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Original Research Article

An Assessment of Early Predictor of Severe Hyperbilirubinemia in Healthy Full-Term Newborns Aged 72 Hours: Prospective Observational Study

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Abstract

Aim: The aim of this study to evaluate the early indicator of significant hyperbilirubinemia in healthy full-term infants at 72 hrs of age.

Methods: This prospective observational study was conducted in the Department of Pediatrics, Darbhanga medical college and Hospital, Laheriasarai, Darbhanga, Bihar, India. 100 patients who full filled the inclusion criteria; Full-term newborns delivered at our Hospital of >36 weeks of gestation, Birth weight >2 kg were included in this study. Bilirubin level at or above high intermediate risk zone at 24 and 48 hrs of age was considered a cut-off value to find out the association with significant hyperbilirubinemia at 72 hrs of age.

Results: Of 100, 54% of the newborn were male and 46% were female. 91(91%) newborns included were between 37 to 40 weeks, and 9% were above 40 wk of gestation. 85(85%) were appropriate for gestational age, 12 newborns (12%) were Short for gestational age, and 3 newborns were Large for gestational age. Out of 100 newborns 5 newborns (33.33%) developed hyperbilirubinemia above high intermediate zone at 48 hrs while 9(30%) newborns developed subsequently developed hyperbilirubinemia at 72 hrs.

Median values for gestational age and birth weight were 38 weeks, 3.1 kg respectively, in study groups. 12 newborns (12%) showed signs of dehydration and out of these 12 newborns, 7 developed hyperbilirubinemia subsequently at 72 hrs of life. 31% received top feeding or mixed feedings, while 17% newborn first feeding was delayed for more than 3 hrs due to inadequacy of lactation on first few days. In our study birth weight <2.5 kg, delayed first feeding, dehydration, and 48 Hr serum bilirubin >11.8 mg/dl were significantly associated with significant hyperbilirubinemia($p<0.05$).

Conclusion: The present study concluded that healthy full-term newborns with birth weight <2.5 kg, higher 24 and 48-hour serum bilirubin were more likely to experience significant hyperbilirubinemia who are often discharged from hospital early.

Keywords: Total serum bilirubin, Neonatal Hyperbilirubinemia, Risk factors, Significant hyperbilirubinemia, Full-term newborn

Introduction

Sixty to 80% of healthy, full-term infants are expected to present with idiopathic neonatal jaundice in the initial postnatal period.[1] Idiopathic neonatal jaundice is attributed to an increased breakdown of heme, immature liver function, low amount of intestinal bacteria, increased enter hepatic circulation of bilirubin and inadequate intake.[2]

Early detection and treatment of significant hyperbilirubinemia may prevent complications. According to some studies, even moderate hyperbilirubinemia is found to be associated with an increased risk of minor neurologic dysfunction in the first year of life which is often considered safe.[3]

Reliable prediction of at-risk neonates may allow clinicians to plan early discharge of low-risk neonates and timely follow-up of high-risk neonates. Simple, non-invasive, and cost-effective methods should be used in high-risk neonates.

Body weight loss (BWL) percentage is an objective and useful tool that may indicate when interventions such as supplemental feeding should be considered.

Previous studies have suggested that 7% to 10% BWL by day 3 in fully breastfed infants is abnormal neonatal BWL.[4,5] However, there are conflicting opinions about what constitutes normal neonatal BWL, and about when supplemental feeding should be considered to prevent significant hyperbilirubinemia. The aim of this study was to analyze the optimum cut-off values of BWL percentages in the first three days after birth to predict neonatal hyperbilirubinemia 72 hours after birth.

Material and methods

This prospective observational study was conducted in the Department of Pediatrics, Darbhanga medical college and Hospital, Laheriasarai, Darbhanga, Bihar, India, India

Inclusion criteria

Full-term newborns delivered at our Hospital of >36 weeks of gestation. Birth weight >2 kg.

Exclusion criteria

Newborns requiring admission to NICU, Infants of a diabetic mother, Newborns with major congenital malformations, Birth trauma, newborns with haemolytic anaemias (Rh, ABO incompatibility), Neonatal sepsis.

Method

100 patients were included in this study. Demographic profile and relevant information was collected by using structured Pro-forma by interviewing the mother and from the mother's case sheet. Gestational age was assessed by New Ballard score. Venous blood samples were collected from the baby at 24, 48 hours and 72 hrs of life. The venous blood sample was collected and serum bilirubin estimation was done within 12 hours of collection of the sample by Diazotized sulfanilic test. Various demographic and clinical variables as socio-economic background, gender, delivery mode, drugs given to mother, maternal risk factors, birth weights, anthropometry, a first feeding, dehydration, and feeding pattern were studied for possible contribution in development of hyperbilirubinemia in such newborns developing significant hyperbilirubinemia.

Bilirubin levels were analysed to find out association with 3 risk zone according to the Bhutani nomogram (Low-risk zone, low intermediate risk zone, and High intermediate-risk zone and above). Bilirubin level at or above high intermediate risk zone (over 75th percentile cutoff value) at 24 and 48 hrs of age was considered a cutoff value to find out the association with significant hyperbilirubinemia at 72 hrs of age.

Statistical Analysis:

Data was entered on the computer using Microsoft Office Excel Software program for Windows, then transferred to the Statistical Package of Social Science Software (SPSS)25.0 program to be statistically analysed. Comparison between groups was performed using the Mann-Whitney test for quantitative variables while comparison for qualitative variables was performed using Chi-square or Fisher's exact test. P values less than 0.05 were considered statistically significant.

Results

100 newborns were enrolled in the study and analysed for the association of various demographic, clinical, and laboratory markers for early prediction of significant hyperbilirubinemia in the study cohort. 54% of the newborn were male and 46% were female. 91(91%) newborns included were between 37 to 40 weeks, and 9% were above 40 wk of gestation. 85(85%) were appropriate for gestational age, 12 newborns (12%) were Short for gestational age, and 3 newborns were Large for gestational age. [Table1] Out of 100 newborns 5 newborns (33.33%) developed hyperbilirubinemia above high intermediate zone at 48 hrs while 9(30%) newborns developed subsequently developed hyperbilirubinemia at 72 hrs.

Median values for gestational age and birth weight were 38 weeks, 3.1 kg respectively, in study groups. 12 newborns (12%) showed signs of dehydration and out of these 12 newborns, 7 developed hyperbilirubinemia subsequently at 72 hrs of life. 31% received top feeding or mixed feedings, while 17% newborn first feeding was delayed for more than 3 hrs due to inadequacy of lactation on first few days. [Table2] Maternal age, social status, parity, cesarean section, and oxytocin induction were not associated with hyperbilirubinemia at 72 hrs of life. While Instrumental delivery using vacuums and forceps had significantly higher chances of developing significant NNHB at 72 hrs. ($p<0.05$ [Table1]

We also studied 24 hrs bilirubin and 48 bilirubin to find out association to significant hyperbilirubinemia. Total bilirubin >6 at 24 hrs and >11.8 at 48 hrs of life which corresponds to high intermediate risk zone cutoff in Bhutani nomogram and we found this association to be statistically significant. Gender, gestational age, fetal growth had no statistical differences in the occurrence of NNHB. In our study birth weight <2.5 kg, delayed first feeding, dehydration, and 48 Hr serum bilirubin >11.8 mg/dl were significantly associated with significant hyperbilirubinemia($p<0.05$). [Table2

Table-1: Demographic risk factors for the association to significant NNHB in term newborn at 72 hrs of life

Variables		Significant NNHB at 72 hrs of age=20	Total	P-value	95 CI	OR
Social status	Middle class	14(17.44%)	72(72%)	0.08	0.39-1.7	0.93
	Lower	6(21.43%)	28(28%)			
Maternal age	25-35	11(16.42%)	67(67%)	0.4	0.4-1.3	0.7
	>35	9(27.27%)	33(33%)			
Parity	Primi	9(24.32%)	37(37%)	0.5	0.7-2.7	1.4
	Multi	11(17.46%)	63(63%)			
Type of Delivery	Cesarean	7(14.89%)	47(47%)	0.5	0.5-2.1	1
	Normal	5(16.13%	31(31%)			
	Instrumental	8(36.36%)	22(22%)	0.001	1.7-6.5	3.4
Oxytocin	yes	11(18.64%	59(59%)	0.49	0.4-1.4	0.8

induction	No	9(21.95%)	41(41%)			
Instrumental delivery using vacuums and forceps had significantly higher chances of developing significant NNHB at 72 hrs of age (p<0.05)						

Table-2: Neonatal risk factors for association to significant hyperbilirubinemia in term newborn at 72 hrs

Variables		Significant NNHB at 72 hrs of age	Total(%)	P-value	95 CI	OR
Gender	Male	11(20.37%)	54(54%)	0.5	0.6-2.1	1.06
	Female	9(19.56%)	46(46%)			
Birth weight	2-2.5	5(33.33%)	15(15%)	0.01	1.6-4.3	2.3
	>2.5	11(20.37%)	54(54%)			
	>3.5	4(12.90%)	31(31%)			
Gestational age	37-40	17(18.69%)	91(91%)	0.7	0.5-2.3	0.8
	>40	3(20%)	9(9%)			
Fetal growth	SGA	3(25%)	12(12%)	0.96	0.6-2.2	1.1
	LGA	1(33.33%)	3(3%)			
	AGA	16(18.82%)	85(85%)			
Dehydration	Yes	4(33.33%)	12(12%)	0.057	1.06-3.9	2.04
	No	16(18.18%)	88(88%)			
Delayed First feeding(>3 hrs)	Yes	10(29.41%)	17(17%)	0.03	1.18-4.4	2.2
	No	10(12.05%)	83(83%)			
Top feeding/mixed feeding	Yes	9(29.03%)	31(31%)	0.07	1.08-4.26	2.1
	No	11(15.94%)	69(69%)			
24 hr serum bilirubin*	>6 mg/dl	5(33.33%)	15(15%)	0.037	1.18-3.1	2.1
48 hr serum bilirubin*	>11mg /dl	9(30%)	30(30%)	0.001	1.8-7.5	3.6
*24 Hr serum bilirubin >6 corresponds to low intermediate zone and 48 Hr serum bilirubin >11.8 to high intermediate risk zone in Bhutani nomogram birth weight <2.5 kg, delayed first feeding, dehydration,24 Hr serum bilirubin >6mg/dl and 48 Hr serum bilirubin >11.8 mg/dl were significantly associated with significant hyperbilirubinemia (p<0.05)						

Discussion

Neonatal hyperbilirubinemia is the most common physical abnormality in newborns, it occurs in about 60-70% of full-term and 80% of preterm newborns. It is also the most common cause of readmission to the hospital during the early neonatal period. Approximately 4% of term neonates who are readmitted during their first week of life, 85% have jaundice.[6]

Reliable prediction of at-risk neonates may allow clinicians to plan early discharge of low-risk neonates and timely follow-up of high-risk neonates. Simple, non-invasive, and cost-effective methods should be used in high-risk neonates. Recently various new strategies are being adopted to predict significant hyperbilirubinemia in these newborns to facilitated early discharge and timely follow-up.[7] But many of these methods are costly and require repeated sampling and close assessment, which sometimes is not practical in a busy government setting handling large numbers of newborns. Several

demographic and clinical factors are described in a recent meta-analysis of available studies in low resource settings to exacerbate physiological hyperbilirubinemia and make these newborns more likely to develop complications of severe hyperbilirubinemia. According to some recent studies, even newborns having moderate hyperbilirubinemia may show minor or subtle neurological abnormality at a later age

Out of 100 newborns 5 newborns (33.33%) developed hyperbilirubinemia above high intermediate zone at 48 hrs while 9(30%) newborns developed subsequently developed hyperbilirubinemia at 72 hrs. Total bilirubin >6mg/dl at 24 and >11mg/dl at 48 hrs of life which corresponds to high intermediate risk zone cutoff in Bhutani nomogram and found this association to be statistically significant. In our study birth weight <2.5 kg, delayed first feeding, dehydration, 24 and 48-hour serum bilirubin >11 mg/dl were significantly associated with significant hyperbilirubinemia ($p<0.05$)

Maternal age, social background, and primiparity are described as risk factors in various studies.8-10 Adebami O et al.[8] found in their study that social background and advanced maternal age were significant risk factors for the development of severe hyperbilirubinemia among Term newborns. Olusanya BO et al.[9] did not find these risk factors to be significant in their observation. We also did not found statistical significance for social background, and maternal age, and Parity of mother as a risk factor for hyperbilirubinemia.

During the first week of life, some newborns may suffer from caloric deprivation due to low volume of feeds and delayed enteral feeding. This condition will lead to decreased gastrointestinal activity, decreased stool frequency, delayed meconium passage further increasing enter hepatic recirculation of bilirubin. Low oral intake may induce a state of fasting in these newborns. Fasting is known to increase enter hepatic circulation by suppressing gastrointestinal motility.[10] Early initiation of feeding and intervals < 3 hours are related to lower bilirubin levels in a study by M. Alex et al.[11] Dehydration or weightless >10% in the first week, Delayed feeding, and mixed feeding was significantly associated with significant Hyperbilirubinemia in few studies.[11-13] We did not find any statistical significance of exclusive breastfeeding in developing significant hyperbilirubinemia. As inadequate breastfeeding is more likely to cause significant hyperbilirubinemia rather than breastfeeding due to resemblance to fasting state and increased enter hepatic recirculation.

On the other hand, dehydration and delayed initiation feeding were a significant risk factors in our study causing weight loss (≥10%) after birth which can be associated with insufficient oral intake during the first week of life. Studies by M. Alex et al.[11], Bilgin et al.[12] and Tiwari et al.[13] also supported our observations. We observed delayed enteral feeding to be significantly associated with increased risk of hyperbilirubinemia at 48 and 72 hrs. Mixed feeding frequency in our study population was found as high as 31%. As our hospital is tertiary care has high rates of cesarean sections leading to further delay in initiation of breastfeeding and prolonged separation leads to poor lactation in mothers. However, we did not find mixed feeding to increase the risk of hyperbilirubinemia in newborns independently.

Delivery mode and anaesthesia during the cesarean section may also influence the hyperbilirubinemia risk in newborns. We did not observe a statistically significant

difference between the cesarean section and newborns born vaginally. Several other studies comparing cesarean section and vaginal delivery also did not found the mode of delivery to be significant in increasing hyperbilirubinemia risk.[12,14] Oxytocin induction was also not found to be associated with significant hyperbilirubinemia in newborns in the present study is supported by the study conducted by Patil S et al.[15].

The present study found that a higher TSB value at 24 & 48 hours is associated with a risk of significant hyperbilirubinemia at 72 hrs. A study by Randhev S et al.[16] with 228 full-term newborns concluded that 24±6 hour TSB value >6.4 mg/dl had a significant correlation with the development of hyperbilirubinemia with 87.5% sensitivity, 97.9% Negative predictive value, and 80.1% speciality.

Alpay et al.[17] and Agarwal, Deorari et al.[18] also found that a bilirubin level of >6 mg/dL during the first 24 h of life, had a significant association with hyperbilirubinemia with >90% sensitivity and an NPV. Some studies on Indian newborns even recommended serum bilirubin level >4.4 at 24 and >6.5 mg per dl at 48 hrs to successfully predict significant hyperbilirubinemia for Indian newborns with a similar demographic profile as in the present study.[19,20]

Conclusion

The present study concluded that healthy full-term newborns with birth weight <2.5 kg, higher 24 and 48-hour serum bilirubin were more likely to experience significant hyperbilirubinemia who are often discharged from hospital early.

Reference

1. Chou RH, Ezhuthachan S: Management of hyperbilirubinemia in newborns: measuring performance by using a benchmarking model. Pediatrics 2003, 112:1264–1273.
2. Berkowitz CD: Pediatrics: a primary care approach. 2nd edition. Philadelphia: WB Saunders Company; 2000:51–52.
3. Hansen TW. Prevention of neurodevelopmental sequelae of jaundice in the newborn. Dev Med Child Neurol. 2011 Sep;53 Suppl 4:24-8.
4. Noel-Weiss J, Gourant G, Woodend AK: Physiological weight loss in the breastfed neonate: a systematic review. Open Medicine 2008, 2:E11–E22.
5. Laing IA, Wong CM: Hypernatremia in the first few days: is the incidence rising? Arch Dis Child Fetal Neonatal Ed 2002, 87:F158–F162.
6. Nelson D, Porta R, Blair K, Carter P, Martin M. The duodenal switch for morbid obesity- modification of cardiovascular risk markers compared with standard bariatric surgeries. Am J Surg. 2012 May;203(5)603-608.
7. Bhutani VK, Johnson LH, Keren R. Diagnosis and management of hyperbilirubinemia in the term neonate-for a safer first week. Pediatr Clin North Am. 2004 Aug;51(4)843-61, vii.
8. Adebami, Olusegun J. "Factors associated with the incidence of acute bilirubin encephalopathy in Nigerian population". Journal of Pediatric Neurology. 2011;9(03)347-353.
9. Olusanya BO, Akande AA, Emokpae A, Olowe SA. Infants with severe neonatal jaundice in Lagos, Nigeria-incidence, correlates and hearing screening outcomes. Trop Med Int Health. 2009 Mar;14(3)301-10.
10. Ameh N, Ameh EA. Timing of passage of first meconium and stooling pattern in normal Nigerian newborns. Ann Trop Paediatr. 2009 Jun;29(2)129- 33.
11. Alex M, Gallant DP. Toward understanding the connections between infant jaundice and infant feeding. J Pediatr Nurs. 2008 Dec;23(6)429-38.
12. Siyah Bilgin B, Altun Koroglu O, Yalaz M, Karaman S, Kultursay N.

Factors affecting bilirubin levels during first 48 hours of life in healthy infants. BioMed research international. 2013.
13. Tiwari PK, Bhutada A, Agarwal R, Basu S, Raman R, Kumar A. UGT1A1 gene variants and clinical risk factors modulate hyperbilirubinemia risk in newborns. J Perinatol. 2014 Feb;34(2)120-4.
14. Alkan S, Tiraş U, Dallar Y, Sunay D. Effect of anaesthetic agents administered to the mothers on transcutaneous bilirubin levels in the neonates. Acta Paediatr. 2010 Jul;99(7)993-6.
15. Patil S S, Manjunatha S, Veena H C, Vinod W. Oxytocin induced neonatal hyperbilirubinemia. Journal of Evidence Based Medicine and Healthcare. 2015;2(21)3098-3103.
16. Randev S, Grover N. Predicting neonatal hyperbilirubinemia using first day serum bilirubin levels. Indian J Pediatr. 2010 Feb;77(2)147-50.
17. Alpay F, Sarici SU, Tosuncuk HD, Serdar MA, Inanç N, Gökçay E. The value of first-day bilirubin measurement in predicting the development of significant hyperbilirubinemia in healthy term newborns. Pediatrics. 2000 Aug;106(2)E16.
18. Agarwal R, Kaushal M, Aggarwal R, Paul VK, Deorari AK. Early neonatal hyperbilirubinemia using first day serum bilirubin level. Indian Pediatr. 2002 Aug;39(8)724-30.
19. Vailaya R C G, Aiyer S. “Early Prediction of Significant Neonatal Hyperbilirubinemia using Serum Bilirubin Levels in Healthy term & near term Newborns”. J Pub Health Med Res. 2014;2(1)14-9.