Seminars in Fetal & Neonatal Medicine 20 (2015) 58–63

Contents lists available at ScienceDirect

Seminars in Fetal & Neonatal Medicine

journal homepage: www.elsevier.com/locate/siny

Review

Societal impact of bilirubin-induced hearing impairment in resource-limited nations

Bolajoko O. Olusanya*

Centre for Healthy Start Initiative, 286A Corporation Drive, Dolphin Estate, Ikoyi, Lagos, Nigeria

Keywords:
Bilirubin encephalopathy
Developing countries
Developmental disabilities
Kernicterus
Newborn screening
Societal costs

SUMMARY

Infants with bilirubin-induced neurologic dysfunction (BIND) are characterized by several developmental disabilities including auditory impairments. This paper explores the societal impact of bilirubin-induced auditory impairments, inclusive of hearing impairments and auditory neuropathy spectrum disorders, on these infants, their families, and on the community in resource-limited countries (per capita income of US$6,000 or less). Auditory impairments have substantial emotional, social, and economic impact on the affected infants, their families and communities. The burden is exacerbated by widespread poverty, unfavorable community attitudes towards disabilities, and lack of requisite health, educational, and social services. Curtailing the incidence of avoidable severe hyperbilirubinemia through proactive and effective management of infants at risk or with severe hyperbilirubinemia is necessary at all levels of healthcare delivery. Early detection and intervention for unavoidable auditory impairments should be widely promoted to provide improved developmental trajectories for the affected infants.

1. Introduction

Jaundice-related mortality and disabilities, rarely reported in the developed world, persist in disturbing proportions in many resource-limited countries [1; T.M. Slusher et al., unpublished data]. For example, in one recent review of the global burden of hyperbilirubinemia, Sub-Saharan Africa and South Asia were reported to be the leading contributors to an estimated 1.1 million babies who yearly would develop severe hyperbilirubinemia [total serum/plasma bilirubin level (TB) >20 mg/dL (342 μmol/L)] worldwide [1]. Another systematic review found that low- and middle-income countries (LMICs) consistently reported substantially higher rates of exchange transfusions and bilirubin-induced neurologic dysfunction (BIND), such as acute bilirubin encephalopathy (ABE) and chronic bilirubin encephalopathy or kernicterus, than in high-income countries [T.M. Slusher et al., unpublished data]. This is principally due to three levels of delay in providing care for infants with or at risk of severe hyperbilirubinemia, namely: making the decision to seek appropriate care, reaching an appropriate health facility, and receiving adequate/appropriate care [2].

The burden of this high prevalence of severe hyperbilirubinemia or kernicterus is perhaps best characterized by the associated adverse neurodevelopmental outcomes from early infancy [3–7]. For example, several studies have demonstrated significant etiological or statistical associations between auditory impairments in children and severe hyperbilirubinemia, with or without evidence of ABE or kernicterus [6,7]. Like many disabilities, significant auditory impairments from early infancy have profound impacts on the affected child, their family, and society over their lifetime [8,9]. This review therefore sets out to explore the societal impact of infants with auditory impairments secondary to BIND in resource-limited countries.

2. Definitions and terminologies

There are presently no consistent definitions of "resource-poor," "resource-constrained," or "resource-limited" countries in the literature. Although LMICs are frequently described as "resource-poor," the term "LMICs" based on the World Bank classification broadly covers ~140 countries with per capita gross national incomes (GNI) ranging from US$150 to 12,615 [10]. In view of the wide variations in income distribution and developmental status among these countries, we considered the 91 countries with per capita GNI of ≤US$6,000 using the Human Development Report 2013 by the United Nations Development Program (UNDP) as "resource-limited" or LMICs. As described previously [2], these

This work was presented in part by the author at the World Health Summit, October 19–22, 2014, Berlin, Germany.

* Tel.: +234 803 33 44 300.
E-mail address: bolajoko.olusanya@uclmail.net.

http://dx.doi.org/10.1016/j.siny.2014.12.009
1744-165X/

countries account for 64.2% of the total annual live births of roughly 135 million globally, have median institutionalized delivery of 65% [interquartile range (IQR): 43.8–82.8%] and a median human development index (HDI) of 0.525 (IQR: 0.436–0.632) compared to 0.878 (IQR: 0.825–0.878) for the 50 most developed countries. HDI is a robust composite measure of the average achievement in three basic dimensions of human development, namely: a long and healthy life (health), knowledge (education), and a decent standard of living (income). By world regions, 42 (46%) countries are from Sub-Saharan Africa, 18 (20%) from East Asia and the Pacific, 10 (11%) from Latin America and the Caribbean, eight (9%) from Middle East and North Africa, seven (8%) from South Asia, and six (6%) from Europe and Central Asia.

Studies from LMICs specifically investigating ABE or kernicterus as the primary outcome measure are rare, as observed from a PubMed search with keywords "bilirubin encephalopathy" or "kernicterus" and "hearing loss." Hyperbilirubinemia of TB ≥26 mg/dL (450 μmol/L) is often described as extreme or hazardous and frequently associated with signs of ABE in developed countries [11,12]. The author therefore chose to use the term "severe hyperbilirubinemia" as surrogate for ABE and kernicterus, as exemplified in other studies [11–13]. This would correspond with TB levels at or near exchange transfusion levels based on postnatal age and etiology [typically TB ≥20 mg/dL (342 μmol/L) in high-risk populations in many LMICs]. Societal impact was examined holistically along its three constitutional dimensions: the individual, family (nuclear and extended), and the community (Fig. 1).

3. Spectrum of bilirubin-induced auditory impairments

Auditory dysfunctions typically associated with severe hyperbilirubinemia include mild-to-profound hearing loss [7,14,15], including high-frequency sensorineural hearing loss [16,17] and auditory neuropathy spectrum disorders (ANSD) [18–20]. Affected infants may also have additional disabilities such as cerebral palsy, gross motor deficits, epilepsy, and behavioral problems [3], but rarely bilirubin-induced intellectual deficits [4,21]. The threshold at which unbound bilirubin (UB) becomes toxic in humans and predictive of permanent auditory impairments is still not fully understood [6,21–23]. However, the type and severity of neurologic damage to the auditory system is likely to be correlated with the amount and duration of exposure of the central nervous system (CNS) to bilirubin neurotoxicity [21,22]. Some studies also indicate a possible role of prior hypoxia or ischemia in precipitating BIND [24].

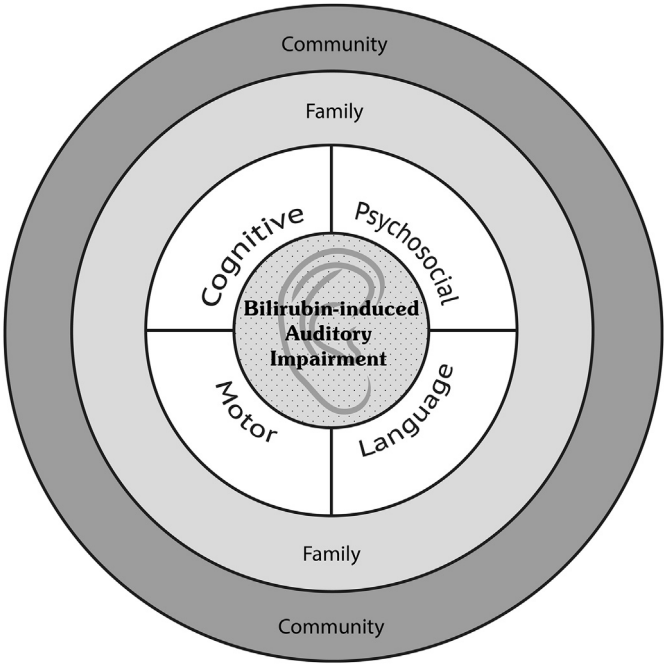

Fig. 1. Dimensions of societal impact of bilirubin-induced auditory impairment.

A frequent limitation in most epidemiological studies from LMICs is the lack of data on TB levels of children diagnosed with auditory impairments secondary to hyperbilirubinemia [25]. Attempts in the literature to quantify the global burden of hyperbilirubinemia based on data of TB levels in infants with these sequelae have often resulted in gross under-ascertainment of the magnitude and pattern of hearing impairments in LMICs [3,6,25]. For example, in one recent systematic review [6], none of the 19 studies selected for the review was from Sub-Saharan Africa, a region arguably with the greatest burden of severe hyperbilirubinemia underpinned by endemic glucose-6-phosphate dehydrogenase (G6PD) deficiency and ineffective management of jaundiced infants [2,26]. The few studies that explored neurodevelopmental risks in infants with hyperbilirubinemia based on predetermined TB thresholds did include auditory brainstem response (ABR) tests [27,28]. In one of the few studies in which ABR tests were carried out on infants in Africa, identification of cases of severe hyperbilirubinemia were based solely on parent-reported history of treatment with phototherapy or exchange transfusion [29]. Similarly, in another systematic review of a broader spectrum of long-term neurodevelopmental sequelae of hyperbilirubinemia using TB diagnostic criteria, only three of the 153 eligible studies were from Africa and no ABR test was reported in any of the studies [3]. Parental or clinical history of treatment with phototherapy and/or exchange transfusion is an indispensable proxy for severe hyperbilirubinemia in LMICs because of the frequently reported delays in presentation of the affected infants prompted by the onset of ABE or kernicterus [2]. It is therefore not surprising to find studies reporting auditory impairments in infants who had received phototherapy and/or exchange transfusion [29,30]. Despite the methodological limitations in available studies, evidence among infants and school-aged children with hearing impairment in LMICs consistently suggests that severe hyperbilirubinemia is associated with the full spectrum of auditory impairments also widely reported in the developed world [29,31–38].

4. Impact of hearing impairment on the child

Early detection of infants with hearing impairments has been shown to be beneficial to optimal communication and developmental outcomes [39,40]. However, unlike the practice in many developed countries, routine screening of newborns for congenital and early-onset hearing impairment is rare in LMICs [41]. Infants with hearing impairments are therefore not detected until a lack of response to a loud sound or a delay in speech prompts parental concern to seek medical intervention. Depending on the severity, a hearing impairment in an infant may not be detected until well over 18 months of life by parental concern or suspicion [42]. In fact, all degrees and configurations of permanent hearing impairments in early childhood can present with great subtlety; most parents are unable to identify their child's hearing impairment before the associated speech and language delays become apparent. In the absence of a systematic effort to screen infants with hearing loss, the average age of detection is well over 2 years and detection may be as late as 6 years and beyond [43,44].

Whereas speech and language difficulties are the most direct consequences of hearing loss, auditory deficits in early childhood