The association of neonatal jaundice and breast-feeding

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ABSTRACT To examine the prevalence of jaundice in neonates and its association with breast-feeding, we studied 100 healthy breast-fed baby boys during the first 3 - 5 days after birth, delivered in Dr. Cipto Mangunkusumo Hospital. This was an analytical, cross-sectional study performed prospectively. The study was conducted from April, 1, 1999 to October 15, 1999. Jaundice was detected in 94 out of 100 infants (94%). Breast-feeding jaundice was encountered in 26 infants (28%) namely infants whose bilirubin levels was >12 mg/dL by day 3 (Cl 95% : 19;37%). Most infants showed bilirubin levels on day two, three and five of 6 – 10 mg/dL (62%), 6 – 10 mg/dL (35%) and 12 – 15 mg/dL (34%), respectively. Several factors found to be contributing to the occurrence of breast-feeding jaundice included : a. breast-feeding frequency (r : - 0.83, p < 0.01), b. mean breast-feeding duration : infants breast-feed for more than 30 minutes have consequences its breast-feeding frequency was less in compared with those breast-fed in less than 30 minutes. c. time of meconium passage (p < 0.05), meconium passage in the first hours after birth played an important part in reducing enterohepatic circulation, d. fecal weight (r =-0.87, p < 0.01), feces retained in the intestine its bilirubin would be deconjugated and reabsorbed subsequently . e. weight loss (p < 0.05). In 11 infants who received blue light therapy there were no abnormalities both in physical and laboratory examinations. **[Paedatr Indones 2001; 41:69-75].**

Keywords: breast feeding, jaundice, term infants.

JAUNDICE IS A CONDITION FREQUENTLY SEEN IN THE first weeks of neonatal life.¹⁻³ In term neonates approximately 25-50% of them develop jaundice.^{1,3} The incidence rates of breast-feeding jaundice in the literature vary between 15-50%.^{4,5} Although most jaundiced neonates looked healthy, this finding make physicians worry,^{2,4} with the consequens that the babies are kept in the hospital longer to get treatment.

Jaundice due to breast-feeding can be divided into 2 forms, namely breast-feeding jaundice and breastmilk jaundice. Breast-feeding jaundice is a physiological jaundice in excess with rapid onset and associaed with inadequate amount of breast-feeding brteastmilk or insufficient intake for infant's need. Breastmilk jaundice is usually late onset (age of infants > 4 days) and associated with contain certain substances such as $3-\alpha$ - 20- β pregnanediol, free fatty acid being actived as competitive inhibitor against enzyme glucuronyl transferase resulting impairment of bilirubin conjugation process by the liver.¹ Breastfeeding jaundice or jaundice due to inadequate breast-feeding is jaundice that begins to appear on early day 3, its bilirubin levels can reach 12 mg/dL or higher and its increase may persist till day 5 to 6 before returning to decrease and disappear by the 11th to 14th day. These infants did not show abnormal clinical manifestations, infants look healthy, no breastfeeding disorder and kernicterus has never been reported.¹ The expenses that must be paid during this physiological jaundice management reach millions dollars annually.⁶ Some study reported the complains of exclusive breast-feeding program because of the steadily increasing number of infants developing hyperbilirubinemia due to inadequate breast-milk production in the first days.7

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With this background, the authors were interested in studying the association of inadequate breastfeeding with excessive physiological neonatal jaundice developing by day three (breast-feeding jaundice).

Methods

We studied 100 healthy infant boys delivered at Obstetrics and Gynecology Department, Medical Faculty, Indonesia University, Cipto Mangunkusumo Hospital Jakarta. Infant boys were chosen as study samples to facilitate fecal examination technique as to avoid urine contamination, and to save the study expenditure. We asked mothers' permission to allow their infants to be investigated for at least 3 days, breast-feeding infants without formula and return for re-examine at infants' age of 5 days. Subjects satisfying inclusion criteria were enrolled by consecutive sampling and informed consent was asked.

The criteria for inclusion were healthy, term infant boys, birth-weight >2500 – 4000 grams, normal pregnancy and delivery, Apgar score one minute >7, delivered at Obstetrics and Gynecology Department, Medical Faculty, Indonesia University, Cipto Mangunkusumo Hospital Jakarta.

We excluded infants with congenital disorders, twins, infants who had not been breast-fed after longer than 3 hours, mothers with DM or took traditional herbal or suspected drugs, history of previous jaundice in infants, the presence of intrapartum infection, cephal-hematoma, jaundice occurred in the first 24 hours or > 4 days, positive Coomb's test, disturbances in Hb, Ht, reticulocyte, morphology of erythrocyte, refused to participate in the study.

The authors recorded the date and time of infant delivery and the hour when they breast-fed for the first time. Infants breast-fed on demand, the investigator and mothers noted the frequency and duration of each breast-feeding daily. Birth-weight was weighed at birth, 24, 48, 72, and 120 hours. The date/ time of first meconium passage, frequency of daily stool were noted. After the first meconium passage, weighed diapers were put on the infants, preceded by plastic urine bag application, diapers were put off every 2 hours to assess whether the infants have defecated. Fecal weight is the diaper weight stained by feces minus the diaper's weight itself. Total bilirubin was studied by day 2, 3 and in control day five (48 \pm 3, 72 \pm 3 and 120 \pm 3 hours) and direct and indirect bilirubin were examined if total bilirubin was ³ 12 mg/dL, using a Microbilirubin analyzer.

Coomb's test was done if total bilirubin levels reached 12 mg/dL. Hb content, Ht, reticulocyte, erythrocyte morphology and blood group determinations were conducted when infants were jaundiced clinically.

Data were analyzed using SPSS for MS windows release 7.5. Significance level chosen for all hypothetical tests was p < 0.05. Confidence interval was 95%.

Results

Baseline data and clinical profile of 100 infants are shown in Table 1. In this study 8 infants were hospitalized only for 2 days so that they were excluded from the day three analysis, but included in the day two analysis. As many as 4 infants did not appear on day 5 so were excluded from that day analysis.

The mean birth weight of the infants was 3204.7 (SD 340.04) grams, with the range from 2500 to 3900 grams.

Among 100 infants, jaundice was seen in 94 infants (94%) whereas 6 infants (6%) were without jaun-

TABLE 1. BASELINE DATA AND CLINICAL PROFILE OF 100 HEALTHY INFANTS

Infant characteristics	
Birth-weight (grams)	
Mean	3204.7
SD	340.04
Range	2500-3900
Jaundice	94 (94%)
Without jaundice	6 (6%)
Breast-feeding jaundice	26 (28.2%)
Received blue light therapy	
2nd day	2 (2.12%)
3rd day	5 (5.31%)
5 th day	4 (4.24%)
Weight loss :	. ,
< 10%	77 (83.6%)
> 10%	15 (16.4%)
> 10%	15 (16.4%)

dice. By day two 8 infants were discharged leaving 92 infants by the 3rd day. Breast-feeding jaundice was found in 26 infants out of 92 infants (28.2%) namely infants whose its bilirubin levels were ³ 12 mg/dL by day three.

Out of 94 infants developing jaundice, blue light therapy was given in 2 infants (2.1%) in the second day with bilirubin levels of 14.2 mg/dl and 16.6 mg/ dl., respectively. Five infants (5.3%) received blue light therapy by day three in which the lowest bilirubin levels was 14.6 mg/dL and the highest was 18.7 mg/dL and 4 infants (4.3%) received blue light therapy by the fifth day with the lowest bilirubin levels was 14.5 mg/dL and the highest was 20 mg/dL. Coomb's tests in all infants receiving blue light therapy were negative, no ABO incompatibility, normal Ht values, normal reticulocyte and morphology of peripheral blood cells and infants looked well.

By day three the weight loss of more than 10% was found in 15 infants (16.4%) and in 77 infants (83. 6%) the weight loss was less than 10%.

By day 2 most infants (62%) showed bilirubin levels range from 6 - 10 mg/dL whereas seven infants showing the bilirubin level of less than 6 mg/dl and only one case with the level more than 15 mg/dl.

TABLE 2. DISTRIBUTION OF BILIRUBIN LEVELS IN THE FIRST 3 DAYS

Bilirubin level (mg/dl)		ay 2 Day 3		Day 5		
ever (mg/u	n	%	n	%	n	%
< 6	7	7	4	4.3	7	7.3
6 – 10	62	62	32	34.8	19	19.8
10 – 12	21	21	30	32.6	28	29.9
12 – 15	9	9	21	22.8	33	34.4
> 15	1	1	5	5.4	9	9.4

By day 3 most infants showed the bilirubin levels range of 6–10 mg/dL (34.8%) and 10–12 mg/dL (32.6%). Breast-feeding jaundice namely bilirubin levels ³ 12 mg/dL was observed in 26 infants (28.2%) with CI of 95%: 19.00 – 37.4. The highest and lowest bilirubin levels in this age were found in other infants with levels of 18.7 mg/dL and 2.7 mg/dL, respectively.

By the fifth day most infants (34.4%) with the bilirubin levels range from 12-15 mg/dL and the remaining (29.9%) showed bilirubin levels between 10 – 12 mg/dL. In this age group the highest bilirubin level was 20 mg/dL and the lowest was 2.0 mg/dL (Table 2).

TABLE 3. THE ASSOCIATION OF WEIGHT LOSS WITH BILIRUBIN LEVELS IN DAY THREE

< 10% 10.3 (SD 2.41	
< 10% 10.5 (SD 2.4))
> 10% 11.7 (SD 3.24	·)

t = - 2.021 df = 90 p = 0.046

Weight loss by day three had a significant correlation with bilirubin levels (p < 0.05) as shown in Table 3. Infants developing weight loss of more than 10% of birth-weight showed higher bilirubin levels (11.7, SD 3.23 mg/dl) compared with those with weight loss of less than 10% (10.3, SD 2.41 mg/dL).

TABLE 4. ASSOCIATION OF MECONIUM PASSAGE WITH BILIRUBIN LEVELS BY DAY TWO AND DAY THREE

Time of meconium passage	Bilirubin levels (mg/dl) Mean±SD			
	Day 2	Day 3		
At birth	7.5 (2.00)	9.3 (2.15)		
< 2 hours	8.8 (2.07)	10.1 (2.60)		
2 – 12 hours	9.4 (2.25)	11.2 (2.82)		
13– 24 hours	9.6 (2.19)	11.2 (3.20)		

Day 2 : F = 4.933 df = 3 p= 0.003 Day 3 : F = 3.117 df = 3 p =0.030

The time of meconium passage showed a significant correlation with bilirubin levels both by day two and by the 3rd day (p< 0.05). Infants who passed the fisrt meconium 12 - 24 hours after birth showed higher

bilirubin levels, i.e., 9.6 mg/dL by day two and 11.2 mg/dL by day three, respectively. Infants who passed the first meconium within 2 to 12 hours after birth had the bilirubin levels of 9.4 mg/dL in day two and 11.2 mg/dL in day three. Infants with meconium passed at birth showed lower bilirubin levels, i.e., 7.5 mg/dL by the second day and 9.3 mg/dL by day three (Table 4).

TABLE 5. THE ASSOCIATION OF BREAST-FEEDING FREQUENCY WITH BILIRUBIN LEVELS

Feeding freq/day		Bilirubin levels (mg/dl) Mean (SD)		
	Day 2	Day 3		
6 – 8 times	10.7 (1.65)	12.8 (2.00)		
9 – 10 times	8.4 (1.59)	10.5 (1.51)		
11 – 12 times	6.1 (1.47)	7.0 (1.71)		

Day 2 : F = 48.201; df = 2; p = 0.000 Day 3 :F = 59.496 df = 2 p = 0.000

Breast-feeding frequency having a significant negative correlation with bilirubin levels (r = -0.83, p < 0.01) (Table 5). Infants whose daily breast-feeding frequency was less (6 – 8 times) showed higher bilirubin levels, i.e., 10.7 (SD 1.65) mg/dL by day two and 12.8 (SD 2.0) mg/dL in the day three, respectively. Most infants were fed in breast-feeding frequencies of 9 to 10 times and by examination bilirubin was found in respective lower levels of 8.4 (SD1.59) mg/dL by day two and 10.3 (SD 1.5) mg/dL by day three. The most frequently breast-fed infants (11 to 12 times) showed the lowest bilirubin levels, namely 6.1 (SD 1.47) mg/dL by the 2nd day and 7.0 (SD 1.71) mg/dL by the 3rd day, respectively.

Breast-feeding duration has a significant correlation with bilirubin levels both by day two and day 3 (p<0.05) (Table 6). By day two infants with breastfeeding duration less than 30 minutes indicated lower bilirubin levels in comparison with infants with mean duration of breast-feeding of more than 30 minutes namely 8.5 (SD 2.13) mg/dL and 9.4 (SD 2.29) mg/ dL. By day three infants with mean breast-feeding duration less than 30 minutes showed lower bilirubin levels compared to infants with breast-feeding duration more than 30 minutes namely 10.1 (SD 2.48) mg/ dL and 11.5 (SD 2.8) mg/dL, respectively. Infants who wre breast-fed less than 30 minutes per feeding were more frequently breast-fed than those with mean breast-feeding duration of more than 30 minutes, i.e., 9.8 vs 9.1 times a day as shown in Table 7.

TABLE 6. ASSOCIATION OF MEAN DURATION OF BREAST-FEEDING WITH BILIRUBIN LEVELS

Feeding duration (minutes)	Bilirubin levels (mg/dl) Mean (SD)		
	Day 2	Day 3	
< 30	8.5 (2.13)	10.2 (2.48)	
≥ 30	9.4 (2.29)	11.5 (2.75)	
Day 2 : t = 4. 02	92 df = 1 p = 0.047		

Day 3 : t = 2.125 df = 0.90 p = 0.036

TABLE 7. ASSOCIATION OF MEAN BREAST-FEEDING DURATION WITH BREAST-FEEDING FREQUENCY

Feedi Mean	ng frequency / day SD
9.8	1.19
9.1	1.18
	Mean 9.8

t = 2.503 df = 0.90 p = 0.014

TABLE 8. ASSOCIATION OF CUMULATIVE FECAL WEIGHT DURING THE FIRST 3 DAYS WITH BILIRUBIN LEVELS BY DAY THREE

Fecal weight (grams)	Bilirubin Mean	levels SD	day 3 (mg/dl) N
< 20	17.2	_	1
20 - 40	12.8	2.00	26
40 - 60	10.1	1.48	55
60 - 80	6.3	1.71	10

F = 44.437 df = 3 p = 0.000

In this study 26 infants were found to have lower cumulative fecal weight during 3 days, namely 20 to 40 grams, and on examination higher bilirubin levels on day three was found 12.8 (SD 2.00) mg/dL. In the remaining (55 infants) whose cumulative fecal weight was larger (40 – 60 grams) lower bilirubin levels was encountered, i. e., 10.6 (SD 1.48) mg/dL. The largest cumulative fecal weight (60 – 80 grams) was observed in 10 infants, and its bilirubin levels were only 6.3 (SD 1.72) mg/dL.

We observed a significant high correlation between cumulative fecal weight during the first 3 days with bilirubin levels on day three (r = -0.87, p < 0.01) (Table 8).

Discussion

In this study it can be seen that bilirubin levels still rises until day five (Table 2). This findings were in accordance with the literature stating that in breastfeeding infants increased bilirubin levels can occur till day 5 to 6.1,4 A meta-analysis study of 12 investigations on 8000 newborns during the first week of life found moderate jaundice (serum bilirubin ³ 12 mg/dL or 205 mmol/L) in 12.9% of breast-fed infants and in 4% of infants receiving formula. Severe jaundice (serum bilirubin ³ 15 mg/dL or 257 mmol/L) was found in 2% breast-fed infants and in only 0.3% of formula-fed infants.5 In this study moderate jaundice was found in 22.8% of infants and severe jaundice in 5.4% of breast-fed infants. This study results were almost similar with those reported by Kuhr et al8 namely moderate jaundice of 22.1% and severe jaundice of 9%.

Butler et al⁹ and Maisels MJ et al¹⁰ in their study found statistically significant weight loss in infants developing breast-feeding jaundice. In this study 15 infants (16.3%) showed weight loss of more than 10% of their birth-weight and by examination higher bilirubin levels (11.7 mg/dL) compared with infants whose weight loss was less than 10% (10.3 mg/dL) (Table 3). Lack of caloric intake resulting in weight loss in association with jaundice has been described by Gartner and Lee.¹¹ During fasting period the unesterified fatty acid levels increase and hamper bilirubin clearance by the liver. These fatty acids can affect bilirubin uptake by inhibiting receptors in liver cells membrane. The fatty acids also compete with unconjugated bilirubin binding to ligandin and may reduce bilirubin clearance by inhibiting the activity of enzyme glucuronyl transferase. Some literature said that in breast-fed infants, because amount of breastmilk on the first days were still small, bilirubin levels were increased, so dehydration it self might be a cause of jaundice.¹²

The time of meconium passage showed a significant correlation with bilirubin levels both by day two and day three (p < 0.05). Infants passing meconium more slowly showed higher bilirubin levels both by day two and day 3. Infants with meconium passage after 12 to 24 hours had high bilirubin levels of 9.6 mg/dL by day two and 11.2 mg/dL by day three, respectively. Infants whose meconium passage took place at birth and at age of less than 2 hours showed respective lower bilirubin levels of 7.5 mg/dL and 8.8 mg/dL by the second day, whereas by day three respective values of 9.3 mg/dL and 10.1 mg/dL (Table 4) were observed. Indirect bilirubin was reabsorbed and entered the blood through enterohepatic circulation in normal condition exerts its highly marked effect in the first hours of life.13 Raised enterohepatic circulation is an important cause of breast-feeding jaundice, so the main effort reduce the incidence of this excessive jaundice in neonates some measures can be taken to accelerate the meconium passage. This hypothesis has been tested in 2 control-case studies. Cottler et al¹⁴ measured the ratio of bilirubin levels of infants whose its axillary temperature was taken and those whose temperature was rectally taken immediately after birth based on the assumption that thermometer insertion in rectum would lead to faster meconium passage. Another study Weisman et al¹⁵ who chose infants randomly to be given glycerin suppository in the first hour of life. From those two studies they found that peak levels of serum bilirubin in infants with rectal stimulation was lower of 1 mg/dL compared with control.

Breast-feeding frequency in this study showed a significant negative correlation with bilirubin levels both by day two and day 3 (r = -0.83, p< 0.01). The lower the frequency, the higher the bilirubin level was detected as shown in Table 5. This finding was in accordance with the study reported by other researchers though they found a slight difference from bilirubin levels obtained.^{16,17} De Carvalho et al¹⁶ found that infants exclusively breast-fed without any other supplementation, if its mean breast-feeding frequency was 6 times a day so the mean bilirubin levels in day three was 11 mg/dL, whereas those breast-fed 7 times

a day the levels was $9.3 \pm 3.5 \text{ mg/dL}$. Infants breastfed 10 times a day showed bilirubin levels of $6.5 \pm 4.0 \text{ mg/dL}$ and those breast-fed 12 times revealed bilirubin levels only of 5 mg/dL (r = 0.66, p < 0.001). Yamauchi and Yamanouchi¹⁸ have investigated 140 healthy and term newborns. They reported that the prevalence of hyperbilirubinemia declined significantly by the sixth day in infants breast-fed at least 9 times in the first 24 hours. The appropriate frequency of breast-feeding that can decrease blood bilirubin levels encountered in this study was in accordance with the study reported by De Carvalho¹⁶ namely 12 times a day. With decreasing breast-feeding frequency fecal excretion becomes slower because of diminished gastrocolic reflex contributing to colonic contraction.¹⁹

From the literature it is stated that in the first weeks of life, breast-feeding is more effective when practised briefly in alternate manner compared to that practised continuously at one side. Most (84%) breastmilk was obtained after 8 – 10 minutes breast-feeding and reach 100% in 20 minutes.²⁰ In the present study a significant correlation of breast-feeding duration and serum bilirubin levels was observed. Infants breastfed longer than 30 minutes showed higher serum bilirubin levels compared with those breast-fed less than 30 minutes (Table 6). This could be explained based on the other fact found in this study that infants breastfed longer than 30 minutes showed less frequent breast-feeding in comparison with infants with breastfeeding duration of less than 30 minutes (Table 7).

Fecal weight showed a significant negative correlation with serum bilirubin levels (r = - 0.87, p < 0.01) (Table 8). These findings were in accordance with the study reported by De Carvalho¹⁶ who found cumulative fecal weight by the third day of 58 grams with bilirubin levels of 9.5 \pm 3.5 mg/dL. The study by Gourley GR et al²¹ observed cumulative fecal mass by day three was far lighter than that of this study namely 11.36 \pm 3.28 grams and blood bilirubin levels obtained that time was 9.0 \pm 4.7 mg/dL.

In this study 11 infants received blue light therapy. No abnormalities were detected in physical and supporting examination: Coomb's test was negative, no ABO incompatibility, and normal peripheral blood pictures. All infants were discharged home with good clinical condition, this was in accordance with some literature stating that infants developing breastfeeding jaundice were generally healthy.^{1,4,6}

Conclusions

The prevalence of neonatal jaundice in this study was 94%, whereas the breast-feeding jaundice was 28.2% (CI 95%: 19.00-37.39). Infants with less breast-feeding frequency had higher serum bilirubin levels, and the effective breast-feeding frequency was 12 times a day. Infants with duration of breast-feeding more than 30 minutes had higher serum bilirubin levels than those with breast-feeding duration of less than 30 minutes and this correlates with breast-feeding frequency. Infants with slower meconium passage had higher serum bilirubin levels. Higher serum bilirubin levels were detected in with lighter faecal weight. Infants whose weight loss was more than 10% showed higher serum bilirubin levels compared with infants whose weight loss was less than 10%. In the present study infants who suffered from breast-feeding jaundice did not show any abnormality of their clinical manifestations.

The prevalence of breast-feeding jaundice was sufficiently high so that parental education on breastfeeding jaundice was needed and parents should be well informed that jaundice generally occurred was not harmful. Breast-feeding jaundice can be reduced with several ways namely breast-feeding more frequently (12 times a day) with duration not longer than 30 minutes, stimulation of meconium passage if it has not passed in the first 12 hours despite frequent breastfeeding, Prevention of dehydration by day 1 up to 5 to will reduce the possibility of jaundice. Implementation of further study enrolling infant girls and study comparing serum bilirubin levels in infants exclusively breast-fed with infants who were given breast-milk and formula as well.

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