Original Research Article

Umbilical cord bilirubin level used as a predictor of significant hyperbilirubinemia in newborns: An observational study

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Abstract

Background: Neonatal Hyperbilirubinemia (NH) is the most common medical problem affecting newborn infants during first week of life. It is recommended to discharge newborns infants early. This carries the increased rate of readmission which is a concern to clinician. This in turn delays the early recognition of significant hyperbilirubinemia. An observational study was done to evaluate the predictive value of umbilical cord blood bilirubin in identifying significant hyperbilirubinemia in full term newborns. **Aim:** To evaluate the umbilical cord blood bilirubin (CBB) level as a predictor of significant hyperbilirubinemia and the occurrence of NH. **Methods:** The study was performed at the Department of Pediatrics of a Rural Tertiary Health Care Centre. Intramurally delivered, 132 healthy full-term newborns during 1-year period were prospectively enrolled. CBB was estimated. Serum bilirubin estimation was done at 48 hours and 5 day of age and later if required. The association between cord blood bilirubin and neonatal hyperbilirubinemia was analyzed by Pearson Chi Square (Fishers Exact) test. **Results:** In the present study the incidence of significant NH was 3.78%. On second postnatal day mean total serum bilirubin was 11.50 ± 2.60 mg/dl and on fifth postnatal day was 10.40 ± 2.30 mg/dl**.** The cut-off value of cord bilirubin ≥3 mg/dl had a sensitivity and specificity of 100% and 98.42 % respectively with positive predictive value of 71.42 % and negative predictive value of 100% in predicting significant hyperbilirubinemia. **Conclusions:** Present study suggests that the healthy term babies (without Rh and ABO incompatibility) with CBB level ≥3mg/dl should be followed more frequently to look for significant NH.
Keywords: Neonate, Jaundice, Rural.

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Received Date: 02/03/2021 Revised Date: 12/04/2021 Accepted Date: 07/05/2021
DOI: https://doi.org/10.26611/10141911

Access this article online	
Quick Response Code:	Website: www.medpulse.in
	Accessed Date: 02 July 2021

INTRODUCTION

Neonatal jaundice is one of common condition affecting neonates which requires urgent medical attention. About 60% of term and 80% of preterm neonates suffer from neonatal hyperbilirubinemia (NH) during first week of life.[1] High serum bilirubin levels can lead to neurological impairment with serious sequelae in a few jaundiced babies which can be prevented with early intervention and prompt treatment.[2] Many newborns get early discharge (within 2 days after birth) especially in resource limited settings in rural areas of developing countries.[3] These newborns are at risk of having neonatal jaundice and its potential complication. Various parameters like cord bilirubin estimation[4,5], bilirubin estimation during 6 to 24 hours of age[6,7,8,9], predischarge hour specific bilirubin estimation,[10] and transcutaneous bilirubin measurement[11,12,13,14] are studied by researchers to predict hyperbilirubinemia and its subsequent course

How to cite this article: Tushar L Sonawane, Vaibhav K Gode. Umbilical cord bilirubin level used as a predictor of significant hyperbilirubinemia in newborns: An observational study. *MedPulse International Journal of Pediatrics.* July 2021; 19(1): 01-04. http://medpulse.in/Pediatrics/index.php

in newborns. It is very challenging to predict which infants are at heightened risk for significant and comparably late hyperbilirubinemia. Umbilical cord blood bilirubin (UCB) level is a cheap and non-invasive method which can be performed by semiskilled healthcare worker in resource limited set up.[8,9] There is an obvious need to develop predictive guidelines that will enable the Paediatricians to identify neonates which are likely to develop significant NH.[2] Hence, it was decided to study a comparison of cord blood bilirubin and serum bilirubin on 48th hour-of-life in term neonates to detect and prevent significant NH in infants getting early discharge.

MATERIALS AND METHODS

The study was conducted in the Department of Pediatrics of a rural tertiary health care centre over a period of 12 months from January 2020 to December 2020. This was a prospective observational study. All healthy term babies (≥37 weeks) delivered at our hospital were prospectively enrolled in the study.

Approval from ethical committee of institute taken. [Approval no 544/SMBT/02/SS/UG/IEC /20/11]

Inclusion criteria: All full term neonates (gestation age ≥37weeks to 42 weeks) and birth weight more than 2500gm irrespective of mode of delivery.

Exclusion criteria: Newborns having risk factors for the development of severe hyperbilirubinemia like jaundice in first 24 hrs, ABO and/or Rh incompatibility [12(66.66%)], cephalohematoma or significant bruising [2(11.11%)], significant co morbidities requiring N.I.C.U. admission [4(22.2%)]. Out of 150 newborns 18 were excluded since they did not meet the inclusion criteria.

Methodology: Informed written consent was obtained from parents. The detailed history was collected from parents by using pre-structured pro-forma. Blood samples were collected from umbilical cord at birth and venous blood samples of the neonates was collected at 48 hours and the end of five days after birth and tested for total, direct and indirect serum bilirubin. For the present study cord blood hyperbilirubinemia was defined as cord blood total bilirubin level ≥3mg/dl. Neonatal hyperbilirubinemia is defined as significant when serum bilirubin level is more than or equal to15 mg/dl. [15] The serum bilirubin levels were monitored more frequently if required. Bilirubin estimations were done using DIAZO method in the biochemistry laboratory. Additional investigations were done as per the case requirements.

Statistical analysis: The data was collected and analyzed in Microsoft excel by using registered version of SPSS 21 (IBN California). The quantitative data like total cord blood bilirubin, day 2 and day 5 bilirubin, birth weight were expressed in mean ± SD while the qualitative data like gender, blood group were expressed in frequency and % distribution. The association between cord blood bilirubin and neonatal hyperbilirubinemia was analyzed by Pearson Chi Square (Fishers Exact) test. The 2×2 table was plotted for calculating the sensitivity, specificity, positive predictive value and negative predictive value. P value < 0.05 was considered as significant.

Sample size: Sample size was calculated by formula from Epi info software using formula

Sample size n = **[DEFF*Np (1-p)]/ [($d^2/Z^2_{1-\alpha/2}$*(N-1) +p*(1-p)]**

Sample size: 132

RESULTS

The study consisted of 132 healthy full term newborns [67 were males and 65 were females] that were followed up for first 5 postnatal days and further if necessary.

Table 1: Baseline characteristics of neonates studied (N=132)

Details of neonate	Number of neonates	%
Gender		
Male	67	50.75
Female	65	49.24
Birth weight (kg)		
2.50-3.00	104	78.78
3.01-3.50	24	18.19
3.51-4.00	4	3.03
Blood group		
A+	30	22.72
B+	41	31.06
AB+	18	13.63
O+	43	32.57

Table 2: Bilirubin profile of the study population

Variable	Minimum	Maximum	Mean ± SD
Cord blood total bilirubin	0.40	3.70	2.60 ± 0.70
Day 2 total bilirubin	3.00	20.70	11.50± 2.60
Day 5 total bilirubin	4.50	21.50	10.40 ± 2.30

The maximum recorded cord serum total bilirubin (STB) was 3.70 mg/dl and the minimum recorded cord STB was 0.4 mg/dl. The mean cord STB was 2.60±0.70 (Table 2). Out of 132 newborns, 7 had umbilical cord bilirubin level more than 3 mg/dl, of whom 5(3.78%) had significant hyperbilirubinemia (TSB ≥ 15 mg/dl). The results obtained were put in a 2×2 table to determine specificity, sensitivity, positive predictive value, negative predictive value and diagnostic accuracy (Table 3 and 4). The correlation between cord blood bilirubin and development of significant hyperbilirubinemia in the first two days was statistically significant (p value < 0.05). The incidence of significant hyperbilirubinemia in the study population is 3.78 %.

Table 3: Sensitivity, specificity, positive and negative predictive values of cord blood bilirubin levels at (>3mg/dl) in diagnosis of significant hyperbilirubinemia

Cord bilirubin at birth	Significant hyperbilirubinemia (At 48 hours of life)	Without significant hyperbilirubinemia (At 48 hours of life)	Total
Cord bilirubin ≥3 mg/dl	5 (100%)	2 (1.6%)	7 (5.5%)
Cord bilirubin <3 mg/dl	0 (0%)	125 (98.4%)	125 (98.4%)
Total	5(0%)	127 (100%)	132 (100%)
Pearson Chi Square (Fishers Exact) =74.24 p value < 0.001			

Table 4

Parameter	Estimate	95% CIs
Sensitivity	100%	(56.55, 100)
Specificity	98.43%	(94.44, 99.57)
Positive Predictive Value	71.43%	(35.89, 91.78)
Negative Predictive Value	100%	(97.02, 100)
Diagnostic Accuracy	98.48%	(94.64, 99.58)

DISCUSSION

The incidence of significant neonatal hyperbilirubinemia is 3.78% in the present study which is lower than the other comparable studies.[5,6,7,8,9,15,16,19] Low incidence can be attributed to the fact that neonates with no risk factors were only included in the study. Variables such as gender of the baby and birth weight [2.5-4 kg] did not have significant association with subsequent development of NH. Cord blood bilirubin level >3 mg/dl had sensitivity and specificity of 100% and 98.43% and can be taken as a cut off value above which, a neonate would develop hyperbilirubinemia and would require phototherapy. The negative predictive value of 100% suggests that the cord blood bilirubin level estimation can help in detection of newborns not requiring further follow up and intervention. Rosenfeld J *et al.* stated that if cord bilirubin level less than 2.0 mg/dl in newborns then has only a 4 percent chance of developing significant hyperbilirubinemia. However, if serum cord bilirubin levels are more than 2.0 mg/dl, the infant has a 25 percent chance of developing subsequent hyperbilirubinemia.[2] Knupfer *et al.*, observed that if cord serum bilirubin level between 1.75-2.34 mg/dl then 3.4% newborns has a chance of significant hyperbilirubinemia and if CBB >2.34 mg/dl, the newborns has a 8.6% chance of developing significant hyperbilirubinemia.[5] Taksande *et al.*, predicted that if cord bilirubin level >2 mg/dl then jaundice occurred in 9.5% newborns and had 89.5% sensitivity, high (98.7%) negative predictive value and fairly low (38.6%) of positive predictive value.[15] Knudsen A found that if cord bilirubin was below 1.17mg/dl, 2.9% became jaundiced as opposed to 85% if cord bilirubin was above 2.34mg/dl with sensitivity of 13%, specificity of 99%, and positive predictive value of 85% and negative predictive value of 72%. Furthermore, 57% of jaundiced infants with cord bilirubin above 2.34mg/dl required phototherapy, but only 9% if cord bilirubin was 2.34mg/dl or lower (p less than 0.003).[17] Rataj J *et al.* reported that if cord bilirubin was less than 1 mg%, jaundice occurred in 2.4% newborns, where as 89% of the infants with cord bilirubin above 2.5 mg% became jaundiced.[18] It is noted that different authors have used different cut off value of umbilical cord blood bilirubin level for predicting significant jaundice. This variability credited to individuality of laboratories to estimate bilirubin level. Therefore, it is important that studies should be done to

find out cut off value that will be used as a predictor for development of significant hyperbilirubinemia.

LIMITATIONS OF THE PRESENT STUDY

In the present study only full term healthy neonates were taken for the study. Since the peak bilirubin level reaches on 3rd and 5th postnatal days, babies are followed till 5 days of delivery. In view of early discharge of the babies delivered vaginally, increased representation of babies extracted by caesarean section are taken.

CONCLUSION

Present study suggests that the healthy term babies (without Rh and ABO incompatibility) with CBB level ≥3mg/dl should be followed more frequently to look for significant NH. Further studies with large sample size with heterogeneous group of neonates are required to establish UCB level > 3mg/dl as predictor of significant NH. It is recommended to have cord blood bilirubin estimation of all healthy term babies delivered in an institution to prevent the dangerous consequences of neonatal hyperbilirubinemia like kernicterus. This can reduce the morbidity and mortality due to hyperbilirubinemia.

ACKNOWLEDGEMENTS:

We wish to thank the consultant paediatricians, pathologists, resident doctors and nursing staff of paediatric department of SMBT medical college, hospital and research centre, Dhamangaon, Igatpuri, Nashik.

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Source of Support: None Declared
Conflict of Interest: None Declared