www.jmscr.igmpublication.org
Impact Factor 5.84
Index Copernicus Value: 83.27
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v5i4.99

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Original Articles

Umbilical Cord Bilirubin-an Early Diagnostic Marker of Significant Neonatal Hyperbilirubinemia

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ABSTRACT

Background: *To study the correlation between umbilical cord blood bilirubin and significant neonatal hyperbilirubinemia in healthy term newborns.*

Methods: *The cord blood bilirubin estimation was done at birth for all enrolled cases. All the neonates were clinically observed for the development of icterus for 5 days and serum bilirubin level was measured in neonates who developed jaundice on clinical evaluation. Significant hyperbilirubinemia was considered when serum bilirubin levels in term newborns was more than or equal to 12 mg/dl at 24 hours of life, 15 mg/dl at 48 hours, and 17 mg/dl at 72 hours.*

Results: *Total of 250 neonates were enrolled. Out of these, 27 newborns (10.8%) had significant hyper-bilirubinemia. Mean ± SD cord blood bilirubin level in no hyperbilirubinemia group and hyperbilirubinemia group was 1.657 ± 0.40 mg/dl and 2.607 ± 0.256 mg/dl respectively. There was significant association between cord blood bilirubin level and hyperbilirubinemia ($p<0.001$). Using Receiver operating characteristic analysis level of cord blood bilirubin at2.2 mg/dl had the high sensitivity (92.6%) and specificity (90.6%) to predict the newborn that would develop significant hyperbilirubinemia with the positive predictive value of 54.3% and the negative predictive value of 99.0%.*

Conclusion: *There is a positive correlation between umbilical cord blood bilirubin level and significant hyperbilirubinemia. Healthy term neonates with umbilical cord blood bilirubin level of 2.2 mg/dl or more are at higher risk for development of significant hyperbilirubinemia with high sensitivity and specificity. Newborns with umbilical cord bilirubin level < 2.2 mg/dl are at much lower risk and hence can be discharged early.*

Keywords: *neonatal hyperbilirubinemia, neonatal jaundice, umbilical cord bilirubin.*

Introduction

Neonatal hyperbilirubinemia is a clinical condition that is common in paediatric practice and constitutes one of the major issues within the neonatal period. It occurs as both physiological and pathological processes in newborns. Most neonatal jaundice is benign, but because of the potential toxicity of bilirubin, newborn must be

monitored to identify those who may develop severe hyperbilirubinemia and, in rare cases, may develop bilirubin encephalopathy.

Incidence of significant hyperbilirubinemia is 10.5% in term newborns and 25.3% in near term newborns [(1)]. Neonatal hyperbilirubinemia is significant when serum bilirubin levels in term newborns are more than or equal to 12 mg/dl at 24 hours of life, 15 mg/dl at 48 hours, and 17 mg/dl at 72 hours [(2)]. Despite improved understanding of the physiologic features of bilirubin and the mechanisms of bilirubin neurotoxicity, our ability to predict which infants are at greatest risk remains imprecise. Early discharge of healthy term newborn after delivery has become a common practice because of medico-social reasons and economic constraints and hence these discharged babies need to be followed up for development of hyperbilirubinemia [(2)]. But a complete follow up is not always possible due to socio economic reasons and patient's noncompl-iance. Early discharge before 72 hrs had significantly increased the risk of readmission with hyperbilirubinemia [(3,4)]. Severe jaundice and even kernicterus can occur in some full term healthy newborns discharged early with no apparent early findings of hemolysis [(5)]. So, it is desirable to identify newborns who are at risk of developing significant hyperbilirubinemia, in order to implement early treatment and minimize the risk of bilirubin induced brain damage. Thus, the investigation of parameters that might help in predicting the development of significant hyperbilirubinemia is justifiable. Present study was conducted to determine whether umbilical cord blood bilirubin levels could predict significant hyperbilirubinemia among full term newborns without complications.

Material and Methods

The present study was conducted in department of Pediatrics, between January 2015 to December 2015. During the study period 250 healthy full term newborns born in ourhospital were enrolled. Newborns with birth weight of less than 2500 grams or who developed significant illness requiring NICU admission, with major congenital malformations and Conjugated hyperbilirubinemia were excluded. This study was approved by ethics and scientific committees of Mata Chanan Devi Hospital and written informed consent was taken from the parents of the all newborns who were enrolled for the study. Relevant maternal and neonatal details were collected.

The cord blood bilirubin estimation was done at birth. All the neonates were clinically observed for the development of icterus for 5 days and serum bilirubin level was measured in neonates who developed jaundice on clinical evaluation. The cord blood bilirubin and after birth serum bilirubin levelswere measured using - a photometric method on Beckman coulter AU480 for estimation of direct and total bilirubin. Significant hyperbilirubinemia was considered when serum bilirubin levels in term newborns were more than or equal to 12 mg/dl at 24 hours of life, 15 mg/dl at 48 hours, and 17 mg/dl at 72 hours.

Statistical Analysis

Statistical testing was conducted by using the socialscience system version SPSS 17.0. Continuous variables were presented a smean±SD or median (IQR) for non-normally distributed data. Categorical variables were expressed as frequencies and percentages. The comparison of normally distributed continuous variables between the groups was performed using Student's t test. Nominal categorical data, between the groups, was compared using Chi-squared test or Fisher's exact test as appropriate. A receiver operating characteristics (ROC) analysis was calculated to determine optimal cutoffvalue for umbilical cord blood total bilirubin level. The area under the curve, the sensitivity, and the specificity was calculated to analyze the diagnostic value of umbilical cord blood total bilirubin level. For all statistical tests, a p value less than 0.05 was taken to indicate a significant difference.

Results

We enrolled 250 healthy term newborns, 135 were male (54%) and 115 were Female (46%), out of which 177 (70.8%) cases were delivered by ceasarian section and 73 (29.2%) cases were vaginal delivery. Mean ± SD Birth weight was 2.98 ± 0.361 kg with mean ± SD gestational age was 37.92 ± 0.89 weeks.

Out of 250 cases 27 newborns developed significant hyperbilirubinemia (10.8%). We found no significant association between the cases who did and who did not develop significant hyperbilirubinemia with respect to various factors such as birth weight, mode of delivery i.e., LSCS or normal vaginal delivery, gestational age, gender with value $P > 0.05$ (table 1).

In our study, hyperbilirubinemia was significantly associated with the presence of maternal-fetal blood group incompatibility (p<0.001). Out of 250 newborns, 46 (18.4%) cases had ABO (O-A or O-B) incompatibility and 18 (7.2%) cases had Rh incompatibility. In neonates with ABO incompatibility, 14 (30.4%) cases had significant hyperbilirubinemia, whereas in cases of Rh incompatibility, 2 (11.1%) developed significant hyperbilirubinemia.

Mean ± SD cord blood bilirubin level in no hyperbilirubinemia group and hyperbilirubinemia group was 1.657 ± 0.40 mg/dl and 2.607 ± 0.256 mg/dl respectively. There was significant association between cord blood bilirubin level and hyperbilirubinemia (p<0.001).

In neonates with significant hyperbilirubinemia, 92.6% were having cord Blood bilirubin level2.2 mg/dl or more and only 7.4% were having cord blood bilirubin level <2.2 mg/dl. While in neonates with no significant hyperbilirubinemia majority (90.6%) were having cord blood bilirubin level < 2.2mg/dl.

Receiver operating characteristic analysis demonstrates that cord blood bilirubin2.2 mg/dl had the high sensitivity (92.6%) and specificity (90.6%) to predict the newborn that would develop significant hyperbilirubinemia. At this level the positive predictive value was 54.3% and the negative predictive value was 99.0%. Area under curve was 0.973. So optimum cut off level for prediction of significant neonatal hyperbilirubinemia using umbilical cord blood bilirubin was 2.2 mg/dl (fig-1).

Fig: 1 –Receiver operating characteristic curve

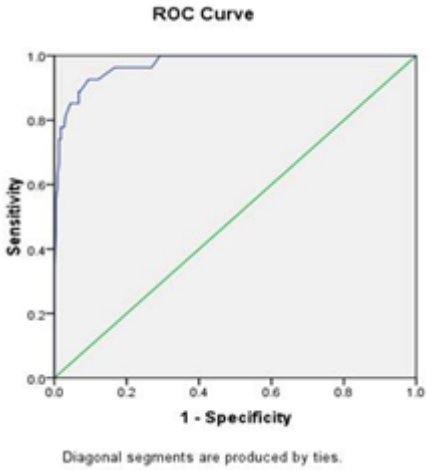

Table 1 Comparison of various factors between no hyperbilirubinemia and significant hyperbilirubinemia group

Variable	No Hyperbilirubinemia	Hyperbilirubinemia	P value
Gender: male/female	118/105	17/10	0.322
Mean Birth weight (kg)	2.97 ± 0.36	3.00 ± 0.36	0.682
Mean Gestational age (weeks)	37.91 ± 0.89	38.03 ± 0.93	0.510
Delivery: LSCS/vaginal	159/64	18/9	0.617
Blood group incompatibility No ABO or Rh/ ABO/Rh incompatibility	175/32/16	11/14/2	<0.001
Mean Cord bilirubin level (mg/dl)	1.657 ± 0.40	2.607 ± 0.256	<0.001

Discussion

Jaundice is common clinical condition in neonates that can be associated with bilirubin encephalopathy or bilirubin-induced neurologic dysfunction. Higher levels of umbilical cord blood bilirubin among neonates who later on developed

significant hyperbilirubinemia indicates that mechanism of subsequent jaundice are active in late fetal life. In their study Bernaldo AJ et al. [6] concluded that in full term neonates, values of cord blood unconjugated bilirubin was significantly higher in newborns who required phototherapy.

In a study done by Eshwara Chary et al. [7] to identify the newborns at risk for developing significant hyperbilirubinemia using cord blood serum bilirubin levels, out of 282 healthy term newborns 51 (18.09%) developed significant hyperbilirubinemia. In their study, the umbilical cord bilirubin cut off point was 2 mg/dl which had good sensitivity (94.12), specificity (90.9%), positive predictive value (69.57%) and negative predictive value (98.59%).

Similarly Amar Taksande et al. [8] in their study on healthy term neonates for prediction of neonatal hyperbilirubinemia, concluded that the cord blood bilirubin level of more than 2 mg/dl had the highest sensitivity (89.5%), and also showed this critical bilirubin level had a very high (98.7%) negative predictive value and a low (38.6%) positive predictive value.

In the present study out of 250 neonates, 27 patients developed significant hyperbilirubinemia with incidence rate of 10.8%. Similar incidence of 9.4% and 14% was seen in study by Nahar Z et al.[9] and Gurdeep Singh Dhanjal et al[10] respectively.

Our study showed significant association between umbilical cord blood bilirubin level and hyperbilirubinemia. In this study using the critical value of 2.2 mg/dl or more, umbilical cord blood bilirubin can predict the newborns who can develop significant hyperbilirubinemia with sensitivity of 92.6% and specificity of 90.6%. At this critical level of 2.2 mg/dl the positive predictive value was 54.3% and the negative predictive value was 99.0%.

Conclusions

Based on our results, we conclude that significant positive correlation is present between umbilical cord blood bilirubin level and significant hyperbilirubinemia. Cutoff umbilical cord blood bilirubin level of 2.2 mg/dl in healthy term neonate can predict significant hyperbilirubinemia with high sensitivity and specificity. Neonates with umbilical cord bilirubin level < 2.2 mg/dl are at low risk of significant hyperbilirubinemia and can be discharged early from hospital. Umbilical cord blood bilirubin level can be used as screening tool for development of significant hyperbilirubinemia.

Acknowledgements – funding none.

Disclosure - The authors declare no conflict of interest.

Author contribution- AKT contributed to conception and design of this study, AG performed and collected the data, AKT and AG drafted and analysed the manuscript, AKT critically reviewed and supervised the whole study. All authors read and approved the final manuscript.

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