Section: Pediatrics

Research

A PROSPECTIVE COHORT STUDY ON PREDICTIVE MARKERS OF NEONATAL HYPERBILIRUBINEMIA IN CORD BLOOD

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Abstract

Background: One of the frequent reasons for hospital readmission in the neonatal period is jaundice. To prevent severe hyperbilirubinemia, accurate predictive markers that allow doctors to determine which neonates may experience major hyperbilirubinemia are now essential. Therefore, we sought to identify early, accurate measures using cord blood bilirubin, albumin bilirubin/albumin ratio and alkaline phosphatase levels to serve as diagnostic markers for newborn hyperbilirubinemia. **Materials and Methods:** This prospective cohort purposive sampling study was conducted between January to December 2019 at the Government hospital in Thoothukudi, India. Three hundred newborns with a gestational age greater than 35 weeks were studied. Cord blood bilirubin, albumin, bilirubin albumin ratio and alkaline phosphatase levels were estimated. Newborns were clinically followed up daily, and serum bilirubin level was measured on day 4 of life. **Result:** When the serum bilirubin level in the AAP nomogram is above the curve based on hours of life, significant jaundice is taken into account. This study found that for cord blood bilirubin, the cut-off value is >2.15 mg/dl. 3.75 g/dl is the cut-off value for cord blood albumin. The threshold value for alkaline phosphatase is >151 IU/L, and the threshold value for the bilirubin albumin ratio is >0.86. **Conclusion:** To predict the incidence of significant jaundice requiring treatment, we advise measuring the bilirubin, albumin, bilirubin albumin ratio, and alkaline phosphatase in cord blood.

INTRODUCTION

More than half of all newborn babies have visible jaundice secondary to hyperbilirubinemia. Hyperbilirubinemia in the neonatal period is a common, benign and temporary issue that is frequently physiologic. Therefore, interventions are typically not required. Total serum bilirubin levels increase during the first week of life due to a rise in bilirubin production and fall after bilirubin clearance. The liver effectively conjugates and excretes bilirubin, and total serum bilirubin concentrations return to normal. When the bilirubin level reaches about 80 mol/L, infants exhibit clinical jaundice. Newborn jaundice is a crucial clinical trait since it may indicate an underlying problem like hemolytic anaemia, infection, an inborn error of metabolism or liver disease. In extreme circumstances, basal ganglia, in particular, can accumulate significant levels of unconjugated hyperbilirubinemia, leading to kernicterus, cerebral palsy and death when Total serum bilirubin levels concentrations are extremely high and rising quickly. Also, hemolytic disease of the foetus and newborn, a risk factor for early-onset HB and bilirubin-induced neurotoxicity, can be brought on by maternal-fetal blood group incompatibility frequently by ABO incompatibility and Rhesus (Rh).[1,2]

Due to social, medical, and financial considerations, it is usual to discharge healthy newborns as soon as possible following delivery. The American Academy of Pediatrics advises that neonates released from the hospital within 48 hours after birth should visit again in two to three days to check for serious jaundice. This is often neglected and overlooked in low-income countries. Scheduled follow-up within 1-2 days of early discharge, pre-discharge serum and transcutaneous bilirubin measurements, umbilical cord bilirubin concentration at birth and other methods are some ways to predict significant hyperbilirubinemia.

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Although these recommendations have been made, hyperbilirubinemia remains the most typical reason for readmission during the early neonatal period. American.[1-5]

The factors mentioned above make it important to establish an early prediction concept to identify newborns at risk of developing significant jaundice. Hence this study was performed primarily to determine the cut-off value for cord blood bilirubin, albumin, bilirubin albumin ratio, and alkaline phosphatase in identifying severe neonatal hyperbilirubinemia (NH) requiring treatment. In addition, the evaluation of the relationship between neonatal jaundice, the mother's parity, and the newborn's gender served as the secondary outcome measure.

MATERIALS AND METHODS

In this prospective cohort, a purposive sampling study conducted between January to December 2019 at the Government hospital in Thoothukudi, India, 300 newborns with a gestational age greater than 35 weeks were studied. Institutional Ethical Board clearance and informed consent were obtained from the mother before the commencement of the study. The sample size was calculated using online openepi.com. With a two-sided confidence interval of 99% and power of 90%, the sample size was calculated as 300.

Inclusion Criteria

Neonates > 35 weeks of gestational age delivered either through normal vaginal delivery or caesarean section.

Exclusion Criteria

Preterm neonates less than 35 weeks of gestational age, those with intrauterine growth restriction with less than 2 kg, respiratory distress syndrome, maternal risk of infection, conjugated hyperbilirubinemia, major congenital malformation and birth asphyxia (APGAR < 7 at 1 min) were excluded from the study.

The antenatal history, obstetric and medical history of the mother were obtained. A structured questionnaire with demographic details of gender, gestational age, birth weight, length and head circumference, delivery method, and Apgar scores at 1 and 5 minutes of life was completed for all newborns. All neonates participating in the trial got a clinical follow-up using Kramer's scale. On day four of life, serum bilirubin tests were performed on all other babies. Newborns thought to have substantial jaundice had their serum bilirubin levels checked sooner. Two ml of placental cord blood was collected, and cord blood, albumin, bilirubin albumin ratio, and alkaline phosphatase were analysed using Beckman Coulter Au2700 and Au680 autoanalyzer (Beckman Coulter Mishima K.K., Sizuoka-ken, Japan). Blood grouping of the baby for mothers having O positive and RH negative groups was also performed from the cord blood sample. The AAP nomogram was used to plot the serum bilirubin (SBR) levels. Significantly jaundiced newborns were admitted to the NICU and given phototherapy.

Statistical Analysis

Data was analysed in the Statistical Package of Social Science Software (SPSS) program, version 23. Data were expressed as means±SD and percentage. Pearson's correlation was used to measure the strength and direction of the association between the two variables. The data were also analysed using a T-test and multiple regression analysis. P values less than 0.05 were considered statistically significant. To investigate the discriminant power of various cord measurements in predicting newborn jaundice, receiver operating characteristics (ROC) curve analysis was carried out. The cut-off values for the variables were also analysed.

RESULTS

The study included 300 newborns (49.3% of female and 50.7% male) with an average birth weight of 2.898 kg. The mean value of gestational age of newborns in the study population is 38.3+ 1 week. There is a statistically significant difference in the mean value of gestational age of jaundiced newborns (37.98+ 1.38) and newborns with insignificant jaundice (38.4+ 0.98) with a p-value of <0.0001. The maternal age ranged from 18 to 43 years, with a mean of 25 years. Vaginal delivery was observed in 21.3 % (n=64), while Caesarean delivery in 78.7 % (n=236).

Fifty-seven (19%) babies experienced severe hyperbilirubinemia. Ten of these newborns developed significant jaundice on day three of life, 46 on day four of life, and 01 on day six of life. In addition, cord blood bilirubin (mean 1.7420 ± 0.74216 SD), cord blood albumin (mean 3.2487 ± 0.32984 SD), cord blood bilirubin albumin ratio (mean 0.5344 ± 0.23959 SD), cord blood alkaline phosphatase (mean 147.7633 ± 62.31091 SD), and day 4 SBR (mean 11.4713 ± 4.33671 SD) were recorded. The characteristics of the study population are represented in [Table 1].

Table 1: Characteristics of the study population

	Minimum	Maximum	Mean	STD Deviation
Maternal age	18.00	43.00	25.2367	4.10897
Gestational age	35.00	40.00	38.3633	1.08100
Birth weight	2.04	4.30	2.8982	.36277
Cord blood bilirubin	.20	4.50	1.7420	.74216

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Cord blood albumin	2.20	4.60	3.2487	.32984
Cord blood bilirubin albumin ratio	.06	1.36	.5344	.23959
Cord blood alkaline phosphatase	18.00	360.00	147.7633	62.31091
Day 4 BSR	4.20	21.20	11.4713	4.33671

Table 2: Independent T Test analysis between cord blood variables and jaundice

	Significant jaundice	Insignificant jaundice
No: of newborns	57	243
Mean value of cord blood bilirubin	2.6228	1.5354
Std. Deviation	0.64642	0.59854
Mean value of cord blood albumin	3.0368	3.2984
Std. Deviation	0.32162	0.31215
Mean value of cord blood bilirubin albumin ratio	0.8574	0.4586
Std. Deviation	0.19781	0.17756
Mean value of cord blood alkaline phosphatase	178.1404	140.6379
Std. Deviation	73.87935	57.14705

Primagravida compared to multigravida mothers: Primigravida was noted in 123 and multigravida in 177 individuals. Out of 300 newborns in the research group, 41% were delivered to primigravida mothers. 32% of the 123 infants born to primigravida moms experienced severe jaundice. Only 10% of infants born to multiparous moms experienced severe jaundice. Significant hyperbilirubinemia is more common (68%) in babies of primigravida mothers than in those of multiparous mothers (32%). Compared to multigravida moms, newborns delivered to primigravida mothers are statistically more likely to experience neonatal jaundice. The odds ratio showed that newborns delivered to primigravida mothers are 4.5 times more likely to exhibit neonatal jaundice than newborns of multigravida mothers.

Gender: In this study, there were 49.3 percent female and 50.7% male newborns. Significant jaundice was noted in 53% of male and 47% of female newborns. In our investigation, the gender of the newborn had no statistically significant impact on the likelihood of substantial hyperbilirubinemia.

ABO and Rh incompatibility: 17.7% of newborns in our study cohort had ABO compatibility issues, while 6% had Rh incompatibility. There was significant hyperbilirubinemia in 34% ABO incompatibility, while 55% in newborns with Rh incompatibility.

Phototherapy duration: Two of the newborns received phototherapy for 1 day, 15 received it for 2 days, 13 for 3 days, 14 for 4 days, 06 for 5 days, 05 for 6 days and two newborns for 7 days.

Distribution of clinical grading of jaundice in the study population: Nine percentage (n=27) developed jaundice on the face, 18.7 % (n=56) developed it on the chest, 28.3 % (n=85) developed it on the abdomen, 27.7 % (n=83) on thighs and 16.3 % (n=49) on legs.

Binomial logistic regression: A logistic model was used to determine the impacts of birth weight, SBR, gender, Obstetric coding (OC), and gestational age on the likelihood of neonatal jaundice in individuals. The logistic regression model was statistically significant, $\chi 2 = 138.711$ ($p < .0001$).

The model explained 59.5% of the variation in newborn jaundice (Nagelkerke R2) and accurately identified 81.0% of cases. Gender ($p= 0.014$), OC ($p<0.0001$), and cord blood bilirubin ($p<0.0001$) all significantly contributed to the model/prediction. In addition, neonatal jaundice was 4.5 times (odds ratio) more likely to occur in primigravida than in multigravida.

Multiple Regressions Analysis

Estimated model coefficients: The general equation for day 4 SBR prediction using gender, OC, and SBR, is:

Predicted day4 SBR = 7.084 – (0.757 x gender) – (0.311 x OC) + (3.452 x cord blood SBR)

In order to predict day 4 SBR from gender, OC, and SBR, a multiple regression was done. The variables significantly and statistically predicted the day 4 SBR, $F (3, 296) = 56.194$, $p < .0001$, $R2 = 0.363$.for gender of newborns: male child-1; female child-2; for obstetric code: primigravida-1; multigravida-2. In addition, SBR by itself greatly improved the prediction statistically ($p <.0001$).

Correlation between cord blood bilirubin and day 4 serum bilirubin level: Pearson correlation demonstrated a moderate positive correlation of 0.595 with a significant p-value of <0.0001 between the variables. The mean cord blood bilirubin level was 1.742 (SD ± 0.742), and the mean value of day 4 SBR was 11.47 (SD ± 4.33).

Correlation between cord blood albumin and day 4 serum bilirubin levels: Pearson correlation between the variables resulted in a negative correlation of -0.204. It showed a mild correlation between cord blood albumin and day 4 SBR level with a significant p-value of <0.0001. The mean value of cord blood albumin is 3.25 (SD ± 0.33).

Correlation between cord blood bilirubin albumin ratio and day 4 serum bilirubin level: Bilirubin levels demonstrate significant (p-value < 0.0001) and moderate positive correlation (r=0.636) with cord blood bilirubin albumin ratio.

Correlation between cord blood alkaline phosphatase and day 4 serum bilirubin level: A mildly significant positive correlation (r= 0.218) with a significant p-value of <0.0001 was noted. The mean value for cord blood alkaline phosphatase was 147.76 (SD ± 62.3).

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Independent T-test analysis: Independent sample T-test demonstrates a significant association ($p<0.0001$) between cord blood bilirubin and the occurrence of neonatal jaundice. Compared to neonates with insignificant neonatal jaundice, those with significant neonatal jaundice have mean cord blood bilirubins of 2.62 and 1.53, respectively. In addition, a significant association ($p<0.0001$) was noted between cord blood albumin and the occurrence of significant neonatal jaundice requiring treatment. The mean value of cord blood albumin in the treatment group is 3.036 and in the non-treatment group is 3.29. Also, a statistically significant association ($p<0.0001$) was detected between the cord blood bilirubin albumin ratio and the occurrence of neonatal jaundice. The mean cord blood bilirubin albumin ratio in the treatment group is 0.857 compared to 0.458 in the non-treatment group. A significant correlation between cord blood alkaline phosphatase and the occurrence of significant jaundice ($p<0.0001$) was observed. The mean cord blood alkaline phosphatase in the treatment group is 170 IU, whereas, in the non-treatment group, it is 140 IU. Table 2 depicts the association between variables.

Nonparametric Correlations:

With a significant p-value of less than 0.0001, Kendall's tau b test shows a strong link between cord blood bilirubin and day 4 clinical grade. The correlation coefficient is 0.533. Similarly, with a significant p-value of 0.001 and a significant negative correlation coefficient of -0.150, Kendall's tau b test shows a strong association between cord blood albumin and day 4 clinical grading. Likewise, the cord blood bilirubin albumin ratio significantly correlates with the clinical jaundice grading on day 4 according to Kendall's tau b testing. With a significant p-value of 0.0001, the correlation coefficient is 0.549. In addition, the alkaline phosphatase level in the cord blood correlates significantly with the clinical jaundice grade on day 4, according to Kendall's tau b testing. Two variables have a 0.169 correlation coefficient, with a significant p-value of 0.0001.

Comparison between gestational age and significant neonatal jaundice:

An independent sample t-test demonstrates a significant correlation between gestational age and the occurrence of jaundice. The mean gestational age in newborns with significant jaundice is 37.98, but it is 38.45 in newborns with insignificant jaundice, with a significant p-value of 0.03. Lower gestational age babies are more likely to experience jaundice.

With a significant P value of 0.0001, Pearson chi-square tests revealed a statistically significant difference in the incidence of newborn jaundice between primigravida and multigravida mothers.

With a non-significant P value of 0.105, the Pearson chi-square test revealed a statistically significant difference in the incidence of jaundice between the ABO incompatibility and Rh incompatibility groups.

Receiver operating characteristic curve and association with variables:

ROC curve study to determine the cut-off level for cord blood bilirubin in predicting the development of significant jaundice showed a significant 0.914 area under the curve [Figure 1]. This shows that substantial neonatal hyperbilirubinemia is highly predictable when measured in cord blood bilirubin. The p-value is significant (< 0.0001). A cut-off value of cord blood bilirubin for developing significant jaundice is 2.15 mg/dl. It has a sensitivity of 84.2% and a specificity of 88.1%.

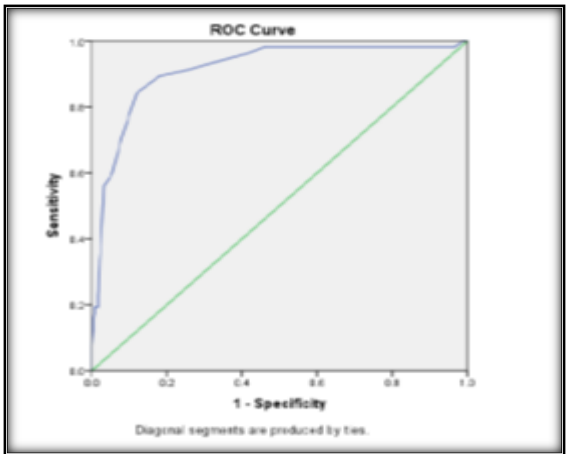

Figure 1: ROC Curve for prediction of neonatal jaundice using cord blood bilirubin

The area under the curve for the ROC curve study for cord blood albumin in the prediction of neonatal hyperbilirubinemia was 0.260 [Figure 2]. This shows neonatal hyperbilirubinemia is mildly predictable by cord blood albumin with a P value < 0.0001. A cut-off value of cord blood albumin for developing significant jaundice is less than 3.75g/dl. It has a sensitivity of 35% and a specificity of 92.2%.

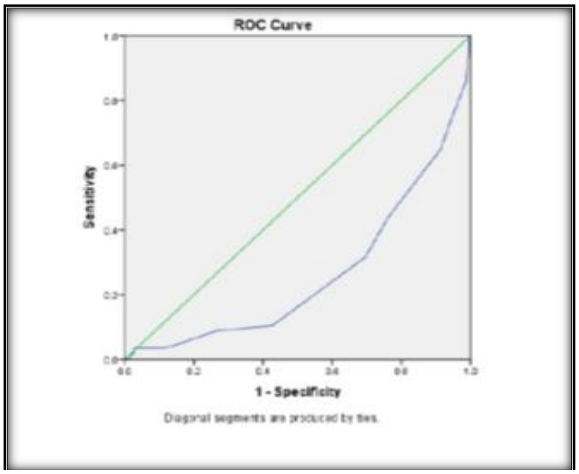

Figure 2: ROC Curve for cord blood albumin in the prediction of neonatal hyperbilirubinemia

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The ROC curve to predict significant neonatal jaundice using cord blood bilirubin albumin ratio demonstrates a large area under the curve of 0.941 [Figure 3]. This shows cord blood bilirubin albumin ratio has a high predictive value in the occurrence of significant jaundice. The p-value is less than 0.0001, which is significant. The Cut-off value of cord blood bilirubin albumin ratio for the development of significant jaundice is 0.86. It has a sensitivity of 54.4% and a specificity of 98.4%.

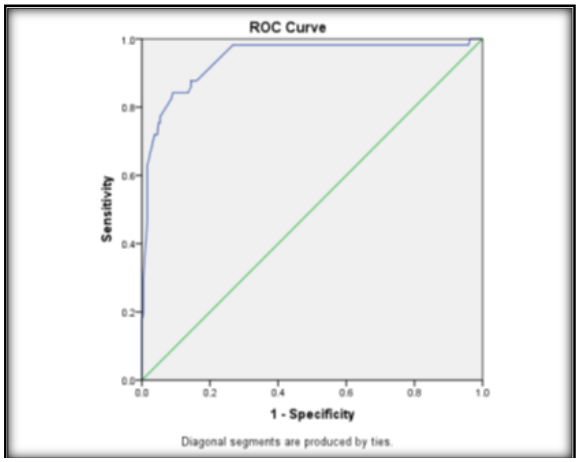

Figure 3: ROC curve for prediction of neonatal hyperbilirubinemia using cord blood bilirubin albumin ratio

The ROC in [Figure 4] curve demonstrates that cord blood alkaline phosphatase has a large area under the curve of 0.650 which shows the moderate predictive value of occurrence of neonatal jaundice (P value < 0.0001). The cut-off value of cord blood alkaline phosphatase level for developing significant jaundice is 151 IU/L. It has a sensitivity of 63.2% and a specificity of 60.9%.

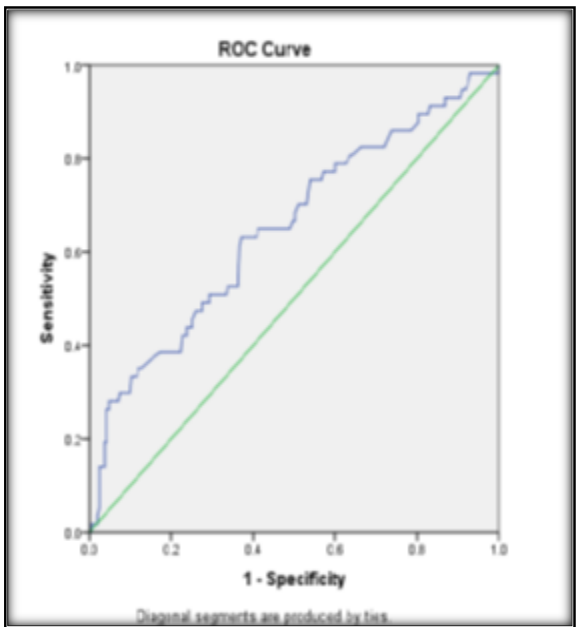

Figure 4: ROC Curve for cord blood alkaline phosphatase in the prediction of significant neonatal jaundice

DISCUSSION

Neonatal jaundice (NJ) occurs when the amount of unconjugated bilirubin builds up to the point where the yellow colour in the skin and conjunctiva of newborns becomes apparent to human eyes. On the other hand, hyperbilirubinemia (HB) refers to a level of total serum bilirubin (TSB) that is higher than what is considered normal for human health. HB is typically present before we recognise this as NJ because our lab methods are more sensitive than our eyes. Although the range of detectability in earlier research was as large as 30-200 mol/L, the lowest TSB level at which NJ can be visually identified in neonates is approximately 46-68 mol/L (2.7-4.0 mg/dL). Visual observers may not see infants with TSB levels at the lower end of these ranges as having jaundice, hence the need for objective tests.[6]

This study of 300 newborns delivered between January 2019 and December 2019 recorded that 57 (19%) had severe jaundice. This incidence is similar to the 19.84 % by Sharma et al. and the 19.86% by Bernaldo et al.[7,8] Given the severe neurological morbidities brought on by bilirubin toxicity, the importance of early jaundice prediction in identifying infants at risk for neonatal hyperbilirubinemia has increased. Furthermore, cord bilirubin levels can be easily measured and may be a promising prediction sign for future hyperbilirubinemia development. Hence various cord blood parameters were assayed, analysed and correlated with hyperbilirubinemia in newborns to assess their diagnostic significance.

Our research demonstrated a statistically significant ($p<0.001$) variation in all parameters of cord blood measured between those newborns with and without significant jaundice. In addition, the levels of CBB in the newborns who developed significant hyperbilirubinemia (Mean±SD 2.62 mg/dl ±0.64) were higher than those who didn't (1.53 mg/dl +0.59).

In a prospective cohort study of 175 neonates, Khairy et al. aimed at identifying early, reliable markers such as cord serum bilirubin and albumin levels and the bilirubin/albumin ratio as early predictors of neonatal hyperbilirubinemia. It was a prospective study done on 175 neonates. 28 neonates (16%) developed significant hyperbilirubinemia, comparable to 19 % of our study. The study found that newborns who developed significant neonatal hyperbilirubinemia had statistically significantly higher cord total bilirubin (2.4± 0.2 mg/dl) versus (1.4 ±0.4 mg/dl), significantly lower cord albumin [(2.8 ±0.3 gm/dl) versus (3.3±0.5 gm/dl), and significantly higher cord B/A ratio (0.86± 0.14) versus (0.44 ±0.19). According to the study's findings, the parameters mentioned above accurately predict newborn hyperbilirubinemia, per the present study findings.[9] Ipek et al. found a CBB cut-off level of 2.60 mg/dl,

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with a positive predictive value of 41.18%, a negative predictive value of 97.9% and a sensitivity of 50%.[10] Shahidukkah ZN et al.found that the cord bilirubin level >2.5 mg/dl has a sensitivity of 77%, specificity of 98.6%, a negative predictive value of 96%, and positive predictive value of 38.8%, which correlates with the present study.[11] In a trial of 418 newborns, the cut-off value of CBB for predicting the occurrence of significant hyperbilirubinemia requiring PT was 1.67 mg/dL, with a sensitivity of 82% and specificity of 99%.[12] According to Trivedi et al., levels of unconjugated bilirubin in cord serum below 2.0 mg/dl and total bilirubin below 2.5 mg/dl appeared to be high-risk indicators for predicting neonatal hyperbilirubinemia.[13] The mean cord serum bilirubin levels in newborns with hyperbilirubinemia were higher in several investigations than in those without.[14,15]

Various levels of cord blood albumin (CBA) have been reported. The mean value of cord blood albumin (CBA) in the treatment group was 3.036 g/dl; in the non-treatment group, it was 3.29 g/dl. Th cut-off value of cord blood albumin for the development of significant jaundice is less than 3.75g/dl. It has a sensitivity of 35% and a specificity of 92.2%. Janaki and Selvakumar found that neonates with umbilical cord blood albumin < 3.15 g/dl in ABO blood group incompatibility require special monitoring to look out for the emergence of severe hyperbilirubinemia, which is in agreement with our findings.[16] According to a study by Venkatamurthy M et al., newborns with umbilical cord serum albumin levels greater than 3.4 g/dl were not shown to be at risk of developing hyperbilirubinemia. Similarly, Sandeep Kumar et al., Sahu S et al., and Meena et al. found CBA levels of >3.4 g/dl, >3.3 g/dl, and > 3.3 gm/dl, respectively, to be safe.[17-20] These results are consistent with our research.

Other studies have noted contrary results. Khairy et al. cut-off value ≤ 3.0 mg/dl had a good predictive value with a sensitivity of 85.7% and specificity of 67.3%.[9] Kumar et al. studied hundred and fifty randomly chosen eligible term neonates for the relationship of cord serum albumin with neonatal hyperbilirubinemia. They found that those with hyperbilirubinemia (≥17mg/dl) had significantly lower levels of cord serum albumin (≤2.8g/dl).[21] Rajpurohit et al. stated a CBA level ≤ 2.6 gm/dl had an 80 % sensitivity and 86.67 % specificity. 22 Trivedi et al. found that cord serum albumin level < 2.8 gm/dl was added risk indicator in predicting NH.[13] Ghada et al. found that values > 3.3 mg/dl were considered safe with no incidence of hyperbilirubinemia, while 2.8 g/dl was associated with severe hyperbilirubinemia in 81.8% of cases.[23] Bhat et al., in their study of 300 newborns, cut-off points to foretell significant hyperbilirubinemia in newborns were CBB >3 mg/dL (sensitivity 60.61%, specificity 97.63%), CBA <2.4 mg/dL (sensitivity 78.79%, specificity 98.13%), CBAR >0.98 (sensitivity 78.79%, specificity 95.51%). These measurements conflict with what we found in our research.[24]

We opted to employ CBAR to assess the sensitivity and specificity of the combination than either CBB or CBA alone. The Mean±SD bilirubin albumin ratio in jaundiced newborns is 0.857±0.19, while it was 0.458±0.17 in those with insignificant jaundice. The cut-off value of cord blood bilirubin albumin ratio (CBAR) for developing significant jaundice is 0.86. It has a sensitivity of 54.4% and a specificity of 98.4%. According to Ramteke et al., if a patient's CBAR is above 0.89, 95.5% of newborns will likely develop NH in the future. This cut-off level is similar to ours at 0.86.25Rehna et al., in their study, summarised that at the CBAR cut-off of 0.59, the risk of hyperbilirubinemia was 36.4%, and at 0.69, it was 46.9. They found a statistically significant positive link with the probability of hyperbilirubinemia.26 Sharma et al. found a CBAR cut-off of 0.719 with 97.4% sensitivity and 62.6% specificity.7Mashad GM et al. noted a cut-off ratio of 0.6 for CABR with a sensitivity of 83.3% and specificity of 85.7%.[27]

The mean±SD of cord blood alkaline phosphatase in jaundiced newborns is 178.14±73.88 compared to 140.63±57 for those without significant jaundice. The cut-off value of cord blood alkaline phosphatase (CBAP) level for developing significant jaundice is 151 IU/L. It has a sensitivity of 63.2% and a specificity of 60.9%. A prospective study in Northern Iran found cord blood alkaline phosphatase level > 314 IU/L was the best cut-off value for predicting severe jaundice with a 63% specificity and an 80% sensitivity, which is considerably higher than our study. Fenton et al. reported a mean level of cord blood alkaline phosphatase 159 ± 49 IU/L, which is closer to the value found in our study.28 El-Amin et al., in their ROC curve analysis, noted that cord ALP cut-off value > 145 IU/l has a good predictive value for NH with a sensitivity of 72% and a specificity of 85.71%.[29] Dasaptjita et al. summarised that the cut-off value for predicting NH in full-term newborns was 163.5 IU/l with 84.7% sensitivity and 77.3% specificity.[30]

The difference in analyte relationships with cut-off values between our study and the other studies could be attributed to different sample sizes, bilirubin estimate techniques and variations in inclusion and exclusion factors.

CONCLUSION

The present study found a statistically significant link between newborn hyperbilirubinemia and the variables tested in the cord blood, including bilirubin, albumin, bilirubin albumin ratio, and alkaline phosphatase. The occurrence of neonatal bilirubin hyperbilirubinemia can be predicted positively using the cut-off values for the cord blood factors.

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Limitation

Preterm or any high-risk babies were not evaluated. Results could be affected by confounding variables such as dehydration brought on by exclusive breastfeeding in mothers who have inadequate milk supply.

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