Diagnostic Accuracy of Umbilical Cord Bilirubin Measurement in Development of Significant Hyperbilirubinemia in Healthy Neonates

Taimur Khalil Sheikh [1], Rubina Zulfiqar [2], Tariq Mahmood [3]

1. Department of Paediatrics, Al-NAfees Medical College;2. Department of Paediatrics, Yusra Medical and Dental College, Rawalpindi ;3. Department of Paediatrics, Holy Family Hospital and Rawalpindi Medical University, Rawalpindi

Abstract

Background: To determine the diagnostic accuracy of umbilical cord blood bilirubin in determining the development of significant hyperbilirubinemia on the 3rd day of life in healthy full term newborns, keeping serum bilirubin as a gold standard.

Methods: In this cross sectional study babies delivered consecutively were taken.Any condition which can aggravate hyperbilirubinemia and any patient with congenital abnormality were excluded. Cord blood sample was collected from the neonatal end of the umbilical cord after it had been cut and investigated for serum total bilirubin (STB). Venous sample was taken on the 3rd day of life and sent for serum total bilirubin. Babies were then discharged or admitted for treatment depending on their serum total bilirubin levels. Mean serum total bilirubin in cord blood and mean total serum bilirubin on 3rd day of life was calculated. A 2 x 2 table was constructed to determine sensitivity, specificity positive and negative predictive values.

Results: The mean cord STB was 2.0 mg/dl ± 0.6. Out of the 115 babies, 26% developed significant hyperbilirubinemia requiring phototherapy, only one needed exchange transfusion. The results showed that cord blood bilirubin ≥2.5mg/dl had the high sensitivity (87%) and specificity (98%) to predict the newborn that would develop significant hyperbilirubinemia. At this level the negative predictive value was 95%. The diagnostic accuracy of cord bilirubin 94.8%.

Conclusion: A cord blood STB of ≥2.5md/dl is predictive of significant hyperbilirubinemia on the 3rd day of life in healthy neonates.

KeyWords: Umblicalcordbilirubin,Hyperbilirubin emia, Healthy Neonates

Introduction

Hyperbilirubinemia is a common clinical condition that occurs in approximately 70% term newborns and 80% of premature newborns. [1] Although jaundice in the newborn is usually a benign condition, accumulation of unconjugated bilirubin in the brain can lead to acute bilirubin encephalopathy, characterized by lethargy, high-pitched cry, and poor feeding in a jaundiced infant. [2] Acute bilirubin encephalopathy must be treated quickly to prevent its progression to kernicterus, which is the chronic, permanent clinical sequelae of bilirubin toxicity. It is characterized by severe athetoid cerebral palsy, paralysis of upward gaze, hearing loss, and intellectual impairment.[2]

Jaundice presents within the first 2-7 days of life in most neonates.[3] Therefore, neonates discharged within 48 hours after birth are likely to return to the hospital with complaint of jaundice, which may require treatment. Such readmission not only exposes the neonate to hospital infection and places financial burden on the family and hospital, but is also a cause of disruption of breast feeding and early weaning. It is recommended that all neonates should be examined within 24 to 72 hours of hospital discharge to assess for jaundice and general well-being and earlier follow ups for babies who had more risk factors for severe hyperbilirubinemia and shorter hospital stays.[2] Pre-discharge bilirubin screening is also effective in reduction of severe hyperbilirubinemia and therefore kernicterus.[4]

In developing countries of the world, the vast number of babies presenting in the hospitals, as well as financial pressures have led to shortened stay of babies and their mothers within hospitals. Mothers who give birth by vaginal delivery are discharged within 24 hours, whereas those giving birth by caesarean section are discharged 48 hours post-operation. These early discharged neonates are likely to be readmitted after the 2nd day of life with elevated hyperbilirubinemia and kernicterus.[2]

Parameters are therefore required in order to predict severe hyperbilirubinemia within the 1st 24-48 hours of

the neonate's life so as to prevent early discharges & subsequent readmissions of neonates with high risk of severe hyperbilirubinemia. Studies have been carried out in India to evaluate cord blood serum bilirubin and serum albumin as predictive factors for severe hyperbilirubinemia. [5,6] Cord blood serum total bilirubin has sensitivity of 61.3% and specificity: 76.8% compared to venous blood serum bilirubin, which is used as a gold standard, which has a sensitivity of 100% and specificity of 98.2% in predicting the development of significant hyperbilirubinemia. [7,8]

Patients and Methods

This cross sectional validation study was conducted in the Paediatric Medicine Unit of Holy Family Hospital in collaboration with the Department of Gynaecology and Obstetrics, from October 2013 to April 2014. One hundred and fifteen babies delivered consecutively were taken.All neonates born within the time period by any mode of delivery, of both genders with gestational age more than 37 weeks, birth weight over 2.5kg, APGAR score of 7 or above at 1 and 5 minutes of life and with or without ABO blood group incompatibility were included. Babies with Rh incompatibility, requiring admission for any other cause, any condition which can aggravate hyperbilirubinemia and any patient with congenital abnormality were excluded. Cord blood sample of 2cc was collected from umbilical cord of all neonates. The sample was taken from the neonatal end of the umbilical cord after it had been cut. It was sent to Holy Family Hospital laboratories and investigated for serum total bilirubin (STB), complete blood count, blood group and Rh factor. All neonates were followed up by Paediatrician daily in the Obstetric ward. They were kept in the obstetric wards with their mothers until their 3rd day of life. Venous sample was taken on the 3rd day of life &sent for serum total bilirubin. Babies were then discharged or admitted for treatment depending on their serum total bilirubin levels. Findings were recorded in the proforma.Frequency was calculated for gender and true positives. Mean weight in kg, the mean serum total bilirubin in cord blood and mean total serum bilirubin on 3rd day of life was calculated. A 2 x 2 table was constructed to determine sensitivity, specificity positive and negative predictive values.

Results

A total of 115 babies were included in the study. None of the babies were lost to follow up and no patient was excluded from study. Sixty (52.2%) were male and 55

(47.8%) were female. Out of the 115 babies, 26%, mostly male babies, developed significant hyperbilirubinemia, for which they were admitted in nursery and given phototherapy (Table 1).

Table 1.Percentage of Patients who developed Hyperbilirubinemia

Significant hyperbilirubinemia	No significant hyperbilirubinemia
26%	74%

Table 2.Gender Distribution of Hyperbilirubinemia

	Number	Percentage
Males who developed hyperbilirubinemia	16	53.3
Females who developed hyperbilirubinemia	14	46.7

Table 3.Cord blood bilirubin levels

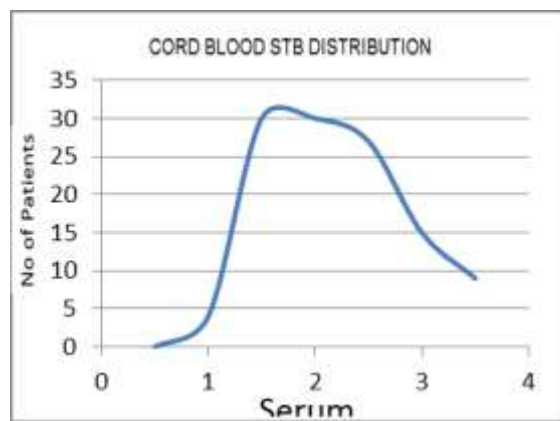| Cord blood bilirubin (mg/dl)	Number of babies
<0.5	0
0.5-1.0	4
1.0-1.5	30
1.5-2.0	30
2.0-2.5	27
2.5-3.0	15
>3.0	9

Figure 1. Cord blood bilirubin distribution

The maximum recorded cord STB was 3.4mg/dl and the minimum recorded cord STB was 0.8 mg/dl. The mean STB was 2.0 mg/dl ± 0.6(Table 3 and Fig. 1).. One patient had hyperbilirubinemia severe enough to require exchange transfusion (Table 4).The results obtained were put in a 2x2 table to determine specificity, sensitivity, positive predictive value, negative predictive value & diagnostic accuracy (Table

5).The results demonstrated that cord blood bilirubin ≥2.5mg/dl had the high sensitivity (87%) and specificity (98%) to predict the newborn that would develop significant hyperbilirubinemia. At this level the negative predictive value was 95%. The diagnostic accuracy of cord STB was 94.8%. The critical cut off value for the development of hyperbilirubinemia was taken as ≥2.5mg/dl.

Table 4.Babies with significant and insignificant serum hyperbilirubinemia

Cord Bilirubin	Significant hyperbilirubi-nemia (on 3rd day of life)	Without significant hyperbiliru-binemia (on 3rd day of life)
Cord bilirubin≥ 2.5mg/dl	26 (TP)	2 (FP)
Cord blood< 2.5 mg/dl	4 (FN)	83 (TN)

True Positive (TP), False Positive (FP), False Negative (FN), True Negative (TN)

Table 5.Sensitivity, specificity and positive and negative predictive values of cord blood bilirubin levels in predicting the development of significant hyperbilirubinemia

Bilirubin level	TP	FN	FP	TN	SN	SP	PPV	NPV
2.5mg/dl	26 (22.6)	4 (3.5%)	2 (1.7%)	83 (72.2%)	87	98	93%	95%

TP- true positive; FN-false negative; FP-false positive; TN -true negative; Sn Sensitivity; Sp-specificity; PPV-positive predictive value; NPV-negative predictive value.

Discussion

There has been a recent increase in the incidence of kernicterus in full term neonates.[2,9] A large number of cases of hyperbilirubinemia go undiagnosed or under diagnosed, owing to the large population and lack of medical facilities in many parts of our country.As mentioned previously, physiologic jaundice appears after 24 hours, is maximum by the 3-4th day of life , and typically resolves by 2 weeks after birth.[10] Bilirubin may be estimated by visual assessment, which although provides a rapid and convenient method for assessing the degree of jaundice but it is not very accurate. [11] It is therefore obvious that this method alone is not to be relied upon for the assessment of the degree of hyperbilirubinemia and the subsequent risk of kernicterus, although the fact does remain that visual assessment is indeed the cheapest method. It is especially useful for overcrowded and underdeveloped countries, where

access to laboratories and adequate medical facilities may be deficient and if available is expensive.

Serum total bilirubin (STB) is the gold standard for measurement of jaundice, making these guidelines a very useful tool for prevention of hyperbilirubinemia. [8] A number of risk factors have been identified for the development of significant hyperbilirubinemia. These include male sex, prematurity, low birth weight, polycythemia, sepsis, haemorrhage and hemolysis .[12] The risk factors of prematurity, sepsis and low birth weight were excluded from our study.

In present study, out of the 115 babies, 52.2% were male and 47.8% were females, in the ratio of 1.09:1 and among the thirty babies, who developed hyperbilirubinemia, again male gender predominated 53.3% versus 46.7%.Male gender is a known factor for development of hyperbilirubinemia.[12,7,13,14] Calkins et al and Jones et al determined the significance of predictive value of cord blood bilirubin (CBB) concentrations for hyperbilirubinemia, in babies at risk for hemolytic disease of newborn. [15,16] Calkins concluded that Cord Blood bilirubin may help to predict severe hyperbilirubinemia and phototherapy in such population.Jones found that in infants of mothers with blood group O, arterial umbilical cord bilirubin predicts development of neonatal jaundice. Chary et al, demonstrated that cord blood bilirubin >2.0 mg/dl had a sensitivity of 94.12% and specificity 90.91% to predict the newborn that would develop significant hyperbilirubinemia. [17] Krishnan et al in his study determined that the cord blood bilirubin is the best predictor and babies with value >1.8mg/dl are at higher risk for developing pathological hyperbilirubinemia. [18] Ninety one percent of newborns who developed pathological jaundice required phototherapy. It may be noticed that in our study, 26% of neonates had hyperbilirubinemia severe enough to require phototherapy.

Ahire et al demonstrated that with serum bilirubin levels ≥ 3 mg/dL in the cord blood, hyperbilirubinemia could be predicted with sensitivity of 100%, specificity of 98.17 % and positive predictive value of 66.67 % and negative predictive value of 100%. [19] Kumaran et al in their study found infants having umbilical cord bilirubin level > 2mg/dl should be followed strictly either in hospital or at an outpatient department on day 5 if practicable. [20]

Pradhan et al concluded that there is a significant correlation between cord blood total bilirubin level and development of pathological hyperbilirubinemia. [21] They found that the sensitivity and specificity of cord bilirubin ≥ 2.5mg/dl was 84.1% and 88.5%

respectively. The positive predictive value of this variable was 98.0% and the negative predictive value was 45.1%.These results also correlate with our study.

Conclusion

1.A cord STB level of ≥2.5mg/dl had a high correlation with development of significant hyperbilirubinemia on the 3rd day of life, with sensitivity of 87%, specificity of 98%, PPV of 93% & NPV 95%

2.In our setting, neonates who have umbilical cord blood TSB ≥2.5 mg/dl should be followed up strictly either in hospital or as an outpatient department on day 3 if practicable. Infants having TSB <2.5mg/dl in cord blood can be discharged early.

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