

Incidence of neonatal hyperbilirubinemia in low, intermediate-low, and intermediate-high risk group infants

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Abstract

Background Neonatal hyperbilirubinemia is commonly found in newborns. Assessment of the risk of hyperbilirubinemia and information on the average time of the occurrence of hyperbilirubinemia are important to prevent the development of severe hyperbilirubinemia.

Objective To find out the incidence of and the time of the development of hyperbilirubinemia in healthy-term newborns.

Method A cohort prospective study was done on healthy-term newborns born at Hasan Sadikin Hospital between November and December 2009. Subjects were divided into 4 groups of risk at discharged, based on Bhutani nomogram. A serial bilirubin level measurement were performed within 6 days.

Results One of 14 newborns at low risk group developed hyperbilirubinemia but did not need phototherapy. Six of 14 newborns at intermediate-low risk group developed hyperbilirubinemia, 2 of them needed phototherapy with total serum bilirubin level of 14.7 mg/dL at 57 hours and 19.8 mg/dL at 111 hours. Nine of 15 newborns of intermediate-high risk group developed hyperbilirubinemia, 1 of them needed phototherapy with total serum bilirubin level of 16.6 mg/dL at 76 hours. There was no newborn categorized as high risk group in this study. The median time the occurrence of hyperbilirubinemia in intermediate-low and intermediate-high risk group was 140 hours and 82 hours, respectively. There was no significant difference in survival curve between intermediate-high and intermediate-low risk groups (95% CI 108.1-125.4).

Conclusion The incidence of hyperbilirubinemia was not different between intermediate-low and intermediate-high risk babies. [Paediatr Indones. 2010;50:351-4].

Keywords: neonatal hyperbilirubinemia, survival, risk.

Hyperbilirubinemia is a common problem in newborns, which may develop to severe hyperbilirubinemia if not managed properly.¹⁻⁶ Early discharge of healthy-term newborn and inadequate breastfeeding might lead to undetected hyperbilirubinemia, which can cause Kern icterus, a reemergency condition.⁷⁻⁹ Therefore, early detection of and acknowledging the risk factors of hyperbilirubinemia are important to be conducted before discharging newborns from the hospital.¹

Bhutani nomogram, which was developed based on postnatal age (in hours) and total serum bilirubin level, is an essential tool to prevent severe hyperbilirubinemia. This nomogram consists of four risk zones for the incidence of severe hyperbilirubinemia i.e. low, intermediate-low, intermediate-high, and high risk zone.¹⁰ The incidence of severe hyperbilirubinemia in high, intermediate-high, intermediate-low, and low risk groups are 39.5%, 12.9%, 2.3%, and 0%, respectively.¹

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It is commonly found in developing countries that parents do not bring their newborn baby to the health services for follow up evaluation due to financial problem. This may result in late detection of hyperbilirubinemia. Therefore, a study of survival analysis is needed to find out more accurately when hyperbilirubinemia develops.

Methods

This prospective cohort study was conducted on healthy-term newborns, who were born at Hasan Sadikin Hospital between 1 November and 31 December 2009. We included single baby, spontaneous delivery, term, appropriate for gestational age, roomed-in with the mother, parents lived in Bandung and obtained parental written consent. We excluded newborns from unmarried couples, and has ABO incompatibility. A minimal sample size of 14 in each group was needed.

Total serum bilirubin level examination was performed at the time of discharge, every 24-48 hours afterwards until the age of 144 hours or in case hyperbilirubinemia occurred (total serum bilirubin level ≥ 13 mg/dL). Total serum bilirubin level according to newborn's age (in hours) was plotted to hyperbilirubinemia nomogram of Bhutani, then categorized as low risk (lower than 40th percentile), intermediate-low risk (40th-75th percentile), intermediate-high risk (75th-95th percentile), and high risk group (higher than 95th percentile).⁹ Risk factors of severe hyperbilirubinemia were recorded from mothers and newborns. Time of hyperbilirubinemia in each group were analyzed with survival analysis and comparison between each survival curve were analyzed by Gehan log-rank test. All statistical analysis was done with SPSS 13.0 software.

Results

During the study period there were 43 newborns, consisted of 14 low-risk babies, 14 intermediate-low risk babies, 15 intermediate-high risk babies, and none of high risk babies. Of 43 newborns there were 14 males and 29 females. All of the newborns did not have a history of hyperbilirubinemia of their sibling(s). The mean age of mother in low, intermediate-low, and intermediate-high risk group were 21, 26.0 (SD 6.0), and 32.7 (SD 2.2) years, consecutively.

Sixteen of 43 (37.2%) newborns developed hyperbilirubinemia, consisted of 10 females and 6 males. Hyperbilirubinemia occurred in 1/14 of low-risk newborns, 6/14 of intermediate-low risk newborns, and 9/15 of intermediate-high risk newborns.

The characteristics of the newborns in a low risk group are presented in **Table 1**. Most newborns were breastfed. Of the breastfed newborns, one developed hyperbilirubinemia. The mean of birth weight was 2953.2 (SD 330.1) grams, age at discharge was 17 (SD 10.8) hours, and bilirubin serum level at discharge was 3.4 (SD 1.2) mg/dL.

Eight of 14 (57.1%) newborns in intermediate-low risk group were breastfed, 2 of them developed hyperbilirubinemia. (**Table 2**). The mean of birth weight was 3325 (SD 328.8) grams, age at discharge was 27.8 (SD 6.7) hours, and bilirubin serum level at discharge was 6.4 (SD 1.3) mg/dL.

In intermediate-high risk group, 60% (9/15) of the newborns developed hyperbilirubinemia. Most (93.3%) of the newborns in this group were breastfed.. Fifty seven percent (8/14) of breastfed newborns and one newborn (100%) who was given formula milk developed hyperbilirubinemia (**Table 3**). The mean birth weight was 2975.8 (SD 301.5) grams, age at discharge was 27.1 (SD 8.0) hours, and bilirubin serum level at discharge was 7.9 (SD 1.5) mg/dL.

Table 1. Characteristics of newborns in low risk group

Characteristics n = 14	Bilirubin level	
	≤ 13 mg/dL	> 13 mg/dL
Breastfed	11	1
Formula milk	2	0
Male	5	0
Female	8	1
Birth weight (g)	2965.8 (334.6)	2700
Age on discharge (SD) (hours)	15.4 (9.6)	38
Bilirubin level on discharge (SD) (mg/dL)	3.1 (0.8)	6.96

Table 2. Characteristics of newborns in intermediate-low group

Characteristics n = 14	Bilirubin level	
	<13 mg/dL	>13 mg/dL
Breastfed	6	2
Formula milk	2	4
Male	2	3
Female	6	3
Birth weight (g)	3137.5 (332.5)	2825.0 (91.7)
Age on discharge (SD) (hours)	25.9 (8.0)	30.3 (4.2)
Bilirubin level on discharge (SD) (mg/dL)	6.5 (1.1)	6.3 (1.5)

Table 3. Characteristics of newborns in intermediate-high risk group

Characteristics n = 15	Bilirubin level		Total
	<13 mg/dL	>13 mg/dL	
Breastfed	6	8	14
Formula milk	0	1	1
Male	1	3	4
Female	5	6	11
Birth weight (g)	3017.5 (234.8)	2933.3 (339.1)	
Age on discharge (SD) (hours)	22.6 (8.9)	30.0 (7.4)	
Bilirubin level on discharge (SD) (mg/dL)	9.8 (1.6)	9.9 (1.5)	

The survival analysis showed that the median of time of the occurrence of hyperbilirubinemia in low risk group was not able to be determined. In intermediate-low and intermediate high risk group, hyperbilirubinemia occurred at 140 hours and of 82 hours, respectively (95%CI 108.1-125.4) (**Figure 1**).

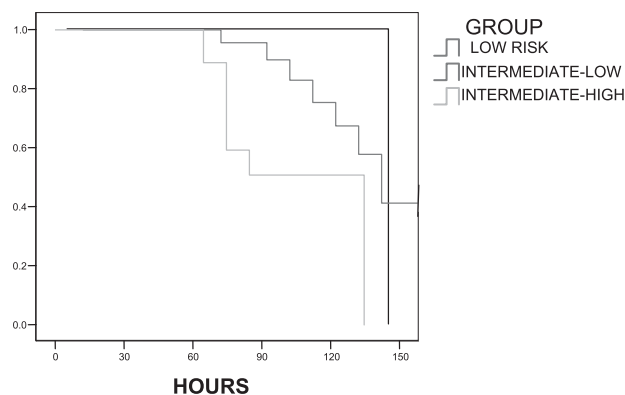


Figure 1. Survival curve in low risk, intermediate-low, and intermediate-high risk with Gehan log-rank test.

Discussion

Hyperbilirubinemia in a healthy-term newborn was influenced by a history of hyperbilirubinemia in siblings, male gender, mother's age >25 years, diabetic mother, inadequate breastfeeding, cephalhematoma,

and asphyxia.^{1,3} None of the subjects in this study had siblings with a history of hyperbilirubinemia. Previous studies showed that the incidence of severe hyperbilirubinemia were found more common in intermediate-high than intermediate-low risk zone and none in low risk zone.^{1,10} Our study showed that hyperbilirubinemia occurred earlier in intermediate-high compared to intermediate-low risk group, and the latest in low risk zone.

Only one of 14 newborns at low risk group reached bilirubin level of 13.6 mg/dL at 133 hours of age (at 38 hours of age, bilirubin serum level was 6.9 mg/dL). This baby was female, had no icteric at discharge, adequately breastfed, and born from 18 years old mother at 40 weeks gestational age. Hyperbilirubinemia in this case was probably caused by breast-milk jaundice. No phototherapy was required for this baby. Six of 14 newborns in intermediate-low risk group had hyperbilirubinemia, 2 of them needed phototherapy with total serum bilirubin level of 14.7 mg/dL at 57 hours (intermediate-high risk zone) and 19.8 mg/dL at 111 hours (high risk zone), respectively. Both were females, adequately breastfed combined with formula-fed, mothers' age were 29 and 27 years respectively. The probable causes of hyperbilirubinemia were G6PD deficiency or other genetic factors. G6PD was examined in this study, but the result was not valid because of procedural error.

In the intermediate-high risk group, nine newborns developed hyperbilirubinemia and one needed phototherapy with bilirubin serum level of 16.6 mg/dL at the age of 76 hours (high risk zone). This newborn was female and was given combined breast and formula milk. The probable cause of hyperbilirubinemia was G-6-PD deficiency or other genetic factors.

A newborn at low risk could become intermediate-low risk zone, while newborns at intermediate-low risk could become intermediate-high or high risk in the first week of life. These changes were in accordance with those of Bhutani's study.^{8,9} With survival analysis, at low risk zone there was no median survival time of hyperbilirubinemia, at intermediate-low risk zone median survival time of hyperbilirubinemia was 140 hours, and at intermediate-high risk zone was 82 hours.

In conclusion, the incidence of hyperbilirubinemia in intermediate-low and intermediate-high groups is not different, but the times when hyperbilirubinemia occurred were different in each group of newborns.

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