Clinical profile of neonates with hypernatremic dehydration in a nephrology clinic

GRAŻYNA KRZEMIEŃ, MAŁGORZATA PAŃCZYK-TOMASZEWSKA, AGNIESZKA ANTONOWICZ-ZAWIŚLAK, AGNIESZKA SZMIGIELSKA

Department of Pediatrics and Nephrology, Medical University of Warsaw, Poland

Clinical profile of neonates with hypernatremic dehydration in a nephrology clinic

Krzemień G, Pańczyk-Tomaszewska M, Antonowicz-Zawiślak A, Szmigielska A.

Department of Pediatrics and Nephrology, Medical University of Warsaw, Poland

The aim *of the study was to assess clinical profile of neonates with hypernatremic dehydration (HD) and identify risk factors associated with acute kidney injury (AKI).*
Material and methods. *A retrospective study included 18 neonates with HD (serum Na ≥150 mmol/L) hospitalized in the Department of Pediatrics and Nephrology between the years 2009-2019.*
Results. *The age at presentation was 7.5±4.7 days (range 2-18), weight loss was 15.9±8.3% (range 7.1-32.6) and serum Na range was 151-192 mmol/L (median 155.5 mmol/L). In 12 (67%) neonates, breast or mixed fed, HD occurred due to inadequate milk intake, in 6 (33%) neonates feeding difficulties were secondary to an acute infection. There was positive correlation between serum Na level and percentage weight loss at presentation (r=0.88; p<0.001). In 6 (33%) patients serious complications of HD were found: AKI in 5 patients, convulsions in one. Percentage weight loss was significantly higher in neonates with HD-associated AKI than in neonates with HD without AKI (p<0.01). Serum Na level was marginally higher in neonates with AKI than in those without AKI (p=0.08). In univariate logistic regression analysis, higher percentage of weight loss and higher serum Na level at presentation were important diagnostic factors of AKI in neonates with HD (both p<0.05). ROC analysis determined good diagnostic profile only for percentage weight loss, with a best cut-off value of 24.8%, for predicting AKI in neonates with HD (AUC 0.862, sensitivity 80%, specificity 100%).*
Conclusion. *Neonatal HD mostly occurs due to inadequate milk intake in breast or mixed fed babies, and rarely due to feeding difficulties in babies affected by an acute infection. Percentage weight loss at presentation has strong association with neonatal HD and is the most important factor of AKI in neonates with HD.*

Key words: *breastfeeding, hypernatremia, hypernatremic dehydration, acute kidney injury, neonates*

Pol Med J, 2020; XLVIII (287); 307–311

Profil kliniczny noworodków z odwodnieniem hipernatremicznym hospitalizowanych w klinice nefrologii

Krzemień G, Pańczyk-Tomaszewska M, Antonowicz-Zawiślak A, Szmigielska A.

Katedra i Klinika Pediatrii i Nefrologii, Warszawski Uniwersytet Medyczny, Polska

Celem pracy *była ocena profilu klinicznego noworodków z odwodnieniem hipernatremicznym (HD) i określenie czynników ryzyka wystąpienia ostrego uszkodzenia nerek (AKI).*
Materiał i metody*. Badaniem retrospektywnym objęto 18 noworodków z HD (Na w surowicy ≥150 mmol/L) hospitalizowanych w Klinice Pediatrii i Nefrologii w latach 2009-2019.*
Wyniki*. Wiek dzieci przy przyjęciu wynosił 7,5±4,7 dni (2-18 dni), utrata masy ciała wynosiła 15,9±8,3% (7,1-32,6%) i stężenie sodu w surowicy 151-192 mmol/L (mediana 155,5). U 12 (67%) noworodków, karmionych piersią lub w sposób mieszany, HD było następstwem niedostatecznej podaży mleka, u 6 (33%) noworodków trudności z karmieniem były wtórne do ostrej infekcji. Stężenie sodu w surowicy korelowało dodatnio z procentem utraty masy ciała przy przyjęciu (r=0,88; p<0,001). U 6 (33%) chorych stwierdzono poważne powikłania HD: AKI u 5 chorych, drgawki u jednego. Procentowa utrata masy ciała była znamiennie wyższa u noworodków z HD współistniejącym z AKI w porównaniu do noworodków z HD bez współistnienia AKI (p<0,01). Stężenie Na w surowicy było nieznamiennie wyższe w grupie z HD i AKI w porównaniu do grupy z HD bez AKI (p=0,08). Jednoczynnikowa analiza regresji logistycznej wykazała, że wyższa procentowa utrata masy ciała i wyższe stężenie Na przy przyjęciu są ważnymi wskaźnikami AKI u noworodków z HD (p<0,5). Analiza ROC wykazała dobry profil diagnostyczny do przewidywania AKI u noworodków z HD tylko dla procentowej utraty masy ciała, z punktem odcięcia 24,8%, [pole pod krzywą (AUC) 0,862, czułość 80%, swoistość 100%].*
Wnioski. *Główną przyczyną odwodnienia hipernatremicznego u noworodków jest niedostateczna podaż mleka u dzieci karmionych wyłącznie piersią lub w sposób mieszany. Rzadziej trudności z karmieniem związane są z ostrą infekcją u noworodka. Procentowa utrata masy ciała przy przyjęciu ma istotny wpływ na wystąpienie HD i jest najważniejszym czynnikiem ryzyka AKI u noworodków z HD.*

Słowa kluczowe*: karmienie piersią, hipernatremia, odwodnienie hipernatrmiczne, ostre uszkodzenie nerek, noworodki*

Pol Merkur Lekarski, 2020; XLVIII (287); 307–311

Hypernatremia is usually defined as a serum sodium (Na) concentration = 150 mmol/L [6,21]. Hypernatremic dehydration (HD) is associated with free water deficit secondary to inadequate fluid intake or fluid losses [24,26]. Neonatal HD mostly occurs due to inadequate daily breast milk intake in exclusively breast-fed babies [1,11]. The incidence of neonatal HD is 2.5 per 10 000 live births; 7.1 per 10 000 breast-fed newborns and 22.3 per 10 000 breastfeeding first time mothers [20]. Other authors stated this value as 7 per 1000 live births [13]. The true incidence of HD is difficult to define because of no blood tests in some babies with weight loss and cultural or methodological difference in the various studies [11,21].

Breastfeeding is a natural way of infant feeding in the first 6 months of life [2]. It has many non-nutritional benefits for the child and the mother. The human milk contains numerous immunomodulatory and antibacterial components that positively influence the development of the child immune system and increase the resistance for the infectious diseases, especially diarrhoea and respiratory infection. Breastfeeding reduces the risk of allergy and other frequent immune related diseases e.g. type 1 diabetes, inflammatory bowels diseases and some childhood cancers [17,27]. Therefore, breastfeeding practise is recommended by the WHO and paediatric societies [1,13,17]. Almost all cases of neonatal HD is observed in children of primi-

parous mothers with no practical experience of breastfeeding, but with strong motivation to breast feed [20]. If HD is not recognised on time, it can cause life-threatening conditions, including like brain damage, peripheral thrombosis and acute kidney injury (AKI) [1,4,25].

The aim of this retrospective study was to assess clinical profile of neonates with HD and identify risk factors associated with AKI.

MATERIAL AND METHODS

This was retrospective study. We reviewed data of 18 neonates with HD hospitalized in the Department of Pediatrics and Nephrology between the years 2009-2019. The neonates were enrolled in the study if they had serum Na ≥150 mmol/L, birth weight loss > 7% and age less than 29 days.

We collected demographic data of the babies from the neonatal unit, including gender, parity, delivery route, gestational age, birth weight, postnatal complication, age and weight loss at the time of neonatal unit discharge. The clinical data such as age and weight at presentation, weight loss (calculated by the difference in weight between admission to the hospital and birth weight), mode of delivery, clinical signs of infection, time of hypernatremia correction, duration of hospital stay and discharge diagnosis were reviewed.

Values of various laboratory parameters like serum sodium, potassium, calcium, creatinine, urea, glucose, bilirubin, pH, bicarbonate and urinalysis, as well as results of ultrasonography of the head and abdomen were recorded. Severe hypernatremia was defined as serum sodium ≥160 mmol/L [21]. Normal values of serum creatinine and urea in local laboratory were 0.6-1.1 mg/dL and 4.3-27.8 mg/dL, respectively for neonates <7 days of age, and 0.3-0.7 mg/dL and 4.3-32.1 mg/dL, respectively for neonates >7 days of age. AKI was defined as a progressive increase of serum creatinine ≥0.3 mg/dL above normal values for age and gestation [1, 12].

Statistical analysis was performed with the use of Statistica package version 13. for Windows (StatSoft; Tulsa, OK, USA). Continuous data were presented as mean ± standard deviation (SD) or median with corresponding 25th and 75th percentiles. Categorical data were described as numbers and percentages. Parametric *Student's t*-test and non-parametric *Mann-Whitney* test were used to compare variables between two groups. Correlations between continuous variables were evaluated by *Spearman's* rank correlation and linear regression analysis. Univariate and multivariate logistic regression analysis was performed to identify variables associated with the presence of AKI. Receiver operating curve (ROC) analysis was employed to determine variables with good diagnostic profile for predict AKI. Statistical significance was defined as *p* values less than < 0.05.

RESULTS

We evaluated 18 neonates with HD. Eight (44%) patients were males, 10 (56%) were females. All neonates were from singleton pregnancies, 14 (78%) neonates were first born. Fourteen (78%) babies were born through a normal vaginal delivery and 4 (22%) babies were born through caesarean section (two with no progress in delivery, one with pelvic alignment, one with threatening asphyxia). All neonates were on-term babies. The mean gestational age of the cases was 39.4±1.0 weeks (range 38-42) and the mean birth weight was 3403±390 g (range 2360-4160). One baby had trisomy 21 and birth weight less than 2500 g. Neonates were discharged from neonatal unit at mean day of age 3.2±0.8 (range 2-5) with mean weight loss of 7.1±3.1% (range 0-13.3). Three babies were transferred to our hospital for care – one with trisomy 21 and congenital heart defect suspicion, one with urinary tract infection (UTI) and AKI and one with otitis media acute. Seventeen (94%) neonates were admitted to the hospital in the first 2 weeks of life (tab. 1).

Table 1. The clinical and laboratory data of neonates with hypernatremic dehydratation (HD) in the Department of Pediatrics and Nephrology
Tabela 1. Kliniczne i laboratoryjne dane noworodków z odwodnieniem hipernatremicznym w Klinice Pediatrii i Nefrologii

Case	Age (days)	Birth weight loss (%)	Sodium (mmol/l)	Cr (mg/dL)	Urea (mg/dL)	Sodium correction (hours)	Discharge diagnosis
1	12	27.9	192	2.0	287.8	96	SEP, MEN PF, AKI
2	9	32.6	189	2.0	260.0	96	PF, AKI
3	14	30.1	182	1.1	206.4	64	PF, AKI
4	10	22.4	171	0.7	119.2	84	PF, HD
5	7	18.2	166	0.8	98.0	35	PF, HD
6	12	24.8	159	1.1	72.3	18	PF, HP, AKI
7	4	13.4	158	1.1	70.0	15	HD
8	3	11.5	158	1.1	46.0	23	HP, HD
9	7	10.6	157	0.7	72.4	12	UTI, HD
10	3	12.5	154	0.9	27.6	6	HP, HD
11	6	13.1	154	0.5	26.0	12	HP, HD
12	5	8.4	153	0.5	22.9	6	HD
13	18	7.1*	153	0.4	50.0	6	DS, PN, ASD, HD
14	5	12.0	153	0.5	25.8	8	HD
15	3	8.0	152	0.8	38.0	9	HP, HD
16	2	7.4	152	0.7	37.5	17	AOM, HD
17	2	8.9	151	1.4	76.7	18	UTI, AKI
18	13	17.7	151	0.5	40.2	6	UTI, HD
	7.5±4.7	15.9±8.3	155.5 (153; 166)	0.9±0.5	60.0 (37.5; 98)	16 (8; 11)	

* weight loss compared to the weight 4 days prior to admission; Cr – creatinine; SEP – sepsis; MEN – meningitis; PF – poor feeding; AKI – acute kidney injury; HD – hypernatremic dehydration; HP – hyperbilirubinemia; UTI – urinary tract infection; DS – Trisomy 21; PN – pneumoniae; ASD – atrial septum defect; AOM – acute otitis media

* utrata masy ciała w porównaniu z masą ciała 4 dni przed przyjęciem; Cr – kreatynina; SEP – sepsa; MEN – zapalenie opon mózgowo-rdzeniowych; PF – zaburzenia odżywienia; AKI – ostre uszkodzenie nerek; HD – odwodnienie hipernatremiczne; HP – hiperbilirubinemia; UTI – zakażenie układu moczowego; DS – Trsomia 21; PN – zapalenie płuc; ASD – otwór w przegrodzie międzykomorowej; AOM – ostre zapalenie ucha środkowego

All babies, except one presented weight loss compared to the birth weight. The girl with trisomy 21 (case 13) demonstrated weight loss compared to the weight evaluated 4 days prior to hospital admission. Eleven (61%) babies were visibly dehydrated at presentation. The most common findings of dehydration were: sunken fontanelle – 11 (61%) cases, doughy feel of skin – 11 (61%), oral mucosal dryness – 10 (56%), decreased urine output – 9 (50%), irritability or lethargy – 8 (44%), refusal of feeds – 7 (39%), poor feeding – 6 (33%), lack of stooling prior to admission – 5 (28%), jaundice – 5 (28%) and fever – 4 (22%). One girl (case 18) presented convulsions 7 days after admission. In this baby serum sodium was 151 mmol/L at admission and 137 mmol/L at the time of convulsion, hypernatremia correction time was 6 hours. Because of 17.7% weight loss at presentation and refusal of feeding, she received intravenous fluid infusion for 3 days. The results of cranial magnetic resonance and ultrasonography imaging were normal, but electroencephalography was incorrect. Severe hypernatremia occurred in 4 (22%) patients and hyperbilirubinemia (19.0-27.7 mg/dL) in 5 (28%) patients. Other metabolic disorders were: hyperkaliemia (6.1-6.8 mmol/L) – 3 cases, hyperglycaemia (110-352 mg/dL) – 3, hypoglycaemia (28-32 mg/dL) – 3, severe metabolic acidosis (pH 7.22-7.29) – 4. In 10 neonates urine density at admission was 1030, in 8 neonates urine analysis was performed after hydration. Ultrasonography of the head and abdomen in all neonates were normal.

Sixteen (89%) neonates were exclusively breast-fed prior to admission and 2 (11%) were mixed fed. In 6 (33%) neonates cause of HD were feeding difficulties secondary to an acute infection: sepsis with meningitis in one case, UTI in three cases, pneumoniae in one and acute otitis media in one (tab. 1). In 12 (67%) neonates the only cause of HD was ineffective breast or mixed feeding. Prerenal AKI was found in 5 (28%) neonates with HD – in four admitted to the hospital from home and in one transferred to our department in the age of 2 days due to UTI and AKI (case 17). In another patient with HD-associated AKI (case 1) we recognize sepsis and meningitis. Thirteen (72%) babies received intravenous hydration, all received oral feeds. Phototherapy was used in all neonates with hyperbilirubinemia. None were dialysed or treated using a central venous line. The median hospital stay was 8 day (IQR 4-11; range 2-30). Six (33%) neonates were breast fed and 8 (44%) neonates were mixed fed on discharge.

Linear regression analysis found positive correlation between serum sodium level and percentage weight loss at admission to hospital ($r=0.88$; $p<0.001$). There was no correlation between serum sodium level and age at admission. Weight loss at admission were significantly higher in neonates with HD-associated AKI than in those with HD without AKI. Serum sodium level were only marginally higher in HD-associated AKI group than in HD without AKI group (tab. 2).

Table 2. Comparison of clinical and laboratory data of neonates with hypernatremic dehydration (HD) and acute kidney injury (AKI) with neonates with HD without AKI
Tabela 2. Porównanie klinicznych i laboratoryjnych danych noworodków z odwodnieniem hipernatremicznym (HD) i ostrym uszkodzeniem nerek (AKI) z noworodkami z HD bez AKI

Variables	HD with AKI (n = 5)	HD without AKI (n = 13)	*p*
Admission age (days)	9.8±4.7	6.6±4.6	ns
Admission weight loss (%)	24.9±9.4	12.5±4,6	<0.01
Serum sodium (mmol/L)	182 (159; 189)	154 (153; 158)	0.08
Serum creatinine (mg/dL)	1.5±0.5	0.7±0.2	<0.001
Serum urea (mg/dL)	180.6 (76.7; 260.0)	40.2 (27.2; 70.0)	<0.01
Hypernatremia correction (hours)	64.0 (18.0; 96.0)	12.0 (6.0; 17.0)	<0.05
Hospital stay (days)	15.0 (11.0; 12.0)	8.0 (3.0; 8.0)	< 0.05

Univariate logistic regression analysis has demonstrated that higher percentage of weight loss at admission and higher serum sodium level were important diagnostic factors of AKI in neonates of HD (tab. 3).

Table 3. Univariate logistic regression analysis to identify risk factors associated with presence of acute kidney injury (AKI) in neonates with hypernatremic dehydration (HD)
Tabela 3. Jednoczynnikowa analiza regresji logistycznej do identyfikacji czynników ryzyka wystąpienia ostrego uszkodzenia nerek (AKI) u noworodków z odwodnieniem hipernatremicznym (HD)

Variable	OR (95%CI)	*p*
Gestational age	0.760 (0.253-2.284)	ns
Birth weight loss at discharge (%)	1.009 (0.009-1.021)	ns
Admission age	1.162 (0.919-1.469)	ns
Weight loss at admission (%)	1.273 (1.035-1.566)	< 0.05
Serum sodium	1.129 (1.007-1.266)	< 0.05

Multivariate analysis did not identify independent predictors of AKI (data not shown). ROC analysis has demonstrated good diagnostic profile for percentage weight loss at presentation, with a best cut-off value of 24.8%, for predicting AKI in neonates with HD [area under the curve (AUC) 0.862, sensitivity 80%, specificity 100%]. Age at admission (AUC 0.685) and serum sodium level (AUC 0.777) were not useful for predicting AKI in neonates with HD.

DISCUSSION

In this retrospective study we assessed 18 neonates, who developed HD due to insufficient breast fed or mixed fed. In one third of patients feeding difficulties were secondary to an acute infection. The most serious complications in neonates were AKI and convulsions in one baby.

Neonatal HD mainly occurs due to inadequate breast milk intake in exclusively breast fed babies, rarely due to improperly mixed fed, feeding difficulties secondary to an acute infection, gastrointestinal losses, nephrogenic or central diabetes insipidus, a diffuse skin condition, salt poisoning and ritual salting of skin [3,14,19,23]. In the studies from the last years the frequency of breastfeeding-associated HD in term or near term hospitalized neonates vary from 1.38% to 3.1% [1,8,13]. There are three possible causes of inadequate breastfeeding: problem with maternal breast milk synthesis such as delay initiating breastfeeding or infrequent breast stimulation and drainage; difficulty with breast milk removal due to inverted nipples, infants facial and oral abnormalities or poor breastfeeding technique; low daily breast milk intake because of long sleep periods, jaundice, infection, maternal social factors e.g. depression, fatigue or lack of support [6,15]. Difficulty with breast milk removal is associated with persistence of high breast milk sodium level. In adequate lactation, breast milk sodium decreased from 64 mmol/L on the first day of life to 7 mmol/ L on the 15th day of life [4,9]. In various studies primiparity, caesarean delivery, postpartum complications and maternal excessive pregnancy weight, advanced age, early postpartum discharge and low education level are considered as risk factors for development of HD [4,10,14,15]. In our study all affected neonates were on-term babies, 78% neonates were first born, 22% were born through caesarean section, 89% were exclusively breast-fed prior to admission. One patient had predisposition to feeding problems due to trisomy 21. In 33% of neonates difficulty in feeding were associated with an acute infection.

Some authors reported that most of neonates with HD were regularly assessed by midwives and general practitioner prior to hospital admission, but feeding difficulties were not recognized [25]. Babies were admitted to the hospital when complications such as excessive weight loss, poor feeding, jaundice, excessive

body temperature, decrease urine output or neurological signs were presented [1,5,14,19]. Neonatal HD is difficult to diagnose on clinical examination. The babies may not be visibly dehydrated because having a better preserved extracellular volume and therefore less overt sings of dehydration [1,5,10,18]. Many experts postulate early postpartum follow-up and routine neonates weighting in the first week of life [7,14]. In the present study only 61% neonates were visibly dehydrated at presentation, which was comparable to the study by Livingstone at al [15]. The most common finding of HD were: sunken fontanelle, doughy feel of skin, oral mucosal dryness, decreased urine output and neurological signs like irritability or lethargy. Neonates can lose 7% of birth weight over the first week of life, but they should recovery birth weight in 10 days. Rapid weight loss or persisting weight fall 7 days after birth, need further evaluations [13,15,18]. Breastfed newborns initially lose more weight and need more time to regain birth weight than formula fed neonates [16].

Breastfeeding-associated HD is usually linked with > 10% weight loss, however *Livingstone at al.* reported that HD may develop even if weight loss is < 10% [4,14,15]. In severe HD serum sodium may be rising ≥200 mmol/L [8,10]. Similar to Boskabadi at al. study [10], we found that 72% neonates with HD had weight loss > 10%, and 28% neonates had weight loss of 7.1- 8.9% in the first 2-5 days of life. We also noted that 22% babies were affected by severe HD with serum sodium of 166-189 mmol/L. A systematic review of literature have shown that 95% of breastfeeding-associated HD was recognized in newborn ≤21 days, most of them in the first 2 weeks of life [14]. In the present study, similar to *Oddie et al.* [21] and *Livingstone et al.* [15] reports, 94% neonates were presented to the hospital in the first 14 days of life, and the mean time of admission was 7.5 days of life (range 2-18). Multiple studies have documented significant correlation of the serum sodium level with age at presentation [1,13,16,21] and with weight loss at presentation [1,5,11,14,15]. We demonstrated a strong positive correlation between serum sodium level and percentage weight loss at admission. We did not find correlation between serum sodium level and age at admission.

Neonates with severe HD can have devastating consequences such as neurological complications, extensive peripheral venous and arteries thrombosis, disseminated intravascular coagulopathy (DIC), necrotizing enterocolitis due to impaired mesenteric perfusion, liver dysfunction and AKI [1,14,20,25]. The most frequent life-threatening conditions of neonatal HD are secondary to neurological complications. HD may be associated with brain damage due to bleeding, oedema, thrombosis, infarction or jaundice, as well as with hydrocephalus, convulsion, coma and death [1,4]. Death in neonates with HD, mostly secondary to cerebral involvement, occurred in 2.3% to 10.77% of patients [10,14]. Hypernatremia in breastfeeding-associated HD neonates is fundamentally different from that observed in gastroenteritis. It develops over a longer time, allowing brain cell to adapt to the increasing osmolality. The brain cell produce osmotically active molecules, which restore the intracellular brain volume. Rapid correction of hypernatremia or administration of hypotonic fluid, leads to brain oedema due to the brain inability to remove these molecules [3,6,20]. Convulsions, which occurred in 5.9-27% of neonates with HD, usually during improper rehydration, are the most common neurological complication of hypernatremia [1,5,8,10]. The coexistence of hypernatremia with significant hyperbilirubinemia, which occurred in 17-64.4% of neonates with HD, may enhance the risk of bilirubin encephalopathy and long-term sequelae [5,8,9,14].

There is no consensus about optimal rehydration in this population [6]. Most authors recommend optimal goal reduction rate of serum sodium level not more than 0.5 mmol/L per hour with correction over 48 hours [22,24]. In *Ben-Shalom et al*. opinion during the first hours of therapy, sodium level in intravenous fluid should be only minimally lower than sodium level in serum [3]. In *Bolat et al.* opinion serum sodium above 160 mmol/L at admission and serum sodium correction rate greater than 0.5 mmol/L per hour are independent risk factor of death and convulsion [8]. In our study 8% of neonates presented irritability or lethargy and in 28% of babies hypernatremia coexisted with significant hiperbilirubinemia. Adequate intravenous hydration was administrated in 72% of neonates, all babies received oral feeds. One girl demonstrated convulsions 7 days after admission. She had mild hypernatremia, normal neuroimaging and abnormal encephalography. In this case we could not exclude complication of fluid therapy. We don't have not information about any potential late neurological sequelae in this girl. Other long-term follow-up studies have shown that severe neonatal HD can lead to permanent brain damage and neurodevelopmental delay, which increased with higher levels of serum sodium, urea and creatinine levels [10,24].

Neonates with severe HD-associated AKI usually presented with prerenal type of AKI, however prolonged dehydration and decreased renal perfusion can lead to the renal type of AKI [28]. In the previous studies AKI in neonates with HD was less often recognized condition [2] and the available published reports were usually only small case series [4,23,25]. In the last years the frequency of HD-associated AKI in neonates vary from 5% to 67% [3, 14, 19, 20], and is more often recognized in breast fed babies than in mixed fed [19]. Study by *Ahmed et al*. has revealed that babies with HD-associated AKI were significantly later admitted to the hospital, they had significantly higher percentage of weight loss and higher serum sodium levels at presentation than neonates with HD without AKI. In this report the percentage of dehydration was an independent marker of AKI in neonates with HD [1]. Based on the results of our study we recognized AKI in 5 (28%) neonates with HD – in 4 babies with weight loss range of 22.4-32.6% and in one baby with weight loss of 8.9%. Two patients with AKI were affected with infection – one had sepsis and meningitis, and one urinary tract infection. In concordance with *Ahmed et al*. study [1], we found significantly higher percentage weight loss in neonates with HD-associated AKI than in neonates with HD without AKI. We did not find significant difference in age between the groups. Serum sodium level were only markedly higher in neonates with AKI group than in neonates without AKI. It may be due to small number of AKI patients and relatively low level of serum sodium in one baby. As we expected, babies with HD-associated AKI demonstrated significantly higher serum urea and creatinine levels and longer time of hypernatremia correction than babies without AKI. Longer time of hospital stay in the first group was related to coexisting infections. Univariate logistic regression analysis has shown that higher percentage weight loss and higher serum sodium level were important diagnostic factors of AKI in neonates with HD. However, ROC analysis has determined good diagnostic profile only for percentage weight loss, with a best cut-off value of 24.8%, for predicting AKI in neonates with HD. Small cohort of children may have contributed to results of univariate analysis and ROC analysis.

In neonates with HD-associated AKI, who do not respond to appropriate hydration treatment, renal replacement therapy is the treatment of choice. This kind of therapy usually is necessary in neonates with HD and sepsis with multiorgan dysfunction or with peripheral vascular thrombosis [25,28]. Several investigators demonstrated that neonates with HD-associated AKI can have a complete recovery or may have residual kidney damage with long-term consequence such as hypertension, proteinuria and chronic kidney disease (CKD) [2,10].

There were some limitations of our study. This was retrospective and single-center study, with a small cohort of neonates and lack of follow-up. It may have contributed to the results of statistical analysis.

CONCLUSIONS

The results of this study show that neonatal HD mostly occurred because of inadequate milk intake in breast or mixed fed babies, rarely due to feeding difficulties in babies with an acute infection. Most of the neonates were admitted to the hospital in the

first 14 days of life with weight loss more than 10%. We found strong positive correlation between serum sodium level with percentage weight loss at admission. In one third of patients serious complications of HD like AKI or convulsion were recognized. We found that percentage weight loss at presentation has strong association with neonatal HD and is the most important factor of AKI in neonates with HD.

REFERENCES

1. Ahmed A, Iqbal J, Ahmad I, et al.: Complications due to breastfeeding associated hypernatremic dehydration. J Clin Neonatol, 2014; 3: 153-157.
2. Barman H, Das BK, Duwarah SG.: Acute kidney injury in hypernatremic dehydration in exclusively breastfed babies: don't ignore it. J Clin Neonatol, 2014; 3: 124-125.
3. Ben-Shalom E, Toker O, Schwartz S.: Hypernatremic dehydration in young children: is there a solution? IMAJ, 2016; 18: 95-99.
4. Bhat MA, Kawoosa MS, Bhat JI, et al.: Hypernatremia and intracranial complications due to inadequate exclusive breast-feed in neonates. J Pediatr Neurol, 2008; 6: 183-187.
5. Bilgin LK, Akcay F, Altinkaynak K, et al.: Hypernatremia in breastfed newborns: a review of 149 cases. J Trop Pediatr, 2012; 58: 332-334.
6. Bischoff A, Dornelles AD, Carvalho CG.: Treatment oh hypernatremia in breastfeeding neonates: a systematic review. Biomed Hub, 2017; 2: 1-10
7. Boer S, Unal S, van Wouwe JP, et al.: Evidence based weighing policy during the first week to prevent neonatal hypernatremic dehydration while breastfeeding. PLoS One, 2016; 11:e01167313.
8. Bolat F, Oflaz MB, Guven AS, et al.: What is the safe approach for neonatal hypernatremic dehydration? A retrospective study from a neonatal intensive care unit. Pediatr Emerg Care, 2013; 29:808-813.
9. Boskabadi H, Maamouri G, Ebrahimi M, et al.: Neonatal hypernatremia and dehydration in infants receiving inadequate breastfeeding. Asia Pac J Clin Nur, 2010; 19: 301-307
10. Boskabadi H, Zakerihamidi M, Moradi A.: Predictability of prognosis of infantile hypernatremic dehydration: a prospective cohort study. J Matern Fetal Neonatal Med, 2020; 14:1-9.
11. Ferrández-González M, Bosch-Giménez V, López-Lozano J, et al.: Weight loss thresholds to detect early hypernatremia in newborns. J Pediatr (Rio J), 2019; 95: 689-695.
12. Kellum JA, Lamiere N, Aspelin P, et al. Kidney Disease: Improving Global Otcomes (KIDIGO). Acute Kidney Injury Work Group. KIDIGO clinical practice guideline for acute kidney injury. Kidney Int, 2012; 2: 1-138.
13. Korgali EÜ, Cihan MK, Oğuzalp T, et al.: Hypernatremic dehydration in breastfed term infants: retrospective evaluation of 159 cases. Breastfeed Med, 2016; 12: 5-11.
14. Lavagno C, Camozzi P, Renzi S, et al.: Breastfeeding-associated hypernatremia: a systematic review of the literature. J Hum Lact, 2016; 32: 67-74.
15. Livingstone VH, Willis CE, Abdel-Wareth LO, et al.: Neonatal hypernatremic dehydration associated with breast-feeding malnutrition: a retrospective survey. CMAJ, 2000; 162: 647-652.
16. Macdonald PD, Ross SRM, Grant L, et al.: Neonatal weight loss in breast and formula fed infants. Arch Dis Child Neonatal, 2003; 88: F472-F476.
17. Michaelsen KF.: Breastfeeding. World Rev Nutr Diet, 2015; 113:92-96.
18. Mujawar NS, Jaiswal AN.: Hypernatremia in the neonate: neonatal hypernatremia and hypernatremic dehydration in neonates receiving exclusive breastfeeding. Indian J Crit Med, 2017; 21: 30-33.
19. Nair S, Singh A, Jajoo M.: Clinical profile of neonates with hypernatremic dehydration in an outborn neonatal intensive care unit. Indian Ped, 2018; 55: 343-344.
20. Oddie S, Richmond S, Coulthard M.: Hypernatraemic dehydration and breast feeding: a population study. Arch Dis Child, 2001; 85: 318-320.
21. Oddie SJ, Craven V, Deakin K, et al.: Severe neonatal hypernatraemia: population based study. Arch Dis Child Fetal Neonatal Ed, 2013; 98: F384-F387.
22. Paramasivam P, Earan SK, Arunagirinadhan A, et al.: Life threatening severe hypernatraemic dehydration in neonates: a report of two cases. J Clin Diagn Res, 2017; 11: 10-12.
23. Peker E, Kirimi E, Tuncer O, et al.: Severe hypernatremia in newborns due to salting. Eur J Pediatr, 2010; 169: 829-932.
24. Sarin A, Thill A, Yaklin CW.: Neonatal hypernatremic dehydration. Pediatr Ann, 2019; 48: e197-e200.
25. Shroff R, Hignett R, Pierce C, et al.: Life-threatening hypernatremic dehydration in breastfed babies. Arch Dis Child, 2006; 91: 1025-1026.
26. Somers MJ.: Clinical assessment and diagnosis of hypovolemia (dehydration) in children. www.uptodate.comÓ2020UpToDate.
27. Tlaskalová-Hogenová H, Kverka M, Hrdý J.: Immunomodulatory components of human colostrum and milk. Nestlé Nutr Inst Workshop Ser, 2020; 94: 1-10 .
28. Yildiz N, Erguwen M, Yildiz M, et al.: Acute peritoneal dialysis in neonates with kidney injury and hypernatremic dehydratation. Perit Dial Int, 2013; 33:290-296.

Disclosure: The authors declare no conflict of interest.

Received: 16.06.2020
Revised: 01.07.2020
Accepted: 26.08.2020

Address for correspondence:
Agnieszka Szmigielska, MD, PhD
Department of Pediatric Nephrology Medical University of Warsaw
Żwirki i Wigury 63a Street
02-091 Warsaw, Poland
Phone: +48 22 317 96 56, Fax +48 22 317 99 54
e-mail: agnieszka.szmigielska@wum.edu.pl