

Differential Risk for Early Breastfeeding Jaundice in a Multi-ethnic Asian Cohort

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Abstract

Introduction: To explore the relationship between ethnic origin and mode of feeding with early neonatal jaundice, we examined maternal and neonatal risk factors for hyperbilirubinaemia in a multi-ethnic Asian cohort of healthy term newborns. **Materials and Methods:** This is an observational cohort study in a maternity ward serving a multi-ethnic cosmopolitan community. The relationship between hyperbilirubinaemia (bilirubin ≥ 150 mmol/L before 48 hours to 72 hours after birth), ethnic origin, weight loss after birth, need for phototherapy, and other factors were examined. Bivariate comparisons and binary logistic regression were used to investigate the relationship between hyperbilirubinaemia/phototherapy with maternal and neonatal risk factors. **Results:** A consecutive group of 1034 neonates (56% Chinese, 24% Indian subcontinent, 9% Malay) with birth weights ≥ 2500 g was investigated. Overall factors that contributed significantly to hyperbilirubinaemia/phototherapy were gestational age, Chinese ethnic origin, weight loss of $\geq 7\%$, vaginal delivery, glucose-6-phosphate-dehydrogenase (G6PD) deficiency, breastfeeding and ABO incompatibility. Chinese neonates who were totally breastfed had a higher risk for jaundice [adjusted odds ratio (OR) = 1.64; 95% confidence intervals (CI), 1.11-2.44; $P < 0.014$], and phototherapy (adjusted OR = 2.75; 95% CI 1.77-4.27; $P < 0.001$) compared to those supplemented with, or totally formula fed. In contrast, the risk of jaundice for non-Chinese infants did not differ according to the mode of feed. Although weight loss as a whole increased the risk for jaundice (adjusted OR = 1.43; 95% CI, 1.03-1.99; $P = 0.031$), jaundice in Chinese neonates was not due to ineffective breastfeeding because both Chinese and non-Chinese breastfed infants lost similar weights. **Conclusions:** Chinese ethnic origin was an independent risk factor for hyperbilirubinaemia and phototherapy. Breastfeeding was not a risk factor for hyperbilirubinaemia/phototherapy in non-Chinese Asian infants.

Ann Acad Med Singapore 2009;38:217-24

Key words: Breastfeeding, Ethnicity, Neonatal jaundice, Phototherapy

Introduction

Early-onset hyperbilirubinaemia is a high-risk condition because it often presents with an acute and rapid rise in bilirubin values. Although the outcome for most is benign, infants with extremely high serum bilirubin can develop acute bilirubin encephalopathy in the absence of urgent intervention.¹ Human milk is universally recognised as the optimal feed for all infants. However, reports from the 1960s indicate that breastfeeding is a risk factor for severe hyperbilirubinaemia.²⁻⁴ Kernicterus has re-emerged as a significant concern in the last 15 years⁵ and breastfeeding has been suggested as a contributing factor, since 98% of kernicteric infants were exclusively breastfed compared to the US national average of 68%.⁶

Despite the numerous articles published on this subject,

many aspects of early neonatal hyperbilirubinaemia and breastfeeding remain controversial.⁷ Increased absorption of breast milk compared to formula, and consequent increased entero-hepatic circulation of bilirubin are thought to increase the risk of hyperbilirubinaemia in breastfed newborns.⁸ However, improved absorbability of formula has reduced differences in absorbability between human and formula milk, resulting in no difference in faecal fat excretion in stools of healthy breastfed versus formula-fed newborns.⁹ Rather than breastfeeding *per se*, inability to establish optimal breastfeeding, decreased caloric intake and subsequent weight loss have been suggested as the underlying factors.¹⁰ Besides well understood causes of early hyperbilirubinaemia such as haemolysis associated with bruising following delivery, ABO/rhesus

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incompatibility or glucose-6-phosphate dehydrogenase (G6PD) deficiency,¹¹ the cause of early neonatal jaundice remains undetermined in up to 60% of cases.⁸ Despite the long-standing observation that Asian ethnic origin may play a role^{10,12,13} the factors and mechanisms underlying this relationship remain unclear. Risk factors for jaundice in breastfed infants need to be clearly defined, so that affected infants can be diagnosed early and given timely treatment. In order to investigate the relationship between the mode of feeding and early neonatal jaundice in a multi-ethnic Asian population, we examined the variables affecting hyperbilirubinaemia and the need for phototherapy in term infants. Particular attention was paid to ethnicity, feeding practices and weight loss, in an environment where mothers and newborns received care in a single ward.

Patients and Methods

This study was approved by the National Health Group Domain-Specific Review Board. All infants delivered in the Department of Obstetrics and Gynecology, National University Hospital, Singapore with gestational age ≥ 37 weeks between June 2005 and February 2007 were considered for inclusion in this study. However infants whose weights were < 2500 g, who required intensive care away from their mothers, or stayed less than 2 days in the ward were excluded from this analysis. Data were collected from only one post-natal ward with ensuite room facilities to minimise differences due to nursing care and ward conditions. Patients received care from a single consultant obstetrician throughout their pregnancy and infants were assessed by a consultant paediatrician. Breastfeeding care was under the supervision of one of the co-authors (LYW). Gestational age was determined according to an early trimester scan. For those without early scans, gestational age was determined using the last menstrual period. Maternal risk factors examined were age of mother at time of delivery, presence of maternal diabetes and/or hypertension, mode of delivery and type of feeding. Mothers with diabetes were classified into those treated adequately with diet alone, or those who also required insulin injections in the antenatal period. Hypertension was diagnosed in those with repeated blood pressures $> 140/90$ mmHg.

Ethnic origin was that recorded in the official birth certificate issued to every baby born in Singapore, and was classified as Chinese, Indian originating from the Indian subcontinent, or Malay. Subjects who did not belong to the above ethnic origins were classified as Others. Mode of delivery was divided into vaginal delivery or caesarean section. The use of vacuum at vaginal delivery or other complications following delivery were noted. At birth, cord blood was obtained for G6PD and ABO-rhesus blood group determinations. Mothers were encouraged to start

nursing in the delivery suite and to breastfeed their infants on demand. They were advised to refrain from water or formula supplementation. Pacifiers were not provided. The number of feedings ranged from 8 to 12 times a day. Breastfeeding referred to infants who were exclusively breastfed. Supplementary feeding referred to infants who were breastfed and received additional formula feeds. Formula feeding referred to infants who were exclusively bottle-fed because mothers declined to breastfeed or their infants presented with contraindications to breastfeeding.

Birth weights were prospectively collected. Infants were weighed at birth and this was checked a few hours later in the post-natal ward using a single digital weighing machine. The weight at birth was recorded as the birth weight if there were < 10 g differences. If the weight in the ward differed ≥ 10 g from that recorded at birth, the baby was weighed twice and the mean weight was taken as the birth weight. Infants were weighed daily and significant weight loss was defined as $\geq 7\%$ of their birth weights after 48 hours to 72 hours of life. This cut-off point was used since a weight loss of $\geq 7\%$ indicated possible breastfeeding problems and dehydration.^{14,15}

Infants were recorded as ABO incompatible if the mother's blood group was O and the infants were either A, B, or AB since these combinations were associated with jaundice in our practice. Rhesus incompatibility was the situation where the mother was rhesus negative and her baby rhesus positive. The G6PD status of all infants was determined. All infants were assessed daily and serum bilirubin determination was performed on those with clinically visible jaundice. Significant jaundice or hyperbilirubinaemia was defined as blood bilirubin levels ≥ 150 $\mu\text{mol/L}$ on, or before, day 3 of life. This relatively low cut-off point was deemed necessary because our population has a high incidence of G6PD deficiency and such infants with bilirubin ≥ 150 $\mu\text{mol/L}$ had a measurable risk of severe hyperbilirubinaemia subsequently.¹⁶ This bilirubin level also corresponds to the "low intermediate risk" zone in Bhutani's normogram for the prediction of subsequent significant hyperbilirubinaemia.¹⁷ Most infants were discharged after 72 hours of life. Infants delivered by caesarean sections or who were significantly jaundiced or presented with significant weight loss stayed longer. Data on bilirubin levels and need for any phototherapy for the cohort during the first 2 weeks of life were collected from the nationwide public hospitals shared electronic medical records system.

Bivariate comparison between hyperbilirubinaemia in term infants and groups of clinical interests was made using *t*-test or Fisher's exact test for continuous and categorical data, respectively. Binary logistic regression was used when investigating the relationship between hyper-

bilirubinaemia in term infants with ethnicity, weight loss, feeding practices as well as other maternal and neonatal risk factors such as G6PD and ABO incompatibility. The effects of potential risk factors on hyperbilirubinaemia respectively, were estimated using odds ratio (OR) and its associated 95% confidence interval (CI). Statistical significance was evaluated at the conventional 5% level based on a 2-sided test. All statistical analyses were generated using STATA version 8.2.

Results

A total of 1034 infants with a mean gestational age of 39.1 (SD 1.07) weeks were retrospectively surveyed and their characteristics were shown in Table 1. About half of the subjects were Chinese (56%) with the other half comprising Indian (24%), Malay (9%) and Other (11%) ethnic origins. During their hospital stay, 381 (37%) infants were visibly yellow and required bilirubin measurement. Of the 1034 infants, 281 (27%) were confirmed to have significant jaundice with serum bilirubin ≥ 150 $\mu\text{mol/L}$ and 6% had severe hyperbilirubinaemia (>221 $\mu\text{mol/L}$) on or before day 3 of life. There were no differences in mean maternal age, gestational age and birth weight between infants with or without jaundice (Table 1). The incidence of jaundiced infants in mothers with or without diabetes, and pregnancy-induced hypertension was not different. Gender and rhesus incompatibility were also not significant risk factors. During the first 2 weeks of life, 18.1% of the cohort had bilirubin levels ≥ 255 $\mu\text{mol/L}$, and 23.9% required some form of phototherapy.

Overall bivariate analyses showed that those of Chinese ethnic origin, breastfeeding, vaginal delivery, G6PD deficiency, ABO incompatibility and weight loss were potential risk factors of jaundice (Table 1). However, as modes of feeding and delivery were closely related because caesarean section reduced the rate of total breastfeeding, we elected to exclude mode of delivery from the logistic regression modelling to resolve the issue of collinearity, as well as to better reveal possible risk factors of breastfeeding jaundice. The impact of all other risk factors on jaundice as identified in the bivariate analyses remained notable in the binary logistic regression analysis (Table 2). Sixty-six per cent of jaundiced infants were Chinese. This was higher than the proportion (56%) of Chinese subjects in the study population ($P < 0.001$). In contrast, the risk of jaundice was not increased in non-Chinese infants such as those of Indian, Malay or Other ethnic origins (Table 1). The proportions of jaundiced subjects of these ethnic origins were similar to, or lower than, their distributions in the study population. Of the total of 1043 infants, the proportions of infants with serum bilirubin ≥ 255 $\mu\text{mol/L}$ within the first two weeks of life were 21% (124/579), 11% (11/96), 15%

(37/246) and 13% (15/113) for Chinese, Malay, Indian and Other races, respectively. Since the rates of phototherapy of Malay, Indian and Other races do not appear to differ materially, infants of non-Chinese ethnic origin were analysed as a group (Table 2). We also looked for independent and significant risk factors for infants requiring phototherapy during the first 2 weeks of life. They were found to be the same as those listed above for significant jaundice with gestational age now being significant (Table 3).

Infants with jaundice had a significantly higher weight loss of 20g or 12.6% ($P < 0.001$) more, compared with those without jaundice. This translated to a 43% (adjusted OR, 1.43; 95% CI, 1.03 to 1.99) increase in risk of jaundice among infants losing $\geq 7\%$ as compared to those who lose $< 7\%$ of their birth weights (Table 2). Weight loss was strongly and independently associated with breastfeeding (adjusted OR, 4.63; 95% CI, 3.31 to 6.45; $P < 0.001$), and the risk of weight loss decreased with increasing gestational age (adjusted OR, 0.86; 95% CI, 0.75 to 0.98; $P = 0.024$) (Table 4). Haemolysis was an important contributor to jaundice as ABO-incompatible and G6PD-deficient infants had a 1.69 (95% CI, 1.15 to 2.50) and 3.87 (95% CI, 1.19 to 12.65) fold higher risks of jaundice (Table 2).

Amongst infants with jaundice, the proportion who were totally breastfed was higher than the non-jaundice infants (64% vs 56%; $P = 0.033$). In the logistic regression model, Chinese infants who were exclusively breastfed had a 64% higher risk of jaundice (95% CI of adjusted OR, 1.11 to 2.44), as compared with infants on supplementary or formula feeds. However, analysis for interactions between mode of feeding and ethnicity revealed no associations with risk of jaundice for non-Chinese newborns. To further investigate the cause(s) for this ethnic difference, a comparison was made of the demographic and clinical characteristics between Chinese and non-Chinese infants, who were exclusively breastfed (Table 5). To exclude the role of common haemolytic diseases, data were re-analysed after removing infants with ABO incompatibility and G6PD deficiency. In this new dataset ($n = 762$), the Chinese still exhibited an increased risk of jaundice (adjusted OR, 1.97; 95% CI, 1.27 to 3.05; $P < 0.01$) compared to no increase in risk for the non-Chinese (adjusted OR, 0.97; 95% CI, 0.55 to 1.71; $P = 0.91$) infants. Similarly, increased risk for phototherapy was also observed in the Chinese (adjusted OR, 2.92; 95% CI, 1.77 to 4.81; $P < 0.001$) compared to non-Chinese (adjusted OR, 0.90; 95% CI, 0.49 to 1.63; $P = 0.71$). Increased risk of jaundice in breastfed Chinese infants (compared to non-Chinese) did not seem to be related to differential weight loss, ABO incompatibility, G6PD status, or any of the other parameters studied. Overall, being Chinese and breastfed, having lost $\geq 7\%$ of birth weight, being ABO incompatible or G6PD

Table 1. Demographic and Clinical Characteristics of Study Subjects

	Total (n = 1034)	No Jaundice (n = 753)	Jaundice (n = 281)	P
Mean gestational age, week (SD)	39.1 (1.07)	39.1 (1.08)	39.2 (1.05)	0.056
Mean birthweight, g (SD)	3206.2 (441.1)	3193.2 (440.0)	3241.2 (443.0)	0.120
Mean maternal age, y (SD)	32.1 (4.32)	32.1 (4.40)	31.9 (4.12)	0.505
Gender (%)				
Male	525 (50.8)	376 (49.9)	149 (53.0)	0.376
Female	509 (49.2)	377 (50.1)	132 (47.0)	
Ethnicity (%)				
Chinese	579 (56.0)	394 (52.3)	185 (65.8)	0.001
Malay	96 (9.3)	70 (9.3)	26 (9.3)	
Indian	246 (23.8)	199 (26.4)	47 (16.7)	
Others	113 (10.9)	90 (12.0)	23 (8.2)	
Type of feed (%)				
Total breastfed	601 (58.1)	420 (55.8)	181 (64.4)	0.033
Mixed feeding	419 (40.5)	321 (42.6)	98 (34.9)	
Total formula-fed	14 (1.4)	12 (1.6)	2 (0.7)	
Mode of delivery (%)				
Vaginal delivery	690 (66.7)	482 (64.0)	208 (74.0)	0.002
Caesarean section	344 (33.3)	271 (36.0)	73 (26.0)	
Gestational diabetes (%)				
Nil	916 (88.6)	666 (88.4)	250 (89.0)	0.076
Diet alone	105 (10.2)	74 (9.8)	31 (11.0)	
Insulin and diet	13 (1.3)	13 (1.7)	0 (0.0)	
Pregnancy-induced hypertension (%)				
Nil	1001 (96.8)	727 (96.5)	274 (97.5)	0.601
PIH	25 (2.4)	19 (2.5)	6 (2.1)	
PE	8 (0.8)	7 (0.9)	1 (0.4)	
Rhesus status (%)*				
Negative	25 (2.5)	18 (2.5)	7 (2.5)	0.973
Positive	975 (97.5)	705 (97.5)	270 (97.5)	
G6PD status (%)				
Normal	1017 (98.4)	745 (98.9)	272 (96.8)	0.025
Deficient	17 (1.6)	8 (1.1)	9 (3.2)	
ABO compatibility (%)*				
Compatible	773 (84.8)	563 (86.6)	210 (80.2)	0.019
Incompatible	139 (15.2)	87 (13.4)	52 (19.8)	
Weight loss (%)				
<7%	746 (72.2)	561 (74.5)	185 (65.8)	0.006
≥7%	288 (27.9)	192 (25.5)	96 (34.2)	

* Information on rhesus and ABO compatibility was not available for 34 and 122 subjects respectively.

Table 2. Association Between Significant Jaundice and Specific Risk Factors

	Adjusted OR (95% CI)	P
Weight loss		
≥7%	1.43 (1.03-1.99)	0.031
<7%	1.00	
ABO incompatibility		
Incompatible	1.69 (1.15-2.50)	0.008
Compatible	1.00	
G6PD		
Deficient	3.87 (1.19-12.65)	0.025
Normal	1.00	
Chinese		
Total breastfeeding	1.64 (1.11-2.44)	0.014
Mixed or total formula feeding	1.00	
Non-Chinese		
Total breastfeeding	0.90 (0.54-1.48)	0.671
Mixed or total formula feeding	1.00	

deficient independently increased the risk for hyperbilirubinaemia and the need for phototherapy.

Discussion

Although the susceptibility of East Asians to neonatal jaundice has been noted for many years,^{18,19} the question arises as to whether all Asians were at similar risk and if so, the factors contributing to pathogenesis. To explore the issue of ethnicity, we examined 3 major races present in Asia: Chinese, Indian and Malay. Chinese infants who were breastfed had a 64% higher risk of early neonatal jaundice compared to non-Chinese infants. Increased risk for jaundice was still apparent when common causes of haemolytic disease such as ABO incompatibility and G6PD deficiency were removed from the analysis. All subjects received nursing care and lactation guidance in 1 ward under the charge of one of the co-authors, reducing possible confounders in the post-natal environment. Our data add caveats to the relationship between Asian ethnic origin and neonatal jaundice.^{12,18,19} Although breastfeeding was a risk factor overall, non-Chinese infants who were breastfed had the opposite tendency, that is, they tend toward a lower risk of jaundice compared to those who had supplementary or formula feeding. Our non-Chinese data are consistent with the observation that jaundice in formula-fed and breastfed Caucasian infants showed no significant differences in transcutaneous bilirubin reading before day 5.²⁰ Infants who needed supplementary feeds, due to the inability to successfully establish total breastfeeding, lost excessive weight and consequently were at a higher risk for jaundice, suggesting a key role for caloric intake.¹⁰ This is consistent

Table 3. Association Between Phototherapy and Specific Risk Factors

	Adjusted OR (95% CI)	P
Gestation age (week)	0.76 (0.65-0.89)	<0.001
Weight loss		
≥7%	1.56 (1.10-2.20)	0.012
<7%	1.00	
ABO incompatibility		
Incompatible	1.66 (1.10-2.51)	0.017
Compatible	1.00	
G6PD		
Deficient	5.97 (1.78-20.02)	0.004
Normal	1.00	
Chinese		
Total breastfeeding	2.75 (1.77-4.27)	< 0.001
Mixed or total formula feeding	1.00	
Non-Chinese		
Total breastfeeding	0.74 (0.43-1.27)	0.274
Mixed or total formula feeding	1.00	

Table 4. Association Between Percent Weight Loss After Birth and Specific Risk Factors

	Adjusted OR (95% CI)	P
Gestational age	0.86 (0.75-0.98)	0.024
Type of feed		
Total breastfeeding	4.63 (3.31-6.45)	<0.001
Mixed or total formula feeding	1.00	
Jaundice		
Yes	1.43 (1.05-1.95)	0.025
No	1.00	

with our data that excessive weight loss overall increased the risk of jaundice 1.4 fold (Table 2). However, breastfed Chinese newborns did not have excessive weight loss compared to breastfed infants of other races, suggesting that weight loss might not be a key causative factor for the ethnic differences observed (Table 5). Thus, the aetiology of early neonatal jaundice risk in our cohort of Chinese breastfed newborns remains to be resolved.

Japanese subjects have a high incidence of defects in the bilirubin uridine diphosphate-glucuronosyltransferase gene, which were associated with delayed conjugation of bilirubin with glucuronic acid and decreased excretion of bilirubin.²¹ In Taiwanese infants, variant uridine diphosphate-glucuronosyltransferase and organic anion transporter 2 gene alleles were at increased risk for severe

Table 5. Demographic and Clinical Characteristics of Chinese and Non-Chinese Neonates Who Were Exclusively Breastfed

	Total(n = 601)	Chinese(n = 337)	Non-Chinese(n = 264)	P
Mean gestational age, week (SD)	39.2 (1.06)	39.2 (1.01)	39.2 (1.12)	0.661
Mean birthweight, g (SD)	3199.9 (410.19)	3198.1 (397.35)	3202.2 (426.8)	0.905
Mean maternal age, y (SD)	31.8 (4.06)	32.1 (3.77)	31.4 (4.39)	0.047
Gender (%)				
Male	311 (51.7)	170 (50.4)	141 (53.4)	0.470
Female	290 (48.3)	167 (49.6)	123 (46.6)	
Mode of delivery (%)				
Vaginal delivery	454 (75.5)	258 (76.6)	196 (74.2)	0.512
Caesarean section	147 (24.5)	79 (23.4)	68 (25.8)	
Gestational diabetes (%)				
Nil	546 (90.8)	300 (89.0)	246 (93.2)	0.135
Diet alone	49 (8.2)	34 (10.1)	15 (5.7)	
Insulin and diet	6 (1.0)	3 (0.9)	3 (1.1)	
Pregnancy-induced hypertension (%)				
Nil	591 (98.3)	331 (98.2)	260 (98.5)	1.000
PIH	7 (1.2)	4 (1.2)	3 (1.1)	
PE	3 (0.5)	2 (0.6)	1 (0.4)	
Rhesus status (%)*				
Negative	18 (3.1)	0 (0.0)	18 (7.0)	< 0.001
Positive	568 (96.9)	328 (100.0)	240 (93.0)	
G6PD status (%)				
Normal	592 (98.5)	333 (98.8)	259 (98.1)	0.516
Deficient	9 (1.5)	4 (1.2)	5 (1.9)	
ABO compatibility (%)*				
Compatible	442 (83.4)	262 (85.3)	180 (80.7)	0.193
Incompatible	88 (16.6)	45 (14.7)	43 (19.3)	
Weight loss (%)				
<7%	367 (61.1)	209 (62.0)	158 (59.8)	0.588
≥7%	234 (38.9)	128 (38.0)	106 (40.2)	

* Information on rhesus and ABO compatibility was not available for 15 and 71 subjects respectively.

hyperbilirubinaemia.²² Intestinal absorption of bilirubin is also facilitated by de-glucuronidation, a process facilitated by β -glucuronidase. Breast milk is rich in β -glucuronidase and administration of L-aspartic acid, a β -glucuronidase inhibitor, may be useful for breastfeeding jaundice.²³ However, this may not apply to Chinese newborns since no differences were observed in faecal beta-glucuronidase enzyme activity between breast and formula fed infants in an ethnic Chinese population, despite the breastfed group having a more than 10-fold higher incidence of unconjugated hyperbilirubinaemia.²⁴ Another possible factor may be that consumption of Traditional Chinese Medicines could cause

haemolysis in Chinese babies, especially those with G6PD deficiencies. We cannot exclude this possibility although a review of medical literature fails to detect any evidence that herbs are significant causative factors for haemolysis in G6PD-deficient infants.²⁵ Whether genetic polymorphisms or other factors were the cause of increased jaundice risk in our breastfed Chinese newborns need to be determined.

Losing $\geq 7\%$ of birth weight was an independent risk factor for early neonatal jaundice in our cohort. Infants with $\geq 7\%$ weight loss had a 1.4-fold risk of jaundice, and jaundiced infants had 12.6% more weight loss. Weight loss was independently and strongly associated with exclusive

breastfeeding and inversely related to gestational age. The relationship between fasting and hyperbilirubinaemia is well known and has been reported both in animal models and humans.²⁶ Starvation increases neonatal jaundice in rats and inadequate breastfeeding with consequent dehydration can increase absorption and enterohepatic circulation of bilirubin.²⁷ Breastfed infants experience their maximum weight loss by day 3 and a median weight loss of 6.6% compared to 3.5% for formula fed neonates has been observed.²⁸ By convention, the newborn is evaluated if weight loss is more than 10%.²⁹ Our data suggest that this rule-of-thumb of more than 10% weight loss might need to be re-examined. Asian infants with $\geq 7\%$ weight loss were at risk for significant jaundice and phototherapy. Such newborns should be monitored and supported closely during the first week for effectiveness of breastfeeding.

As expected, increased haemolysis due to G6PD deficiency and ABO incompatibility were significant contributors of neonatal jaundice. In particular, G6PD deficiency is relatively common in Singapore and is associated with increased haemolysis, impaired bilirubin conjugation and delayed bilirubin excretion.¹⁶ Our cohort of newborns was screened for G6PD deficiency, and affected infants (1.6% overall) were at a >3-fold higher risk of neonatal jaundice. Just as in other studies, ABO incompatibility was a significant risk factor for jaundice. Caesarean section protected against jaundice. A possible explanation is that stressed infants produce more conjugating enzymes and less transplacental circulation after caesarean section. The latter reason is less likely in view of the recent meta-analysis indicating that late clamping of umbilical cord to allow greater transplacental infusion of blood resulted in increased haematocrit but not jaundice.³⁰ In our study, modes of delivery and feeding were closely related. Infants who were delivered by caesarean section tended to be supplemented with formula until breastfeeding was well established. Only 24% of infants who were exclusively breastfed were delivered by caesarean section as compared with 33% in the study population. To better reveal factors for breastfeeding jaundice, we therefore excluded the mode of delivery from the logistic regression.

In this study, 58% of mothers were breastfeeding exclusively on discharge from hospital, improving on the 20% to 30% first week breastfeeding rates reported for Singapore³¹ and is comparable to affluent Asian societies such as Taiwan (17.9%)³² and Hong Kong (33.5%).³³ However, our breastfeeding rates were lower than that reported from the USA and other localities, (~70% of mothers totally breastfed on discharge^{10,34}), where breastfeeding practices were more entrenched. These differences may be due to cultural or societal attitudes

towards total breastfeeding. In this setting, we used a serum bilirubin of 150 $\mu\text{mol/L}$ at 48 hours to 72 hours of life as our cut-off level for significant jaundice, as infants with readings above this value were at risk for severe hyperbilirubinaemia in G6PD-deficient infants,¹⁶ a genetic defect relatively common in the population. Using this yardstick, the independent risk factors for jaundice in our cohort were weight loss, ABO incompatibility, G6PD-deficiency and breastfed newborns of Chinese ethnic origin. It is worthwhile to note that the occurrence of late jaundice, occurring after the fourth day and lasting several weeks after, was not studied in our population. Nonetheless, our findings that early jaundice and breastfeeding were associated with weight loss and breastfed Chinese infants were at increased risk for jaundice raises health economic issues. Although breastfeeding clearly improves the health of infants and may result in cost savings for parents, attention has to be given to diagnostic and therapeutic costs associated with neonatal jaundice and its sequelae.³⁵ Early identification and closer out-patient monitoring of infants with specific risk factors such as those defined in our study, may reduce such costs especially with regard to current trends to encourage breastfeeding coupled with reduced length of hospital stay.³⁶

Acknowledgement

We are grateful to Dr Roy Joseph for supervising the weight measurements and for very helpful discussions. Dr Chong Yap Seng, Ms Doris Fok and members of Obstetrics, Gynecology and Neonatology Departments for their support. Thanks also to all the dedicated nurses who have contributed so much to this study and the health of our mothers and babies.

Funding

ELY is BMRC Clinician-Scientist Investigator.

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