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Cord Blood Albumin; A Predictor of Neonatal Jaundice

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Authors Contribution

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ABSTRACT

Objective: To determine significance of cord blood albumin as predictor of neonatal hyperbilirubinemia.

Methodology: This cross-sectional was conducted in 6 months from 24-4-2021 to 23-9-2021 at Department of neonatology, Recep Tayyip Erdogan Hospital, Muzaffargarh. Early preterm, late preterm and term neonates, age less than 1 week were included in the study. Patients were divided in three groups on basis of gestational age. Group 1 was included early preterm; group 2 was included late preterm and group 3 was including term neonates. Cord blood samples were taken in sterile vials for serum albumin at birth. Patients were followed from 2nd to 7th day of life for development of jaundice. Patients who had transcutaneous bilirubin more than 5mg/dl were selected for serum bilirubin level estimation.

Results: A total of 73 newborn babies were studied; with an average age of approximately 4.94+1.68 days. There were 52.1% male and 47.9% female babies. There were no significant differences in average blood cord albumin and direct bilirubin levels among these groups. However, significant variations were observed in terms of total bilirubin and indirect bilirubin levels, with early and late preterm babies displaying higher levels compared to term babies. Moreover, the study established significant inverse correlations between cord blood albumin levels and both total bilirubin ($r \approx -0.389$, $p = 0.001$) and indirect bilirubin levels ($r \approx -0.313$, $p = 0.007$).

Conclusion: Study provides compelling evidence to support the role of cord blood albumin as a predictor of neonatal jaundice through its observed inverse correlations with bilirubin levels. The findings underscore the potential clinical utility of cord blood albumin as an early diagnostic marker for identifying newborns at risk of developing jaundice.

Key words: Newborn Jaundice, cord blood albumin, indicator.

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Introduction

Jaundice refers to the yellowing of the eyes' white part (sclera) and skin, and it is a frequent occurrence in both full-term and preterm newborns.[1] Elevated bilirubin levels in newborns can arise from either physiological or pathological factors.[2] Physiological jaundice occurs when heightened bilirubin production coincides with an underdeveloped bilirubin conjugation and liver excretion system.[3] The elevated bilirubin burden in newborns stems from the escalated production of bilirubin, primarily attributed to a larger volume of red blood cells that have a shorter lifespan within the neonatal context. The reduced elimination of bilirubin is attributed to a lack of the uridine diphosphate glucuronosyltransferase (UGT) enzyme, which in newborns exhibits only around 1% of the liver activity seen in adults.[2] Pathologic jaundice occur on first day of life and urgent attention is needed to find the cause. It is often due to sepsis, hemolysis (RH, ABO incompatibility) and internal haemorrhage e.g cephalhematoma, spleen or liver hematoma,[4] with pathological neonatal jaundice, there is an increased risk for developing bilirubin-induced neurologic dysfunction (BIND), such as acute bilirubin encephalopathy, and its sequelae, kernicterus. Because unbound bilirubin, which is bilirubin not bound to albumin easily enters the brain, serum unbound bilirubin.[3] The water-soluble albumin combines with unconjugated bilirubin and ultimately

makes it less toxic. After entering liver, the bilirubin detaches from albumin and leaves the liver through hepatocytes.[3] Serum albumin levels and bilirubin binding capacity (BBC) are lower in preterm and growth-restricted infants, leading to an increase in free bilirubin levels. Limited data in preterm infants suggest that the mean serum albumin levels in infants born before 30 weeks' gestation are approximately 1.9 g/dl and only approach normal values of 3.0 g/dl at term gestational age. Capacity of bilirubin to bind albumin is a surrogate measure of a neonate's ability to cope with an excessive bilirubin load.[5] Globally, among all live births 85% have neonatal jaundice. The rate of disease is very high in under developed countries especially in low-income countries as compare to developed countries.[6] According to study done in Karachi Pakistan, the incidence of hyperbilirubinemia (bilirubin >5mg/dl) among 1690 newborns was 39.7/1000 live births.[7] According to a study done by Asit kumar mishra in 2018 a cord serum albumin level ≤2.8 g/dl was seen in 95% of term newborns who developed hyperbilirubinemia. In the group where cord serum albumin was ≥3.4 g/dl, none of the term newborns developed hyperbilirubinemia.[8] Despite the emerging interest in using cord blood albumin levels as a potential predictor of neonatal jaundice, there is a noticeable gap in the existing research landscape that warrants further investigation. While preliminary studies have shown a correlation between low cord blood albumin levels and an increased risk of neonatal jaundice, there is limited consensus on its predictive accuracy across diverse populations and clinical settings. The purpose of this study was to determine association between cord blood albumin and neonatal hyperbilirubinemia. By screening neonates with cord blood albumin, detect neonates who are at high risk of developing significant hyperbilirubinemia can be detected and by early detection and treatment of hyperbilirubinemia can be decrease the morbidity and mortality.

Methodology

This cross-sectional study was done at department of neonatology, Recep Tayyip Erdogan Hospital, Muzaffargarh. Study duration was 1 year from 24-4-2021 to 23-9-2021**.** The **s**ample size of this study was 73 and it is calculated by Open EPI software at confidence interval 95%. It is calculated from a reference study in which 95% of patients in a group developed hyperbilirubinemia at cord albumin less than 2.8mg/dl.[8] All the early preterm, late preterm and term neonates, age less than 1 week of either gender were included. Neonate with congenital anomalies, neonates with incomplete or missing cord blood albumin or bilirubin data and lack of consent were excluded. After taking detailed history a detailed examination of the patient was carried out. Patients were divided in three groups on basis of gestational age. Group 1 was included early preterm (gestational age from 24 to 33 weeks); group 2 was included late preterm (34 to 36 weeks of gestation) and group 3 was included term neonates (gestational age from 37 weeks to 41 week). Cord blood sample was taken in sterile vials for serum albumin at birth to evaluate the serum albumin level. Hypoalbuminemia, was defined as a serum albumin <2.5 g\dl in preterm and less than 3g\dl in term neonate. Patients were followed from 2nd to 7th day of life for development of jaundice. Those patients who have transcutaneous bilirubin more than 5mg/dl were selected for serum bilirubin level estimation. All the data will be gathered on proforma and results will be analyzed with SPSS version 20.

Results

The study involved a group of subjects, presumably newborn babies, where the mean age of the subjects was approximately 4.94 days, with a standard deviation of 1.68 days. The study comprises 52.1% male babies and 47.9% female babies. All the neonates had dark color stool. About 63.0% of the neonates had dark yellow urine, while the remaining 37.0% had light yellow urine and feto-maternal blood groups are presented in table I.

The study investigated the relationship between blood cord albumin levels, direct bilirubin levels, total bilirubin levels, and indirect bilirubin levels among newborn babies categorized as early preterm, late preterm, and term. The findings revealed that there were no statistically significant differences in average blood cord albumin and direct bilirubin levels among these three groups of babies ($p > 0.05$). However, notable distinctions were observed in terms of total bilirubin and indirect bilirubin levels. The average total bilirubin and indirect bilirubin levels were found to be significantly higher in both early and late preterm babies compared to term babies ($p < 0.05$), results shown in table II.

A statistically significant inverse correlation was observed between cord blood albumin and total bilirubin levels, with a correlation coefficient (r) of approximately -0.389 ($p = 0.001$). Similarly, another significant inverse correlation was identified between cord blood albumin levels and indirect bilirubin levels, with a correlation coefficient (r) of around -0.313 ($p = 0.007$). This indicates that as cord

blood albumin levels decreased, total bilirubin and indirect bilirubin levels tended to increase. Figure 1 and 2

Table II: Average cord blood albumin and bilirubin level as per the gestational age. (n=73)

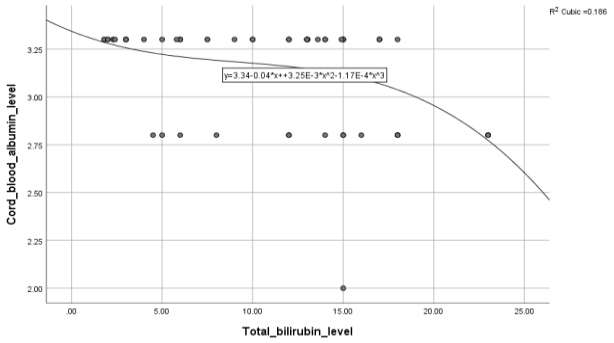
Groups	Cord blood albumin		p-value
Early preterm vs late preterm	3.17±0.22	3.04±0.34	0.237
Early preterm vs term	3.17±0.22	3.20±0.20	0.910
Late preterm vs term	3.04±0.34	3.20±0.20	0.120
Total bilirubin level			
Early preterm vs late preterm	12.00±6.07	13.01±5.85	0.810
Early preterm vs term	12.00±6.07	6.48±4.87	0.002
Late preterm vs term	13.01±5.85	6.48±4.87	0.001
Direct bilirubin level			
Early preterm vs late preterm	0.91±0.68	0.80±0.57	0.823
Early preterm vs term	0.91±0.68	0.77±0.55	0.708
Late preterm vs term	0.80±0.57	0.77±0.55	0.986
Indirect bilirubin level			
Early preterm vs late preterm	9.63±5.50	12.08±5.53	0.228
Early preterm vs term	9.63±5.50	6.90±5.42	0.052
Late preterm vs term	12.08±5.53	6.90±5.42	0.006

Table I: Descriptive statistics of demographic characteristics. (n=73)

Variables		Statistics	
Age of baby	(mean±SD)	4.94±1.68 days	
Neonatal weight	(mean±SD)	2.11±0.64 kg	
Gender of baby	Male	38	52.1%
	Female	35	47.9%
Gestational age	Early preterm	27	37.0%
	Late preterm	21	28.8%
	Term	25	34.2%
Maternal blood group	A-	2	2.7%
	A+	23	31.5%
	AB+	3	4.1%
	B-	2	2.7%
	B+	28	38.4%
	O-	5	6.8%
	O+	10	13.7%
Blood group of babies	A-	3	4.1%
	A+	14	19.2%
	Ab+	7	9.6%
	B-	3	4.1%
	B+	23	31.5%
	O+	23	31.5%
Colour of stool	Dark color stool	73	100.0%
Colour of urine	Dark yellow color	46	63.0%
	light yellow color	27	37.0%
Phototherapy required	Yes	33	45.2%
	No	40	54.8%

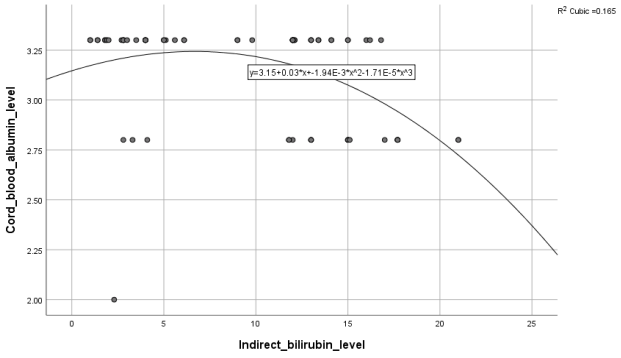
Discussion

Jaundice is a common condition in newborns, caused by elevated bilirubin levels. Identifying reliable predictors for its occurrence, especially in the early stages of life, holds the promise of timely interventions and proactive management. This study's findings contribute to the growing body of research exploring the relationship between cord blood albumin levels and the risk of neonatal jaundice. This study involved a group of subjects, presumably newborn babies, where the mean age of the subjects was approximately 4.94±1.68 days, 52.1% male babies and 47.9% female babies. These findings were supported by the Aiyappa GKC et al[16] as the males were 52.7% and female were 47.3%. However, the average body weight in this study was 2.11±0.64 kg, which was lower in contrast to Aiyappa GKC et al[16] and this may because they enrolled term babies in their study. On the other hand, Mahmoud Alalfy et al[17] also found similar findings as 54.7% were male babies and 45.3% were female babies.



(r=value -.389, p=value 0.001)

Figure 1. Correlation of cord blood albumin with total bilirubin. (n=73)



(r=value -.313, p=value 0.007)

Figure 2. Correlation of cord blood albumin with indirect bilirubin. (n=73)

This study examined the correlation between blood cord albumin levels, direct bilirubin levels, total bilirubin levels, and indirect bilirubin levels in newborns categorized by gestational age (early preterm, late preterm, and term). The results indicated no significant differences in average blood cord albumin and direct bilirubin levels among the three groups ($p > 0.05$). However, noteworthy variations were observed in total bilirubin and indirect

bilirubin levels. Both early and late preterm babies exhibited significantly higher average total bilirubin and indirect bilirubin levels compared to term babies ($p < 0.05$). In the comparison of this study Chiluka S et al[18] reported that the occurrence of jaundice is higher in late preterm infants, with approximately 95.45% of them experiencing jaundice, compared to term infants, where the prevalence is about 91.8%. Overall, out of the total newborn infants studied, 92.77% developed jaundice. According to our findings 54.8% neonates underwent phototherapy, which were almost similar to the study by Chiluka S et al[18] as Out of a total of 154 cases with clinical jaundice, 16 individuals needed phototherapy as a form of treatment. Zeitoun AA et al[19] also reported that the phototherapy treatment was required by 0.4% of the preterm cases. Higher bilirubin levels in late preterm and early preterm babies compared to term babies can be attributed to several factors related to their physiological development and metabolism. In preterm babies, especially those born late preterm or early preterm, the liver is not fully matured and might not efficiently process bilirubin. This can lead to an accumulation of bilirubin in the bloodstream, resulting in higher bilirubin levels.

In this study there was a statistically significant inverse correlation was observed between cord blood albumin and total bilirubin levels, with a correlation coefficient (r) of approximately -0.389 ($p = 0.001$). Similarly, another significant inverse correlation was identified between cord blood albumin levels and indirect bilirubin levels, with a correlation coefficient (r) of around -0.313 ($p = 0.007$). This indicates that as cord blood albumin levels decreased, total bilirubin and indirect bilirubin levels tended to increase. Consistently Sapkota P et al[20] found a significant negative correlation ($r = -0.455$, $p = 0.000$) between cord blood albumin levels and bilirubin levels on the fourth day after birth. This suggests that as cord blood albumin levels decreased, bilirubin levels increased. In the comparison of this series Awad HM et al[21] also observed that the significant correlation exists between the level of albumin in cord serum and the occurrence of neonatal hyperbilirubinemia among healthy full-term neonates weighing 2.5 kg or more at birth. The albumin level measured from umbilical cord blood emerges as a reliable method for predicting neonatal hyperbilirubinemia in healthy term infants.[21] In another study by Bhat JA et al[22] reported that there were significant statistical associations were identified between cord blood bilirubin, albumin, and the ratio of bilirubin to albumin in relation to the occurrence of neonatal hyperbilirubinemia. While the study provides valuable insights into the relationship between cord blood albumin levels and neonatal jaundice, it only examines the immediate postnatal period with limited sample size. However, the long-term outcomes related to neonatal health and the potential impacts of lower cord blood albumin levels on later health conditions remain unexplored. A comprehensive study sample size and more extended follow-up period would provide a comprehensive understanding of how this predictor might influence health outcomes beyond the neonatal.

Conclusion

As per the study conclusion, strong evidence observed which supporting cord blood albumin's ability to predict neonatal jaundice, as indicated by its noticeable inverse connections with bilirubin levels. These results highlight the valuable potential of cord blood albumin as an early diagnostic indicator, aiding in the identification of newborns with a higher likelihood of developing jaundice. The observed inverse correlations between cord blood albumin and bilirubin levels underscore the need for further research to understand the underlying mechanisms and potential interventions to mitigate the risk of neonatal jaundice.

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