

Significant weight loss in term breastfed infants readmitted for hyperbilirubinemia

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ABSTRACT

Background: Hyperbilirubinemia and feeding problems are the most common indications for readmission in the first 2 weeks of life. Inadequate oral intake causes weight loss and increases the bilirubin enterohepatic circulation

Objective: To describe the association between total serum bilirubin (TSB) levels and weight loss in healthy term infants readmitted for hyperbilirubinemia after birth.

Methods: We included breastfed term infants readmitted to Caja Petrolera de Salud Clinic in La Paz, Bolivia, during January 2005 through October 2008 with criteria for phototherapy according to TSB levels.

Results: Seventy-nine infants were studied (64.6% were males). The overall readmission rate due to hyperbilirubinemia was 6.4%. Infants were readmitted at a median age of 4 days. Mean TSB level was 18.6±3 mg/dL. Thirty (38%) had significant weight loss. A weak correlation between TSB levels and percent of weight loss was identified ($r=0.20$; $p<0.05$). The frequency of severe hyperbilirubinemia among infants with significant weight loss was notably higher (46.7% vs. 18.4%; $p<0.05$). The risk of having severe hyperbilirubinemia was approximately 4 times greater for infants with significant weight loss (OR: 3.9; 95% CI: 1.4–10.8; $p<0.05$). Infants with severe hyperbilirubinemia were readmitted approximately 2 days later than those with hyperbilirubinemia alone ($p<0.05$).

Conclusions: significant weight loss seems to be an important factor associated with severe hyperbilirubinemia and both should be identified early in follow-up programs. Further prospective studies are needed.

KEYWORDS

Neonatal hyperbilirubinemia – Breastfeeding – Weight loss from birth – Patient readmission

INTRODUCTION

In the current worldwide context of short postpartum hospital stays, it is important to assess factors associated with potentially preventable causes of newborn readmissions such as hyperbilirubinemia and feeding difficulties with or without dehydration [1-6]. Both are the most frequent indications for readmission in the first 2 weeks of life [6-7] and strongly related each other due to inadequate oral intake, particularly in term infants [8-11]. Exclusively breastfed healthy term infants in whom breastfeeding has not been well established by the time of discharge are at greater risk of poor caloric intake, dehydration associated with decreased volume and frequency, and the secondary delayed gastrointestinal motility determines an increase in the enterohepatic circulation of bilirubin [8, 12-13]. Weight loss in the infant of greater than 7% from birth weight indicates possible breastfeeding problems [14]. Several studies have previously reported significant weight loss in patients with extreme hyperbilirubinemia [15-16]; however, only few have analyzed separately this association in otherwise healthy term breastfed infants. The objective of this study was to determine the overall readmission rate due to hyperbilirubinemia and to describe its association with weight loss during the first two weeks of life in term infants who were discharged home after birth hospitalization and considered to be well infants.

METHODS

This cross-sectional study included term otherwise healthy breastfed infants who were readmitted for hyperbilirubinemia at ages 2 to 14 days during January 2005 through October 2008 at the Caja Petrolera de Salud Clinic, a tertiary care facility in La Paz, Bolivia which is part of a Health Maintenance Organization. In our nursery, neonates are routinely discharged around 48 hours after vaginal delivery, and those of mothers who had undergone cesarean section at 72-96 hours. Breastfeeding is encouraged. Before discharge, all newborns are evaluated for clinical jaundice.

A readmission was defined as admission of an infant for hyperbilirubinemia after a first hospital discharge diagnosis of healthy term infant. Readmission rate was calculated by using the number of readmissions as the numerator, divided by the total number of healthy term infants born during the period of study. To avoid potential confounding causes of readmission, we excluded infants with hemolytic disease, infection, anomalies that required more intensive care or other underlying causes. Cephalohematoma and mild bruising were also exclusion criteria.

On readmission, all patients had criteria for phototherapy according to total serum bilirubin (TSB) levels [12]. Only breastfed term infants with a birth weight > 2500 g were included in this study. Birth weight was obtained using an electronic baby weighing scale with a precision of 5g (Seca 728 Ultimate Digital Baby Scale, Seca Corporation, Hamburg, Germany). The same instrument was used to determine the weight on readmission in order to estimate the percent of weight loss from birth weight. Significant weight loss was defined as weight loss from birth

weight greater than 7%. A bilirubin level ≥ 20 mg/dL (342 μ mol/L) was chosen to define severe hyperbilirubinemia since an infant with this degree of jaundice is thought to be at major risk for neurologic damage [9, 17-19].

Statistical comparisons were done using *t*-tests for continuous variables and χ^2 tests for categorical variables. Pearson correlation was calculated to compare TSB levels and percent of weight loss from birth. The risk was estimated by odds ratio (OR) and confidence intervals (CI) using contingency tables. All statistical tests were two-tailed and P-values <0.05 were considered statistically significant. The data were analyzed using SPSS 17.0 for Windows.

RESULTS

From a population of 2140 live term births, 137 (6.4%) term infants were readmitted for hyperbilirubinemia during their first two weeks of life. About 90% of these neonates were exclusively breast-fed infants. Fourteen infants were excluded (6 patients had simultaneously diagnosis of infection, 4 had minor congenital anomalies, 3 had hemolytic disease, and one had a cephalohematoma). One hundred eight infants met the criteria of being exclusively breastfed otherwise healthy term infants. Of these infants, only 79 infants had sufficient data on medical records for analysis. Characteristics of these infants are summarized in **Table 1** according to the severity of hyperbilirubinemia on admission.

Table 1. Characteristics of exclusively breastfed term infants readmitted for hyperbilirubinemia (n=79)

	Severe hyperbilirubinemia (≥ 20 mg/dL) n=23	Significant hyperbilirubinemia (<20 mg/dL) n=56	p
Perinatal history			
Birth weight (g) Mean \pm SD	3060 \pm 482	3197 \pm 505	0.69
Gender male/female (%)	69.6/30.4	62.5/37.5	0.55
Maternal age (yr) Mean \pm SD	29.4 \pm 5.6	30.3 \pm 6.1	0.50
Birth from vaginal delivery (%)	39.1	37.5	0.89
On admission			
Age (d) Mean \pm SD	6.3 \pm 3.6	4.0 \pm 2.1	< 0.05
Weight (g) Mean \pm SD	2920 \pm 367	2880 \pm 475	0.69

Infant's weight loss from birth (g) Mean \pm SD	277 \pm 221	179 \pm 149	<0.05
Percent of weight loss from birth Mean \pm SD	8.8 \pm 4.8	5.9 \pm 4.7	< 0.05
Length of hospital stay (d)	3.0 \pm 1.6	2.4 \pm 1.1	0.13
Significant weight loss (%)	60.9	28.6	<0.05

Breastfed term infants with hyperbilirubinemia were readmitted at a median age of 4.7 days. Approximately two-thirds of these infants were males (64.6%). Mean TSB level on admission was 18.6 \pm 3.0 mg/dL (range: 15.1 – 31.3 mg/dL). Thirty (38%) infants readmitted for hyperbilirubinemia had significant weight loss. Two thirds of these patients (60%) had weight loss >10%. Mean TSB levels of the infants with hyperbilirubinemia alone was significantly lower than mean TSB levels in infants with hyperbilirubinemia and significant weight loss (19.5 vs. 18.0 mg/dl; p <0.05) A weak positive correlation between TSB levels and percent of weight loss was identified (r=0.20; p <0.05) (**Figure 1**). The frequency of severe hyperbilirubinemia among infants with significant weight loss was higher (46.7% vs. 18.4%; p<0.05). The risk of having severe hyperbilirubinemia was approximately 4 times greater for infants with significant weight loss compared with infants who had acceptable weight loss (OR: 3.9; 95% CI: 1.4–10.8; p<0.05). The risk was greater for infants who had weight loss > 10% (OR: 4.2; 95% CI: 1.4–12.7; p <0.05).The length of hospital stay (median: 2 days) did not differ between groups (3.0 vs. 2.4 days; p=0.13). The route of delivery did not influence significantly on differences between TSB levels (p=0.65), age at admission (p=0.93), and percent of weight loss at admission (p=0.66). Infants with severe hyperbilirubinemia were readmitted at a mean of 6.3 days and those with hyperbilirubinemia alone at 4 days (p<0.05). Extreme hyperbilirubinemia (>25 mg/dL) was identified in three patients (3.8%).

DISCUSSION

In this study, significant weight loss was notably associated with hyperbilirubinemia in readmitted, exclusively breastfed healthy term infants. Excluding infants with hemolytic disease, congenital anomalies, significant prematurity, low birth weight, and other underlying illness, we attempted to select a typical “well-infant” discharged from a newborn nursery.

The overall readmission rate was 64 per 1000 term infants, and approximately 50 per 1000 exclusively breastfed term infants. Hyperbilirubinemia readmission rates in term infants usually vary from 2 to 21.7 per 1000 [2-6, 10, 20-21]. Hyperbilirubinemia and feeding problems are the most common causes of readmission of term and near-term infants [1, 5-7, 22, 25-26]. The risk of readmission for hyperbilirubinemia is higher among infants who are breastfed during the birth

hospitalization [10]. Exclusive breastfeeding is not only a major risk factor for hyperbilirubinemia but also for dehydration, particularly if nursing is not going well and weight loss is excessive [12, 22-25]. Significant weight loss from birth reflects feeding problems [8]. Weight loss > 5% was observed in about 25% of breastfed infants during their first 24 hours of life [27]. Approximately one-third of breastfed term infants readmitted for hyperbilirubinemia (mean TSB level of 22.8 mg/dL) showed to have weight loss from birth > 12% [6]. In addition, dehydration and/or feeding problems were detected in approximately 25% of infants readmitted for hyperbilirubinemia [10]. Breastfed infants with significant hyperbilirubinemia (> 12.9 mg/dl - 221 μ mol/L) showed greater weight loss from birth than bottle-fed infants (6.9% vs. 4.2%) [11]. Also, significant hyperbilirubinemia was associated with a greater weight loss after 72 hours of life (8.0% vs. 6.4%), but no direct relationship with breastfeeding was found [8]. Fasting and poor caloric intakes seem to have a greater effect on the regulation of serum bilirubin than breastfeeding *per se* [8, 11]. We found a significant difference in percent of weight loss between infants with severe and significant hyperbilirubinemia (8.8% vs. 5.9%, respectively). This study also showed that approximately 60% of infants readmitted for severe hyperbilirubinemia had significant weight loss and consequently, major risk of bilirubin-induced neurologic dysfunction (BIND). Infant's weight loss from birth \geq 12% was observed in 41% of patients who underwent exchange transfusion for extreme hyperbilirubinemia (>25 mg/dL) [15]. Similarly, weight loss >10% was detected in 26.2% of infants with idiopathic extreme hyperbilirubinemia [16].

A mean age at admission of 4.7 days found in this study is comparable to previous reports [1, 4-6, 10, 23, 28] and supports the concept that the third and fourth days are critical for assessment of breastfeeding [6]. Breastfed infants experience their maximum weight loss by day 3 [12]. In a previous study, the majority of newborns readmitted for feeding problems were 4 to 7 days old, and many had concurrent dehydration and jaundice (34.3%) [26]. In addition, exclusively breastfed infants readmitted for dehydration in whom sodium serum was measured, levels of 150 mMol/L or greater were detected in 25-33% of cases [24-25]. Since infants with severe hyperbilirubinemia were readmitted approximately 2 days later than infants with hyperbilirubinemia alone, we could assume that a significant proportion of these infants would have been detected early in follow-up visits based on weight loss from birth according to the weak positive correlation found in this study. Therefore, if weight loss >10% lead to interventions to improve nutrition and hydration, no association with extreme hyperbilirubinemia is found [13].

Numerous studies regarding newborn readmissions due to hyperbilirubinemia, dehydration and feeding difficulties have established associations with many other variables. Similar to other reports [1, 12, 23], we found that males are readmitted for hyperbilirubinemia more frequently than females. Inexperienced parenting and/or breastfeeding difficulty and maternal age >30 years were also risk factors for readmission [1]. The latter association was not identified in the present study. Interestingly, the percentage of infants delivered by cesarean section was unexpectedly

higher in this report. There are some possible explanations. First, gestational diabetes, pregnancy-induced hypertension, and premature rupture of membranes are risk factors for readmissions in term and near-term infants [1, 10]. If one of these situations were indications for this procedure, it would explain partially this association. Second, length of stay after a C-section is a significant predictor of readmission in near-term and term infants. This effect may be attributable to breastfeeding difficulties, mainly because lactogenesis was shown to occur later for women after cesarean delivery either for physiologic reasons or because of a delay in the initial feeding after surgery [1]. In contrast, several studies have showed that cesarean section is a protective factor for neonatal hyperbilirubinemia. Cesarean section would reduce the risk of admission for increased maternal rest, teaching, and enhanced lactation during the third hospital day [6]. Furthermore, longer inpatient hospital stays have been associated with breastfeeding success after cesarean delivery [29]. Also, it has been suggested that infants born by emergency cesarean section are stressed before birth and, therefore, induce conjugating enzymes before delivery. Finally, less placental transfusion in infants born by cesarean section has also been proposed as a protective factor [8]. In our study, although the history of cesarean delivery was frequent among term infants readmitted for hyperbilirubinemia, this variable does not seem to affect the severity of weight loss, age of presentation, or TSB levels on admission.

Early hospital discharge contributed to the reappearance of bilirubin encephalopathy in the United States [12, 20]. Initially, length of hospital stay (LOS) < 48 hours showed to be a risk factor for hospital readmission due to hyperbilirubinemia [3, 4]; however, inadequate nursing seemed to have the greatest impact on hospital readmission since jaundiced infants showed greater weight loss than non-jaundiced infants (6.8 vs. 4.0 %) suggesting . This suggests less adequate fluid and caloric intake in the jaundiced infants [4]. Accordingly, recent regression analysis revealed no increased odds of readmission with LOS < 2 days. Infants delivered vaginally with 1 night of hospital stay and adequate prenatal and postnatal care outside the hospital had no increased risk of readmission [2]. In addition, no significant increased risk of readmission for hyperbilirubinemia was found among infants who were born vaginally and discharged <24h after birth compared with those discharged between 24 and 48h [10]. Similarly, no association between dehydration and neonatal or maternal LOS was reported [22]. Finally, early discharge following an uncomplicated postpartum hospital stay appeared to have no independent effect on the risk of readmission in infants with feeding-related problems [26]. Based on these reports, the best intervention would be to help mothers to nurse their infants more effectively from the moment of birth [1]. Outpatient follow-up strategies occurring between 24 and 48 hours after discharge would prevent dehydration and hyperbilirubinemia [22]. Therefore, discontinuing early hospital discharge practices may not be the best means to decrease the risk of hospital readmission for hyperbilirubinemia [3]. The specific age at time of discharge after their birth hospitalization was not determined in this study, but we agree that improving our follow-up programs will have a greater impact on reducing the risk of severe hyperbilirubinemia rather than modifying the current global tendency of short newborn hospital stays.

A major limitation of this analysis is the lack of information regarding infant feeding. Several assessment tools to evaluate lactation are currently available. The second major limitation of this report is the absence of data related to the timing and extent of newborn follow-up in the outpatient setting. As mentioned above, the timing of follow-up may reduce readmissions if jaundice and/or feeding problems are caught early enough. One additional limitation is our inability to compare these results with a normal newborn population and therefore, to establish specifically the causal relationship of other variables such as length of hospital stay and other socio-demographic factors (race, primiparity, prenatal care, and education) which were not considered in the present study. Another important consideration is that the use of neonatal readmission as a primary outcome has advantages and disadvantages, which have been extensively reviewed and discussed [1]. Finally, the study was conducted in a high-altitude city (3600 m above sea level). At similar altitude, incidence of neonatal hyperbilirubinemia, defined as TSB levels >12 mg/dl, showed to be approximately four times the incidence reported in the literature for sea level [30].

Despite the limitations of this study, we found that weight loss and probably feeding problems are strongly associated with readmission due to hyperbilirubinemia in exclusively breastfed term infants. Significant weight loss increase approximately 4 times the risk to develop severe non-hemolytic hyperbilirubinemia in term breast-fed infants and it seems to be worst when the cut point to define significant weight loss is higher (infants with a weight loss of 10% have odds 4.2 times higher). Both hyperbilirubinemia and dehydration persist worldwide despite well-intentioned guidelines for care showing that practice related to newborn care and follow-up seem to be resistant to change, particularly in less-developed countries.

If breastfed infants are targeted for intervention on the third and fourth days of life, it is conceivable that this population at risk can receive assistance that will avoid costly readmissions [6]. Preventing readmissions is a desirable goal and can prevent stress and trauma to the infant and family during this particularly vulnerable period surrounding childbirth [1, 6]. Because of the increasing number of studies which have reported association between dehydration, hypernatremia and hyperbilirubinemia related with feeding problems [6, 24-25, 27], we suggest that serum sodium and glucose become part of the routine workup in infants readmitted for hyperbilirubinemia, particularly if breastfeeding problems are suspected as possible etiology.

Our findings also highlight the need for better data about the content of outpatient follow up visits. Recently, many successful interventions have been published. A family-centered systems approach has demonstrated to prevent effectively severe neonatal hyperbilirubinemia and kernicterus [20-21]. The institution of a prehospital-discharge newborn bilirubin screening program also showed to reduce readmissions for hyperbilirubinemia [31]. Finally, postnatal home nursing visits for prevention of hospital management of hyperbilirubinemia and dehydration have also showed to reduce significantly readmission rates and costs [32]. Which is the best intervention in settings with a similar socio-economic context should be analyzed in

large future research projects based on prospective models to identify not only association but also a relationship of cause and effect in term and near-term infants.

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Figure 1. Linear correlation between TSB levels and percent of weight loss in exclusively breastfed term infants readmitted for hyperbilirubinemia

