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THE USEFULNESS OF CORD BLOOD BILIRUBIN LEVEL IN PREDICTING SIGNIFICANT HYPERBILIRUBINEMIA IN NEWBORNS WITH ABO INCOMPATIBILITY

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ABSTRACT **Introduction-** Neonatal jaundice is a condition in newborns, where yellowish discoloration of the skin and sclera is seen due to high bilirubin. Neonatal hyperbilirubinemia (NNH) is a common clinical condition which can occur physiologically or pathologically. Over 50% of all newborn infants suffer this condition. On the other hand, neonatal jaundice is an important clinical feature as it can be a sign of an underlying disorder (i.e. hemolytic anemia, infection, an inborn error of metabolism or liver disease). ABO incompatibility is the commonest cause of hemolytic jaundice in the newborns. The diagnosis of ABO incompatibility is suspected by early onset of jaundice which usually appears during first 24 to 72 hours of life, mild splenomegaly and anaemia being rare manifestations whereas hydrops-fetalis is extremely rare. **Method-** The study was conducted at Dr. D.Y. Patil Hospital, Kadamwadi, Kolhapur. The time period of the study was from Dec 2020 to Aug 2022 and the sample size taken was 80. Maternal blood will be collected to determine blood group. Cord blood will be collected to determine blood group, bilirubin level of neonate. TRANSCUTANEOUS BILIRUBINOMETER will be noted on 1st, 2rd, 3rd day to find bilirubin levels. Any time if yellowish discoloration of baby is below the chest clinically based on Kramer's criteria. Then we send the sample of baby for Bilirubin levels. We compare cord blood level bilirubin, TRANSCUTANEOUS BILIRUBINOMETER bilirubin levels and sample bilirubin levels. **Results-** The incidence of hyperbilirubinemia was more common in B+ neonates with ABO incompatibility. AB+ blood group neonates with ABO incompatibility were least affected with hyperbilirubinemia than other blood groups. Total cord TOTAL BILIRUBIN at cut off point >3.2 mg/dl showed a specificity of 83.33%, sensitivity of 97.06%, PPV of 83.33%, NPV of 97.06%, and diagnostic accuracy of 95%. **Conclusion-** Cord TOTAL BILIRUBIN ≥3.2 mg/dl can predict hyperbilirubinemia in new-born babies.

KEYWORDS : Jaundice, hyperbilirubinemia, new-born babies, Transcutaneous Bilirubinometer, blood group

Introduction

Neonatal jaundice is a yellowish discoloration of the skin and sclera in a newborn by raised serum bilirubin level. Neonatal hyperbilirubinemia (NNH) is a common clinical condition that can occur physiologically or pathologically. [1]Over 50% to 70% of all full-term newborn infants become visibly physiologically jaundiced. High levels of unconjugated bilirubin can deposit in the brain, especially in the basal ganglia, where they can lead to kernicterus. [2] On the other hand, neonatal jaundice is an important clinical feature as it may be a sign of an underlying disorder (i.e. hemolytic anemia, infection, an inborn error of metabolism, or liver disease). [3] After discharge from PNC ward during the early newborn period is neonatal hyperbilirubinemia. The most often reported reason for readmission during the early newborn period is hyperbilirubinemia. [4-6] A future moderate to severe hyperbilirubinemia occurs in 0.36 percent of healthy-term babies who are discharged after 72 hours of life with no more than mild hyperbilirubinemia. [7] With the declining incidence of Rhesus disease (Rh disease), as it is preventable by the use of prophylactic anti-D immediately after the birth of the baby, ABO incompatibility is the commonest cause of hemolytic jaundice in newborns. Approximately 20% of all pregnancies are associated with ABO incompatibility between the mother and the fetus and only <10% of all these cases manifest ABO-hemolytic diseases of the newborn (ABO-HDN). [8] ABO incompatibility causes a range of hemolytic diseases, the severe end of which is known as ABO hemolytic illness and occurs in 15% to 20% of all pregnancies. [9]

ABO incompatibility occurs in 'A', 'B' and 'AB' blood group babies born to 'O' blood group mothers. In a mother with type A and type B blood group, antibodies of IgM class are present which do not cross the placenta whereas, in a type O blood group mother, antibodies are of IgG class which cross the placenta. Low antigenicity of A and B factors and wide expression in a variety of tissues besides RBCs, accounts for the relatively low incidence and milder nature of ABO hemolytic disease. [10] The diagnosis of ABO incompatibility is suspected by early onset of jaundice which usually appears during the first 24 to 72 hours of life, with mild splenomegaly and anemia being rare manifestations whereas hydrops-fetalis is extremely rare. All neonates with the risk factors for increasing the blood level of indirect bilirubin are at risk for bilirubin encephalopathy. Bilirubin toxicity can be transient and acute (with early, intermediate and advanced phases) or be permanent, chronic (kernicterus), and lifelong with tetrad of symptoms including visual (upward gaze palsy), auditory (sensory neural hearing loss), dental dysplasia abnormalities, and extrapyramidal disturbances (choreoathetosis cerebral palsy). [11] We thus looked at the use of cord bilirubin measurement in predicting the emergence of major hyperbilirubinemia level and bilirubin value at 24hrs, 48hrs, and 72hrs with the use of Transcutaneous bilirubinometer and cord bilirubin at 4th day and if bilirubin is more according to Bhutani chart than giving the treatment of phototherapy. The main objective of this study is to predict ABO incompatibility in A +VE, B+VE, AB+VE babies by using Cord bilirubin levels among hospital deliveries at Dr.D.Y. Patil Hospital & Research Institute, Kolhapur. Also, to compare cord bilirubin of A +ve, B +ve and AB +ve babies for prediction of developing significant Neonatal hyperbilirubinemia in a new-born and find the appropriate level of cord bilirubin which can pick up the maximum number of new-borns who would go for significant hyperbilirubinemia.

Materials and Methods-

The study was conducted at, Dr. D. Y. Patil Hospital & Research Institute, Kolhapur from December 2020 to August 2022. All the necessary permissions were taken from the institutional ethics committee. OPD and IPD patients were included in the study. Written and informed consent was taken from the parents of the neonate for participation in the study.80 neonates who were A +ve or B +ve or AB +ve babies born to O +ve mothers, newborn of gestational age > 37 weeks, newborn of Body weight > 2.5 kg and < 4kg, newborn delivered by any mode of normal delivery or Caesarian section for indications not causing hyperbilirubinemia, having Apgar >7 in newborn and exclusively breastfeeding babies were included in this study. Whereas, babies with rhesus blood factor incompatibility, having O +ve blood

group and complications causing hyperbilirubinemia like birth asphyxia, sepsis, birth trauma, and congenital malformation were excluded from the study. Also, mothers having significant diseases, which can cause hyperbilirubinemia in newborn, like gestational diabetes mellitus, preeclampsia, chronic liver disease were also excluded.

Maternal blood was collected to determine blood group and cord blood was withdrawn to determine blood group and bilirubin level in neonates. TRANSCUTANEOUS BILIRUBINOMETER was noted on the 1st, 2nd, and 3rd days to find bilirubin levels. Any time if yellowish discoloration of a baby is below the chest, clinically based on Kremer's criteria. Then the sample was sent to test the bilirubin levels of the baby. A later comparative study was done between cord blood level bilirubin, TRANSCUTANEOUS BILIRUBINOMETER bilirubin levels, and sample bilirubin levels.

RESULTS-TOTAL BILIRUBIN

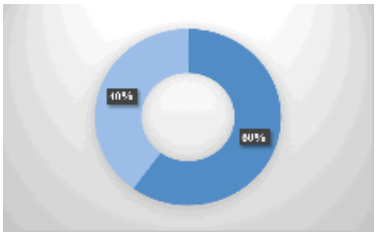
Data was entered in the Ms-Excel and then imported into SPSS for analysis. Data were evaluated using SPSS V 1.2.5001 software. Continuous variables were shown in mean±SD whereas, categorical variables were presented in percentage and frequency. Comparison variables between both groups were assessed using the student T-test. The Pearson correlation coefficient test was used to find the correlation. P<0.05 was considered statistically significant.

Table 1. Distribution of neonates according to Gestational Age

GA (weeks)	Frequency (n)	Percentage (%)
37-38	7	8.75
39-40	39	48.75
>40	34	42.50
Total	80	100

The mean GA of the neonates was 38.44±1.08 weeks. Most of the neonates were of 39-40 weeks GA followed by >40 weeks and 37-38 weeks. The detailed distribution of neonates according to GA is depicted in table 1

Figure 1. Distribution of subjects according to birthweight



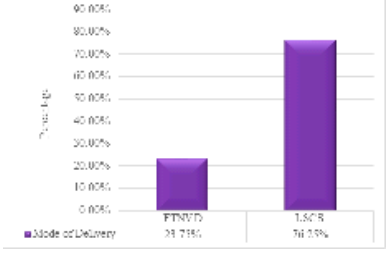
The mean birthweight of the babies was 2.98±0.36 kg. Most of the neonates were belong to the 2.5-3 kg weight category whereas 40% belonged to the 3.1-3.5 kg weight category. The detailed distribution of subjects according to birthweight is shown in figure 1.

Table 2. Distribution of babies according to sex

Birthweight (Kg)	Frequency (n)	Percentage (%)
Female	38	47.50
Male	42	52.50
Total	80	100

The majority of neonates were male followed by females. The detailed distribution of babies according to sex is illustrated in table 2.

Figure 2. Distribution of neonates according to the mode of delivery



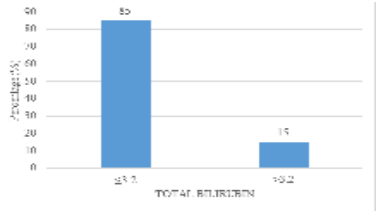
In 76.25% of patients, the mode of delivery was LSCS whereas 23.75% had FTNVD. The detailed distribution of neonates according to the mode of delivery is depicted in figure 2.

Table 3. Distribution of subjects according to blood group

Blood groups	Frequency (n)	Percentage (%)
A+	26	32.50
B+	32	40
AB+	22	27.50
Total	80	100

In 40% of the babies, the blood group was found to be B+ whereas, 32.50% and 27.50% of the babies had A+ and AB+ blood groups respectively. The detailed distribution of subjects according to blood group is shown in table 3.

Figure 3. Distribution of neonates according to TOTAL BILIRUBIN categories



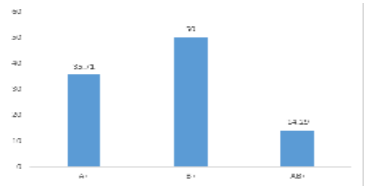
The mean TOTAL BILIRUBIN, DIRECT BILIRUBIN, and INDIRECT BILIRUBIN were found to be 2.69±1.07, 0.51±0.42, and 2.18±0.92 respectively. The TOTAL BILIRUBIN >3.2 was found in 15% (n=12) of neonates whereas 85% (n=68) neonates had TOTAL BILIRUBIN ≤3.2. The distribution of neonates according to TOTAL BILIRUBIN categories is shown in figure 3

Table 4. Distribution of subjects according to outcomes

Outcomes	Frequency (n)	Percentage (%)
Normal	66	82.5
Phototherapy	14	17.5
Total	80	100

In 17.5% of the patients, phototherapy was performed whereas in 82.5% of patients the outcomes were normal. The distribution of subjects according to outcomes is depicted in table 4.

Figure 4. Distribution of blood groups according to outcomes



Most of the babies with who had phototherapy had B+ blood group followed by A+ and AB+ figure 4.

Table 5. Predictive measures of total cord bilirubin according to individual blood group

Predictive measures	Blood groups		
	A+	B+	AB+
Sensitivity	73.23%	95.32%	69.12%
Specificity	87.12%	97.21%	74.25%
PPV	73.14%	85.14%	71.41%,
NPV	84.06%,	97.25%	74.19
Accuracy	83%	97%	80%

The diagnostic measures of cord TOTAL BILIRUBIN A+ blood group neonate with ABO incompatibility specificity of 73.23%, sensitivity of 87.12%, PPV of 73.14%, NPV of 84.06%, and diagnostic accuracy of 83%. The diagnostic measures of cord TOTAL BILIRUBIN B+ blood group neonate with ABO incompatibility specificity of 95.32%, sensitivity of 97.21%, PPV of 85.14%, NPV of 97.25%, and diagnostic accuracy of 97%. The diagnostic measures of cord TOTAL

BILIRUBIN AB+ blood group neonate with ABO incompatibility specificity of 69.12%, sensitivity of 74.25%, PPV of 71.41%, NPV of 74.19%, and diagnostic accuracy of 80% (table 5)

Table 6. Overall predictive measures of total cord bilirubin

Statistic	Value	95% CI
Sensitivity	83.33%	51.59% to 97.91%
Specificity	97.06%	89.78% to 99.64%
Positive Predictive Value	83.33%	55.50% to 95.25%
Negative Predictive Value	97.06%	90.30% to 99.15%
Accuracy	95.00%	87.69% to 98.62%

Total cord TOTAL BILIRUBIN at cut-off point >3.2 mg/dl showed a specificity of 83.33%, sensitivity of 97.06%, PPV of 83.33%, NPV of 97.06%, and diagnostic accuracy of 95% (table 6)

Discussion

Jaundice can cause severe issues in new-borns causing delayed discharge or readmission. [1,14,15]Thus, the determination of jaundice has the utmost importance in the diagnosis of high-risk neonates due to hyperbilirubinemia which also can cause adverse neonatal outcomes. [16] Assessment of serum bilirubin is an easily available, cost-effective, and non-invasive procedure that can give insight regarding hyperbilirubinemia or could aid in the decision of early discharge. The study was conducted to assess the usefulness of cord blood bilirubin level in predicting significant hyperbilirubinemia in a new-born with ABO incompatibility in babies born of O +ve mothers. The significant findings of the study were the most common blood group in babies was B+ followed by A+ and AB+. The most common mode of delivery in the present study was LSCS. The TOTAL BILIRUBIN >3.2 was found in 15% (n=12) of neonates whereas 85% (n=68) neonates had TOTAL BILIRUBIN ≤3.2. In most of the neonates with TOTAL BILIRUBIN >3.2, phototherapy was performed. The most common blood group in babies who had phototherapy was B+ (n=9 out of n=14). The assessment of TOTAL BILIRUBIN at cut off >3.2 had good sensitivity, specificity, PPV, NPV, and accuracy. In this study, the average gestational age of neonates was 38.44±1.08 weeks. The majority of neonates (48.75%) belonged to 39-40 week GA followed by >40 weeks (42.50%), and 37-38 weeks (8.75%). The mean birthweight of the babies was 2.98±0.36 kg. Most of the neonates [13] were belong to the 2.5-3 kg weight category whereas 40% belonged to the 3.1-3.5 kg weight category. Here males were predominantly present compared to females (42% vs 38%). In the majority of the babies (76.25%) the mode of delivery was LSCS followed by FTNVD (23.75%). These findings are comparable with previous reports. [17, 12] Moreover, in premature neonates abnormal liver function is unable to remove bilirubin which is evidenced by previous reports suggesting a significant association between hyperbilirubinemia and gestational age. However, no association of hyperbilirubinemia with sex, birthweight, and mode of delivery was reported. [12,18]] Babies born with A, B, and AB blood to the O blood group mother are at increased risk for the development of subsequent hyperbilirubinemia due to immunity associate Hb breakdown. However, the type of blood group does not affect the severity of hyperbilirubinemia. [19] In this study, we included babies with ABO incompatibility. Among these infants, 40% of the babies had the B+ blood group whereas 32.50% and 27.50% of the babies had A+ and AB+ blood groups respectively. In the study of Eldho HP. et al. the blood group of 33.33%, 42.50%, and 24.17% of the babies were with A, B, and AB blood groups.[20]

Literature has suggested that cord TOTAL BILIRUBIN is significantly associated with serum bilirubin in neonates with hyperbilirubinemia. [21, 22] In this study, the average cord TOTAL BILIRUBIN, DIRECT BILIRUBIN, and DIRECT BILIRUBIN were found to be 2.69±1.07, 0.51±0.42, and 2.18±0.92 respectively. Based on the cord TOTAL BILIRUBIN range in neonates with hyperbilirubinemia, we used 3.2mg/dl as the cut-off point to predict the risk of hyperbilirubinemia. Here, n=12 (15%) neonates had cord TOTAL BILIRUBIN >3.2 mg/dl while 85% had <3.2 mg/dl. In our study assessment of diagnostic measures in all neonates, cord TOTAL BILIRUBIN is an acceptable predictor for the development of hyperbilirubinemia in the initial hours of life with a cut-off value of cord TOTAL BILIRUBIN of 3.2 which showed a specificity of 83.33%, sensitivity of 97.06%, PPV of 83.33%, NPV of 97.06% and diagnostic accuracy of 95%. Various studies with different cut-off values reported the effective predictive ability of cord TOTAL BILIRUBIN. The detailed comparison between the studies is illustrated in table 7. These findings suggested cord TOTAL BILIRUBIN ≥3.2 mg/dl can predict hyperbilirubinemia in new-born babies.

CONCLUSION-

The study aimed to assess the usefulness of cord blood bilirubin level in predicting significant hyperbilirubinemia in a new-born with ABO incompatibility in babies born of O +ve mothers. A+ blood group neonate with ABO incompatibility were less prone to hyperbilirubinemia. The diagnostic measures of cord TOTAL BILIRUBIN A+ blood group neonate with ABO incompatibility specificity of 73.23%, sensitivity of 87.12%, PPV of 73.14%, NPV of 84.06%, and diagnostic accuracy of 83%. The incidence of hyperbilirubinemia was more common in B+ neonates with ABO incompatibility. The diagnostic measures of cord TOTAL BILIRUBIN B+ blood group neonate with ABO incompatibility specificity of 95.32%, sensitivity of 97.21%, PPV of 85.14%, NPV of 97.25%, and diagnostic accuracy of 97%. AB+ blood group neonates with ABO incompatibility were least affected with hyperbilirubinemia than other blood groups. The diagnostic measures of cord TOTAL BILIRUBIN AB+ blood group neonate with ABO incompatibility specificity of 69.12%, sensitivity of 74.25%, PPV of 71.41%, NPV of 74.19%, and diagnostic accuracy of 80%. Total cord TOTAL BILIRUBIN at cut-off point >3.2 mg/dl showed a specificity of 83.33%, sensitivity of 97.06%, PPV of 83.33%, NPV of 97.06%, and diagnostic accuracy of 95%. These findings suggested cord TOTAL BILIRUBIN ≥3.2 mg/dl can predict hyperbilirubinemia in new-born babies. Further studies are warranted to confirm the present study findings.

REFERENCES:

1. Peeters B, Geerts I, Van Mullem M, Micalessi I, Saegeman V, Moerman J. Post-test probability for neonatal hyperbilirubinemia based on umbilical cord blood bilirubin, direct antiglobulin test, and ABO compatibility results. European journal of pediatrics. 2016 May;175(5):651-7.
2. Sharkey D, Lissauer T, Carroll W. Neonatal Medicine. In Illustrated TexTotal Bilirubinook of Paediatrics. 5th edition Elsevier; 2018 p.181.
3. Chen HL, Wu, SH, Hsu SH Liou BY, Chen HL, Chang MH. Jaundice revisited: recent advances in the diagnosis and treatment of inherted cholestic liver diseases. J Biomed Sci. 2018; 25:75.
4. Fei F, Marques MB, Staley EM, Williams LA. Correlation of Direct Antiglobulin Test Strength in Umbilical Cord Blood and Hyperbilirubinemia in ABO Incompatible Neonates with Two Methods. Blood. 2018 Nov 29; 132:5072.
5. Munir S, Ijaz S, Singh M, Kareem AA, Mehmood K. Frequency of ABO Incompatibility in Neonates Presenting with Unconjugated Hyperbilirubinemia. Research on Health Benefits of Coconut. 2021 Aug;32(8):133.
6. Abbas SH, Nafea LT, Abbas RS. Prevalence of ABO Incompatibility and its effect on Neonates Hyperbilirubinemia. Research Journal of Pharmacy and Technology. 2020;13(1):141-6.
7. Gopu S, Begum A. A study on neonatal hyperbilirubinemia due to ABO incompatibility in sick new-born care unit, Telangana. Indian Journal of Child Health. 2018 Jun 28;5(6):425-7.
8. Kalakheti BK, Singh R, Bhatta NK, Karki A, Baral N. Risk of neonatal hyperbilirubinemia in babies born to 'O' positive mothers: A prospective cohort study. Kathmandu University Med J. 2009;7(1):11-15.
9. Chowdhary S, Devi U, Giridhar S. Predicting Significant Hyperbilirubinemia in ABO Incompatibility: Is Cord Direct Antiglobulin Test Useful?. Indian Journal of Hematology and Blood Transfusion. 2022 Jan 25:1-5.
10. Behrman RE, Kliegman RM, Jensen HB, eds. Nelson TexTotal Bilirubinook of Pediatrics. 17th ed. Philadelphia, WB saunders Co. 2004;596-605.
11. Karimzadeh P, Fallahi M, Kazemian M, Taleghani NT, Nouripour S, Radfar M. Bilirubin induced encephalopathy. Iranian journal of child neurology. 2020;14(1):7.
12. Pradhan A, Lamichaney R, Sharma V. Cord blood bilirubin level as a predictor of development of pathological hyperbilirubinemia in new-borns. Int J Contemp Pediatr. 2017 Jul;4(4):1519-24
13. Ipek IO, Bozaykut A, Çağrıl SC, Sezer RG. Does cord blood bilirubin level help the physician in the decision of early postnatal discharge?. The Journal of Maternal-Fetal & Neonatal Medicine. 2012 Aug 1;25(8):1375-8.
14. Schiltz NK, Finkelstein Rosenthal B, Crowley MA, Koroukian SM, Nevar A, Meropol SB, et al. Rehospitalization during the first year of life by insurance status. Clin Pediatr (Phila). 2014;53:845-53.
15. Harron K, Gilbert R, Cromwell D, Oddie S, van der Meulen J. Newborn length of stay and risk of readmission. Paediatr Perinat Epidemiol. 2017;31:221-32.
16. Wennberg RP, Watchko JF, Shapiro SM. Maternal empowerment----an underutilized strategy to prevent kernicterus? Curr Pediatr Rev. 2017;13:210-19.
17. Pahuja M, Dhawan S, Chaudhary SR. Correlation of cord blood bilirubin and neonatal hyperbilirubinemia in healthy new-borns. Int J Contemp Pediatr. 2016 Jul;3(926):e30.
18. Dhanwadkar SS, Christo S. Rasalam, Masoodet Z. Effectiveness of early clinical assessment and bilirubin estimation for prediction of neonatal hyperbilirubinemia. International J. Contemporary Pediatrics. 2016;3:477-84.
19. Akgül S, Korkmaz A, Yiğit S, Yurdakök M. Neonatal hyperbilirubinemia due to ABO incompatibility: does blood group matter. Turk J Pediatr. 2013 Sep 1;55(5):506-9.
20. Eldho HP, Baruah MN, Biswanath P. Correlation of cord blood bilirubin and NHB in the setting of ABO incompatibility. Int J Contemp Pediatr 2022;9:451-6.
21. Singh R, Jain H. Prediction of significant hyperbilirubinemia by estimating cord blood bilirubin in neonates with ABO incompatibility. International journal of contemporary paediatrics, 2019;6(2):670-5.
22. Knupfer M, Pulzer F, Gebauer C, Robel-Tillig E, Vogtmann C. Predictive value of umbilical cord blood bilirubin for postnatal hyperbilirubinaemia. Acta Paediatr. 2005; 94(5):581-7