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Umbilical Cord Blood Bilirubin and Determination of Neonatal Hyperbilirubinemia

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[1,3]Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work, Final approval of the version to be published,[2,4,5]Drafting the work or revising it critically for important intellectual content, [6]Active participation in active methodology

Funding Source: None
Conflict of Interest: None

Received: May 25, 2022
Accepted: Jan 1, 2023

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ABSTRACT

Objective: To determine accuracy of cord blood bilirubin in identifying significant neonatal hyperbilirubinemia.

Methodology: A Cross sectional study was conducted in Pediatric department of Fauji Foundation Hospital Rawalpindi from Jan.2019 to June 2019. Cord blood samples were sent for the blood group and bilirubin levels. Neonates with cord bilirubin level > 2mg/dl and < 5 mg/dl were enrolled and admitted for 3 days and serum bilirubin level were done on 3rd day. Those developing significant hyperbilirubinemia were further investigated for hemoglobin, reticulocyte count, Coomb's test and other causes.

Results: Total 74 newborns at >35 weeks of gestation were included in the study of which 35 (47.3%) were male and 39 (52.7%) were female (male: female: 1:1.1). The data was analyzed using SPSS 17. At 3rd day of life mean ± SD cord blood bilirubin was 8.4 ± 2.7 mg/dl, mean direct bilirubin was 1.6 ± 0.9 mg/dl and mean indirect bilirubin was 6.8 ± 2.3mg/dl. Significant hyperbilirubinemia developed in 16 (21.6%) newborns at >35 weeks of gestation, who had a cord blood bilirubin level of > 2 mg/dl, so that the accuracy of cord blood bilirubin level (true positives) in determining significant hyperbilirubinemia was 21.6%.

Conclusion: Cord blood bilirubin level >2mg/dl in all healthy term newborns predicts significant hyperbilirubinemia.

Keywords: Jaundice, Hyperbilirubinemia, Cord blood bilirubin.

Cite this article as: Tahir A, Abid U, Batool I, Zaman N, Ahmad N, Khaleel S. Umbilical Cord Blood Bilirubin and Determination of Neonatal Hyperbilirubinemia. Ann Pak Inst Med Sci. 2023; 19(1):20-23. doi. 10.48036/apims.v19i1.649

Introduction

Neonatal jaundice is a very common problem in newborns especially in the first week of life. It is the most common cause of newborn admission in the hospital, thus a major cause of concern for both parents and clinicians.[1, 2] Of all the cases of neonatal jaundice, about 5-10% require intervention for management of pathological jaundice.[3] In most of neonates a transient unconjugated hyperbilirubinemia is a normal physiological event, as neonate's premature liver is unable to conjugate increased levels of bilirubin. But if levels rises above a certain limit it can lead to serious neurological complication 'kernicterus' and even death.[4,5] Bilirubin induced brain damage has increased the concerns to detect jaundice early that occurs in healthy term infants even with no evidence of haemolysis.[6,7] Therefore, it is necessary to identify those newborns who are at risk of developing significant hyperbilirubinemia, doing early intervention, to decrease the risk of readmission and prevent complications .[8,9]

As practice of early discharge after delivery is becoming increasingly common in developing countries like ours due to economic burden, severe hyperbilirubinemia risk is also increased. Therefore different methods have been introduced and tried to predict severe hyperbilirubinemia in certain neonates. In one study done on early neonates demonstrated that umbilical cord bilirubin was a very good predictor of hyperbilirubinemia at 48 h of life [AUC = 0.80 (95% CI 0.78–0.82)].[10] Another study also showed that umbilical cord blood bilirubin advantage when performed clinically well with an area under the receiver-operating

characteristic curve (AUC) of 0.82 (95 % CI 0.80-0.84).[11] In one other study early detection and intervention by using first day cord blood bilirubin levels showed that with bilirubin levels of 6 mg/dl and above, subsequent hyperbilirubinemia developed in 21 (27.2%) babies with 95% sensitivity and 70.6% specificity with a positive predictive value of 27.2% and negative predictive value of 99.3%. [12]

In our study we aim to highlight the importance of cord blood bilirubin estimation and to make sure its routine use to identify neonates with risk of developing hyperbilirubinemia, subjecting them to early preventive measures, phototherapy and also to lessen readmission rates and serious complications.

Methodology

This Descriptive Cross sectional study was conducted in The Pediatric department of Fauji Foundation Hospital Rawalpindi for duration of 6 months (Jan.2019 to June 2019) after taking ethical clearance. An informed consent was taken from the parents/guardians included in the study following guidelines. A total of 74 newborns at ≥35 weeks of gestation of both sex, delivered by vaginal and C-section with weight > 2 kg, absence of congenital malformations and cord blood bilirubin > 2mg/dl and< 5mg/dl were included in the study. The exclusion criteria includes pre-terms < 35 weeks with weight < 2 kg, having Septicemia / DIC and co-morbid conditions like respiratory distress syndrome, birth asphyxia, necrotizing enterocolitis etc and presence of direct hyperbilirubinemia. Neonates with cord bilirubin level > 2mg/dl and < 5 mg/dl were enrolled and admitted for 3 days and serum bilirubin level were done on 3rd day. Those who developed significant hyperbilirubinemia were further evaluated for hemoglobin, reticulocyte count, coomb's test and other causes. The entry and analysis of data was done using SPSS 17. Descriptive statistics like Mean ± SD were calculated for quantitative variables like serum bilirubin at 3rd day of life, cord blood bilirubin at birth and weight. Frequency and percentage were calculated for qualitative variables like gender, significant hyperbilirubinamia, mother's & baby's blood group and true positives.

Results

A total of 74 newborns at ≥ 35 weeks of gestation were included in this study. Of the enrolled neonates, 35 (47.3%) were male and rest 39 (52.7 %) were female (Male: Female is 1:1.1). Distribution of mother's & neonate's blood group is shown in table I. B positive was the most common blood group i.e. in 25 mothers (33.8%) and in 23 neonates (31.1%). Mean (± SD) cord blood bilirubin at birth was 3.1 ± 0.85mg/dl while Mean (±SD) serum total bilirubin at 3rd day of life was 8.4± 2.7 mg/dl, mean direct bilirubin at 3rd day of life was 1.6± 0.9mg/dl and mean indirect bilirubin at 3rd day of life was 6.8±2.3mg/dl, as shown in table II.

Table I: Distribution of mothers and neonates blood groups (n= 74)

Blood Group	Mother's	Baby's
A +ve	18 (24.3 %)	14 (18.9%)
A –ve	2 (2.7 %)	0
B +ve	25 (33.8%)	23 (31.1%)
B –ve	4 (5.4%)	0
AB +ve	1 (1.4%)	8 (10.8%)
AB –ve	2 (2.7%)	5 (6.8%)
O +ve	17 (22.9%)	22 (29.7%)
O –ve	5 (6.8%)	2 (2.7%)

Table II: Mean serum bilirubin concentration (n= 74)

Investigations	Min – Max	Mean ± SD
Cord Blood Bilirubin (mg/dl) (at birth)	2.1 – 4.9	3.1 ± 0.85
Serum Total Bilirubin (mg/dl) (at Day 3)	0.4 – 16.1	8.4 ± 2.7
Direct Bilirubin (mg/dl) (At Day 3)	0.3 – 5.8	1.6 ± 0.9
Indirect Bilirubin (mg/dl) (at Day 3)	2 – 13.7	6.8 ± 2.3

Significant hyperbilirubinemia (serum total bilirubin > 15mg/dl on 3rd day of life) developed in 16 (21.6%) newborns at ≥ 35 weeks of gestation, who had a cord blood bilirubin of > 2mg/dl, so that the accuracy of cord blood bilirubin level (true positive) in determining significant hyperbilirubinemia was 21.6%. Mean (±SD) hemoglobin in neonates with significant hyperbilirubinemia was 14.9±1.6, mean direct & indirect bilirubin was 1.8±0.7 mg/dl and 9.8±1.7 mg/dl as shown in table III. Coomb's test was positive in 2 (12.5%) neonates with significant hyperbilirubinemia and interventions were required in 10 (62.5%) neonates.

Table III: Laboratory investigations in neonates with significant hyperbilirubinemia (n = 16)

Investigations	Min – Max	Mean ± SD
Hemoglobin (gm/dl)	11.2 -17.2	14.9 ± 1.6
Direct Bilirubin (mg/dl)	0.7 – 3.1	1.8 ± 0.7
Indirect Bilirubin (mg/dl)	8 – 14	9.8 ± 1.7
Reticulocyte count	2 – 8	3.5 ± 1.5

Discussion

This study demonstrates that the accuracy of cord blood bilirubin level (true positives) in determining significant hyperbilirubinemia was 21.6% making cord blood bilirubin estimation as a useful tool to detect neonates at risk of developing hyperbilirubinemia. Although our study has several limitations but it is the first study in our hospital to enhance the importance of measuring cord blood bilirubin. We can subject these newborns to early preventive therapies like early feeding and phototherapy to reduce the complications.[13] It is not a new idea to use cord blood bilirubin to detect bilirubin levels in neonates as its area of interest since 1950s highlighting its importance.[14]

In 2019, Jehangir, et al revealed in their study that cord blood bilirubin level <2.5 mg/dl has 8.82% sensitivity and 83.92% specificity of not developing hyperbilirubinemia while cord bilirubin levels >3mg/dl has 97% sensitivity and 99% specificity to develop raised bilirubin levels.[15] In another study done in 2019 by Muhammad Rafi cord blood bilirubin level of ≥2mg/dl had sensitivity of 90.48%, specificity 84.88% in prediction of neonatal hyperbilirubinemia encouraging it to be used as an early predicting tool.[16] In 2019 Vincenzo et al reported that newborns diagnosed with hyperbilirubinemia had higher cord blood bilirubin.[17] Selma, et al in 2019 concluded that cutoff value of 1.67 mg/dL of cord blood bilirubin with 82% sensitivity and 53% specificity.[18] One latest study done in India in 2022, showed serum bilirubin levels ≥2.5 mg/dL in the cord blood has 100% sensitivity and 99.30 % specificity. [19]

Hence, almost all the studies showed that using cord blood bilirubin level of 2 mg/dl will help us to detect significant hyperbilirubinemia in infants especially those requiring phototherapy during initial life days.[20] Therefore in our setting neonates with umbilical cord blood bilirubin level greater than 2 mg/dl should have follow up either in the hospital or on OPD basis, if feasible. Infants having serum total bilirubin less than 2.5 mg/dl in cord blood can be discharged safely.

Conclusion

On the basis of the results of this study it may be concluded that the use of critical cord bilirubin level of 2 mg/dl in all healthy term newborns will predict significant hyperbilirubinemia. This critical cord bilirubin level of greater than 2 mg/dl is a fairly good predictor of significant hyperbilirubinemia as depicted by a number of studies. To avoid crippling conditions like kernicterus, bilirubin estimation in cord blood is suggested to be uniformly applied to all the Obstetric units of the country, and make it a standard protocol. This will also subject it to a multicenter and multivariate analysis, further revealing its true statistical significance.

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