



# Umbilical Cord Blood Hemoglobin as a Predictor of Significant Neonatal Hyperbilirubinemia in Term Newborns in a Tertiary Care Centre in North Kerala

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## **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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## **ABSTRACT**

**Aims:** Neonatal hyperbilirubinemia is one of the most common problems during first week of life and is the most common cause of readmission in early neonatal period. The present study aimed to predict the development of significant hyperbilirubinemia in term neonates using cord blood hemoglobin.

**Study Design:** Prospective study.

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**Place and Duration of Study:** Department of Paediatrics, MMCH & RC, Kozhikode, Kerala from March 2021 to July 2022.

**Methodology:** The prospective study enrolled 162 appropriate for gestational age term newborns, delivered at MMCH & RC. Cord blood hemoglobin was measured and bilirubin estimation was done at 48-72 hours of life. Hyperbilirubinemia was considered significant if serum bilirubin value was above standard as per American Academy of Pediatrics guidelines. Data was entered in Microsoft Excel and analysed using SPSS 20.0 version. The relationship between cord hemoglobin in predicting significant neonatal hyperbilirubinemia was studied using appropriate statistical tests. Sensitivity and specificity of the variables were defined using ROC curve and Pearson correlation coefficient to determine the correlation between the variables.

**Results:** Out of the total 162 neonates enrolled, 86 were boys (53.1%) and 76 were girls (46.9%). The mean cord hemoglobin value was 15.3g/dl. 20 neonates (12.3%) had developed significant hyperbilirubinemia and required phototherapy while none of them needed exchange transfusion. Correlation between cord hemoglobin with serum bilirubin showed weak correlation ( $r=0.194$ ) but the correlation was statistically significant ( $p<0.05$ ). On ROC curve analysis, cord hemoglobin cut off value  $\geq 14.9$ g/dl showed 75% sensitivity and 39.4% specificity to predict significant neonatal hyperbilirubinemia.

**Conclusion:** There is significant correlation between umbilical cord blood hemoglobin level and neonatal hyperbilirubinemia. Cord hemoglobin  $\geq 14.9$ g/dl can predict future development of significant neonatal hyperbilirubinemia. This will be useful in very low resource centres to plan early discharge of newborns without fear of hyperbilirubinemia.

*Keywords: Cord blood hemoglobin; neonatal hyperbilirubinemia.*

## 1. INTRODUCTION

Jaundice is one of the most common abnormal physical findings during the first week of life [1]. Almost all newborn babies have serum or plasma total bilirubin (TB) concentrations that are  $>1$ mg/dl, in contrast to healthy adults, whose normal total bilirubin level is  $<1$  mg/dl. Most preterm infants and around 85% of term neonates develop clinical jaundice. Peak total bilirubin levels  $>12.9$  mg/dl are present in 6.1% of normal-term neonates. Total blood bilirubin levels in well-term newborns exceed 15 mg/dl in 3% of cases [2].

Jaundice is visible in the skin and eyes of a newborn when total serum bilirubin content exceeds 5-7 mg/dl. Three mechanisms contribute to the increased total bilirubin concentration in newborns: increased production from red blood cell breakdown, decreased clearance by immature hepatic mechanisms, and enhanced reabsorption by enterohepatic circulation. Some babies may develop bilirubin-induced neurological dysfunction as a result of high serum bilirubin levels. Jaundice is benign in most cases and doesn't need any therapeutic intervention. About 5–10% of them have clinically significant jaundice that needs to be treated [3].

Jaundice caused by the physiological immaturity of newborns to handle increased bilirubin

production is referred to as "physiological jaundice. Pathological jaundice is taken into consideration when total bilirubin concentrations are not in the physiological jaundice range [3]. Any total bilirubin level of 17 mg/dl or more should be regarded as pathologic and should be evaluated for the cause and possible intervention, such as phototherapy [4].

Neonatal hyperbilirubinemia is the most common cause of readmission in the early neonatal period. Early discharge of healthy term newborns after normal delivery is a common practice due to medical factors like prevention of nosocomial infection, social factors, and economic factors. Parents also want early discharge during pandemic seasons like COVID-19 in order to minimize the hospital stay. Early treatment of jaundice with phototherapy is cheap, effective, and simple. Treatment of severe neonatal jaundice by exchange transfusion is costly, time-consuming, and associated with complications.

The American Academy of Pediatrics (AAP) recommends that neonates discharged within 48 hours should be followed up after 48-72 hours for significant jaundice and other problems [5]. This recommendation is not appropriate for our country because of the limited follow-up facilities. So, the follow-up, detection, and early treatment of jaundice have become more difficult due to early discharge from the hospital. So, the

concept of predicting neonatal hyperbilirubinemia at birth using cord blood offers a non-invasive option to implement follow-up and treatment for high-risk groups, thereby reducing mortality and morbidity, and also allowing for the early discharge of low-risk newborns. The present study to find out the predictive ability of cord blood hemoglobin with significant neonatal hyperbilirubinemia will be a useful tool for Paediatricians.

## 2. MATERIALS AND METHODS

The present hospital based prospective study carried out in the Department of Paediatrics, Malabar Medical College Hospital & Research Centre (MMCH & RC), Kozhikode, Kerala, India from March 2021 to July 2022. All term newborns who are appropriate for gestational age and delivered at MMCH & RC were included in the study. Preterm term babies, post term babies, babies with APGAR score less than 7 at 5 minutes of life, Rh incompatibility (DCT positive), babies born by instrumental delivery, babies with major congenital anomalies, early neonatal sepsis, neonates with cord hemoglobin <10g/dl and cord bilirubin >5mg/dl were excluded from the study.

After delivery, a 2ml blood sample was taken in an EDTA bottle for hemoglobin, blood grouping and Rh estimation. APGAR score at 1 and 5 minutes, birth weight, gender, gestational age using LMP or first trimester USG and the mother's blood group were recorded. Hemoglobin was estimated by Colorimetric method using Sodium Lauryl Sulphate as reagent. Machine used for Colorimetric method was Sysmex XN 550 and serial number was 14583. All babies in the study were followed up daily for jaundice using Kramer's rule, features of sepsis and blood group incompatibility up to 72

hours of life. During the period of observation, babies with exclusion criteria were excluded. 2ml of venous blood was drawn from all the newborns in the study for estimation of serum bilirubin at 48-72 hours, which is a routine investigation for all neonates. If the baby developed significant jaundice earlier, a serum bilirubin test was performed sooner, and appropriate treatment was started. Hyperbilirubinemia was considered significant if the serum bilirubin value was above standard as per AAP guidelines [5].

Data was entered in Microsoft Excel and analysed using SPSS 20.0 version. The relationship between cord blood hemoglobin in predicting significant neonatal hyperbilirubinemia was studied using appropriate statistical tests. Continuous variables were tested by t test and categorical variables were tested by Chi square test. The sensitivity and specificity of the variables were defined using the ROC curve and the Pearson correlation coefficient to determine the correlation between the variables. A P value of <0.05 was considered as statistically significant.

## 3. RESULTS

One hundred and sixty-two healthy term newborns were enrolled in the present study, out of which 86 (53.1%) were males and 76 (46.9%) were females. There were 32.1% primigravidae and 67.9% multigravida mothers. The majority of the babies in the study group were delivered vaginally (61.1%), while the rest were delivered via caesarean section (38.9%). Most of the babies in the current study (52.5%) belonged to the O blood group. The majority of the newborns had birth weight between 2.5 - 3.5 kg, and the mean birth weight of the study was 3.104 kg ± 0.299 kg.

**Table 1. Comparison of baseline characteristics with neonatal hyperbilirubinemia**

Neonatal characteristics		Total	Hyperbilirubinemia		P-value
			Yes n=20	No n=142	
Gender	Male	86	10 (11.6%)	76 (88.4%)	.77
	Female	76	10 (13.2%)	66 (86.8%)	
Mode of delivery	Vaginal	99	16 (16.2%)	83 (83.8%)	.06
	Caesarean section	63	4 (6.3%)	59 (93.7%)	
Birth weight	2.5-3 kg	67	10 (14.9%)	57(85.1%)	.56
	3-3.5 kg	76	8 (10.5%)	68 (89.5%)	
	>3.5 kg	19	2 (10.5%)	17 (89.5%)	

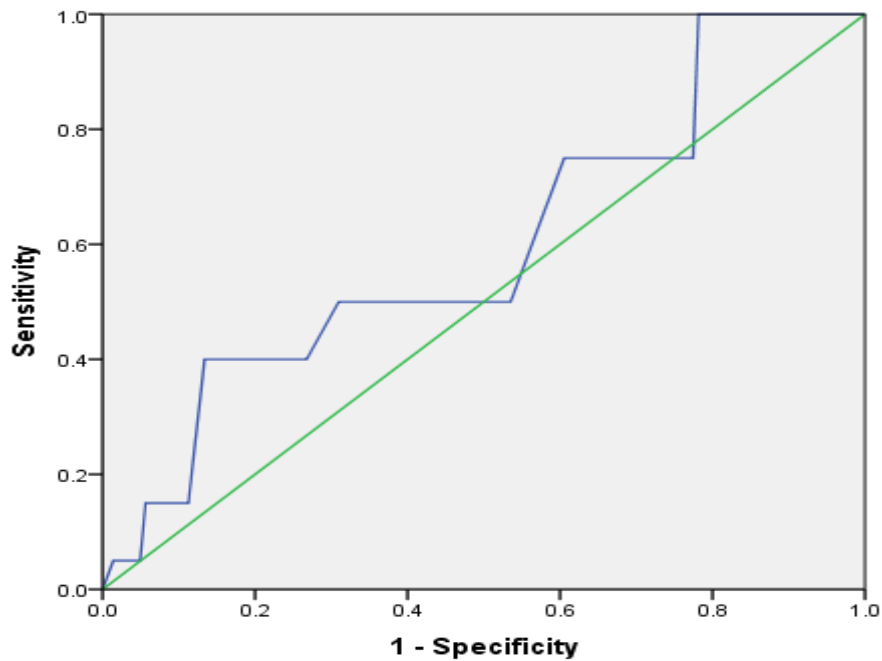


Fig. 1. ROC curve for cord hemoglobin and neonatal hyperbilirubinemia

Table 2. Association between neonatal hyperbilirubinemia and cord hemoglobin

Haemoglobin (g/dl)	Hyperbilirubinemia		Total (N=162)
	Yes	No	
≥14.9	15	88	103
<14.9	5	54	59
Total	20	142	162

The mean cord blood hemoglobin was  $15.322 \pm 1.537$  g/dl and the mean total serum bilirubin at 48-72 hours of life was  $12.018 \pm 3.258$  mg/dl. Twenty neonates (12.3%) had developed significant hyperbilirubinemia and required phototherapy while none of them needed exchange transfusion. Significant newborn hyperbilirubinemia was present in 11.6% of boys and 13.2% of girls. Association between hyperbilirubinemia and gender, mode of delivery, and birth weight was showed no association ( $P>.05$ ). Correlation between cord hemoglobin with serum bilirubin showed weak correlation ( $r=0.194$ ) but the correlation was statistically significant ( $P<.05$ ).

On ROC curve analysis, haemoglobin has an area under the curve of 0.598 and it is not statistically significant ( $P>.05$ ). Cord haemoglobin level of  $\geq 14.9$ g/dl was chosen as the cut off value based on ROC analysis which showed 75% sensitivity, 38% specificity, 14.6% positive predictive value, 91.5% negative predictive value for predicting significant neonatal hyperbilirubinemia. The sensitivity and negative predictive value of cord blood hemoglobin were

high, but the specificity and positive predictive value were low.

#### 4. DISCUSSION

Neonatal hyperbilirubinemia is one of the most common reasons for newborn readmission. The rising trend of early newborn discharge has resulted in the re-emergence of bilirubin-related neurological sequelae. Therefore, it is important that early detection of hyperbilirubinemia be made in neonates who have been discharged early from the hospital. Umbilical cord blood screening is less invasive and therefore easier to perform in various peripheral centers. Keeping these factors in mind, our study was conducted on term-healthy neonates. In this present study, we assessed the cord blood haemoglobin as a tool for screening for the risk of subsequent neonatal hyperbilirubinemia.

In present study, out of 162 babies, 53.1% were males and 46.9% were females and there was no statistical significance between development of significant neonatal hyperbilirubinemia and gender. Previous studies done by Onwuanaku et

al. [6], Amar Taksande et al. [7], Patel A et al. [8] and Venkatamurthy et al. [9] found no correlation between neonatal hyperbilirubinemia and newborn gender. Rudy Satrya et al. showed a significant correlation between the gender of the newborn and neonatal hyperbilirubinemia ( $P < 0.05$ ) [10]. The present study is in correlation with the studies done by Onwuanaku et al. [6], Amar Taksande et al. [7] and Venkatamurthy et al. [9]. Among the 99 neonates born vaginally, 16 had significant hyperbilirubinemia, while out of 63 caesarean deliveries, 4 had significant jaundice, and there is no significant relationship between neonatal hyperbilirubinemia and mode of delivery, with a P value of .06. This was in correlation with the results of studies done by Amar Taksande et al. [7], Rostami et al. [11] and Rudy Satrya et al. [10].

In the present study, 20 neonates developed significant hyperbilirubinemia, giving an incidence of 12.3%, which was similar to Alpay et al. [12], Pradhan et al. [13] and Randev et al. [14] while a higher incidence for the development of significant jaundice (27.34%) was reported by Gupta S et al. [15] and a lower incidence (8.35%) by Phuapradit et al. [16]. All neonates with significant hyperbilirubinemia were treated with phototherapy and none of them required an exchange transfusion.

The mean value of cord hemoglobin among neonates in the study was  $15.322 \pm 1.537$  g/dl. Correlation between cord hemoglobin with serum bilirubin showed weak correlation ( $r = 0.194$ ) but the correlation was statistically significant ( $P < 0.05$ ). On ROC curve analysis, cord hemoglobin cut off value  $\geq 14.9$ g/dl showed 75% sensitivity, 38% specificity, 14.6% positive predictive value, 91.5% negative predictive value to predict significant neonatal hyperbilirubinemia.

A study done by Nakagawa et al. showed that significant neonatal hyperbilirubinemia requiring phototherapy mostly occurred in association with high cord blood hemoglobin, which is increased by delayed cord clamping [17]. A study done by Ankit Sharma et al. showed, the mean value of cord hemoglobin on delayed cord clamping (18.69 g/dl) was more compared to immediate cord clamping (17.27g/dl). Also found that the risk of developing neonatal hyperbilirubinemia is an issue of concern in delayed cord clamping [18]. Study by Yuksel Yasartekin et al. also showed similar results comparing early and delayed cord clamping [19]. A study done by Krishnan et al. showed that babies with cord haemoglobin

$< 15.1$ g/dL are more prone for pathological hyperbilirubinemia [20].

The present study which correlates with study done by Nakagawa et al. [17] and Ankit Sharma et al. [18]. The high cord blood hemoglobin values in newborns with significant neonatal hyperbilirubinemia can be attributed to the practice of delayed cord clamping.

Limitations: The limitations of the study are that the sample size was small and preterm or high-risk babies were not evaluated. Despite the fact that the peak bilirubin level peaks on the third and fifth postnatal days, newborns are only monitored for three days following delivery, which is another limitation of the study.

## 5. CONCLUSION

Incidence of significant neonatal hyperbilirubinemia was 12.3% in the current study. There is significant correlation between umbilical cord blood hemoglobin level and neonatal hyperbilirubinemia. Cord blood hemoglobin with cut off  $\geq 14.9$ g/dl was found to have sensitivity, specificity, NPV and PPV values of 75%, 38%, 14.6% and 91.5% in relation to significant neonatal hyperbilirubinemia. Cord hemoglobin  $\geq 14.9$ g/dl can predict future development of significant neonatal hyperbilirubinemia. This will be useful in very low resource centres to plan early discharge of newborns without fear of hyperbilirubinemia.

## CONSENT

Informed written consent was obtained from all the parents before starting the study.

## ETHICAL APPROVAL

The study was conducted after getting approval from the institutional ethical committee.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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