International Journal of Medical and Health Research
ISSN: 2454-9142
www.medicalsciencejournal.com
Volume 4; Issue 5; May 2018; Page No. 69-72

The value of umbilical cord blood bilirubin measurement in predicting the development of significant hyperbilirubinemia in healthy newborn

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Abstract
Introduction: Hospital readmission for neonatal hyperbilirubsinemia is a cause of concern among clinicians in neonatal departments. While early Hospital discharge of neonates is currently recommended by the neonatologists, it carries the risk of delayed recognition of hyperbilirubinemia and the possibility of brain damage due to kernicterus. In our study we aimed to study whether umbilical cord serum (UCS) bilirubin values could predict the risk of significant hyperbilirubinemia requiring treatment in newborns.
Patients and Methods: In a prospective study carried out at the Neonatal Department of Krishna institute of medical sciences (KIMS), umbilical cord serum (UCS) bilirubin was collected from 117 newborns who were categorized into three groups according to UCS bilirubin levels, 4mg/dl respectively. All demographic data was collected from all included newborns and compared among the three groups. Maternal and neonatal blood groups were checked as well cord hemoglobin and hematocrit concentration. The neonates were then followed by TcB at 24hrs, 48hrs & 72hrs of postnatal age and those who showed significant high TcB values according to the hour-specific nomogram, were then sampled by venous blood for total & indirect bilirubin levels. Significant hyperbilirubinemia was interpreted as the need for medical intervention in the form of phototherapy and/or exchange transfusion.
Results of study: A cut-off value of neonatal hyperbilirubinemia in cord blood was 2mg/dl and the end point of the study was the need for treatment. The mean value for total bilirubin in cord blood was significantly higher among newborns whose bilirubin values required phototherapy. The specificity reached 94.2% with a negative predictive value (NPV) of 96.32%. At cut-off cord serum bilirubin level >4mg/dl, the specificity was 98.92% and the NPV was 99.1%.
Conclusion: Cord blood serum bilirubin can be used as a useful screening test for predicting neonatal hyperbilirubinemia and allowing safe postnatal Hospital discharge.

Keywords: hyperbilirubsinemia, umbilical cord serum (UCS)

Introduction

Babies are called newborns during their first month of life. Jaundice is yellow discoloration of skin and sclera. About 60% of term and 80% of preterm neonates are clinically jaundiced. However, jaundice in the newborn might signal a serious, potentially treatable illness and may cause neurological damage, if the bilirubin level is sufficiently elevated.

In this study we are mainly focused on Cord Bilirubin and its significance in predicting neonatal jaundice. Most babies have mild jaundice. It usually gets better or goes away on its own within a week or two without causing problems. Generally jaundice should be taken seriously, it may be physiological or pathological. In rare cases, if the bilirubin level stays high and isn't treated, it can cause brain damage called kernicterus. At times this condition becomes life threatening if it's not properly taken care which may lead to hyperbilirubinemia. We are mainly concerned about various causes, ill effects as well the prevention mechanism of it.

Jaundice is the visible manifestation in skin and sclera of elevated serum concentration of bilirubin. Neonatal jaundice may not appear until serum bilirubin exceeds 5 to 7 mg/dl. Any serum total bilirubin (STB) elevation exceeding 17 mg/dl is considered pathologic and warrants investigations for a cause and possible therapeutic intervention. Neonatal hyperbilirubinaemia is the most common reason of readmission after early hospital discharge.

Early discharge of healthy term newborns after delivery has become a common practice because of medical and social reasons and economic constraints. However, an association between the decreased length of stay and the risk of readmission to the hospital has previously been shown, and it is significant that the most common cause for readmission during the early neonatal period is hyperbilirubinemia.

Thus, the recognition, follow-up, and early treatment of jaundice has become more difficult as a result of earlier discharge from the hospital. Severe jaundice, and even kernicterus, can occur in some full-term healthy newborns discharged early with no apparent early findings of hemolysis

The American Academy of Pediatrics recommends that newborns discharged within 48 hours should have a follow up visit after 2-3 days for any significant jaundice and other problems. And as such, from the obvious need to design and implement a follow up programme, the present study was conducted to find out the critical value of serum bilirubin in the cord blood in predicting the subsequent development of hyperbilirubinemia in healthy newborn.

Aim of the study

The present study was conducted to evaluate the predictive

value of umbilical cord serum (UCS) bilirubin level for identifying term and near term Cord Blood Bilirubin as a Predictor of Neonatal Hyperbilirubinemia newborns with subsequent hyperbilirubinemia. We presume that the use of UCS bilirubin values as a screening tool may help recognizing neonates at risk of developing hyperbilirubinemia requiring treatment.

Patients and Methods

This study was conducted at the Neonatal Department of Krishna institute of medical sciences (KIMS). A total of 117 healthy full-term (>_ 37weeks) and near term (35-<37 weeks) newborns born consecutively at the hospital during a six months period- July 2017 to December 2017 - were eligible for enrolment in the study. Clinical data of all studied neonates was collected including: Birth-weight,gestational age, mode of delivery, sex, Apgar score more than 7 at 1 and 5 minutes, birth trauma, history of Rhisoimmunization, history of previous sibling with neonatal hyperbilirubinemia requiring phototherapy (PT). Cord blood serum (UCS) bilirubin, and newborn's blood group were obtained from all neonates at birth. The cord blood sample was collected by clamping the umbilical cord after delivery of the newborn, then the isolated section is cut and a blood sample is collected into a plane specimen tube. The blood sample was centrifuged and serum was used for estimation of conjugated, unconjugated and total serum bilirubin levels using Colorimetric method using green filter with 450m wavelength by digital bilirubinmeter. The maternal blood group was obtained from the maternal medical record. All neonates in the studied groups were assessed following birth, the neonates who were transferred with their mothers to the maternal ward, were carefully observed by pediatric resident for 48 hours at least, for the development of hyperbilirubinemia. After their discharge, the parents were asked to bring their baby for follow-up 24 hours later for confirmation of serum bilirubin values. Neonates who failed to come for follow-up and the third result of transcutaneous bilirubin (TcB) was not collected were excluded from the study.

All neonates were monitored for developing hyperbilirubinemia by measurement of (TcB) using a non-invasive bilichek, at 24, 48 & 72 hours of age or daily till discharge. TcB was measured on the newborn's forehead, using the BiliCheck device, protected them from direct sunlight and avoiding areas with hair, bruises, nevi or other skin anomalies. The BiliCheck device is a hand-held bilirubinometer that measures TcB levels using multi-wave length spectral reflectance analysis. All measurements were taken with the same BiliCheck device, which was calibrated before each measurement in accordance with the manufacturer's recommendations. The BiliCheck device displays a calculated average of five measurements for each bilirubin estimation.

The neonates were categorized into three groups according to the umbilical cord serum (UCS) bilirubin level. Group (1) UCS bilirubin <2mg/ml, group (2) UCS bilirubin >_ 2-4mg/ml, and group (3) UCS bilirubin >4mg/ml. Group (1) will act as the control group.

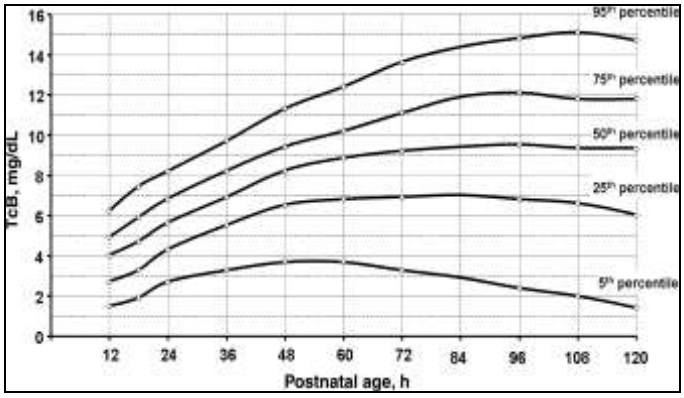

Fig 1

If Tc bilirubin exceeds the appropriate values for gestational age, as matched to values on the percentile-based hourspecific transcutaneous nomogram and risk zones, were subjected to a serum venous bilirubin sample collection according to the clinical guidelines of our department for managing hyperbilirubinemia and the appropriate treatment was then applied accordingly.

The need for phototherapy was determined according to AAP 2004 guidelines, on the basis of gestational age, postnatal age, and the presence or absence of risk factors. All neonates who developed significant hyperbilirubinemia were evaluated with hematocrit measurement, peripheral blood smear, reticulocyte count, blood group analysis and direct Coombs test. Gestational age was determined on the basis of the date of the last menstrual period and was confirmed with the expanded New Ballard Score within 24 hours after birth. Enrolled neonates were discharged from the Hospital according to department policy if Tc bilirubin did not cross the low risk zone for gestational age on the bilirubin hour-specific nomogram. Venous serum bilirubin samples were analyzed using the colorimetric method. The frequency of hyperbilirubinemia at different postnatal ages and the need for phototherapy (PT) were compared among the three groups. An analysis of umbilical cord serum bilirubin (UCS bilirubin) as a predictor of later development of jaundice was performed.

Inclusion Criteria

- Sequentially born, any type of delivery, both genders.
- Gestational age >35 weeks.
- Absence of any major congenital malformations.
- Apghar more than 7 at 1 and 5 minutes
- Birth weight >2 kg

Exclusion Criteria

- Any complication arising during the Hospital stay that could aggravate the hyperbilirubinemia.
- Neonates with direct hyperbilirubinemia.
- There were no signs of cephalhematoma, prolong rupture of membrane, septicemia, bruising, absence of major congenital malformations.

Ethical Aspects

Parental counceling was done and an informed consent was obtained from all parents or gaurdians of the newborns enrolled in the study.

Analysis of results

Maternal and neonatal clinical data was collected. Data was analyzed using descriptive analysis, chi-square, and t-tests. p-values of <0.05 were taken as statistically significant. Sensitivity, specificity, and positive and negative predictive values of different cut-points of the cord total bilirubin were obtained. Receiver Operating Characteristics(ROC) curve analysis was carried out to evaluate the usefulness of cord bilirubin level for identifying neonates at risk.

Results

A total of 117 healthy terms and near term (62 boys & 55 girls) neonates completed the study. The studied neonates were categorized into three groups based on umbilical cord serum (UCS) bilirubin levels: 69 (58.97%) neonates in group(1), 34 boys & 35 girls; 38 (32.48%) neonates in group (B) 20 boys & 18 girls; & 10 (8.55%) neonates in group (3), 5 boys & 5 girls. The characteristics of the neonates who became jaundiced with CSB levels >2.0mg% [group (2) & group (3)] were compared with the nonjaundiced group (1) with CSB levels <2.0mg% are listed in Table(1) As shown there is no statistically significant difference among the three groups as regards gestational age, birth weight & gender. The mean gestational ages in the three studied groups were 38.5±2.93 in group (1), 38.4±2.45 in group (2) & 37.8±2.85 in group (3). The mean birth-weight, in grams, in groups (1), (2) & (3) was 2773±391, 2732±485 & 2694±430 respectively.

A history of neonatal jaundice in a previous sibling was reported in 26 cases (37.7%) in group 1; 8 (21%) in group 2 and 5 (55%) in group 3. Group (2) showed a lower statistically significant value than groups(1) & (3) ($p<0.05$).

Table 1: Clinical characteristics of the study population

Groups (n)	Group 1 (69)	Group 2 (38)	Group 3(10)
Gestational age (mean +- SD)	38.5 +- 2.93	38.4 +- 2.45	37.8 +- 2.85
Birth weight (mean +- SD)	2773±391	2732±485	2694±430
Male : female	34/35	20/18	5/5
NVD/LSCS	47/23	27/11	7/3
Birth trauma N	2	1	1
Rh-ABO incompatibility N	2	4	1
Jaundice in previous siblings (mean +- SD)	26 cases (37.7%)	8 (21%)	5 (55%)

There was no significant difference among the three groups regarding the mode of delivery, whether vaginal delivery or cesarean section, as shown in Table (1)

There was no statistically significant difference among the three groups regarding the occurrence of birth trauma. Group (1) had 2 cases (2.2%) of birth trauma: 1 case of cephalohematoma due to ventous extraction, 1case of assisted breech delivery with superficial bruises. One case (2.6%) of birth trauma were reported in Group (2) neonates: it was a case of cephalohematoma despite spontaneous vaginal delivery. One case (5%) of birth trauma reported in Group (3) was due to Erb's palsy.

The presence of Rh & ABO incompatibility was statistically significantly higher in Group (3) compared to Groups (1) & (2) (65% versus 3% & 10.5% respectively).

There was no statistically significant difference among the cord blood haemoglobin as well.

Table (2) shows that the mean (±SD) TcBilirubin level among the three groups, showed statistically significant increase in Group (3) compared to Groups (1) & group (2) at 24 hours of age, 3.3 ±0.75 & 5.5±2.2 in Groups (1) & (2) respectively against 10 ±3.1 in Group (3) ($p<0.01$)

Table 2: Comparison of CSB, TcB at 24, 48 & 72 hours of age among the three groups

	Group 1	Group 2	Group 3
Cord bilirubin (mg/dl) (mean±SD)	1.58±0.38	2.71±0.46	4.25±0.26
Serum bilirubin (mg/dl) at 24 h	3.3±0.75	5.5±2.3	10±3.1
Serum bilirubin (mg/dl) at 48 h	4.9± 1.44	8.1±2.8	14±3.6
Serum bilirubin (mg/dl) at 72 h	7.2±2.79	12±3.9	16±4.1
Peak serum bilirubin (mg/dl)	10±4.7	14±4.6	17±4.3
Time of Peak serum bilirubin (mg/dl)	92±20.1	88±15.7	66±17.5
Phototherapy N	3	16	10

There was progressive rise in mean total serum bilirubin (TSB) level as measured in the three groups to reach a peak of 10 ±4.7mg/dl at a mean postnatal age of 92±20.1 hours in group (1) neonates & 14 ±4.6 at a mean peak age of 88 ± 15.7 in group (2) compared to a more significant & rapid rise in group (3) (17 ±4.3mg/dl, $p<0.05$) at an earlier postnatal age (66 ± 17.5 hour of age) Neonates in Group (3) had a statistically significant higher peak of serum bilirubin level ($p<0.01$). Differences in cord blood bilirubin levels between the three groups were statistically significant ($p<0.001$). Neonates with UCS bilirubin level <2 mg% accounted for 59% of the study population. Only 6 % of these neonates developed significant hyperbilirubinemia requiring phototherapy treatment.

The frequency of patients with hyperbilirubinemia or phototherapy increased with increasing UCS bilirubin levels. While patients with UCS bilirubin levels between 2-4mg% had a 44.6% chance to develop significant hyperbilirubinemia requiring phototherapy.

The optimum cut-off level for prediction of neonatal jaundice using umbilical cord blood bilirubin was 2.0mg/dl. The probability of neonates with a CSB value <2.0mg/dl developed hyperbilirubinemia was 34.94% (positive predictive value, PPV). Likewise, the probability that neonates who did not develop significant hyperbilirubinemia (not requiring medical intervention) had CSB values <2.0mg/ dl was 94.2% (specificity), while the probability of neonates without significant hyperbilirubinemia had CSB values <2.0 mg/dl was 97.32% (negative predictive value, NPV).

The receiver operating characteristic (ROC) curve demonstrates that UCS bilirubin >4mg/dl had a high sensitivity approaching 97% and specificity 98.92% that predict the newborn that would develop significant

hyperbilirubinemia requiring medical intervention and a NPV of 99.1% The area under curve = 0.8722 (Fig. 2).

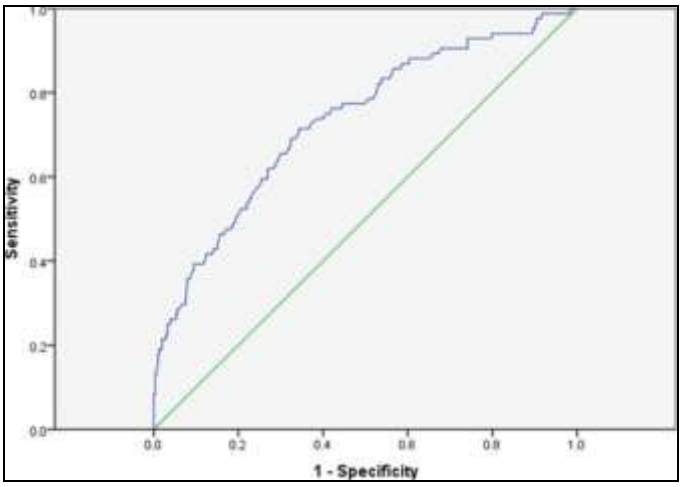

Fig 2

Discussion

Higher cord bilirubin levels among neonates who later became jaundiced compared to cord bilirubin levels in nonjaundiced neonates indicate that mechanisms of importance for the subsequent jaundice are already active in late fetal life. Nearly all fetal bilirubin is unconjugated, due to a limited ability of the fetal liver to conjugate bilirubin.

A clear correlation between umbilical cord serum bilirubin (UCB) & subsequent development of hyperbilirubinemia was shown among all the three studied groups. Newborns presenting levels higher than 4mg were a group at risk of developing severe hyperbilirubinemia and should be reassessed, since this group presented mean serum bilirubin levels that were higher than 16mg/dl at 72 hours of postnatal age with a peak level of 17 ±4.3mg/dl at 66± 17.5 hours of postnatal age. There was also a significant association between the serum bilirubin in cord blood and the newborn's bilirubin level at several postnatal ages.

In the present study, the most useful cut off point for the serum bilirubin levels in cord blood was 2.0mg/dl. With this cut off point, whenever values that were equal to or greater than this were found, the newborn had a probability of more than 50% that phototherapy would be needed.

Adélia & Conceição in 2004, speculated that it may be considered that the umbilical cord blood to be a kind of “file” for the newborn, as it could be collected, stored and used for further analysis of bilirubin levels, should a slightly or moderately jaundiced neonate be considered for early discharge from hospital. Such a proposal may therefore constitute an additional predictive method that is available for evaluating the occurrence of severe hyperbilirubinemia by the third day of life. Accordingly, this proposal may help in assuring safer early discharge for these newborns.

Bernaldo and Segre investigated the predictability of umbilical cord blood unconjugated bilirubin concentration on subsequent hyperbilirubinemia and need for therapy. Utilizing a cut-off point of un-conjugated bilirubin of 2.0 mg/dl, they showed that 53% babies needed phototherapy and raising the cut-off value to 2.5 mg/dl predicted that 72% babies need phototherapy.

In our study, the cord bilirubin level of >2mg/dl had the highest sensitivity (89.5%), and this critical bilirubin level had a very high (98.7%) negative predictive value and fairly low (38.6%) positive predictive value. According to our findings, the critical cut-off level of cord bilirubin 2mg/dl, predicted 90% of the newborns who developed jaundice.

Conclusion

The results of this study confirm that measurement of umbilical cord serum bilirubin level can be used as a screening tool for predicting the development of significant hyperbilirubinemia.

References

1. Stoll BJ, Kleigman RM. Jaundice and hyperbilirubinemia in newborn. In: Behrman R.E., Kliegman Rm, Jenson H.B. ed. Nelson Textbook of Pediatrics 16th edn, WB Saunders Company, 2000, 513-517.
2. Bhutani VK, Johnson L, Sirieri EM. Predictive ability of a predischarge hour-specific serum bilirubin for subsequent hyperbilirubinemia in healthy term and near-term newborns. Pediatrics. 1999; 103(1):6-14.
3. Bhutani VK, Gourley GR, Adler S, Kreamer B, Dalin C, Johnson LH. Noninvasive measurement of total serum bilirubin in a multiracial predischarge newborn population to assess the risk of severe hyperbilirubinemia. Pediatrics. 2000; 106(2):E17.
4. American Academy of Pediatrics: Practice parameter: Management of hyperbilirubinemia in the healthy term newborn. Pediatrics. 1994; 94:558-567.
5. Ballard JL, Khoury JC, Wedig K *et al*. New Ballard Score, expanded to include extremely premature infants. J. Pediatrics. 1991; 119:417-423.
6. Lee KS, Perlman M, Ballantyne M. Association between duration of neonatal hospital stay and readmission rate. J. Pediatr. 1995; 127:758-766.
7. Maisels MJ, Newman TB. Kernicterus in otherwise healthy, breast-fed term newborns. Pediatrics. 1995; 96:730-733.
8. Adélia Jeha Nasser Bernaldo, Conceição Aparecida de Mattos Segre. Bilirubin dosage in cord blood: could it predict neonatal hyperbilirubinemia? São Paulo, Brazil. Sao. Paulo. Med. J. 2004; 122(3):99-103.
9. Bernaldo AJN, Segre CA, de Mattos. Bilirubin dosage in cord blood: could it predict neonatal hyperbilirubinaemia? Sao Paulo Medical Journal. 2004; 122:99-103.