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Common Clinical Presentation and Associated Laboratory Findings of Neonatal Hypernatremia

Mohammed El. A. Zayed[1]*, Sarah Omer Mohammed Gadim[2] and Omer Saeed Magzoub[3]*

[1]Assistant professor of Pediatric and Child Health, Faculty of Medicine and Health Science, Kordofan University, Kordofan, Sudan.

[2]Pediatric Specialist, Mistry of Health, North Kordofan State, Sudan.

[3]Specialist General Pediatrician at Ain Al-Khaleej Hospital, Al-Ain, Abu Dhabi, UAE.

***Correspondence:**
Mohammed El. A. Zayed, Assistant professor of Pediatric and Child Health, Faculty of Medicine and Health Science, Kordofan University, Kordofan, Sudan, Mobile No: 00249128750205.

Dr. Omer Saeed Magzoub, Specialist General Pediatrician, Ain Al-Khaleej Hospital, Al-Ain, Abu-Dhabi, UAE, Mobile No: 0097564993763.

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ABSTRACT

Serum sodium concentration of ≥ 150mmol/l in neonates is known as neonatal hypernatremia. The risk of hypernatremia is high in newborns as result of inability to control their fluid intake and their large body surface area to weight or height ratio which results in high insensible water losses.

Objectives: *To determine clinical presentation and associated laboratory findings of hypernatremia in Neonates admitted to Al-Obied Specialized Pediatric Hospital, North Kordofan State, Sudan during the period from January 2020 - January 2022.*

Methods: *This is a descriptive, observational, cross-sectional and hospital-based study conducted at Al-Obied Specialized Pediatric Hospital. Data was extracted from the patient records and then re-entered into a predesigned data collection form. Data then cleaned and entered into Microsoft excel data sheet and analyzed using SPSS version21.*

Results: *A total of 206 of the participants were included in this study. Most patients (92.2%) were delivered at term with normal APGAR score in (86.9%). The birth weight for majority 104 (50.5%) of the respondents was found to be from 1.5 to 2.5 kg. Serum Na was found to be 151 -170 mmol/l in 124 (68.9%), 170 – 190 mmol/l in 41 (22.8%), 190 – 200 mmol/l in 10 (5.6%) of them and more than 200 mmol/l in 5 (2.8%) of the participants. The most commonly reported associated neonatal complication was found to be sepsis which reported in 185 (89.8%) of the participants followed by neonatal jaundice which reported in 64 (31.1%) of the neonates, feeding refusal in 55 (26.7%) of neonates, diarrhea in 28 (13.6%), vomiting in 25 (12.1%) of the neonates and 22 (10.7%) were with congenital malformations. Neurological symptoms (convulsions, irritability & lethargy) were reported in 70 (34%) of the participants. The most reported maternal complications were febrile illness in 35 (17%) of the participants 23 (11.2%) were with UTI 20 (9.7%) had PIH. C-reactive protein (CRP) was found elevated in all participants. Renal function tests (RFTs) was impaired in 180 (87.4%) of the participants and normal in 26 (12.6%).*

Conclusion: *Birth weight significantly associated with Hypernatremia. The most common reported clinical presentation was found to be sepsis, followed by neonatal jaundice, feeding refusal, diarrhea, vomiting and congenital malformations. Neurological symptoms (convulsions, irritability & lethargy) were reported as well. Other complications included sepsis and acute kidney injury (AKI). The most common laboratory findings which found to be associated with neonatal hypernatremia were elevated C-reactive protein (CRP), urea and creatinine.*

Keywords
Clinical presentation, Laboratory findings, Neonatal hypernatremia.

Introduction
Hypernatremia in neonates is defined as a total serum sodium concentration of ≥ 150mmol/L. Newborns are at increased risk of hypernatremia due to inability to control their fluid intake and their large body surface area to weight or height ratio which results in high insensible water losses [1]. The incidence of neonatal hypernatremia varies widely depending on countries regions geographic settings or socioeconomic status and has been increasing over the past three decades [2].

Due to the gradual occurrence of dehydration and hypernatremia diagnosis of neonatal hypernatremic dehydration is difficult and dehydration is often not recognized. Thus infants with hypernatremic dehydration may not see a doctor until there are complications of reduced urination, lethargy, weakness, neurologic symptoms, thrombosis or seizure [3]. Other complications of hypernatremia can be hyperglycemia, hypokalemia and renal tubular damage as hypernatremia results in endocrine dysfunction. Available evidence shows that hypernatremia and hyperosmolarity are related to impaired glucose metabolism by insulin and impaired glucose release by glucagon [3].

Etiology
The etiological list of hypernatremic dehydration in newborn infant is not long. Depending on amount of deficit in total body fluids hypernatremia is described as either hypovolemic euvolemic or hypervolemic. Infants are worst affected because of (a) immaturity of the kidney that hinders its ability to excrete an excess sodium load (b) babies have limited or no ability to express thirst and (c) infants can't feed themselves and depend on caregivers to provide adequate and appropriate fluids and feeds [4]. Hypernatremic dehydration may be caused by pure water loss (diabetes insipidus) hypotonic fluid loss (vomiting or diarrhea) or hypertonic sodium gain (hypertonic feeding preparations such as improperly prepared infant formula). Sodium content of breast milk at birth is high and declines rapidly over subsequent days. Sodium content of colostrum in the first five days is (22±12) mmol/L and of transitional milk from day five to ten is (13±3) mmol/L and of mature milk after 15 day is (7±2) mmol/L. The Breastfeeding hypernatremic dehydration results when a mother-infant feeding interaction is inadequate. Here human milk production is limited and the physiologic decline in human milk sodium concentration does not occur. The infant becomes dehydrated while the kidneys are mature enough to retain sodium ions [4].

Clinical Presentation
The clinical presentation of hypernatremic dehydration is usually around ten days with a range from 3 to 21 days. Parents may fail to identify that the infant is ill and professionals may also falsely reassure about infant's apparent well-being. Signs may be non-specific including lethargy and irritability occasionally there is an acute deterioration which precipitates the infant's emergency admission to hospital. During acute isonatremic or hyponatremic dehydration clinicians may rely on sunken eyes and depressed anterior fontanelle as signs of total body water loss. In hypernatremic dehydration however there may be changes in brain cell osmolality and cerebral oedema and the resultant fullness of the anterior fontanelle may mislead the underlying dehydration. Clinical examination of these infants at presentation is variable. Some present with lethargy; others may be alert hungry and clinically dehydrated [5]. There may be jaundice, seizure and excessive weight loss. In moderate to severe hypernatremic dehydration skin turgor is normal there may be fever tachycardia with poor perfusion and hypotension with hypovolemia. Skin is thick doughy and may even feel moist due to perspiration. Mucous membrane is dry. An important observation of hypernatremic dehydration is intense thirst [5].

Complications
Brain is the most vulnerable organ from hypernatremia. Plasma hypertonicity and the subsequent intracellular water loss causes the brain cells to shrink leading to rupture of bridging vessels with hemorrhages in subarachnoid and brain parenchyma and thrombosis. Brain responds over a period of several hours by acquiring new intracellular solutes known as 'idiogenicosmoles' to protect intracranial volume [6]. If rehydration is rapid with relatively hypotonic intravenous fluids excess water enters cerebral cells leading to rebound cerebral oedema. Permanent cognitive impairment, cerebral dysfunction, spastic paralysis and seizure disorders have been described [7]. Extensive pontine and extra-pontine myelinolysis have also been reported [8,9]. Children with early onset of seizures or impairment of consciousness have a 50% chance for neurologic sequel. Other recognized complications of hypernatremia include hyperglycemia hypocalcemia renal tubular injury and renal vein thrombosis [10]. Mortality in acute cases with serum sodium >160 mmol/L is around 45% (15-70%), while it is around 10% in chronic hypernatremia [8].

Hypernatremia previously thought to be unusual in breast feed babies but recent reports suggested that the incidence of hypernatremia and hypernatremic dehydration is rising. The condition carries an acute morbidity and mortality. Hypernatremic dehydration is a potentially lethal condition in neonate which adversely affects central nervous system leading to devastating consequences like intracranial hemorrhage thrombosis and death [4].

This study aimed to orient our health care professionals specially pediatricians concerning some essential aspect of such important issue for early recognition and timely intervention of this condition so that devastating consequences in neonate can be avoided.

Materials and Methods
Cross sectional, descriptive, observational and hospital-based study conducted among neonates admitted to **Al-Obied Specialized Pediatric Hospital**, North Kordofan State from June 2020 to June 2022 (2-years duration). The study included all neonates admitted

to the hospital with hypernatremia during the study period and excluded those with incomplete records.

Total coverage approach was used in which all neonates admitted during study period with serum sodium >150 were selected from patient's records in the same orders of original report. Data was collected from patients records using structural questionnaires and entered into Microsoft excel data sheet and were analyzed used SPSS version 21. P value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests and level of confidence.

Results

A total of 206 of the participants were included in this study. 190 (92.2%) were delivered at term 16 (7.8%) were preterm of those who were preterm; 14 (87.5%) were 30 - 35 week gestational age preterm and 2 (12.5%) were 25 - 30 week gestational age preterm and none of the preterm was less than 25 week of gestational age (Table 1). Apgar score was normal in 179 (86.9%) of the neonates and low in 27 (13.1%) of them. Resuscitation was done for all 27 (100%) of the neonates with low Apgar score (Table 2).

The birth weight for most 104(50.5%) of the respondents was found to be from 1.5 to 2.5 kg 58 (28.2%) having birth weight of 2.5 to 3.5 kg 2 (1%) were having birth weight of more than 3.5 kg and none of them had birth weight of less than 1 kg (Figure 1). Most of the respondents 109 (52.9%) were having newborn in his first week 68 (33%) of the respondents were having a newborn in his second week 16 (7.8%) were having third week neonate and 13 (6.3%) were having a 4th week neonate (Figure 2).

The most commonly reported associated neonatal complication was found to be sepsis which reported in 185 (89.8%) of the participants followed by neonatal jaundice which reported in about 64 (31.1%) of the neonates then feeding refusal as found to be in 55 (26.7%) of neonates 28 (13.6%) were found to be having diarrhea 26 (12.6%) were diagnosed as Hypoxic ischemic encephalopathy (HIE) 25 (12.1%) of the neonates were having vomiting 22 (10.7%) were with congenital malformations and 16 (7.8%) were with congenital heart disease (CHD). The least reported associated neonatal complications were HSD and oral thrush with each represented with 1 (0.5%) of the respondents (Table 3).

Voiding was normal in 89 (43.2%) of the participants 83 (40.3%) were oligouric 32 (15.5%) were anuric and 2 (1%) were polyuric. In regards to hydration status about 144 (69.9%) were euvolumic 57 (27.7%) were hypovolemic and 5 (2.4%) were hypervolemic. Neurological symptoms were absent in 136 (66%) of the participants and present in 70 (34%) of the participants. Convulsions were found in 70 (34%) of the participants irritability in 32 (15.5%) of the participants lethargy in 26 (12.6%) of the participants and confusion in 20 (9.7%) (Table 4).

Concerning sepsis workup; CRP titer was from 6 – 20 mg/l in 59 (28.6%) of the participants 20 – 50 mg/l in 54 (26.2%) of the participants 50 – 100 mg/l in 52 (25.2%) and more than 100 mg/l in 41 (19.9%) of the participants. TWBCs was from 10000 – 25000 in 116 (56.3%) of the participants 3000 - 10000 in 51 (24.8%) of the participants more than 25000 in 26 (12.6%) of the participants (Table 5).

RFT was impaired in 180 (87.4%) of the participants and normal in 26 (12.6%) of them. Urea was found to be 100 – 200 mg/dl in about 53 (29.4%) of the participants urea level was 200 – 300 mg/dl in about 51 (28.3%) of them urea was found to be more than 300 mg/dl in 44 (24.4%) of the participants and 51 – 100 mg/dl in about 32 (17.8%) of the participants. Serum creatinine was 1 – 3 mg/dl in 93 (51.7%) of the participants 3 – 6 mg/dl in 38 (21.1%) of the participants 6-10 mg/dl in 37 (20.6%) of the participants and more than 10 mg/dl in about 12 (6.7%) of the participants. Serum Na was found to be 151 -170 mmol/l in 124 (68.9%) of the participants 170 – 190 mmol/l in 41 (22.8%) of the participants 190 – 200 mmol/l in 10 (5.6%) of them and more than 200 mmol/l in 5 (2.8%) of the participants (Table 5).

Time of diagnosis was found to be day 1 in 150 (72.8%) of the participants 56 (27.8%) were diagnosed at (day 2 3 4). Duration of treatment of hypernatremia was found to be 1 day in about 40 (19.4%) of the participants 2 days in 42 (20.4%) 3 days in 38 (18.4%) of the participants 4 days in 24 (11.7%) and 8 days in 20 (9.7%) of the participants (Table 6).

Birth weight significantly associated with Hypernatremia (P. value = .000). Those with birth weight between 1 – 2.5 kg more frequently have sodium level 151 – 170 mmol/l. Those with impaired RFT significantly have high sodium level (P. value = .000). High blood urea and serum creatinine significantly associated with sodium level 151 – 170 mmol/L.

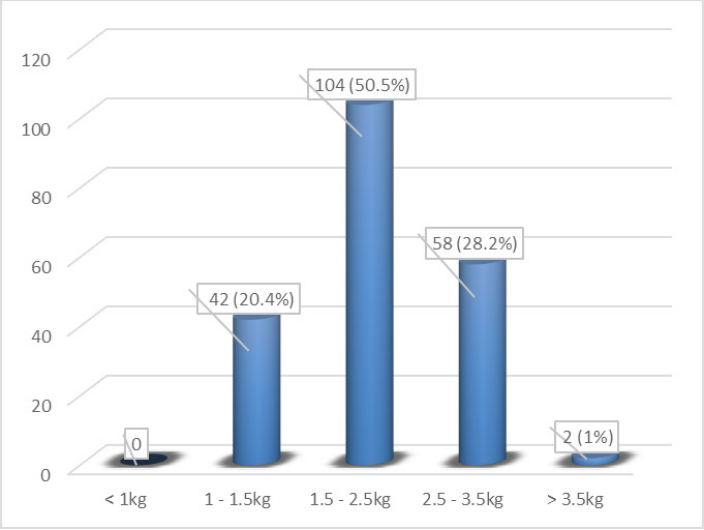

Figure 1: Birth weight of the respondents.

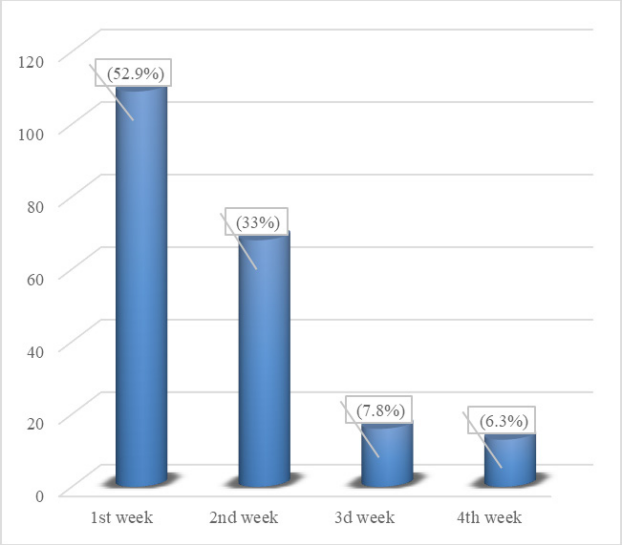

Figure 2: Age groups.

Table 1: Gestational age.

GA	Frequency (%)
Term	190 (92.2%0
Preterm	16 (7.8%)
< 25wk	0 (0%)
25 – 30wk	2 (12.5%)
30 – 35wk	14 (87.5%)

Table 2: Apgar score and need for resuscitation.

	Frequency (%)
APGAR score	
Normal	179 (86.9%)
Low	27 (13.1%)
Resuscitation	
Yes	27 (100%0
No	0 (0%)

Table 3: Associated neonatal presentation & complications.

Complications	Frequency (%)
Vomiting	25 (12.1%)
Diarrhea	28 (13.6%)
Sepsis	185 (89.8%)
RDS	15 (7.3%)
HIE	26 (12.6%)
Jaundice	64 (31.1%)
Congenital malformation	22 (10.7%)
Malaria	15 (7.3%)
Meconium aspiration	6 (2.9%)
Refuse of feeding	55 (26.7%)
Oral thrush	1 (.5%)
Trisomy 21	7 (3.4%)
Cleft lip	11 (5.3%)
CHD	16 (7.8%)
LI	13 (6.3%)
HDON	4 (1.9%)
HSD	1 (.5%)
FTT	8 (3.9%)
Meningitis	12 (5.8%)

Table 4: Signs of hypernatremia.

Clinical features	Frequency (%)
Voiding	
Normal	89 (43.2%)
Anuric	32 (15.5%)
Oligouric	83 (40.3%)
Polyuric	2 (1%)
Hydration status	
Euvolemia	144 (69.9%)
Hypovolemia	57 (27.7%)
Hypervolemia	5 (2.4%)
Neurologic symptoms	
Absent	136 (66%)
Present	70 (34%)
Lethargy	26 (12.6%)
confusion	20 (9.7%)
Convulsion	70 (34%)
Coma	7 (3.4%)
Irritability	32 (15.5%)

Table 5: Sepsis workup.

Investigation	Frequency (%)
CRP	
6 – 20	59 (28.6%)
20 – 50	54 (26.2%)
50 – 100	52 (25.2%)
>100	41 (19.9%)
TWBCs	
<3000	13 (6.3%)
3000 – 10000	51 (24.8%)
10000 – 25000	116 (56.3%)
>25000	26 (12.6%)
RFT	
Normal	26 (12.6%)
Impaired	180 (87.4%)
Urea	
51 – 100	32 (17.8%)
100 – 200	53 (29.4%)
200 – 300	51 (28.3%)
>300	44 (24.4%)
S. creatinine	
1 – 3	93 (51.7%)
3 – 6	38 (21.1%)
6 – 10	37 (20.6%)
>10	12 (6.7%)
Serum Na	
151 – 170	124 (68.9%)
170 – 190	41 (22.8%)
190 – 200	10 (5.6%)
>200	5 (2.8%)

Table 6: Time to diagnosis.

	Frequency (%)
Early (Day 1)	150 (72.8%)
Late (day 2, 3, 4)	56 (27.2%)
Day 2	27 (48.2%)
Day 3	27 (48.2%)
Day 4	2 (3.6%)

Discussion

Birth weight significantly associated with hypernatremia as those with birth weight of 1 – 2.5 kg more frequently have sodium level 151 – 170 mmol/L. The vast majority (92.2%) was delivered at term and (7.8%) were preterm. The majority (87.5%) of those who were preterm were 30 - 35 week gestational age preterm and (12.5%) were 25 - 30 week gestational age preterm and none of the preterm was less than 25 week of gestational age. Apgar score was normal in most (86.9%) of the neonates and low in (13.1%) of them. Apgar score was found to be normal in all of the participants with hypernatremia in the study which conducted by Boskabadi et al in which reported normal apgar scores among all neonates including those with hypernatremia [11].

The most commonly reported associated neonatal complication was found to be sepsis which reported in (89.8%) of the participants followed by neonatal jaundice which reported in about one third (31.1%) of the neonates and this was higher than that reported in Kenya in which prevalence of neonatal sepsis was found to be 28.6% [12].

In our study, (40.3%) were oligouric (15.5%) were anuric and (1%) were polyuric and the rest of them were normal. Concerning fluid status (69.9%) were euvolemic (27.7%) were hypovolemic and 5 (2.4%) were hypervolemic. Neurological symptoms were present in (34%) of the participants. Convulsions were found in (34%) of those who had neurological symptoms irritability in (15.5%) of the participants lethargy in (12.6%) of the participants and confusion in (9.7%) of them this was in consistent with the findings reported in the study by Fleicsher et al. which also stated that seizures are the most common neurological manifestation of hypernatremia in neonates [13].

Regarding sepsis workup; TWBCs were from 10000 – 25000 mg/ml in more than half (56.3%) of the participants 3000 – 10000 mg/ml in (24.8%) of the participants more than 25000 mg/ml in (12.6%) of the participants. CRP titer was from 6 – 20 mg/l in (28.6%) of the participants and 20 – 50 in (26.2%) of the participants 50 – 100 mg/l in (25.2%) and more than 100 in (19.9%) of the participants in regards to the previously mentioned CRP reading it was positive in nearly all patients with neonatal sepsis where as in the parallel study carried out by Hisamuddin et al. which found that only two-thirds of CRP were positive at initial assessment of neonates with sepsis [14].

Concerning renal function test (RFT) it was impaired in the vast majority (87.4%) of the participants; urea was found to be 100 – 200 in about (29.4%) of the participants urea level was 200 – 300 in about (28.3%) of them urea was found to be more than 300 in (24.4%) of the participants and 51 – 100 in about 32 (17.8%) of the participants. Serum creatinine was 1 – 3 mg/dl in about half (51.7%) of the participants 3 – 6 mg/dl in (21.1%) of the participants 6- 10 in (20.6%) of the participants and more than 10 in about 12 (6.7%) of the participants as hypernatremia and dehydration were considered to be an important risk factors for AKI in and about 18% of total cases which documented in the study conducted in India [15].

Those with impaired RFT significantly have higher sodium levels compared to others and this was reported in the congruent study conducted by Habib et al which linked acute kidney injury (AKI) with hypernatremic dehydration [16].

Conclusion

The most common reported clinical presentation was found to be sepsis, followed by neonatal jaundice, feeding refusal, diarrhea, vomiting and congenital malformations. Neurological symptoms convulsions, irritability & lethargy were reported as well. Other complications included sepsis and acute kidney injury (AKI). The most common laboratory findings which found to be associated with neonatal hypernatremia were elevated C - reactive protein (CRP), urea and creatinine.

Recommandations

We would like to recommend the following:

1. Check the renal function test (RFT) and électrolytes routinly to all hospitalized neonates.
2. Increase the awarness among doctors & medical profisionals to recognize clinical presentaion of neonatal hypernatremia.

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Consent

Ethical approval for this study was obtained from concerned authority of Sudan Medical Spcialization Broad, Ministry of Health, North Kordofan State and Al-Obied Specialized Pediatric Hospital Administration.

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