

## **Original Research Article**

## CORRELATION OF CORD BLOOD ALBUMIN AND NEONATAL HYPERBILIRUBINEMIA IN NEWBORNS WITH ABO SETUP: A HOAPITAL BASED STUDY

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#### ABSTRACT

**Background:** There is lack of data about Cord serum albumin levels in predicting hyperbilirubinemia. The objective is to estimate the levels of albumin in cord blood and determine their relationship with the occurrence of neonatal hyperbilirubinemia in ABO incompatibility

**Materials and Methods:** It is a hospital based prospective study centered in Gadag Institute of Medical Sciences, Mallasamudra, Gadag. The study was conducted during the period of March 2021 to March 2022 in the department of Paediatrics at Gadag institute of Medical science, Mallasamudra, Gadag.

**Results:** Mean birth weight in our study was  $2.932\pm0.333$ kgs. Age of development of significant hyperbilirubinemia was found to be highest at 48-72 hours of life that is 70%. In our study 51% of newborns with blood group of A positive and 49% of newborns with blood group of B positive. Blood group distribution to development of significant jaundice was statistically insignificant by Pearson chi square test. Our study provided cut off values of newborns with cord albumin <3.5 g/dl in ABO blood group incompatibility should be followed up closely to watch for the development of significant hyperbilirubinemia requiring treatment in the form of phototherapy with or without exchange transfusion.

**Conclusion:** Babies with cord blood albumin <3.5 g/dl in ABO blood group incompatibility should be followed up closely to watch for the development of significant hyperbilirubinemia requiring treatment in the form of phototherapy with or without exchange transfusion while those babies with cord blood albumin >3.5g/dl can be safely discharged early.

Keywords: Albumin, ABO blood group incompatibility, hyperbilirubinemia.

## **INTRODUCTION**

Hyperbilirubinemia is the most common clinical condition requiring evaluation and treatment in the newborn and a frequent reason for hospital readmission during the first week of life. Although generally a benign, postnatal transitional phenomenon, a few neonates develop marked potentially hazardous bilirubin levels that can pose a direct threat of serious brain injury.<sup>[1]</sup>

ABO incompatibility occurs in about 15% of pregnancies. Only less than 1 percentage of these babies develop significant hyperbilirubinemia requiring treatment.<sup>[2]</sup>

Many factors have been identified to increase the risk of developing significant hyperbilirubinemia in newborns to necessitate treatment like blood group incompatibility, cephalhematoma, significant bruising, injuries, history of neonatal jaundice in previous sibling and predischarge TSB or TcB in high risk zone. Though our understanding of neonatal hyperbilirubinemia has improved in the recent years, we are still not able to precisely predict those babies at risk of developing significant hyperbilirubinemia. Since then, many researchers studied the correlation between the umbilical cord blood bilirubin and predicting significant albumin in neonatal hyperbilirubinemia. However, no study has established a single cut off value for umbilical cord serum albumin especially in ABO incompatibility to allow us to predict at birth those babies who will develop significant hyperbilirubinemia to require therapeutic intervention.

Hence, the present study was conducted to evaluate the predictive ability of the umbilical cord blood albumin for significant neonatal hyperbilirubinemia in ABO incompatibility.

## MATERIALS AND METHODS

This Prospective cross sectional study was conducted in Gadag Institute of Medical Sciences, Mallasamudra, Gadag. The study will be conducted during the period of March 2021 to March 2022 in the department of Paediatrics at Gadag institute of Medical science, Mallasamudra, Gadag.

Sample size: Total sample size 198

# Sampling method: Purposive sampling Inclusion Criteria

- Healthy Term Neonates with A or B blood group born to healthy mother with O positive blood group
- Born by normal delivery or cesarean section
- Birth weight 2.5kg to 4kg
- Apgar score of 7 or more at 1 min

#### **Exclusion Criteria**

- Rhesus blood factor incompactability
- Significant illness requiring NICU admission
- Major congenital malformation
- Delivered by instrumental delivery
- h/o meconium stained liquor or at risk of sepsis [premature rupture of membranes more than 12 hours]

Informed consent will be obtained from the parents. A detailed history including mothers age, maternal complication, family history of neonatal jaundice and type of delivery is obtained by interviewing the mother and from maternal hospital records. A complete physical examination is done at birth to

assess the gestational age and to look for the presence of birth trauma, congenital anomalies and cephalhematoma. APGAR score at 1<sup>st</sup> minute and at 5<sup>th</sup> minutes of life recorded. About 3ml of cord blood is collected at birth for blood grouping, Rh typing and estimation of serum albumin and bilirubin.

Babies will be examined daily and looked for development of jaundice. Serum bilirubin will be estimated in all newborns at 24 hours and 72 hours of life. Serum bilirubin will be estimated by diazo method using erba system pack reagent in autoanalyzer. Serum albumin will be measured by using erba system pack reagent containing bromocresol green by biuret method.

The development of significant hyperbilirubinemia will be treated with phototherapy with or without exchange transfusion as per AAP guidelines. Complete blood count, peripheral blood smear, reticulocyte count and direct coombs test will be done in all babies who developed significant hyperbilirubinemia. The development of significant hyperbilirubinemia requiring phototherapy with or without exchange transfusion as per AAP will be taken as major outcome of the study.

Statistical method: The data was entered and analysed using the latest SPSS 24th edition, the results were calculated using Pearson correlation coefficient calculating ROC, Sensitivity, Specificity of the test and Regression analysis. Statistical association by chi square test.

## RESULTS

In our study, out of 198 newborns 94 were females and 104 were males. Out of 198 neonates, 83 neonates are seen to have jaundice.

Fable 1: Gender and significant Jaundice						
Gender	Count			%		
	Jaundice		Total	Jaundice		Total
	Yes	No		Yes	No	
Male	49	55	104	47%	53%	53%
Female	34	60	94	36%	64%	47%
Total	83	115	198	41.4%	58.6%	100.0%

In our study out of 152 neonates born by LSCS, 69 neonates developed significant jaundice and 14 out of 46 neonates born by NVD developed significant jaundice.

Around 110 neonates were between 2.5-2.9kg of weight which is highest. 72 neonates were born with weight between 3.0-3.4 kgs and 16 with 3.5-4.0kgs.

Fable 2: Birth Weight (Kgs) and Jaundice						
Birth Weight Count					%	
	Jaundice		Total	Jaundice		Total
	Yes	No		Yes	No	
2.5-2.9 kg	46	64	110	41%	59%	55%
3.0-3.4 kg	27	45	72	37%	63%	36%
3.5-4.0kg	10	6	16	62%	38%	9%
Total	83	115	198	41%	59%	100.0%
Pearson Chi-Square		2.915a	df	2	Sig	0.233

#### Not Significant

Among birth weight of 2.5 - 2.9 kgs, out of 110 newborns, 46 developed jaundice. With birth weight of 3.0-3.4 kgs 27 out of 72 newborns developed jaundice. Among birth weight of 3.5-4.0 kgs 10 out of 16 newbors developed jaundice.

Majority of the patients developed jaundice at 49-72 hrs of life that is 59 patients. Least number of patients that is 2 were seen to develop jaundice after 72 hours.

Fable 3: Baby Blood Group and R.H. Typing					
Baby Blood Group and R.H. Typing	Count	Percent			
A Positive	102	51.5%			
B Positive	96	48.5%			
Total	198	100.0%			

In our study, total number of neonates with A positive blood group is 102 that constitute 51 % and with B blood group is 96 that constitute 48%.

Among neonates with blood group A 44 out of 102 developed jaundice that constitute to 43% and among neonates with blood group B 39 out of 57 developed jaundice. By Pearson chi square test it is satistically insignificant

Table 4: CORD serum albumin					
C.S.Albumin	Count	Percent			
< 2	8	4.0%			
2-2.5	23	11.6%			
2.6-3.0	38	19.2%			
3.1-3.5	36	18.2%			
3.6-4.0	45	22.7%			
>4.1	48	24.2%			
Total	198	100.0%			

Maximum number of neonates that is 48 were seen to have C.S.Albumin >4.1g/dl and least was of around 8 neonates seen to have C.S.Albumin <2g/dl. C.S.Albumin <2g/dl constitute about 4% and C.S.Albumin >4.1g/dl constitute about 24%.C.S.Albumin with 2-2.5g/dl,2.6-3.0g/dl,3.1-3.5g/dl 3.6-4g/dl constitutes and about 11.6%,19.2%,18.2%,22.7% and 24.2% respectively.

C.S. Albumin	Count			%		
	Jaundice		Total	Jaundice		Total
	Yes	No		Yes	No	
< 2	1	7	8	12.5%	87.5%	4.0%
2-2.5	19	4	23	82%	18%	11.6%
2.6-3.0	32	6	38	84%	16%	19.2%
3.1-3.5	17	19	36	47%	53%	18.2%
3.6-4.0	9	36	45	2%	98%	22.7%
>4.1	5	43	48	10%	90%	24.2%
Total	83	115	198	41.4%	58.6%	100.0%
Pearson Chi-Square		72.123a	df	5	Sig	0.000

With C.S.Albumin level of 2-2.5g/dl and 2.6-3.0g/dl, significant number of neonates developed jaundice that constitute about 19 out of 23 and 32 out of 38 neonates respectively. With C.S.Albumin of 3.1-3.5g/dl, 17 out of 36 neonates developed significant jaundice. with C.S.Albumin 3.6-4.0g/dl and >4g/dl only 9 out of 45 and 5 out of 48 neonates developed

jaundice respectively. With C.S.Albumin above 3.5g/dl have low chance of developing jaundice.

Around 83 neonates were given phototherapy among which maximum number of phototherapy was given for a period of 1 day that is 41 and second maximum number of days for which phototherapy given was for 2 days that is 30 neonates. Least of neonates that is 2 were given phototherapy for 4 days.

Fable 6 - Mean and Standard Deviation of the Parameters				
Parameters	Mean±Std.			
Mothers Age	24.89±3.716			
Baby Birth Weight (kgs)	2.932±0.333			
C.S.Albumin	3.408±0.891			
C.S.B total	1.912±0.883			
72 hrsS.B.I	11.60±3.539			
Age at the development of Jaundice	60.57±20.77			

Hemoglobin	15.25±2.169
R.B.C. count	4.079±0.878
Hematocrit	45.54±6.502

R.O.C. Curve between CORD SERUM ALBUMIN and JAUNDICE

The sensitivity vs. specificity values is plotted in the R.O.C. curve as the cut off point moves from 0 to 1.

In the study, there were 198 patients, of which 83 of them had jaundice, and the remaining 115 did not.

Fable 7: R.O.C. Curve between CORD Serum Albumin and JAUNDICE				
Jaundice	Valid N (listwise)			
Positive	83			
Negative	115			
Larger values of the test result variable(s) indicate stronger evidence for an actual positive state.				
a. The actual positive state is Yes.				

A model with high sensitivity and specificity will have a ROC curve that touches the upper left corner of the plot. A curve nearly perpendicular to the diagonal line at a 45-degree angle indicates a model with low sensitivity and specificity. From the study 198 neonates, it is clear that the model does a decent job of forecasting the jaundice CUTOFF. The area under the curve indicates the model's ability to distinguish between a neonate with and without jaundice. The model performs better at accurately classifying outcomes when the A.U.C. is larger. However, the AUC value in the study is 0.204 when the significance value is 0.000, which is comparatively lower in predicting the jaundice CUTOFF when C.S.Albumin in place.

Table 8: A	able 8: Area under the Curve between cord serum albumin and jaundice						
Area Und	Area Under the Curve						
Test Resu	lt Variable(s):						
Area	Area Std. Errora Asymptotic Sig.b Asymptotic 95% Confidence Interval						
			Lower Bound	Upper Bound			
0.204	0.034	0.000	0.137	0.270			
The test result variable(s): C.S.Albumin has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.							
a. Under th	a. Under the nonparametric assumption						
b. Null hyp	oothesis: true area =	0.5					



In the ROC curve's sensitivity and specificity for various cutoff, positions are shown in the final table. Here the threshold of 0.9500 has been taken; then in that case, it can predict that neonates with a C.S.Albumin value below the given cutoff will be considered to have jaundice else, the neonates does not have jaundice. By using the given cutoff, there would be 100% sensitivity and 1 - specificity would be 98.3%.

Table 9: ROC curve's sensitivity and specificity for various cutoff, positions					
Positive if Greater Than or Equal Toa	Sensitivity	1 - Specificity			
-0.2000	1.000	1.000			
0.8500	1.000	0.991			
0.9500	1.000	0.983			
The test result variable(s): C.S.ALBUMIN has at least one tie between the positive actual state group and the negative actual state group.					
a The smallest cutoff value is the minimum ob	served test value minus	1 and the largest is the maximum value minus 1. All the other			

a. The smallest cutoff value is the minimum observed test value minus 1, and the largest is the maximum value minus 1. All the othe cutoff values are the averages of two consecutive ordered observed test values.

## Correlation between CORD SERUM ALBUMIN and JAUNDICE

There is a negative correlation of 42.3% between C.S.Albumin and Jaundice.

Table 10: Correlation between CORD SERUM ALBUMIN, and JAUNDICE				
		Jaundice	Result	
C.S.ALBUMIN	Pearson Correlation	423**	Significant	

	Sig.	0.000				
	N	198				
**. Correlation is significant at the	**. Correlation is significant at the 0.01 level (2-tailed).					

There is a significant difference between the 72 hrs Serum bilirubin and Jaundice as per 83 jaundice and 115 non-jaundice neonates.

## **DISCUSSION**

In our study around 46 neonates were born by normal vaginal delivery and rest other by LSCS. As because early discharge in normal vaginal delivery many cases are missed out.

In our study 89 neonates were born to multiparous mother and rest to primigravid that is Primi mothers were 55 % and multiparous mother were 45%, Around 110 out of 198 were with birth weight of 2.5-2.9 kgs which constitute 55 %. Neonates with birth weight of 3-3.4 kgs constituted with 36 % and 3.5-4 kgs constituted with 9%. By Pearson chi square test it is statistically insignificant in relation to birth weight and development of significant hyperbilirubinemia. Mean birth weight in our study was  $2.932\pm0.333$  kgs.

Significant neonatal jaundice in Sex distribution in our study is statistically insignificant.

Among neonates with blood group B, 38 out of 96 developed significant jaundice which constitute for 40%. By Pearson chi square test it is statistically insignificant.Mean age of development of significant jaundice in our study is60.57±20.77 hrs.

Maximum number of neonates that is 48 were seen to have C.S.Albumin >4.1g/dl and least was of around 8 neonates seen to have C.S.Albumin <2g/dl .C.S.Albumin <2g/dl constitute about 4% and C.S.Albumin >4.1g/dl constitute about 24%.C.S.Albumin with 2-2.5g/dl,2.6-3.0g/dl,3.1-3.5g/dl and 3.6-4g/dl constitute about 11.6%, 19.2%,18.2%,22.7% and 24.2% respectively. Mean C.S.Albumin is 3.408±0.891g/dl. Neonates with cord serum albumin <3.5 g/dl have high risk of developing significant jaundice.

When cord serum albumin level of <2g/dl, out of 8 neoates,1 neonate developed jaundice. With C.S.A level of 2-2.5g/dl and 2.6-3.0 g/dl significant number of neonates developed jaundice that constitute about `19 out of 23 and 31 out of 38 neonates respectively. With C.S.Albumin of 3.1-3.5g/dl, 17 out of 36 neonates developed significant jaundicewith C.S.Albumin 3.6-4.0g/dl and > 4g/dl only 9 out of 45 and 5 out of 48 neonates developed jaundice. With C.S.Albumin above 3.5g/dl have low chance of developing jaundice. Accordingly, by Pearson chi square test it is statistically significant.

Gurdeep Singh Dhanjal et al conduted study in 2018, observed in his study that the sensitivity of C.S.Albumin level <2.8 g/dl to predict risk of development of neonatal hyperbilirubinemia is 87.50% and specificity was 75.72% while positive predictive value (PPV) was 34.31% and negative predictive value (NPV) was 97.66%. Correlation of C.S.Albumin level < 2.8 g/dl to predict risk of development of significant neonatal hyperbilirubinemia was statistically highly significant (P value = <0.0001),cut off for C.S.Albumin is lower than my study in predicting significant hyperbilirubin.<sup>[3]</sup>

In such and et al conducted a study in 2017, Cord serum albumin level of  $\leq 2.8$  g/dl is a risk indicator in predicting the development of neonatal hyperbilirubinemia at birth, which is comparable to our study.<sup>[4]</sup>

In Janaki et al study, conducted in2017 the cutoff point for umbilical cord serum albumin for development of significant hyperbilirubinemia was 3.15 g/dl. This value predicts the development of significant hyperbilirubinemia with a sensitivity of 76.5%, specificity of 78.7% and an accuracy of 77.6%. This study also correlates to my study but this study was case control study.<sup>[5]</sup>

In sandeep et al study in 2016 Cord serum albumin level of  $\leq 2.8$  g/dl can be used a risk indicator in predicting the development of neonatal hyperbilirubinemia at birth which was less than my study comparatively in predicting the significant hyperbilirubinemia.<sup>[6]</sup>

By ROC analysis, the cutoff point for umbilical cord serum albumin for development of significant hyperbilirubinemia for the study population is < 3.5g/dl. This value predicts the development of significant hyperbilirubinemia with there would be 100% sensitivity and 1 - specificity would be 98.3%.Here the threshold of 0.9500 has been taken then in that case, it can predict that neonates with a C.S.Albumin value below the given cutoff will be considered to have jaundice else, the neonates does not have jaundice. The AUC value in the study is 0.204 when the significance value is 0.000, which is comparatively lower in predicting the jaundice CUTOFF when C.S.Albumin is in place.

Around 83neonates were given phototherapy among which maximum number of phototherapy was given for a period of 1 day that is 41neonates with significant hyperbilirubinemia and second maximum number of days for which phototherapy given was for 2 days that is 27neonates with significant jaundice. Least of 2 neonates with significant jaundice were given phototherapy for 4 days. 3 out of 83 neonates developed significant hyperbilirubinemia requiring exchange transfusion in my study.

## **CONCLUSION**

In umbilical cord blood, the mean serum albumin in babies with blood group A+ve or B+ve born to O+ve mothers was 3.408±0.891 g/dl. The umbilical cord serum albumin correlates well with the development of significant neonatal hyperbilirubinemia requiring treatment in the form of phototherapy with or without exchange transfusion.

Umbilical cord serum albumin level of less than or equal to 3.5 g/dl predicts the development of significant hyperbilirubinemia with a there would be 100% sensitivity and 1 - specificity would be 98.3%. We recommend routine measurement of albumin levels in umbilical cord blood at birth.

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