

ORIGINAL ARTICLE

Decreased Cord Blood Albumin: A Predictor of Neonatal JaundiceErum Rashid Chaudhry¹, Abdul Khaliq Naveed², Amena Rahim³, Zunnera Rashid Chaudhry⁴**ABSTRACT****Objective:** To determine the significance of cord blood albumin estimation as a predictor of neonatal jaundice.**Study Design:** It was a prospective observational study.**Place and Duration of Study:** This study was carried out in Gynae/OBS department, neonatal intensive care unit and pathology laboratory at Railway Hospital Rawalpindi in collaboration with the Biochemistry Department of Islamic International Medical College from June 2015 to March 2016.**Materials and Methods:** Ninety full term neonates were divided into three groups based on their cord blood albumin concentration. Group I, with albumin less than 2.8 gm/dl, Group II with albumin between 2.8 - 3.3 gm/dl and Group III greater than 3.3 gm/dl. Serum Bilirubin level more than 1mg/dl was taken as standard for all the groups. Follow up was done for those neonates who had albumin less than 3 gm / dl and bilirubin more than 1 mg/dl. The babies were followed up on 7th and 15th day for the appearance of jaundice. Depending upon the extent, and delayed recovery from jaundice they were followed up to 20th post delivery day.**Results:** It was found that all neonates of group I and II who had albumin levels less than 3.3gm/dl, developed jaundice. Out of these 16.75% from group I received phototherapy and only 3% needed exchange transfusion. Whereas 10% jaundice neonates from group II received phototherapy. Out of 30 neonates in group III, 60% neonates developed jaundice but none required phototherapy or exchange transfusion.**Conclusion:** It is concluded that low albumin levels in the cord blood taken after birth is a good predictors of neonatal jaundice.**Key Words:** *Albumin, Bilirubin, Cord Blood, Neonatal Jaundice, Predictor.***Introduction**

Neonatal jaundice is one of the most common conditions requiring medical attention in newborn babies. About 60% of neonates born at term and 80% of neonate born before term (preterm) develop jaundice in the first week of life.¹ It is also known as icterus neonatorum and in the first postnatal week, approximately two thirds of all newborns develops icterus neonatorum in which bilirubin deposition occurs in the skin and mucous membrane. In majority of neonates such deposition is of little consequence.² It is mostly physiological since liver is not mature enough to handle the bilirubin load and this increased load is due to a higher circulating erythrocyte volume, a shorter erythrocyte life span,

and a larger bilirubin peak.³ Bilirubin is a yellow colored pigment which is produced from hemoglobin during destruction of erythrocyte. So increased production, impaired uptake of bilirubin by liver and in-effective conjugation causes increase level of unconjugated bilirubin leading to hyperbilirubinemia.⁴ For the detection of potential severity of neonatal hyperbilirubinemia the main criterion is the serum concentration of free bilirubin, or if it cannot be determined, the bilirubin/albumin ratio is taken.⁵ Bilirubin is normally glucuronidated and excreted by the liver into bile. Failure of this system can lead to a buildup of conjugated bilirubin in the blood, resulting in jaundice.⁶ There are several neurotoxic effects attributed to jaundice like sensorineural deafness, neonatal seizures, auditory neuropathy, cerebral palsy and apnoea.⁷ It has been observed that during the first week of life unconjugated serum bilirubin level is more than 1 mg/dL (17 mol/L), in almost all neonates.⁸ Albumin is the major protein present in abundant amount in the blood and has the property of binding to many hormones and nutrients.⁹ Albumin has a specific site for binding with bilirubin and is responsible for transporting it to the liver, its flexible structure of the helps it to adapt readily to ligands, and it has three

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domain in its structure which offers a different kinds of binding sites.⁹ In liver Glucouronyltransferase an enzyme binds this unconjugated bilirubin with glucuronic acid. This conjugated bilirubin (water soluble) can now be readily excreted in bile.¹⁰ In the term babies the normal lower limit of the serum albumin at the time of birth is 2.8gm/ dl.¹¹ In the developing countries like, Sub-Saharan Africa, Asia and Latin America, there is increased incidence of neonatal morbidity and mortality, attributed to neonatal jaundice (NNJ). Increase level of unconjugated bilirubin causes brain damage, kernicterus is a term for NNJ when it involves brain leading to neurological handicap and early death of affected infants.¹² kernicterus occurs when the molar bilirubin- to- albumin (B: A) ratio is >0.8.¹³ However, this can be avoided by the appropriate use of phototherapy and exchange blood transfusion to control serum bilirubin levels.¹² Most of the healthy term infants are discharged earlier because of medical, social and economic reasons. It has been observed that commonest cause for readmission during the early neonatal period is hyperbilirubinemia. Such readmissions are exposes a healthy newborn to the hospital environment, causing emotional problems that involves extra expenses for both family and the institution along with the risks of poor breast-feeding.¹⁴ Hence early prediction of level of albumin in cord blood can not only be used for early detection of neonatal jaundice but can be helpful to prevent re-hospitalization of babies. It will also reduce the economic burden of re-hospitalization on family.

Materials and Methods

This study was carried out in Gynae/OBS department, neonatal intensive care unit , Pathology laboratory at Railway Hospital Rawalpindi in collaboration with the Biochemistry Department of Islamic International Medical College from June 2015 to March 2016. Ninety term neonates were selected and randomly divided in 3 groups with thirty neonates in each group. Term babies of both genders with any mode of delivery, Birth weight above 2000 gm, APGAR score over 7 and absence of significant illness or major congenital malformation were included in our study.

Babies having Significant illness (sepsis, RDS, asphyxia, IDM that could aggravate hyper

bilirubineia) Gestational age <37 weeks Birth weight below 2000 gm, Rh incompatibility were excluded from the study. After the informed consent of the parents 2 ml of blood was collected from the cord vein and serum was separated in the lab. Quantitative in vitro-estimation of serum albumin was done by calorimetric biuret method. Total bilirubin was estimated with jendrassik Grof method on photometric system - Micro Lab 300. 2 ml of cord blood was taken from the neoente with 5ml syringes and tranferred to gel tubes. All neonates were assessed for the appearnce of jaundice at time of discharge, and neonates who had serum albumins less than 3gm/dl amd bilirubin more than 1mg/dl were followed up from 7th till 20th post delivery day. Those babies who were physically jaundiced were re-admitted and their total serum bilirubin levels were repeated.

Depending upon their bilirubin levels all neonates in Group I with serum albumin less than 2.8 gm/dl, Group II with albumin between 2.8 - 3.3 gm/dl and Group III greater than 3.3 gm/dl were managed accordingly. All of our data was tested for normality. Kruskal –wallis test was performed to compare the parameters in between the groups, MannWhitney-U test was applied to compare the parameters within the groups. A p-value of < 0 .05 was considered significant. Correlation analysis was carried out using spaermans corelation test.

Results

In whole study group 86.7% neonates suffered from neonatal jaundice in group I and II 100% of neonates suffered from jaundice and in group III 60% had jaundice.

Table I: Median IQR of study groups on the basis of cord blood albumin and bilirubin concentration (n=90)

Biochemical parameters	Group I	Group II	Group III
Serum Albumin g/dl	2.0 (1.8 – 2.5)	3.1 (3.0 – 3.3)	4.5 (4.1 – 4.8)
Serum Bilirubin mg/dl	3.6 (2.7 – 3.9)	2.2 (2.1 – 2.6)	1.9 (1.8 – 2.1)

When compared by kruskalwallis a statistically significant difference of (p=0.00) was found, between all groups. when compared by using Mann-whitney U test a statistically significant difference of (p=0.00) was seen between group I and II and between group I and III. P value of (0.02) was found between group II and III.

Table II: Comparison of cord bilirubin in all groups by Mann-whitneyU test

Group	P Value
Group I	0.00
Group II	
Group I	0.00
Group III	
Group II	0.02
Group III	

phototherapy was to be given to 26.7% of the whole study population. In group I, 16.7 % received conventional phototherapy for the treatment of jaundice. In group II, 10.0 % received phototherapy. In group III, none of the neonate needed hospital intervention like phototherapy.

Table No III: Frequency distribution of phototherapy in all groups

Phototherapy	Group I (n=30)		Group II (n=30)		Group III (n=30)	
	Frequency	Percentage %	Frequency	Percentage %	Frequency	Percentage %
Hospital Phototherapy	5	16.7	310.0	-		-
No phototherapy	-	-	-	-	30	0

Discussion

This study was commenced to distinguish the relation of serum albumin and bilirubin with neonatal jaundice. Cord blood albumin and bilirubin was measured after the delivery of neonates. A total of 90 neonates of both genders with weight ranging between 2 - 4 kg were selected. It was found out that all the neonates with low albumin and high bilirubin developed jaundice and 16.7% in group I and 10% in the group II received phototherapy and one neonate required exchange transfusion.

In this study it was found that neonate of group I with albumin less than 2.8 mg/dl developed jaundice within 72 hrs after birth and 16.7% required phototherapy in hospital. Sahu, et.al (2011)³ conducted a study on neonates and suggested that infants with low levels of albumin showed high bilirubin level and needed intensive phototherapy than those with high albumin level. Only one neonate from this group needed exchange transfusion and 83.3 % did not require any intervention like phototherapy or exchange transfusion.

None of the baby from group III with cord blood albumin greater than 3.3 gm/dl required

phototherapy or exchange transfusion. Sahu et al, in his study suggested that neonates with cord blood albumin level greater than 3 gm/dl require any interventional therapy or exchange transfusion.³

Our study showed that decreased serum albumin level leads to increased serum bilirubin level. This can be due to decreased availability of serum albumin to bind with bilirubin and transport it to excretory organs. Bairagi et al 2015, suggested that albumin has binding sites for bilirubin in subdomain 2A.¹⁵

Phototherapy has a standard role in treating neonatal hyperbilirubinemia. It lowers the serum bilirubin level as it uses light energy from the light source in altering the structure and the shape of bilirubin, converting bilirubin into isomers that are water-soluble and are not dependent on the process of conjugation for their elimination from the body. Even when normal conjugation is deficient it converts bilirubin to molecules that can be easily excreted. Bernaldo and Serge in one of their study stated that the neonates having bilirubin levels in the serum that are above 2 mg / dl have 53% of probability of receiving phototherapy.¹⁴

In our study, in group I about 16.7% neonates received phototherapy. In group II, a total of 10% received phototherapy. These results are in accordance with the results of the study done by Bernaldo and serge.¹⁴ In group III, none received phototherapy. This is supported by study done by Sahu et al.³ In addition to Phototherapy, exchange transfusion are extensively used world-wide for treating hyperbilirubinemia. It is considered as gold standard treatment for neonatal jaundice.¹⁶ In our study only one child required exchange transfusion due to raised bilirubin levels upto 20 gm/dl. M. Rahman in 2015 in one of his study suggested that neonates require exchange transfusion due to hyperbilirubinemia, septicemia or G6PD deficiency.¹⁷

Conclusion

The result of the present study revealed that the albumin taken from the cord blood immediately after the birth of the neonates can be used for the prediction of neonatal jaundice. It is further concluded that low albumin levels less than 2.8 gm/dl is not sufficient to bind with high level of bilirubin produced in neonates, leading to hyperbilirubinemia causing neonatal jaundice.

Further well designed research with large sample size is recommended for more clarification and assesment of relation of low level of albumin with neonatal jauindice.

REFERENCES

1. Rennie J, Burman Roy S, Murphy MS. Guideline Development Group. Neonatal jaundice: summary of NICE guidance. *BMJ*. 2010; 340: 1190-6.
2. Lauer BJ, Spector ND. Hyperbilirubinemia in the newborn. *Pediatrics in Review-Elk Grove*. 2011; 32: 341-6.
3. Sahu S, Abraham R, John J, Mathew AA, George AS. Cord blood albumin as a predictor of neonatal jaundice: *Int J Biol Med*. 2011; 2: 436-8.
4. Nazer H, Katz J. Unconjugated Hyperbilirubinemia. 2013; emedicine.medscape.com/article/178841.
5. Petit FM, Gajdos V, Parisot F, Capel L, Aboura A, Lachaux A, et al. Paternal isodisomy for chromosome 2 as the cause of Crigler–Najjar type I syndrome. *European journal of human genetics*. 2005; 13: 278-82.
6. Van de Steeg E, Stránecký V, Hartmannová H, NoskováL, Hřebíček M, Wagenaar E, et al. Complete OATP1B1 and OATP 1B3 deficiency causes human Rotor syndrome by interrupting conjugated bilirubin reuptake into the liver. *The Journal of clinical investigation*. 2012; 122: 519-28.
7. Amin SB, Lamola AA. Semin Perinatol New born Jaundice Technologies: Unbound Bilirubin and Bilirubin Binding Capacity in Neonates. *PubMed - indexed for MEDLINE*—2011; 35: 13440.
8. Maisels MJ. What's in a name? Physiologic and pathologic jaundice: the conundrum of defining normal bilirubin levels in the newborn. *Pediatrics*. 2006; 118: 805-7.
9. Roche M, Rondeau P, Singh NR, Tarnus E, Bourdon E. The antioxidant properties of serum albumin. *FEBS letters*. 2008 ; 582: 1783-7.
10. Nikolaev AV, Rozhilo YA, Starozhilova TK, Sarnatskaya VV, Yushko LA, Mikhail ovskii SV, etal. Mathematical Model of Binding of Albumin-Bilirubin Complex to the Surface of Carbon Pyropolymer. *Bulletin of experimental biology and medicine*. 2005; 140: 365-9.
11. Burtis CA, Ashwood AR, Bruns DE. *Tietz Textbook of Clinical Chemistry and Molecular Diagnostics*. Elsevier Health Sciences; 4th ed. 2008.
12. Ogunfowora OB, Daniel OJ. Neonatal jaundice and its management: knowledge, attitude and practice of community health workers in Nigeria. *BMC Public Health*. 2006; 6; 1-5.
13. Bunt JE, Rietveld T, Schierbeek H, Wattimena JD, Zimmermann LJ, van Goudoever JB. Albumin synthesis in preterm infants on the first day of life studied with [1-13C] leucine. *American Journal of Physiology-Gastrointestinal and Liver Physiology*. 2007; 292: 1157-61.
14. Bernaldo AJ, Segre CA. Bilirubin dosage in cord blood: could it predict neonatal hyperbilirubinemia. *Sao Paulo Med*. 2004; 122: 99-103.
15. Bairagi U, Mittal P, Mishra B. Albumin: A Versatile Drug Carrier. *Austin Therapeutics*. 2015; 2: 1021-6.
16. Badiie Z. Exchange transfusion in neonatal hyperbilirubinaemia: experience in Isfahan, Iran. *Singapore medical journal*. 2007; 48: 421-3.
17. Rahman M, Sarkar PK, Nazrin T, Chowdhury K, Jahan RA, Islam MS, et al. Study on neonates who received exchange transfusion at Dhaka shishu hospital. *Northern International Medical College Journal*. 2015; 6: 70-2.