

A study on Cord Blood Albumin as an Indicator of Neonatal Hyperbilirubinemia Among Preterm Babies

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Abstract

Introduction: Neonatal hyperbilirubinemia (NH) affects nearly 60% of term and 80% of preterm neonates during the first week of their life. Because of the potential toxicity of bilirubin, newborn infants must be monitored to identify those who might develop severe hyperbilirubinemia and, in rare cases, acute bilirubin encephalopathy or kernicterus. Neonatal hyperbilirubinemia is the most common reason for readmission after early hospital discharge.

Objective : To find out critical value of Cord Serum albumin in predicting the subsequent development of significant neonatal hyperbilirubinemia requiring interventions like phototherapy or exchange transfusion.

Methodology: It is a Hospital based prospective observational study of a sample of 100 preterm babies with birth weight <2.5 kg selected by simple random sampling. Cord blood was collected from the placental side at the time of delivery. Cord blood Albumin estimation was done by using auto-analyser while Serum bilirubin estimation (Total and direct) was done using venous blood of children having jaundice involving palms and soles on any day of follow up, using Diazotized Sulfanilic test by spectrometry.

Results: In our study out of hundred patients 71 patients had hyper bilirubinemia requiring either phototherapy (PT) or Exchange transfusion (ET). They were divided in three groups according to Cord blood albumin in group 1, 2, 3 with CBA <2.8, 2.8-3.1, >3.1 g/dl. Statistical analysis was conducted and it showed <2.8 g/dl CBA is critical and associated with higher relation with hyperbilirubinemia requiring phototherapy (95.65%) and also requiring Exchange transfusion 47.83%. CBA >3.1 g/dl is less association with Hyperbilirubinemia, that is about in 9.52% cases.

Conclusion: Cord blood albumin can be considered as a risk indicator rather than diagnostic tool, which can give a clue to the possibility of severe jaundice during neonatal period. It may help treating doctors and the parents stay alert to take action at the earliest.

Keywords: Cord blood albumin, Neonatal hyperbilirubinemia, Preterm

INTRODUCTION:

Neonatal hyperbilirubinemia (NH) is usually a normal physiologic condition occurring during the transitional period after birth. It is not a singular disease in itself, but a physical finding associated with multiple possible etiologies.[1] It affects nearly 60% of term and 80% of preterm neonates during the first week of their life.[2]

Jaundice is one of the most common conditions requiring medical attention in newborn babies. The physical findings like yellowish discoloration of the skin and sclera in the newborns is due to the accumulation of unconjugated bilirubin (UCB). In most infants, unconjugated hyperbilirubinemia reflects a normal physiological phenomenon and is of little consequence. But in some infants the bilirubin levels may become extremely high and can lead to many complications.[3] Because of the potential toxicity of bilirubin, newborn infants must be monitored to identify those who might develop severe hyperbilirubinemia and, in rare cases, acute bilirubin encephalopathy or kernicterus.[4, 5]

Early discharge of healthy term newborns after normal vaginal delivery has become a common practice, because of medical reasons like prevention of nosocomial infections, social reasons like early naming ceremony, and also due to economic constraints.[6,7] Neonatal hyperbilirubinemia is the most common reason for readmission after early hospital discharge in a significant number of term neonates.[8, 9] Hyperbilirubinemia in preterm infants is more prevalent, more severe, and its course more protracted than in term neonates, as a result of exaggerated neonatal red cell, hepatic, and gastrointestinal immaturity. Several developmental and clinical phenomena contribute to the greater degree and duration of neonatal jaundice in premature infants.[10] Albumin is a major binding protein in the human neonate.[11] Low production of albumin will lower its transport and binding capacity, especially in preterm neonates.[12] Free bilirubin is anticipated when

there is reduced binding of bilirubin by albumin and it is this free bilirubin that can cross the blood brain barrier (BBB).[11] Early recognition of NH, its follow-up, as well as early treatment and prevention of bilirubin induced encephalopathy has become more difficult as a result of earlier discharge from the hospital. Though The American Academy of Pediatrics (AAP) recommends that newborns discharged within 48 hours should have a followup visit after 48 to 72 hours for any significant jaundice and other problems,[4] it is not possible in our country due to limited follow up facilities. The treatment of severe NH by exchange transfusion (ET) is costly and is associated with complications.[13, 14] Whereas treatment of jaundice with phototherapy is effective, simple and cheap.[15] Phototherapy (PT) is now a viable alternative to the planned use of exchange transfusion in the treatment of even moderate to severe Hemolytic Disease of Newborn (HDN).[16]

Till date only few predictors of neonatal jaundice have been studied, these are cord blood albumin, cord blood bilirubin, cord blood albumin to bilirubin ratio and alpha fetoprotein⁶ but cord blood albumin to predict hyperbilirubinemia in preterm neonates has been studied in this part of Odisha. By predicting the newborns developing significant neonatal jaundice early at birth, we can design and implement the follow-up of the high-risk groups cost effectively. In this way early treatment could be started, which could reduce the risk of bilirubin dependent brain damage and other morbidity. There is paucity of studies on cord blood albumin (CBA) as a predictor of severity of neonatal hyper- bilirubinemia, hence our study is aimed to evaluate the predictive value of cord serum albumin as predictor of significant neonatal hyperbilirubinemia in healthy preterm neonates and subsequent requirement of phototherapy or exchange transfusion. This study may throw light on association between cord blood albumin and hyperbilirubinemia in preterm babies. Thereby helping in early intervention and photo therapy.

AIM & OBJECTIVES

The present study is conducted to find out critical value of Cord Serum albumin in predicting the subsequent development of significant neonatal hyperbilirubinemia requiring interventions like phototherapy or exchange transfusion. Thus, the aim of the present study includes:

- 1 To find out the association between various levels of cord serum albumin (CSA) and significant neonatal hyperbilirubinemia requiring interventions like phototherapy or exchange transfusion.
- 2 To predict the proportion of new born requiring intervention for Neonatal Hyperbilirubinemia (phototherapy or exchange transfusion) based on cord serum albumin level at birth.

To correlate the hospital, stay in relation to the level of cord serum albumin in the preterm neonates with hyperbilirubinemia.

MATERIALS & METHOD

STUDY DESIGN-Hospital based prospective observational study **SAMPLING METHOD** - Simple random sampling

STUDY POPULATION – Preterm (<37 weeks of GA) admitted in Dept. Of Pediatrics (SVPPGIP) & Preterm born in Department of Obstetrics & Gynecology SCBMCH, CUTTACK

STUDY PERIOD - November 2019 to October 2021 **SAMPLE SIZE** – 100

INCLUSION CRITERIA

All preterms (<37 weeks of GA) babies of both genders, Birth weight <2.5kg.

EXCLUSION CRITERIA

Term, Rh incompatibility, Neonatal sepsis, Instrumental delivery Birth asphyxia, Respiratory distress, Meconium stained amniotic fluid, Infant of diabetic mother.

PARAMETER TO BE STUDIED

Gender, Gestational, Mode of Delivery, Cord albumin After obtaining clearance from institutional ethical committee & informed consent from the parents of the defined population, data will be collected in the predesigned proforma for the study. Cord blood was collected from the placental side at the time of delivery. Gestational age to was calculated using New Ballard Score wherever the LMP was not available. The cases were assessed at the time of birth for inclusion and exclusion criteria. All those who had given consent and met inclusion criteria were enrolled for in the study and were followed up at least till day 7 of life for development of severe jaundice (involving palms and soles). Serum bilirubin estimation (Total and direct) was done using venous blood of children having jaundice involving palms and soles on any day of follow up. Those who will develop desired criteria for intervention on follow up days were given phototherapy or exchange transfusion and further will follow up till discharge. Any complications develop during phototherapy was noted. The data were collected using a pre-designed and pre-tested tool. Data was partly collected using interview with the mother and partly using case sheets of mother and laboratory investigation reports. Cord Serum Albumin estimation was done by using auto-analyser while serum bilirubin estimation was done using Diazotized Sulfanilic test by spectrometry. All the tests were done following standard laboratory procedure in the laboratory of SCBMCH, CUTTACK by a single laboratory technician. The data so obtained were contemplated in different tabular form & analysed using appropriate statistical methods. Serum Bilirubin (Total & Direct) at Day – 1, Day-3, Day-5 & Day-7.

RESULTS

Table 1: Gender distribution of newborns:

Gender	Percentage (%)
MALE	58.0%
FEMALE	42.0%
TOTAL	100.0%

Above table shows that among 100 preterm newborns, 58 were males & 42 were females in this study. Thus male outnumbered female preterm newborns.

Table 2: Distribution of Gestational age:

Birth Weight	Percentage (%)
<1.5	31.0(%)
>=1.5	69.0(%)
Total	100.0(%)

Above table shows out of 100 newborns, majority 52% belonged to Gestational age of 32-34 weeks & each 24% had Gestational age of 28-31 weeks & 35-<37 weeks.

Gestational Age	Percentage (%)
28-31 weeks(Group-1)	24.0%
32-34 weeks(Group-2)	52.0%
35-<37 weeks(Group-3)	24.0%
Total	100.0%

Table 3: Distribution of Birth Weight:

Above diagram shows that majority of the newborns had birth weight above 1.5 kg (69%) & rest 31% had birth weight less than 1.5 kg.

Table 4: Distribution of Mode of Delivery:

Mode of Delivery	Percentage (%)
NVD	60.0(%)
LSCS	40.0(%)
Total	100.0(%)

The above table shows there were more numbers of Vaginal deliveries i.e 60% in compared to Cesarean deliveries(40%).

Table 5: Distribution of Cord Albumin:

Group	Cord blood albumin(g/dl)	Percentage(%)
1	<2.8	23.0(%)
2	2.8-3.1	56.0(%)
3	>3.1	21.0(%)
	Total	100.0(%)

Among 100 newborns, Group 1 consisted of 23% newborns who had CBA <2.8 gm/dl, Group 2 belonged to majority 56% & had CBA 2.8gm/dl-3.1gm/dl while Group 3 had 21% with CBA >3.1gm/dl.

Table 6: Distribution of Phototherapy (PT) requirement:

PT received	Numbers	Percentage (%)
NO	29	29%
YES	71	71%
Total	100	100%

The above table shows those who developed neonatal hyperbilirubinemia & required phototherapy i.e 71% whereas rest 29% didn't receive phototherapy.

Table 7: Distribution of Exchange Transfusion(ET)requirement:

ET received	Number of patients	Percentage(%)
NO	47	66.1%
YES	24	33.9%
Total	71	100%

Table shows that out of 71 newborns those developed hyperbilirubinemia, only few newborns (24) required exchange transfusion.

Table 8: Distribution of Duration of Hospital stay:

Hospital Stay(Days)	Percentage(%)
<=3	51.0%
>3	49.0%
Total	100.0%

The above table shows that there is almost equal duration of hospital stay irrespective of the among the newborns with hyperbilirubinemia.

Table 9: Association between cord blood albumin(CBA) & Gender of newborns:

		Cord blood albumin(mg/dl)				Total	
		<2.8	2.8-3.1	>3.1		p Value	Significance
Gender	MALE	12(52.17)	33(58.93)	13(61.9)	58(58)	0.790	Not Significant
	FEMALE	11(47.83)	23(41.07)	8(38.1)	42(42)		
Total		23(100)	56(100)	21(100)	100(100)		

This table shows that CBA is independent of gender of the newborns & there is no statistical significance between two of them.

Table 10: Association between cord blood albumin(CBA) & Gestational Age(GA):

		Cord blood albumin(mg/dl)				Total	
		<2.8	2.8-3.1	>3.1		p Value	Significance
GA	28-31 weeks	14(60.87)	10(17.86)	0(0)	24(24)	<0.001	Significant
	32-34 weeks	9(39.13)	39(69.64)	4(19.05)	52(52)		
	35- <37 weeks	0(0)	7(12.5)	17(80.95)	24(24)		
Total		23(100)	56(100)	21(100)	100(100)		

The above table shows that there is significant correlation between Cord blood albumin & gestational age with P value of <0.001.

Table 11: Association between cord blood albumin(CBA) & Birth weight(BW):

0		Cord blood albumin(mg/dl)				Total	
		<2.8	2.8-3.1	>3.1		p Value	Significance
BW	<1.5	18(78.26)	13(23.21)	0(0)	31(31)	<0.001	Significant
	>=1.5	5(21.74)	43(76.79)	21(100)	69(69)		
Total		23(100)	56(100)	21(100)	100(100)		

This table shows that there is a statistical significance association between CBA & birthweight with P value <0.001.

Table 12: Association between Cord blood albumin(CBA) & Mode of delivery:

		Cord blood albumin(mg/dl)				Total	
		<2.8	2.8-3.1	>3.1		p Value	Significance
Mode of	NVD	14(60.87)	31(55.36)	15(71.43)	60(60)	0.438	Not Significant

Delivery						
	LSCS	9(39.13)	25(44.64)	6(28.57)	40(40)	
Total		23(100)	56(100)	21(100)	100(100)	

The above table shows there is no statistical significance between CBA & Mode of delivery.

Table 13: Association between Cord blood albumin(CBA) & Requirement of phototherapy (PT):

		Cord blood albumin(mg/dl)				Total	
		<2.8	2.8-3.1	>3.1	p Value	Significance	
PT	NO	1(4.35)	9(16.07)	19(90.48)	29(29)	<0.001	Significant
	YES	22(95.65)	47(83.93)	2(9.52)	71(71)		
Total		23(100)	56(100)	21(100)	100(100)		

The above table shows that there is statistical significance between CBA & Phototherapy with P value of 0.001.

Table 14: Association between Cord blood albumin(CBA) & requirement of Exchange Transfusion(ET):

		Cord blood albumin(mg/dl)				Total	
		<2.8	2.8-3.1	>3.1	p Value	Significance	
ET	NO	12(52.17)	46(82.14)	18(85.71)	76(76)	0.009	Significant
	YES	11(47.83)	10(17.86)	3(14.29)	24(24)		
Total		23(100)	56(100)	21(100)	100(100)		

The above table shows that there is statistical significance between CBA & requirement of ET with P value of 0.009.

Table 15: Association between Cord blood albumin(CBA) & Neonatal hyperbilirubinemia:

		Cord blood albumin(mg/dl)				Total	
		<2.8	2.8-3.1	>3.1	pValue	Significance	
Hyperbilirubinemia	NO	1(4.35)	9(16.07)	19(90.48)	29(29)	<0.001	Significant
	YES						
Total		23(100)	56(100)	21(100)	100(100)		

The above table shows there is statistical significance between CBA & chance of neonatal hyperbilirubinemia with P value of <0.001.

Table 16: Association between requirement of Phototherapy(PT) & Gender of the newborns:

		Gender		Total		
		MALE	FEMALE	p Value	Significance	
PT	NO	17(29.31)	12(28.57)	29(29)	0.936	Not Significant
	YES	41(70.69)	30(71.43)	71(71)		
Total		58(100)	42(100)	100(100)		

This data shows there is no statistical significance between requirement of phototherapy with gender of the newborns.

Table 17: Association between requirement of Phototherapy(PT) & Gestational age(GA) of newborns:

		GA			Total		
		28-31 weeks	32-34 weeks	35-<37 weeks	pValue	Significance	
PT	NO	1(4.17)	9(17.31)	19(79.17)	29(29)	<0.001	Significant
	YES	23(95.83)	43(82.69)	5(20.83)	71(71)		
Total		24(100)	52(100)	24(100)	100(100)		

This table shows there is statistical significance between requirement of phototherapy with Gestational age with P value of <0.001.

Table 18: Association between requirement of Phototherapy(PT) & Birth weight(BW):

		BW		Total		
		<1.5	>=1.5	p Value	Significance	
PT	NO	1(3.23)	28(40.58)	29(29)	<0.001	Significant
	YES	30(96.77)	41(59.42)	71(71)		
Total		31(100)	69(100)	100(100)		

The above table shows there is statistical significance between requirement of phototherapy with birth weight of the

newborns with P value of 0.001.

Table 19: Association between requirement of Phototherapy(PT) & Mode of delivery:

		Mode of Delivery			Total		
		NVD	CS		p Value	Significance	
PT	NO	17(28.33)	12(30)	29(29)	0.857	Not Significant	
	YES	43(71.67)	28(70)	71(71)			
Total		60(100)	40(100)	100(100)			

The above table shows comparison of requirement of phototherapy with mode of delivery. No statistical significance is seen.

Table 20: Association between cord blood albumin(CBA) & requirement of phototherapy (PT):

		Cord blood albumin(mg/dl)			Total		
		<2.8	2.8-3.1	>3.1	p Value	Significance	
PT	NO	1(4.35)	9(16.07)	19(90.48)	29(29)	<0.001	Significant
	YES	22(95.65)	47(83.93)	2(9.52)	71(71)		
Total		23(100)	56(100)	21(100)	100(100)		

The above table shows that there is statistical significance between CBA & requirement of phototherapy with P value of <0.001.

Table 21: Association between requirement of exchange Transfusion(ET) & Gender of the newborns:

		Gender			Total		
		MALE	FEMALE		p Value	Significance	
ET	NO	43(74.14)	33(78.57)	76(76)	0.608	Not Significant	
	YES	15(25.86)	9(21.43)	24(24)			
Total		58(100)	42(100)	100(100)			

This table shows comparison of requirement of exchange transfusion with gender of the newborns. No statistical significance is seen.

Table 22: Association between requirement of exchange Transfusion(ET) & Gestational age(GA)

		GA			Total		
		28-31 weeks	32-34 weeks	35-<37 weeks	p Value	Significance	
ET	NO	11(45.83)	45(86.54)	20(83.33)	76(76)	<0.001	Significant
	YES	13(54.17)	7(13.46)	4(16.67)	24(24)		
Total		24(100)	52(100)	24(100)	100(100)		

This table shows there is statistical significance between requirement of exchange transfusion & gestational age with P value of < 0.001.

Table 23: Association between requirement of exchange Transfusion(ET) & Birth weight(BW):

		BW		Total		
		<1.5	>=1.5		p Value	Significance
ET	NO	18(58.06)	58(84.06)	76(76)	0.005	Significant
	YES	13(41.94)	11(15.94)	24(24)		
Total		31(100)	69(100)	100(100)		

This table shows there is statistical significance between requirement of exchange transfusion & birth weight of the newborns with P value of 0.005.

Table 24: Association between requirement of exchange Transfusion(ET) & Mode of delivery:

		Mode of Delivery			Total		
		NVD	CS		p Value	Significance	
ET	NO	45(75)	31(77.5)	76(76)	0.774	Not Significant	
	YES	15(25)	9(22.5)	24(24)			
Total		60(100)	40(100)	100(100)			

This table shows comparison between requirement of exchange transfusion & mode of delivery. There is no statistical significance.

Table 25: Association between requirement of exchange Transfusion(ET) & cord blood albumin(CBA):

		Cord blood albumin(mg/dl)				Total	
		<2.8	2.8-3.1	>3.1		p Value	Significance
ET	NO	12(52.17)	46(82.14)	18(85.71)	76(76)	0.009	Significant
	YES	11(47.83)	10(17.86)	3(14.29)	24(24)		
Total		23(100)	56(100)	21(100)	100(100)		

This table shows there is statistical significance between CBA & requirement of exchange transfusion with P value of 0.009.

Table 26: Correlations between cord blood albumin & serum bilirubin:

albumin(mg/dl)		Serumbilirubin	Serumbilirubin	Serumbilirubin	Serumbilirubin
		D-1(mg/dl)	D-3(mg/dl)	D-5(mg/dl)	D-7(mg/dl)
<2.8	Mean	8.40	12.55	10.53	6.70
	Median	8.00	12.70	10.90	6.80
	Std. Deviation	1.97	2.23	1.85	1.26
2.8-3.1	Mean	8.52	12.83	10.60	7.17
	Median	9.00	12.80	10.55	7.05
	Std. Deviation	2.81	3.51	2.32	2.00
>3.1	Mean	7.88	9.78	10.10	7.00
	Median	7.60	9.40	9.30	6.70
	Std. Deviation	1.94	2.43	2.73	1.83
p Value		0.342	<0.001	0.235	0.538
Significance		Not Significant	Significant	Not Significant	Not Significant

This table shows the correlation of variables like CBA with the serum bilirubin on Day1, Day3, Day 5 & Day7. There is statistical significance between serum bilirubin value of Day3 with cord blood albumin (P value=0.001)

Table 27: Correlation between requirement of Phototherapy & serum bilirubin:

		Serumbilirubin	Serumbilirubin	Serumbilirubin	Serumbilirubin
		D-1(mg/dl)	D-3(mg/dl)	D-5(mg/dl)	D-7(mg/dl)
YES	Mean	9.03	13.56	11.03	7.26
	Median	9.00	13.20	11.00	7.10
	Std. Deviation	2.29	2.62	1.83	1.83
	p Value	<0.001	<0.001	<0.001	0.088
SIGNIFICANCE		Significant	Significant	Significant	Not Significant

Above table shows that the mean value of serum bilirubin on D-1, D-3, D-5 were 9.03mg/dl, 13.56mg/dl & 11.03 mg/dl respectively. It showed that serum bilirubin had statistically significant correlation with requirement of phototherapy with P value of less than 0.001.

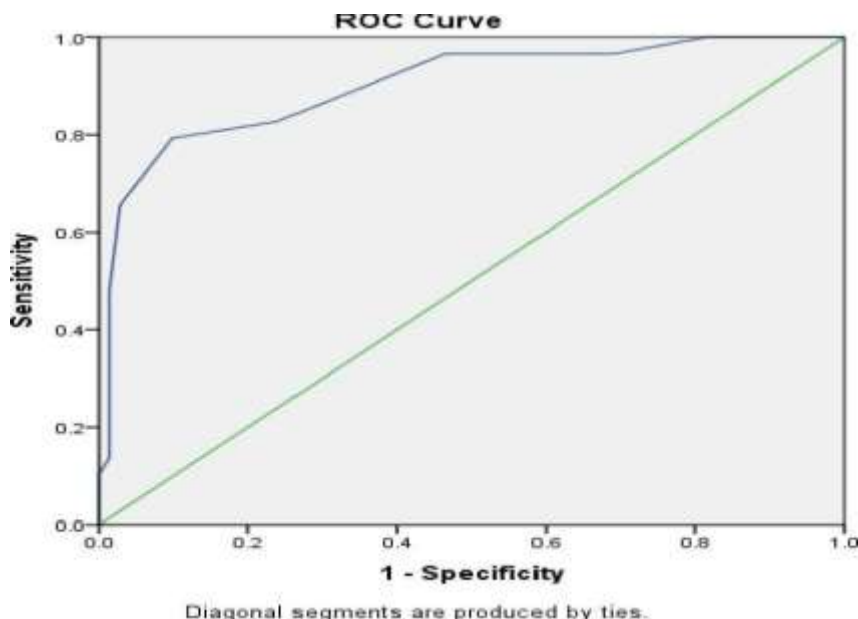
Table 28: Correlation between requirement of exchange Transfusion & serum bilirubin:

EXCHANGE TRANSFUSION		D-1	D-3	D-5	D-7
YES	Mean	8.75	14.59	11.59	7.22
	Median	8.25	14.60	12.00	7.20
	Std. Deviation	2.31	2.99	1.72	1.69
	p Value	0.542	<0.001	<0.001	0.765
		Significant			Significant

Above table showed that serum bilirubin value on D-3 & D-5 were significant & required exchange transfusion treatment. There was significant correlation between the two with P-value of less than 0.001.

Table 29: Diagnostic predictability of cord blood albumin(CBA) For Neonatal hyperbilirubinemia(NH)

Parameter	TP	TN	FPFN	Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
Cord blood albumin(mg/dl)	64	23	6 7	90.14	79.31	91.43	76.67	87.00



Area Under the Curve

Test Result Variable(s): Cord blood albumin(mg/dl)

Area	Std. Error	p Value	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.902	0.036	<0.001	0.832	0.972

CUT OFF 3.05

		Cord blood albumin(mg/dl)		Total
		>3.05	<=3.05	
Hyperbilirubinemia	NO	23	6	29
	YES	7	64	71
Total		30	70	100

This table shows that diagnostic predictability of cord blood albumin in Newborns in relation to neonatal jaundice. There was 91.43% chance of developing NH & if CBA was <3g/dl while if CBA > 3 g/dl there was 76.67% chance of not developing NH. The sensitivity is 90.14% & specificity is about 79.31% with diagnostic accuracy of 87.0%.

DISCUSSION:

Gender distribution : In the present study, out of 100 newborns 58 (58%) were males & rest were female 42(42%). Other studies by Dhanjal *et al*(2017)[77], Sapkota *et al*(2020)[78], were done in term neonates where male newborns outnumbered females members with percentage of 57.59% & 67% respectively. Above studies are in correlation with this study. **Distribution of Birth weight :** In our study, we had 31% newborns with birth weight less than 1.5 kg where as 69% newborns had birth weight >/ 1.5 kg. A study done by Sapkota *et al*(2020)[78] where term newborns were divided into 3 groups I.e. weight <2.6kg(10%), 2.6-3.5 kg(73%) & >3.5kg(17%). In our study we had taken birth weight <2.5 kg as inclusion criteria, hence all the neonates with birth weight <2.5 kg only were included. **Distribution of mode of delivery :** In the present study, total of 60% neonates were born out of vaginal deliveries while 40% were extracted by caesarean delivery. Similarly studies done in term newborns like Sapkota *et al*(2020) [78], Aiyappa *et al*(2017)[79] more numbers of neonates were born out of vaginal deliveries I.e. 70% & 51% respectively. Our study is in correlation with Sapkota *et al*[78] & Aiyappa *et al*[79]. **Distribution of gestational age :** In our study, preterm neonates were grouped into Group 1(28-31 weeks), Group-2 (32-34 weeks) & (35- <37 weeks) that were consisted of 24%, 52% & 24% newborns were respectively. All the previous studies were done in terms newborns & all of them had gestational age of more than 37 weeks. **Distribution of cord blood albumin(CBA) :** In present study, 100 preterm neonates were categorised into 3 groups based on level of cord blood albumin. Group 1(<2.8 g/dl) constituted 23% where as Group-2(2.8-3.1 g/dl) & Group- 3(>3.1g/dl) had 56% & 21% respectively. **Gender & NH :** In our study we found out that there was no statistical correlation between gender of newborns & development of NH.(P-value=0.936). Similarly in the studies conducted by Rostami *et al*(2005)[80], Amar Taskande *et al*(2005)[81] & Onwuanaku *et al*(2011)[82] showed similar results with P-value of >0.05, 0.107 & 0.453 respectively. These were done in term newborns. It suggested that present study is in correlation with above mentioned studies.

Birth Weight & NH :In this study, we saw that 96.77%(30) newborns who developed hyperbilirubinemia had birth weight of less than 1.5 kg while 59.42%(41) had weight $>/$ 1.5 kg showing there was statistical correlation between them.(P-value <0.001).This is comparable to the study done by Sapkota *et al*(2020)[78], out of those who developed neonatal hyperbilirubinemia 11.8% had weight of >3.5 kg while only 4.1% had 2.6-3.5 kg of birth weight. It showed that NH was independent of birth weight.(P-value =0.386).Our study is not in correlation with previous study.This may be,our study was done on preterm newborns but previous studies were done in term neonates.

Most of the newborns with weight less than 1.5kg were more premature according to the distribution of cases.**Mode of delivery & NH :**In our study no significant association was noted between NH & mode of delivery.(P-value =0.857).Similar results were found in the previous studies done by Amar Taskande *et al*(2005)[81], Rudy Satrya *et al*(2009)[83] with P-value of 0.536,0.885 respectively.It indicates that our study is in correlation with previous studies.**Gestational age & NH :**In the present study we noted that newborns who developed neonatal hyperbilirubinemia 95.83%(23) had gestational age of 28-31 weeks followed by 82.69%(43) & 20.83%(5) who belonged to 32-34 weeks & 35- <37 weeks respectively.

All the previous studies were done in term neonates. Hence there no previous data regarding comparison between gestational age & neonatal hyperbilirubinemia.**Cord blood albumin(CBA) & NH :**In our study we had categorised cohort group into Group-1(<2.8 g/dl),Group-2(2.8 – 3.1g/dl) & Group-3(>3.1 g/dl). Out of them 95.65%(22) from group-1,83.93%(47) from group-2 & 9.52%(2) had developed neonatal hyperbilirubinemia. There was statistically significant correlation between them with P-value of <0.001 .It is comparable to the previous studies that were done in term newborns.In Dhanjal *et al* (2017)[77] out of all newborns who developed hyperbilirubinemia majority 87.50%(35) had CBA <2.8 g/dl & 11.50%(5) had CBA 2.8-3.4 g/dl. But none of the neonates with CBA >3.4 g/dl developed neonatal hyperbilirubinemia.(P-value <0.001). Sahu *et al*(2011) [84] & Trivedi *et al* (2013)[85] also showed significant correlation with P- value of <0.001 & <0.05 respectively.We also got similar results as other studies done before.**Requirement of intervention based on Cord blood albumin(CBA) :**We noted that in the present study maximum cases who required phototherapy 95.65%(22) & exchange transfusion 47.83%(11) belonged to Group-1(CBA level <2.8 g/dl) showing statistical significance between them with P-value of <0.001 .Similar study done by Dhanjal *et al*(2017)[77] concluded that majority cases with neonatal hyperbilirubinemia(87.50%) were with CBA level <2.8 g/dl. (P-value <0.001). Another study done in 2016 by Raj *et al*[86] concluded most of the newborns who developed neonatal jaundice had CBA level less than 2.8 g/dl showing statistical significance with P-value of <0.05 . None of the term newborns from previous studies required exchange transfusion.It signifies that our study is in correlation with previous studies mentioned above.

Cord Blood albumin(CBA) & Duration of hospital stay :Significant association of cord blood albumin with duration of hospital stay was noted. (P- value 0.047). Preterm newborns admitted neonatal hyperbilirubinemia having cord blood albumin level of less than 2.8 g/dl had longer duration of hospital stay in compared to others, which indirectly indicates severity of neonatal jaundice.

LIMITATIONS

- As our study population had a small numbers of newborns & the data from such small group in the study may not yield a conclusive evidence. As only preterm newborns were taken into account, the result was influenced by gestational age & birth weight. Preterm newborns can develop neonatal jaundice on Day-5 & Day-7 of postnatal days, they are followed upto day 7.

□

CONCLUSION

Neonatal Jaundice is found in about 80% of preterm newborns especially in early preterm & very low birth weight neonates but it is independent of gender of newborns and mode of delivery. Neonates with cord albumin level of less than 3 g/dl have more risk of neonatal jaundice requiring intervention along with increased duration of hospital stay while those with more than 3 g/dl are comparatively safe for early discharge.

Cord blood albumin can be considered as a risk indicator rather than diagnostic tool, which can give a clue to the possibility of severe jaundice during neonatal period. It may help treating doctors and the parents stay alert to take action at the earliest. Thus, it can be a useful tool in preventing Kernicterus or any other form of toxicity due to hyperbilirubinemia.

RECOMMENDATIONS

The present study was done to assess the usefulness of the cord serum albumin estimation as a risk indicator to predict significant neonatal hyperbilirubinemia in a healthy preterm newborn who require phototherapy & exchange transfusion subsequently. Neonates with umbilical cord blood albumin level more than 3gm/dl can be safely discharged early as 76.67% negative predictive value (NPV) in the present study suggests that in healthy term neonate, cord serum albumin >3.3 g/dl can help to identify those neonates who are unlikely to require further evaluation and intervention whereas neonates with albumin levels <3.3 gm/dl will need a close follow up to check for development of jaundice. Neonates with cord albumin

level less than 2.8 gm/dl shouldn't be discharged early after delivery whether there is a risk factor for neonatal jaundice or not.

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