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Original Research Article

Cord Serum Albumin (CSA) Measurement and Prediction of Newborn Hyperbilirubinemia Based on CSA Values: Prospective Observational Study

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Abstract

Aim: Aim of this study was measuring the Cord Serum Albumin level (CSA) and predicting neonatal hyperbilirubinemia based on cord serum albumin levels. **Methods:** This prospective observational study was carried out in the Department of Pediatrics, Indira Gandhi Institute of Medical Sciences, Sheikhpura, Patna, Bihar, India from August 2019 to July 2020. Total 110 born term healthy neonates were included in this study. 3 ml of cord blood was collected at birth in a Serum-separating tube and was sent for estimation of cord blood albumin and TSH. On detecting the presence of icterus, Blood was sent for estimation of Total Bilirubin (TB). **Results:** In the study a total of 110 babies were registered. Out of this 58(52.73) % were female and 52(47.27%) were male. Depending on the cord albumin levels the babies were grouped into two: >2.8 gm/dl (Group 1) and <2.8 gm/dl (Group 2). Lower normal limit for cord serum albumin in term babies is 2.6g m/dl. There was a total of 88 babies in Group 1 and 22 babies in Group 2. The mean gestational age was among Group 1 was 38.95±2.31 weeks and Group 2 was 37.98±2.33. It was noted that babies born at a lower gestational age had a higher chance of having a low albumin value and subsequent hyperbilirubinemia ($p=0.001$). The anthropometric profile of both the groups were compared and it was noted that only the birth weight had a significant correlation with cord albumin ($p<0.001$). A significant correlation was noted between the Cord TSH and cord Albumin levels in this study. Out of 110 babies, 53 babies developed icterus. Under group 1, 36 babies developed icterus and under group 2, 17 babies developed icterus. The total bilirubin levels were significant in Group 2 ($p<0.001$). 22 babies of the 53 with icterus required phototherapy and it was noted that majority of these babies were from group 2 ($p<0.05$). Only 1 baby required exchange transfusion and it belonged to group 2. In our study, the sensitivity of cord albumin to detect hyperbilirubinemia in newborn was determined and found to be 74.55%, while specificity was 63.64%. The positive predictive value was found to be 42.73% and the negative predictive value was found to be 91.82%. The accuracy rate was 68.18%. **Conclusion:** Cord albumin levels help to determine and predict the possibility of

hyperbilirubinemia among neonates. Hence this can help to identify the at-risk neonates. So, routine determination of cord albumin can be advocated to keep a track on at risk neonates.
Keywords: Cord Albumin, Hyperbilirubinemia, Icterus.

Introduction

Jaundice is the visible manifestation of elevated serum bilirubin in skin and sclera. Thousands years ago, it was described in Chinese literature and in the 18th century Junker first differentiated between true jaundice and the yellowish tinge observed in many neonates.[1,2] Approximately 60% of term and 80% of preterm neonates develop jaundice in first week of life and significant neonatal hyperbilirubinemia is a cause of concern for the parents and pediatricians as well and it occurs in 3-5% of healthy term infants.[3,4] Early discharge of healthy term newborn after delivery has become a common practice because of medical, social and economic reasons.[5] The most common cause for readmission during the early neonatal period is hyperbilirubinemia. The American Academy of Pediatrics (AAP) recommends that newborn discharged within 48 hours should have a follow up visit after 2-3 days to detect significant jaundice and other problems.[6] In developing countries like India, this recommendation is not practical due to limited follow up facilities. Liver is the site of synthesis of albumin appears at approximately the 7-8 weeks in the human fetus and it increases in inverse proportion to that of α-fetoprotein, which is the dominant fetus protein. It binds to unconjugated bilirubin and helps in the transport. Around 8.5mg of bilirubin will bind tightly to 1gram of albumin. Free bilirubin is anticipated when the bilirubin to albumin ratio is >0.8. Although bilirubin may have a physiologic role as an antioxidant but elevations of unconjugated bilirubin are potentially neurotoxic. The concept of prediction of jaundice offers an attractive option to pick up babies at risk of developing significant neonatal hyperbilirubinemia. Physical examination is not a reliable measure of the serum bilirubin. Under these circumstances it would be desirable to predict the risk of neonatal hyperbilirubinemia in order to implement early treatment and thereby minimize the risk of bilirubin dependent brain damage. By predicting the neonates likely to develop significant neonatal jaundice early at birth, we can design and implement the follow-up programme in these high risk group effectively. Objective of the study was measuring the Cord Serum Albumin level (CSA) and predicting neonatal hyperbilirubinemia based on cord serum albumin levels.

Material and methods

This prospective observational study was carried out in the department of Department of Pediatrics, Indira Gandhi Institute of Medical Sciences, Sheikhpura, Patna, Bihar, India from August 2019 to July 2020

Methodology

Total 110 born term healthy neonates were included in this study. Neonates with ABO or Rh incompatibility, Major congenital malformations, Cephalhematoma, Early onset sepsis and Preterm babies were excluded from the study. 3 ml of cord blood was collected at birth in a Serum- separating tubes and was sent for estimation of cord blood albumin and TSH. Cord Albumin was assessed using the Biuret reaction technique using an automated analyzer. Babies were examined daily for the presence of icterus upto the 5th day following which they were discharged. On detecting the presence of icterus, Blood was sent for

estimation of Total Bilirubin (TB) and the results were plotted on the chart to identify the type of intervention the baby required. The data was entered into the Performa in which the gender, gestational age, mode of delivery anthropometric measurements at birth, cord TSH, Cord albumin and total and direct bilirubin of the babies were noted. Cord blood was collected at birth and was sent for estimation of cord blood albumin and TSH. Babies were examined daily for the presence of icterus up to the day of discharge. On detecting the presence of icterus, Blood was sent for estimation of Total Bilirubin (TB) and the results were plotted on the chart to identify the type of intervention the baby required. Data was collected as per the performa after obtaining consent from the parents of the neonates. The main outcome of the study was inferred in terms of neonatal hyperbilirubinemia.

Statistical analysis

All the data was entered in Microsoft excel sheet and SPSS Version 20.0. Statistical data were analysed with t test, chi-square test and ANOVA. Sensitivity, specificity, negative and positive predicative value of the tests was calculated. The cord albumin levels having highest specificity and sensitivity was determined with the Receiver operating characteristics (ROC) curve analysis.

Results

In the study a total of 110 babies were registered. Out of this 58(52.73)% were female and 52(47.27%) were male. There was no significant difference in the number of male and female babies. Depending on the cord albumin levels the babies were grouped into two: >2.8 gm/dl (Group 1) and <2.8 gm/dl (Group 2). Lower normal limit for cord serum albumin in term babies is 2.6g m/dl. There were a total of 88 babies in Group 1 and 22 babies in Group 2. The mean gestational age was among Group 1 was 38.95±2.31 weeks and Group 2 was 37.98±2.33. It was noted that babies born at a lower gestational age had a higher chance of having a low albumin value and subsequent hyperbilirubinemia (p=0.001). 59 babies were born by normal vaginal delivery and 51 were born by LSCS and there was no significant difference between the babies developing icterus based on the mode of delivery. The anthropometric profile of both the groups were compared and it was noted that only the birth weight had a significant correlation with cord albumin (p<0.001) (Table 1). A significant correlation was noted between the Cord TSH and cord Albumin levels in this study (Table 2). Out of 110 babies, 53 babies developed icterus. Under group 1, 36 babies developed icterus and under group 2, 17 babies developed icterus. The total bilirubin levels were significant in Group 2 (p<0.001) (Table 3). 22 babies of the 53 with icterus required phototherapy and it was noted that majority of these babies were from group 2 (p<0.05) (Table 4). Only 1 baby required exchange transfusion and it belonged to group 2. In our study, the sensitivity of cord albumin to detect hyperbilirubinemia in newborn was determined and found to be 74.55%, while specificity was 63.64%. The positive predictive value was found to be 42.73% and the negative predictive value was found to be 91.82%. The accuracy rate was 68.18%.

Table 1: Gestational age and anthropometric data (N=110)

	Group 1=88	Group 2=22	P value
Gestational age (weeks)	38.95±2.31	37.98±2.33	0.001
Birth weight kgs	3.217±0.244	2.702±0.632	<0.001
Length (cms)	47.49±3.19	47.87±2.87	0.321
Head circumfere (cms)	35.01±2.45	34.98±2.76	0.634

Table 2: Relation between cord TSH and cord albumin

	Group 1	Group 2	P value
Cord TSH (micro UL/mL)	11.02±8.21	16.87±7.31	<0.001

Table 3: Relation between cord albumin and bilirubin

	Total number	Total Bilirubin value	P value
Group 1	36 (40.91%)	12.01±3.54 (mg/dl)	<0.001
Group 2	17(77.27%)	16.02±4.21 (mg/dl)	
Direct bilirubin value			
Group 1	0.669±0.32 (mg/dl)		0.596
Group 2	0.691±1.79(mg/dl)		

Table 4: Relation between cord albumin and Interventions required.

	Group 1	Group 2	P value
Neonates with Icterus	36	17	<0.0005
Newborns requiring phototherapy	9	13	<0.05

Discussion

Studies and literatures have shown that neonates have an immature liver function as compared to that of adults. As a result, there is decreased production and synthesis of all the major proteins in the newborns. On the other hand, liver at times may not be able to handle the excess production of bilirubin that may occur due to various reasons in newborn. The decrease in the production of various proteins means that there is a decrease in the production of albumin, which has a major 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 the present study, we assessed the ability if cord albumin in assessing and acting as a tool for screening for neonatal jaundice. Albumin in a neonate is the major binder of bilirubin and decrease the binding and transport of it.[7] In the study a total of 110 babies were registered. Out of this 58(52.73)% were female and 52(47.27%) were male. There was no significant difference in the number of male and female babies. However, studies done by Satrya and Maisels and Kring had showed that male babies are at a higher risk of developing icterus and subsequent intervention for icterus.[8,9] But the presentation study is in correlation with study done by Taksande et al which states that there is no relation between neonatal hyperbilirubinemia and the sex of the baby.[10] Similar types of sex distribution are reported in various studies while few studies document that females outnumbered the males.[11-13]

In this study, it was noted that the gestational age at which the baby was born had a positive correlation with the presence lower albumin levels. It was noted that lower the gestational age higher was the chance of the baby developing icterus.

In this study 59 babies were born by normal vaginal delivery and 51 were born by LSCS and there was no significant difference between the babies developing icterus based on the mode of delivery. This was in correlation with the studies done by Sun G et al and Sahu et al.[14,15] When the birth weight of the neonate was considered it was seen that babies born with lower weight had a significantly higher chance of developing of icterus and the babies mostly had low cord albumin levels. Whereas previous studies by

Knusden et al, Awathi and rehman had stated that there was no significant correlation between the birth weight and low cord albumin values.[16,17]

Out of 110 babies, 53 babies developed icterus. Under group 1, 36(67.92%) babies developed icterus and under group 2, 17(32.08%) babies developed icterus. The total bilirubin levels were significant in Group 2 ($p<0.001$). 19 babies of the 53 with icterus required phototherapy and it was noted that majority of these babies were from group 2 ($p<0.05$). Trivedi et al, in their study involving 605 neonates had concluded that majority of the infants who required phototherapy had a cord albumin level lower than 2.8 mg/dl.[18] Suchanda et al in a study of 40 neonates found that 80% neonates with cord albumin less than 2.8 mg/dl required phototherapy.[15]

In our study, the sensitivity of cord albumin to detect hyperbilirubinemia in newborn was determined and found to be 74.55%, while specificity was 63.64%. The positive predictive value was found to be 42.73% and the negative predictive value was found to be 91.82%. The accuracy rate was 68.18%.

Pahuja M et al in their had noted that predictive value of cord albumin for development of neonatal hyperbilirubinemia was 75% which implies a fair predictive value of the criteria with 61.3% sensitive and 76.8% specific and is in correlation with the present study.[19] A study by Nahar et al showed cord bilirubin level >2.5 mg/dl had a sensitivity of 77%, specificity of 98.6% with negative predictive value of 96% which is in correlation with the present study.[20]

Sahu et al, showed that 70% newborn who developed significant Neonatal hyperbilirubinemia had cord albumin level <2.8 gm/dL, 30% newborn had cord albumin level 2.9-3.3 gm/dL and none of the newborns with cord albumin level >3.4 gm/dL developed hyperblirubinemia.[15]

Conclusion

Cord albumin levels help to determine and predict the possibility of hyperbilirubinemia among neonates. Hence this can help to identify the at-risk neonates. So, routine determination of cord albumin can be advocated to keep a track on at risk neonates.

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