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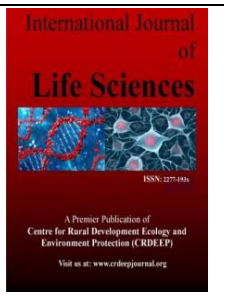

Full Length Research Paper

Predictive Value of Cord Blood Albumin level in Neonatal Hyperbilirubinemia

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ABSTRACT

Objective: To detect the correlation between cord blood albumin levels and development of neonatal jaundice (hyperbilirubinemia) in full term healthy neonates. Methods: this is a Prospective study was done on 90 term healthy term neonates at department of obstetrics and gynecology Al Azhar university Damietta from June 2018 to May 2020 taking into consideration the gender gestational age, anthropometric measurements. There was no other risk factor for hyperbilirubinemia detected in the neonates. The neonates were divided into two groups A and B based on the cord albumin levels of <2.8 mg/dl or >2.8 mg/dl. Results: 90 babies included in this study, 51 babies were under Group 1 and 39 under Group 2. 30 babies (34%) in group 1 and 28 babies (71.7%) in group 2 (p<0.0005) developed clinical icterus of which 16 in group 1 and 19 in group 2 required phototherapy (p<0.05). one baby in group 2 required exchange transfusion. The sensitivity and specificity of cord albumin level in detecting neonatal hyperbilirubinemia in this study was determined to be 70.8% and 64.1%, respectively. Conclusion: we can determine and predict the possibility of hyperbilirubinemiaamong neonates by Cord albumin levels. So this can help and identify the neonates who are at risk. So, routine determination of cord albumin can be advocated to keep a track on at risk neonates.

Introduction

In many countries neonatal Jaundice or icterus neonatrum has been developed in new-born babies. It was that first differentiated between true jaundice and the physiological yellowish tinge observed in many neonatesin the early 18th century by Juncker [1]. Hyperbilirubinemia is also the most common cause for readmission during the early neonatal period [1]. Approximately 50% of term and 80% of preterm newborns develop hyperbilirubinemia, which usually appears 2–4 days after birth, and resolves spontaneously after 1–2 weeks [2]. Because of the increasing number of early discharged newborns, there is a corresponding danger of failing to diagnose severe hyperbilirubinemia in time, as reports about kernicterus in full-term healthy newborns demonstrate [3]. In Egypt, it is common that infants are discharged at less than 24 h of age with little or no evaluation for the risk of developing jaundice or any instructions for follow-up. In fact, clinical or laboratory assessment of jaundice was almost nonexistent even among those who were discharged after the second day of life [4],

About 80% of the new-borns are developed neonatal hyperbilirubinemia and it is considered as the most common cause for admission to the hospital during this period [2]. Severe hyperbilirubinemia is when the total serum bilirubin [TSB] level is more than 20 mg per dL and it occurs in less than 2% of term infants and can lead to kernicterus. Hence it is important to evaluate all newborns for clinical signs of hyperbilirubinemia. The risk factors for the hyperbilirubinemia includesignificant bruising,early gestational age, cephalhematoma or, exclusive ineffective breastfeeding, and a family history of neonatal jaundice [3]. In addition to hyperbilirubinemia, preterm baby, hemolysis, sepsis, and IUGR are associated with the development of bilirubin encephalopathy. According to the guidelines set down by the American Academy of Pediatrics neonates discharged within 2 days of birth must report back for a follow-up visit within 48-72 h after discharge [4].

Physiological jaundice is a result of immature liver cell which have low uridine diphosphoglucuronosyl transferase activity when compared to mature hepatocyte, low concentration of albumin which is a bilirubin binding ligand and increased number of erythrocytes which have a shorter life span. Physiological jaundice is a normal response on the part of the baby due limitations in the ability to excrete bilirubin. Neonates develop an unconjugated hyperbilirubinemia due to increased level of unconjugated Bilirubin above 1.0 mg/dl. Early treatment with phototherapy is effective, simple and cheap.

This is the appropriate treatment for exaggerated neonatal jaundice [5]. Albumin synthesis occurring in the liver. It binds to unconjugated bilirubin and helps in the transport. This in turn reduces the bilirubin toxicity on the tissues and thus competing with

tissues for bilirubin binding. Extremely avid binding to albumin may be detrimental, however, because it limits the rate of hepatic removal of unconjugated bilirubin from the plasma [6,7].

Decrease production of albumin will lower its transport and binding capacity and hence determination of neonates who at risk early this will help to avoid the complications associated with neonatal jaundices [8]. It was noted that there is a intense decrease in the hospital stays of healthy neonates over the past. It also noted that the neonates that appear healthy are usually discharged within 48 hours of birth [9]. So it is important to define the neonates who are at risk for developing hyperbilirubinemia following an early discharge from the hospital. Henceforth, the present our study was directed in order to determine the correlation between cord albumin level and developments of neonatal hyperbilirubinemia.

Materials and Methods

This was prospective study and was conducted in the department of obstetrics and gynecology with pediatric department at Al Azhar University Damietta from June 2018 to May 2020. The study group consisted of 90 simultaneously born full term healthy neonates delivered at AL Azhar Hospital. Ethical clearance was obtained.

Ethical consideration

The study was approved by the Ethical Committee of Al Azhar university hospital, Damietta, and an informed consent was obtained from all participants' guardian before the study commenced.

Selection criteria for the patients

the participants included in this study were selected according to inclusion and exclusion criteria. A healthy term new-born during the study period were included in the study after obtaining consent from the parents. The inclusion criteria included neonates with gestational age 38 weeks or more, any mode of delivery, both sexes, APGAR score over 7 at the first minute and 10 at fifth minute of life, absence of significant illness, or a major congenital malformation.

Exclusion criteria

Conditions that aggravate hyperbilirubinemia as:

The Neonates with ABO or Rh incompatibility
Major anomalies
Cephalhematoma
Sepsis
Preterm babies
Respiratory distress syndrome
Infants of diabetic Mather
Hypoxia

All cases were subjected to the following:

Full history taking with emphasis on the antenatal and perinatal history (maternal illness, maternal drugs, and fever); risk factors for hyperbilirubinemia, for example, ABO or Rh incompatibility; and individual data from the mothers' medical records, for example, mode of delivery, the cause for lower segment cesarean section, recent and previous obstetric history, single or multiple pregnancies, and past medical history.

Full clinical examination immediately after birth such as general examination (vital signs, anthropometric measures, and presence of cephalohematoma), systemic examination (cardiac, abdominal, chest, and neurological examination), gestational age assessment using Ballard score, and clinical and laboratory follow-up for level of hyperbilirubinemia

Laboratory investigations: cord blood samples (3 ml) will be collected from all newborns that complied with the protocol inclusion criteria. The samples will be sent for the assaying of total, unconjugated, conjugated bilirubin and albumin levels and baby's blood group and rhesus.

All data will be calculated and entered into the Performa in which the mode of delivery,gestational age, gender, anthropometric measurements at birth, cord blood TSH, Cord blood albumin and total and direct bilirubin of the babies were measured.

Method of umbilical cord blood collection

After delivery of the newborn, the umbilical cord was double clamped and transected within 15 s. As soon as the newborn was removed from the operative field, cord blood was collected as follows. The placenta-side part of the umbilical cord was held straight at a slight angle downward. After identification of a suitable puncture site, the umbilical cord was cleaned, the umbilical vein was then punctured with sterile syringe, 3 ml of cord blood from umbilical vein collected in a test tube and was sent for lab for estimation of cord blood albumin and TSH. The Cord Albumin was assessed using the Biuret reaction technique using an automated analyzer. Neonateswill be examined daily for the presence of icterus up to the 5th day following which they were discharged. When detecting the presence of icterus, Blood was sent for the estimation of Total Bilirubin (TB) level and the results were planned on the chart to recognize the type of intervention the baby required. The 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.

Follow-up of babies was done after 72 h of age for serum bilirubin (total and direct) using a peripheral venous sample.

Statistical analysis

Results were analyzed and tabulated using Microsoft Excel version 2016 (Microsoft Corporation, New York, New York, USA) and SPSS v. 16 (SPSS Inc., Chicago, Illinois, USA). Qualitative data were expressed as number and percentage and quantitative data were expressed as mean ± SD and multiple regressions, and Wallis analysis of variance for comparing categorical data. Receiver operating characteristic (ROC) curve was constructed with area under curve analysis performed to detect best cut-off value of cord blood albumin and bilirubin for detection of positive cases. A value of P was less than 0.05 was indicated statistically significant.

Results

In this study a total of 90neonates were included. Out of this 52.2% were female and 47.7% were male. There was no significant difference in the number of male and female babies. According to the cord albumin levels the babies were grouped into two: >2.8 mg/dl (Group 1) and <2.8 mg/dl (Group 2). Lower normal limit for cord serum albumin in term babies is 2.8gm/dl [10].Group 1 included51 babies and in Group 2 included 39 babies. The mean gestational age was among Group 1 was 39.022 ± 1.144 weeks and Group 2 was 38.194 ± 2.039. We noted that babies born at a lower gestational age had a higher chance of having a low albumin value and subsequent hyperbilirubinemia (p=0.002). 41 babies were born by assistant vaginal delivery and 49 were born by LSCS and there was no significant difference between the babies developing icterus among 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**).

Variable	Group 1	Group 2	P value
Gestational age	39.022 ± 1.144	38.194 ± 2.039	0.002
Birth weight	3.042 ± 0.387	2.642 ± 0.544	<0.001
Length	47.5 ± 3.45	47.64 ± 2.30	0.239
Head circumference	34.68 ± 2.026	34.59 ± 2.468	0.805

Table 2. Gestational age and Anthropometric data

	Group 1	Group 2	P value
Cord TSH	10.384 ± 7.013	17.045 ± 6.220	<0.001

Table 3. Relation between cord TSH and cord albumin

	Group 1	Group 2	P value
Total number	30 (34%)	28 (71.7%)	<0.001
Total bilirubin value	28 (71.7%)	15.96 ± 3.960	<0.001
Direct Bilirubin Value	0.638 ± 0.199	0.6564 ± 194	0.714

Table 4. Relation between cord albumin and bilirubin

	Group 1	Group 2	P value
Neonates with Icterus	30	28	<0.0005
New-borns requiring phototherapy	16	19	<0.05

Table 4. Relation between cord albumin and interventions required

Items	Group 1(no 51)	Group 2 (no 39)	P value
Sex			
Male	23 (25.55%)	20 (22.22%)	<0.001
female	28 (31.11%)	19 (21.11%)	
Mode of delivery			
CS	26 (28.88%)	23 (25.55%)	<0.048
NVD	25 (27.77%)	16 (17.77%)	
Maternal RH			
Positive	49 (54.44%)	33 (36.66%)	<0.001
negative	2 (2.22%)	6 (6.66%)	
BABY RH			
Positive	45 (50%)	38 (42.22%)	0.038
negative	6 (6.66%)	1 (1.11%)	
Treatment			
Not	35 (38.88%)	19(21.11%)	0.014
Phototherapy	16 (17.77%)	19 (21.11%)	
Exchange transfusion		1 (1.11%)	

Discussion

There is no relation between the mode of delivery and the development of icterus and the cord albumin levels. in correlation with the other studies done by Sun et al. (15) and Sahu et al. it was noted that 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. Where previous studies by Knusden et al. (16), Awasthi et al.(16), had stated that there no significant correlation between the birth weight and low cord albumin values.

Of 90 neonates included in our study, 69.8% and 33.9% babies from group A and B developed icterus. In group a 75.9% required phototherapy and 48% required exchange transfusion while in Group B 14.7% required phototherapy and none underwent exchange transfusion. In other study by Trivedi et al. involving 605 neonates had concluded that majority of the infants who required phototherapy had a cord albumin level lower than 2.8 mg/dl. Sahu et al. (17) in a study of 40 neonates found that 80% neonates with cord albumin less than 2.8 mg/dl required phototherapy.

Regarding the levels of cord blood albumin, the current study showed that at cord albumin levels less than 2.8 g/dl, 81.8% (27 cases) of cases developed significant hyperbilirubinemia. At cord albumin 2.8–3.3 g/dl, 46.9% of cases developed significant hyperbilirubinemia, whereas levels greater than 3.3 g/dl were considered safe, with no incidence of hyperbilirubinemia. Our study results are similar to many other studies, where at cord serum albumin levels less than 2.8 g/dl, 58.35% [9], 82% (12) and 95% [8] of newborns developed significant hyperbilirubinemia in all of the aforementioned studies. At levels greater than 3.3 g/dl, no infants developed hyperbilirubinemia. However, in the study by Trivedi et al. [9], 12.68% developed hyperbilirubinemia at cord serum albumin greater than 3.5 g/dl.

Pahujaet al. (15) 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. A study by Nahar et al. (16) 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. Sahu et al. (16) showed that 70% new-born who developed significant Neonatal hyperbilirubinemia had cord albumin level <2.8 g/dL, 30% new-born had cord albumin level 2.9-3.3 g/dl and none of the new-borns with cord albumin level >3.4 g/ dL developed hyperbilirubinemia. In this study it was noted that between cord albumin and development of neonatal hyperbilirubinemia (p value <0.001) there was a significant correlation. Trivedi et al. (16) studied a total of 605 new-borns. Off these, 205 new-borns developed significant neonatal hyperbilirubinemia in study group with 58.35% (120/205) of the neonates with cord albumin level <2.8 g/dl developing significant neonatal hyperbilirubinemia ($P \leq 0.05$). Our study results correlated with these studies.

Despite most of the studies confirming the usefulness of CB in predicting the development of hyperbilirubinemia, it was concluded from a previous study by Carbonell et al. (15) that CB level of 2.2 mg/dl showed scant sensitivity (22.2%) but a high NPV (97.4%), which excluded CB as a useful predictor of subsequent neonatal jaundice. Moreover, another study carried out by Rostami and Mehrabi (6) concluded that assessment of CB level could not help identifying newborns with neonatal hyperbilirubinemia

Conclusion

Using Cord Albumin levels in a healthy term neonate can predict the possibility of the neonatal hyperbilirubinemia. This can help to determine the neonates who are at a higher risk for developing jaundice. predictive value less than 2.8 mg/dl has found to be more associated with clinical icterus. So routine determination of cord albumin along with TSH can be determining the neonates who are developing jaundice.

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