

# Cord Blood Albumin as a Predictor of Significant Hyperbilirubinemia in Term and Preterm Neonates

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## Abstract

**Background:** Jaundice is the most common condition requiring medical attention and readmission. As neonates are discharged within 48 hours of birth, close follow up is very important to look for jaundice. In developing countries, follow up visits are difficult. Therefore, it is important to identify at risk neonates before discharge. This study helps in identifying neonates at risk for hyperbilirubinemia. This study includes both healthy pre-term and full term neonates. **Aim & Objective:** To find correlation between cord blood albumin level with serum bilirubin level in healthy term and preterm neonates and correlation between maternal serum albumin level with cord blood albumin. **Subject and Method:** This study included 106 neonates (full-term and pre-term) born in Lilavati Hospital, Mumbai during period of March to December 2017. **Result:** Out of 106 neonates, 42(39.6%) developed significant hyperbilirubinemia. 17 (58.6%) neonates with cord blood albumin below 2.8 g/dl required phototherapy against 24 (50%) with cord blood albumin between 2.8-3.3 g/dl. In this study, 11 (73.3%) out of 15 pre-term and 6 (42.9%) of 14 full-term neonates with cord blood albumin below 2.8 g/dl developed significant hyperbilirubinemia and required phototherapy. A significant association was observed between maternal and cord blood albumin level. **Conclusion:** Significant association observed between cord blood albumin and tendencies of significant hyperbilirubinemia. So, cord blood albumin can be used as a surrogate marker for screening newborns for development of significant hyperbilirubinemia

**Keywords:** Cord blood albumin, Significant hyperbilirubinemia, Phototherapy.

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## Introduction

Jaundice is the most common condition that requires medical attention in newborns as 84% of the new-borns are affected by neonatal hyperbilirubinemia. It is considered as the most common cause of readmission to the hospital during this period.<sup>[1]</sup> Physiological jaundice is a normal response by neonates due to limitations in the ability to excrete bilirubin. Albumin binds unconjugated bilirubin and helps in its transport. This in turn reduces the bilirubin toxicity on the tissues. It has been noted that there is a dramatic decrease in the hospital stays of neonates over the past few decades. It is a common practise to discharge normal appearing neonates within 48 hours of birth.<sup>[2]</sup> Hence it is important to identify neonates who are at risk of developing hyperbilirubinemia following an early discharge from the hospital. Hence, the present study was conducted to determine the correlation between cord blood albumin and development of neonatal significant hyperbilirubinemia. Low production of albumin will lower its transport and binding capacity and hence determining the cord blood albumin helps identifying at risk neonates early to avoid the complications associated with neonatal jaundice.

## Aims and objectives

To find a correlation between cord blood albumin level with the serum bilirubin levels in healthy term and preterm neonates.

To find correlation between maternal serum albumin level with cord blood albumin of term and preterm neonates.

## Subjects and Methods

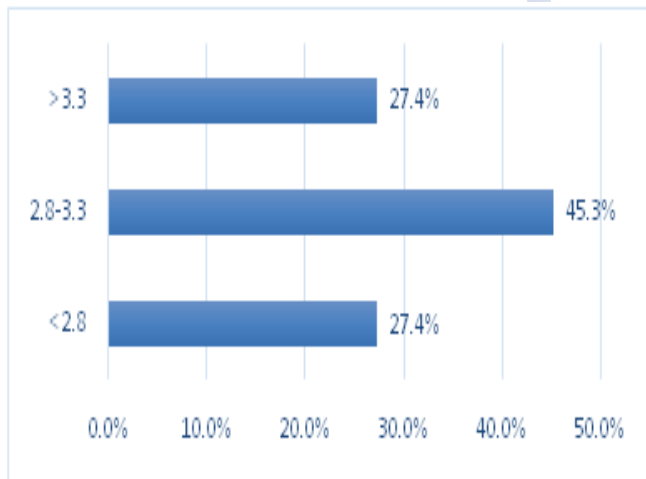
This is a prospective cross-sectional study conducted in Lilavati Hospital, Mumbai from March 2017 and December 2017 on full term and pre-term (>32 weeks) healthy neonates. The permission was taken from the Ethical committee of the hospital. The informed written consent was taken from the either of the parents. All the relevant history of mother and neonate was noted, and neonates were monitored daily for development of jaundice. At the time of delivery, two ml of cord blood was collected and sent for cord blood albumin estimation. The serum albumin level was measured by Immunoturbidometric method. Those suspected to have jaundice as per Kramer dermal chart were tested for serum bilirubin levels by calorimetric assay by diazonium method on day 3-5. Neonates were categorised in three groups according to cord blood albumin levels <2.8

g/dl, 2.8-3.3 g/dl and > 3.3 g/dl respectively. The main outcome of the study was inferred in terms of significant hyperbilirubinemia which needed phototherapy or exchange transfusion. The quantitative data was represented as their mean ± SD. Categorical and nominal data were expressed as frequency and percentage. The t-test was used for analysing quantitative data and categorical data was analysed using chi-square test. The significance threshold of p value was set at <0.05.

## Results

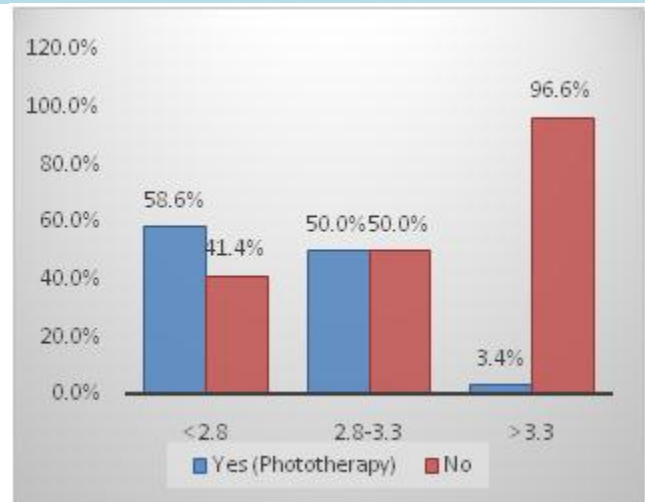
Study included 46 females (43.4%) and 60 male (56.6%) neonates. In this study, 24(57.1%) of 46 female neonates developed significant hyperbilirubinemia against 18 (42.9%) of 60 male neonates. Development of significant hyperbilirubinemia was observed to be associated with female gender in present study (p<0.05).

Study included 40 pre-term(>32 weeks) and 66 term neonates. Cord blood albumin level below 2.8 g/dl seen in 27.4% neonates while in 45.3% and 27.4% neonates, it was between 2.8 to 3.3 g/dl and >3.3 g/dl, respectively.



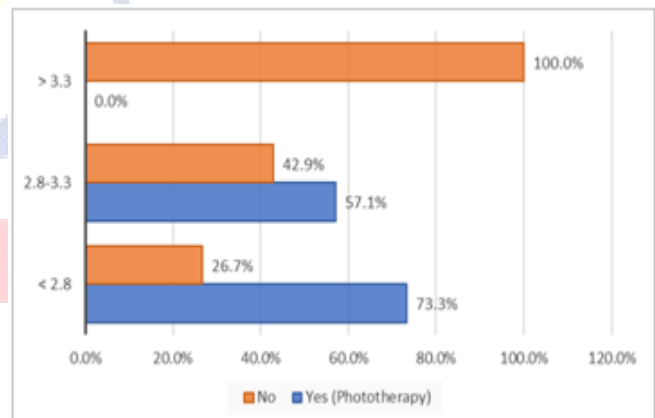
**Figure 1: Distribution of subjects as per cord blood albumin level**

In present study, a total of 42 neonates (39.6%) had significant Hyperbilirubinemia and required phototherapy. Out of these 42 neonates, only 1 had cord blood albumin level above 3.3 g/dl. Out of total 29 cases with cord blood albumin level of < 2.8 g/ dl, 17 neonates (58.6%) developed significant hyperbilirubinemia and required treatment in the form of phototherapy. None of the neonates required exchange transfusion. The association of low cord blood albumin level with development of significant hyperbilirubinemia was statistically significant with sensitivity and specificity of 97.6% and 43.8% at level of 3.3 g/ dl (p<0.01).



**Figure 2: Association of cord blood albumin level with hyperbilirubinemia**

In pre-term neonates, 23(57.3%) developed significant hyperbilirubinemia and of these 11 neonates had cord blood albumin < 2.8 g/dl. Only 4 neonates had cord blood albumin levels > 3.3 g/dl and none of them developed hyperbilirubinemia.



**Figure 3: Association of cord blood albumin level with hyperbilirubinemia in Pre-term neonates.**

In term neonates, out of 66 only 19 (28.8%) developed significant hyperbilirubinemia. The association of low cord blood albumin level with development of significant hyperbilirubinemia was statistically significant in term babies, 6 out of 8 neonates (42.9%) with cord blood albumin below 2.8 g/dl developed significant hyperbilirubinemia compared to only 1 out of 24 (4%) with cord blood albumin above 3.3 g/dl (p<0.01).

This study also found a significant association between maternal and cord blood albumin level. Lower serum albumin level in mothers were associated with lower cord blood albumin level (p<0.01).

In this study, visual assessment of severity of hyperbilirubinemia as estimated by Kramer staging was not observed to be statistically related to cord albumin levels (p=0.13). Hence, visual inspection is unreliable for identifying

hyperbilirubinemia in neonates.

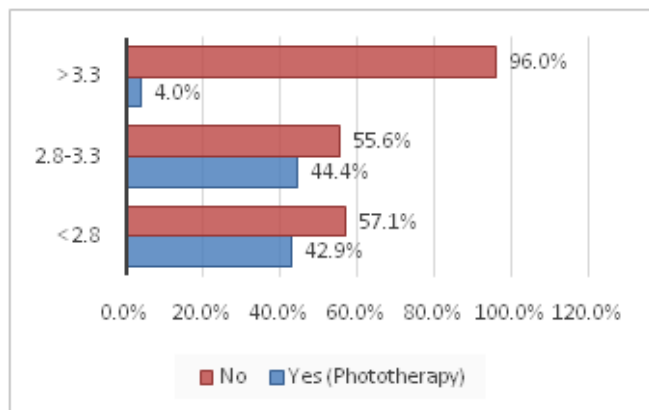


Figure 4: Association of cord blood albumin level with hyperbilirubinemia in term neonates

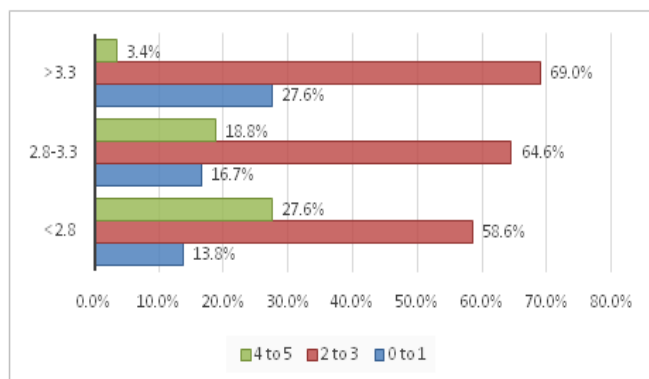


Figure 5: Association of cord blood albumin level with clinical Jaundice (Kramer Stage).

No neonates required exchange transfusion in this study. This study did not find any significant correlation of significant hyperbilirubinemia with mode of delivery, type of feeding.

## Discussion

In present study, overall, 39.6% neonates developed significant hyperbilirubinemia (Term – 28.8% and Pre-term – 57.5%) requiring phototherapy. The prevalence of significant hyperbilirubinemia was observed as 28% in the study by Meena JK et al<sup>[3]</sup> and 41.3% and 54.6% prevalence in term and pre-term babies in study by Reshad et al.<sup>[4]</sup> In a study on 40 term newborns by Sahu et al<sup>[5]</sup> significant hyperbilirubinemia was observed in 50% neonates.

A statistically significant association of low cord blood albumin level with development of significant hyperbilirubinemia was observed in our study. The prevalence of significant hyperbilirubinemia among various cord albumin level groups was: < 2.8 g/dl- 58.6%, 2.8-3.3 g/dl- 50% and; > 3.3 g/dl- 3.4% respectively. In a study by Meena JK et al<sup>[3]</sup> on the term neonates the prevalence of significant hyperbilirubinemia among group A, B and C was

90.9%, 26.6% and 2.4%. Similarly, Sahu S et al<sup>[5]</sup> found that 82% of neonates who had cord blood albumin level less than 2.8 g/dl developed hyperbilirubinemia requiring phototherapy and about 12% needed exchange transfusion. At higher levels of cord blood albumin that is 2.8 - 3.3 g/dl, 40% needed phototherapy and with cord blood albumin > 3.3 g/dl, none of the neonates needed any intervention for hyperbilirubinemia.

In present study, 11 out of 15 pre-term neonates (73.3%) with cord blood albumin <2.8 g/dl developed significant hyperbilirubinemia compared to none with cord blood albumin >3.3 g/dl (p<0.01). Also, 6 out of 8 term neonates (42.9%) with cord blood albumin < 2.8 g/dl developed significant hyperbilirubinemia compared to only 1 out of 24 (4%) with cord albumin above 3.3 g/dl (p<0.01). Reshad M et al<sup>[4]</sup> in a similar study found that in the term group, 19 (61.2%) newborns with cord blood albumin < 2.8 g/dL developed neonatal hyperbilirubinemia while 13 (32.3%) newborns with cord blood albumin level between 2.9- 3.3 g/dL, and only 2 (6.5%) of the newborns with cord blood albumin level ≥3.4 g/dL developed significant neonatal hyperbilirubinemia. In the preterm group, 33 (80.5%) newborns that developed significant hyperbilirubinemia and their cord blood albumin was < 2.8 g/dL. None of the newborns with cord blood albumin level >3.4 g/dL developed neonatal hyperbilirubinemia (p<0.01).

In present study, the sensitivity, specificity, positive and negative predictive value of cord albumin level < 2.8 g/dl was 97.6%, 43.8%, 53.2% and 96.6% in predicting significant hyperbilirubinemia among term and preterm neonates.

We also observed a significant association between maternal and cord blood albumin levels in this study. Lower serum albumin levels in mothers were associated with lower cord albumin levels in neonates (p<0.01). Maher JE et al<sup>[6]</sup> in their study observed a significant correlation between maternal serum levels of albumin and albumin levels in newborns. Stanier MW et al<sup>[7]</sup> also observed a significant correlation between low maternal serum albumin levels and fetal cord blood albumin (p<0.05).

## Conclusion

There is a significant association between cord blood albumin (<2.8 g/dl) and the tendency to develop significant neonatal hyperbilirubinemia. Hence, cord blood albumin can be used as a surrogate marker for screening newborns for development of significant hyperbilirubinemia. It is a cost-effective investigation and safe to implement in daily clinical practice. Visual inspection of jaundice using Kramer dermal score is unreliable and may mislead about the severity of jaundice. We can reduce the length of hospital stay and reduce readmission rates due to hyperbilirubinemia if we have ways to know at risk neonates for hyperbilirubinemia. Our study results will help to identify such neonates and reduce the morbidity and mortality due to

hyperbilirubinemia in resource limited set ups.

Limitation of study- This was a prospective cross-sectional study conducted in a single tertiary centre conducted on small number of full term and pre-term neonates. The population studied were not indicative of general population as study was conducted in a tertiary centre.

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