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The relationship between hypernatremia and breast milk sodium levels in newborns with hypernatremic dehydration

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ABSTRACT

Objectives: Breast-feeding with high sodium content milk may cause hypernatremic dehydration in neonates (NHD). The number of cases with NHD tends to increase particularly in the higher temperature seasons. In this prospective case-control study, the relationship between NHD and breast milk sodium (Na) levels and demographic features of NHD were investigated during the summer season.

Methods: The study included term newborns admitted to the neonatal intensive care unit of our hospital with the diagnosis of hypernatremic dehydration between June 2009 and October 2009. Serum sodium level ≥ 150mEq/L was accepted as hypernatremia. Among 109 NHD patients, breast milk sodium level was evaluated in 50 cases. Term infants without hypernatremic dehydration were taken as the control group (50 cases).

Results: Postnatal age at admission ranged between 2 and 12 days and mean serum Na concentration was 152 mEq/L (150-173 mEq/L). A significant weight loss of >10% was determined in 85% of cases. Breast milk Na was significantly higher in the hypernatremic group (24.3 ± 20.3 mEq/L) compared to the control group (12.6 ± 6.79 mEq/L) ($p < 0.001$). In primiparous mothers, the mean breast milk Na level was statistically higher than that of multipara mothers (21.16 ± 19.9 mEq/L vs 15.48 ± 9.96 mEq/L, $p < 0.016$).

Conclusions: In this study, we demonstrated that high breast milk sodium level was closely related with NHD and being a primiparous mother appeared as a significant factor for high breast milk sodium content. In this respect, all pregnant women especially primiparous should be educated about infant nutrition and neonatal dehydration. Health care providers should emphasize importance of frequent milking and more fluid intake, especially in summer.

Keywords: Breast milk sodium, hypernatremic dehydration, newborn

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Hypernatremic dehydration of the newborn (NHD) is mostly observed in breast-fed newborns and can cause serious complications [1, 2]. Hypernatremia in all ages may occur in association with reduced fluid intake, excessive fluid loss, or excessive Na intake [3]. Neonatal hypernatremic dehydration has mostly been reported in the infants of primiparous mothers with the lack of education on breast-feeding [4]. The etiology of NHD has been suggested to be related to the insufficiency and high sodium content of breast milk. The inadequate volume and high sodium concentration of breast milk have been linked with a delay in the maturation of breast milk [4, 5]. The number of cases with hypernatremic

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dehydration (HD) tends to increase particularly in the summer because of higher temperatures, which can cause dehydration in both the mother and her infant [6, 7]. In the literature, a relationship was reported between weight loss was more than 10% and high serum sodium concentration [8].

In this study, demographic data, as well as clinical and laboratory findings of newborns with HD were evaluated and the relationship between hypernatremia and breast milk sodium (Na) level was investigated during a summer season. It was also aimed to provide suggestions to reduce the number of NHD cases.

METHODS

One hundred and nine term newborns hospitalized for NHD between June and October 2009 at the neonatal intensive care unit (NICU) of Dr. Behçet Uz Children's Hospital (İzmir, Turkey) were enrolled. Neonates with congenital anomalies, chromosomal abnormalities, congenital heart diseases, perinatal asphyxia, metabolic or endocrine disorders, sepsis, prematurity and those born to mothers with intrauterine infections were excluded. Serum Na level > 150 mEq/L and > 160 mEq/L were considered to indicate hypernatremia and severe hypernatremia, respectively [3]. A detailed maternal and infant history was taken, including gestational age, birth weight, postnatal age at admission, presenting symptoms, feeding type, maternal parity, mode of delivery, maternal age, and education level. Physical examination findings, body weight on admission, and percentage weight loss were evaluated. Length of hospital stay, presence of any accompanying comorbidities and complications (renal failure, disseminated intravascular coagulation (DIC), intraventricular hemorrhage, seizure, dural thrombosis, brain damage), and the mortality rate were determined. Complete blood count and serum sodium, glucose, blood urea nitrogen (BUN), creatinine, potassium, chlorine, calcium, serum alanine amino transferase (ALT), serum aspartate amino transferase (AST), total bilirubin, arterial blood gas, C-reactive protein (CRP), and urinalysis were obtained from all patients. Metabolic acidosis was defined as a serum pH < 7.35 and a base deficit ≥ 5 (with normal CO2 level) [3, 9]. Serum glucose level < 40 mg/dL was defined as hypoglycemia and > 125 mg/dL was defined as hyperglycemia [7, 9]. DIC was defined as prolonged activated partial thrombin time (aPTT) and prothrombin time (PT), increased fibrin degradation products, and a thrombocyte count < 100,000/mm^3 [9].

Physiological body weight loss was described as 1-3% per day or < 7% in the first week after birth [10]. The free water deficit was calculated for all patients and added to their daily required fluid intake. Fluid therapy for the patients was adjusted to Na concentration of 77 mEq/L. Hypernatremia was corrected at a maximum decline of 0.5-1.0 mEq/L/h. Serum Na measurements were repeated every 4-6 hours. Treatment period was arranged according to initial serum Na levels. Any complication observed during treatment were recorded.

The fractional sodium excretion (FeNa) was calculated in order to differentiate pre-renal and renal etiology of kidney failure in patients with acute kidney injury. Pre-renal azotaemia for newborns was defined as a fractional excretion of sodium < 2.5%. A renal failure index ≥ 2.5% was considered to indicate acute intrinsic renal failure. Fever was defined as axillary body temperature ≥ 38°C. Blood and urine cultures were obtained in cases with fever or any suspected infection. In patients with neurological symptoms, transfontanel ultrasonography (USG), magnetic resonance imaging (MRI) and electroencephalogram (EEG) were performed.

Healthy mothers without any contraindications for breast-feeding (such as chronic diseases or use of certain medications) were included in the study. Mothers using diuretics while breastfeeding were excluded. Samples of 3-5 ml breast milk were obtained from each mother using an AmedaSMB 50 breast pump. Each sample was placed in dry-flat biochemistry tubes and centrifuged at 3,500 rpm for 5 minutes and the supernatant was stored at -20° C until assayed. The samples were thawed at room temperature before the assay. Breast milk Na concentration was analysed with the indirect ion selective electrodes (ISE) method using a Beckman UnicelDxC 800 Chemistry Analyzer. The results were reported as mEq/L. The control group consisted of normonatremic, normovolemic healthy term newborns whose serum sodium levels were < 150 mEq/L and whose weight losses were no more than 6% in the first week of life. Breast milk Na concentrations were

classified according to the day of the sample collection and were compared with normal values determined in previous studies [9]. The study and control groups were compared to detect any risk factor that might lead to high breast milk sodium concentration, such as parity, delivery mode, maternal age and educational level. Approval for the study was granted by the ethics committee of Dr. Behçet Uz Children's Hospital (İzmir, Turkey) (date/number: 06.11.2009/7) and informed consent was obtained from each contributing mother before enrollment.

Statistical Analysis

Statistical analyses were performed using SPSS version 16.0 (SPSS, Inc., Chicago, IL, USA). Qualitative and quantitative (continues) variables were shown as the number of cases (n) with percentages (%) and mean ± standard deviation (SD), respectively. The t-test and Analysis of variance (ANOVA) were used for comparison of continuous variables between the study groups. Pearson correlation analysis was applied to examine the relationship between variables of interest. A value of $p < 0.05$ was accepted as statistically significant.

RESULTS

Among 1,235 term infants hospitalized at the NICU during a 5-month period, 109 cases having NHD were included in the study. The incidence of NHD was 8.82% during the study period. With the exception of two cases, all the other infants were born in a hospital. The mean gestational age of the NHD patients was 38.9 ± 1.12 weeks. Postnatal age at admission ranged from 2 to 12 days, with 91.7% of cases being in the first five days of life and a median age of three days. The mean percentage weight loss of NHD patients was 13.7% ± 4.7% and more than two-thirds of infants had > 10% weight loss. Fifty-six (51.3%) infants were delivered by C-section, 61.5% of the mothers were primiparous and 82.6% of the infants were exclusively breast fed. Nearly half of the mothers were graduated from a primary school and when they were questioned about the amount of their milk, only seven were aware of an insufficiency of amount of breast milk. The demographic and clinical

Table 1. The characteristics of the all neonatal hypernatremic dehydration patients (n = 109)

Characteristics	Data
Birth weight (g)	3,319.10 ± 507.93
Gestational age (week)	38.9 ± 1.12
Admission age (day)	3.6 ± 1.93
Admission weight (g)	2,863.57 ± 450.84
Weight loss (%)	13.7 ± 4.73
Maternal age (year)	27.8 ± 5.3
Gender, female	54 (49.5%)
Delivery mode, cesarean section	56 (51.3%)
First-time mothers	67 (61.5%)
Primary school educated mothers	59 (54.2%)
Feeding type	
Only breast milk	90 (82.6%)
Mix (breast milk+ formula)	17 (17.6%)
Only formula	2 (1.8%)
Weight loss degree ≥ 10%	92 (84%)
Weight loss degree < 10%	17 (16%)
Presenting symptom	
Jaundice	76 (68.5%)
Fever	72 (65%)
Poor infant suck	28 (24%)
Decreased urine output or bloody urine	8 (7.3%)
Weight loss	6 (7.3%)
Lethargy	3 (2.7%)
Seizure	1 (0.9%)
Others[a]	5 (4.5%)
Complications	
IHB	78 (72%)
Acute renal failure	70 (65%)
Pre-renal-renal asotemia	53 (49%)
Acute intrinsic renal failure	17 (16%)
Elevated liver enzymes	40 (37%)
DIC	10 (9.2%)
Hypoglycemia on admission	5 (4.6%)
Hyperglycemia on admission	4 (3.8%)
Metabolic acidosis on admission	15 (13.7%)
Seizure	2 (1.8%)
Intracranial hemorrhage	1 (0.9%)
Mortality	0 (0%)

Data are shown as mean± standard deviation or number (%). [a]Others: Vomiting, diarrhea, cutaneous eruption, respiratory distress, DIC = Disseminated intravascular coagulation, IHB = Indirect hyperbilirubinemia

Table 2. Mothers and infant characteristics of the study and control groups

Characteristics	Study group (n = 50)	Control group (n = 50)	*p* Value
Gestational age (week)	38.7 ± 1.14	38.5 ± 0.97	0.440
Birth weight(g)	3,263 ± 538	3262 ± 446	0.996
Gender (female/male)	27/23	29/21	0.687
Admission age (day)	3.6 ± 1.9	5.8 ± 4.7	**< 0.001**
Admission weight(g)	2,831.4 ± 457.9	3,215.8 ± 397.7	**< 0.001**
Cesarean section delivery mode	29 (58%)	23 (46%)	0.234
Maternal age(year)	27.8 ± 5.08	28.56 ± 5.04	0.467
First-time mothers	32 (64%)	21 (42%)	**0.028**
Primary school educated mothers	27 (54%)	26 (52%)	0.841
Serum sodium (mEq/L)	153.60 ± 4.84	138.08 ± 2.70	**< 0.001**
BUN (mg/dL)	25.57 ± 24.82	9.94 ± 5.42	**< 0.001**
Creatinine (mg/dL)	1.16 ± 0.45	0.56 ± 0.47	**< 0.001**
Glucose (mg/dL)	67.50 ± 23.79	83.0 ± 18.9	**< 0.001**
Breast milk Na concentration, (mEq/L)	24.38 ± 20.54	12.62 ± 6.79	**< 0.001**
High breast milk Na concentration	26 (52%)	13 (26%)	**0.008**

Data are shown as mean± standard deviation or number (%). BUN = Blood urea nitrogen

features of all NHD patients are summarized on Table 1.

The mean serum sodium level of the all NHD patients was found 153.19 ± 4.08 mEq/L (range; 150-173 mEq/L). Severe hypernatremia was observed in seven cases. While serum sodium concentration was positively correlated with the amount of weight loss and postnatal age on admission (r = 0.596, $p < 0.05$ and r = 0.549, $p < 0.01$, respectively), it was not related to gestational age, birth weight, gender or mode of delivery ($p > 0.05$). A positive correlation was determined between serum sodium and BUN, creatinine, and uric acid levels (r = 0.675, $p < 0.01$; r = 0.586, $p < 0.01$; and r = 0.452, p < 0.01, respectively). The mean length of hospital stay was 4.3 ± 2.03 days. The average time for the normalization of serum Na level was 30.52 ± 20.09 hours for all cases with hypernatraemia, and 64 ± 30 hours for cases with severe hypernatraemia. There was a positive correlation between the duration of treatment and the serum sodium level as well as the percentage weight loss (r = 0.515, $p < 0.01$ and r = 0.498, $p < 0.01$, respectively).

Transfontanel USG was applied to seven patients with neurological symptoms (hypotonia, seizure, cephalhematoma, cyanosis, lethargy). Only one had grade one subependimal haemorrhage, while the others were totally normal. Seizures were observed in two (1.8 %) patients within the first 48 hours of rehydration therapy. No abnormalities were observed on EEG, transfontanel USG, or MRI.

A total of 50 single samples were collected from the mothers of the NHD group at postpartum 2-14 days. Mean breast milk Na concentration was 24.48 ± 20.54 mEq/L, with respect to the sample collection day, 52% of cases had high breast milk Na content. The control group was composed of 50 cases, and the sample collection days were identical to the study group. In the control group, mean breast milk Na concentration was 12.62 ± 6.79 mEq/L and 26% of cases had a high breast milk Na content with respect to the day of sample collection. The characteristics of both groups are summarized on Table 2. The breast milk sodium concentrations were significantly higher in the mothers of dehydrated infants compared to the control group ($p = 0.008$). A statistically significant

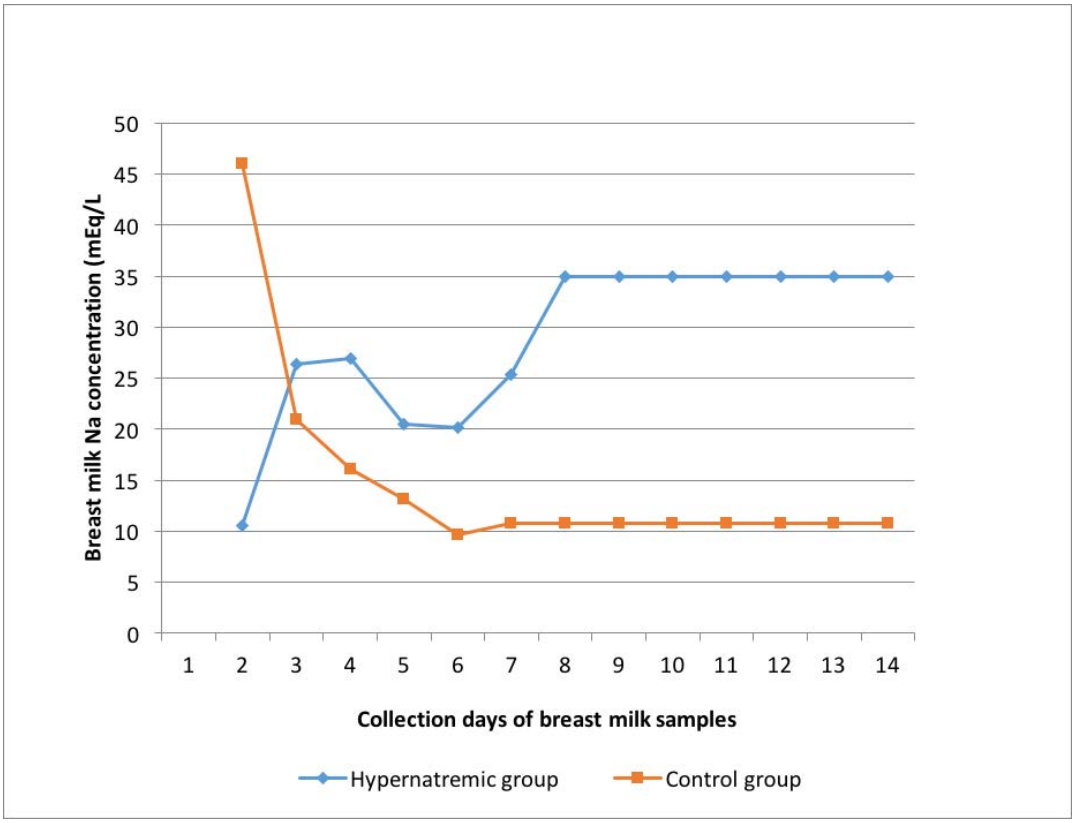

Figure 1. Postpartum changes in mean breast milk sodium level.

correlation was determined between breast milk Na concentration and primiparity ($p < 0.05$). The mean breast milk Na concentration of primiparous women (21.16 ± 19.9 mEq/L) was statistically higher than that of multiparous women (15.48 ± 9.96 mEq/L ($p < 0.016$). Postpartum changes in the mean breast milk sodium level of the study and control groups are demonstrated in Figure 1. No statistically significant correlation could be demonstrated between breast milk Na concentration and maternal age or mode of delivery.

The highest breast milk Na concentration was 98 mEq/L, which was measured on the 14th postpartum day. This infant was hospitalized with complaints of vomiting, fever, and sleepiness on day 13. His birth weight was 3100 g and his total weight loss was 27%. His serum sodium was measured to be 170.6 mEq/L. His mother was subjected to a detailed education on adequate fluid intake and breastfeeding. After regular feeds and milking, her breast milk sodium level decreased gradually to 10 mEq/L on the 20th postpartum day. There was a positive correlation between serum sodium level and postnatal age on admission, degree of weight loss, and breast milk sodium level. Gender, type of delivery, gestational age, birth weight, and maternal age were not related to the development of hypernatremia ($p > 0.05$).

DISCUSSION

Hypernatremic dehydration in the neonatal period is an important problem which can lead to serious, life-threatening complications [9]. This single-center study with a large cohort want to evaluate demographic features of NHD patients and to evaluate the relation of breast milk and NHD. The results of this study showed that breast milk sodium content is closely related to NHD and the breast milk sodium concentrations were significantly higher in the mothers of dehydrated infants compared to the control group.

Lactation failure is the most important etiological factor in NHD. Some of the risk factors associated with lactation failure include prematurity, primiparity, C-section delivery, low maternal education level, infrequent breastfeeding, nipple problems and breastfeeding incompatibility between mother and her

infant [11-13]. In the current study, 61.5% of mothers were primiparous and nearly half of the mothers were graduated from a primary school. There was a statistically significant correlation between primiparity and NHD (p = 0.028). However, the correlation between NHD and low maternal education level was not significant (p = 0.841).

In the current study, the breast milk sodium concentrations adjusted to the postpartum day showed a statistically significant difference between the groups. The mean breast milk sodium concentration of primiparous women was statistically higher than that of multiparous women. Although most reports showing a higher incidence of NHD included neonates delivered by C-section, which is known to decrease breast milk production, some reports have claimed that delivery type does not have any influence [5, 14, 15]. In the current study, the proportion of neonates delivered vaginally or by C-section were similar and hence we concluded that delivery type does not have any effect on NHD (p = 0.07).

Although most publications have emphasized that the amount of breast milk is more important than the milk sodium content, a high level of sodium in breastmilk has been reported to lead to clinical symptoms in some hypernatremic neonates [7, 16]. In a study by Koo and Gupta [17], the electrolyte composition of breast milk was evaluated from the 1st to the 28th postpartum days. The mean sodium concentration of breast milk immediately after delivery was reported to be 64.8 mEq/L and this level continued to decrease progressively. On postpartum third day, it was measured as 21.4 mEq/L and at the end of the second week it was measured 7 mEq/L [17]. A gradual decrease in breast milk sodium level is considered as an indication of successful breast-feeding [17, 18]. The opposite is accepted to be true for unsuccessful breast-feeding [2, 19]. Breast milk having high levels of sodium and low free water portion has been reported to cause a hyperosmolar status in infants [5]. In a study involving 208 mothers by Manganaro *et al*. [20], it was claimed that hypernatremic dehydration was related to insufficient daily milk output rather than high sodium concentration in breast milk. Likewise, Ingram *et al*. [21] showed that primaparous mothers have a lower volume of milk than multiparous mothers especially in the first four postpartum weeks.

The present study was carry out during a summer season for our country and the incidence of hypernatremic dehydration was found to be higher than incidence of NHD reported in literature. In the literature, the incidence of breast feeding-associated NHD ranges between 0.6-4.1% [5, 11, 22]. Although in some studies, alterations of seasonal heat were considered to be an important contributing factor, in others no statistical significance was reported [6, 7]. In neonatal hypernatremic dehydration, the most frequent time of hospital admission is the first 10 days of life [4, 5]. In the current study, the postnatal age at admission ranged from 2-12 days, where 91.7% of infants were between 2-5 postnatal days. Positive correlations were found between the degree of weight loss and the postnatal age at admission and serum Na levels in our study (p = 0.019 and p = 0.022; respectively). Therefore we believed that seasonal heat changes may be considered as a causative factor for dehydration in both newborns and their mothers and newborns may become dehydrated more earlier in heat seasons. The American Academy of Pediatrics (AAP) emphasizes that all newborns who are discharged from hospital before 48 hours of age must be seen by a physician for the evaluation of jaundice and dehydration over the first 3-5 days [10]. It is also suggested that possible feeding problems should be investigated in infants who have lost ≥ 7% of their birth weight within the first week of life and a more intensive evaluation of breast-feeding efficiency is required [10]. In some studies, it has been reported that dehydration is detected during a routine pediatric examination and most families are not aware of the condition and as a mother is not informed well enough, she cannot understand that her milk is insufficient [4]. In our study, 93% of mothers of dehydrated infants believed to have sufficient amount of breast milk. In this respect, we believe that evaluation of all neonates for weight loss and signs of dehydration in the first 3-5 days of life is very important for the detection and prevention of NHD.
The treatment regimen should be planned according to the initial serum Na level and monitorized closely because the degree of hypernatremia is very important for prognosis [1, 23, 24]. Seizure in NHD may occur as a presenting symptom but it usually develops during dehydration therapy with hypotonic fluids [1, 23]. Seizure rates have been reported to vary from 6%

to 38% [6, 9, 23]. In the current study, only one patient was admitted with seizure and two patients had seizures during rehydration period. The overall seizure rate was 2.7%. The mortality rate of NHD is unclear but severe hypernatremia may lead to adverse outcomes and increase the mortality rate [24]. In the current study, we did not have any patient loss. Due to our careful treatment regimen, we did not observe any life-threatening complication either.

Limitations

This single-center study is a large cohort study involving comparative measurements of breast milk sodium in mothers of hypernatremic infants and healthy term infants. The major limitations of the study are that we could not obtain milk samples from mothers of all NHD patients and we did not evaluate the breast milk volume which might have influenced our interpretation of milk sodium levels and we could not obtain milk samples from mothers of all NHD patients in this study. A large, multicenter, prospective study which evaluated milk sodium content and milk volume together including control group may give further information about lactation failure.

CONCLUSION

In conclusion, hypernatremic dehydration in the neonatal period is an important problem which can lead to serious, life-threatening complications. High breast milk sodium content may closely related to NHD. Early recognition and an adequate treatment approach are important to prevent complications. In this respect, we suggest all pregnant women should be educated, both prenatally and postnatally, about infant nutrition and neonatal dehydration. All neonates should be evaluated for weight loss and any sign and symptom of dehydration in the first 3-5 days of life. This is very important for early detection, prevention and proper treatment of NHD.

Authorship Declaration

All authors listed meet the authorship criteria according to the latest guidelines of the International Committee of Medical Journal Editors, and all authors are in agreement with the manuscript.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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