http:// ijp.mums.ac.ir
Original Article (Pages: 609-617)

Evaluation of the Sodium Serum Level in Infants with Jaundice

Hassan Boskabadi[1], Gholamali Maamouri[1], Fatemeh Khatami[1], Mohammad Ali Kiani[2], Abbas Abdollahi[3], *Maryam Zakerhamidi[4], Nafiseh Saghafi[5], Amir Hosein Ghazizadeh Hashemi[6]

[1]Department of Pediatrics, Neonatal Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.
[2]Department of Pediatrics, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
[3]Resident of Pediatrics, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
[4]Department of Midwifery, Tonekabon Branch, Islamic Azad University, Tonekabon, Iran.
[5]Department of Gynecology, Mashhad University of Medical Sciences, Mashhad, Iran.
[6]Assistant Professor of Otorhinolaryngology, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Abstract

Introduction

Inadequate milk intake during the first year of neonate's life can result in weight loss, severe hyperbilirubinemia, and sometimes hypernatremia. We aimed to determine the relationship between neonatal weight loss and hypernatremia in term breastfed infants with idiopathic jaundice, as well as the necessity of sodium concentration measurement in newborns with idiopathic jaundice via weight loss measurement.

Materials and Methods

In this cross-sectional study, we examined 273 infants with jaundice of unknown etiology at Ghaem Hospital, Mashhad- Iran, in 2008 to 2012. The study sample consisted of 226 infants in the control group (serum sodium concentration <150 mg/dl) and 47 infants in the case group (serum sodium concentration ≥150 mg/dl). The subjects were evaluated in terms of weight change and neonatal risk factors. Finally, we assessed the sensitivity, specificity, and positive and negative predictive values of weight loss in the measurement of serum sodium concentration.

Results

The mean sodium concentration was 155.8±5.51 mg/dl in the case group, and 139.4±4.09 mg/dl in the control group. There was a significant relationship between weight loss and hypernatremia (P<0.001). With 70% sensitivity and 83.6% specificity, the positive predictive value of ≥ 1.5% daily weight loss was 50% for hypernatremia, in infants younger than 10 days of age; the negative predictive value was 92% (P≤0.001).

Conclusion

According to the results, the measurement of sodium concentration is not required in the first ten days of neonate's life if total weight loss is less than 7% or daily weight loss is less than 1.5%.

***Key Words*:** Infant, Jaundice, Sodium Serum Level, weight loss.

* ***Corresponding Author:***

Zakerhamidi Maryam, Department of Midwifery, Tonekabon Branch, Islamic Azad University, Tonekabon, Iran.
E-mail: maryamzakerihamidi@yahoo.co.nz

Received date: Feb 20, 2015 ; Accepted date: Mar 7, 2015

Introduction

Neonatal jaundice, a common condition among breastfed infants, is a leading cause of neonatal admission during the first week of infant's life (1). Insufficient milk intake in the first days of life can lead to neonate's weight loss and even jaundice. As milk intake reduces, newborn's kidneys try to reabsorb urinary sodium and maintain the fluid as a defense mechanism; this process leads to hypernatremia. Moreover, insensible fluid loss from liver and body continues due to the immaturity of infant's skin, which can lead to intensified dehydration (2).

Weight loss accompanied by hypernatremia, as a result of insufficient milk intake, can result in serious complications such as stroke, brain hemorrhage, and thrombus in neonates (1).

In recent years, the incidence of neonatal hypernatremic dehydration has increased, and insufficient milk intake is considered the most important risk factor. Early hospital discharge after delivery, inadequate training of mothers, lack of attention to the adequacy of milk intake, and poor breastfeeding techniques contribute to the neonate's poor oral intake (1).

Neonatal hypernatremia dehydration is a dangerous condition in neonates, which is accompanied by acute complications (renal failure, cerebral edema, and cerebral hemorrhage) and chronic complications (developmental delay) (3).

Hypernatremia has detrimental effects on various physiologic functions and was shown to be an independent risk factor for increased mortality in critically ill patients. Mechanisms of hypernatremia include sodium gain and/or loss of free water and can be discriminated by clinical assessment and urine electrolyte analysis (4).

There have been debates among pediatricians as to when sodium concentration measurement is required for neonates with jaundice and whether hypernatremia severity could be determined by the amount of weight loss. Neonatal jaundice is the most common cause of neonatal admission in Iran, and approximately 1.5-3% of infants present with hypernatremia (1, 5).

In neonates with jaundice, who show signs of weight loss or dehydration, the appropriate time for the assessment of serum sodium concentration has not been determined. Moreover, the risk factors for hypernatremia are not yet defined in newborns with jaundice.

According to previous studies, jaundice is associated with reduced or increased sodium concentration. However, we still do not know in which cases of jaundice, neonates should be evaluated in terms of hypernatremia.

In this study, we aimed to find a cut-off point for serum sodium measurement in infants with jaundice of unknown etiology. In addition, in this cross-sectional study, we tried to determine the relationship between weight loss and contributing factors in term breastfed infants with idiopathic jaundice and to measure hypernatremia severity via weight loss measurement.

Materials and Methods

In this study, 300 term neonates were evaluated in the Neonatal Intensive Care Unit (NICU) and the Neonatal Ward of Ghaem Hospital, Mashhad, Iran; in 2008 to 2012. The informed consents were obtained from all parents.

The exclusion criteria were as follows: 1) Prematurity, 2) Formula-feeding, 3) Sepsis, 4) Meningitis, 5) Urinary Tract Infection (UTI), 6) Chromosomal abnormality, 7) Congenital heart disease, 8) 1-minute APGAR (Appearance, Pulse, Grimace, Activity, and Respiration) score < 7, and 9) Jaundice with a known cause

(e.g., blood group or Rh incompatibility, hypothyroidism, and hematoma).

Twenty-seven neonates were excluded due to the following reasons: 3 cases of ABO incompatibility; 2 cases of Rh incompatibility; 2 cases of spherocytosis; 3 cases of Glucose-6-phosphate Dehydrogenase (G6PD) deficiency; 1 case of positive blood culture; 2 cases of hypothyroidism; 2 cases of intestinal obstruction; 3 cases of anomalia including myelomeningocele (1 case), Toxoplasmosis, Rubella, Cytomegalovirus, Herpes simplex, and HIV (TORCH) (1 case), and down syndrome (1 case); 1 case of cephalohematoma; and 8 cases of Utilitarianism (UTI).

Therefore, 273 neonates remained in the study. Neonates with non-hemolytic jaundice and weight of ≥ 2.5 kg were divided into case (47 subjects, serum sodium concentration ≥150 mg/dl) and control (226 subjects, serum sodium concentration <150 mg/dl) groups, based on serum sodium concentration. The sample size was calculated using the following formula:

$$n = \frac{p(1-p)z^2}{d^2}$$

According to a study by Jarkan (2), entitled "weight loss and hypernatremia in breast-feeding infants with jaundice" and a 12% estimate of hypernatremia accompanied by weight loss in neonates with hyperbilirubinemia, the sample size was calculated to be 260 subjects in each group, considering the P-value of 0.12, 95% confidence interval, and 0.04 accuracy.

$$n = \frac{0.12 \times 0.88 \times (1.96)2}{(0.04)2}$$

Full examination and weight measurement of the neonates were performed and laboratory test records, as well as neonatal medical history, were recorded. The researcher-made questionnaire consisted of neonatal characteristic. Neonatal factors included age, gender, weight at birth, current weight, gestational age, 5-minute APGAR score, signs and symptoms at admission, cause of admission, breastfeeding duration, urination and bowel movements per day, and the first defecation. The data were recorded for both groups.

The study sample consisted of 226 infants in the control group (serum sodium concentration <150 mg/dl) and 47 infants in the case group (serum sodium concentration ≥150 mg/dl). Also, excessive weight loss was defined as total weight loss exceeding 10% in neonates younger than 7 days.

The validity of the questionnaire was confirmed using reliable sources and experts' comments. For this purpose, 5 faculty members of Mashhad University of Medical Sciences were selected and asked to assess the validity of each question regarding the association between breastfeeding position and serum sodium level; accordingly, the questionnaire was revised based on the given comments. The reliability of the questionnaire was confirmed through test-retest, and Cronbach' alpha was calculated as r=0.8.

In order to evaluate breastfeeding positions, the following criteria were assessed: breast growth during pregnancy, postpartum breast enlargement and fullness, breast fullness before each lactation, and breast sagginess after each breastfeeding.

The let-down reflex was defined as a response evoked by suckling, causing the release of mother's milk; normally, when the mother breastfeeds the newborn, milk is released from the other breast, too.

If information regarding Complete Blood Count (CBC), blood culture, cytology evaluation, Cerebrospinal Fluid (CSF) culture, urine culture, Arterial Blood Gas (ABG) test, Vertical Banded Gastroplasty (VBG), and levels of total and direct

bilirubin, urea, creatinine, sodium, potassium, sugar, and blood calcium was required, the related clinical tests were performed.

After data collection, the total rate of weight loss was determined. Afterwards, by dividing the total weight loss by the number of neonate's days of life, the rate of daily weight change was calculated. The two groups were compared in terms of changes in sodium concentration level and weight. Considering the amount of weight loss, the presence of hypernatremia was assessed. Moreover, by drawing the Receiver Operating Characteristic curve (ROC curve), the specificity, sensitivity, and positive and negative predictive values of weight loss for hypernatremia were determined.

The analysis was performed with regard to the study design (descriptive), by using tables, diagrams, and statistical indices. Statistical analysis was performed by SPSS version 16. For normally distributed data, the correlations between variables were assessed using Pearson's correlation coefficient, t-test, and ANOVA. However, if the data were not normally distributed, Spearman's correlation coefficient, Mann-Whitney test, and Kruskal-Wallis test were performed. Chi-square was used to determine the relationships between nominal variables. P-value less than or equal to 0.05 was considered statistically significant. For determination of the cut-off point, ROC curve was used.

Results

In this study, 56% and 44% of the subjects were male and female neonates, respectively. In total, the neonates had an APGAR score higher than 8. The neonates' characteristics in the two groups are summarized in (Table.1).

Table 1: Neonatal characteristics in both groups

Neonatal characteristics*	Case group (47 infants)	Control group (226 infants)	P-value
Age (day)	5.32 ±3.05	8.10±4.83	<0.001
Weight at birth (g)	3239.14±518.52	3122.92±460.90	0.125
Weight during hospitalization (gr)	2913.19 ±460.38	316.68±520.61	0.002
Weight loss (%)	10.8±4.3	6.3±4.2	<0.001
Gestational age	39.06±1.00	39.02±1.10	0.813
Gender (male or female)	18.29	102.124	0.390
First feeding time	11.21±5.05	6.13±2.11	0.002
Feeding frequency per day	11.76±6.28	14.80±7.08	0.008
Feeding duration	20.17±14.45	20.74±12.23	0.302
Frequency of urination	5.31±3.13	6.76±3.36	0.004
Defecation frequency	4.31±3.10	4.76±3.36	0.312
First defecation (h)	12.06±11.55	11.87±11.60	0.904
Abnormalities in suckling	5 (10.6%)	6 (2.7%)	0.011

*Values are presented as mean± standard deviation or number (percentage, %)

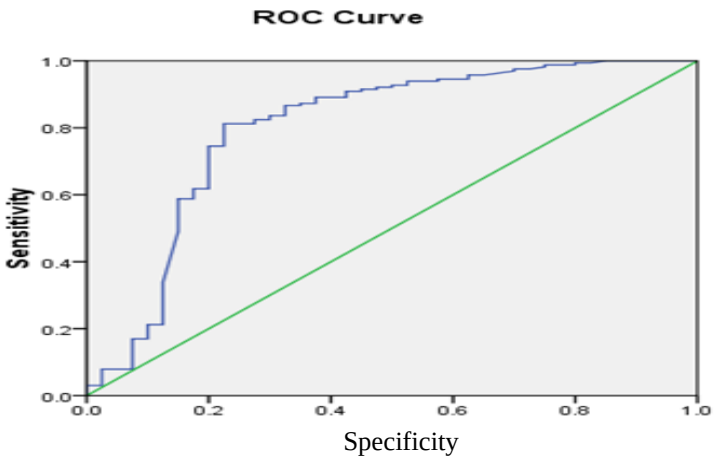

Fig. 1: The relationship between daily weight loss and hypernatremia in infants younger than 10 days

Major symptoms after jaundice were weight loss (47.6%), lethargy (14.2%), restlessness (10.2%), hyperthermia (6.6%), and mucus dryness (%6.6).

After jaundice, the most common sign was weight loss, observed in 80.8% and 40.9% of the neonates in case and control groups, respectively. The average weight loss was 10.8±4.3% (2-27%) in the case group and 6.3±4.2% (1-17%) in the control group. Also, excessive weight loss (total weight loss >10% or daily weight loss>2%, compared to weight at birth) was reported in neonates younger than 7 days of age (64.9% of the case group and 12.3% of the control group) (P≤0.001).

According to the results, there was no significant correlation between jaundice severity and weight loss (P=0.538). Also, there was no significant association between jaundice severity and hypernatremia (P=0.465); however, the relationship between weight loss and hypernatremia severity was significant. Also, in neonates younger than 7 days of age, a linear and direct relationship was observed between total daily weight loss

and sodium serum concentration (Figure. 1, 2) (P≤0.001).

In a total of 205 neonates younger than 10 days of age, the serum sodium level was < 150 mg/dL in 165 neonates and ≥ 150 mg/dL in 40 neonates. With 75% sensitivity and 81.8% specificity, the positive predictive value (i.e., total weight loss ≥ 7% in neonates younger than 10 days indicates hypernatremia) was 50%; the negative predictive value (i.e., lack of total weight loss or total weight loss < 7% in neonates younger than 10 days does not indicate hypernatremia) was 93% (P≤0.001).

Also, with 70% sensitivity and 83.6% specificity, the positive predictive value (i.e., daily weight loss ≥ 1.5% in neonates younger than 10 days indicates hypernatremia) was 50%; the negative predictive value (i.e., lack of weight loss or daily weight loss ≤ 1.5% in neonates younger than 10 days does not indicate hypernatremia) was estimated to be 92% (P≤0.001) (Tables. 2, 3).

Table 2: Comparison between sensitivity and specificity of total weight loss ≥ 7% and < 7% in both groups (younger than 10 days)

Total weight loss	Serum sodium concentration<150 mg /dl		Serum sodium concentration≥150 mg/dl		Total	
Variables	Percentage	Frequency	Percentage	Frequency	Percentage	Frequency
Total weight loss ≥ 7%	18.2	30	75	30	29.3	60
Without total weight loss or < 7% total weight loss	81.8	135	25	10	70.7	145

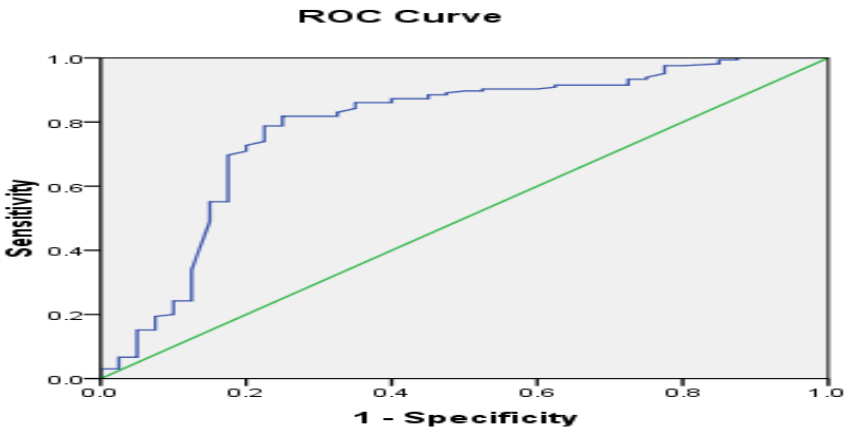

Fig.2: Comparison between total weight loss and hypernatremia in infants younger than 10 days

Table 3: Comparison between the two groups (younger than 10 days) in terms of sensitivity and daily weight loss ≥ 1.5% and <1.5%

Daily weight loss	Serum sodium concentration<150 mg/dl		Serum sodium concentration≥150 mg/dl		Total	
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
Daily weight loss ≥ 1.5%	27	16.4	28	70	55	26.8
Without weight loss or < 7% weight loss	138	83.6	12	30	150	73.2

The average sodium concentrations in the case and control groups were 155.8±5.51 (150-174) and 139.4±4.09 (128-149) mg/dl, respectively. The two groups were significantly different in terms of creatinine level (P≤0.001), hematocrit level (P=0.006), and urine specific gravity (P=0.022). Improper breastfeeding position was mostly observed in the case group, compared to the control group (P<0.001); on the other hand, let-down reflex was mostly present in the control group (P=0.002).

There was no significant difference between the control and case groups in terms of sufficient breast development

during pregnancy (P= 0.357) and breast enlargement/fullness after delivery (P= 0.136). However, breast fullness before every lactation (P=0.009) and its sagginess after it in the case group were significantly less than the control group (P=0.001). Puerperal mastitis in the case group was more significant than the control group (P=0.038).

Moreover, according to ANOVA test, there was a statistically significant difference in white blood cell count, urine specific gravity, and urea, creatinine, and hematocrit levels between the two groups; the obtained values were higher in the case group, compared to the control group. Mann-Whitney test was used to compare data, which were not normally distributed, such as white blood cell count, urine PH, urine specific gravity, and urea, creatinine, direct bilirubin, and sugar levels between the two groups; t-test was used to compare bilirubin, potassium, hematocrit, calcium, and platelet count. According to Mann-Whitney test results, length of hospital stay was significantly different between the groups. Length of hospital stay was 127.47 days in the control group and 180.15 in the case group (longer in the case group). As to Mann-Whitney test results, frequency of supplement intake was not significantly different between the groups; supplement intake was 137.05 in the control group and 136.77 in the case group.

Discussion

In our study, 56% and 44% of the subjects were male and female neonates, respectively. The fact that jaundice is more common among male neonates is well established in many studies (5, 6); however, the underlying cause is still unknown.

In the current study, the most common clinical manifestation in neonates was weight loss, which was observed in half of the infants; weight loss in the case group was twice as common as the control group. Severe weight loss was reported in 64.9% and 12.3% of the neonates in the case and control groups (7 days of age), respectively; there was a linear and direct relationship between weight loss and hypernatremia. Boskabadi (2014) showed that 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) (7). In some previous studies (8), 62.5% of neonates with hypernatremia, (9) 70% of neonates with dehydration, and (1) 73% of neonates with hypernatremia experienced weight loss (over 10% weight loss). In another study, 10% weight loss was observed in 88.6% of hypernatremic neonates, and the average weight loss in the case group was almost twice as much as the control group (10).

In the present study, similar to previously mentioned studies, weight loss in the case group was reported to be 80.8%; the large number of cases with weight loss is probably due to the inclusion of only breast-fed infants with jaundice and the late admission of neonates in our study. Therefore, considerable attention should be paid to weight loss in the first week of life, especially in the first few days.

Based on our finding, the incidence of hypernatremia in neonates without weight loss or total weight loss <7% was very low and serum sodium measurement was not necessary in these cases. Also, in case the neonates were admitted during the first week of life with signs of daily weight loss < 1.5%, sodium measurement was not necessary.

We recommend that neonates younger than 7 days of age, with total weight loss > 7% or daily weight loss > 1.5%, be evaluated in terms of sodium blood level. Also, considering the direct relationship

between blood sodium level and levels of blood urea, creatinine, and urine specific gravidity, these variables should be examined in case of hypernatremic dehydration.

In the current study, breastfeeding frequency in the case group was lower than the control group, which shows the necessity of frequent nutrition in early days of life. Frequency of urination in the case group was lower than the control group, which was inconsistent with some previous studies (8, 10, 11). This shows that attention to weight loss in the first weeks and urine output is necessary, since it indicates the status of milk intake; in fact, decrease in the frequency of urination is a sign of insufficient neonatal nutrition.
Improper feeding position and lack of lactation reflex were more frequent in the case group, compared to the control group; therefore, more attention should be paid to mother's breastfeeding training, breastfeeding techniques at hospital, and let-down reflex. In a previous study (2), mothers of neonates, who had more than 10% dehydration as well as hypernatremia, had insufficient breast milk or low breast milk sodium concentration. Hypernatremic dehydration is relatively common among exclusively breastfed neonates. It is a serious condition with many serious complications and even results in death if detected late. Then Health care providers have increasing responsibilities of promoting proper breastfeeding techniques and taking measures for early diagnosis and treatment of this problem. Also, regular weight monitoring, proper breastfeeding and environmental temperature control should be encouraged for preventing breastfeeding-associated hypernatremia (12, 13).

In another study (11), insufficient breast development during pregnancy and lack of breast fullness and sagginess before and after every lactation, respectively, were mostly observed in the mothers of subjects with hypernatremia.

In the case group, breast sagginess after every breastfeeding was an indicator of improper breast suckling or mother's insufficient training; this problem leads to future breast problems and lactation disorders. Poor milk drainage in the first days of infant's life, which is intensified by supplement intake, can justify the insufficient secretion of milk from breasts and lactation disorders in the first few days. However, mother's milk should reach the sufficient level within 4 days after neonate's birth; also, for infant's sufficient milk intake, frequent lactation in the first few days is more important than milk volume or feeding duration. Mothers should be evaluated in terms of breast growth and lactation signs in the first few days, and necessary examinations should be performed in order to prevent dehydration due to insufficient milk intake (14).

The limitations of this study include lack of a rigorous evaluation of pregnancy- and childbirth-related complications, accurate estimation of breast milk intake, and frequency of urination and bowel movements. No matching the age between case group and control group is one of the limitations was noted in the current study. According to hypernatremia and dehydration in case group, they had referred to the hospital sooner than control group.

Conclusion

According to the results, considerable attention should be paid to weight measurement in neonates with jaundice, especially in the first two weeks of life. In case of a total weight loss> 7% or daily weight loss >1.5% in the first 10 days of life, it is recommended to check blood sodium levels.

Conflict of interests: None.

References

1. Moritz ML, Manoho MD, Bogen DL, Ajus JC, Michael L, Breast Feeding Associated Hypernatrenia. Are we missing the Diagnisis? Pediatrics 2005; 116: 343 -47.
2. Jarcan A, Tiker F, Nilgun S. Weight loss and hypernatremia in breast-fed babies' frequency in neonate with non-hemolytic jaundice In: Pediatric child heath 2005; 41(9): 484-7.
3. Boskabadi H, Anvarifar F, Nourizadeh N. Could Neonatal Hypernatremia Dehydration Influence Hearing Status? Iran J Otorhinolaryngol 2014; 26(74): 13–18.
4. Lindner G, Funk G. Hypernatremia in critically ill patients. J Crit Care 2013; 28(2):216.e11-20.
5. Boskabadi H, Maamouri G, Mafinejad S. The Effect of Traditional Remedies (Camel's Thorn, Flixweed and Sugar Water) on Idiopathic Neonatal Jaundice. Iranian Journal of Pediatrics 2011;21(3):325-30.
6. Bertini G, Dani C, Tronchin M, Rubaltelli F F. Is breastfeeding really favoriting early neonatal jaundice? In: Pediatrics 2001; 107(3): 232-7.
7. Boskabadi H, Maamouri Gh, Bagheri S. Significant Neonatal Weight Loss Related to Idiopathic Neonatal Hyper Bilirubinemia. Int J Pediatr 2014; 2(4-1): 225-31.
8. Gomes SM, Fernandes CA, Ramos H, Fernandes E , Santos M , Nascimento O , et al.Breastfeeding-associated hypernatraemic dehydration. In: Einstein 2009; 7(2): 206-10.
9. Unal S, Arhan E, Kara N, Unca N, Alifendioglu D. Breast-feeding associated hypernatremia. In: Pediatric 2008; 50(1): 29-34.
10. Boskabadi H, Ebrahimi M, Maamouri GH, Ghayour-Mobarhan M, Esmaeily H, Ferns A. Neonatal hypernatremia and dehydration in infants receiving inadequate breast feeding. Asia Pac J Clin Nutr 2010; 19(2):577-84.
11. Yaseen H, Salem M, Darwich. Clinical presentation of hypernatremic dehydration in exclusively breast-fed neonate. In: Indian j Pediatr 2004:71(12); 1059-62.
12. Basiratnia M, Pishva N, Dehghani A. Prevalence of Breastfeeding–associated Hypernatremia among Hospitalized Hyperbilirubinemic Neonates. Iranian journal of neonatology 2014; 5(2): 12-16.
13. Ahmed A, Iqbal J, Ahmad I, Charoo BA, Ahmad QI, Ahmad SM. Complications due to breastfeeding associated hypernatremic dehydration. J Clin Neonatol 2014; 3(3):153-7.
14. Maisels MJ. Mcdonald MG, Seshia MK, Mullet MD. Pathology Pathophysiology & Management of Hyperbilirubinemia in the Newborn. In: Avery's Neonatalogy. Philadelphia: The Newborn. Philadelphia; 2005.