

## Significant Neonatal Weight Loss Related to Idiopathic Neonatal Hyperbilirubinemia

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### Abstract

#### Introduction

Inadequate intake of breast milk in the first days of life leads to weight loss in neonates. Jaundice is also more prominent in these infants. In this cross-sectional study, we tried to evaluate the extent of weight loss in term breastfed infants who were hospitalized for idiopathic hyperbilirubinemia.

#### Materials and Methods

This prospective cross sectional study involved 1072 infants >48 hours old, who were admitted to Ghaem Hospital of Mashhad-Iran, with idiopathic hyperbilirubinemia, between may 2007 - 2013. Infants were divided into two groups based on the amount of weight loss. Case groups (> 7% weight loss) and control (weight loss ≤ 7%). The profile of maternal and neonatal risk factors were compared between them.

#### Results

Average birth weight, gestational age, mode of delivery, maternal age, duration of mother's stay at hospital did not show any significant difference between two groups ( $P>0.05$ ). Age at presentation, weight on admission, extent of weight loss, percentage of daily weight loss, duration of neonatal hospitalization, age at onset of hyperbilirubinemia, serum bilirubin and hematocrit levels were significantly different between two groups ( $p<0.05$ ).

#### Conclusion

According to this study's findings, about one thirds of neonates presenting with idiopathic hyperbilirubinemia, had severe weight loss and hyperbilirubinemia was also more severe in this group. The average weight loss in the neonates with severe hyperbilirubinemia (>20 mg/dl) was three times that of moderate hyperbilirubinemia (< 20 mg/dl).

**Key Words:** Breastfeeding, Hyperbilirubinemia, Neonate, Weight loss.

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Received date: May25, 2014 ; Accepted date: Jun 22, 2014

## Introduction

Hyperbilirubinemia and feeding problems are two of the most common complaints in the first weeks of life (1). Insufficient milk intake during the first days of life increases the enterohepatic cycle and thus increasing bilirubin levels. On the other hands, neonatal hyperbilirubinemia causes maternal anxiety and separation of mother - infant for phototherapy during the first days postpartum which has adverse effects on establishment of proper breast feeding (2). Also, lack of sufficient milk intake in the first days of life results in neonatal weight loss. Little milk intake and thus receiving inadequate calories leads to decreased intestinal movements and thus accentuating the enterohepatic cycle of bilirubin and also retards the maturation of bilirubin conjugation liver enzymes. This two latter, play a role in breast feeding jaundice in the first week of life (3).

It is normal over the first week of life for the neonate to lose as much as 5-7% of its birth weight. Weight loss more than 7 % in the first week of life can be an indicator of low milk intake by the neonate. Probable causes of little milk intake can be lack of maternal education about breast feeding problems in the first days post partum, early maternal discharge before establishment of proper nursing, too many cesarean sections, maternal breast problems, lack of suitable post discharge maternal follow up and the use of traditional supplements such as glucose water and camel thorn (2). Many studies have been undertaken about neonatal hyperbilirubinemia but few of them have evaluated the relationship between weight loss and jaundice (3,4). So in this prospective cross sectional study we tried to evaluate the relationship between weight loss and it's affecting factors on

breastfed term infants presenting with idiopathic hyperbilirubinemia.

## Materials and methods

This study was performed between May 2007 to May 2013. 2400 breastfed term infants who were hospitalized for hyperbilirubinemia in Ghaem Hospital of Mashhad-Iran, were studied. This hospital is affiliated with Mashhad University of Medical Sciences. 1072 infants whose hyperbilirubinemia could not be attributed to a specific cause (idiopathic hyperbilirubinemia) were included in this study. Exclusion criteria were as follows:

- 1) Preterm infants or birth weight < 2.5 kg;
- 2) Formula fed infants;
- 3) Infants with septicemia, meningitis, urinary tract infection, multiple anomalies, chromosomal anomalies or congenital heart disease;
- 4) Fifth minute Apgar score of less than 7;
- 5) Infants with hyperbilirubinemia with a specific etiology (Hemolytic disease of the newborn (ABO) or RH incompatibility, hypothyroidism, cephalhematoma, skin ecchymosis, glucose 6 phosphate dehydrogenase deficiency).

The study was approved by Medical Ethics Committee of Mashhad University of Medical Sciences prior to performance and all patients' parents signed informed consent. These infants were divided according to their degree of weight loss into case (weight loss > 7 % ) and control ( weight loss  $\leq$  7 % ) groups.

The research questionnaire was developed by the researchers and consisted of 2 parts:

1. Neonatal data: age, birth weight, weight on admission, 5 minute Apgar score, gestational age, sex, reason for hospitalization, signs and symptoms and complaints on admission, duration of hospitalization, frequency and duration of feeding.
2. Maternal factors including: age, parity, problems during pregnancy,

mode of delivery and duration of postpartum hospitalization.

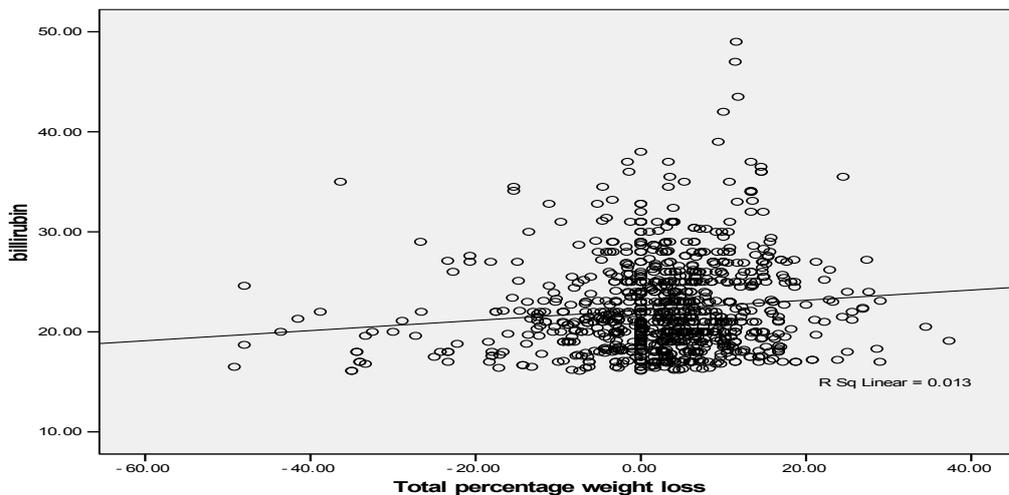
Complete blood count (CBC), serum bilirubin level, reticulocyte count, direct and indirect coombs test, maternal and neonatal blood group and RH and if needed blood culture, urinalysis and urine culture, urea, creatinin and sodium levels were tested and recorded.

**Data analysis and statistical methods**

Data were analyzed using SPSS software, version 14. The group comparisons were assessed by the Pearson correlation test, Student's t-test and ANOVA tests (in case of normally distributed data) and nonparametric tests include Spearman correlation test, mann-whitney test and kruskal-wallis test (in case of non-normally distributed data). Chi-square test was used to analyze the relationship between variables with nominal scales. For all tests level of significance in terms of p value was <0.05.

**Results**

From among 1072 evaluated infants, 764 had weight loss of  $\leq 7\%$  or did not have any weight loss (control group) and 308 had weight loss of more than 7% (case group) (Figure.1).



**Figure 1:** Diagram of distribution of bilirubin in newborns according to weight loss.

Average birth weight of neonates was 3175 ±470 gr and average weight on admission was 3073 ±520 gr. All neonates had first Apgar score of more than 8. Characteristics of case and control groups are shown in (Table.1). 47% percent of neonates who were first child had pathologic weight loss, whereas 32 % of

infants of higher order pregnancies had this severe weight loss. On the initial physical examination 687 (90.8 %) of infants were normal and 10 % had accompanying symptoms. 92% were admitted with the complaint of jaundice. Although 34.3% of infants had severe weight loss, only 8 % were brought to

clinic for weight loss. Average birth weight, gestational age, mode of delivery, maternal age, duration of mother's stay at hospital did not show any significant difference between two groups ( $p > 0.05$ , Table 1 ). Age and weight on admission, degree of weight loss, percentage of daily

weight loss, and duration of infant's hospitalization, age at the onset of hyperbilirubinemia, bilirubin and hematocrit levels were significantly different between two groups ( $p < 0.05$ , Table 1, 2).

**Table 1:** Characteristics of case and control mothers and infants

Variables	Case group (Mean ± SD)	Control group (Mean ± SD)	P Valau
Age (days)	7.04 ± 3.6	8.13 ± 5	0.000
Birth weight (gr)	3196 ± 477	3138 ± 4507	0.070
Weight at admission(gr)	2782 ± 439	3184 ± 4096	0.000
Sex (female / male)	132/141	265/418	0.004
Mode of delivery(C / S / NVD)	123/120	342/285	0.167
The duration of neonatal hospital stay (days)	3.5 ± 2.8	2.9 ± 1.9	0.02
Maternal age (years)	26.56 ± 5.5	26.23 ± 5.3	0.405
Duration of maternal hospital stay (days)	1.55 ± 0.6	1.42 ± 0.6	0.065
Time of first feeding (h)	2.11±5.05	1.6±2.11	0.002

Values are expressed as mean±sd, number or percentage. Comparisons between control and case groups were made using the Student's *t* test (in case of normally distributed data), mann-whitney

test (in case of non-normally distributed data) or chi-square test (in case of categorical variables). Average percentage of daily weight loss in case group was (2.6±1.03) which was (0.6 ±0.75) for control group.

**Table 2:** Changes in weight based on the severity of hyperbilirubinemia(Less or more than 20mg / dl)

The groups study	Bilirubin ≥20 mg / dl	Bilirubin <20 mg / dl	Mann-weightney test
Variables			
Daily rate of weight loss(gr / day)	23.54 ± 46.51	48.41 ± 17.38	0.011
The overall weight loss(gr)	109.58 ± 294.11	32.60 ± 393.68	0.009

## Discussion

Findings of this study show that neonates with severe hyperbilirubinemia have 3 times more severe weight loss and serum bilirubin levels increases with the severity of weight loss too. In our study, average age of neonates was 7.62 ±4.69 days. In a study in Turkey age at presentation was 5 days (5). In another

study in Iran, age at presentation for hemolytic hyperbilirubinemia was 6 days (6). These studies show that most of our jaundiced neonates are brought to clinic by the end of the first week of life, which seems to be late and this can worsen the complications of hyperbilirubinemia. So it seems that educating the families about the

importance of hyperbilirubinemia and the role of seeking early medical attention in reducing the complications of jaundice can be very helpful. In comparison between case and control groups we found that the neonates of case group were younger and this shows the importance of attention and careful care about nursing problems and weight loss in the first days of life.

In this study, the prevalence of hyperbilirubinemia in male neonates was 1.5 times that of girls. The greater prevalence of hyperbilirubinemia in male neonates has been shown in several other studies (2,7,8) but the real etiology for this greater prevalence is unknown. Important to notice in our study was that, weight loss in girls was two times that of boys and there was no similar study on this subject. The reason for this greater weight loss in girls remains unknown. In our study the rate of normal vaginal delivery (NVD) was 53.9 % and 46.1% for cesarean section. In another study this was 81.4-94.7% for NVD and 5.3-19.6 % for Caesarean section (CS) (7, 8). One other study reported that 58.1 % of jaundiced neonates were born through NVD and 41.9 % by cesarean section (9). Although the prevalence of cesarean section was high in our study but mode of delivery did not show any significant difference between two groups. Though it's presumed that because of the problems of cesarean, these problems must be seen more in neonates of cesarean deliveries, but because our neonates were all icteric, the difference was not noticeable in this population. In a study about the relationship between mode of delivery and degree of hyperbilirubinemia, no relation was found (9).

In this study, most of our jaundiced neonates were first child (52.2 %). In other studies neonates with breastfeeding

jaundice were mostly of primiparous mothers (7,10). This shows the importance of educating young mothers about hyperbilirubinemia and weight loss and also educating mothers about proper breastfeeding techniques before hospital discharge. The average maternal age in our study was less than 26 years old. In another study average maternal age was 26.1 years old (11). With regards to low maternal age of icteric neonates and their mostly being of first parity and the early onset of breastfeeding jaundice in the first week of life, educating young and primiparous mothers about the importance of breastfeeding, proper feeding techniques and the possibility of hyperbilirubinemia in the first week seems necessary ( 12,13 ).

In comparison between case and control groups, delayed initiation of breastfeeding was more common in the case group, which was reported in another study too (13). Though, this was not correlated with the results of Gomez et al. study (10). So breastfeeding initiation as soon as possible after birth is necessary and all factors affecting early breastfeeding initiation must be identified and resolved (13).

Frequency of urination in case group was less than control and this was also reported in other studies (9,5,11). Urinary output of neonates in the first weeks of life is an important indicator of sufficient milk intake. On the other hands, decreased urination is an early sign of inadequate feeding in an infant (13).

About one thirds of our jaundiced neonates had significant weight loss (more than 7%). In one other study 33% of infants with pathologic hyperbilirubinemia (more than 13 mg/dl) had weight loss more than 12% (4). Another study showed that 37% of infants who had weight loss were also

icteric (13). Geiger et al. in a survey of risk factors for neonatal jaundice reported that 24.2% of these infants were dehydrated and 26.8% had feeding problems (14). In another study comparing icteric neonates with bilirubin >13mg/dl with those of lower bilirubin levels (<13 mg/dl) a significant weight loss was reported in those with higher bilirubin levels and it was concluded that starvation plays an important role in the pathogenesis of hyperbilirubinemia (4). Early breast feeding jaundice which is manifested in the first week of life is due to insufficient intake of milk and is called by some authors exaggerated physiologic jaundice. Decreased milk intake causes a delay in meconium passage which contains high amounts of bilirubin , thus absorption of bilirubin through gastrointestinal tract increases ( 4,15 ).

Though all neonates who experience significant weight loss during their first week of life are not icteric but an association between weight loss and hyperbilirubinemia is seen and although it does not seem that weight loss is the etiology of hyperbilirubinemia but the possibility that it aggravates the jaundice is great (4,13 ). Low caloric intake and the resulting weight loss is a severe problem in neonates that can be a risk factor for exaggerating their hyperbilirubinemia. So, frequent breast feeding in the first days of life, in addition to the establishment of breast feeding, decreases neonatal weight loss and according to this study, decreases the severity of their hyperbilirubinemia. So, we recommend frequent breast feeding in order to reduce weight loss and hyperbilirubinemia in neonates.

According to this study's findings, severe hyperbilirubinemia (>20 mg/dl) is more frequent in infants with pathologic weight loss. That is average weight loss in infants with severe hyperbilirubinemia(>20

mg/dl) was three times more than that of neonates with moderate hyperbilirubinemia ( $\leq 20$  mg/dl).

It is shown that weight loss due to decreased caloric intake in the first days of life plays a role in the severity of hyperbilirubinemia. The probable mechanism for this phenomenon could be the accentuation of enterohepatic cycle and also delay in the maturation of enzyme UDP-glucoronyltransferase (UGT) (3). Early maternal discharge before establishment of a successful nursing leads to decreased milk and calori intake and thus delays intestinal movements and finally increases the enterohepatic cycle ( 3,16,17 ).

### **Conclusion**

Weight loss in neonates can accentuate hyperbilirubinemia and frequent breast feeding inhibits pathologic weight loss and thus idiopathic hyperbilirubinemia. So in neonates with feeding problems if suitable feeding interventions is not instituted promptly we should await significant weight loss and hyperbilirubinemia.

### **Conflict of interest**

The authors have no conflicts of interest.

### **Acknowledgment**

The researchers must appreciate the cooperation of dear colleges, nurses and also dear their parents of Neonatal unit of Qaem Hospital, Mashhad.

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