Cord Blood And 1st Day Bilirubin Level As A Predictor Of 3rd Day Hyperbilirubinemia In Newborns With Birth Weight >2000g (A Prospective Non Randomized Study)

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Abstract: Aims: To evaluate whether bilirubin levels in cord blood and 1st day could predict neonatal hyperbilirubinemia to their third day of life. Settings and Design: Prospective non randomized study in tertiary care hospital and medical college. Methods and Material: In 100 healthy newborns with birth weight > 2000g, cord blood bilirubin, serum bilirubin at days 1 (20 to 25 h) and 3 (65 to 75 h) of life was obtained. Newborns with signs of ecchymosis, cephalhaematoma, septicemia, G6PD deficiency and APGAR <7 at 1min were excluded from the study. Total bilirubin ≥ 14 mg/dl measured on 3rd day was considered as significant hyperbilirubinemia. Cord and 1st day bilirubin was used as a predictor of 3rd day hyperbilirubinemia (3DHB). Statistical analysis: T-test, chi-square, Receiver Operating Characteristics (ROC) curve. Results: 22 newborns developed 3rd day hyperbilirubinemia (≥ 14 mg/dl). Cord blood bilirubin level of ≥1.75mg/dl has sensitivity 81%, specificity 77%, positive predictive value 50% and negative predictive value of 90% in predicting the risk of 3DHB. 1st day (20-25h) bilirubin level of ≥4.1 mg/dl has a sensitivity 62 %, specificity 93 %, positive predictive value 77 % and the negative predictive value of 87 % in predicting the risk of 3DHB. There was significant association between 3DHB with oxytocin induction of labour (p=0.0185) and mean cord blood bilirubin (p=0.0001). Conclusions: Cord blood bilirubin level of ≥1.75mg/dl (moderately positive correlation-0.53) or 1st day level of ≥4.1 mg/dl (moderately positive correlation-0.65) can predict the development of 3rd day hyperbilirubinemia (S. Bilirubin ≥14 mg/dl). Oxytocin induction of labour has significant correlation with 3rd day hyperbilirubinemia. [Parekh N Natl J Integr Res Med, 2019; 10(5):11-14]

Key Words: Newborns, Hyperbilirubinemia, Cord Bilirubin, 1st Day Bilirubin

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Introduction Hyperbilirubinemia is a common problem during the neonatal period and is the most common reason for readmission after early hospital discharge. It can be a physiologic condition or a severe disease resulting into brain damage.[1, 2,3]Hyperbilirubinemia is common in newborns; it affects nearly 70% of term and 80% of preterm neonates during the first week of life. A short hospital stay for less than 48 hours after birth, results in an increase in neonatal readmissions for hyperbilirubinemia.

The American Academy of Pediatrics recommends that newborns discharged within 48hours shouldhave a follow-up visit after 2-3 days to detect significant jaundice and other problems.Bilirubin toxicity remains a significant problem despite recent advances in the care of jaundiced neonates. Kernicterus, though infrequent, is the cause of 10% of mortalities and at least 70% of long-term morbidities among newborns. Recent increases in early hospital discharges, coupled with a rise in breast feeding rates, has led to a rise in the rate of preventable kernicterus resulting from undetected hyperbilirubinemia. If significant hyperbilirubinemia can be prevented, then almost all cases of kernicterus are avoidable. Reliable strategies to predict hyperbilirubinemia can identify such babiesand reduce hospital stay for normal babies.

Methods: A prospective non randomized study was conducted in post natal ward of tertiary care hospital from December 2013 to August 2014.The protocol was approved by the hospital's institutional review board.

Inclusion criteria:
Birth weight > 2kg, -Mode of delivery (normal and c- section), APGAR ≥ 7/10 at 1.

Exclusion criteria:
Mode of delivery, forceps or vacuum, Birth injuries (cephalhaematoma, ecchymosis), Sepsis,Congenital anomalies,G6PD deficiency, -Admission and treatment in NICU for cause other than jaundice.

Informed written parental consent was obtained from all cases. Medication during labour, details of delivery, APGAR score and maternal blood

group were collected from the maternal file. Cord blood bilirubin was done at birth. 1st day (between 20 to 25 h) and 3rd day (between 65 to 75 h) serum bilirubin was estimated using - modified Jendrassik-Grof method, a photometric method for estimation of direct and total bilirubin. The main outcome of the study was inferred in terms of hyperbilirubinemia. Serum bilirubin ≥ 14 mg/dl on 3rd day (between 65 to 75 h)of life was considered as significant hyperbilirubinemia. Cord and 1st day bilirubin were used as predictor of 3rd day hyperbilirubinemia by statistical analysiswith the independent sample t test, the descriptive analysis, and chi-square tests. Sensitivity, specificity, negative and positive predictive value of the test was calculated. The critical cord bilirubin level having the highest sensitivity and specificity was determined with the Receiver operating characteristics (ROC) curve analysis.

Results: The study group consisted of 100 neonates with birth weight > 2000 gram (flow chart). Table 1 presents descriptions of the 100 newborns. Out of 100 newborn, 22 (22%) developed significant 3rd day hyperbilirubinemia (≥14 mg/dl) (3DHB). Table 2 shows association between modes of delivery, timing of initiation of breast feeding and oxytocin induction of labour with 3DHB.

Table 1:Clinical characteristics of the study population.

Birth weight (grams)	2669 ± 381 (mean ± SD)
Male: female ratio	49/51
Gestational age- week days	38 wk 2 d ± 5 d (mean ± SD)
Apgar 1st minute	Median 9, Minimum/Maximum: 8/10
Mode of delivery (VD/CS)	61 /39
Rh & ABO incompatibility N (%)	28(28%)
Cord blood haemoglobin (mg/dl)	13.9 ± 1.14 (mean ± SD)

*VD= vaginal delivery, CS= caesarean section delivery

The cord blood bilirubin values (mg/dl) of the two groups of the neonates who eventually did develop (mean ±SD: 2.27 ±0.58) and did notdevelop (mean ±SD 1.55 ±0.55) 3DHB, was having a statistically significant (p=0.0001) correlation.

The blood group of the mothers wasO in 31, followed by B in 26, A in 19 and AB in 10. The blood group among the newborns was Ain 46, followed by B in 32, O in 15 and AB in one. 72 out of 100 did not show ABO or Rh blood incompatibility and 28had incompatibility; of whom 12 had O-A,seven had O-B and ninehad Rh incompatibility. The cord blood serum bilirubin (mg/dl)with and without blood group incompatibility was (mean ±SD: 2.466±0.5) and (mean ±SD: 2.146±0.62); the difference was not statistically significant (p=0.126).

Table 2: Association of mode of delivery, initiation of breast feeding and oxytocin induction of labour, with 3DHB

	Neonatal Hyper-bilirubinemia (≥ 14mg/dl)		p value
	Yes	No	
Vaginal delivery	14	47	0.774
Caesarean delivery	8	31	
Brest feeding within 30 min	10	35	0.961
Breast feeding after 30 min	12	43	
With oxytocin	10	16	*0.018*
Without oxytocin	12	62	

Cord blood bilirubin level of ≥ 1.75mg/dl was chosen based on the Receiver operating characteristics analysis (area under curve - 0.828) (Figure1) and hadmoderately positive correlationwith 3DHB; with Correlation coefficient of0.53 (Figure 2). Cord serum bilirubin of ≥ 1.75 mg/dl had the sensitivity 81%, specificity 77%, positive predictive value 50% and the negative predictive value of 93% in prediction of 3DHB (S. bilirubin ≥ 14mg/dl).

On ROC curve analysis 1st day (20-25h) bilirubin level of ≥ 4.1 mg/dl was selected(area under curve - 0.916) (Figure3) and hadmoderately positive correlationwith 3DHB;with Correlation coefficient of 0.65 (Figure 4). 1st day serum bilirubin of ≥ 4.1 mg/dl had sensitivity 62 %, specificity 93 %, positive predictive value 77 % and the negative predictive value of 87 % in prediction of 3DHB (S. bilirubin ≥14mg/dl).

Discussion: In present study, we assessed the ability of cord bilirubin level to be a tool for screening of subsequent 3DHB.

The incidence of 3DHB was 22%. These results were not agreement with those of other investigators like Alpay[4] who reported that 12.5% of newborns had significant jaundice after 3rd day of life.

Present study shows cut-off value of total cord blood bilirubin for development of 3DHB to be ≥ 1.75mg/dl by ROC analysis. Although, the cord blood bilirubin level of ≤ 1.75mg/dl did not completely exclude the development of 3DHB; only 4/63newborns with cord blood bilirubin level < 1.75mg/dl developed hyperbilirubinemia. Rosenfeld[5] showed that infants with cord bilirubin levels less than 2 mg/dl have only 4% chance of developing hyperbilirubinemia. However, infants with cord bilirubin > 2mg/dl would have 25% chance of developing subsequent hyperbilirubinemia. Amar Taksande[6] concluded that increased cord blood bilirubin can be used as a predictor of the development of neonatal hyperbilirubinemia. Cord bilirubin level of >2mg/dl at 3rd day of life had the highest sensitivity (89.5%), and very high (98.7%) negative predictive value and fairly low (38.6%) positive predictive value. Knudsen[7] showed if cord bilirubin was below 20.5mmol/l, 2.9% of infants developed jaundiced as opposed to 85% if cord bilirubin was above 43mmol/l.

Present study shows the cut-off point of 1st day serum bilirubin for development of 3DHB to be ≥ 4.1mg/dl by ROC analysis.Alpay[4], showed that 1st day bilirubin level of ≥ 6mg/dl has a sensitivity 90%, specificity 65.3%, positive predictive value 26.3% and negative predictive value of 97.9% in predicting neonatal hyperbilirubinemia.Awasthi[8] showed that 1st day bilirubin level of ≥ 3.99mg/dl has a sensitivity 68.6%, specificity 71%, positive predictive value 35% and negative predictive value of 96% inpredicting neonatal hyperbilirubinemia. Rina Trisiah[9], showed that 1stday bilirubin level of >4.5mg/dl has a sensitivity 90%, specificity 71.9%, positive predictive value 50% and negative predictive value of 96.8% in predicting neonatal hyperbilirubinemia.

Our study indicated that blood group incompatibility did not always result in rise in cord blood bilirubin.Bernaldo**[10]**,Robinson[11] showed that infants with blood group incompatibility had developed 3rdday higher cord blood bilirubin level.

There was a significant relationship between usage of oxytocin and 3DHB(p <0.018), which wasin agreement with the Rostami[12] and Awasthi[8] but disagreed with results of Amar Taksande[5] which showed no significant association (p 0.245) between the Oxytocin induction of labour and 3DHB.

In our study analysis, there was no significant association between the 3DHB and the mode of delivery and time of initiation breast feeding after birth. This matched with results of Amar Taksande[6]and Awasthi.[8]

In the present study, the infants were followed up for up to the third day of life. Therefore, infants who might have developed late jaundice would have been missed.

Conclusion: Sexes, mode of delivery, time of initiation of breast feeding and cord blood haemoglobin level are not associated with 3rd day hyperbilirubinemia. Oxytocin induction of labour has significant correlation with the development of 3DHB. Cord bilirubin level ≥ 1.75mg/dl and 1st day (20-25h) level≥4.1 mg/dl could predict the development of hyperbilirubinemia(≥14mg/dl) on the third day of life in neonates weighing > 2k.

In a study of 100 healthy newborns weighing > 2 k at birth;Cord blood bilirubin of ≥1.75 mg/dl,or S. bilirubin of ≥4.1 mg/dl collected at 24 hr age,could predict the development of hyperbilirubinemia(serum bilirubin ≥14 mg/dl) on day three.

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