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Original research article

Does Weight Loss Predict Hyperbilirubinemia Requiring Readmission for Phototherapy in Term Infants?

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ABSTRACT

Encouraging exclusive breastfeeding after delivery is recommended, but infants may have subpar breastmilk intake and then present with initial weight loss. Neonatal hyperbilirubinemia is a frequent complication from inadequate breastfeeding, developing in the first week of life and very often requiring readmission for phototherapy. We looked at correlations between bodyweight loss (BWL) during the first 2 days after birth in term infants with hyperbilirubinemia requiring readmission for phototherapy. Term infants born between June 1st, 2018 and April 19th, 2019 were enrolled in this prospective cohort study. Baseline characteristics and percentage of BWL during the first 2 days of life were analyzed. The optimal BWL cutoff was calculated using receiver operating characteristic curves to predict possibilities of hyperbilirubinemia requiring readmission. With a total of 2841 infants, 115 (3.8%) with hyperbilirubinemia were readmitted for phototherapy, leaving 2726 in the non-hyperbilirubinemia group. The number of exclusively breastfed infants was not different (67%) between the two sets. Two days after birth, infants with hyperbilirubinemia had statistically significant higher BWL percentages than those without: 6.0 ± 2% and 5.4 ± 2%, $p < 0.01$. The appropriate cutoff BWL percentage seems to be ≥ 5% on the first 2 days after birth (sensitivity: 79.82%, specificity: 38.85%, positive likelihood ratio: 1.31, and negative likelihood ratio: 0.52). BWL during hospitalization was associated with readmission for phototherapy in term infants. Infants losing weight, especially ≥ 5% in the first 2 days of life, need follow-up.

Keywords: Bodyweight; Bodyweight loss; Jaundice; Neonatal hyperbilirubinemia; Term infant

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1. Introduction

The most common problem in newborns is neonatal hyperbilirubinemia, with approximately 60% of term infants developing it in the first week of life [1-3]. Infants with severe hyperbilirubinemia can have irreversible neurodevelopmental impairments [3, 4]. The WHO recommends mothers exclusively breastfeed infants. However, potentially poor caloric intake and/or dehydration is associated with inadequate breastfeeding, and this may contribute to hyperbilirubinemia. Infants, then, can require readmission for phototherapy treatment. A term, exclusively breastfed infant usually loses 7% of the maximum allowable weight as part of typical physiological weight loss in the first 3 days after birth [5]. Outside of these parameters, significant weight loss or dehydration is associated with neonatal jaundice [2, 6-8].

Exclusive breastfeeding rates after delivery are increasing at our hospital. In our nursery, most infants are routinely discharged after 48-72 hours of life. To prevent severe neonatal hyperbilirubinemia, as well as avoid any possible adverse neurodevelopmental outcomes, we looked at the association between bodyweight loss (BWL) during first 2 days of life and neonatal hyperbilirubinemia in term infants requiring readmission for phototherapy.

2. Materials and Methods

All infants who were born at term at Thammasat University Hospital between March 1st and July 31th, 2017, were enrolled in this prospective cohort study. Infants who had chromosomal anomalies such as Trisomy 13, 18, or 21; were admitted to neonatal intensive care unit or sick newborn unit for more than 24 hours; had non-contactable parents 14 days after birth; had parents who could not understand Thai or English; had incomplete patient informat-ion; had neonatal hyperbilirubinemia within 48 hours of age were excluded. This study was approved by the Human Research Ethics Committee of Thammasat University.

Baseline characteristics including maternal data such as age, delivery method, and underlying diseases as well as infant information such as gestational age, birthweight, and Apgar score were collected. Weight loss was defined as the difference between birthweight and bodyweight: infants were routinely weighed every day at 6 AM. Microbilirubin levels were regularly checked at 48 hours of age and/or when infants looked jaundice.

Infants were divided into two groups. One group consisted of infants not admitted for phototherapy, the second being those who returned to our hospital for treatment. Infants were readmitted for phototherapy when total serum bilirubin level exceeded or was within 1 mg/dl of the hour-specific range indicating phototherapy by American Academy of Pediatrics (AAP) guidelines [4]. Feeding methods were classified as either exclusively breastfed or mixed-feeding *i.e.* infants fed both breastmilk and infant formula. All infants were followed up at 7 days old whether they had significant hyperbilirubinemia or not.

Statistical analyses: Continuous data were calculated using mean; standard deviation and categorical data were gathered using frequencies and percentages. Fisher's exact test and T-test were used to compare variables. $p < 0.05$ was considered statistical-ly significant. We also analyzed our data by receiver operator characteristic (ROC) curve, sensitivity, specificity, area under the ROC curve (AUC), positive likelihood ratio (LR+), and negative likelihood ratio (LR–) at the various cutoff percentages for BWL.

3. Results and Discussion

Of the 3520 infants born during our study, a total of 520 infants were excluded for various reasons: chromosomal anomalies and major organ anomalies (n=5), neonatal intensive care unit or sick newborn unit admission of more than 24 hours (n=387), parents who could not understand Thai or English (n=10), neonatal hyperbilirubinemia within 48 hours of age (n=116), and incomplete information (n=2). With the remaining 3000, 159 were then removed from the study (5.3%) as their parents could not be contacted 7-10 days after birth, resulting in a new total of 2841 infants. Of this, 115 patients (3.8%) were readmitted for phototherapy composing the hyperbilirubinemia group, leaving 2726 (96.2%) as the non-hyperbilirubinemia cohort.

3.1 Demographic and clinical characteristics

There were significant differences in gestational age, rates of cesarean section, and microbilirubin levels at 48 hours of age between the two sets. Those in the non-hyperbilirubinemia group had a GA of 38.8±0.9 weeks, making them older, versus a GA of 38.4±1 in the hyperbilirubinemia infants ($p<0.01$). Cesarean sections occurred more often (65.2% of the time) for those with hyperbilirubinemia, significantly more than for those without (49.7%). Microbilirubin levels at 48 hours of age in our hyperbilirubinemia group were 10.4±1.3 mg/dL, again higher than for the infants not readmitted (8.3±1.6 mg/dL). The amount of exclusively breastfed infants did not differ in either cohort, around 67% (Table 1).

3.2 Bodyweight loss within 2 days after birth

Our results did not display any notable differences in BWL and percentage of BWL on the first day after birth. Two days after birth, infants with hyperbilirubinemia had a BWL of 186.2 ± 61.8 (6.0 ± 2 %), significantly higher than the 165 ± 64.1 grams (5.4 ± 2 %) lost in the non-hyperbilirubinemia group (Table 2).

Logistic regression analysis showed BWL over 4% presented a higher risk for phototherapy readmission. Our finding determined that any BWL of more than 4, 5, 6, and 7% clearly demonstrated an increased, but variable, risk with odd ratios of 2.61, 2.1, 2.37 and 2.76, respectively (Table 3). Under ROC analysis, the optimal cutoff BWL percentage at 2 days of age for predicting hyperbilirubinemia would be having a BWL percentage≥5% (AUC=0.59, 95% CI=0.56-0.63, sensitivity=79.82%, specificity=38.85%, LR+1.31 and LR-0.52) (Table 4, 5) (Fig. 1).

3.3 Discussion

Breastfeeding is known to convey several advantages. Nonetheless, research has demonstrated inadequate breastfeeding can cause excessive weight loss. When BWL is greater than 7% [9], infants are at risk. Many studies have also reported an association between inadequate consumption of milk, resulting in BWL and significant hyperbilirubinemia [10-13].

Viriyaudomsiri [14] found that in Thai infants, BWL was associated with breastfeeding jaundice within 72 hours of age. The optimal cutoff percentages of BWL ≥ 5.1% and ≥ 7.7% at 24 and 48 hours after birth, respectively, were used to predict breastfeeding jaundice. Tarcan et al. [15] showed infants with idiopathic hyperbilirubinemia had severe weight loss on admission. Furthermore, Salas et al. [16] found significant weight loss in breastfed term infants led to a 4-times higher readmission rate for hyperbilirubinemia.

Chou [17] reported the incidence of hyperbilirubinemia, defined as total serum bilirubin levels meeting or exceeding age-specific AAP criteria, was 2.74%. An observational retrospective cohort study by Huang et al. [18] reported that a BWL ≥ 7% on, or before, day 3 of life, was an independent risk factor for early neonatal jaundice needing phototherapy during the first 2 weeks of life; in addition, infants with a BWL ≥ 7% had a 1.4-fold increased risk of jaundice.

Of note, Yang et al. [19] stated BWL in the first three days was a significant risk factor associated with neonatal hyperbilirubinemia in term infants but feeding methods were not. Although BWL ≥ 7.6% by day 2 is the cutoff point to predict significant hyperbilirubinemia 72 hours after birth, accuracy is low (AUC=0.63, 95% CI=0.58- 0.68).

The authors concurred with Chou's results in the sense that this study's incidence of readmission for phototherapy was 3.8%. Our number of exclusively breastfed infants did not differ between the jaundice and non-jaundice cohorts, but BWL at the second day of life in our hyperbilirubinemia group was significantly more severe compared to the non-hyperbilirubinemia infants.

However, similar to Yang WC et al., breastfeeding was not associated with readmission for phototherapy for this study's infants. This seems to demonstrate that an important factor in readmission for hyperbilirubinemia is actually poor intake versus breastfeeding itself. The authors found that BWL ≥ 4 to ≥ 7% (Table 3) indicated twice the increased risk, higher than shown by Huang et al. Our optimal cutoff BWL percentages at 2 days of age, for predicting hyperbilirubinemia, should be BWL ≥ 5%, lower than all previously cited studies using ≥ 7% as a benchmark.

There are likely to be some variations between neonatal care programs from hospital to hospital. Our hospital provides most mothers an evaluation of breastfeeding practices by a full-time lactation nurse. Our accuracy of BWL ≥ 5% at 2 days of age with AUC=0.59, 95% CI=0.56-0.63, sensitivity=79.82%, specificity=38.85%, was also as low as Yang's et al. Generally, the most common diagnosis in the initial postnatal period in healthy, full-term infants is declared to be inconclusive jaundice. Certainly, there are multiple factors associated with this: genetic variations [20] in hepatic bilirubin clearance e.g. uridine diphosphate glucuronosyl transferase (UGT) enzyme and glucose 6 phosphate dehydrogenase (G6PD) enzyme. These are not investigated in routine newborn screening.

Despite BWL percentage having low accuracy, this study suggests that it is, indeed, important neonatal hyperbilirubinemia risk factors, among others. General pediatricians would be wise to monitor BWL percentages as the part of neonatal hyperbilirubinemia follow-up guidelines.

4. Conclusion

There was significant weight loss during the 2 days of hospitalization in term infants with neonatal hyperbilirubinemia, requiring readmission for phototherapy. Therefore, infants with BWL ≥ 5% need careful follow-up.

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Table 1. Demographic and clinical characteristics.

Characteristics	Hyperbilirubinemia (n=115)	Non-hyperbilirubinemia (n=2726)	p
Maternal age (year), mean ±SD	30.4 ± 5.4	29.6 ± 6	0.17
Maternal hypertension, n (%)	4 (3.5)	44 (1.6)	0.13
Maternal diabetes, n (%)	15 (13)	237 (8.7)	0.1
Gestational age (weeks), mean ±SD	38.4 ± 1	38.8 ± 0.9	<0.01
Parity, median (range)	1 (1-4)	2 (1-8)	0.7
Cesarean section, n (%)	75 (65.2)	1355 (49.7)	<0.01
Apgar at 1 min, median (range)	9 (6-9)	9 (3-9)	0.04
Apgar at 5 min, median (range)	10 (7-10)	10 (8-10)	0.6
Male, n (%)	65 (56.5)	1346 (49.4)	0.13
Birthweight (g), mean ±SD	3127.4±385	3118.2±380.2	0.8
Exclusive breastfeeding, n (%)	78(67.8)	1826 (67)	0.36
Microbilirubin levels (mg/dL), mean ±SD	10.4 ± 1.3	8.3 ± 1.6	<0.01

Table 2. Bodyweight loss within 2 days after birth.

Bodyweight (BW) Bodyweight loss(BWL)	Hyperbilirubinemia (n=115)	Non-hyperbilirubinemia (n=2726)	p
Day 1: BW (g), mean ±SD	3021.9±372.3	2999.7±372.8	0.54
Day 2: BW (g), mean ±SD	2920.3±355.9	2926.7±363.4	0.85
Day 1: BWL (g), mean ±SD	85.3±68.8	92.5±51.2	0.14
Day 1: BWL %, mean ±SD	2.7±2.1	3±1.6	0.07
Day 2: BWL (g), mean ±SD	186.2±61.8	165±64.1	<0.01
Day 2: BWL %, mean ±SD	6±2	5.4±2	<0.01
BWL > 5% at Day 2, n (%)	91 (73.1)	1656(60.8)	<0.01
BWL > 7% at Day 2, n (%)	32 (27.8)	532 (19.5)	0.03

Table 3. Bodyweight loss percentages 2 days after birth: phototherapy readmission risk.

Bodyweight loss percentages	Odds Ratio	95% Confidence Interval	p
≥ 4	2.61	1.39 – 4.89	<0.01
≥ 5	2.1	1.22 - 3.65	<0.01
≥ 6	2.37	1.37 – 4.1	<0.01
≥ 7	2.76	1.54- 4.97	<0.01

Table 4. Bodyweight loss percentage cutoff values at 2 days of age.

Bodyweight loss percentages Cut point	Sensitivity	Specificity	LR+	LR-
≥ 0	98.26%	1.36%	1.00	1.28
≥ 1	98.26%	2.79%	1.01	0.62
≥ 2	98.26%	5.32%	1.04	0.33
≥ 3	97.78%	10.71%	1.06	0.49
≥ 4	90.43%	21.57%	1.15	0.44
≥ 5	79.13%	39.14%	1.30	0.53
≥ 6	53.91%	60.67%	1.37	0.76
≥ 7	27.83%	80.45%	1.42	0.9
≥ 8	7.83%	93.43%	1.19	0.99

Table 5. Bodyweight loss percentage 2 days after birth cutoff values.

Bodyweight loss Cut point	AUC	95% Confidence Interval	p
≥ 5	0.59	0.56-0.63	<0.01
≥ 7	0.54	0.5-0.58	

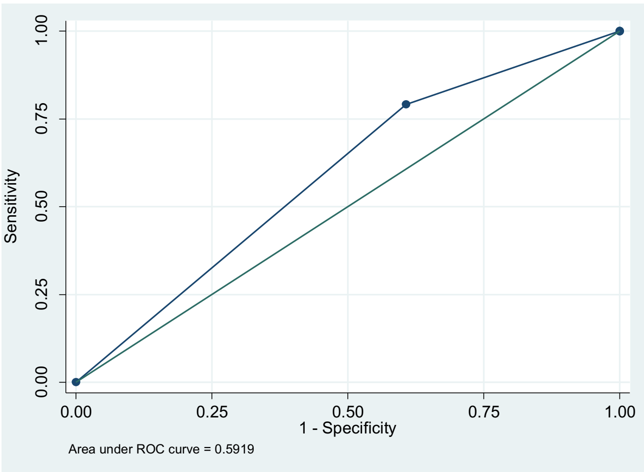

Fig. 1. ROC curves of ≥ 5% bodyweight loss 2 days after birth (AUC=0.59, 95% CI= 0.56- 0.63).

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