RESEARCH PAPER

Brain Injury Patterns in Neonates With Hypernatremic Dehydration: Single Center Experience

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Objective: To find out the incidence, spectrum, and topographical distribution of brain lesions in neonatal hypernatremic dehydration. **Method**s: We prospectively enrolled 100 consecutive neonates admitted with hypernatremic dehydration. 93 neonates underwent magnetic resonance imaging brain to identify the nature and site of neurological injury. **Results**: Neuroradiological lesions were found in 42 (45.2%) babies. Edema was the most common finding in 37 (39.8%), followed by hemorrhage in 13 (13.9%) and thrombosis in 6 (6.4%).Edema predominantly affected juxtacortical/subcortical white matter followed by periventricular white matter and centrum semiovale, posterior part of internal capsule, and basal ganglia/thalamus. Occipital horns of lateral ventricle were the main sites of hemorrhage. Thrombotic lesions predominantly involved sagittal, straight and transverse sinuses. Brain lesions were observed only in severe hypernatremia group. **Conclusion**: In neonatal hypernatremic dehydration, edema was the most common neurological lesion, followed by hemorrhage and thrombosis. Subcortical/juxtacortical white matter was the most commonly affected site.

Keywords: *Edema, Hemorrhage, Neuroimaging, Thrombosis*.

Neonatal hypernatremic dehydration (NHD) is a serious and potentially devastating condition, with cases being increasingly reported from all over the world [1]. Neurological involvement in NHD is considered dangerous, as it may not only produce acute neurological dysfunction, but also permanent brain damage [2]. In a recent study, one fourth of NHD cases had abnormal development at 6 months follow up [3].

Neuro-radiological changes developing in NHD still remain an under-researched area. Previous small studies have reported cerebral edema, brain hemorrhage, and cerebral venous sinus thrombosis in these neonates [4]. The exact incidence of brain lesions and patterns of injury are largely not known. This study was conducted to study magnetic resonance imaging (MRI) identified brain lesions, in the neonates admitted with hypernatremic dehydration.

METHODS

This study was conducted in 30-bedded dedicated extramural neonatal intensive care unit (NICU) of a teaching hospital among 93 neonates consecutively seen between August, 2018 and July, 2019. Ethical approval was taken from the institutional ethics committee, and written informed consent was obtained from the caregivers of enrolled neonates.

Our study population was outborn term neonates admitted with hypernatremic dehydration. Presence of any one of excessive weight loss (≥10%), oliguria or delayed skin turgor was considered as a clinical feature of dehydration. Serum sodium levels of these neonates were estimated along with other routine investigations. All neonates with serum sodium levels >150 mmol/L were enrolled. Those neonates who had any congenital malformation, history of delayed cry or Apgar score <8 at 1 minute after birth, hypoglycemia, sepsis, suspected inborn errors of metabolism, coagulopathy, history of abortion or unexplained sibling death, history of stroke, deep venous thrombosis, early age myocardial infarction or thromboembolic phenomena in family were excluded.

Fully automated analyzer (EM360, ERBA Diagnostics Manheim GmBH) was used to measure serum sodium levels. For MRI brain, 1.5 Tesla MRI machine (Achieva 1.5 T, Philips) was used. T1, T2, fluid attenuated inversion recovery, diffusion weighted imaging, apparent diffusion coefficient map, and gradient echo sequences were taken in all the cases. MRI reporting was done for all neonates by a single senior radiologist. Standard treatment protocols were universally followed in all babies (**Web Box I**).

The study by Unal, et al. [5] has reported the incidence of neuroradiological changes among hypernatremic dehydrated infants to be around 10% (with some newborns having more than one change). Assuming an incidence of 10%, with 5% absolute precision and 95% confidence interval, the calculated sample size was 94 neonates. Assuming an attrition of 5% due to in-hospital deaths, the final sample size was calculated to be 100.

Statistical analysis: Data were collected in Microsoft Excel sheet and were analyzed using SPSS 20.0 software.

RESULTS

A total of 100 hypernatremic neonates were enrolled; out of which seven died during hospital stay due to decompensated shock and associated respiratory failure, and remaining 93 were analyzed. Decreased urine output was the most common presentation (*n*=90, 96.8%), followed by poor acceptance of feed (*n*=76, 81.7%), fever (*n*=74, 79.6%), seizures (*n*=39, 41.9%), and jaundice (*n*=21, 22.6%). On examination, 54 (58%) babies were lethargic and 15 (16.1%) were irritable; and neonatal reflexes (Moro's, grasp, rooting and sucking reflexes) were depressed in 76 (81.7%) babies. Mean gestational age, birth weight and age at MRI scan were 39.61 (1.43) weeks, 2889 (0.48) grams and 11.81(1.03) days, respectively. Mean serum sodium, blood urea nitrogen and serum creatinine levels were 177.12 (11.90) mmol/L, 33.58 (19.7) mmol/L, and 309.47 (207.79) µmol/L, respectively. Most of the babies (*n*=46, 49.5%) had serum sodium levels exceeding 180 mmol/L, followed by 42 (45.2%) in 161-180 mmol/L category, and only 5 (5.4%) had mild hypernatremia.

Table I Magnetic Resonance Imaging Patterns of Cytotoxic Edema in Neonates With Hypernatremic Dehydration (N=37)

Site of lesion	*No. (%)*
Juxtaventricular white matter/ deep white matter (n=26)	
Periventericular white matter	14 (37.8)
Centrum semiovale	14 (37.8)
Internal capsule	13 (35.1)
Corona radiate	10 (27)
Capsuloganglionic region	9 (24.3)
Corpus callosum	9 (24.3)
Subinsular	1 (2.7)
Juxtacortical/subcortical white matter (n=21)	
Frontal	21 (56.7)
Parietal	21 (56.7)
Occipital	17 (45.9)
Temporal	14 (37.8)
Subinsular	1 (2.7)
Basal ganglia/thalamus	11 (29.7)
Cerebral cortex (n=6)	
Frontal	6 (16.2)
Parietal	6 (16.2)
Occipital	6 (16.2)
Temporal	3 (8.1)
Insular	1 (2.7)

Brain lesions were noted in 42 (45.2%) hypernatremic neonates with edema being the most common (*n*=37, 39.8%), followed by hemorrhage in 13 (13.9%), and thrombosis in 6 (6.4%) babies. Among the isolated lesions, cytoxic edema alone was noted in 24 (25.8%), and hemorrhage alone in 4 (4.3%) babies. None of the neonates developed isolated thrombosis, or both hemorrhage and thrombosis. Among combination of lesions, edema was associated with thrombosis in 4 (4.3%) babies, with hemorrhage in 7 (7.5%) babies, and with both thrombosis and hemorrhage in 2 (2.15%) babies. Cytotoxic edema predominantly affected juxtacortical/ subcortical white matter (*n*=21, 56.7%), followed by periventricular white matter and centrum semiovale (*n*=14, 37.8% each). Isolated white matter edema dominated the picture, it was observed in 21 (56.7%) brain edema patients (**Table I**). Fifteen hemorrhagic lesions were observed in 13 patients. Intraventricular hemorrhage (IVH) was the most common. Eight thrombotic lesions were observed in six patients. Superior saggital, transverse and straight sinuses were the most commonly affected site (**Table II**). Edema, hemorrhage and thrombosis were noted only when serum sodium levels exceeded 160, 170 and 180 mmol/L, respectively.

DISCUSSION

In the present hospital-based study conducted among 93 hypernatremic neonates; we observed brain lesions in 45.2% babies. The incidence of edema, hemorrhage, and thrombosis was 39.8%, 14%, and 6.4%, respectively. Cytotoxic edema affected both gray and white matter, but isolated involvement of white matter was more common. Brain edema, hemorrhage and thrombosis were noted only when serum sodium levels exceeded 160, 170 and 180 mmol/L, respectively.

The major limitations of our study are lack of a comparison group, and non-uniform timing of MRI brain scan. In our study MRI scan was carried out only after ensuring stability of the baby in the MRI suit. Lesions observed in our study cannot be purely ascribed to hypernatremic dehydration, as some of the complications might have evolved during rehydration therapy. However, for clinical purpose, outcome lesions (ultimate lesions at discharge) are more important than the initial insult.

As compared to previously available retrospective data [5], the incidence of brain edema, hemorrhage and thrombosis are approximately 5-10 times higher in the present study. Lack of neuroimaging in all cases,

WHAT THIS STUDY ADDS?

- Subcortical/juxta cortical white matter edema is the most common lesion in neonatal hypernatremic dehydration.

Table II Magnetic Resonance Imaging Patterns of Hemorrhagic and Thrombotic Brain Lesions in Neonates With Hypernatremic Dehydration (N=19)

Type	*No (%)*
Hemorrhagic lesions	13 (13.9)
Intraventricular hemorrhage (IVH)	
Bilateral occipital horns+ choroid plexus	3 (23)
Bilateral occipital horns	2 (15.3)
Left occipital horns+ choroid plexus	1 (7.7)
Subacute subdural hemorrhage (SDH)	
Overlies right temporal and right parietal lobe	1 (7.7)
Overlies left paramedian cerebellar convexity	1 (7.7)
Overlies posterior interhemispheric falx, tentorium, and posterior occipito parietal convexity	1 (7.7)
Late subacute subarachnoid hemorrhage (SAH)	1 (7.7)
Parenchymal hemorrhage	
Right frontoparietal, right centrum semiovale, left superior frontal	1 (7.7)
Left cerebellar hemisphere	1 (7.7)
Micro/punctiform hemorrhage	
Right parietal and left temporal lobe	1 (7.7)
Right occipital and right temporal lobe	1 (7.7)
Bilateral cerebellar hemisphere	1 (7.7)
Thrombotic lesions	6 (6.4)
Dural venous sinus thrombosis/ Subacute occlusive thrombosis of veins	
Straight sinus, trocula and bilateral transverse sinuses	2 (33.3)
Superior sagittal sinus	1 (16.7)
Anterior half of superior sagittal sinus, superior frontal cortical vein	1 (16.7)
Left transverse and sigmoid sinus, trocula, posterior one third of superior sagittal sinus, straight sinus, vein of galen, right internal cerebral vein, right basal vein of rosenthal	1 (16.7)
Vein of galen and bilateral internal cerebral veins	1 (16.7)

predominant use of ultrasonography and computerized tomography (CT) scan for brain imaging, and less severe hypernatremia might explain the lower incidence of brain lesions in the previous study. The most common type of lesion and/or combination of lesions has not been defined in previous studies [2,4,6,7], as these were based on few case reports/small case series or retrospective analyses. The most common site of lesions also remained inconclusive in the past except for thromboses, which in most case reports showed predominant involvement of sagittal, straight and transverse sinuses [8-11], similar to our findings. These findings are in contrast to adults with hypernatremia, in whom osmotic demyelination syndrome has been noticed as the most common neuroradiological lesion; extra pontine myelinolysis (EPM) being more common than central pontine myelinolysis (CPM) [12,13].

In our population besides hypernatremia, associated presence of uremia and metabolic acidosis might also have contributed to the neurological insults. Uremia predominantly affects the basal ganglia followed by cortical/subcortical regions and white matter. This pattern of injury has an important bearing on neurodevelopment, as reversibility is less and outcome is poor [12, 14]. Most of our babies had isolated white matter edema which usually carries a good prognosis. Associated involvement of basal ganglia and cortical/subcortical white matter might have been contributed by uremia and acidosis.

Our center caters to a wide spread of population of the Thar desert. Some of the settlements are located more than 300 km away from our center. Long travel probably further aggravates the dehydration in the neonates coming from far-flung areas. As almost half (49.5%) of our babies had serum sodium levels higher than 180 mmol/L, the present findings may not be generalizable to the predominantly mild hypernatremia group.

MRI brain should be advocated in all neonates admitted with hypernatremic dehydration, especially in severe hypernatremia (serum sodium levels exceeding 160 mmol/L). Further multi-centric research is required to focus on neuroradiological and neurodevelopmental outcomes of this high risk population. As brain edema, which was the most common lesion in our study, usually evolves during rehydration therapy, choice of rehydrating fluid and its rate of infusion also needs exploration.

Note: Additional material related to this study is available with the online version at *www.indianpediatrics.net*

Ethics clearance: Institutional Ethics Committee, Dr SN Medical College, Jodhpur. No. SNMC/IEC/2019/55 dated March 16, 2019.

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Web Box I Management Protocol of Hypernatremia Followed in the Study

Clinical status and intervention
Fluid resuscitation in shock Intravenous bolus of isotonic saline, 10 mL per kg, repeated as required
Initial rehydration and correction of hypernatremia Free water deficit (36-48 ml per kg per 24 hour) plus usual maintenance fluid, targeting reduction in serum sodium at a rate of 0.5mmol/l per hour
Subsequent rehydration and correction of hypernatremia Serum sodium levels were checked every 6 hour. Subsequent composition of fluid and its rate of infusion was guided by drop in serum sodium levels and urine output
Parameters monitored
Clinical and non-invasive monitoring Heart rate, respiratory rate, SpO_2, and temperature were continuously monitored. Blood pressure, capillary refill time and Urine output were checked at every one hour.
Blood/serum parameters Serum electrolytes (sodium, potassium, and calcium), blood sugar and blood gas - every 6 hourly initially. Renal function tests (serum urea, creatinine), and liver function tests (serum bilirubin, serum aspartate aminotransferase, serum alanine aminotransferase) – daily initially. Complete hemogram was done on admission, and was repeated, if abnormal hematocrit or platelet deficiency was observed or required correction.