Research Article

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20162367

Correlation of cord blood bilirubin and neonatal hyperbilirubinemia in healthy newborns

Mayank Pahuja^{1*}, Shikha Dhawan², Sanjata Roy Chaudhary¹

¹Department of Pediatrics, Rohilkhand Medical College and Hospital, Bareilly, Uttar Pradesh, India

Received: 14 April 2016 **Revised:** 03 June 2016 **Accepted:** 08 June 2016

*Correspondence: Dr. Mayank Pahuja,

E-mail: dr.mayankpahuja@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Jaundice is one of the commonest problems that can occur in a newborn. During the first week of life all new-borns have increased bilirubin levels by adult standards, with approximately 60% of term babies 1 and 85% of preterm babies having visible jaundice. This physiological rise in bilirubin causes indirect hyperbilirubinemia after 24 hours of birth, rises progressively with age and resolves gradually with no intervention in majority of cases. A small percentage may however require phototherapy or exchange transfusion when the bilirubin levels exceed the normal range.

Methods: This study was performed at the Neonatal Intensive Care Unit, Department of Pediatrics of Rohilkhand Medical College and Hospital, Bareilly. All the healthy newborns <37weeks-41weeks>, delivered at this hospital fulfilling the inclusion and exclusion criteria were enrolled in the study during One year from January 2014 to January2015. Inclusion criteria was healthy new-borns (37weeks-41weeks) delivered at Rohilkhand Medical College and Hospital and exclusion criteria was Setting of ABO incompatibility, ABO incompatibility, Rhesus blood factor incompatibility. The present study was conducted on 100 term healthy neonates delivered at tertiary care hospital. Serum bilirubin level was estimated at birth (cord blood) and at 3rd day of life. The main outcome measured was significant hyperbilirubinemia requiring treatment (phototherapy/exchange transfusion). Serum bilirubin was estimated clinically as indicated and on day 3 of life.

Results: The area under curve was observed to be 0.75, i.e., the predictive accuracy of the criteria is 75% which implies a fair predictive value of the criteria. Receiver operator curve analysis revealed that a cut-off of 1.875 was 61.3% sensitive and 76.8% specific.

Conclusions: Cord blood bilirubin level of more >1.87mg/dl can reliably predict neonatal hyperbilirubinemia in healthy term neonates.

Keywords: Jaundice, Bilirubin, Neonatal hyperbilirubinemia

INTRODUCTION

Jaundice is one of the commonest problems that can occur in a new-born. During the first week of life all new-borns have increased bilirubin levels by adult standards, with approximately 60% of term babies and 85% of preterm babies having visible jaundice. This physiological rise in bilirubin causes indirect hyperbilirubinemia after 24 hours of birth, rises

progressively with age and resolves gradually with no intervention in majority of cases. A small percentage may however require phototherapy or exchange transfusion when the bilirubin levels exceed the normal range, It is important to identify babies at risk of hyperbilirubinemia, as it can cause acute bilirubin encephalopathy and kernicterus/chronic encephalopathy, which have a high mortality and significant morbidity with long term sequalae.^{2,3}

²Department of Obstetrics and Gynaecology, Rohilkhand Medical College and Hospital, Bareilly, Uttar Pradesh, India

Bilirubin is produced from heme released from destruction of senescent RBCs in the reticuloendothelial system. It is transported to liver by binding to albumin. It is conjugated in the liver and excreted in stool and urine. During intrauterine life, the placenta removes bilirubin from the fetus and after birth; this function is taken over by the liver. However, it may take some time for the liver to be able to do this efficiently.

New-borns produce bilirubin at a rate of approximately 6 to 8 mg per kg per day. This is more than twice the production rate in adults, primarily because of relative polycythaemia and increased red blood cell turnover in neonates.⁴

This exceeds the conjugating capacity of the neonatal liver leading to indirect hyperbilirubinemia. Bilirubin binding to albumin is influenced by acidosis, hypoalbuminemia, lower gestational age, postnatal age (age <3 days) and interference by drugs such as sulpha and some cephalosporins. Indirect bilirubin can cross the blood brain barrier and cause acute encephalopathy. Acute bilirubin encephalopathy can manifest as hypotonia, high pitched cry, retro Collis and seizures.

Risk factors for elevated indirect bilirubin include maternal age, race, maternal diabetes, prematurity ,drugs like vitamin K etc., altitude, polycythaemia, male sex, trisomy 21, cutaneous bruising, blood extravasation (cephalohematoma), Rh isoimmunisation, ABO incompatibility, oxytocin induction, breastfeeding, weight loss/dehydration, delayed bowel movement and a family history of a sibling who had physiological jaundice.

It is difficult to predict the level of serum bilirubin by examination alone. The observer variability and the influence of skin color in clinically evaluating hyperbilirubinemia by 'Kramer index' has been the 'Achilles' heel of this method.⁵ Hence, identifying and treating hyperbilirubinemia at earliest is prudent and a preventable cause of cerebral palsy. A high index of suspicion, clinical examination and monitoring of blood bilirubin levels are absolute prerequisites to achieve this.

When the new-born stays at the hospital for a 72-hour post-delivery period, it is possible to observe the peaking of the physiological jaundice, thus allowing medical intervention, if necessary. However, early discharge of healthy term new-borns after delivery has become a common practice because of medical and social reasons as well as economic constraints leading to readmissions for management of subsequent hyperbilirubinemia.

METHODS

This study was performed at the Neonatal Intensive Care Unit, Department of Pediatrics of Rohilkhand Medical College and Hospital, Bareilly during One year from January 2014 to January 2015.

Study population

All the healthy new-borns <37weeks-41weeks>, delivered at this hospital fulfilling the inclusion and exclusion criteria were enrolled in the study.

Inclusion criteria

Healthy new-borns (37weeks-41weeks) delivered at Rohilkhand Medical College and Hospital

Exclusion criteria

- Setting of ABO incompatibility
- ABO incompatibility
- Rhesus blood factor incompatibility.
- Significant illness requiring NICU admission.
- Major congenital malformations.
- Chronic maternal illness (like DM)
- History of intake of drugs affecting fetal liver
- Presence of cephalhaematoma
- Those who didn't give consent

Method of collection of data

An informed consent was obtained from the parents of the new-born before enrolling them in the study. Demographic profile and relevant information was collected by using structured and pretested proforma by interviewing the mother. Gestational age was assessed by New Ballard score. Cord blood bilirubin, Complete blood counts, Baby Blood group and Direct Coombs test were estimated. Repeat serum bilirubin estimation was done at 72 hours of age. Serum bilirubin was repeated as whenever need was felt. Other investigation like random blood sugar was done if required. Babies were examined daily and looked for evidence of jaundice, sepsis, illness or birth trauma. All the babies were followed up daily for first 3 postnatal days.

Laboratory investigation

- Mother's blood group was done before delivery
- Cord blood (2 ml) was collected from placental side after its separation and subjected to following investigation.
 - Blood group
 - Total and Direct Serum Bilirubin.
 - Complete blood counts
 - Direct coombs test

Venous blood samples were collected from the baby at 72 hours of life. These samples were subjected to following investigation

- Total and Direct Serum Bilirubin.
- complete blood counts

Serum bilirubin estimation was done by diazo method. This method for Bilirubin estimation was based on principle that Bilirubin reacts with Diazotised Sulphanilic acid in acidic medium to form pink colored Azobilirubin with absorbance directly proportional to Bilirubin concentration. Direct Bilirubin, being water soluble directly reacts in acidic medium. However indirect or unconjugated Bilirubin is made soluble using a surfactant and then it reacts similar to direct Bilirubin.

The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 15.0 statistical Analysis Software. The values were represented in Number (%) and Mean±sd.

RESULTS

The present study was conducted in the Neonatal Intensive Care Unit Department of Pediatrics of Rohilkhand Medical College and Hospital, Bareilly over a period of 12 months i.e. from January 2014 to January2015. All the healthy new-borns <37weeks-41weeks>, delivered at this hospital fulfilling the inclusion and exclusion criteria were enrolled in the study but only 100 subjects whose parents gave written and informed consent for cord blood collection and blood collection after a follow up of 72 hours for serum bilirubin levels for diagnosis of hyperbilirubinemia were included in the study.

Table 1: Maternal factors study population.

| Maternal factors | Number of neonates (%) |
|--------------------------------|------------------------------|
| Age of mother (years) | |
| Up to 20 | 15 (15) |
| 21-25 | 51 (51) |
| 26-30 | 30 (30) |
| 31-35 | 4 (4) |
| Total | 100 (100) |
| Range: 18-35 years; M | ean age: 24.79 <u>+</u> 3.54 |
| Multipara | 54 (54) |
| Pregnancy induced hypertension | 28 (28) |

Age of mothers of study subjects ranged from 18 to 35 years. Majority of mothers' age was between 21-30 years (81.0%). Mean age of mothers was 24.79±3.54 years. Out of 100 mothers, 54 were multipara and rests 46 were primipara. Pregnancy induced hypertension was observed in 28 mothers.

Birth weight of approximately 1/3rd of babies was 2.5-2.75 kg (33%); similarly 1/3rd babies had birth weight 2.76-3.00 kg. Birth weight 3.01-3.50 kg was found in only 29 subjects and birth weight >3.51 kg was found in only 5 (5.0%) babies.

Table 2: Distribution of study population according to birth weight.

| Birth weight | Number of neonates (%) |
|--------------|------------------------|
| 2.5-2.75 Kg | 33 (33) |
| 2.76-3.00 Kg | 33 (33) |
| 3.01-3.50 Kg | 29 (29) |
| >3.50 | 5 (5) |
| Total | 100 (100) |

Table 3: Distribution of study population according to gestational age.

| Gestational age (weeks) | Number of neonates (%) |
|-------------------------|------------------------|
| 37 wks – 39 wks 6 day | 57 (57) |
| 40 wks – 42 wks | 43 (43) |
| Total | 100 (100) |

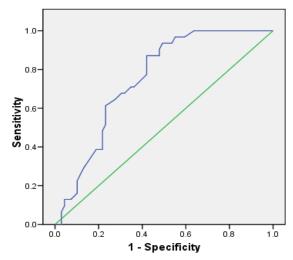
Out of 100 subjects included in the study, gestational age of 37 weeks to 38 weeks 6 days was found in majority of subjects (57%) while rest of the 43 subjects had gestational age 40 weeks to 42 weeks (43%).

Mode of delivery of approximately 2/3 subjects was normal vaginal delivery (64%) and of rest was LSCS.

Table 4: Distribution of study population according to mode of delivery.

| Mode of delivery | Number of neonates (%) |
|-------------------------|------------------------|
| LSCS | 36 (36) |
| Normal vaginal delivery | 64 (64) |
| Total | 100 (100) |

ROC Curve



Diagonal segments are produced by ties.

Figure 1: Receiver-operator curve analysis (ROC).

Table 5: Area under curve to evaluate the diagnostic efficacy of cord blood bilirubin levels to predict neonatal hyperbilirubinemia.

| Area under curve | SE | Significance | 95% Co limit Upper bound | nfidence Lower bound |
|------------------------|-------|--------------|-----------------------------------|----------------------------|
| | | | boulla | Doulla |
| 0.750 | 0.048 | < 0.001 | 0.657 | 0.843 |

Under the nonparametric assumption; Null hypothesis: true area = 0.5

The area under curve was observed to be 0.75, i.e., the predictive accuracy of the criteria is 75% which implies a fair predictive value of the criteria. Receiver operator curve analysis revealed that a cut-off of 1.875 was 61.3% sensitive and 76.8% specific.

All the neonates receiving phototherapy responded well to treatment and no adverse outcome was reported.

Table 6: Sensitivity, specificity, positive and negative predictive values of cord bilirubin level for prediction of 3rd day significant hyperbilirubinemia.

| Cord- bilirubin cut off points (mg/dl) | Specificity | Sensitivity | Negative predictive value | Positive predictive value |
|--|-------------|-------------|---------------------------------|---------------------------------|
| 1 | 20.3 | 100.0 | 100.0 | 36.0 |
| 1.5 | 52.2 | 87.1 | 90.0 | 45.0 |
| 2 | 78.3 | 41.9 | 75.0 | 46.4 |
| 2.5 | 95.7 | 9.7 | 70.2 | 50.0 |
| 1.875 | 76.8 | 61.3 | 81.5 | 54.3 |

DISCUSSION

A total of 100 full-term new-borns delivered and who fulfilled the inclusion criteria at Rohilkhand Medical College and Hospital were enrolled in the study.

On evaluating the maternal profile a total of 15 (15%) mothers were aged \leq 20 years of age whereas a total of 4 (4%) were above 30 years of age. Both advancing age as well as pregnancies at younger age have been reported to be associated with risk of NICU admission. In India, prevalence of teenage pregnancies has been reported to be varying from 8.7% to 24% from various set ups. On the other hand prevalence of late pregnancy (in fourth decade or above) is relatively lowers (6.5%) in India. Trends seen in Indian subcontinent reveal that rates of child bearing is maximum between 20 to 30 years of age and prevalence of pregnancy beyond the age of 30 years is relatively lower. The findings of present study also endorsed maximum proportion of women in 20-30 years age group and pregnancy beyond 30 years to be minimum.

In present study, almost half the mothers (54%) were multipara and a total of 28 (28%) had pregnancy induced hypertension. Relationship between parity and NICU admission has been viewed variedly. In a study by Başer et al, for advancing age pregnancy (≥40 years) the NICU admission rate was almost twice in nullipara (15.2%) as compared to multipara (5.7%), whereas in mothers aged 20-30 years the rate of NICU admission was lower in nullipara (6.9%) as compared to multipara (8.9%). Although, none of the mothers in present study were aged ≥40 years and as such proportional distribution of multipara to nullipara in present study (54/46; 1.17:1) is similar to that reported in the cited study (1.29:1). Pregnancy induced hypertension is a known risk factor for NICU admission.

Funding: No funding sources Conflict of interest: None declared

Ethical approval: The study was approved by the

Institutional Ethics Committee

REFERENCES

- Canadian Paediatric Society. Position Statement (FN 2007-02). Guidelines for detection, management and prevention of hyperbilirubinaemia in term and late preterm new-born infants (35 or more weeks' gestation). Pediatr Child Health. 2007;12:1B-12B.
- American Academy of Paediatrics Subcommittee on Hyperbilirubinemia. Management of Hyperbilirubinemia in the Newborn Infant 35 or more weeks of gestation. Pediatr. 2004;114(1):297-316
- Demott K, Bick D, Norman R, Ritchie G, Turnbull N, Adams C, et al. Clinical Guidelines and Evidence Review For Postnatal Care: Routine Post Natal Care of Recently Delivered Women And Their Babies. National Collaborating Centre for Primary Care and Royal College of General Practitioners. Cited 2009 Feb 12. Pp. 290-296.
- 4. Gartner LM, Herschel M. Jaundice and breast-feeding. Pediatr Clin North Am. 2001;48:389-99.
- Kramer LI. Advancement of dermal icterus in the jaundiced newborn. Am J Dis Child. 1969;118:454-58.
- Yüksel B, Greenough A, Dobson P, Nicolaides KH. Advanced maternal age and smoking: risk factors for admission to a neonatal intensive care unit. J Perinat Med. 1996;24(4):397-403.
- De Jongh BE, Locke R, Paul DA, Hoffman M. The differential effects of maternal age, race/ethnicity and insurance on neonatal intensive care unit admission rates. BMC Pregnancy and Childbirth. 2012;12:97.
- 8. Nili F, Rahmati MR, Sharifi SM. Maternal and neonatal outcome in teenage pregnancy in Tehran Valiasr Hospital. Acta Medica Iranica. 2002;40(1):55-9.
- 9. Sharma AK, Chhabra P, Gupta P, Aggarwal QP, Lyngdoh T. Pregnancy in Adolescents: A

- Community Based Study. Ind J Prev Soc Med. 2003;34(1-2):24-32.
- 10. Mahavarkar SH, Madhu CK, Mule VD. A comparative study of teenage pregnancy. J Obstet Gynaecol. 2008;28(6):604-7.
- Banerjee B, Pandey GK, Dutt D, Mondal M, Deb S. Teenage Pregnancy: A Socially Inflicted Health Hazard. Indian J Community Med. 2009;34(3):227-31
- 12. Kumar A, Chaudhary K, Prasad S. Maternal indicators and obstetric outcome in the north Indian population: A hospital-based study. J Postgrad Med. 2010;56:192-5.
- 13. Sahu TM, Agarwal A, Das V. Advanced maternal age and obstetric outcome. J Obstet Gynecol India. 2007;57(4):320-3.
- 14. Hanif HM. Association between maternal age and pregnancy outcome: implications for the Pakistani society. JPMA. 2011;61(3):313-9.
- 15. Başer E, Seçkin KD, Erkılınç S, Karslı MF, Yeral IM, Kaymak O, et al. The impact of parity on perinatal outcomes in pregnancies complicated by advanced maternal age. J Turkish-German Gynecol Assoc. 2013;14:205-9.

Cite this article as: Pahuja M, Dhawan S, Chaudhary SR. Correlation of cord blood bilirubin and neonatal hyperbilirubinemia in healthy newborns. Int J Contemp Pediatr 2016;3:926-30.