# Encephalopathy with acute gastroenteritis: an Upper Egypt tertiary center study

Mena M. Attia, Gamal A. Askar, Shereen M. Galal

Department of Pediatrics, Faculty of Medicine, Assiut University, Assiut, Egypt

Correspondence to Mena M. Attia, MSc, Department of Pediatrics, Faculty of Medicine, Assiut University, Assiut, Egypt.
Postal Code 4111;
Tel: +20 122 073 4934;
e-mail: menamagdykolta1@yahoo.com

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**Introduction**

Gastroenteritis is a digestive tract infection that can be caused by viral, bacterial, and parasitic pathogens. The most common symptoms include diarrhea and vomiting, which can be accompanied by fever and abdominal pain. Encephalopathy is a generalized disorder of cerebral function that may be acute or chronic, progressive, or static. Encephalopathy was defined as depressed or altered level of consciousness, lethargy, or personality change lasting more than 24 h. The aim of this study was to identify the frequency and outcome of encephalopathy with acute gastroenteritis (AGE) owing to various metabolic causes such as hyponatremia, hypernatremia, hypocalcemia, and hypoglycemia for children younger than five years admitted at the gastroenterology unit.

**Materials and methods**

A cross-sectional study was carried out at the gastroenterology unit of Assiut University Children Hospital from May 1, 2018 to April 30, 2019 during a period of 1 year. A total of 2236 cases complaining of AGE were admitted during this period, and the study comprised 100 children complaining of encephalopathy with AGE.

**Results**

Among 100 patients, males were 55% and females were 45%. Overall, 62% were younger than 12 months of age, 35% were within 12–24 months of age, and 3% were above 24 months of age. All 100 patients enrolled in this study had signs of encephalopathy with acute diarrhea. Overalll, 51% had hyponatremia, 46% had hypernatremia, 21% had hypocalcemia, and 13% had hypoglycemia.

**Conclusion**

Electrolyte disturbances such as hyponatremia, hypernatremia, hypocalcemia, and also hypoglycemia are still major causes of encephalopathy with AGE.

**Keywords:**
diarrhea, encephalopathy, hypernatremia, hypocalcemia, hypoglycemia, hyponatremia

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## Introduction

Acute diarrhea is one of the principal causes of morbidity and mortality among children in low-income countries. Mostly, gastroenteritis occurs in the winter and early spring, and the most common cause for this is rotavirus [1]. Diarrhea is a common cause of deaths in all children and is the second most common cause in those aged over 1 month [2]. An average of 1.66 billion deaths occurred in 2014 in infants younger than the age of 5 years in developing countries, of whom ~80% were from Africa, South Asia, and Middle East [3]. The leading causes of mortality from acute diarrhea are dehydration, electrolyte disorders, and their associated complications [4]. Identifying the specific etiologic agent responsible for the acute gastroenteritis (AGE) rarely changes management. However, it may be helpful to differentiate between viral, bacterial, parasitic, and noninfectious causes of diarrhea. Rotavirus represents the most important viral pathogen worldwide, responsible for 37% of diarrhea-related deaths in children younger than 5 years [5]. The major complications from diarrhea from any cause are dehydration, electrolyte, acid-base derangements, bacteremia, disseminated intravascular coagulation, and hemolytic uremic syndrome, which can be life-threatening. Avoiding delays in diagnosis and treatment and appropriate supportive care using either oral, enteral, or intravenous hydration can prevent or treat most of these conditions [6]. The aim of the study was to identify the frequency and outcome of encephalopathy with AGE owing to various metabolic causes such as hyponatremia, hypernatremia, hypocalcemia, and hypoglycemia for children younger than 5 years admitted at the gastroenterology unit.

## Materials and methods

A cross-sectional study was carried out at the gastroenterology unit from May 1, 2018 to April 30,

2019 during a period of 1 year. A total of 2236 cases complaining of AGE were admitted during this period, and the study comprised 100 children complaining of encephalopathy with AGE.

### Inclusion criteria

Children younger than 5 years of age who complained of AGE (Loose motion at least three episodes in 24 h of < 14 days), presenting with one or more of the signs of encephalopathy, including altered mental status, irritability, and Convulsion, during the episode of AGE owing to electrolyte disturbances (hyponatremia, hypernatremia, and hypocalcemia) or hypoglycemia were included.

### Exclusion criteria

The following were the exclusion criteria:

(1) Children who have a diarrhea lasting more than 14 days.
(2) Children having associated other diseases such as protein-energy malnutrition, liver cirrhosis, heart failure, renal failure, and congenital malformations related to epilepsy.
(3) Children with neurological diseases or epilepsy.
(4) Children with intracerebral inflammation (meningitis or encephalitis).
(5) Noninfectious causes of encephalopathy (toxic or metabolic encephalopathy owing to other than electrolyte disturbance or hypoglycemia).
(6) Systemic diseases causing irritability in children such as otitis media and urinary tract infection.
(7) All cases included in our study had not been vaccinated by rotavirus vaccine.

### Clinical evaluation

All patients included in this study were subjected to the following:

(1) The data were collected through a preformed proforma by taking consent from the parents, and all such maneuvers were as per the medical ethics.
(2) Each child with AGE was assessed by taking history from mother/caregiver. For each patient, we asked about age, sex, residency, history of rotavirus vaccination, fever (defined as body temperature >37.5°C), gastrointestinal symptoms (vomiting and its frequency and duration, diarrhea and its frequency and duration, and presence or absence of bloody stool).
(3) Family history of convulsions (febrile convulsion, neurological diseases, or epilepsy).
(4) Physical and systemic examination. Anthropometric measurements such as weight, height, BMI, and head circumference were done. Hydration status was assessed.
(5) Complete neurological, chest, heart, and abdominal examination was done. Urological and ENT examination was also done to exclude urinary tract infection and otitis media, respectively, as causes of fever and irritability in children.
(6) Investigations:
    (a) Serum electrolytes (serum sodium and ionized calcium).
    (b) Random blood glucose.
    (c) Cerebrospinal fluid examination (in selected febrile cases).
    (d) Electroencephalography (in selected cases).
    (e) Neuroimaging: computed tomography brain (in selected cases).

### Ethical considerations

The aim of the study was explained to the parents of each child before the beginning of the process. A written consent was obtained from those who agreed to participate in the study. Privacy and confidentiality of all data were assured. The study was approved and monitored by the Medical Ethics Committee, Assiut Faculty of Medicine. IRB#17100038.

### Sampling

After admission of each child, 2 ml of whole blood was collected under complete aseptic conditions at the time of insertion of intravenous cannulation before giving intravenous fluids to measure serum levels of sodium, ionized calcium, and random blood glucose. Lumbar puncture and cerebrospinal fluid examination were done for febrile patients to exclude central nervous system infection (meningitis and encephalitis) as a cause of encephalopathy.

### Statistical analysis

The data were tested for normality using the Kolmogorov–Smirnov test and for homogeneity variances before further statistical analysis. Categorical variables were described by number and percentage,

**Table 1 Sociodemographic characteristics of patients**

| Parameters | Range | Mean±SD |
|---|---|---|
| Sex [*n* (%)] | | |
| Male | 55 (55) | |
| Female | 45 (45) | |
| Age level [*n* (%)] (months) | | |
| <12 | 62 (62) | 9.97±5.07 |
| 12-24 | 35 (35) | |
| >24 | 3 (3) | |
| Length range (m) | 0.49-0.83 | 0.69±0.07 |
| Weight range (kg) | 3-12 | 7.76±2.13 |
| BMI range | 9.47-21.3 | 15.82±2.39 |

where continuous variables were described by mean and SD. $\chi^2$-test used to compare between categorical variables where comparison between continuous variables was done by *t*-test (one-way analysis of variance). A two-tailed *P* less than 0.05 was considered statistically significant. All analyses were performed with the IBM SPSS 20.0 software (International Business Machines Corporation is an American multinational technology company headquartered in Armonk, New York).

## Results

Tables 1–7. Majority of patients admitted were below 24 months of age i.e., 97 (97%). 62 patients (62%) were below 12 months of age, 35 patients (35%) were within 12-24 months of age and three patients (3%) were above 24 months of age. Among 100 patients males were 55 (55.0%) and females were 45 (45.0%).

All 100 patients enrolled in this study had signs of encephalopathy. 22 patients (22%) had a mild encephalopathy (GCS=13-15). 71 patients (71%) had a moderate encephalopathy (GCS=9-12). 7 patients (7%) had a severe encephalopathy (GCS<9). The mean GCS was 11.72 ± 1.22 (the range was 8-13). 2 0 patients had convulsions. 13 patients had generalized tonic-clonic (GTC) Convulsions and 7 patients (38.9%) had focal convulsions (p. value = 0.001).

Of 100 patients, 56 patients (56%) had a fever (p. value <0.030). 43 patients of them (76.8%) had a low grade fever (37.5°C-38.3°C) (p. value <0.001) and 13 of them (23.2%) had a high grade fever (>38.3°C).

Among 100 patients, 51 patients (51%) had hyponatremia. one patient of them (2%) had a mild hyponatremia. 7 patients of them (13.7%) had a moderate hyponatremia. 43 patients of them (84.3%) had a severe hyponatremia.

46 patients (46%) had hypernatremia. 38 patients of them (82.6%) had a moderate hypernatremia. 8 patients of them (17.4%) had a severe hypernatremia.

21 patients (21%) had a hypocalcemia. 13 patients (13%) had a hypoglycemia.

Regarding the outcome of all 100 studied cases, most cases had clinical improvement and were discharged [89 cases (89%)], no cases (0%) had permanent neurological sequelae, and 11 cases (11%) died (p. value=0.016). The mean duration of hospital admission

**Table 2 Duration and frequency of diarrhea and presence of bloody diarrhea in relation to patients' age**

| Parameters | Age levels | | *P* |
|---|---|---|---|
| | <12 months (*n*=62) | 12-60 months (*n*=38) | |
| Acute diarrhea | | | |
| 1-6 days | 52 (83.9) | 26 (68.4) | 0.117 |
| 7-13 days | 10 (16.1) | 12 (31.6) | 0.116 |
| Bloody diarrhea | 8 (12.9) | 4 (10.5) | 0.967 |
| Frequency of diarrhea | | | |
| <5 times/day (mild diarrhea) | 2 (3.2) | 0 | 0.708 |
| 5-10 times/day (moderate diarrhea) | 37 (59.7) | 21 (55.3) | 0.823 |
| >10 times/day (severe diarrhea) | 23 (37.1) | 17 (44.7) | 0.587 |
| Dehydration | | | |
| Moderate | 35 (56.5) | 24 (63.2) | 0.651 |
| Severe | 27 (43.5) | 14 (36.8) | 0.653 |

**Table 3 Presence or absence of fever and grades of fever in relation to patients' age**

| Parameters | Age levels | | *P* |
|---|---|---|---|
| | <12 months (*n*=62) | 12-60 months (*n*=38) | |
| Fever | | | |
| Present | 29 (46.8) | 27 (71.1) | 0.030* |
| Absent | 33 (53.2) | 11 (28.9) | 0.031* |
| Grade | | | |
| Low grade (37.5-38.3°C) | 21 (72.4) | 22 (81.5) | <0.001* |
| High (>38.3°C) | 8 (27.6) | 5 (18.5) | 0.637 |

*Statistically significant.

**Table 4 Grades of encephalopathy and characteristics of convulsion in relation to acute diarrhea duration**

| Parameters | Acute diarrhea duration | | *P* |
|---|---|---|---|
| | 1-6 days (*n*=78) | 7-13 days (*n*=22) | |
| Encephalopathy | 78 (100) | 22 (100) | 1.000 |
| Encephalopathy grade | | | |
| Mild (GCS=13-15) | 21 (26.9) | 1 (4.6) | 0.051 |
| Moderate (GCS=9-12) | 53 (68) | 18 (81.8) | 0.316 |
| Severe (GCS<9) | 4 (5.1) | 3 (13.6) | 0.364 |
| Convulsion | 18 (23.1) | 2 (9.1) | 0.251 |
| GTC | 11 (61.1) | 2 (100) | 0.001* |
| Focal | 7 (38.9) | 0 | 0.001* |

GCS, Glasgow coma scale; GTC, generalized tonic-clonic.
*Statistically significant.

**Table 5 Serum electrolytes and random blood glucose in relation to acute diarrhea duration**

| Parameter | Acute diarrhea duration | | *P* |
|---|---|---|---|
| | 1-6 days (*n*=78) | 7-13 days (*n*=22) | |
| Hypernatremia | | | |
| Moderate (150-169 mEq/l) | 28 (35.9) | 10 (45.5) | 0.568 |
| Severe (>170 mEq/l) | 7 (9) | 1 (4.5) | 0.809 |
| Hyponatremia | | | |
| Mild (130-134 mEq/l) | 1 (1.3) | 0 | 0.505 |
| Moderate (125-129 mEq/l) | 5 (6.4) | 2 (9.1) | 0.972 |
| Severe (<125 mEq/l) | 34 (43.6) | 9 (40.9) | 0.986 |
| Hypocalcemia (<0.8 mmol/l) | 18 (23.1) | 3 (13.6) | 0.503 |
| Hypoglycemia (<50 mg/dl) | 12 (15.4) | 1 (4.5) | 0.325 |

**Table 6 Serum electrolytes and random blood glucose in relation to encephalopathy grade**

| Parameters | Encephalopathy grade | | | *P* |
|---|---|---|---|---|
| | Mild (GCS=13-15) (*n*=22) | Moderate (GCS=9-12) (*n*=71) | Severe (GCS<9) (*n*=7) | |
| Isolated hypernatremia | 5 (22.7) | 22 (31) | 1 (14.3) | <0.001* |
| Isolated hyponatremia | 9 (40.9) | 29 (40.8) | 3 (42.9) | <0.001* |
| Hypernatremia+hypocalcemia | 2 (9.1) | 8 (11.3) | 0 | 0.114 |
| Hypernatremia+hypoglycemia | 0 | 5 (7) | 2 (28.6) | 0.450 |
| Hyponatremia+hypocalcemia | 1 (4.5) | 3 (4.2) | 0 | 0.617 |
| Hyponatremia+hypoglycemia | 1 (4.5) | 2 (2.8) | 1 (14.3) | 0.779 |
| Hyponatremia+hypocalcemia+hypoglycemia | 1 (4.5) | 1 (1.4) | 0 | 0.480 |

*Statistically significant.

**Table 7 Outcome and duration of hospital stay in relation to patients' age**

| Parameters | Age levels | | *P* |
|---|---|---|---|
| | <12 months (*n*=62) | 12-60 months (*n*=38) | |
| Outcome | | | |
| Survivors | 52 (83.9) | 37 (97.4) | 0.138 |
| Deaths | 10 (16.1) | 1 (2.6) | 0.016* |
| Hospital stay | | | |
| Duration (days) | 4-12 | 1-12 | |
| Mean±SD | 6.97±1.67 | 7.06±2.01 | 0.809 |

*Statistically significant.

in days at age 1–12 months was 6.97 ± 1.67 (range was 4–12 days) and at age more than 1–5 years was 7.06 ± 2.01 (range was 1–12 days).

## Discussion

Encephalopathy with AGE owing to electrolyte disturbance and/or hypoglycemia is common between infancy and early childhood, younger than five years of age.

Our study found that most patients (97%) were younger than 2 years, 62 patients (62%) were younger than 12 months, and 35 patients (35%) were between 12 and 24 months, whereas only three patients (3%) were above 2 years of age and median age was 9 months. Male patients (55%) were more than females (45%). Shah *et al.* [7] also found that most patients (70%) were younger than 2 years of age. There were 37 (65%) males and 20 (35%) females.

Regarding the type and frequency of convulsion among all 100 studied cases, we found that 13 cases (65%) had a generalized tonic-clonic type and seven cases (35%) had a focal type. This is in agreement with the study done by Zerr *et al.* [8] who mentioned that the most common type of convulsion of nonfebrile illness seizures associated with a history of diarrhea was the generalized tonic-clonic type (86%) followed by the focal type (6%).

Regarding the laboratory investigation, it was observed that hyponatremia was present in 51 cases (51%), hypernatremia as a complication of AGE was present in 46 cases (46%), and hypocalcemia was present in 21 cases (21%). Our study also had found that hyponatremia was the most common electrolyte disturbance occurring owing to AGE, leading to encephalopathy in 51 patients (51%), and three of them had GTC convulsions. Zifman *et al.* [9] and Ueda *et al.* [10] suggested that hyponatremia or rapid decline in serum sodium levels (but a mild degree of hyponatremia) may result in seizure. Shah *et al.* [7] found that the most common electrolyte disturbance was hyponatremia (56%), whereas hypernatremia was present in 10% of cases. The pathogenesis of hyponatremia in diarrhea is due to a combination of Sodium loss and water loss, and water retention is needed to compensate the volume depletion. The explanation for hypernatremia could be owing to inadequate free water intake or increased sodium intake through improperly prepared oral rehydration solution. According to a study by Chouchane *et al.* [11], hypernatremia was present in 11.51% cases of all kinds of dehydration. Kari Johansen *et al.* [12] also reported in a Swedish study that hypernatremia was caused as a result of RV + AGE (Rotavirus-positive AGE) in ~10% of cases. Hypernatremia is indicative of hypertonic dehydration and puts children at special risk for neurological sequelae, either due to hypertonicity itself or due to cerebral edema, which may be caused by too rapid decrease of sodium concentration in serum after initiation of intravenous rehydration. As more than 75% of cases with hypernatremia were due to RV infection, prevention of RV infection is the key. This is best achieved by vaccination of all infants against RV. Children with ongoing AGE should receive early oral rehydration therapy with low sodium concentrations (60 mmol/l) [13].

In our study, 21 patients (21%) had hypocalcemia, which was an important cause of encephalopathy, focal and GTC convulsions. Either it was isolated hypocalcemia or mixed with hyponatremia, hypernatremia, or hypoglycemia. In a case-control observational study about serum calcium level in acute diarrhea, Purohit *et al.* [14] found that 28 (28%) of 100 cases had hypocalcemia, based on the cutoff value

for defining hypocalcemia in their study of less than 8.5 mg/dl. In another study of 66 cases and 66 controls about 'Hypocalcemia in AGE', Devrajani *et al.* [15] found hypocalcemia in 94% cases of acute diarrhea, based on the cutoff value for defining hypocalcemia in their study of less than 9.0 mg/dl.

Hypoglycemia was present in 13 cases (13%). This is in agreement with the a study done by Vafaei *et al.* [16] who stated that hypoglycemia was found in 7.2% of cases. There is a lack of literature describing hypoglycemia as a complication of dehydration owing to AGE; a study by Reid *et al.* [17] about hypoglycemia complicating dehydration owing to AGE mentioned that seizure was present in 35% of cases.

Regarding the outcome of all 100 studied cases, most cases had clinical improvement and were discharged [89 cases (89%)], no cases (0%) had permanent neurological sequelae, and 11 cases (11%) died. The mean duration of hospital admission in days at age 1–12 months was 6.97 ± 1.67 (range was 4–12 days) and at age more than 1–5 years was 7.06 ± 2.01 (range was 1–12 days). This is in agreement with a study conducted in Tabriz Children's Hospital during 2001 to 2016 by Vafaei *et al.* [16] about the determinant factors in seizure following gastroenteritis, and it was noticed that most cases had a good prognosis, Moreover, the findings was also in agreement with the study by Hong *et al.* [18].

## Conclusion

AGE is one of the principal causes of morbidity and mortality among children in low-income countries. The major complications from diarrhea from any cause are dehydration; electrolyte or acid-base derangements; intussusception; bacteremia; hemolytic uremic syndrome; seizures; or encephalopathy, which can be life-threatening. The small age group (<12 months) was more susceptible to complications than older age group. In the present study, electrolyte disturbances such as hyponatremia, hypernatremia, and hypocalcemia and also hypoglycemia were still the major causes of encephalopathy with AGE. Outcome of the cases enrolled in our study was good. Most of the cases survived and were discharged. Few cases died. No permanent neurological sequelae were observed in our survived cases.

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**Conflicts of interest**
There are no conflicts of interest.

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