Original Article

Association between Bodyweight Change and Significant Neonatal Hyperbilirubinemia in Term Infants

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Background: Neonatal jaundice is one of the most common problems in newborns, and approximately 60% of term infants develop hyperbilirubinemia in the first week of life. Neonatal jaundice is caused by high levels of unconjugated bilirubin, which is neurotoxic. Severe neonatal hyperbilirubinemia leads to permanent brain damage. Inadequate breastfeeding causes significant weight loss which may be associated with further jaundice in the first week of life.

Objective: To explore association between bodyweight changes during the first 48 hours of life and significant neonatal hyperbilirubinemia within the first week of life in healthy term infants.

Materials and Methods: This was a prospective, cross-sectional study conducted from March 1st, 2017 to July 31st, 2017. Term infants with BW ≥2,500 grams were enrolled. Relationship between weight change during the first 48 hours of life and occurrence of hyperbilirubinemia requiring phototherapy was explored.

Results: Of 269 infants, 35 (13.0%) presented with significant hyperbilirubinemia within 7 days after birth; 21 (60%) presented in the first 48 hours. Mean birthweight was 3,178.2±356.1 g; mean percentage weight loss during the first 48 hours was 5.6±2.1%. Infants with significant hyperbilirubinemia had non-statistically significant higher weight loss than those without, (6.0±1.5% and 5.5±2.2%, $p = 0.21$).

Conclusion: Infants with significant hyperbilirubinemia has slightly higher weight loss at 48 hours of life, although not statistically significant. Therefore, infants with excessive weight loss should be monitored for development of severe significant hyperbilirubinemia.

Keywords: Term infant, Jaundice, Neonatal hyperbilirubinemia, Weight loss, Bodyweight change

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Neonatal jaundice is a common problem in newborn infants, with approximately 60% of term infants developing hyperbilirubinemia in the first week of life[1-3]. It is caused by the accumulation of unconjugated bilirubin, mainly from heme protein breakdown in blood components and other organs. High levels of unconjugated bilirubin induce permanent brain damage and affect long term neurosensory impairment[3,4].

Several factors contribute to pathological jaundice. Hence, breast feeding associated jaundice takes substantial risk from inadequate volume or energy intake, along with potential feeding problems, leading to increase enterohepatic circulation which usually evolves during the first several days after birth. Normally, breastfed infants do not lose weight beyond 6% of that birthweight within the 3 days after birth. Significant weight loss or dehydration is also a cause of neonatal jaundice[2,5-7].

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According to our institutional policy, we encourage early and exclusive breastfeeding for all healthy term infants during their hospitalization and they are typically discharged home after 48 to 72 hours of life. Some infants might develop complications of weight loss such as hyperbilirubinemia which is the most common neonatal morbidity. Therefore, the authors decided to study the association between bodyweight change during first 2 days of life and significant neonatal hyperbilirubinemia during the first 7 days of age.

Materials and Methods

This was a prospective cohort study. All Thai infants who were born at term with birth weight ≥2,500 grams at Thammasat University Hospital between March 1st and July 31th, 2017, were enrolled in the present study. Infants were excluded if they had chromosomal anomalies (such as trisomy 13,18, 21), admitted to neonatal intensive care unit or sick newborn unit, had no microbilirubin screening on the second day of life, cannot be contacted 7 to 10 days after birth, or had incomplete medical records. The present study protocol was approved by the Human Research Ethics Committee of Thammasat University.

All Infants received routine postnatal care including

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screening microbilirubin and hematocrit at 48 hours of life and were followed-up at 7 days old whether they had significant hyperbilirubinemia or not. Maternal and infants' demographic data and other relevant risk factors of hyperbilirubinemia included feeding type were prospective collected. Feeding methods had 2 categories: breastfeeding infants who were exclusively breastfed, and mixed feeding which refers to infants who were breastfed and received additional formula.

Infants were weighed with the same scale that was daily tested by using a calibrated equipment. Weight change was defined as the difference between birthweight that was the first record at the postpartum unit and each weight recorded subsequently once daily at 6 AM as a routine practice.

A significant neonatal hyperbilirubinemia was defined as having total serum bilirubin level in the range indicated for phototherapy by American Academy of Pediatrics (AAP) guidelines[4].

Data was analyzed by using descriptive statistics (percentage, mean, standard deviation) for demographic data. The t-test was used to compare weight change. A *p*-value <0.05 was considered statistically significant.

Results

Of the 300 infants were eligible, 31 infants were excluded due to lost follow-up (n = 29) and had incomplete information (n = 2). Total infants were 269 patients. We found 35 patients (13.0%) had significant neonatal hyperbilirubinemia in the first week of life, 14 (40%) had jaundice with onset after 48 hours. Seventeen infants (48.6%) had neonatal jaundice from breastfeeding.

There were no significant differences in maternal characteristics, but there was a significant difference among GA. Those in the non-significant hyperbilirubinemia group had a GA of 38.8±0.9 weeks, older than the GA of 38.4±1.2 in the significant hyperbilirubinemia group (p<0.01). Sixteen (45.7%) infants of the significant hyperbilirubinemia group were exclusively breastfed which was not significantly more than the non-significant hyperbilirubinemia (Table 1).

Two days after birth, the significant neonatal hyperbilirubinemia group had a weight loss of 192.7±175 gram (6.0±1.5%) which had no statistically significant more than the 175.5±74.5 grams (5.5±2.2%) of weight loss in the non-significant hyperbilirubinemia group. Microbilirubin levels at 48 hours after birth were 12.6±2.5 and 8.5±1.6 mg/dl in the significant hyperbilirubinemia group and the non-significant hyperbilirubinemia group, respectively; this was statistically significant (Table 2).

For newborns with significant neonatal hyperbilirubinemia due to breast feeding, 2 days after birthweight loss was 204.4±38.5 gram (6.3±1.2%) which was greater than the non-significant hyperbilirubinemia group but without statistical significance (Table 3).

Discussion

Excessive weight loss for exclusive breastfeeding infants, especially greater than 7% from birthweight, indicates possible breastfeeding problems[8]. Many studies have reported an association between breast feeding and significant

Table 1. Demographic and clinical characteristics

Clinical characteristics	Significant hyperbilirubinemia (n = 35)	Non-significant hyperbilirubinemia (n = 234)	*p*-value
Maternal data			
Age (year) (mean ± SD)	31.8 (±6.4)	29.9 (±5.9)	0.44
Delivery (n, %)			0.88
Spontaneous vaginal delivery	17 (48.6)	109 (46.6)	
Caesarian section	18 (51.4)	124 (53.0)	
Assisted delivery (forceps extraction or vacuum extraction)	0	1 (0.4)	
ABO blood group (n, %)			0.37
A	5 (14.3)	39 (16.8)	
B	13 (37.1)	77 (33.2)	
O	17 (48.6)	98 (42.2)	
AB	0	18 (7.8)	
Rh blood group (n, %)			
Rh positive	34 (97.1)	232 (100)	0.13
Gestational diabetic mellitus (n, %)	7 (20.0)	25 (10.7)	0.38
Infants' data			
Gestational age (weeks) (mean ± SD)	38.4 (±1.2)	38.8 (±0.9)	<0.01
Birthweight (g) (mean ± SD)	3,212.3 (±321.0)	3,173.1 (±361.4)	0.54
Male gender (n, %)	20 (57.1)	113 (48.3)	0.37
Exclusive breastfeeding (n, %)	16 (45.7)	72 (30.8)	0.09

Table 2. Bodyweight change within 2 days after birth

Data	Significant hyperbilirubinemia (n = 35)	Non-significant hyperbilirubinemia (n = 234)	*p*-value
Birthweight (g)	3,192.2 (±322.9)	3,148.6 (±358.7)	0.50
BW 1st day after birth (g)	3,095.6 (±310.9)	3,049.3 (±355.1)	0.47
BW 2nd days after birth (g)	2,999.5 (±302.6)	2,973.1 (±337.2)	0.66
BWL on the 1st day (g)	96.6 (±50.9)	99.2 (±51.7)	0.78
BWL on the 2nd day (g)	192.7 (±175.0)	175.5 (±74.5)	0.19
Percent of BW changing on the 1st day	3.0 (±1.5)	3.2 (±1.6)	0.58
Percent of BW changing on the 2nd day	6.0 (±1.5)	5.5 (±2.2)	0.21
Microbilirubin level at 48 hours (mg/dl)	12.6 (±2.5)	8.5 (±1.6)	<0.01

Data shown as mean ± SD
BW = bodyweight, BWL = bodyweight loss

Table 3. Bodyweight of the exclusively breastfed infants with significant hyperbilirubinemia, compared the non-significant hyperbilirubinemia group

Bodyweight	Significant hyperbilirubinemia (n = 17)	Non-significant hyperbilirubinemia (n = 234)	*p*-value
Birthweight (g)	3,265.8 (±282.5)	3,148.6 (±358.7)	0.19
BW 1st day after birth (g)	3,150.7 (±280.4)	3,049.3 (±355.1)	0.25
BW 2nd days after birth (g)	3,061.4 (±277.4)	2,973.1 (±337.2)	0.29
BWL on the 1st day (g)	115.1 (±44.4)	99.2 (±51.7)	0.22
BWL on the 2nd day (g)	204.4 (±38.5)	175.5 (±74.5)	0.11
Percent of BW changing on the 1st day	3.5 (±1.3)	3.2 (±1.6)	0.36
Percent of BW changing on the 2nd day	6.3 (±1.2)	5.5 (±2.2)	0.17

Data shown as mean ± SD
BW = bodyweight, BWL = bodyweight loss

hyperbilirubinemia[9,10].

For term infants with birthweight ≥2,500 grams, 13% had neonatal jaundice within 7 days after birth (40% had onset after 48 hours). The most common cause was breastfeeding jaundice (48.6%).

Breastfeeding and associated problems can be caused by inadequate consumption of ingested milk and energy per day, resulting in weight loss which may be associated with hyperbilirubinemia[11,12]. Tarcan A, et al[13] showed that infants with idiopathic hyperbilirubinemia had severe weight loss (more than 10% or not regain their birthweight by postnatal day 10) on admission. Salas AA, et al[14] found that significant weight loss in the breast fed term infants had a 4-times higher for readmission for hyperbilirubinemia. A previous retrospective cohort study, Yang WC, et al[15], stated that weight loss of healthy term newborn infants in the first three days significantly increased incidences of neonatal hyperbilirubinemia and that weight loss of more than 7.6% is the cutoff point to predict significant hyperbilirubinemia 72 hours after birth.

In the present study result, bodyweight loss at the second day of age was 6.0±1.5%. This was more severe when compared to the non-significant hyperbilirubinemia group but without statistical significance. Breastfeeding was not associated with significant hyperbilirubinemia. Thus, an important factor in developing significant hyperbilirubinemia would be poor intake more than breast feeding. This result was as a previous study although it did not show statistical significance. The definition of significant hyperbilirubinemia as well as our study design differed due to hospital policy and practice. For examples, our hospital has a full-time lactation nurse, using AAP guideline as a standard management and our study was prospective.

Conclusion

As 60% of the infants who had neonatal jaundice requiring phototherapy presented within 48 hours after birth, screening of neonatal jaundice at 48 hours remains essential.

Forty percent of these were readmitted due to significant hyperbilirubinemia within 7 days of age, of which the most common cause was breastfeeding jaundice. Although there was no significant difference in weight loss during the 2 days of hospitalization in our study, careful follow-up is needed, especially for infants who have significant weight

loss i.e. more than 6% of birthweight in the first 2 to 3 days to monitor breastfeeding problems and neonatal jaundice conditions.

What is already known on this topic?

Breastfeeding and associated problems can be caused by inadequate consumption of ingested milk and energy per day, resulting in weight loss which may be associated with hyperbilirubinemia.

What this study adds?

Most term infants may develop significant hyperbilirubinemia and have breastfeeding problems within 7 days of age. Body weight change during the 2 days of hospitalization was not associated with significant hyperbilirubinemia in the first week of life, but infants who have significant weight loss, are required to follow-up.

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Potential conflicts of interest

The authors declare no conflicts of interest.

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ความสัมพันธ์ของการเปลี่ยนแปลงของน้ำหนักตัวกับการเกิดภาวะตัวเหลืองในทารกเกิดครบกำหนด

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ภูมิหลัง: ภาวะตัวเหลืองในทารกแรกเกิดเป็นปัญหาที่พบได้บ่อยโดยร้อยละ 60 ของทารกเกิดครบกำหนดจะมีภาวะตัวเหลืองในสัปดาห์แรกของชีวิต ภาวะตัวเหลืองเกิดจากมีระดับของบิลิรูบินที่สูง ซึ่งเป็นอันตรายกับระบบประสาท ภาวะตัวเหลืองที่รุนแรงทำให้เกิดความพิการทางระบบประสาทอย่างถาวร การที่ทารกกินนมแม่ไม่เพียงพอทำให้ทารกมีน้ำหนักตัวลดลงมาก ซึ่งอาจมีความสัมพันธ์กับการเกิดภาวะตัวเหลืองในทารกเกิดครบกำหนดในช่วงสัปดาห์แรกของชีวิต

วัตถุประสงค์: เพื่อศึกษาความสัมพันธ์ระหว่างการเปลี่ยนแปลงน้ำหนักตัวใน 48 ชั่วโมงแรกของชีวิตกับการเกิดภาวะตัวเหลืองในสัปดาห์แรกของชีวิตของทารกเกิดครบกำหนดที่มีสุขภาพแข็งแรงดี

วัสดุและวิธีการ: เป็นการศึกษาชนิดเปรียบเทียบแบบไปข้างหน้า ณ ช่วงเวลาตั้งแต่วันที่ 1 มีนาคม พ.ศ. 2560 ถึง วันที่ 31 กรกฎาคม พ.ศ. 2560 ทารกเกิดครบกำหนดที่มีน้ำหนักแรกเกิดตั้งแต่ 2,500 กรัมขึ้นไปจะนำเข้าร่วมการศึกษา เพื่อหาความสัมพันธ์ระหว่างการเปลี่ยนแปลงน้ำหนักในช่วง 48 ชั่วโมงแรกของชีวิตและการเกิดภาวะตัวเหลืองซึ่งต้องได้รับการส่องไฟ

ผลการศึกษา: จากการศึกษาในทารกแรกเกิดทั้งหมด 269 คน พบทารกที่เกิดภาวะตัวเหลืองใน 7 วันหลังเกิดจำนวน 35 คน (ร้อยละ 13.0) โดยทารก 21 คน เกิดภาวะตัวเหลืองใน 48 ชั่วโมง หลังเกิดน้ำหนักแรกเกิดเฉลี่ย 3,178.2±356.1 กรัม ทารกแรกเกิดมีน้ำหนักตัวที่ลดลงโดยเฉลี่ยที่ 48 ชั่วโมงแรกหลังเกิดเท่ากับร้อยละ 5.6±2.1 ของน้ำหนักแรกเกิดในกลุ่มทารกที่มีภาวะตัวเหลืองน้ำหนักตัวลดลง (ร้อยละ 6.1±1.5) มากกว่ากลุ่มทารกที่ไม่มีภาวะตัวเหลือง (ร้อยละ 5.5±2.2) แต่ไม่มีนัยสำคัญทางสถิติ ($p = 0.21$)

สรุป: ทารกที่มีภาวะตัวเหลืองมีน้ำหนักตัวลดลงที่ 48 ชั่วโมงหลังเกิดนั้นมากกว่ากลุ่มทารกที่ไม่มีภาวะตัวเหลือง ถึงแม้ว่าจะไม่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติ อย่างไรก็ตามทารกที่มีภาวะน้ำหนักตัวลดลงมากควรได้รับการติดตามเนื่องจากมีโอกาสเกิดภาวะตัวเหลือง