



Umbilical Cord Bilirubin Levels as a Predictor of Subsequent Development of Clinically Significant Neonatal Hyperbilirubinemia

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Abstract

Aims and Objectives: *To assess the usefulness of cord bilirubin level as a predictor of occurrence of clinically significant neonatal hyperbilirubinemia in healthy full term neonates.*

Study Setting and Design: *prospective cohort study conducted at a pediatric hospital over a period of 9 months.*

Materials and Methods: *A prospective cohort study was conducted on 60 consecutively born healthy term babies (gestational age > 37 weeks), irrespective of mode of delivery. The babies were divided into 4 groups A, B, and C, D and E depending upon cord blood bilirubin levels. All the neonates were examined daily clinically for development of clinically significant jaundice from birth to day 8 of life or till discharge from hospital whatever was later. If the clinical examination revealed clinically significant jaundice then immediate laboratory workup was done to determine the severity and type of hyperbilirubinemia. The baby was managed according to standard protocol of management. The data was analyzed and incidence of clinically significant jaundice requiring treatment for hyperbilirubinemia (phototherapy or exchange transfusion) in each group was calculated.*

Results: *During the study period 84 children were born in our hospital. Out of these 84 newborn babies 60 neonates were included in the study. 24 babies were excluded from the study because either they were preterm, had ABO or Rh incompatibility, birth asphyxia or congenital anomalies. Out of these 60 neonates 32 (53%) were males and 28 (47%) were females with a M: F ratio of 1: 0.88. Amongst the studied neonates 34 (56.66%) babies were delivered by normal vaginal deliveries, 22 (36.66%) were born by lower segment cesarean section (LSCS) and another 4 (6.66%) were delivered by assisted vaginal delivery (AVD). Since prematurity was an exclusion criteria all neonates were full term (> 37 weeks of gestational age). The birth weight of majority of the neonates was in between 2.1-2.5 kg. Cases were divided into 5 Groups depending upon the cord bilirubin level. Group A, B, C, D and E had 25, 13, 9, 5 and 2 newborns respectively. Amongst neonates in group A, 5 (20%) developed clinically significant jaundice, whereas 5 (38.46%) neonates in group B developed clinically significant jaundice. In group C, 5(55.56%) neonates developed clinically significant jaundice. In group D and E 4(80%) and 2 (100%) babies developed clinically significant jaundice.*

Conclusion: *Our study show that total serum bilirubin in cord blood can be used as a predictor of the development of clinically significant jaundice and need for treatment (phototherapy or exchange transfusion) in healthy full term neonates born by any mode of delivery.*

Keywords: *Cord bilirubin levels, clinically significant jaundice, phototherapy, Exchange transfusion.*

Introduction

Jaundice in neonates is a common occurrence. More than 50% of full term and around 80% of preterm babies develop some degree of jaundice in neonatal period ^[1]. While the most common cause of jaundice in newborns is physiological and doesn't need any active treatment there are conditions which may predispose a newborn for development of severe jaundice. Pathological jaundice leading to severe hyperbilirubinemia is a risk for newborn because unconjugated bilirubin can cross blood brain barrier and lead to neurological complications like kernicterus ^[2]. It is a common knowledge that more severe the hyperbilirubinemia more it is likely to cause complication in newborn. But various studies have shown that there is no "safe" level of hyperbilirubinemia and any neonate can get kernicterus. Various factors affecting the rate of complications due to hyperbilirubinemia in a particular newborn are birth weight, age of gestation, presence of Rh and ABO incompatibility and associated co-morbid conditions like sepsis, hypoalbuminemia and acidosis ^[3]. Given the condition of over-burdened health institutions in India it is not uncommon to discharge a healthy neonate who is taking proper breast feeding and have no active complaints on or after D3 of life. The American Academy of Pediatrics has recommended that all neonates who have been discharged within 2 days should have a follow-up visit after 2-3 days to detect clinically significant jaundice and other problems ^[4]. Though ideal this recommendation of American academy of pediatrics is sometimes not practical in our country due to lack of awareness amongst the parents and limited health care facilities especially in rural areas. For this reason the researchers have been trying to predict the risk of clinically significant jaundice in neonates so that at risk babies either will not be discharged or even if they are discharged then their parents could be forewarned and advised to remain in follow up ^[5]. In this regard hour specific percentile charts at different post natal ages have been developed.

These percentile charts help in prediction of clinically significant jaundice by plotting hour specific bilirubin levels on these charts. A total serum bilirubin level of more than 6mg/dl within 21 hours of birth was found to be associated with significant hyperbilirubinemia in neonates ^[6]. Cord bilirubin levels at birth as a predictor of later development of clinically significant hyperbilirubinemia requiring phototherapy or exchange transfusion have also been studied in many studies. The concept of predicting the chances of development of clinically significant hyperbilirubinemia is a very attractive proposition for pediatricians working in busy neonatology units as it can differentiate between low risk neonates who can safely be discharged from hospital and high risk patients who either need delayed discharge or a close follow up ^[7].

The present study was conducted to evaluate the predictive value of cord bilirubin levels in identifying neonates who are at risk of developing clinically significant hyperbilirubinemia requiring some or the other form of therapy like phototherapy or exchange transfusion.

Materials and Methods

This was a prospective cohort study comprising of full term newborn babies born by any mode of delivery. out of 84 consecutively born newborn babies 24 were excluded from the study because they were meeting one or more exclusion criteria. The babies were divided into 5 groups A, B, and C, D and E depending upon cord blood bilirubin levels. The cord bilirubin level was noted in all the neonates. All newborn babies were examined daily clinically for development of clinically significant jaundice from birth to day 8 of life or till discharge from hospital whatever was later. The clinical finding of significant jaundice if found was confirmed by appropriate laboratory tests. The tests were also done to determine the type, severity and complications of neonatal jaundice. The baby was managed according to standard protocol of management. The data was analyzed and incidence of clinically significant

jaundice requiring treatment for hyperbilirubinemia in each group was calculated.

Inclusion criteria:

1. All full term babies delivered by any mode of delivery
2. Gestational age should be 37 weeks or more.

Exclusion Criteria

1. Preterm babies (Gestational age < 37 weeks)
2. Birth asphyxia (Apgar score less than 7 at 1 minute)
3. Risk factors for development of pathological jaundice Rh or ABO incompatibility.
4. Any significant congenital anomaly.

Results

During the study period 84 children were born in our hospital. Out of these 84 children 24 were excluded from the study because they met one or more of the exclusion criteria ie either they were preterm, had birth asphyxia or some form of congenital anomaly. Out of 60 neonates included in the study 32 (53%) were males and 28 (47%) were females with a male to female ratio of 1: 0.88.

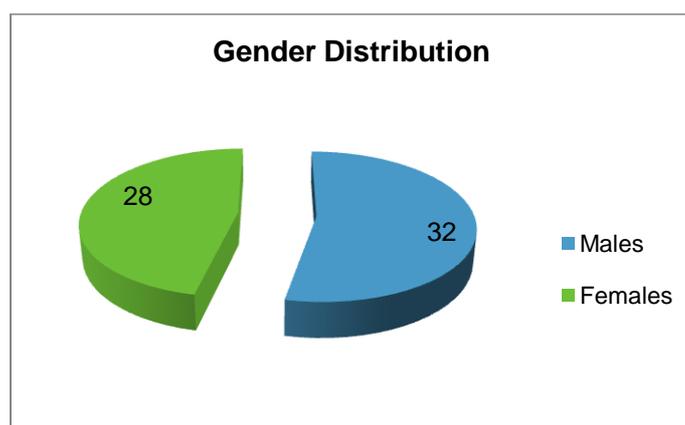


Figure 1: Gender distribution of the studied cases.

Out of the 60 neonates included in the study 34 (56.66%) babies were delivered by normal vaginal deliveries, 22 (36.66%) were born by lower segment cesarean section (LSCS) and another 4 (6.66%) were delivered by assisted vaginal

delivery (AVD). Since preterm babies, those with ABO and Rh incompatibilities were part of exclusion criteria hence there was no neonate belonging to this group in the studied cases.

Table 1: Mode of delivery of the studied cases.

Mode Of Delivery	Number of neonates	Percentage
Normal Vaginal Delivery	34	56.66%
Assisted Vaginal	22	36.66%
LSCS	4	6.66%

Since prematurity was one of the exclusion criteria in this study all studied cases had gestational age of more than 37 weeks. Low birth weight babies were included in this study. There were no babies having birth weight of less than 1.5 kg. 16 (26.66%) babies had birth weight in between 1.5 to 2 kg and 26 (43.33%) babies had birth weight in between 2.1 to 2.5 kg. 18 (30%) babies had birth weight more than 2.5 kg. All low birth weight babies included in this study were small for gestational age rather than premature because prematurity was an exclusion criteria of this study.

Table 2: Birth weight of the studied cases

Birth weight	Number of cases	Percentage
<1.5kg	0	0
1.5-2 kg	16	26.66%
2.1-2.5 kg	26	43.33
>2.5 kg	18	30%

Since Rh and ABO compatibilities are independent risk factors for neonatal hyperbilirubinemia and in these cases the neonates are usually not discharged early these cases were also excluded from the study and Rh and ABO incompatibility were exclusion criteria in our study. Moreover in cases of RH and ABO incompatibility the risk of hyperbilirubinemia is also modified by independent variables like parity of the mother, whether anti-D injections were taken after delivery of Rh positive baby in previous pregnancies and whether there is only isolated Rh incompatibility or there is combination of Rh and ABO incompatibilities.

The analysis of cord bilirubin levels showed that out of 60 studied cases out of 60 patients 25 (46.3%) patients had a cord bilirubin level between 1-1.5 mg/dl. 13 (24.07%) neonates had the cord bilirubin level of 1.6-2 mg/dl. 9 (16.67%) babies had cord bilirubin levels of 2.1-2.5 mg/dl while 5 (9.26%) babies had cord bilirubin between 2.1- 2.5gm/dl and 2 (3.7%) babies had cord bilirubin level above 3gm/dl.

Table 3. Cord bilirubin levels in the studied cases

Cord bilirubin levels	Number	Percentage
1-1.5 mg/dl	25	46.3%
1.6-2 mg/dl	13	24.07%
2.1- 2.5 mg/dl	9	16.67%
2.6 – 3 mg/dl	5	9.26%
> 3 mg/dl	2	3.7%

Most of the babies had a serum bilirubin level clustered between 1-2 mg/dl. The analysis of the studied cases for development of clinically significant jaundice within 1 week of birth and its correlation with cord bilirubin levels was done.

Out of 2 neonates having cord bilirubin level more than 3mg/dl, 2(100%) developed clinically significant jaundice and later was confirmed to be having level of hyperbilirubinemia requiring phototherapy. out of 5 patients having bilirubin levels 2.6 – 3 mg/dl 4 (80 %) developed clinically significant jaundice and required phototherapy. Out of 9 patients found to be having cord bilirubin levels of 2.1- 2.5 mg/dl 5 (55.56%) developed clinically significant jaundice requiring phototherapy. Out of 13 patients having cord bilirubin level 1.6-2 mg/dl 5 (38.46 %) developed clinically significant jaundice and lastly out of 25 neonates having cord bilirubin levels of 1-1.5 mg/dl 5 (20%) developed clinically significant jaundice requiring phototherapy. No neonate having cord bilirubin less than 1mg/dl developed clinically significant jaundice in this study. Out of 21 newborn babies who developed clinically significant jaundice 18 babies were treated with phototherapy

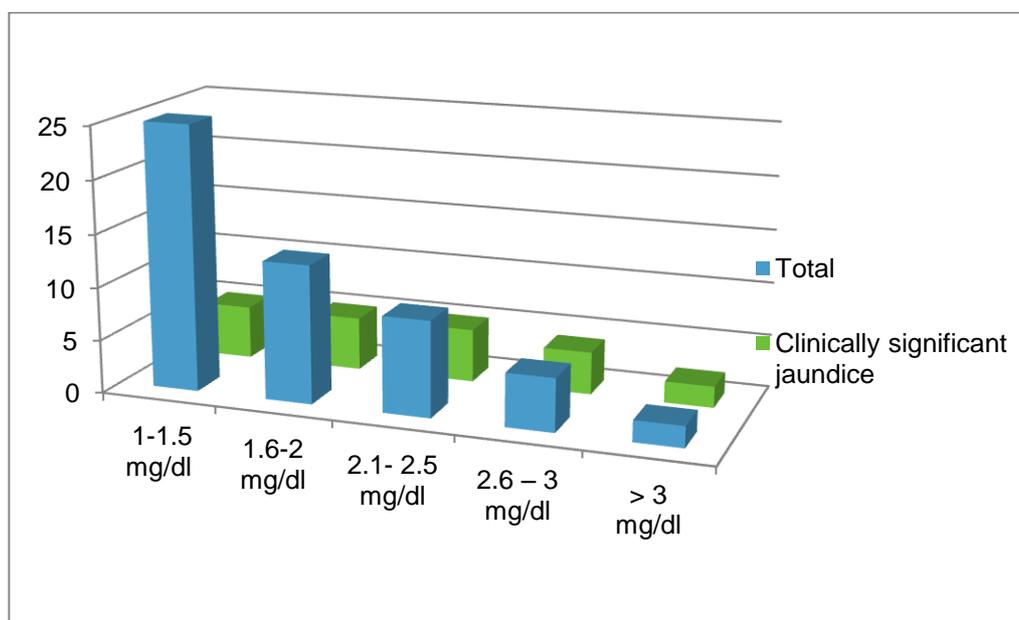


Figure 2: Cord bilirubin levels and its correlation with development of clinically significant hyperbilirubinemia requiring treatment.

The analysis of the cord bilirubin levels of the full term neonates and its correlation with clinically significant hyperbilirubinemia within first week of neonatal period showed that there was a

significant correlation between the cord bilirubin levels and risk of subsequent development of clinically significant neonatal hyperbilirubinemia requiring phototherapy. This is important because

in many developing countries the mother or the family is not willing to remain in hospital after having delivered a healthy baby. In these circumstances estimation of cord bilirubin level can predict the babies in whom there is an increased risk of clinically significant hyperbilirubinemia. All such babies either should not be discharged or if it's necessary to discharge them then the mother or caregiver should be forewarned about the chances of development of jaundice requiring treatment.

Discussion

Jaundice is one of the most common causes of pediatric consultations in neonatal age group. In majority of the cases jaundice reflects a normal transitional phenomenon and hardly requires any treatment. The factors which predispose neonate for occurrence of jaundice are immature hepatic enzymes required for conjugation of bilirubin, increased turnover of red blood cells in neonates and increased enterohepatic circulation owing to intestinal stasis. Jaundice occurring due to these physiological causes usually appears between 2nd to 5th day and never go above 15 mg/dl and rate of rise in bilirubin is less than 5mg/dl. Jaundice occurring in neonates predisposed to developing hyperbilirubinemia due to causes such as sepsis, Rh and ABO incompatibility is called pathological jaundice. If jaundice occurs within 24 hours of birth, Total serum bilirubin levels more than 17mg/dl, persistence of jaundice beyond 3 weeks of life and conjugated hyperbilirubinemia should be presumed to be pathological and investigated accordingly^[8].

Clinical examination to determine the level of jaundice was originally described by Kramer. He showed that the yellowish discoloration of skin due to jaundice progresses in cephalocaudal direction. For this examination broad day light is preferable. The skin overlying sternum can be blanched with mild digital pressure and underlying color of skin and subcutaneous tissue is noted. The severity of jaundice can be assessed by the extent of discoloration which is seen

progressing in cephalocaudal direction. The other more precise form of estimation of serum bilirubin levels are transcutaneous bilirubinometer and estimation of bilirubin by spectrophotometry^[9].

Though one of the important criteria of differentiating physiological and pathological jaundice is total serum bilirubin level there is no definite "safe" or "unsafe" level of serum bilirubin and some babies may get kernicterus even at lower levels of serum bilirubin^[10].

The factors predisposing a newborn for severe neonatal hyperbilirubinemia are Rh and ABO incompatibilities, sepsis, maternal diabetes, galactosemia, and neonatal hypothyroidism and Gilbert syndrome^[11].

In developing countries like that of India where health resources are scarce and there is lack willingness of the patient to remain in hospital after a normal delivery it is not unusual for a patient to be discharged on 3rd or 4th postpartum day. In these cases of early discharges the newborn babies are at increased risk of complications including admission in the hospital for neonatal jaundice. Many studies have concluded that Infants discharged from the hospital early were at increased risk for jaundice adjusted for birth year, gestational age, maternal race and age, parity, and infant sex. Also in many instances of neonatal re-admission for neonatal jaundice there was no predisposing factor for hyperbilirubinemia at the time of discharge^[12].

The need for predicting the occurrence of clinically significant neonatal jaundice in the newborns had always been felt by the neonatologists. Many investigators have tried predicting the occurrence of clinically significant neonatal jaundice on the basis of various parameters like day 1 total serum bilirubin levels, cord bilirubin levels and hour specific bilirubin normogram^[13]. The exercise was done in the hope of being able to accurately predict the chances of clinically significant hyperbilirubinemia in certain infants who then on the basis of such a determination will either not be discharged

from hospital or in case they were discharged a proper follow up can be advised .

Cord bilirubin level as a predictor of subsequent development of clinically significant neonatal hyperbilirubinemia has been studied by many investigators. Rosenfeld in his study concluded that the neonates with a cord bilirubin level of more than 2gm/dl had 25 percent chance of developing subsequent hyperbilirubinemia. The author recommended this level to be used to identify the neonates at risk of development of subsequent clinically significant neonatal hyperbilirubinemia ^[14]. Similar conclusions were drawn by Sun G et al who concluded that umbilical cord serum bilirubin levels may help detect infants at low or high risk for hyperbilirubinemia and minimize an unnecessary prolongation of hospitalization ^[15].

Our study also concluded that umbilical cord bilirubin levels of more than 2mg/dl were associated with an increased risk of subsequent development of clinically significant jaundice. All such neonates having an umbilical cord bilirubin level of more than 2 mg/dl either should not be discharged early and if at all they are discharged for some reason then parents should be counseled properly and advised regular follow up.

Conclusion

Our study shows that total serum bilirubin in cord blood can be used as a predictor of subsequent development of clinically significant jaundice and need for treatment (phototherapy or exchange transfusion) in healthy full term neonates born by any mode of delivery. This knowledge can be used to decide about early discharge of a newborn. In neonates having high cord bilirubin level (>2mg/dl) the discharge either should be delayed or if that is not possible then the caregivers should be warned about development of clinically significant jaundice.

Conflict of interest: None

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