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Original Article

Risk Factors and Neurological Outcomes of Neonatal Hypernatremia

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ABSTRACT

Background: Hypernatremia might lead to neurological and developmental disabilities. This study aimed to determine the frequency, risk factors, and one-year neurological prognosis of hypernatremia in newborns. The findings of the present study may assist the prevention of hypernatremia mortality and complications.
Methods: This cross-sectional study was conducted on all neonates admitted to the neonatal ward and the Neonatal Intensive Care Unit (NICU) of Bahrami Children's Hospital, Tehran, Iran from September 2013 to September 2014. All the newborns, who were diagnosed with hypernatremia (serum sodium>150 mEq/L) were included in this study. The data were collected using a form, which included clinical symptoms and risk factors for neonatal hypernatremia in addition to the laboratory data. Additionally, the patients were subjected to the developmental examination for one year. Another form was used during the follow-up period to collect all the relevant data.
Results: A total of 1,923 newborns were examined in the present study. The results demonstrated that 74 (3.8%) neonates had sodium levels of >150 mEq/L. Furthermore, jaundice was found to be the most prevalent presentation of hypernatremia, which was reported in 57% of the admitted neonates. Additionally, weight loss was the most common observation on the follow-up examinations. Neonates admitted at older ages (>7 days) had higher sodium levels (160.71±8.98 mEq/L). There were 18 neonates with seizures before or during the hospitalization and 19 (25.7%) cases showed abnormal development during the one-year follow-up. Moreover, a statistically significant relationship was observed between the abnormal development and the presence of seizure (OR: 2.543, CI: 1.358-4.763).
Conclusion: The findings of the current study demonstrated the critical role of weighing the newborns 72-96 h after birth and monitoring for jaundice in the prevention of the neonatal hypernatremia. Furthermore, seizures in these patients were associated with an increased risk of future developmental problems; however, more studies are required in this regard.

Keywords: Hypernatremia, Neurologic manifestations, Newborn, Outcome assessment, Risk factors

Introduction

Hypernatremia is defined as the serum sodium levels of > 145 mEq/L; however, it is often considered as sodium values above 150 mEq/L (1). Most of the children with hypernatremia exhibit signs of dehydration. Nevertheless, even in the absence of dehydration, this condition can be a cause for central nervous system (CNS) disorders that depend on the sodium levels and the speed of increase in these levels (2-5). Several studies support the beneficial role of early post-discharge visits, breastfeeding training, and daily infant weighing in the prevention of neonatal hypernatremia (6-15).

Various national and international studies have reported the prevalence of 1.8% for hypernatremic dehydration and different neuro-developmental outcomes in neonates inflicted with hypernatremia (11, 16). However, further studies are required due to the neonatal mortality and morbidity (abnormal development) rates caused by hypernatremia, which can be prevented in numerous cases. It is necessary to

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develop new guidelines and/or modify the previous ones to address the care and training of the pregnant and lactating mothers in the healthcare systems. Regarding this, the present study aimed to determine the prevalence of hypernatremia in the hospitalized neonates and assess the risk factors and complications of hypernatremia to provide advice on prevention of this condition.

Methods

This cross-sectional study was conducted on all the neonates admitted to the neonatal ward and the NICU of Bahrami Children's Teaching Hospital, Tehran, Iran, from September 2013 to September 2014. All the patients were initially divided into two groups of with and without hypernatremia based on their serum sodium levels (cutoff point of >150 mEq/L).

After giving explanations about the research project, informed consent was obtained from the parents. The data collection form 1 was completed according to the interviews and physical examinations of the neonates diagnosed with hypernatremia. This form included clinical symptoms and risk factors for neonatal hypernatremia in addition to the laboratory data, including the serum sodium and urea levels and the electroencephalography (EEG) results.

Weight loss was one of the signs of hypernatremia in data collection form 1, which was calculated as the difference between the birth weight and the weight upon admission. We took into consideration the fact that the newborns under 10 days lose weight naturally; therefore, the normal neonatal weight on the tenth day after birth would equal the birth weight. We regarded the weight loss as abnormal when the calculated weight loss was greater than the normal expected loss.

Over a one-year period, the neonates with hypernatremia underwent monthly examinations conducted by a neonatologist who recorded the data concerning weight gain, head circumference, height, growth index, reflexes, and neurodevelopmental state (i.e., motor skills, behaviors, learning, and other neurological functions) in the patients' medical records.

At the end of the one-year follow-up, the data that pertained to developmental status (i.e., weight gain, raise in head circumference, or increased height according to the curve for weight gain, head circumference, height or abnormal neurodevelopmental state) were assessed and recorded on form 2 using the patients' medical records.

Statistical analysis

Data analysis was performed in SPSS, version 16, using Student's t-test and Chi-square test. Furthermore, descriptive statistics were utilized to determine the mean and frequency. The dependent variable was one-year neurological outcomes, and the independent variables included gravidity, gender, age, route of delivery, mode of nutrition, weight loss, as well as serum sodium and urea levels.

Binary logistic regression with forward stepwise (conditional) was used to compare the outcomes in patients with varying neurodevelopmental states. P-value less than 0.05 was considered statistically significant.

Results

In this study, out of 1,923 (96.2%) newborns, 1,849 cases had sodium level of < 150 mEq/L, among whom 1,052 cases were male (56.9%). Therefore, 74 (3.8%) neonates had sodium values of > 150 mEq/L, which consisted of 28 (37.8%) female and 46 (62.2%) male. No statistically significant difference was observed regarding hypernatremia between the genders (P=0.37), routes of delivery (P=0.3), and gravidity (P=0.5). Furthermore, there was a statistically significant relationship between the elevated serum sodium levels and season of admission (P=0.03). The children with serum sodium levels of > 150 mEq/L were hospitalized throughout the year (winter [32.4%], fall [31.1%], summer [25.7%], and spring [10.8%]).

In newborns with hypernatremia, there were 53 and 21 cases had serum sodium levels of 150-160 and ≥ 160 mEq/L, respectively. The serum sodium concentration among the 74 newborns diagnosed with hypernatremia was 157.2±6.64 mEq/L on admission. The mean serum sodium level was significantly high in neonates older than seven days, had weigh loss over than 10% and neonates with abnormal neurodevelopment state which they are mentioned in table 1 (Table 1).

Among the neonates with hypernatremia, 25 (33.8%), 25 (33.8%), and 24 (32.4%) subjects had serum urea levels of ≤ 40, 40-80, and > 80 mg/dL, respectively. The mean urea level for all neonates with hypernatremia was 93.1 mg/dL. Moreover, the mean concentration of this metabolite was not significantly different among the various seasons of admission (P>0.05). Nonetheless, a significant

Table 1. The relationship of mean serum sodium level and hypernatremia with gravidity, gender, development, age group, route of delivery, mode of nutrition, and weight loss

		Mean Serum Sodium Level	SD	P-value*
Gravidity	1	156.85	6.33	0.09
	2	155.75	5.36	
	3	160.25	6.40	
	4	165.67	12.90	
Gender	Boy	157.33	5.89	0.86
	Girl	157.06	7.83	
Development	Normal	156.2	6.05	0.02
	Abnormal	160.16	7.51	
Age Groups	≤ 3 days	156.48	5.95	0.04
	3-7 days	155.97	5.15	
	> 7 days	160.71	8.98	
Route of Delivery	NVD	159.55	8.33	0.09
	C/S	156.23	5.58	
Mode of Nutrition	Breastfeeding	157.45	6.86	0.62
	Formula	154.25	1.5	
	Mix	156	5.29	
Weight Loss	< 5%	152.33	2.95	0.008
	5-10%	154.1	5.02	
	> 10%	158.58	6.81	

*: P-value of < 0.05 is considered as significant

difference was observed between the weight loss groups in this regard (P=0.001). In neonates with hypernatremia, the mean urea level for those with normal development was 71 mg/dL, whereas it was 157 mg/dL in the abnormal development group (P<0.001).

Therefore, higher urea levels were indicative ofincreased probability of abnormal development. Furthermore, there was a significant relationship between serum sodium and urea levels (r=0.738, P<0.001), which suggested a direct association between the serum urea and sodium concentrations. The serum urea level could elevate up to 9.86 mg/dL by each 1 mEq/L rise in serum sodium level.

In this study, the most common presentation of hypernatremia was jaundice as observed in 57% of the neonates with hypernatremia. Overall, 79.5% of the evaluated neonates were admitted to the neonatal ward and 34.3% were admitted to the NICU. A significant relationship was found between jaundice occurrence and the serum sodium level of > 160 mEq/L (P<0.001). Exchange was performed for two out of five (6.8%) newborns diagnosed with hypernatremia, who had jaundice at the exchange level.

At the one-year follow-up, 74.3% of the neonates with hypernatremia showed normal development, whereas 25.7% of the hypernatremia patients had abnormal development. This included 84.6% (normal) and 15.4% (abnormal) of the newborns in the neonatal ward. Additionally, in the NICU, 62.9% and 37.1% of the cases had normal and abnormal development, respectively, during the follow-up. The comparison made between the two sodium groups (<160 and ≥160 mEq/L) revealed there was a significant difference between the two groups regarding the developmental state (P=0.001).

The frequencies of disturbed development at the one-year follow-up were 10.5%, 26.3%, and 63.3% in the neonates with hypernatremia, who had serum urea levels of ≤ 40, 40-80, and > 80 mg/dL, respectively. The mean weight loss was 16.05% in the newborns diagnosed with hypernatremia and abnormal development, and 12.62% in those with hypernatremia and normal development (P>0.05).

The prevalence of abnormal development and its relationship with weight loss groups, gender, age, and serum sodium levels are presented in Table 2. Out of the 18 newborns with hypernatremia, 13 cases were deceased. Accordingly, a statistically significant relationship was found between mortality and seizure in patients with hypernatremia (P=0.042). According to the results of the mentioned model, the most effective risk factors were history of seizure and serum urea level, respectively (Table 4).

Table 2. The relationship between neurodevelopmental states of the neonates and hypernatremia, weight loss, gender, age, and level of serum Na

		Normal Development	Abnormal Development	Total
Weight Loss < 5%	Count	6	3	9
	Percent	66.67%	33.33%	100%
Weight Loss 5-10%	Count	10	0	10
	Percent	100%	0%	100%
Weight Loss ≥ 10%	Count	39	16	55
	Percent	70.9%	29.1%	100%
P-value*		0.13		
Boy	Count	34	12	36
	Percent	73.9%	26.1%	100%
Girl	Count	21	7	38
	Percent	75%	25%	100%
P-value		0.9		
Age: ≤ 3 days	Count	17	6	23
	Percent	73.9%	26.1%	100%
Age: 3-7 days	Count	29	5	34
	Percent	85.3%	14.7%	100%
Age: > 7 days	Count	9	8	17
	Percent	52.9%	47.1%	100%
P-value		0.045		
Na < 160	Count	45	8	53
	Percent	84.9%	15.1%	100%
Na ≥ 160	Count	10	11	21
	Percent	47.6%	52.4%	100%
P-value		0.001		

*: P-value of < 0.05 is considered as significant

Table 3. The relationship between the neurodevelopmental states of neonates and hypernatremia and seizure

		Without Seizures	Pre-treatment Seizures	Post-treatment Seizures	Pre- and Post-treatment Seizures	Total	P-value*
Normal Development	Count	48	2	5	0	55	0.001
	Percent	87.3%	3.6%	9.1%	0	100%	
Abnormal Development	Count	8	2	3	6	19	
	Percent	42.1%	10.5%	15.8%	31.6%	100%	
Total	Count	56	4	8	6	74	
	Percent	75.7%	5.4%	10.8%	8.1%	100%	

*: P-value of < 0.05 is considered as significant

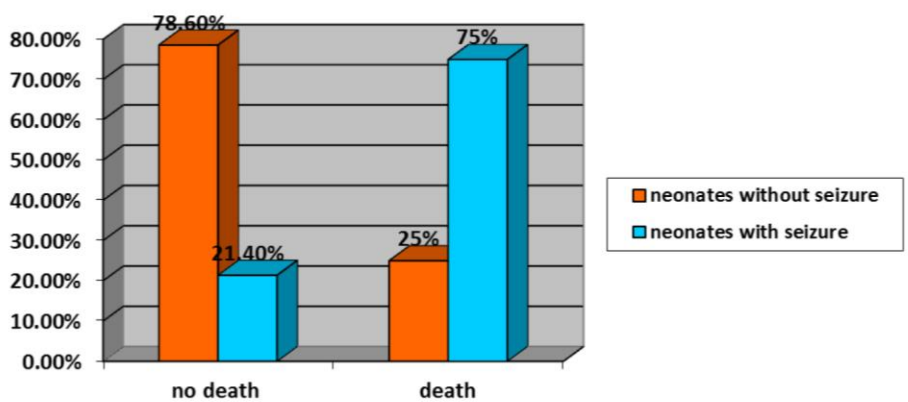

Figure 1. The relationship between seizure in neonates with hypernatremia and the risk of mortality

Table 4. The relationship between the risk factors and the neurodevelopmental state according to the logistic regression

Risk Factor	Estimate[1]	SE[2]	P-value[3]	OR[4]	CI[5]
Serum Sodium Level	0.007	0.004	0.05	1.007	1.000-1.014
Seizures	0.933	0.320	0.004	2.543	1.358-4.763

1: B regression coefficient
2: Standard Error
3: P-value of <0.05 was considered as statistically significant
4: Odds Ratio (First level compared to the second and third levels)
5: Confidence interval 95%

Discussion

In the current study, we discovered a statistically significant relationship between the sodium level of neonates and the season of admission among the referred neonates. In the neonates with hypernatremia, jaundice was the most common presentation. The mean serum sodium level was significantly higher in neonates with abnormal neurodevelopment state who were older than seven days and had weigh loss over 10%. In these patients, the mean serum urea level was significantly higher in the weight loss and neurodevelopmental disorder groups compared to neonates with less weight loss and normal neurodevelopmental state. Furthermore, there was a relationship between the mortality and presence of seizure and also between the serum sodium and urea levels.

In this study, 57% of the neonates with hypernatremia had jaundice. In the current study, the most prevalent symptom of hypernatremia was jaundice (57%), followed by poor feeding (40.5%) in the newborns diagnosed with hypernatremia.

A retrospective study performed on 4,136 neonates admitted to the Ministry Hospital in Ankara, Turkey during 2004-2005 reported a direct relationship between the sodium, blood urea nitrogen, and bilirubin levels. However, there was no specific relationship between the In a study conducted by Breauning et al. in 2006, a strong linear relationship was reported between the dehydration percentage and blood sodium concentration. On average, 16 mEq/L raise was observed by each 10% increase in the percentage of dehydration (6).

Furthermore, in the present study, there was no statistically significant relationship between the mean sodium level and gender (P=0.86), route of delivery (P=0.09), mode of nutrition (P=0.62), and gravidity (P=0.09). Moreover, the mean sodium level had a statistically significant relationship with neurodevelopmental state (P=0.02), age (P=0.04), and weight loss (P=0.008). We observed that serum urea levels augmented up to 9.86 mg/dL by each 1 mEq/L increase in serum sodium.

In a retrospective study carried out on 116 neonates with hypernatremia over a period of six years in Turkey, 50% of the newborns had developmental problems at the twelve-month follow-up (7). In another study performed at Gazi Hospital in Turkey, 15 out of the 28 NICU neonates diagnosed with hypernatremia were followed for one year. In the mentioned study, there were two and five newborns with severe and moderate developmental delays, respectively (17). In the current study, 25.7% of all the hypernatremic neonates had developmental delays at the one-year follow-up, which made up 29% of all the neonates admitted to the NICU.

In another study, 81 out of 4,280 (1.8%) newborns had hypernatremic dehydration. The highest and lowest mortality rates were reported in the groups with serum sodium levels of > 170 (66.6%) and 150-160 mEq/L (3.6%), respectively. In the mentioned study, seizure was the most common complication during treatment of the hypernatremia (22 patients). In addition, there was a statistically significant difference between the high and low serum sodium groups in terms of Denver Developmental Screening Test II results (11). In our study, the sodium concentrations were 160.16±7.51 and 156.2±6.05 mEq/L in the newborns with abnormal and normal development, respectively (P=0.02). Moreover, the mortality rates were 75% and 25% in the patients with and without seizures, respectively.

Several studies (6, 7, 13, 14) have supported the role of early weighing and examination (72-96 h after birth, especially in case of early neonatal discharge. A chart for hypernatremia was established in the study conducted by Paula Van Dommeleu in Netherlands (2014). There was a difference concerning the weight loss between the healthy breastfed newborns and the hyper-natremic neonates in chart that supports our study results (13).

In another study carried out in Kilifi Country Hospital on the Kenyan Coast in 2016, the neonates had increased risk of hypernatremia, compared to the non-neonates (68.2% vs. 38.1%, P<0.001), and hypernatremia was common in neonatal tetanus (14). In a study performed in Shiraz, Basiratnia et al. reported the incidence of hypernatremia among the exclusively and non-exclusively breastfed neonates as 9.3% and 2.7%, respectively. In the mentioned study, a correlation was observed between the hypernatremia and weight loss (P=0.008). Additionally, hypernatremia was found to have a higher incidence in the summer and winter, compared to the other seasons (P=0.042) (18).

In another study conducted on 65 hypernatremic neonates in Mashhad, Iran, it was demonstrated that this group had developmental issues during the first year of their lives. In the mentioned study, the major signs and symptoms of neonates with hypernatremic dehydration included poor feeding (61.5%), seizure (23.1%), hyperthermia (7.7%), and lethargy (7.7%). Additionally, the severity of hypernatremia was correlated with poor developpmental states (P=0.001) (16), which was consistent with our findings.

Conclusion

Hypernatremia in neonates can be associated with mortality and long-term complications that are likely to even exacerbate in case of delayed presentation. The results of the current study demonstrated the critical role of monitoring for jaundice and weighing the newborns 72-96 h after birth in the prevention of neonatal hypernatremia. High serum urea levels and seizures in these patients were associated with an elevated risk of future developmental problems, which highlights the necessity of performing further studies.

Limitations of the Study

One of the limitations of the current study was the poor parental involvement in the clinic follow-up. Furthermore, the initial delay in test preparation might have led to a delayed first visit by the colleagues. In case of significant weight loss, it was recorded in the initial form. Additionally, the cross-sectional design of this study did not allow evaluating the delay or priority of risk factors and outcomes.

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Conflicts of interests

The authors of present study declare no conflicts of interest.

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