

Correlation of Neonatal Hyperbilirubinemia by Clinical Assessment, Total Serum Bilirubin and Transcutaneous Bilirubin among Healthy Neonates

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Abstract

Neonatal hyperbilirubinemia one of the most common clinical signs encountered in newborn babies. It is the result of bilirubin deposited in the skin and mucus membrane. Reticuloendothelial system is the major source of bilirubin due to breakdown of senescent RBC. Bilirubin is conjugated by the liver in to water soluble product which is excreted easily. Due to immaturity of the neonatal hepatic enzymes newborns are at risk of developing jaundice. The free bilirubin crosses the blood-brain barrier easily which causes encephalopathy called kernicterus in the immediate period, and has a potential to damage brain causing cerebral palsy and other complications. The mainstay treatments to prevent and manage bilirubin encephalopathy are phototherapy and exchange transfusion which has been a major subject of investigation over the last 6-7 decades. To prevent bilirubin induced neurologic damage requires repeated blood withdrawal to ascertain exact bilirubin levels. So non-invasive and painless screening by use of transcutaneous bilirubinometer is becoming more acceptable. However, in preterm neonates the use of transcutaneous bilirubinometer is still under scrutiny. Transcutaneous bilirubin measuring devices have undergone changes to make them overcome previous inconsistency of results in preterms and dark skinned newborns. Studies have shown the results of newer generation TCBs correlate well with serum bilirubin irrespective of skin pigmentation but with respect to gestational age the findings are different. In some studies among preterm babies it shows acceptable correlation between transcutaneous and serum bilirubin. This study aims at establishing the relation between transcutaneous and serum bilirubin levels among healthy newborn babies and its use as a screening tool.

Keywords: Neonatal hyperbilirubinemia; Jaundice; Unconjugated bilirubin; Birth weight; Caesarean section; Gestational age; Gender

Introduction

Neonatal hyperbilirubinemia (NH) is a common problem for newborn and cause of concern for parents and pediatricians [1]. It affects nearly 60% of term and 80% of preterm neonates during 1st 7 days of life [2]. Neonatal hyperbilirubinemia is the commonest cause of readmission after early hospital discharge. Concerns regarding jaundice have increased due to reports of hyperbilirubinemia causing brain injury in healthy neonates even without hemolysis [3,4]. Preventing kernicterus in term or late preterm babies is one of the main goals of newborn care. To prevent significant hyperbilirubinemia, members of the American Academy of Pediatrics Subcommittee on Hyperbilirubinemia recommended that all newborns must be screened for icterus before discharge with a total serum bilirubin (Tsb) or transcutaneous bilirubin (Tcb) measurement [1]. Tcb screening is an attractive modality because it is quick, non-invasive test to screen for hyperbilirubinemia [5]. It is easy to perform and multiple measurements can be taken on the same newborn without pricking for blood. In addition, rather than to wait for a serum bilirubin test to be performed in a laboratory and the result is instantaneous. Finally, the use of Tcb as a screening tool for hyperbilirubinemia, lead to substantial cost savings [6] with Tsb reserved for neonates with a reading above cut off value.

In a study conducted by the BORN (Better Outcomes through Research for Newborns) to determine the research priorities of its

members, the utility of Tcb meter as a screening tool for jaundice in newborn infants, was in the 10 most important topics for investigation [7]. Levels of bilirubin can be determined with device that noninvasively estimates Tsb levels by measurement of light transmitting through the skin of newborns. There are many Tcb meters are available, and previous studies of various Tcb meters have shown that there is a linear relation exists between Tcb and Tsb [$r=0.87$ to 0.96] [8-13]. But, when Tsb (>15 mg/dL), the accuracy of Tcb is less clear. The literature supports the use of Tcb as a screening tool for the initial assessment of neonatal jaundice so that decreasing the number of pricks on neonates. If the Tcb is high, a subsequent serum bilirubin is required for confirmation [6,8,10-17]. The precision of Tcb meters has been gauged in newborns from different ethnicity including, African, Indian and Asian [9,18,19]. Early discharge of healthy newborns has become a common trend because of medical, social as well as economic constraints [20,21]. Thus, the recognition, follow-up, and early treatment of jaundice has become more tough. The American Academy of Pediatrics (AAP) advocates that newborns who are discharged within 48 hours of life should have a follow-up visit after 2-3 days for detection of significant hyperbilirubinemia along with other problems, but this recommendation is not possible in our country due to financial and social constraints. The gold standard for evaluating icterus in neonates is measurement of total serum bilirubin [22]. The transcutaneous measurements of bilirubin have a linear correlation with total serum bilirubin and may be useful as screening devices to detect significant jaundice so decreasing the need to assess serum bilirubin [23]. Currently the standard treatment for hyperbilirubinemia is phototherapy which is effective but in some

cases, when the serum bilirubin concentration elevates or rapidly rises in spite phototherapy, exchange transfusion is indicated but it has more serious complications than phototherapy. The mortality rate from the exchange transfusion is around 0.3-2% [23-25]. Phototherapy has light of wavelength in the 430 to 490 nm and it is much safer than exchange transfusion [24-30].

The results from studies have shown that newer generation of TcB meters correlate well with total serum bilirubin irrespective of skin colour but when gestational age is considered the findings are different. The present study was done at our tertiary centre to establish the correlation between TcB meter reading and total serum bilirubin levels among healthy newborns and its utility as a screening tool.

Aims and Objectives

- To determine correlation between clinical assessment, serum bilirubin levels and transcutaneous bilirubin measurement
- To determine how transcutaneous bilirubin (TcB) levels and total serum bilirubin (TsB) levels are related, in healthy neonates without phototherapy
- To determine how transcutaneous bilirubin levels would influence decision to start phototherapy
- To determine how site of reading of transcutaneous bilirubin measurement and gestational age influence the correlation between the two methods.

Materials and Methods

Hospital based prospective observational study was conducted at Department of Pediatrics, D.Y. Patil University School of Medicine during June 2015 to June 2018. All 121 consecutive patients satisfying the inclusion criteria were taken in the study after 3 informed consents. Study was conducted by taking a detailed history, clinical examination, management and outcome as per the case record proforma. The device used in the study is an ISO certified device the details and product description is Model:-MS1006 Bilisense, Certification:- ISO 13485/ISO 9001 2008/CE.

Observation/Result

Significant association was found in results with those undergone phototherapy according to TsB and TcB levels and it is also evident that TsB significantly affected by gender, gestational age birth weight, mode of delivery, feeding habits, and age of assessment. The outcome of this study supports the use of the transcutaneous bilirubin measurement for screening of clinically significant hyperbilirubinemia in newborns. The TcB meter had superb sensitivity, so it is doubtful that a newborn with a notable level of hyperbilirubinemia would escape detection with TcB measurement. Though the specificity of the TcB level was about 66%, The TcB meter was able to recognize a notable number of infants that did not need invasive testing for the evaluation of jaundice. Based on our results, we recommend that all normal, term, infants should be screened for jaundice initially with TcB meter and if the results are above 75th percentile for age, a TsB level must be obtained.

Discussion

A hospital based prospective study was done with 121 patients to establish the correlation between transcutaneous and serum bilirubin levels among healthy neonates and its utility as screening tool. Most of the participants in our study were female i.e. 62.8%. According to birth

weight most of the participants were of normal birth weight range 2.5 to 3 kg (56.2%), while remaining 43.8% have more birth weight than normal limits. Mean birth weight was 3100 g.

In our study population 52.1% was from caesarean section which was equivalent to those from normal delivery (47.9%). The study of Pendse et al. noted that rate of Caesarean Section was 46.7%. Radfar et al. 112 study evaluated the accuracy of transcutaneous bilirubin measurement in a large population of newborn infants, before and during the phototherapy found incidence of caesarean section was 68.5%.

Most of the healthy neonates in our study were exclusively breast fed (72.7%). 16.5% were both breast fed and formula fed. Rest 10.7% was only formula fed. It is evident that gestational age most commonly seen among study population was 37 to 38 weeks (55.4%) followed by 39 to 41 weeks (33.1%). Mean gestational age was 39 weeks. Age of assessment of neonates in hours was 72 to 96 hours in most of the neonates (43%) followed by 48 to 72 hours (31.4%). Therefore most babies have been found to have age of assessment between 48-96 hours. TsB values ranged from 9.3 to 20.8 mg/dL, with 48.8% of neonates below the 75th percentile for age, 19% with levels between the 75th and 95th percentiles for age, and 32.2% with levels above the 95th percentile for age. In our study we have included only full term babies. The TcB of forehead and sternum was assessed in our study. This study included sternum site for reason that it is often shielded to some extent from ambient light. These differences did not vary much as evident in table. 37.2% of forehead and 42.1% of sternum TcB more than 95 percentile while 14% of forehead and 14% of sternum TcB less than 40 percentile. The reason for this might be due to light exposure to the forehead and scarcity of subcutaneous fat in the sternal area. It is evident in the present study that clinical evaluation by Kramers rule in neonates have most of the participants between 40 to 75 percentile (34.7%) followed by 27.3% above 95 percentile. Kramer identified the cephalocaudal advancement of icterus with increasing total serum bilirubin levels and divided the body of baby into 5 zones, with a total serum bilirubin level measurement associated with each zone. Least number of participants was of 75 to 95 percentile (16.5%) on clinical evaluation by this rule. Most of the TcB neonates have received phototherapy (62.8%) in comparison to those with high TsB receiving phototherapy (51.2%). Thus transcutaneous bilirubin level determines and influences decision to start phototherapy more in comparison to TsB levels. Therefore Kramer's clinical evaluation was found less accurate in comparison with TsB level. However TcB measurements were more accurate as compared to Kramer's rule.

It is evident in our study that TsB significantly affected by gender, birth weight, mode of delivery, feeding habits, gestational age and age of assessment. 52 Females (68.4%) were affected from hyperbilirubinemia but only 23 (19%) required phototherapy as compared to 45 males out of which 39(86.6%) had serum bilirubin above 75th percentile and required phototherapy.

Provaluk et al., Zecca et al. and Nanjundaswamy et al. studies have demonstrated a good agreement between TsB and patched TcB during PT in preterm neonates. However, in a study by Jangaard, et al. reported TcB measurement during PT was not found to be as sensitive in preterm compared to term neonates. In our study we have not studied the TcB or TsB values in preterm which might open up a scope for another study in preterm babies.

We saw a significant relation between neonatal hyperbilirubinemia and birth weight. 68 babies between 2.5 kg to 3 kg serum bilirubin

above 40th percentile whereas 41 babies between 3.1 kg to 3.5 kg had serum bilirubin above 75th percentile and required phototherapy.

Out of 63 babies delivered by LSCS 29 (46%) had serum bilirubin above 75th percentile and required phototherapy whereas 33(56.8%) out of 58 vaginal delivered babies had serum bilirubin above 75th percentile and required phototherapy. Due to individual variance, any clinical decision has to be taken on the basis of the transcutaneous trend more than on a single value. A transcutaneous bilirubinometer is good to use in clinical settings as evident from above significant results. Significant association was found in results by kramer's rule and TcB assessment from sternum and forehead. This implies significant association between clinical assessment, TCB and TsB measurements. Significant association was found in results with those undergone phototherapy according to TsB and Tcb levels Serial TcB measurements from the patched site after starting PT could have been a better guide to evaluate the trends in correlation during the course of PT. This study has major implications for developing countries where the rate of prematurity is high, necessitating prolonged NICU admissions, phlebotomy losses and unavailability of micro-methods for bilirubin estimation in most laboratories.

References

- Mishra S, Agarwal R, Deorari AK, Paul VK (2008) Jaundice in the newborns. *Indian J Pediatr* 75: 157-163.
- Piazza AJ, Stoll BJ (2008) Jaundice and hyperbilirubinemia in the Newborn. In: Kliegman RM, Behrman RE, Jenson HB, Stanton BF (eds.) *Nelson Text book of Pediatrics* (18th edn), Saunders Elsevier, New Delhi, India, pp: 756-766.
- Penn AA, Enzmann DR, Hahn JS, Stevenson DK (1994) Kernicterus in a full term infant. *Pediatrics* 93: 1003-1006.
- Maisels MJ, Newman TB (1995) Kernicterus in otherwise healthy, breast-fed term newborns. *Pediatrics* 96: 730-733.
- Maisels MJ, Bhutani VK, Bogen D, Newman TB, Stark AR, et al. (2009) Hyperbilirubinemia in the newborn infant > or=35 weeks' gestation: an update with clarifications. *Pediatrics* 124: 1193-1198.
- Maisels MJ, Kring E (1997) Transcutaneous bilirubinometry decreases the need for serum bilirubin measurements and saves money. *Pediatrics* 99: 599-601.
- Simpson E, Goyal NK, Dhepyasuwan N, Flaherman VJ, Chung EK, et al. (2014) Prioritizing a research agenda: a Delphi study of the Better Outcomes through Research for Newborns (BORN) network. *Hosp Pediatr* 4: 195-202.
- Bhutani VK, Gourley GR, Adler S, Kreamer B, Dalin C, et al. (2000) Noninvasive measurement of total serum bilirubin in a multiracial predischargenewborn population to assess the risk of severe hyperbilirubinemia. *Pediatrics* 106: e17.
- Bhat V, Srinivasan S, Usha TS, Puri RK (1987) Correlation of transcutaneous bilirubinometry with serum bilirubin in South Indian neonates. *Indian J Med Res* 86: 49-52.
- Maisels MJ, Ostrea EM Jr, Touch S, Clune SE, Cepeda E, et al. (2004) Evaluation of a new transcutaneous bilirubinometer. *Pediatrics* 113: 1628-1635.
- Rubaltelli FF, Gourley GR, Loskamp N, Modi N, Roth-Kleiner M, et al. (2001) Transcutaneous bilirubin measurement: a multicenter evaluation of a new device. *Pediatrics* 107: 1264-1271.
- Tayaba R, Gribetz D, Gribetz I, Holzman IR (1998) Noninvasive estimation of serum bilirubin. *Pediatrics* 102: e28.
- Carbonell X, Botet F, Figueras J, Rui-Godo A (2001) Prediction of hyperbilirubinemia in the healthy term newborn. *Acta Paediatr* 90: 166-170.
- Ebbesen F, Rasmussen LM, Wimberley PD (2002) A new transcutaneous bilirubinometer, BiliCheck, used in the neonatal intensive care unit and the maternity ward. *Acta Paediatr* 91: 203-211.
- Briscoe L, Clark S, Yoxal CW (2002) Can transcutaneous bilirubinometry reduce the need for blood tests in jaundiced full term babies? *Arch Dis Child Fetal Neonatal* Ed 86: F190-192.
- Nanjundaswamy S, Petrova A, Mehta R, Bernstein W, Hegyi T (2004) The accuracy of transcutaneous bilirubin measurements in neonates: a correlation study. *Biol Neonate*; 85: 21-25.
- Yap SH, Mohammad I, Ryan CA (2002) Avoiding painful blood sampling in neonates by transcutaneous bilirubinometry. *Ir J Med Sci* 171: 188-190.
- Slusher TM, Angyo IA, Bode-Thomas F, Akor F, Pam SD, et al. (2004) Transcutaneous bilirubin measurements and serum total bilirubin levels in indigenous African infants. *Pediatrics* 113: 1636-1641.
- Janjindamai W, Tansantiwong T (2005) Accuracy of transcutaneous bilirubinometer estimates using BiliCheck in Thai neonates. *J Med Assoc Thai* 88: 187-190.
- Catz C, Hanson JW, Simpson L, Yaffe SJ (1995) Summary of workshop: early discharge and neonatal hyperbilirubinemia. *Pediatrics* 96: 743-745.
- Escobar GJ, Braveman PA, Ackerson L, Odouli R, Phox KC, et al. (2001) A Randomized comparison of home visits and hospital-based group follow-up visits after early postpartum discharge. *Pediatrics* 108: 719-727.
- Hemmati F, Kiyani Rad NA (2013) The value of bilicheck® as a screening tool for neonatal jaundice in the South of Iran. *Iran J Med Sci* 38: 122-128.
- Ip S, Chung M, Kulig J, O'Brien R, Sege R, et al. (2004) An Evidencebased Review of Important Issues Concerning Neonatal Hyperbilirubinemia. American Academy of Pediatrics. Subcommittee on Hyperbilirubinemia. *Pediatrics* 114: e130-153.
- Jackson JC (1997) Adverse events associated with exchange transfusion in healthy and ill newborns. *Pediatrics* 99: E7.
- Patra K, Storfer-Isser A, Siner B, Moore J, Hack M (2004) Adverse events associated with neonatal exchange transfusion in the 1990s. *J Pediatr* 144: 626-631.
- Keenan WJ, Novak KK, Sutherland JM, Bryla DA, Fetterly KL (1985) Morbidity and mortality associated with exchange transfusion. *Pediatrics* 75: 417-421.
- Aspberg S, Dahlquist G, Kahan T, Kallen B (2010) Confirmed association between neonatal phototherapy or neonatal icterus and risk of childhood asthma. *Pediatr Allergy Immunol* 21: e733-e739.
- Aspberg S, Dahlquist G, Kahan T, Kallen B (2007) Is neonatal phototherapy associated with an increased risk for hospitalized childhood bronchial asthma? *Pediatr Allergy Immunol* 18: 313-319.
- Maisels MJ, McDonagh AF (2008) Phototherapy for neonatal jaundice. *N Engl J Med* 358: 920-928.
- Dahlquist G, Kallen B (2003) Indications that phototherapy is a risk factor for insulin-dependent diabetes. *Diabetes Care* 26: 247-248.