ORIGINAL RESEARCH

Comparison Of Umbilical Cord Blood Bilirubin And Bilirubin Albumin Ratio In Predicting Neonatal Hyperbilirubinemia

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ABSTRACT

Introduction: In newborns, hyperbilirubinemia is a common medical issue. When bilirubin levels rise to unusually high levels and cause neurological issues, it becomes troublesome. The aim of present study is to compare the umbilical cord blood bilirubin and bilirubin albumin ratio in predicting neonatal hyperbilirubinemia.

Material & methods: The prospective observational study was conducted at NICU and post natal wards for a period of 1 year. Until five days or until they were discharged, babies were checked every day for signs of jaundice. If clinical icterus was detected within 72 hours of delivery or at any point following, according to Kramer's guideline, venous blood was sent for bilirubin measurement. The p-value<0.05 was considered statistically significant.

Results: Out of 100 patients 25% had hyperbilirubinemia. Male patients (55%) were more as compared to females (45%). Most common mode of delivery was vaginal (69%). 77% had birth weight 2.5-3.5kg. Correlation of UCB cut-off of 2 mg/dL and UCB cut-off of 2.5 mg/dL to predict neonatal hyperbilirubinemia were both highly statistically significant with p-value of <0.001. Statistically significant correlation between the BAR and neonatal hyperbilirubinemia with a p-value <0.001 with both BAR cut-offs of 0.59 and 0.69. UCB cut-off of 2 mg/dL had a better sensitivity and UCB 2.5 mg/dL had a better specificity. BAR 0.59 has a better sensitivity and BAR 0.69 has a better specificity.

Conclusion: Neonatal hyperbilirubinemia can be predicted well by both UCB and BAR, However UCB is a stronger predictor than BAR.

Keywords : Cord blood albumin, Neonates, Prediction tool, Umbilical cord bilirubin

INTRODUCTION

In newborns, hyperbilirubinemia is a typical physiological occurrence. By days 2 to 4, it affects 60–70% of term babies and 80% of preterm babies [1]. In cord blood, mean bilirubin concentrations vary from 1.4 to 1.9 mg/dL [2,3]. Bilirubin is produced daily by newborns at a rate of roughly 6 to 8 mg per kg [4]. On the third or fourth day of life, the average total blood bilirubin level typically peaks at 5 to 6 mg per dL and subsequently resolves within 1-2 weeks [5]. A heightened form of physiologic jaundice in which the total blood bilirubin level can increase to 17 mg/dL is possible in infants with numerous risk factors [6]. Reduced Red Blood Cell (RBC) survival, increased enterohepatic circulation, and temporary bilirubin conjugation deficit are the main causes of hyperbilirubinemia in newborns [1]. If left untreated, hyperbilirubinemia can progress to kernicterus, a clinical disease linked to seizures, neurological delays, and even death [7, 8]. The majority of jaundice instances are benign in origin, but because bilirubin can be toxic, newborns need to be closely watched to see whether any develop severe neonatal hyperbilirubinemia (NNH), which could lead to neurotoxicity [9]. Approximately 5–10% of patients require exchange transfusions or phototherapy as a clinically necessary NNH intervention.[10] Early in fetal life, the liver synthesizes albumin [11]. Serum albumin levels in term newborns should not exceed 2.8 mg/dL, with 3.1±0.3 g/dL being the usual range [12]. Amounts 70–75% of plasma oncotic pressure are made out of albumin. It facilitates the movement of several substances throughout the body, including cysteine, free fatty acids, and bilirubin. 1mg of albumin is bound by 8.5 milligrams of bilirubin [13]. The risk of neonatal hyperbilirubinemia is decreased by the binding of bilirubin to albumin. Before being released from the hospital, the American Academy of Paediatrics (AAPs) advises screening all newborns for hyperbilirubinemia [14]. In addition, if a neonate is released earlier than 72 hours, the AAP advises reviewing all of them after 48 to 72 hours for the

onset of jaundice [15]. Since it is uncertain at what level neurotoxicity develops and the conditions under which toxicity develops are not well characterized, there is currently little consensus over what constitutes a safe bilirubin level [16]. An intriguing extra metric in the therapy of NNH is the bilirubin albumin ratio (BAR), which serves as a stand-in for free bilirubin. Hence the present study was done to compare the umbilical cord blood bilirubin and bilirubin albumin ratio in predicting neonatal hyperbilirubinemia.

MATERIAL & METHODS

The prospective observational study was conducted at NICU and post natal wards for a period of 1 year. Ethical permission was taken from institutional ethical committee of allied medical college and hospital before commencement of study. Total 100 newborn babies were selected for the study on the basis of following inclusion and exclusion and exclusion criteria:

Inclusion criteria- Term neonates with gestational age >37 weeks of either gender, from either normal vaginal delivery or caesarean section with birthweight ≥2 kg and Apgar score ≥7 at first minute of life .

Exclusion criteria- Preterm babies, babies with ABO and Rh incompatibility and whose Apgar score were <7 at first minute of life, babies born by instrumental delivery, neonates with sepsis, respiratory distress and major congenital anomalies. Written informed consent was taken from parents/guardian after explaining the complete procedure of the study. Relevant antenatal history was taken by interviewing the mother or from antenatal records. Following the baby's delivery, the umbilical cord was clamped twice. Two milliliters of cord blood were drawn into two simple bottles; one vial was sent to be analyzed for the baby's blood type, and the other was used to estimate albumin and bilirubin levels. By employing the colourimetric diazo technique in a semi-automated assay, cord bilirubin was evaluated. Using the semi-automated bromocresol green method, umbilical cord albumin was tested. An analysis of the baby's blood group was also sent. Thus, the newborns' rhesus, blood group, and total cord bilirubin as well as cord albumin were measured. Throughout the course of five days, or until their discharge, whichever came first, the neonates were checked every day for the onset of jaundice. After 72 hours, a peripheral venous blood sample was supplied for bilirubin measurement. If Kramer's rule indicated clinical icterus at any point, venous blood should be extracted and sent for bilirubin evaluation. The National Neonatology Forum of India (NNF) clinical practice Guidelines [17] stated that bilirubin >13 mg/dL on day 2 or ≥17 mg/dL on day 3 was the requirement for phototherapy. With cord bilirubin cutoff values of 2 mg/dL and 2.5 mg/dL and BAR of 0.59 and 0.69, the risk of hyperbilirubinemia was examined. Data was analyzed using SPSS version 25.0. Qualitative data were expressed as number and percentage and quantitative data were expressed as mean±Standard Deviation (SD). The statistical data were analysed with t test, Chi-square test and Pearson's correlation. The p-value ≤0.05 was considered as statistically significant.

RESULTS

In the present study out of 100 patients 25% had hyperbilirubinemia. Male patients (55%) were more as compared to females (45%). Most common mode of delivery was vaginal (69%). 13% patients had birth weight 2-2.5kg , 77% had birth weight 2.5-3.5kg and 10% had birthweight greater than 3.5 kg. There were no statistically significant differences in the baseline characteristics between those with/without neonatal hyperbilirubinemia as shown in table 1.

Table: 1 showing baseline characteristics of two groups

Variable		Hyperbilirubinemia		P value
		Present N=25	Absent N=75	
Gender	Male	13 (52)	42 (56)	0.156
	Female	12 (48)	33 (44)	
Mode of delivery	Vaginal	19 (76)	50 (66.6)	0.17
	C section	6 (24)	25 (33.4)	
Birth weight (kg)	2-2.5	3 (12)	10 (13.3)	0.363
	2.5-3.5	19 (76)	58 (77.3)	
	>3.5	3 (12)	7 (9.4)	

36.1% of patients having hyperbilirubinemia had bilirubin value above 2 mg/dL and 15% had bilirubin value below 2 mg/dL while 52.1% of patients had bilirubin level above 2.5mg/dL and 16.8% had bilirubin value below 2.5 mg/dL. Correlation of UCB cut-off of 2 mg/dL and UCB cut-off of 2.5 mg/dL to predict neonatal hyperbilirubinemia were both highly statistically significant with p-value of <0.001 as shown in table 2.

Table: 2 showing association between cut-off cord bilirubin 2 mg/dL and 2.5 mg/dL and neonatal hyperbilirubinemia

Cut off values	Umbilical cord bilirubin (mg/dL)	Hyperbilirubinemia		Total	P value
		Present	Absent		
Cut off 2	>2	17 (36.1)	30 (63.9)	47	<0.001
	<2	8 (15)	45 (85)	53	
Cut off 2.5	>2.5	12 (52.1)	11 (47.8)	23	<0.001
	<2.5	13 (16.8)	64 (83.2)	77	

53.4% of patients having hyperbilirubinemia had BAR value above 0.59 and 3.5% had BAR below 0.59 while 71.4% of patients had BAR above 2.5 and 12.6% had BAR below 2.5. There was a statistically significant correlation between the BAR and neonatal hyperbilirubinemia with a p-value <0.001 with both BAR cut-offs of 0.59 and 0.69 as shown in table 3.

Table: 3 showing association between cut-off cord bilirubin albumin ratio(BAR) 0.59 and 0.69 and neonatal hyperbilirubinemia

Cut off values	Bilirubin albumin ratio (BAR)	Hyperbilirubinemia		Total	P value
		Present	Absent		
Cut off 0.59	>0.59	23 (53.4)	20 (46.5)	43	<0.001
	<0.59	2 (3.5)	55 (96.4)	57	
Cut off 0.69	>0.69	15 (71.4)	6 (28.5)	21	<0.001
	<0.69	10 (12.6)	69 (87.3)	79	

The sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of UCB 2 mg/dL in predicting the risk of neonatal hyperbilirubinemia were 76.3%, 61.2%, 38.3% and 89.3% respectively. The sensitivity, specificity, PPV and NPV with cut-off of UCB >2.5 mg/dL are 33.7%, 88.1%, 50.7% and 81.2%, respectively. Cut-off value of BAR at 0.59 had a sensitivity, specificity, PPV and NPV of 68%, 65.4%, 37.3% and 84.3%, respectively. Cut-off BAR 0.69 had sensitivity, specificity, PPV, NPV of 44.3%, 80.1%, 40.2% and 81.2%, respectively as shown in table 4.

Table: 4 showing Sensitivity, Specificity, Positive Predictive Value (PPV), and Negative Predictive Value (NPV).

Variable	Sensitivity	Specificity	Positive predictive value	Negative predictive value
UCB>2mg/dL	76.3	61.2	38.3	89.3
UCB <2mg/dL	33.7	88.1	50.7	81.2
BAR>0.59	68	65.4	37.3	84.3
BAR<0.69	44.3	80.1	40.2	81.2

DISCUSSION

In the initial days following birth, jaundice is a frequent condition in newborns that needs medical treatment. With the exception of a tiny percentage that requires intervention such as phototherapy, exchange transfusion, or other novel treatment modalities, the majority of jaundice that occurs in newborns falls within the physiological range. The devastating repercussions of kernicterus, which can include mental retardation, the choreoathetoid type of cerebral palsy, or hearing impairments, must be avoided by prompt diagnosis and prompt treatment. The past ten years have seen a significant drop in these side effects as a result of public awareness education campaigns. However, a tiny percentage of newborns continue to suffer from the devastating side effects of neonatal hyperbilirubinemia, particularly in poorer nations, due to inadequate follow-up, a lack of resources, and—most importantly—a lack of emotional attachment from their parents. Certain parents wish to avoid any pain—not even from a single needle prick—for their child. Considering all of these variables, the goal of this study was to establish the bilirubin/albumin ratio and cord blood bilirubin cut-off values in the hopes that these values may be utilized to forecast the emergence of eventual newborn hyperbilirubinemia.[18] The incidence of neonatal hyperbilirubinemia was 25% . This was consistent with the Satrya R et al study, which found that 24% of patients had hyperbilirubinemia [19]. There are studies that show a higher prevalence of 34% as well as those that show a lower incidence of 12.8% and 10.6% than this [20-22]. There could be several causes for the discrepancy. The research has been carried out across diverse racial and geographic contexts. The diazo method and the enzymatic method, which employs bilirubin oxidase, are two different approaches used to estimate bilirubin. High-risk and near-term newborns were included in Zeitoun AA et al's study, which raised the rate of hyperbilirubinemia [22]. In our study out of 100 patients male (55%) were more as compared to

females (45%). Most common mode of delivery was vaginal (69%). Maximum (77%) patients had birth weight 2.5-3.5 kg . The birth weight, sex of the baby and mode of delivery have no statistically significant differences between the babies who developed hyperbilirubinemia or not. Correlation of UCB cut-off of 2 mg/dL and UCB cut-off of 2.5 mg/dL to predict neonatal hyperbilirubinemia were both highly statistically significant with p-value of <0.001. According to research by Kara L. et al, infants who got phototherapy had greater levels of bilirubin in their umbilical cord blood compared to those who did not. They came to the conclusion that bilirubin from umbilical cord blood may be able to predict the likelihood of severe hyperbilirubinemia and phototherapy [23]. According to a recent study conducted at this center, the umbilical cord bilirubin (UCB) can predict neonatal hyperbilirubinemia, which is why it is recommended that all newborns have their UCB estimated [24]. In our study 53.4% of patients having hyperbilirubinemia had BAR value above 0.59 and 3.5% had BAR below 0.59 while 71.4% of patients had BAR above 0.69 and 12.6% had BAR below 0.69. There was a statistically significant correlation between the BAR and neonatal hyperbilirubinemia with a p-value <0.001 with both BAR cut-offs of 0.59 and 0.69. In the research done by Mashad GM et al [25], this was quite close to the cut-off ratio of 0.6 . In study done by, Sharma I et al and Khairy MA et al they discovered cutoffs of 0.719 and 0.78, respectively [26,27]. UCB cut-off of 2 mg/dL had a better sensitivity and UCB 2.5 mg/dL had a better specificity. Haridas K et al., found that the relation between cord bilirubin level and the requirement of phototherapy is present and that the sensitivity was 58.33% and specificity was 96.49% [28]. BAR 0.59 has a better sensitivity and BAR 0.69 has a better specificity for the detection of neonatal hyperbilirubinemia. Bhat JA et al., found that cord blood bilirubin/albumin ratio >0.98 can predict hyperbilirubinemia with sensitivity 78.79% and specificity 95.51% [18]. The different sample sizes and different methods of bilirubin estimation would have contributed to this variation in the BAR.

Small sample size and not involvement of pre-term and high risk babies are some limitations of the study

CONCLUSION

This study showed that for the purpose of identifying neonatal hyperbilirubinemia, both UCB and BAR are potentially helpful screening methods. It was discovered, however, that UCB is a more accurate predictor of the emergence of newborn hyperbilirubinemia than BAR, with a greater specificity of 2.5 mg/dL and a better sensitivity of 2 mg/dL for UCB. Therefore, when it came to detecting hyperbilirubinemia, UCB outperformed BAR in terms of both sensitivity and specificity.

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