# Cord Blood Albumin as a Predictor of Neonatal Jaundice

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## ABSTRACT

**Background:** Neonatal jaundice is a very common condition worldwide occurring in up to 60% of term and 80% of preterm newborns in the first week of life. Even though extreme hyperbilirubinemia is rare in developed countries it is still quite rife in developing countries often resulting in kernicterus with its attendant medical, economic and social burden on the patient, family and society.

**Objective:** The present study was conducted to evaluate the predictive value of umbilical cord blood albumin level for subsequent neonatal jaundice in healthy full-term neonates.

**Patients and Methods:** The current study was carried out in the Pediatric Department, Faculty of Medicine, Aswan University Hospital. The study was conducted on 100 healthy full-term newborn after obtaining consent from parents. Cord blood was collected at birth and cord blood albumin estimation was done.

**Results:** The incidence of neonatal hyperbilirubinemia in our study (64%). In terms of demographic data: males represented (32.5 %) of the jaundiced cases in the study and females represented (62.5 %); the difference was statistically insignificant (P value 0.325). Cord serum albumin level of (> 3.3) g/dl has a sensitivity of (86%) and specificity of (80%), PPV (81%), NPV of (85%) and the accuracy rate was (83 %) in predicting neonatal hyperbilirubinemia.

**Conclusion:** There is significant correlation between cord serum albumin level and neonatal hyperbilirubinemia in healthy full-term neonates ≥ 2.5 kg birth weight and that serum albumin level taken from the blood of the umbilical cord is an effective way to predict neonatal hyperbilirubinemia in term healthy infants.

**Keywords:** Cord Blood Albumin, Predictor of Neonatal Jaundice, Hyperbilirubinemia.

## INTRODUCTION

Bilirubin is a yellow colored pigment which is produced from hemoglobin during destruction of erythrocyte. So increased production, impaired uptake of bilirubin by liver and ineffective conjugation causes increase level of unconjugated bilirubin leading to hyperbilirubinemia [(1)].

Bilirubin is non-polar, insoluble in water and is transported to the liver bound to serum albumin. Bilirubin that is bound to albumin does not usually enter the central nervous system. Hence it is thought to be non-toxic. Free bilirubin circulates in the body when the level of albumin is low and this is toxic to the body [(2)].

Liver is the site of synthesis of albumin. It binds to unconjugated bilirubin and helps in the transport. This in turn reduces the bilirubin toxicity on the tissues and thereby competing with tissues for bilirubin binding [(3)].

Clinical guide to the level of jaundice which was originally described by Kramer as the dermal staining of bilirubin may be used and confirmation can be done by measuring the levels of bilirubin. Dermal staining in an infant advance in a cephalo-caudal direction. The skin should be blanched with digital pressure and the underlying color of the skin should be analyzed. It gives a rough guide for the level of bilirubin dermal staining (Face 4-6 mg/dl, Chest and upper abdomen 8-10 mg/dl, Lower abdomen and thighs 12-14 mg/dl, Arms and lower legs 15-18 mg/dl, Palms and soles 15-20 mg/dl) [(2)].

In term babies physiological jaundice is seen to appear between 36 to 72 hours of age, maximum intensity of jaundice is seen on 4$^{th}$ day of life. Physiological jaundice never appears before 24 hours of life. In certain conditions, the bilirubin levels may exceed this duration and may cause complications like brain injury which can be prevented if detected and treated early with simple treatments like phototherapy [(2)].

The American Academy of Pediatrics (AAP) recommends that newborns discharged within 48 hours should have a follow-up visit after 48-72 hours to detect significant jaundice and other problems [(4)].

In developing countries, this recommendation is not practical due to limited follow up facilities. Severe jaundice and kernicterus has been found in some healthy full term newborns discharged early with no apparent hemolysis. It is difficult to predict which of these newborns are at risk for developing significant hyperbilirubinemia (Total serum bilirubin ≥ 15 mg/dl) [(5)].

Thus, the concept of prediction of jaundice offers an attractive option to pick up babies at risk of neonatal hyperbilirubinemia in order to implement early





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treatment and thereby minimize the risk of bilirubin dependent brain damage [6].

There is paucity of studies on cord blood albumin levels as a predictor of neonatal hyperbilirubinemia.

Study of **Sahu *et al.*** [7] conducted on neonates and suggested that infants with low levels of cord albumin showed high bilirubin level and needed intensive phototherapy than those with high albumin level.

Study of **Reshad *et al.*** [6] showed that cord blood albumin can be used as a 'surrogate marker' for screening the newborns for development of neonatal hyperbilirubinemia.

**Aiyappa *et al.*** [3] in their study involving healthy neonates had concluded that majority of the infants who required phototherapy had a cord albumin level lower than 2.8 mg/dl and that cord albumin levels in a healthy term neonate helps to predict the possibility of the neonate having hyperbilirubinemia.

The purpose of this study is to evaluate the predictive value of umbilical cord blood albumin level for subsequent neonatal jaundice in healthy full-term neonates in order to early detection of hyperbilirubinemia and to implement the appropriate therapeutic strategies to prevent bilirubin induced neurologic damage.

## PATIENTS AND METHODS

The study is a prospective clinical study which carried out in Pediatric Department, Faculty of Medicine, Aswan University Hospital. The study included 100 healthy full-term neonates delivered in the hospital after obtaining consent from parents.

**Inclusion criteria:** Healthy term babies ≥37 weeks of both genders with any mode of delivery, birth weight ≥ 2.5 kg. and Apgar score more than 7 at 1 minute and 5 minutes of life.

**Exclusion criteria:** Preterm < 37 weeks, multiple pregnancies, neonates with ABO or Rh incompatibility, neonatal jaundice within 24 hours of life, significant illness requiring NICU admission (neonatal sepsis, birth asphyxia, respiratory distress, IDM and meconium aspiration), major congenital malformations, instrumental delivery, cephalohematoma, history of intake of drugs affecting fetal liver and those who didn't give consent.

**Methods:**

**History:** Maternal informations was collected by interviewing the mother and from mother's case sheet with particular emphasis on: maternal mode of delivery, parity, gravidity, blood group, previous abortion, type of feeding and history of previous sibling affected.

**Physical examination:** Complete clinical examination to all systems was done to all neonates. Gestational age was assessed by New Ballard score. Apgar score and weight of the newborn were recorded.

**Laboratory investigations:** Mother's blood group and Rh factor were done before delivery. Cord blood samples (2 ml) were collected from all newborns that complied with the protocol inclusion criteria.

**Method of umbilical cord blood collection:**

After delivery of the newborn, the umbilical cord was double clamped and transected within 10 seconds. As soon as the newborn was removed from the operative field, cord blood was collected as follows:

- The placental 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.
- Approximately 2 ml of blood were withdrawn from umbilical vein then put in a plain tube to be separated by centrifuging and then the serum was tested for albumin [8].
- **Cord blood albumin:**
  Albumin analyzed by semi-automated spectrophotometer by quantitative colorimetric method [8].

All enrolled babies were followed up for 5 days and clinically assessed for jaundice according to Kramer dermal scale. The babies were followed up daily and interventions undertaken as per hyper-bilirubinemia American Academy of Pediatrics guidelines for management of neonatal hyperbilirubinemia.

**Venous blood samples were collected from all neonates at 72-96 hours of life. These samples subjected to the following investigation:**

a) Total serum bilirubin.
b) Direct serum bilirubin.
c) Complete blood count with reticulocyte count.
d) Blood group and Rh factor.

- **Serum bilirubin (total, direct and indirect):**
  Bilirubin level was estimated using the automated chemistry analyser (BT-3500) [9].

- **CBC and reticulocytic count:**
  Complete blood picture was done on automated cell counter (Sysmex-XP 300) with complete red blood cell indices assessment (RBCs count, Hct, MCV, MCH, MCHC and RDW). Manual reticulocytic count was done using Brilient Cresyle blue stain [10].

  A complete blood count or CBC is a blood test that provides several pieces of information about a person's state of health based on the content of certain components within the blood. The CBC is one of the most routinely performed laboratory tests. It is a valuable screening tool for a wide variety of disorders, including:

  a) Anaemia
  b) Infection
  c) Blood diseases [10].

- **Blood group of newborn:**
  Analysed by antisera method: Babies' blood groups were identified manually using both anti-A and anti-B sera against the babies' serum and also rhesus D blood group analysis were made manually [8].

**Ethical consideration:**

**The current study received approval from the Ethics Committee of the Faculty of Medicine, Aswan University.** The steps of the study, the aims, the potential benefits and dangers, all were discussed for each child with his/her legal guardian. Each patient's care-giver was required to sign a written consent form before starting the study. Confidentiality was assured for all patients. The legal guardian had the right to withdraw his/her newborn from the study at any time with neither jeopardizing the right of the newborn to be treated nor affecting the relationship between the newborn and the care provider.

***Statistical analysis***

Recorded data were analyzed using the statistical package for the social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage. Independent-samples t-test of significance was used when comparing between two means. Chi-square ($x^2$) test of significance was used in order to compare proportions between two qualitative parameters. The confidence interval was set to 95% and the margin of error accepted was set to 5%. The P-value <0.05 was considered significant. P-value <0.001 was considered as highly significant. P-value >0.05 was considered insignificant.

**RESULTS**

A total of 131 cases were delivered and parents gave consent, out of which 31 cases did not meet inclusion or met exclusion criteria or they did not complete the follow-up. Samples collected from these cases were discarded.

Table (1) shows that: There was no statistically significant relation between jaundice and gestational age/week, sex of newborns, birth weight. There was statistically significant relation between jaundice and cesarean section (C.S.).

**Table (1): Socio-demographic and obstetric data differences between not jaundiced and jaundiced Cases.**

| | Non-Jaundiced (No.=36) | Jaundiced (No.=64) | P-value |
|---|---|---|---|
| **Gestational Age/weeks** | 38.33 ± 1.0 | 38.30 ± 1.1 | 0.893 |
| **Sex** | | | 0.325 |
| **Male** | 10 (27.8%) | 24 (37.5%) | |
| **Female** | 26 (72.2%) | 40 (62.5%) | |
| **Mode of Delivery** | | | |
| **C.S.** | 23 (63.9%) | 55 (85.9%) | **0.011** |
| **Vaginal** | 13 (36.1%) | 9 (14.1%) | |
| **Birth Weight (Mean ± SD)** | 3.11 ± 0.2 | 3.07 ± 0.3 | 0.476 |

Table (2) shows that: There was no statistical significant relation between jaundice and maternal age/years or exclusive breast feeding. Statistically significant association was found between jaundice and gravidity and parity. The most risk factor which may affect the appearance of jaundice was previous sibling affected with jaundice and those previous siblings who received phototherapy.

**Table (2): Maternal and Clinical Data Differences between Not jaundiced and Jaundiced Cases.**

| | Not jaundiced (No.=36) | Jaundiced (No.=64) | P-value |
|---|---|---|---|
| **Maternal Age/years** | 27.17 ± 4.5 | 25.53 ± 3.8 | 0.056 |
| **Gravidity (Mean ± SD)** | 2.81 ± 1.3 | 2.17 ± 0.9 | **0.006** |
| **Parity (Mean ± SD)** | 2.42 ± 1.0 | 1.97 ± 0.9 | **0.028** |
| **Exclusive BF** | | | |
| No | 24 (66.7%) | 39 (60.9%) | 0.569 |
| Yes | 12 (33.3%) | 25 (39.1%) | |
| **History of Previous Sibling Affected with Jaundice (n=74)** | | | |
| No | 25 (80.6%) | 8 (18.6%) | **< 0.001** |
| Yes | 6 (19.4%) | 35 (81.4%) | |
| **History of Previous Sibling Received Phototherapy (n=42)** | | | |
| No | 6 (100%) | 26 (72.2%) | **< 0.001** |
| Yes | 0 (0%) | 10 (27.8%) | |

Depending on the cord albumin levels the babies were grouped into 3 groups (Table 3).

**Table (3)** shows that: All the 17 neonates in group 1 were icteric. Out of the total 40 neonates in group 2 were icteric. Out of the total 43 neonates in group 3 were icteric.

**Table (3)**: **Groups based on serum albumin level.**

| Cord blood albumin levels | Group 1 <2.8 g/dl (n=17) | Group 2 2.8-3.3 g/dl (n= 40) | Group 3 >3.3 g/dl (n= 43) |
|---|---|---|---|
| **Neonates developing hyperbilirubinemia (%)** | 17 (100%) | 34 (85%) | 13 (30.23%) |
| | P1 0.079 | P2 **<0.001** | P3 < **0.001** |
| **Number of newborns requiring phototherapy (%)** | 16 (94.1%) | 6 (15%) | 0 |
| | P1 **<0.001** | P2 **<0.001** | P3 **<0.001** |
| **Number of newborns requiring exchange transfusion (%)** | 1 (5.88%) | 0 | 0 |
| | P1 0.096 | P: Non applicable | P **<0.001** |

**P1** *comparison between group 1 and group 2*
**P2** *comparison between group 2 and group 3*
**P3** *comparison between group 1 and group 3*

**Table (4) shows that:** Mean value of Cord blood Albumin in non-jaundiced cases was statistically significantly higher than jaundiced cases. There was no statistically significant relation between jaundiced and not jaundiced as regards hemoglobin (Hb), hematocrit Hct), reticulocytes, platelets, and total leucocytes Count.

**Table (4): Cord blood albumin and other laboratory data characteristics in not jaundiced and jaundiced cases.**

| | | Not jaundiced (No.=36) | Jaundiced (No.=64) | P-value* |
|---|---|---|---|---|
| **Cord Blood Albumin** | **Mean ± SD** | **3.60 ± 0.3** | **3.03 ± 0.4** | **< 0.001** |
| **Hb (g/dL)** | **Mean ± SD** | 16.06 ± 0.9 | 16.19 ± 0.8 | 0.458 |
| **Hct** | **Mean ± SD** | 46.89 ± 2.8 | 46.54 ± 3.1 | 0.580 |
| **Reticulocytes** | **Mean ± SD** | 1.76 ± 0.3 | 1.71 ± 0.3 | 0.694 |
| **Platelet $10^3$/µl** | **Mean ± SD** | 293.11 ± 6.1 | 280.08 ± 6.2 | 0.325 |
| **Total Leucocytes Count $10^3$/µl** | **Mean ± SD** | 16.50 ± 3.1 | 16.28 ± 3.3 | 0.744 |

**Table (5) shows that:** Cord blood albumin correlates positively and significantly with birth weight/kg, time of jaundice appearance/hours. On the other hand, cord blood albumin correlates negatively and significantly with TSB level.

**Table (5): Correlations of cord blood albumin and clinical and laboratory parameters in all patients (n = 100)**

| Parameter | Cord Blood Albumin | |
|---|---|---|
| | r* | P-value |
| **Gestational Age/weeks** | 0.028 | 0.392 |
| **Birth Weight/kg** | **0.211** | **0.018** |
| **Maternal Age/years** | 0.005 | 0.482 |
| **Gravidity** | 0.020 | 0.420 |
| **Parity** | -0.008 | 0.468 |
| **Time of Jaundice Appearance/hours** | **0.416** | **< 0.001** |
| **TSB** | **-0.684** | **< 0.001** |
| **Haemoglobin gm/dl** | -0.085 | 0.202 |
| **Hct** | -0.041 | 0.343 |
| **Reticulocytes** | 0.041 | 0.343 |
| **Platelet Count $10^3$/µl** | 0.239 | 0.808 |

| | | |
|---|---|---|
| **TLC $10^3$/µl** | 0.005 | 0.479 |

Table (6) shows that the area under the curve (AUC) of cord blood albumin was 0.847.

**Table (6): Diagnostic performance of cord blood albumin for diagnosis of Neonatal Jaundice, analyzed as area under the curve (95% CI)**

| | AUC* | SE** | P-value | 95% CI+ |
|---|---|---|---|---|
| **Cord ALP** | **0.847** | **0.040** | **< 0.001** | **0.768 - 0.925** |

***AUC = Area under the Curve**
****SE = Standard Error +CI = Confidence Interval**

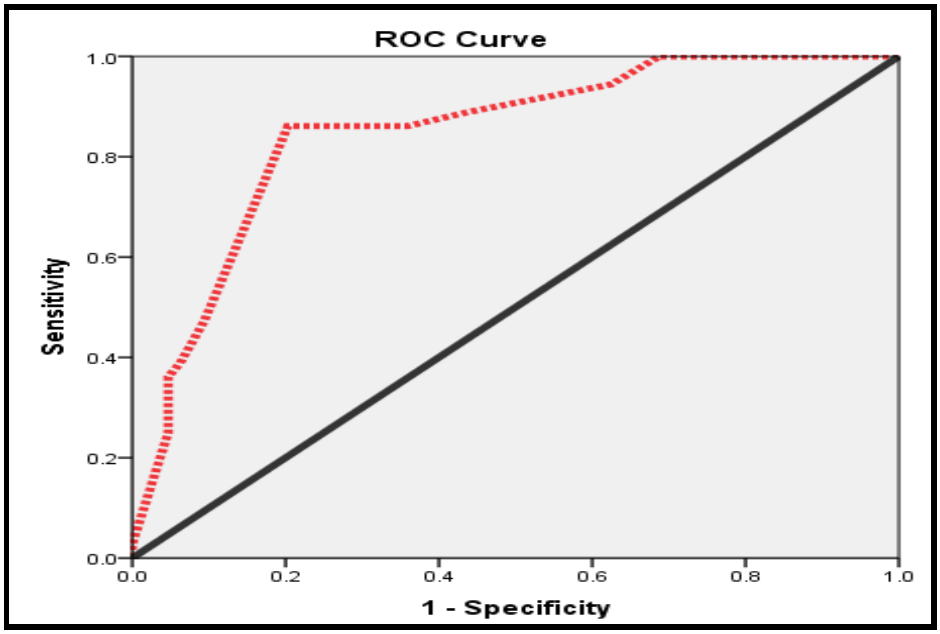


**Figure (1): ROC curve for cord blood albumin for diagnosis of neonatal jaundice in the studied cohort**

**Table (7) shows:** Goodness criteria of cord blood albumin for diagnosis of neonatal jaundice in the studied sample: **Cut off value** of cord blood albumin was 3.3

**Table (7): Goodness criteria of cord blood albumin for diagnosis of neonatal jaundice in the studied sample**

| Goodness Criteria | Cord Blood Albumin |
|---|---|
| **AUC** | **0.847** |
| **Cut-off** | **3.3** |
| **Accuracy** | **83%** |
| **Sensitivity, %** | **86%** |
| **Specificity, %** | **80%** |
| **PPV, %** | **81%** |
| **NPV, %** | **85%** |

PPV: positive predictive value NPV: negative predictive value

## DISCUSSION

We found neonatal hyperbilirubinemia in 64% of cases; 22% of infants underwent phototherapy; 1% of infant underwent exchange transfusion and 77% needed no intervention at all. We report a quite high incidence of neonatal hyperbilirubinemia in our study. This high incidence is similar to previous studies in Egypt as **Khairy *et al.*** [10] (67.9%) and **Alalfy *et al.*** [8] (56%). Many other studies have reported a lower incidence, **Kumar *et al.*** [11] (10%) and **Thakur *et al.*** [12] (9.3%). This difference may be attributed to the differences in racial and ethnic groups in different populations studied for jaundice.

In terms of socio-demographic and obstetric data, the mean gestational age of our study population was 38.11 ±1.1 weeks, their mean birth weight was 3.08 ± 0.3 kg, males represented 32.5 % of the jaundiced cases in the study and females represented 62.5 %; with no statistically significant relation between jaundice and sex of newborns. The present study is in correlation with the study done by **Rajpurohit *et al.*** [4] who assessed predictive value of cord blood bilirubin and albumin for significant neonatal hyperbilirubinemia in which the study group was uniformly distributed with 110 male and 90 female babies and there was no significant correlation between the development of neonatal hyperbilirubinemia and the sex of the newborn. Also, this was in agreement with a study carried out by **Reshad *et al.*** [6] who studied cord blood albumin as a predictor of significant neonatal hyperbilirubinemia in term and preterm neonates and has found no statistical significance in the gender of his study newborns. The study done by **Aiyappa *et al.*** [3] showed that there is no correlation between the neonatal hyperbilirubinemia and the sex of the new born.This was in disagreement with a study carried out by **Satrya *et al.*** [13], that showed significant correlation between the sex of the newborn and neonatal hyperbilirubinemia; with p value <0.05 in 88 healthy term newborn in which there were more males than females among jaundiced cases. This could be explained on the basis that in developing countries male neonates are taken care more in comparison to the female neonate because of gender discrimination prevalent in society of the developing countries. But, unlike **Keren *et al.*** [14] study, who conducted a prospective cohort study of 823 term and near-term newborns admitted to the well-infant nursery and found that female gender was associated with an increased, rather than decreased, risk of hyperbilirubinemia that is explained by his limited samples included.

Our study showed no statistically significant difference between the jaundiced and the non-jaundiced cases regarding the gestational age. This came in agreement with the study of **Bilgin *et al.*** [15] that showed that there was no correlation between the neonatal hyperbilirubinemia and the gestational age of the newborn (p>0.05). While was incompatible with **Newman *et al.*** [16] who studied 51387 newborns born at 36 weeks or later found that gestational age was the strongest predictor of significant hyperbilirubinemia. Also, our study was in disagreement with the study done by **Aiyappa *et al.*** [3] in which it was noted that the lower the gestational age the higher was the chance of the baby developing icterus.

In the present study association between the neonatal hyperbilirubinemia and the mode of delivery was studied as there was statistically significant relation between jaundice and C.S. This was consistent with **Eskicioğlu *et al.*** [17] study in which a total of 511 neonates delivered by vaginal route or cesarean section were included in the study, stated that total bilirubin levels in the first 24 hours for C/S groups were significantly higher than vaginal delivery groups. Also, our study was in agreement with **Ozdemirci *et al.*** [18] study that found that the ratio of hyperbilirubinemia in the cesarean group was higher than that of the neonates in the vaginal group. This in disagreement with **Dhanjal *et al.*** [19] study, in which out of 316 babies 163 (51.58%) babies were born by LSCS and 153 (48.42%) were vaginally delivered, with no significant difference among the babies developing neonatal hyperbilirubinemia based on the mode of delivery. Also, our results disagreed with **Bilgin *et al.*** [15] study**,** who reported that the mode of delivery is not a risk factor for rate of hyperbilirubinemia. But unlike **Han *et al.*** [20] study who showed that peak serum bilirubin was significantly higher in neonates delivered by vaginal delivery and are supposedly explained by placental transfusion or timing of cord clamping.

The age of onset of jaundice in our study in majority of neonates was on 3$^{rd}$ and 4$^{th}$ postnatal day (mean 69.58 ± 19.3 hours). This was in agreement with the study done by **Meena *et al.*** [21] in which the mean age of onset of jaundice was 72 ± 16.8 hrs. Also, it is in agreement with **Trivedi *et al.*** [22] who found that among 205 babies who exhibited hyperbilirubinemia, 83.80% babies developed jaundice in the range of 3$^{rd}$ to 5$^{th}$ day and this supports the observation of **American Academy of Pediatrics (AAP)**[23] that non-hemolytic jaundice in term babies appears mostly on 3$^{rd}$ day of life because of increase production of bilirubin, delayed maturation of liver enzymes and increased enterohepatic circulation.

In our study we found that cord blood albumin in jaundiced cases was statistically significantly lower than non-jaundiced cases and our data clearly demonstrated that there was negative significant correlation between cord blood albumin and total serum bilirubin level. This means that the lesser the

cord serum albumin levels the more was the chances of newborns developing hyperbilirubinemia. But there was no significant difference as regard to hemoglobin, Hct, Reticulocyte count, PLT and TLC. This was in agreement with studies done by **George *et al.* [2], Reshad *et al.* [6], Alalfy *et al.* [8], and Dhanjal *et al.* [19],** as they concluded that there is significant correlation between cord serum albumin level and neonatal hyperbilirubinemia in healthy full term neonates >2.5 kg birth weight and that serum albumin level taken from the blood of the umbilical cord is an effective way to predict neonatal hyperbilirubinemia in term healthy infants.

The correlation between birth weight and cord serum albumin groups in our study was statistically significant. Came in agreement to our results the study done by **Dhanjal *et al.* [19]** who stated that lower the birth weight, the lower are the cord serum albumin levels. Also, it came in agreement with **Aiyappa *et al.* [3]** who stated 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.

In our study no significant relationship was found between cord blood albumin levels and other variables like sex, mode of delivery, gestational age, mode of feeding, maternal age and parity. Similar results were reported by **Meena *et al.* [21]** and **Reshad *et al.* [6].**

According to the levels of cord blood albumin our study cohort (100 neonates) were grouped into Group 1, Group 2, Group 3, based on cord serum albumin level (< 2.8 g/dl), (2.8-3.3 g/dl) and (> 3.3 g/dl) respectively. 100%, 85%, 30% newborns developed jaundice in group 1, 2, and 3 respectively. In group 1, 94.12% (16 cases) required phototherapy and 5.88% (1 case) required exchange transfusion. In group 2, 15% (6 cases) required phototherapy and no one required exchange transfusion, while in group 3 none of them required phototherapy nor exchange transfusion. Similarly, **Meena *et al.* [21]** study out of 100 neonates 95.5%, 79.4%,36.4% newborns developed jaundice in group 1, 2, and 3 respectively. In group 1, (81.8%) required phototherapy and (8.2%) required exchange transfusion. In group 2, (26.5%) required phototherapy and no one required exchange transfusion, while in group 3, only (2.3%) required phototherapy and none of them required exchange transfusion. In **Alalfy *et al.* [8]** study at cord albumin < 2.8 g/dl; (81.8%) of cases (27 cases) developed neonatal hyperbilirubinemia, with (75.8%) of them (25 cases) needed phototherapy and about (6.1%) (2 cases) needed exchange transfusion. At cord albumin 2.8-3.3 g/dl; (46.9%) of cases (15 cases) developed neonatal hyperbilirubinemia requiring phototherapy for all of them with no need for exchange transfusion. At cord albumin > 3.3 g/dl; no cases developed neonatal hyperbilirubinemia that requiring any intervention. The present study is in correlation with these studies. When 3.3 gm/dL of cord blood albumin was taken as cut off, to predict neonatal jaundice at birth, it is clear from data that those with <3.3 gm/dl cord blood albumin group were at increased risk of developing neonatal jaundice requiring phototherapy when compared with those infants with >3.3 gm/dl albumin group. Neonates with umbilical cord blood albumin level more than 3.3 gm/dl can be safely discharged early whereas neonates with albumin levels <3.3 gm/dl will need a close follow up to check for development of jaundice.

While analysing the diagnostic predictability of cord serum albumin levels for neonatal hyperbilirubinemia in our study, the sensitivity was (86%) and the specificity was (80%). The positive predictive value was (81%) and the negative predictive value was (85%). The accuracy rate was (83 %) and the same has been depicted in ROC curve (AUC = 0.847). **Alalfy *et al.* [8]** performed a ROC curve analysis to find a cut-off point level of cord blood albumin for development of neonatal hyperbilirubinemia. It was 2.75 g/dl; with a low sensitivity (64.3%), (81.8%) specificity, PPV (81.8%) and NPV (64.3%). **Aiyappa *et al.* [3]** reported the sensitivity of cord albumin to detect hyperbilirubinemia in newborn was determined and found to be (71.8%), while specificity was (65.1%). The positive predictive value was (38.9%) and the negative predictive value was (88.2%). The accuracy rate was (67.3 %) and the area under the ROC was (0.684).

Various tests were studied to predict hyperbilirubinemia in healthy full term newborns. **Banasia *et al.* [24]** used the cord blood bilirubin level to predict subsequent neonatal hyperbilirubinemia in a healthy term infants who require phototherapy. By a cord bilirubin cut-off level of 2.15 mg/dl; this revealed a sensitivity of (65%), specificity of (65%) and a negative predictive value (81%). **Khairy *et al.* [10]** suggested that, the bilirubin/albumin ratio (B/A) might provide a better estimate of free bilirubin (Bf) because it contains 2 of the 3 factors determining Bf (TSB, albumin and the albumin binding affinity). However, the value of B/A ratio may be reduced because of some factors that influence the intrinsic albumin-bilirubin binding constant (it may be decreased by drugs (e.g. ceftriaxone) and the presence of other plasma constituents that bind unconjugated bilirubin (as apolipoproteins and alfa fetoprotein) and they concluded that cord bilirubin/albumin ratio cut off value > 0.61 had a good predictive value with a sensitivity of 100% and specificity of 88.4%. Cord blood alkaline phosphatase level used as predicting marker for neonatal jaundice with sensitivity and specificity of 80% and 63% respectively in cut off

level > 314 IU/L [25]. A cut-off level of haptoglobin in cord blood of 7.5 mg/dl was determined to have sensitivity (100%), specificity (81%), and positive predictive value (89%) in the prediction of occurrence of neonatal hyperbilirubinemia [26]. **Riskin *et al.*** [27] checked umbilical cord alfa fetoprotein (UCAFP) as a marker of hepatic immaturity in 174 term babies to predict an increased risk for neonatal hyperbilirubinemia. Mean UCAFP was 60.2±45.9 mg/L. Its levels were linearly correlated with subsequent bilirubin levels, and statistically significantly higher bilirubin levels were found in neonates whose UCAFP levels were ≥100 mg/L. But in spite of significant correlation between UCAFP and subsequent bilirubin levels this was not recommended for use in clinical practice because of its inability to serve as a screening tool for hyperbilirubinemia in the new-borns. **Chou *et al.*** [28] measured cord blood hydrogen peroxide level for prediction of neonatal hyperbilirubinemia. The cord blood hydrogen peroxide signal level of 2500 counts/10 seconds was an appropriate cutoff for predicting severe hyperbilirubinemia with sensitivity and negative predictive value of 6.2% and 93.3%, respectively.

## CONCLUSION AND RECOMMENDATIONS

Neonatal Hyperbilirubinemia is one of the most common and major issues during the neonatal period.

In the present study, there is significant correlation between cord serum albumin level and neonatal hyperbilirubinemia in healthy full-term neonates ≥ 2.5 kg birth weight and that serum albumin level taken from the blood of the umbilical cord is an effective way to predict neonatal hyperbilirubinemia in term healthy infants.

Neonates with umbilical cord blood albumin level more than 3.3 gm/dl can be safely discharged early as 85% 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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