that empowers mothers to share in their babies' management should they develop jaundice is based on the hypothesis that mothers are the most vested caretakers of their offspring, and that, given focused information and incentive, they will make appropriate decisions. The proposed content of antenatal training (jaundice identification, risky behavior avoidance, early signs of toxicity, Table 3) provides information on par or greater than existing training modules for CHEWs and far exceeds current information on jaundice proposed in the 2013 WHO recommendations on postnatal care of the mother and newborn. It acknowledges that, despite good intentions, dependence on a community provider led system has limitations. Assumptions that trained community health workers in LMICs will be able to provide 2-3 home visits in the first week may be unrealistic [80]. Empowering mothers as a component of integrated maternal-child health care would complement current WHO/UNICEF/USAID strategies that emphasize training community health workers to provide Essential Newborn Care. The value of parent-provider sharing in care and referral decisions when parents are restrained by illiteracy, social, family, and cultural barriers, may be questioned, but limited data on response to training, suggest

that the fraction of 'non-responders' is small when the message is well presented. WHO advises a minimum of four antenatal clinic visits to achieve a complete package of perinatal information. A major task of community health workers is to identify high social risk pregnancies and facilitate their attendance at antenatal clinics where they will be exposed to perinatal education and care.

CONCLUSION

The high rates of very early discharge and home deliveries in LMICs combined with uncertain guidance and monitoring by health care providers during the critical 2-5 days of life place increased demand for parents to participate in health care for their infants. Although lacking randomized trials, there is cumulative observational evidence in both low and high income environments that empowering mothers with knowledge and skills to recognize jaundice, avoid ineffective therapies, understand early signs of ABE, and, where G6PD deficiency is endemic, to avoid known hemolytic triggers will lead to timely care seeking and a lower incidence of ABE. There is a need for further robust evaluation of the impact of maternal education on outcome, but pending this reinforcement, maternal empowerment through education offers a very low cost and likely effective component to the strategy of preventing kernicterus worldwide.

LIST OF ABBREVIATIONS

AAP	=	American Academy of Pediatrics
ABE	=	Acute Bilirubin Encephalopathy
CHEW	=	Community Health Extension Worker
G6PDd	=	Glucose-6-phosphate Dehydrogenase Deficiency
LMIC	=	Low-middle Income Country
NICE	=	National Institute for Health and Care Excellence
TSB	=	Total Serum Bilirubin
WHO	=	World Health Organization

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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