

University of Groningen

## Improving the Management of Hyperbilirubinemia in a Limited-Resource Area

Sampurna, Mahendra

DOI:  
[10.33612/diss.172716035](https://doi.org/10.33612/diss.172716035)

**IMPORTANT NOTE:** You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

*Document Version*  
Publisher's PDF, also known as Version of record

*Publication date:*  
2021

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*  
Sampurna, M. (2021). *Improving the Management of Hyperbilirubinemia in a Limited-Resource Area*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen. <https://doi.org/10.33612/diss.172716035>

### Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

### Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

## **Chapter 8**

# **General discussion**

## **Introduction**

---

The studies described in this thesis were conducted to try to reduce the incidence of hyperbilirubinemia in newborn infants in Indonesia. Studies from Low/Middle Income Countries (LMICs) including Indonesia found a higher incidence of hyperbilirubinemia in these countries compared to High Income Countries (1). The aim of the studies described in this thesis is to identify potential causes for this higher incidence and to provide potential ways to reduce the incidence.

It is acknowledged that in this thesis no study is done that shows that hyperbilirubinemia is higher in Indonesia compared to for instance the Netherlands. This project was started with a registry of cases with hyperbilirubinemia in Indonesia. Unfortunately, there was no support from the Pediatric Community in Indonesia to participate in this registry. Despite many efforts, there was an almost complete lack of interest of pediatricians and other health care workers to participate in this registry. Why pediatricians did not collaborate is not clear. It might be that pediatricians feel not secure enough to show their data. There is not a strong tradition in Indonesia to conduct research, and not at all to conduct a multicenter study. The supposition that hyperbilirubinemia in Indonesia is seen more frequent than in developed countries therefore is based on studies published in literature (1).

## **Knowledge and adherence on the hyperbilirubinemia management**

---

In chapters 2 and 3 data are shown on adherence of pediatricians and other health care workers to existing guidelines for the diagnosis and treatment of hyperbilirubinemia. That the adherence is rather low among midwives, general practitioners, and pediatricians (4). In chapter 3 it is shown that residents in pediatrics also do not always follow the existing guidelines. Studies conducted in other countries also found that pediatricians not always follow accepted guidelines. Atkinson *et al* (2) found that in the USA only 54% of infants who received phototherapy in agreement with the AAP guidelines. This is consistent with Tartaglia's and our studies (3,4). Tartaglia's showed that campaigns to improve the adherence to guidelines are effective, for example one aimed at increasing the awareness of the AAP guideline in the Children's Hospital in Columbus, USA (3). The compliance score increased

from 60% before an intervention to 90% thereafter. Darling *et al* investigated the implementation of new guidelines made by the Canadian Pediatric Society in 100 hospitals in Canada. Seventy-nine of these hospitals indicated to have implemented these guidelines. However, only 70% of these hospitals implemented measuring the bilirubin level before discharge, although this is recommended in the guidelines.

We found in the first questionnaire that only 54% of midwives and 46% of general practitioners followed the guidelines. The study done before and after the introduction of a new national guideline (5) and a web-based app (6) showed that before the introduction only 38% of infants received the correct treatment, phototherapy when indicated according to the guidelines and no therapy when there was no indication. After the introduction of the new guideline and the app the percentage of correct treatment increased to 51%, forty-nine percent of infants did not receive PT while this was indicated, received PT while this was not indicated or received PT although the bilirubin level was not measured (Chapter 4). The question therefore is why pediatricians in Indonesia often do not follow guidelines. Pediatricians in Indonesia seem not to be familiar with using guidelines in their daily practice. Another explanation might be the difficulties in obtaining bilirubin measurements. When it is difficult to measure the bilirubin levels, pediatricians might want to be on the safe side and give PT also when this is not indicated according to the guidelines. This might explain why 28% of infants received PT while this was not indicated according to the guideline. More studies are needed to understand why pediatricians in Indonesia seem not very motivated to follow guidelines. These studies are also important when more, guidelines on other diseases than hyperbilirubinemia, are introduced.

### **Validating minimal invasive devices for hyperbilirubinemia diagnosis in Indonesia**

---

As mentioned above is correct, non-invasive measurement of the serum bilirubin level very important to prevent hyperbilirubinemia. In chapter five we evaluated two bed-side methods, the Transcutaneous measured Bilirubin (TcB) and a point of care method, the Bilistick® (BS) and compared these to the gold standard, the measurement of total bilirubin in serum. (TSB). The TcB showed a good correlation with the TSB, however with an

overestimation of ( $\pm$  SD) of 26 ( $\pm$  30)  $\mu\text{mol/L}$  with a 95% CI of 21 to 32  $\mu\text{mol/L}$ . Negative aspects of the TcB are the costs of these apparatus and the need for daily calibration. The BS has an almost equal correlation with the TSB, but we observed ten outliers, including four severe outliers in a range where PT was indicated. A study done in Thailand also found that the Bilistick® gave unpredictable false readings in high humidity for 67 cases out of 84 subjects with error readings (7). As long as these problems are not solved, is the use of the Bilistick® not recommended as single measurement for hyperbilirubinemia. For now, is in our opinion, the TcB is the preferred method, despite the costs. However, when cases of sequela due to hyperbilirubinemia are prevented by using the TcB, the costs for the treatment and care for a child with a severe handicap will be saved. The care of a child with a severe handicap for the society might be as high as 50.000 USD only for cochlear implant. A good cost/benefit study on the use of TcB units across Indonesia is urgently needed (8,9).

### **Improving practice phototherapy in Indonesia** —————

A cornerstone in the prevention and treatment of hyperbilirubinemia is the use of phototherapy (PT). PT can be given by blue light bulbs or LED systems. Studies in the Netherlands and elsewhere have shown a decreasing irradiation output with the time the lamp was on (10). To prevent inadequate output of these lamps it is needed to measure the output. Systems to measure the output are presently not available in Indonesia. In chapter six we described that almost 50% of systems used in the hospitals we visited, had an output under the accepted minimum level. The use of PT units with insufficient output might be a reason for the high incidence of hyperbilirubinemia in Indonesia. PT units must be checked regularly to be sure about the output of the PT system. The costs of systems to measure the output of PT systems are rather high. We therefore suggest that each central/teaching hospital is equipped with one of these devices and that these hospitals are responsible also for the PT systems in the hospitals in their area. In this way it is not necessary that irradiation measurement systems are bought by all hospitals, while at the same time the incidence of severe hyperbilirubinemia can be reduced because the output of the PT device is guaranteed.

The risk to develop bilirubin levels that require intervention are higher for preterm than term infants (11). In guidelines like that of the AAP it is advised to measure the bilirubin level in preterm infants daily after birth (12). This however might be difficult in countries with limited resources (13). In chapter seven, we therefore studied if the bilirubin level measured at 24 hours after birth can predict the risk to develop bilirubin levels that need intervention. We found that a bilirubin level of 4.5 mg/dl in infants of 1000-1499 and 5.8 mg/dl in infants 1500-1999 g measured at 24 hrs after birth were predictive for the need for PT. Unfortunately, we could not find other studies in preterm infants where the bilirubin level at 24 hours was used to identify infants at risk to develop hyperbilirubinemia. More studies therefore are needed to confirm our findings.

Finally, we -again- propose a national registry of patients with hyperbilirubinemia. It is very important to know the present incidence of this preventable disease in Indonesia. A registry is also needed to evaluate the efficacy of measures to reduce the incidence of hyperbilirubinemia, as suggested in this thesis, are introduced and are effective.

In conclusion, in this thesis we identified factors that might be related to the high incidence of hyperbilirubinemia in Indonesia, 1. non-adherence to guidelines, problems with measuring bed-side the bilirubin level and 3. insufficient output of PT units. As solutions we designed and introduced a new national guideline, and we developed a web-based app (chapter four) to assist the practitioners to adhere to the guidelines. We identified and advised which non-invasive bilirubin method is most suitable for Indonesia and how the output of PT units can be secured.

## References

---

1. Greco C, Arnolda G, Boo NY, Iskander IF, Okolo AA, Rohsiswatmo R, et al. Neonatal Jaundice in Low- and Middle-Income Countries: Lessons and Future Directions from the 2015 Don Ostrow Trieste Yellow Retreat. *Neonatology*. 2016;110(3):172–80.
2. Atkinson LR, Escobar GJ, Takayama JI, Newman TB. Phototherapy use in jaundiced newborns in a large managed care organization: do clinicians adhere to the guideline? *Pediatrics*. 2003;111(5 Pt 1).
3. Tartaglia KM, Campbell J, Shaniuk P, McClead RE. A Quality Project to Improve Compliance With AAP Guidelines for Inpatient Management of Neonatal Hyperbilirubinemia. *Hosp Pediatr*. 2013;3(3):251–7.
4. Sampurna MTA, Ratnasari KA, Etika R, Hulzebos C V., Dijk PH, Bos AF, et al. Adherence to hyperbilirubinemia guidelines by midwives, general practitioners, and pediatricians in Indonesia. *PLoS One*. 2018;13(4):1–8.
5. Menteri Kesehatan Republik Indonesia. Pedoman Nasional Pelayanan Kedokteran Tata Laksana Hiperbilirubinemia. 2019;(2):1–97. Available from: <http://repositorio.unan.edu.ni/2986/1/5624.pdf>
6. Sampurna MTA, Ratnasari KA, Irawan ZS, Etika R, Utomo MT, Corebima B, et al. Evaluation of A Mobile Application Tool ( BiliNorm ) To Improve Care for Newborns with Hyperbilirubinemia in Indonesia. :1–15.
7. Thielemans L, Hashmi A, Priscilla DD, Kho Paw M, Pimolsorntong T, Ngerseng T, et al. Laboratory validation and field usability assessment of a point-of-care test for serum bilirubin levels in neonates in a tropical setting. *Wellcome Open Res* 2018;3:110. <https://doi.org/10.12688/wellcomeopenres.14767.1>.
8. Shapiro SM, Nakamura H. Bilirubin and the auditory system. *J Perinatol*. 2001;21:S52–5.
9. De Vries LS, Lary S, Whitelaw AG, Dubowitz LMS. Relationship of serum bilirubin levels and hearing impairment in newborn infants. *Early Hum Dev*. 1987;15(5):269–77.
10. van Imhoff DE, Hulzebos C V., van der Heide M, van den Belt VW, Vreman HJ, Dijk PH, et al. High variability and low irradiance of phototherapy devices in Dutch NICUs. *Arch Dis Child Fetal Neonatal Ed*. 2013;98(2).
11. Bhutani V, Wong R. Bilirubin neurotoxicity in preterm infants: Risk and prevention. *J Clin Neonatol*. 2013;2(2):61.

12. American Academy of Pediatrics. Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation. *Pediatrics* [Internet]. 2004;114(1):297–316. Available from: <http://www.citeulike.org/group/11862/article/5941222>
13. Mabogunje CA, Olaifa SM, Olusanya BO. Facility-based constraints to exchange transfusions for neonatal hyperbilirubinemia in resource-limited settings. *World J Clin Pediatr*. 2016;5(2):182.



