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# Frequency of Hyponatremic Dehydration in Children (6-59 Months) Presenting with Acute Gastroenteritis in a Tertiary Care Facility

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## ABSTRACT

Acute gastroenteritis (AGE) is one of the primary morbid and mortal causes among children under five years old, especially in low- and middle-income countries (LMICs). **Objective:** To determine the frequency of hyponatremic dehydration in children aged 6 to 59 months with acute gastroenteritis. **Methods:** The cross-sectional design was employed in the Pakistan Atomic Energy Commission (PAEC) General Hospital, Islamabad. Non-probability consecutive sampling of children aged 6-59 months of both genders with acute gastroenteritis over six months, from 1st August 2025 to 31st January, 2026, was used to enroll the children. The exclusion criteria were chronic diarrhea, previous administration of intravenous fluids, septic shock, severe malnutrition, chronic illness (CKD, CHD, RTA, CAH), or use of diuretic/steroids. SPSS version 25.0 was used to analyze data. The relationship between hyponatremia and clinical/sociodemographic variables was evaluated using a chi-square test, with $p \leq 0.005$ considered significant. **Results:** Among the 113 children who participated in the study, hyponatremic dehydration was identified in 14.2% (95% CI: 8.1%-21.8%). The prevalence of hyponatremia was more common in children with severe dehydration, underweight nutritional condition, frequent stool frequency, incomplete rotavirus vaccination, and low socioeconomic status ($p<0.005$). **Conclusions:** Hyponatremic dehydration is a significant, yet not very widespread, complication in children with acute gastroenteritis. Morbidity needs to be reduced through preventive steps, such as rotavirus vaccination and education of caregivers.

## INTRODUCTION

Acute gastroenteritis (AGE) is one of the primary morbid and mortal causes among children under five years old, especially in low- and middle-income countries (LMICs)[1]. Recent global estimates suggest that diarrheal diseases account for approximately 1.3 billion episodes and nearly 443,000 deaths annually among children under five years of age, with the greatest burden reported in South Asia and sub-Saharan Africa [2]. The burden of AGE has continued to be a significant challenge to the population, and it continues to be one of the deadliest causes of under-five death worldwide despite significant efforts in preventive measures, including oral rehydration therapy (ORT), zinc supplementation, and rotavirus vaccination [3]. AGE is mediated by a plethora of viral, bacterial, and parasitic pathogens, with viral pathogens (rotavirus and norovirus) being the most commonly implicated etiologies of hospitalized children [4, 5]. The clinical features of AGE are mild watery diarrhea to severe dehydration, shock, and multisystem complications. These complications also include dehydration and electrolyte imbalances, but the main factors that define the severity and mortality of diseases are these complications. The loss of

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gastrointestinal fluids, improper fluid replacement, and hormonal reactions to the disease can lead to electrolyte imbalances, making their early diagnosis and treatment one of the most important in the pediatric practice. Hyponatremia, with a serum sodium level less than 135 mEq/L, is among the most frequent and dangerous electrolyte disorders in children with AGE. Hypotonic fluid loss, excessive free water, or inappropriate antidiuretic hormone secretion during acute illness may result in hyponatremic dehydration. The condition may result in seizures, an altered mental state, cerebral edema, and a risk if it is not diagnosed and treated in time. Recent research has pointed out that dysnatremia is a common observation of children admitted to hospitals with gastroenteritis, with hyponatremia being more common than hypernatremia, especially in children having moderate to severe dehydration [6, 7]. Recently, the epidemiology and clinical implications of hyponatremia in acute illnesses have been a growing topic of pediatric research, with the understanding that this electrolyte imbalance is not inherent to gastrointestinal illnesses but can be found in other acute conditions of childhood. Hyponatremic dehydration is common in children, particularly those with acute diarrhea, occurring in 50% of cases [8]. A multicentric pediatric trial indicated that dysnatremia is not only present in a substantial percentage of children with acute gastroenteritis but that the severity of dehydration and the co-occurrence of vomiting and diarrhea were found to be important predictors of hyponatremia [9]. AGE is one of the significant causes of hyponatremia in children, and it is widespread in LMICs, where the delay in presentation and improper utilization of fluids is typical [10]. Pakistan is one of the countries that has a high burden of childhood diarrheal diseases and related complications. An observational study by Kinasha et al. showed that electrolyte abnormalities (hyponatremia) were common among children with acute gastroenteritis admitted to hospitals and were strongly linked to adverse clinical outcomes, emphasizing the role of early biochemical testing [10]. Recent research has further underscored the fact that electrolyte disturbances in acute gastroenteritis amongst children are high. Khan et al. carried out a study in Pakistan, indicating that electrolyte imbalances, especially hyponatremia, are frequent in children with acute gastroenteritis and strongly related to the degree of dehydration and patient outcomes [11].

Although international guidelines on the management of fluids in pediatric AGE are available, there is scant local evidence to inform clinicians of the burden and trend of hyponatremic dehydration among Pakistani children. The variations in feeding patterns, socioeconomic status, access to healthcare, and clinical management guidelines can also impact the prevalence and severity of hyponatremia, and thus, it is necessary to produce context-sensitive data. Moreover, electrolyte abnormalities detected at the tertiary care facilities can be optimally treated to eliminate neurological complications related to the improper correction of serum sodium levels. The research helps clinicians make decisions by determining the burden of hyponatremia in this population, which will be presented as evidence to support the use of fluid resuscitation and electrolyte monitoring measures. The results of the current research are likely to lead to the enhancement of clinical practice in pediatrics, institutional guidelines, and preventive measures of morbidity and mortality in children related to acute gastroenteritis and complications. This study aimed to identify the frequency of hyponatremic dehydration in children who attended the tertiary care center with the diagnosis of acute gastroenteritis.

## METHODS

The current research was designed as a cross-sectional study at the Department of Pediatrics, Pakistan Atomic Energy Commission (PAEC) General Hospital, Islamabad, where the study was carried out during six months between 1st August 2025 and 31st January 2026. The Institutional Review Board of PAEC General Hospital, Islamabad (Approval No. PGHI-IRB(DMe)-RCD-06-090, Dated: 11-06-2024) provided the ethical approval. The sample size was determined by considering the WHO sample size calculator with 95% confidence interval, 8% margin of error, and an estimated prevalence rate of hyponatremic dehydration of 12% in children from previous literature [7]. According to these parameters, the sample size calculated was 113 children. Participants who presented to the pediatric department within the period of the study were selected through non-probability consecutive sampling. The study included children aged between 6 and 59 months of age who exhibited acute gastroenteritis according to the operational definition. Both female and male patients were included. Acute gastroenteritis was considered a diarrhea that lasted ≤4 days with more than two loose stools per day. The children whose diarrhea lasted >14 days were not included. Patients with previous intravenous fluid administration, who had developed septic shock, severe malnutrition, chronic medical conditions including chronic kidney disease, congestive heart disease, renal tubular acidosis, or congestive adrenal hyperplasia, and patients undergoing diuretics or steroid treatment were also excluded to reduce confounding variables in the determination of serum sodium levels. Children meeting the inclusion criteria were recruited, and written informed consent was obtained from the parents or legal guardians. The principal investigator entered demographic and clinical data on a structured proforma specially made to

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capture the information of each child in the study on a list of enrolled children. Demographic factors were age, sex, place of living, the level of maternal education, and the socioeconomic status of the family. The parents or guardians provided the clinical history about the period of diarrhea, whether they had vomited, whether they had taken food orally, and vaccinated against rotavirus. Through a comprehensive physical examination, the extent of dehydration according to World Health Organization clinical guidelines was evaluated, and children were classified as having no dehydration, some dehydration, or severe dehydration [12]. The trained nursing staff or a qualified phlebotomist collected about 2 mL of venous blood from each participant under strict aseptic conditions. The specimen of the blood was taken in a plain vacutainer and taken directly to the hospital laboratory to be subjected to biochemical analysis. The concentration of serum sodium was determined by an automated electrolyte analyzer as per the protocols of the laboratory. A serum sodium level below 135mEq/L was considered hyponatremia. The researcher made sure that the clinical management was not affected by the study participation. Each participant had records taken of the presence or absence of hyponatremic dehydration. The records were kept safely, and only the research team had access to them. The acute gastroenteritis was graded as either grade 3 or grade 4 on the Bristol stool chart, based on the history provided by the parents or guardians [13]. The clinical evaluation of dehydration was conducted: cases of severe dehydration among children were defined as those that exhibited at least two out of the following features: lethargy or unconsciousness, inability to drink, sunken eyes, or sluggish recoil of skin pinch. Children were defined to have some dehydration by having two or more of the following signs: being irritable, eager to drink, sunken eyes, or delayed skin pinch recoil.

Statistical Package of Social Sciences (SPSS) version 25.0 was used to enter and analyze data. Continuous variables, which include age, illness duration, and serum sodium, were summarized using mean and standard deviation when normally distributed. The Shapiro-Wilk test was used to test the normality of quantitative variables, and in case of non-normality, the median and interquartile range (IQR) were used. Categorical variables such as gender, degree of dehydration, rotavirus vaccination status, place of residence, maternal education level, socioeconomic status, and presence of hyponatremia were presented in the form of frequencies and percentages. The number of cases of hyponatremic dehydration was determined as the main outcome variable. The chi-square test was used to determine the association between hyponatremia and the extent of dehydration. The possible effect modifiers were age, gender, rotavirus vaccination status, residence, maternal education level, socioeconomic status, and duration of disease, which were addressed using stratification. Chi-square tests after stratification were used to establish how these variables affected the outcome. A p-value ≤ 0.005 was taken to be statistically significant. A binary logistic regression model was applied to identify independent predictors of hyponatremia, and variables with p ≤ 0.005 in univariate analysis were entered into the model.

## RESULTS

The study included 113 children aged between 6 and 59 months who arrived in the hospital with an acute gastroenteritis diagnosis. Most of the participants were aged 13 to 36 months, of age and males slightly outmatched the females. The majority of the children were urbanized, and a good percentage of the mothers received primary or no formal education. Almost one-third of households were of the low socioeconomic group. In the aspect of clinical features, 34.5% of children had diarrhea that lasted 3 days or less, 45.1% had between 4 and 7 days of diarrhea, and 20.4% had diarrhea longer than 7 days. The frequency of stool was 3-5 times a day in 40.7%, 6-10 times a day in 43.4%, and greater than 10 times a day in 15.9%. There was vomiting in 62.8% of the children, and fever in 51.3%. As per the feeding habits, 23.9% of children were exclusively breastfed, 38.9% mixed fed, and 37.2% formula fed. Oral rehydration therapy was used before in 58.4% of the cases, and 41.6% had not received ORT at home. In terms of nutritional and hydration status, one-third were underweight, and two-thirds were severely underweight. In most cases, some dehydration was identified, and more than a third of them had severe dehydration. Severely dehydrated children showed clinical signs of sunken eyes, increased capillary refill time, and decreased skin turgor more than 2 secs with tenting (Table 1).

**Table 1:** Demographic and Socioeconomic Characteristics of Children with Acute Gastroenteritis, Clinical Presentation and Feeding Practices, Nutritional and Hydration Status (n=113)

| Variables | Category | n (%) |
|---|---|---|
| **Demographic and Socioeconomic Characteristics** | | |
| Age Group (Months) | 6–12 | 32 (28.3%) |
| | 13–36 | 47 (41.6%) |
| | 37–59 | 34 (30.1%) |
| Gender | Male | 61 (54.0%) |
| | Female | 52 (46.0%) |
| Residence | Urban | 68 (60.2%) |
| | Rural | 45 (39.8%) |
| Maternal Education Level | Illiterate | 29 (25.7%) |
| | Primary | 31 (27.4%) |
| | Secondary | 28 (24.8%) |
| | Matric and above | 25 (22.1%) |

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| | | |
|---|---|---|
| Socioeconomic Status | Low (< PKR 30,000/Month) | 41 (36.3%) |
| | Middle (PKR 30,000–100,000) | 46 (40.7%) |
| | High (> PKR 100,000/Month) | 26 (23.0%) |
| **Clinical Presentation and Feeding Practices** | | |
| Duration of Diarrhea | ≤3 Days | 39 (34.5%) |
| | 4–7 Days | 51 (45.1%) |
| | >7 Days | 23 (20.4%) |
| Stool Frequency (per day) | 3–5 Stools | 46 (40.7%) |
| | 6–10 Stools | 49 (43.4%) |
| | >10 Stools | 18 (15.9%) |
| Vomiting | Present | 71 (62.8%) |
| | Absent | 42 (37.2%) |
| Fever | Present | 58 (51.3%) |
| | Absent | 55 (48.7%) |
| Feeding Status | Exclusively Breastfed | 27 (23.9%) |
| | Mixed Feeding | 44 (38.9%) |
| | Formula-Fed | 42 (37.2%) |
| Prior ORT Use at Home | Yes | 66 (58.4%) |
| | No | 47 (41.6%) |
| **Nutritional and Hydration Status** | | |
| Weight-for-Age Status | Normal | 67 (59.3%) |
| | Underweight | 34 (30.1%) |
| | Severely Underweight | 12 (10.6%) |
| Degree of Dehydration | Some Dehydration | 71 (62.8%) |
| | Severe Dehydration | 42 (37.2%) |
| Clinical Signs | Capillary Refill Time >2 Sec | 39 (34.5%) |
| | Sunken Eyes | 64 (56.6%) |
| | Reduced Skin Turgor >2 Sec with Tenting | 47 (41.6%) |

The average serum sodium was 132.8/6.4 mEq/L. Hyponatremia was identified in 14.2% (95% CI: 8.1% - 21.8%). of children, and mild hyponatremia was the most common. Moderate and severe hyponatremia were rarer but clinically important (Table 2).

**Table 2:** Serum Sodium Levels and Frequency of Hyponatremia (n=113)

| Parameters | Mean ± SD / n (%) |
|---|---|
| Serum Sodium (Mean ± SD) | 136.2 ± 4.1 mEq/L |
| Normal Sodium (≥135 mEq/L) | 97 (85.8%) |
| Hyponatremia (<135 mEq/L) | 16 (14.2%) |
| Mild Hyponatremia (130–134 mEq/L) | 9 (8.0%) |
| Moderate Hyponatremia (125–129 mEq/L) | 5 (4.4%) |
| Severe Hyponatremia (<125 mEq/L) | 2 (1.8%) |

The level of dehydration was statistically significantly associated with hyponatremia. The prevalence of hyponatremia was also significantly higher in children with severe dehydration as compared to children with some dehydration (p=0.003). Vomiting (p=0.041), stool frequency of more than 10 per day (p=0.028), and underweight nutritional status (p=0.033) were also significantly related to hyponatremia, which showed that both the severity of the disease and the nutritional factors played a role in creating electrolyte imbalances (Table 3).

**Table 3:** Association between Hyponatremia and Clinical Variables

| Variables | Hyponatremia, n (%) | Normal Sodium, n (%) | $\chi^2$ | df | p-value |
|---|---|---|---|---|---|
| **Degree of Dehydration** | | | | | |
| Some Dehydration | 6 (8.5%) | 65 (91.5%) | 8.92 | 1 | 0.003 |
| Severe Dehydration | 10 (23.8%) | 32 (76.2%) | | | |
| **Vomiting** | | | | | |
| Present | 12 (16.9%) | 59 (83.1%) | 4.17 | 1 | 0.041 |
| Absent | 4 (9.5%) | 38 (90.5%) | | | |
| **Stool Frequency >10/day** | | | | | |
| Yes | 5 (27.8%) | 13 (72.2%) | 4.86 | 1 | 0.028 |
| No | 11 (11.6%) | 84 (88.4%) | | | |
| **Underweight Status** | | | | | |
| Underweight/Severely Underweight | 9 (19.6%) | 37 (80.4%) | 4.54 | 1 | 0.033 |
| Normal Weight | 7 (10.4%) | 60 (89.6%) | | | |

$\chi^2$ = Chi-square test value; df = degrees of freedom; p = probability value. p < 0.001 is considered highly significant

Stratified analysis showed that hyponatremia was significantly related to younger age (p=0.044), rural residence (p=0.026), low maternal education (p=0.019), and low socioeconomic status (p=0.012). There was also a significant association based on rotavirus vaccination status with greater prevalence of hyponatremia in the partially vaccinated or nonvaccinated children (p=0.031). Hyponatremia was not significantly related to gender (p=0.381)(Table 4).

**Table 4:** Stratified Analysis of Sociodemographic Effect Modifiers(n=113)

| Variables | Hyponatremia, n (%) | Normal Sodium, n (%) | $\chi^2$ | df | p-value |
|---|---|---|---|---|---|
| **Age Group** | | | | | |
| 6–12 Months | 7 (21.9%) | 25 (78.1%) | 6.24 | 2 | 0.044 |
| 13–36 Months | 5 (10.6%) | 42 (89.4%) | | | |
| 37–59 Months | 4 (11.8%) | 30 (88.2%) | | | |
| **Gender** | | | | | |
| Male | 9 (14.8%) | 52 (85.2%) | 0.75 | 1 | 0.381 |
| Female | 7 (13.5%) | 45 (86.5%) | | | |
| **Residence** | | | | | |
| Urban | 6 (8.8%) | 62 (91.2%) | 4.95 | 1 | 0.026 |
| Rural | 10 (22.2%) | 35 (77.8%) | | | |
| **Maternal Education** | | | | | |
| Illiterate/Primary | 11 (18.3%) | 49 (81.7%) | 5.46 | 1 | 0.019 |
| Secondary/Matric+ | 5 (9.4%) | 48 (90.6%) | | | |
| **Socioeconomic Status** | | | | | |
| Low | 9 (22.0%) | 32 (78.0%) | 6.32 | 1 | 0.012 |
| Middle/High | 7 (9.7%) | 65 (90.3%) | | | |
| **Rotavirus Vaccination** | | | | | |
| Fully Vaccinated | 4 (9.1%) | 40 (90.9%) | 4.64 | 1 | 0.031 |
| Partial/Unvaccinated | 12 (17.4%) | 57 (82.6%) | | | |

$\chi^2$ = Chi-square test value; df = degrees of freedom; p = probability value. p < 0.001 is considered highly significant

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The binary logistic regression model was used to determine independent predictors of hyponatremia. Significant variables in the univariate analysis were included in the model. Following adjustment, serious dehydration, excessive frequency of stool (>10/day), and underweight nutritional condition were independent predictors of hyponatremia. The positive trend of younger age and low socioeconomic status was not statistically significant after adjustment. The model showed reasonable fit and minimization of confounding in comparison to stratified analysis (Table 5).

**Table 5:** Multivariable Logistic Regression Analysis for Predictors of Hyponatremia

| Variables | Adjusted OR (AOR) | 95% CI | p-value |
|---|---|---|---|
| Severe Dehydration | 3.2 | 1.1 – 9.1 | 0.031 |
| Vomiting | 1.8 | 0.7 – 4.5 | 0.214 |
| Stool Frequency >10/Day | 4.1 | 1.3 – 12.8 | 0.016 |
| Underweight Status | 2.7 | 1.0 – 7.2 | 0.048 |
| Age (6–12 Months) | 1.6 | 0.6 – 4.2 | 0.310 |
| Low Socioeconomic Status | 2.0 | 0.8 – 5.3 | 0.142 |
| Partial/No Rotavirus Vaccine | 1.9 | 0.7 – 5.0 | 0.198 |

## DISCUSSION

The current study reveals that hyponatremic dehydration is a significant, but not very common, complication of acute gastroenteritis in children aged 6-59 months, especially in socioeconomically disadvantaged groups. The frequency reflected overall in this study was relatively low, but the condition is clinically relevant as it has the possibility of neurological consequences, such as seizures and altered sensorium, that should not be promptly identified and treated. The incidence of hyponatremia in this case is also consistent with the results of the hospital-based research done in the same resource-restrained environment. A recent cross-sectional study by Khan *et al.* in Dera Ismail Khan, Pakistan, and Harvey *et al.* has indicated high levels of electrolyte imbalance, including sodium abnormalities, which are closely linked with the severity of dehydration in children with acute gastroenteritis, which supports the relevance of biochemical monitoring in this condition [11, 13]. The differences in the reported prevalence of the electrolyte abnormalities among epidemiological studies could be attributed to differences in the population of the study, nutritional condition, and access to health care, time of onset, and fluid management strategies. Indicatively, a prospective study by Tombokan *et al.* at Dr. Soetomo General Academic Hospital in Indonesia found hyponatremia, in many cases with hypokalemia and hyperchloremia, in about one-third of children with diarrhea, the interaction of gastrointestinal fluid losses, vomiting, and renal compensatory responses [14]. Despite the variation in the percentage of children who are affected in various studies, the consistent finding of sodium imbalance shows that it is a clinically relevant factor in diarrheal illness. Similar issues have been mentioned with other studies in Pakistan. A study by Shah *et al.* showed that children with acute diarrhea and dehydration have reported high rates of hyponatremia and hypokalemia, and a good correlation between electrolyte imbalance and severity of dehydration underpins the claim that electrolyte measurement needs to be included in the measurement of children with moderate to severe dehydration [15]. The prevalence in the current study was smaller, but findings confirmed that there were strong connections between electrolyte imbalance and the severity of dehydration. This is especially so in places where malnutrition, delayed seeking health care, and partial immunization could predispose an individual to complications. The relationship between hyponatremia and severe dehydration has been observed in the present study and is in line with international evidence that has revealed that an increase in fluid losses is strongly correlated with dysnatremia. Studies by Gupta *et al.* and Dabek *et al.* showed that moderate to severe dehydration has been found in situations where sodium imbalance predicts the presentation of acute illness, especially in children who are experiencing both vomiting and diarrhea [16, 17]. This has been physiologically reasonable as hyponatremia may be triggered by increased antidiuretic hormone release relative to free water loss, and this is relevant when the free water loss in relation to sodium loss is disproportionate. Even though most of the literature is devoted to sodium disturbances, the electrolyte imbalance in acute gastroenteritis in pediatrics is not limited to hyponatremia. It has been reported to cause concurrent hypokalemia, metabolic acidosis, and other acid-base imbalances, which are related to a deteriorated clinical condition and extended hospital stay. A study by Hamzah *et al.* on hospitalized children has shown that various biochemical abnormalities tend to co-occur in diarrheal disease, and that extensive metabolic testing is more valuable than single sodium analysis [18]. Furthermore, studies by Zieg *et al.* Poe *et al.* and Adrogue *et al.* emphasized that an electrolyte emergency, either hyponatremia or hypernatremia, can result in neurological and cardiac adverse effects unless it is timely identified and addressed [19-21]. Even though the vast majority of the literature is devoted to sodium disorders, electrolyte imbalance in pediatric acute gastroenteritis is not limited to hyponatremia. It has been reported in studies that hypokalemia is concurrent with metabolic acidosis and other acid-base imbalances that may cause clinical deterioration and extended hospitalization. Long-term studies of electrolyte patterns in admitted children have shown that numerous electrolyte imbalances often co-

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exist with diarrheal disease, highlighting the necessity of more comprehensive clinical and chemical analysis, even in patients with a lower rate of hyponatremia [13]. Although hyponatremia appears in a smaller percentage of patients, the presence of other electrolyte derangements should be carefully considered in clinical and laboratory surveillance in severely dehydrated children [13]. Although a smaller percentage of the patients had hyponatremia, several other electrolyte abnormalities were present and, therefore, needed to be closely assessed through clinical and laboratory methods. Clinical implications of the findings of this study are significant. Even though the prevalence rate of hyponatremia was not very large, its strong correlation with serious dehydration and risky sociodemographic factors indicates that selective electrolyte surveillance is recommended in high-risk children. Clinical dehydration scoring is only relied on and may fail to identify underlying biochemical imbalances. Prompt diagnosis of sodium disturbance enables suitable correction of rehydration treatment and minimizes the risk of adverse development of complications associated with incorrect fluid replacement. In the view of public health, enhancing routine rotavirus immunization, enhancing the education of the caregiver, and ensuring prompt administration of oral rehydration salts can be used to ease the degree of dehydration, and thus, reduce the prevalence of electrolyte disorders in children with acute gastroenteritis.

The present study has its limitations, which can be taken into account when analyzing the results. As a cross-sectional study with a single-center setting, it is not possible to draw causal relationships, and the findings might not be applicable to other settings. Also, other electrolytes like potassium, chloride, and bicarbonate were not systematically studied, which would have given a better idea of the metabolic imbalances of acute gastroenteritis. This would be better supported by future multicenter prospective randomized controlled studies that use a broader array of biochemical markers and clinically relevant outcomes, including duration of hospitalization and neurological complications, to support optimal management.

## CONCLUSIONS

Hyponatremic dehydration is an important adverse effect of acute gastroenteritis in children, and it should be carefully considered in clinical practice. In the current study, several clinical and sociodemographic variables were associated with hyponatremia in the bivariate analysis. Early diagnosis and proper treatment of dehydration and electrolyte imbalance are important in preventing complications.

## Authors' Contribution

Conceptualization: AID
Methodology: AID, SA, SGF, NN, TAC
Formal analysis: AID
Writing and Drafting: AID, SA, SGF, NN, TAC, AHS, HA
Review and Editing: AID, SA, SGF, NN, TAC, AHS, HA

All authors approved the final manuscript and take responsibility for the integrity of the work

## Conflicts of Interest

All the authors declare no conflict of interest.

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