# Stroke from systemic vascular disorders in Saudi children

## *The devastating role of hypernatremic dehydration*

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## ABSTRACT

Systemic vascular disorders, leading to childhood stroke, include volume depletion or systemic hypotension and hypernatremic dehydration. We describe 3 cases of stroke following systemic vascular disorders. These were diagnosed during a prospective and retrospective study on childhood stroke, which included 104 patients. Post-gastroenteritis hypernatremic dehydration is an important, potentially preventable, cause of stroke in Saudi children.

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A variety of systemic vascular disorders are known to cause stroke during childhood with significant morbidity and mortality. These include volume depletion on systemic hypotension and hypernatremic dehydration.[1,2] In the present report, we describe 3 cases of stroke due to systemic vascular disorders, who were diagnosed during a prospective (February 2001 to March 2003) and retrospective (July 1992 to February 2001) combined study on childhood stroke which extended for 10 years and 7 months.[3]

**Case Reports.** Three children had stroke due to systemic vascular disorders following cardio-respiratory arrest in one patient, and hypernatremic dehydration in another 2. A summary of the clinical features of these patients is shown in **Table 1**.

***Patient One.*** This 34-month-old boy sustained a stroke due to cardiopulmonary arrest following general anesthesia for orchiopexy and herniorrhaphy. Neurological sequelae of the cerebral insult consisted of generalized seizures, bilateral motor deficit, aphasia and cognitive deficits. Investigations showed normal complete blood count (CBC), erythrocyte sedimentation rate (ESR), prothrombin time (PT), activated partial thromboplastin time (APTT), anion gap estimation, and serum lactate. An EEG revealed diffuse slowing bilaterally. Visual evoked response (VER) showed no reproducible potentials whereas electroretinogram (ERG), brainstem auditory evoked potentials (BAEP), ECG, and chest x-ray were normal. Brain MRI depicted lacunar infarcts in the brainstem and cerebellum.

***Patient 2.*** A 27-month-old boy was evaluated at the Division of Pediatric Neurology (DPN) because of spastic diplegic cerebral palsy. He was developing normally until the age of 7 months when he had an episode of diarrhea complicated by hypernatremic dehydration. He was admitted to a regional hospital where he remained on a ventilator for one month

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**Table 1-** Characteristics of patients with stroke due to systemic vascular disorders.

| Patient | Gender | Age at onset of initial stroke (years) | Age when evaluated at DPN (years) | Focal cranial CT/MRI lesions | Underlying cause | Neurological features | Duration of follow-up (years) | Outcome |
|---|---|---|---|---|---|---|---|---|
| 1 | Male | 2.8 | 2.8 | Lacunar infarcts in the brainstem and cerebellum | Cardiorespiratory arrest following general anesthesia for orchiopexy and herniorrhaphy | Generalized seizures, bilateral motor deficit | 1.5 | Alive |
| 2 | Male | 0.6 | 2.3 | Bilateral frontal cystic lesions. Features of previous hemorrhage in the region of left basal ganglia | Hypernatremic dehydration secondary to diarrheal disease | Spastic diplegia, dysphasia and cognitive deficits | 7.5 | Alive |
| 3 | Female | 0.8 | 0.8 | Gyral petechial hemorrhages. Widespread gyral and subcortical enhancement involving grey/white matter junction after contrast injection. Features of global hypoxic/ischemic insult | Hypernatremic dehydration secondary to diarrheal disease | Coma, decerebrate abnormal movement with right hand twitching. Spastic quadriplegia | 2 | Alive |

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because of respiratory failure associated with acute renal failure. On examination, he was wheelchair bound and had spastic diplegia associated with retarded cognitive development. Brain MRI (**Figure 1**) showed bilateral, well-defined cystic lesions in the frontal lobes, marginating the anterior horns of the lateral ventricles. Diffuse, symmetrical, T2-hyperintensity was seen in the periventricular distribution representing periventricular leukomalacia. Diffuse thinning of the corpus callosum was also seen. There was a T2-hypointense lesion in the left basal ganglia region consistent with hemosiderin effect from previous bleed in this location. Other investigations revealed normal PT, APTT, visual evoked potentials (VEPs) and ERG. Serum was negative for brucella antibodies. The BAEP revealed mild left conductive hearing loss. He showed sustained improvement with rehabilitation and orthopedic surgeries, and at the age of 11 years he could walk when aided. His intelligence quotient (IQ) was 40%.

***Patient 3.*** A 10-month-old girl was admitted to the Pediatric Intensive Care Unit (PICU) at King Khalid University Hospital (KKUH) in hypovolemic shock secondary to severe diarrhea and vomiting. Her blood pressure was unrecordable, and she was comatose and severely acidotic. Her eyes were slightly sunken, cornea and lips were dry, and skin was doughy. Axillary temperature was $37^0$C, initial serum sodium on admission was 174 mmol/L and serum osmolality was 360 mOsmol/kg $H_2O$ (N=275-295). Neurologically, she showed decerebrate posture with hypertonia and hyperreflexia and was ventilated empirically because of her general condition. Her clinical course in the PICU was complicated by the development of cerebral edema, epilepsy (in the form of hand twitching associated with tachycardia), pulmonary hemorrhage, features of disseminated intravascular coagulation, supraventricular tachycardia and one episode of cardiac arrest. Her serum sodium was fluctuating from the start, and the highest recorded level was 185 mmol/L. She was managed with slow fluid correction over 4 days and serum sodium was reduced to 140 mmol/L. An EEG (recorded one day after admission) showed features of severe degree of encephalopathy. Other tests included VEP, ERG, BAEP and echocardiography. All of these showed normal results. Brain MRI (carried out 25 days after admission) showed hyperintense signal in some of the gyri of both frontal lobes (**Figure 2**). These were seen on T1 and T2 - weighted proton density and fluid-attenuated inversion recovery (FLAIR) images, and represented ischemic insult with gyral petechial

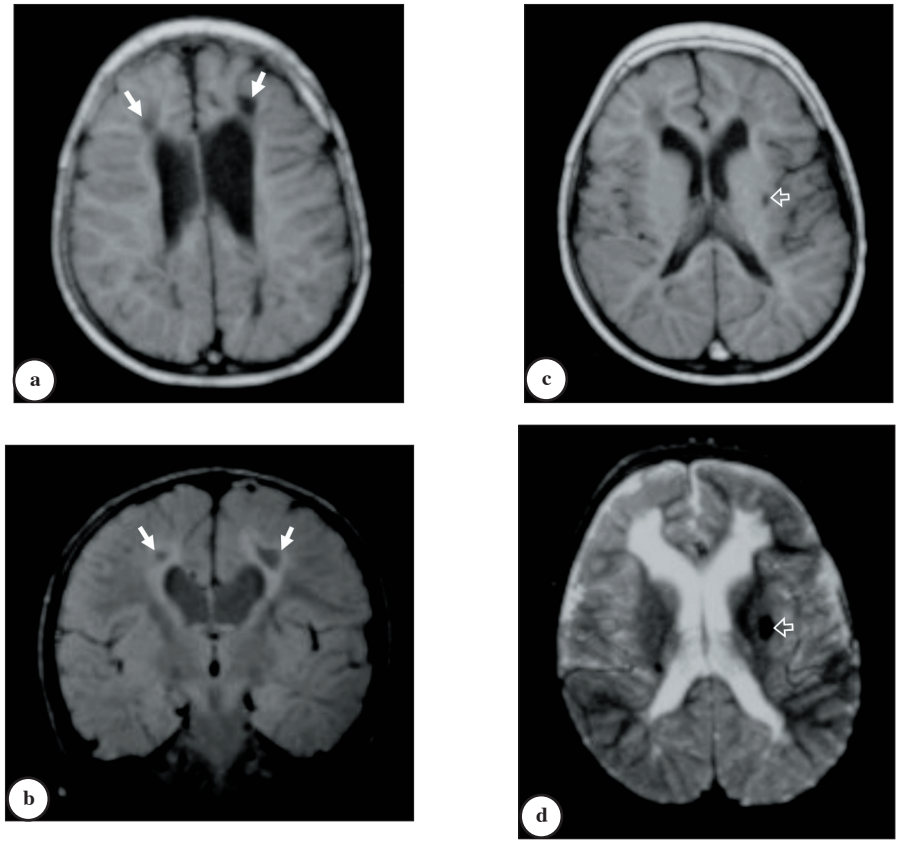


**Figure 1 -** **a)** Axial T1-weighted (T1W) and **b)** coronal proton density-weighted MR images of the brain of a child with cystic leukomalacia (arrows) due to prior ischemic insult. **c)** Axial T1W image and **d)** T2W (spin-echo) image showing focal area of hemosiderin deposition (open arrow) in the region of left basal ganglia. Note that the lesion appears larger on T2W image due to magnetic susceptibility effect.

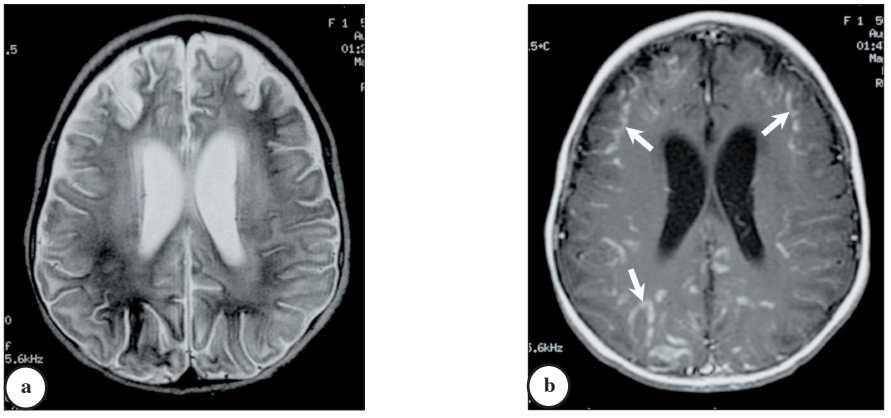


**Figure 2 -** **a)** Axial T2-weighted MR image of the brain showing cortical and white matter high signal intensity areas due to ischemic insult. **b)** Enhanced axial T1-weighted MR image showing multiple areas of enhancement at the grey/white matter junction (arrows).

hemorrhages. Mild to moderate enlargement of the ventricular system and widened cerebral sulci were also seen. After gadolinium injection (**Figure 2**), there was striking gyral and subcortical enhancement involving the grey/white matter junction. Meningeal enhancement was also seen in some areas. The cerebellum and brainstem were not involved. She survived the stormy illness with residual spastic quadriplegia, severe cognitive deficits, and complex partial seizures.

**Discussion.** In this cohort of 104 Saudi children, stroke following systemic vascular disorders manifested in 3 (2.9%). The mechanism of cerebral injury (**Table 1**) was due to systemic hypotension in a 34-month-old boy who had cardiorespiratory arrest following general anesthesia for orchiopexy and herniorrhaphy. The other 2 children (**Table 1**: Patients 2 and 3) had stroke following episodes of hypernatremic dehydration. Hemorrhagic encephalopathy is a well-recognized complication of hypernatremia,[4-6] which usually follows dehydration secondary to childhood diarrheal diseases.[7-10] The mechanism of hemorrhage is probably due to hyperosmolar endothelial damage and venous rupture following traction which results from shrinkage of the surrounding brain tissue.[7-11] Multiple pericapillary hemorrhages, or capillary thrombosis are characteristic, although intraparenchymal hemorrhage and sinovenous thrombosis have been documented.[12-15]

Hypernatremic dehydration following gastroenteritis has been well documented in Saudi Arabia. In a prospective study by Karrar and Abdullah[16] from Riyadh over a 4-month period (September 1980 – February 1981), hypernatremia occurred in 12.6% of 254 children admitted with gastroenteritis. Almost 85% of the 254 children were under one year old, 46.5% were <5 months and 65.4% were bottle-fed. Only 20% of the mothers used boiling or chemical means of sterilizing the bottles. The incidence of second and third-degree malnutrition was 38.8%. While mothers of children with hypotonic dehydration tended to dilute the feeds, mothers of hypertonic dehydrated children tended to concentrate them. The authors[16] expressed their concern about the high incidence of bottle-feeding and its consequences to infant health. Approximately 5 years later, a prospective study from the Northern Region[17] described 25 children who had hypernatremic dehydration. These belonged to a group of 520 children who were admitted with gastroenteritis during June 1985 – June 1986. All of the 25 children with hypernatremia were <1 year of age and 23 (92%) were under 6 months. All babies were bottle-fed, and the majority of mothers did not know the appropriate water/milk proportions or how to prepare food hygienically. Moreover, the majority of infants were underweight for their age and 20 (80%) came from families who lived in the villages and had a poor educational background. Two children died, and one had residual neurological sequelae. The authors[17] reaffirmed the importance of breastfeeding and the need for public education in the proper preparation of bottle feeds when breast-feeding is not possible. A study,[18] carried out more than a decade later in another similar population, reiterated the same recommendations. A study from Riyadh by Abdullah[19] on 300 children (mean age of 14 months) admitted with gastroenteritis between 1984 and 1988 showed that only 11% of them had exclusive breast-feeding. Hypernatremic dehydration was present in 2%. Oral rehydration solution (ORS) was used in 22%, and 13% were given intravenous fluids plus ORS. The author[19] highlighted the urgent need to encourage the use of ORS. It is noteworthy that in a later publication, Altuntas et al[20] reported successful management of hypernatremic dehydration following acute gastroenteritis with ORS. Also, the following years witnessed an increase in the use of ORS in Saudi Arabia. A national survey[21] carried out in 1991, found that ORS was used in 73% of children under 5 years with diarrhea. There was a 25% increase in the use of ORS over the previous Saudi findings in 1987.

Two other studies from the Western and Eastern Provinces reported similar findings. The earlier one was a cross-sectional study of diarrhea in the under-fives in a semi-urban community in the Eastern Province.[22] The point prevalence of diarrhea was found to be 5.4% and the period prevalence was 12.5%. In children <1 year, the prevalence of diarrhea was significantly associated with age of the child and type of feeding. Other significant associations with diarrhea were parental age and education, and the number of children <5 years in the household. The authors[22] recommended the establishment of health education programs to educate mothers on diarrhea, and establishing "under-fives" clinics. The second study was from the Western Province,[23] reported on 1726 diarrhea cases (mean age of 20.2 months) and found that mothers of affected children were mostly housewives with low educational level. Bottle-fed children showed higher proportions (53.1%) of diarrhea than children fed otherwise, suggesting the feco-oral route of infection and the effect of poor sanitation. A recent study[24] using the setting of primary health care centres (PHCCs) in Riyadh estimated that in children <2 years of age, the diarrheal episodes were about 6 per child per year. Approximately 25% of mothers stopped or decreased breast-feeding

during diarrheal episodes, 11.3% reduced the volume of fluids given to their children, and 22.7% of affected children were fed less solid/semi-solid foods. The authors[24] concluded that diarrhea is still common in children <2 years old in Riyadh City and recommended that intervention (based in PHCCs) be undertaken to correct the faulty practice of mothers during diarrhea episodes in their children.

Recently, the incidence and complications of breastfeeding-associated hypernatremic dehydration in neonates caused worrying epidemiological concerns. It was reported by Moritz et al[25] to affect 1.9% of 3718 breastfed neonates, the cause being lactation failure usually in primiparous women (87%) who were discharged from hospital within 48 hours after birth (90%). This insufficient breast milk syndrome, which leads to high sodium concentration in breast milk, has been reported from Saudi Arabia[26] as well as the Gulf Region.[27] The study from Saudi Arabia[26] suggested measures to combat this potentially life-threatening condition. These consisted of encouraging initiation of lactation in the delivery room, discouraging artificial feeding in the first few postnatal days, close supervision of lactating mothers especially primiparous and providing emotional as well as technical support for nursing mothers.

The study highlights the significant role which post-gastroenteritis hypernatremic dehydration plays in the causation of stroke in Saudi children and the inherent risks in its management. Most recently, repeated diffusion MR imaging studies were found to be useful in monitoring the rehydration therapy program by allowing an in vivo insight into brain changes during hypernatremic dehydration.[28] Preventive measures at primary and secondary levels can eliminate this dangerous form of dehydration due to hypernatremia and the inherent risk of therapy.

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