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Original Research Article

Study of the association of cord serum albumin with neonatal hyperbilirubinemia among neonates with neonatal hyperbilirubinemia among neonates in a teritary care hospital

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ABSTRACT

Background: Neonatal hyperbilirubinemia (NH) is the most prevalent aberrant physical finding in the first week of life, affecting about 60% of term and 80% of preterm neonates. Hyperbilirubinemia is more common in preterm infants due to a variety of causes, although it can also occur in healthy term infants. The liver produces albumin, which aids in the transport of unconjugated bilirubin. Hyperbilirubinemia can be predicted early, allowing newborns and mothers to be discharged sooner and stay in the hospital for less time. Objective were to study cord albumin levels, to study the proportion of newborn requiring intervention for neonatal jaundice (phototherapy or exchange transfusion) based on different levels of cord blood albumin (CBA) level at birth and thereby defining the critical cord blood albumins values with respect to significant neonatal jaundice.
Method: The 200 cases who filled the inclusion and exclusion criteria were included into the study for predictive value of CBA for NH. Then the data was analyzed using epi info and descriptive and inferential statistics were used.
Result: In the present study, term group had 49 males and 45 females, while preterm group had 62 males and 47 females respectively. There was no significant association between gender and NNHB in either of the two groups (0.75 in term; 0.09 in preterm). There was also no association found between NH and the mode of delivery, in both term and preterm neonates with p=0.88 in term group and 0.84 in preterm group respectively. In our study, in the term group, only 1 (100%) with birth weight less than 2.5 kg developed significant NH. Only 33 (35.5%) out of 93 newborns with birth weight more than 2.5 kg developed NH. With p=0.01, there was significant association between birth weight and significant NH. Among preterm newborns, there was a significant association between birth weight and development of significant NH (p=0.0001).
Conclusions: In present study findings showed that CBA level can be used as a predictor of NH in a term as well as preterm newborn soon after birth. As cord blood is easily available in an institutional delivery and albumin estimation also easily done which can help in recognizing risk group (low CBA) and strict vigilance should be followed.

Keywords: CBA, Preterm, Term, Phototherapy, NH, Mode of delivery

INTRODUCTION

NH is a normal physiologic condition which occurs after birth. It is not a singular disease in itself, but a physical finding associated with multiple possible etiologies.[1] In most infants, unconjugated hyper-bilirubinemia 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.[2] Hyperbilirubinemia in preterm infants is more common, has more severity and has longer course than in term neonates as a result of exaggerated neonatal red cell, hepatic and gastrointestinal immaturity.[3] Albumin is one of the major binding proteins in

neonates.[4] Low production of albumin will lower its transport and binding capacity, especially in preterm neonates.[5]

The concept of prediction of jaundice offers a valuable option to pick up babies at risk of developing NH. By predicting the newborns likely to develop significant neonatal jaundice early at birth, we can design and implement the follow-up program in these high-risk groups effectively. The present study was designed to evaluate the predictive value of CBA among both term and preterm newborns with subsequent hyperbilirubinemia.

METHOD

This was a prospective study carried out over a period of two years from May 2020 to April 2021, at Indira Gandhi medical college and hospital, Shimla. The study group consisted of 200 newborns of which 94 were term babies and 106 preterm babies, irrespective of gender. All live neonates born at KNH Shimla irrespective of their gender, mode of delivery and period of gestation were included in the study. VLBW babies, SGA babies, babies with hemolytic disease (Rh), instrumental delivery (forceps and vacuum) babies and those babies with significant illnesses like neonatal sepsis, birth asphyxia, respiratory distress syndrome, and meconium aspiration syndrome, maternal drug which increases NNH were excluded from the study. Those babies whose apgar score was <7 at 1 minute and who developed neonatal jaundice within 24 hours of life were also excluded.

The neonates were categorized in to four: 1) term neonates 2) <32 weeks of gestation 3) 32-34 weeks of gestation 4) 34-37 weeks of gestation. Both term and preterm groups were further divided in to three groups each, based on their CBA levels (≤2.8 g/dl, 2.9-3.3 g/dl and ≥3.4 g/dl respectively.

Informed consent was taken from the parents of the neonates enrolled in the study. Demographic profile and relevant information were collected by interviewing the mother and from mother's case sheet. Assessment of gestational age was done by new Ballard score and corresponded with the LMP. CSA level was evaluated at birth. All enrolled babies were followed up and clinically assessed for jaundice according to Kramer dermal scale for term neonates and clinically for preterm neonates.[6] Total serum bilirubin (TSB) estimation was done as and when neonate was clinically icteric for estimation of serum total bilirubin and indirect bilirubin.

The cord blood (2 ml) collected at birth was analyzed by auto analyser method using Merilyser AutoQuant 100 machine for cord serum albumin level. The main outcome of the study was inferred in terms of NH requiring intervention. Interventions like phototherapy and exchange transfusion were undertaken as per hyperbilirubinemia management guidelines.[7,8]

Data was tabulated in Microsoft excel and analysed using Epi info Software from CDC Atlanta. Proportions and Chi square test was used to analyse data. P value less than 0.05 was considered significant. Study was approved by the institude ethic board.

RESULT

The study COHORT consisted of 200 neonates who fulfilled the inclusion criteria. The study group was categorized in to four groups: term neonates and preterm neonates of gestation <32 weeks, 32-34 weeks of gestation, 34-37 weeks of gestation which was further divided based on cord serum albumin level in to 3 groups (Table 1).

Table 1: Groups based on cord serum albumin (g/dl) level.

Period of gestation (weeks)	Cord blood albumin, n (%)		
	<2.8	2.8-3.2	≥3.3
	N (%)	N (%)	N (%)
<32	11 (10.2)	7 (10)	3 (13.6)
32-34	19 (15.8)	18 (25)	4 (17.3)
34-37	25 (23.3)	18 (25)	7 (30)
>37	52 (48.5)	27 (39)	9 (39.1)
Total	107	70	23
Chi square: 6.3, p=0.38			

The demographic variables and the variables, which influence NH directly or indirectly, for term and preterm neonates were compared and are shown in Table 2 and 3 respectively.

In Table 2, statistical significance can be seen between cord serum albumin and NH (p=0.001). In Table 3, statistical significance can seen with birth weight (0.001) and CBA (0.001) for subsequent occurrence of NH.

Table 2: Correlation of clinical variables with need for phototherapy-term.

Variables	Need of phototherapy in term, n (%)		P value
	Yes	No	
CBA			
CBA <2.8	26 (44.8)	32 (55.2)	0.02
CBA 2.8-3.2	8 (29.6)	19 (70.4)	
CBA ≥3.3	0	9 (100)	
Gender			
Female	17 (37.8)	28 (62.2)	0.75
Male	17 (34.7)	32 (65.3)	
Mode of delivery			
Caesarean	13 (37.1)	22 (62.9)	0.88
Vaginal	21 (35.6)	38 (64.4)	
Birth weight (kg)			
1.5-2.5	1 (100)	0	0.01
>2.5	33 (35.5)	60 (64.5)	

Table 3: Correlation of clinical variables with need for phototherapy-preterm.

Variables	Need of phototherapy in pre-term, n (%)		P value
	Yes	No	
CBA			
CBA <2.8	37 (75.5)	12 (24.5)	0.02
CBA 2.8-3.2	21 (48.8)	22 (51.2)	
CBA ≥3.3	7 (50)	7 (50)	
Gender			
Female	33 (70.2)	14 (29.8)	0.09
Male	32 (54.2)	27 (45.8)	
Mode of delivery			
Caesarean	21 (60)	14 (40)	0.84
Vaginal	44 (62)	27 (38)	
Birth weight (kg)			
<1	13 (100)	0	0.000
1-1.5	17 (94.4)	1 (5.6)	
1.5-2.5	33 (56.9)	25 (43.1)	
>2.5	2 (11.8)	15 (88.2)	

DISCUSSION

In comparison to adults, neonates have an underdeveloped liver function, according to studies and literature. As a result, the generation and synthesis of all main proteins in infants is reduced. On the other hand, the liver may be unable to cope with excessive bilirubin generation in newborns due to a variety of factors. As the production of various proteins declines, so does the production of albumin, which plays a critical role in the conjugation of bilirubin. Albumin acts a carrier protein for the transport of bilirubin, which eventually helps in the transfer of bilirubin to the liver where conjugation occurs. This process is interrupted due to decreased albumin levels in newborns. The impact is more so in preterm newborns, which have an even decreased albumin levels. In this present study, we assessed the CSA level as a tool for screening for the risk of subsequent NH, in both term and preterm neonates and compared its efficacy in both the groups.

In the present study, term group had 49 males and 45 females, while preterm group had 62 males and 47 females respectively. There was no significant association between gender and NNHB in either of the two groups (0.75 in term; 0.09 in preterm). There was also no association found between neonatal hyper-bilirubinemia and the mode of delivery, in both term and preterm neonates with p=0.88 in term group and 0.84 in preterm group respectively.

In our study, in the term group, only 1 (100%) with birth weight less than 2.5 kg developed significant NH. Only 33 (35.5%) out of 93 newborns with birth weight more than 2.5 kg developed NH. With p=0.01, there was significant association between birth weight and significant NH. Among preterm newborns, there was a significant association between birth weight and development of significant NH (p=0.0001). Romagnoli et al and Onwuanaku et al in their respective studies concluded that there was a significant association between birth weight and NH among preterm newborns. Satrya et al in a study on 88 newborns, showed that there is no association (p=0.885) between birth weight and NH, among term newborns.[9-11] The present study was in correlation with these studies.

In the term group, 26 (44.8%) newborns with CSA <2.8 g/dL developed NH. The 8 (29.6%) newborns had CSA level between 2.9-3.3 g/dl and none of the newborns with CSA level ≥3.4 g/dl developed significant NH. The p value was significant (0.02). In the preterm group, 37 (75.5%) newborns that developed significant hyperbilirubinemia had a CSA level <2.8 g/dl, 21 (48.8%) newborns had a CSA level between 2.9 and 3.3 g/dl 7 (50%) of the newborns with CSA level >3.4 g/dl developed NH. There was a significant p=0.001.

Study of Sahu et al showed that 70% (14/20) newborn who developed significant NH had CSA level <2.8 g/dl, 30% (6/20) newborn had CSA level 2.9-3.3 g/dl and none of the newborns with CSA level >3.4 g/dl developed NH.[4] There was a statistical significance noted between CSA and development of NH (p<0.001). Trivedi et al studied a total of 605 newborns and 205 newborns developed significant NH in study group with 58.35% (120/205) of the neonates with CSA level <2.8 g/dl developing significant NH (p<0.05). Our study results correlated well with both these studies.[12]

Few studies were done on term newborns to find the correlation between CBA and NH, but none have been done on preterm newborns.[4,12,13] In the present study, it was found that there was a significant association between CBA values and the tendency to develop significant NH that may require intervention, and also the risk is the same for both term and preterm newborns when CBA levels are less than 2.8 g/dl. Between 2.9 g/dL, the risk is comparatively less and with value above 3.4 g/dl, newborns have a very less chance of developing significant NH.

Limitation

The limitation of our study was that it had a small sample size and only healthy neonates, in both term and preterm groups, were taken for the study.

CONCLUSION

Few studies were done on term newborns to find the correlation between CBA and NH, but none on preterm newborns.

In the present study the findings showed that CBA level can be used as a predictor of NH in a term as well as preterm newborn soon after birth. As cord blood is easily

available in an institutional delivery and albumin estimation also easily done which can help in recognizing the risk group (low CBA) and strict vigilance should be followed.

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