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ORIGINAL ARTICLE

Electrolyte imbalance and its association with the severity of dengue fever.

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ABSTRACT… Objective: To assess the electrolyte imbalance in the patients with dengue and severe dengue fever and correlate their abnormalities with the severity of illness in pediatric population. **Study Design:** Cross-sectional study. **Setting:** Department of Pediatrics, The National Institute of Child Health (NICH), Karachi, Pakistan. **Period:** November 2024 to April 2025. **Methods:** A total of 196 children aged 6 months to 12 years with dengue, confirmed by NS1 antigen or IgM ELISA, were enrolled using non-probability consecutive sampling. Data collected included demographic, clinical, and laboratory parameters, with patients classified according to WHO dengue severity criteria. Electrolyte disturbances were defined using standard cutoffs. Data analysis was performed using SPSS v24, applying the Chi-square test, with $p < 0.05$ considered significant. **Results:** In a totaof 196 children, the mean age was 4.9±3.6 years, while 50.5% children were male. There were 41 (20.9%) children who had dengue fever, 118 (60.2%) dengue with danger signs, and 37 (18.9%) had severe dengue. Hyponatremia was observed in 72 (36.7%) children, most frequent in dengue with danger signs (44.9%) and severe dengue (37.8%), while hypernatremia was seen only in severe dengue (24.3%). Hypokalemia and hypocalcemia were found in 19.4% and 58.2% of cases, respectively. All 17 (8.8%) deaths occurred in severe dengue and were associated with hyponatremia, hypernatremia, and hypocalcemia. **Conclusion:** Electrolyte imbalances are common in paediatric dengue, with hyponatremia, hypocalcemia, and hypernatremia strongly associated with increased severity and mortality.

Key words: Dengue Fever, Fever, Hypernatremia, Hypocalcemia, Hypokalemia, Mortality.

INTRODUCTION

Dengue fever is an acute febrile illness and is the second most common serious vector borne disease after malaria globally transmitted by Aedes aegypti and Aedes albopictus mosquito.[1-3] In Pakistan, the first case was reported in 1985 and 5.2 million cases including 91 deaths were reported in 2019 out of which the majority 41 of the deaths were from Sindh.[2,4] Out of 500 thousand people requiring hospitalization each year with severe dengue approximately 90% of them are children less than 5 years of age and mortality among them is about 2.5%.[5] There are several factors leading to frequent epidemics of dengue fever in Pakistan including burgeoning population, rise in urbanization rate and ineffective vector control in rainy season.

WHO has categorized dengue into 2 major categories as dengue (with/without warning signs), and severe dengue. Dengue without warning signs presents with high grade fever (40C) whereas Dengue with warning signs manifest with severe headache, pain behind eyes, myalgia, arthralgia, nausea, vomiting, rash and swollen glands. Severe Dengue, on the other hand, is characterized by severe abdominal pain, bleeding gums, hematemesis and hypotension. Severe dengue can lead to potentially fatal complication, due to plasma leaking, fluid accumulation, respiratory distress, severe bleeding, or organ impairment.[4]

An association between dengue fever and electrolyte disturbances has been reported in the past.[6] Several proposed mechanisms are there for it and direct action of immune complexes on glomeruli is one of them.[7] Routine assessment of serum electrolytes is done in hospitalized patients with dengue fever or severe dengue.[8]

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Treating dengue fever primary approaches from supportive care, appropriate and vigilant fluid therapy, targeted organ support and correction of any metabolic abnormalities.[9] Correcting and managing electrolyte imbalance greatly alter mortality as well as morbidity in dengue fever.[2] The prevalence of different electrolyte imbalance varies across different part of world, hyponatremia has been reported globally ranging from 11% to 58%. Hypokalemia occurring in 11% including case reports of acute hypokalemic quadriparesis further complicated with hypomagnesemia. Hypocalcemia has been observed with a prevalence rate of 86.9%.[2] Despite high burden of dengue fever in Pakistan, there is paucity of data on dengue fever, its severity and association with electrolyte imbalance in pediatric population. Given the variability of data in pediatric population it is ascertain to determine the pattern of electrolyte imbalance in children and its relation with its severity. This study aims to fill the gap and determine the trend of electrolyte imbalance and its association with the severity in the pediatric population of Pakistan to enhance the outcome and optimize a better management in different settings. The objective was to assess the electrolyte imbalance in the patients with dengue and severe dengue fever and correlate their abnormalities with the severity of illness in pediatric population.

METHODS

This cross-sectional study was conducted at departments of Pediatrics, National Institute of Child Health (NICH), Karachi, Pakistan. The study was carried out during November 2024 to April 2025, following approval from the Institutional Ethics Review Board (Letter: IERB-15/2024, dated: 26th October, 2024). The sample size was calculated to be 196, using the WHO sample size calculator, based on a confidence level of 95%, a confidence limit of 7%, and a proportion value of 53.3% for mild hyponatremia in children with dengue.[5] The study population included children aged 6 months to 12 years who were diagnosed with dengue fever, confirmed by either NS1 antigen or IgM ELISA testing. Exclusion criteria included children with height and weight below the 5th percentile for age, those with pre-existing kidney or liver dysfunction, patients presenting with any other febrile illness or co-infection, and those with underlying conditions such as diabetes mellitus or Addison's disease. A non-probability consecutive sampling technique was used to recruit participants.

After obtaining written informed consent from parents or guardians, all eligible children were enrolled. Demographic information and detailed clinical history including onset, duration, and progression of illness were collected. Laboratory investigations, including hemoglobin, white blood cell count, platelet count, hematocrit, and serum levels of sodium, potassium, calcium, magnesium, and phosphorus, were obtained for all participants. Based on clinical features and duration of fever, patients were categorized as having either non-severe dengue or severe dengue according to established WHO criteria. Dengue fever was defined as an acute febrile illness lasting between 2 to 7 days, accompanied by two or more symptoms such as headache, retro-orbital pain, myalgia, arthralgia, rash, or hemorrhagic manifestations. Non-severe dengue was characterized by high-grade fever (40°C) along with symptoms such as severe headache, pain behind the eyes, myalgia, arthralgia, nausea, vomiting, rash, or swollen glands. Severe dengue was identified by the presence of severe abdominal pain, gum bleeding, hematemesis, or hypotension. Serum sodium levels were considered normal between 135–145 mEq/L. For potassium, normal serum levels ranged from 3.5–4.5 mEq/L. Corrected serum calcium levels were calculated using the formula as measured calcium plus 0.8 multiplied by (4.0 minus serum albumin), with normal values ranging from 8.5–10.5 mg/dL. Normal calcium levels were considered as 8.5-10.5 mg/dl. Normal serum magnesium levels were considered 1.5–2.5 mg/dL.

Data were analyzed using IBM SPSS Statistics for Windows, Version 24.0. Categorical variables such as gender and clinical features (including fever, body aches, lethargy, drowsiness, muscle aches, and respiratory distress) were described using frequencies and percentages. Continuous variables, such as age, duration of illness, and

electrolyte levels, were summarized as mean and standard deviation. The association between the severity of dengue and the frequency of electrolyte disturbances was assessed using the Chi-square test, or Analysis of variance, takin $p<0.05$ as significant.

RESULTS

In a total of 196 children, the mean age was 4.9±3.6 years, and 99 (50.5%) children were male. The mean duration of illness at presentation was 5.0±1.2 days. Among 196 children, 41 (20.9%) were categorized as dengue fever, 118 (60.2%) as dengue with danger signs, and 37 (18.9%) as severe dengue. Regarding clinical presentation, fever was reported in all children (100%), while headache occurred in 70 (35.7%), retro-orbital pain in 28 (14.3%), myalgia in 38 (19.4%), arthralgia in 15 (7.7%), nausea in 155 (79.1%), vomiting in 130 (66.3%), rash in 98 (50.0%), abdominal pain in 108 (55.1%), gum bleeding in 43 (21.9%), hematemesis in 6 (3.1%), lethargy in 108 (55.1%), and respiratory distress in 47 (24.0%) children.

Children with severe dengue were significantly younger (3.9±3.4 years) compared to those with dengue fever (6.7±3.6 years), with $p=0.002$. The duration of illness was relatively shorter in the severe dengue children (4.1±0.9 days) as compared to dengue with danger signs (5.2±1.2 days) and dengue fever (5.8±0.9 days), with $p< 0.001$. Table-I is showing association of demographic and clinical characteristics of children with dengue severity.

Hematological parameters revealed a mean leukocyte count of $8.4\pm2.8\times10^9$/L in dengue fever, $7.2\pm3.3\times10^9$/L in dengue with danger signs, and $10.0\pm5.1\times10^9$/L in severe dengue ($p < 0.001$). Platelet counts were lower in the danger signs group ($70.3\pm72.9 \times 10^9$/L) compared to dengue fever ($107.8\pm142.3\times10^9$/L), and severe dengue ($81.8\pm70.2 \times 10^9$/L), although the difference was not statistically significant ($p=0.080$).

Hyponatremia was found in 72 (36.7%) children, with the highest frequency among those with dengue with danger signs (44.9%), and severe dengue (37.8%), compared to dengue fever (12.2%), with $p<0.001$). Hypernatremia was seen only in the severe dengue children (24.3%, $p<0.001$). Hypokalemia was documented in 38 (19.4%) children, most frequently in severe dengue (24.3%), and dengue fever (22.0%), with $p=0.824$. Hypocalcemia was observed in 114 (58.2%) children, with 70 (59.3%) cases in dengue with danger signs, and 23 (62.2%) in severe dengue, with $p=0.571$. All children had normal magnesium levels. Table-III is showing details about the association of electrolyte parameters with dengue severity.

Regarding outcomes, mortality was observed in 17 (8.8%) children, all of whom had severe dengue. Among children with severe dengue, mortality was associated with hyponatremia (100%), hypernatremia (100%), and hypocalcemia (100%). None of the children with normal sodium or calcium levels died. No deaths were reported in children with only dengue fever or dengue with danger signs (Table-IV).

DISCUSSION

Hyponatremia emerged as a prevalent electrolyte disturbance in children with dengue fever, particularly in those with more severe disease. Hyponatremia was observed in 36.7% of all participants, reaching its highest frequency among those with dengue with danger signs (44.9%) and severe dengue (37.8%), compared to 12.2% in the dengue fever group. Only patients with severe dengue developed hypernatremia (24.3%). Choudhary et al.[5], documented hyponatremia in 58.9% of patients with dengue fever, with the majority (53.3%) presenting with mild hyponatremia. These figures are higher than those identified in the present cohort. In contrast, the current data identified a substantial, but somewhat lower, frequency of hyponatremia, with more pronounced abnormalities in severe dengue cases. Shankar et al.[10], reported a mean serum sodium of 133.7 mEq/L in their study population, which is similar to the mean sodium levels reported in the present cohort's severe dengue group.

Variables		Dengue Fever (n=41)	Dengue with Danger Signs (n=118)	Severe Dengue (n=37)	P-Value
Gender	Male	21 (51.2%)	55 (46.6%)	23 (62.2%)	0.255
	Female	20 (48.8%)	63 (53.4%)	14 (37.8%)	
Age, years		6.7±3.6	4.8±3.6	3.86±3.4	0.002
Duration of illness, days		5.8±0.9	5.2±1.2	4.1±0.9	<0.001
Presenting symptoms / complaints	Fever	41 (100%)	118 (100%)	37 (100%)	1
	Headache	17 (41.5%)	42 (35.6%)	11 (29.7%)	0.558
	Retro-orbital pain	9 (22.0%)	14 (11.9%)	5 (13.5%)	0.279
	Myalgia	12 (29.3%)	23 (19.5%)	3 (8.1%)	0.062
	Arthralgia	-	6 (5.1%)	9 (24.3%)	<0.001
	Nausea	23 (56.1%)	104 (88.1%)	28 (75.7%)	<0.001
	Vomiting	14 (34.1%)	85 (72.0%)	31 (83.8%)	<0.001
	Rash	18 (43.9%)	55 (46.6%)	25 (67.6%)	0.057
	Swollen glands	-	3 (2.5%)	-	0.365
	Abdominal pain	14 (34.1%)	66 (55.9%)	28 (75.7%)	0.001
	Gum bleeding	3 (7.3%)	20 (16.9%)	20 (54.1%)	<0.001
	Hematemesis	-	-	6 (16.2%)	<0.002
	Lethargy	6 (14.6%)	65 (55.1%)	37 (100%)	<0.001
	Respiratory distress	-	13 (11.0%)	34 (91.9%)	<0.001

Table-I. Association of demographic and clinical characteristics of children with dengue severity (N=196)

Variables	Dengue Fever (n=41)	Dengue with Danger Signs (n=118)	Severe Dengue (n=37)	P-Value
Heart rate (beats/minute)	112.1±11.5	121.6±14.5	134.2±18.9	<0.001
Systolic blood pressure (mmHg)	101.4±8.0	94.1±10.0	88.5±11.1	<0.001
Diastolic blood pressure (mmHg)	60.6±5.2	56.1±6.7	51.9±7.0	<0.001
Respiratory rate (resp/minute)	26.9±5.2	28.9±5.5	37.5±5.6	<0.001
Hemoglobin (g/dl)	10.9±1.9	10.9±1.6	11.5±2.0	0.263
Leukocytes count (10^9/L)	8.4±2.8	7.2±3.3	10.0±5.1	<0.001
Platelets (10^9/L)	107.8±142.3	70.3.8±72.9	81.8±70.2	0.080

Table-II. Association of vital signs and laboratory parameters with dengue severity (N=196)

Electrolyte Parameters		Dengue Fever (n=41)	Dengue with Danger Signs (n=118)	Severe Dengue (n=37)	P-Value
Serum sodium	Normal	36 (87.8%)	65 (55.1%)	14 (37.8%)	<0.001
	Hyponatremia	5 (12.2%)	53 (44.9%)	14 (37.8%)	
	Hypernatremia	-	-	9 (24.3%)	
Serum potassium	Normal	26 (63.4%)	75 (63.6%)	22 (59.5%)	0.824
	Hypokalemia	9 (22.0%)	20 (16.9%)	9 (24.3%)	
	Hyperkalemia	6 (14.6%)	23 (19.5%)	6 (16.2%)	
Serum calcium	Normal	20 (48.8%)	48 (40.7%)	14 (37.8%)	0.571
	Hypocalcemia	21 (51.2%)	70 (59.3%)	23 (62.2%)	

Table-III. Association of electrolyte parameters with dengue severity (N=196)

Electrolyte Parameters		Outcomes	Dengue Fever	Dengue with Danger Signs	Severe Dengue	P-Value
Serum sodium	Normal	Discharged	36 (32.1%)	65 (58.0%)	11 (9.8%)	<0.001
		Death	-	-	3 (100%)	
	Hyponatremia	Discharged	5 (7.8%)	53 (82.8%)	6 (9.4%)	<0.001
		Death	-	-	8 (100%)	
	Hypernatremia	Discharged	-	-	3 (100%)	<0.001
		Death	-	-	6 (100%)	
Serum potassium	Normal	Discharged	26 (23.2%)	75 (67.0%)	11 (9.8%)	<0.001
		Death	-	-	11 (100%)	
	Hypokalemia	Discharged	9 (23.7%)	20 (52.6%)	9 (23.7%)	<0.001
		Death	-	-	-	
	Hyperkalemia	Discharged	6 (20.7%)	23 (79.3%)	6 (17.1%)	<0.001
		Death	-	-	6 (100%)	
Serum calcium	Normal	Discharged	20 (24.4%)	48 (58.5%)	14 (17.1%)	<0.001
		Death	-	-	-	
	Hypocalcemia	Discharged	21 (21.6%)	70 (72.2%)	6 (6.2%)	<0.001
		Death	-	-	17 (100%)	

Table-IV. Association of electrolyte parameters with outcomes among children with dengue (N=196)

This trend of declining serum sodium with increasing severity of illness aligns with the findings of Yanda and Karimulla[11], who also demonstrated a positive correlation between serum sodium levels and dengue severity. The variations in prevalence of hyponatremia between the current study and prior reports may be attributable to differences in study settings, diagnostic criteria, thresholds for defining severity, and timing of sample collection relative to the disease course. In the current population, strict exclusion of children with underlying chronic disease or co-infections may have reduced confounding factors, possibly resulting in a more accurate reflection of hyponatremia due solely to dengue infection. Some researchers have found a higher prevalence of hyponatremia, such as Lumpaopong et al.[12], where 61% of dengue fever and 72% of dengue hemorrhagic fever patients were hyponatremic. Another study reported hyponatremia in only 22% of adult dengue patients, suggesting that age, severity, and hospital setting significantly influence the prevalence and clinical impact of this electrolyte disturbance.[13] From a clinical perspective, the frequent occurrence of hyponatremia among paediatric dengue cases, especially in those with warning signs or severe disease, underscores the need for routine monitoring of serum sodium.[14,15] Early detection and timely correction may reduce the risk of neurological complications and other adverse outcomes, especially in settings where access to paediatric intensive care is limited. The finding that all mortality in this cohort was associated with either hyponatremia or hypernatremia, and that no child with normal sodium died, further emphasizes the prognostic significance of sodium disturbances in severe dengue.

Hypokalemia was observed in 19.4% of children in the current cohort, most commonly in severe dengue (24.3%) and dengue fever (22.0%), but no significant association with severity was established (p=0.824). Choudhary et al.[5], described mild hypokalemia in 35.6%, moderate in 4.5%, and severe in 1.1% of their study subjects. Relwani et al.[16], found hypokalemia in 10.6%, and Rajalekshmy and Vadivelan found a higher prevalence of 34%. Rehman et al.[9], identified hypokalemia in 23.2% of a large cohort, and Shankar et al.[10], reported a mean potassium level of 3.58 mEq/L, comparable to the mean for the present study population.

Hypocalcemia was noted in 58.2% of children in the current study, with the highest frequencies in the dengue with danger signs (59.3%) and severe dengue groups (62.2%). This pattern mirrors the high rates observed by Ali et al.[17], in Sudan, where hypocalcemia was present in 30% of adults with dengue. Haider et al.[18], also reported significant reductions in serum calcium in all clinical subgroups of dengue patients compared to controls. Relwani et al.[16], similarly emphasized the high frequency of hypocalcemia in dengue infection, yet the pathophysiological basis remains poorly understood. Proposed mechanisms include capillary leak syndrome leading to hypoalbuminemia, direct viral effects on parathyroid hormone secretion, or transient renal tubular dysfunction impairing calcium reabsorption.[19] In this study, hypocalcemia was strongly associated with mortality in severe dengue, with all deaths occurring in hypocalcemic children.

No patients in the present cohort developed hypomagnesemia or hypermagnesemia. This finding diverges from Anwar et al.[2], who documented hypomagnesemia in 14.6% of paediatric patients, and Ali et al.[17], who reported low magnesium in 13% of their study group. The absence of magnesium abnormalities in this cohort could be related to differences in population characteristics, dietary patterns, or institutional protocols regarding electrolyte supplementation and monitoring. Variability in laboratory reference ranges or thresholds for clinical intervention might also explain the differing prevalence reported across studies.

The association of hyponatremia, hypernatremia, and hypocalcemia with increased mortality in severe dengue is particularly noteworthy. All children who died in this study were found to have one or more of these electrolyte disturbances, and no deaths occurred in children with normal sodium or calcium levels. This strong association is mirrored in the findings of Anwar et al.[2], who demonstrated that hyponatremia and hypophosphatemia were significantly related to severe dengue. Rehman et al.[9], did not find a significant relationship between electrolyte abnormalities and in-hospital mortality or length of stay, suggesting that mortality in dengue may be influenced by additional factors, including the timing and quality of supportive care, and the presence of comorbidities such as renal dysfunction or diabetes mellitus. The integration of electrolyte assessment into standard care pathways for paediatric dengue may improve risk stratification, guide fluid management, and enable targeted supportive therapy.[19-22] Given the rapid progression to severe disease in some patients, point-of-care testing for electrolytes in the emergency or paediatric intensive care setting may be especially valuable.

The cross-sectional design precludes assessment of causality or longitudinal changes in electrolyte levels during the disease course. The study was conducted at a single tertiary centre, which may limit generalizability, particularly to rural or primary healthcare settings with differing patient profiles or resources. The exclusion of children with pre-existing conditions or coinfections reduces confounding but may underestimate the true burden of electrolyte abnormalities in the broader paediatric population. The sample size, though adequate for the primary outcome, limited the power for subgroup analyses, especially regarding rare outcomes such as hypernatremia.

CONCLUSION

Electrolyte imbalances are common in paediatric dengue, with hyponatremia, hypocalcemia, and hypernatremia strongly associated with increased severity and mortality. The absence of significant potassium or magnesium disturbances in this cohort contrasts with some prior reports, emphasizing the importance of population-specific data. Routine monitoring and early correction of sodium and calcium abnormalities should be prioritized in paediatric dengue management protocols.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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1	**Nimra Fatima:** Data collection, drafting, responsible for data's integrity, approved for publication.
2	**Muhammad Ashfaq:** Study concept and design, proof reading, critical revisions, approved for publication.
3	**Wajid Hussain:** Study concept and design, proof reading, critical revisions, approved for publication.
4	**Mariam Raza:** Study concept and design, proof reading, critical revisions, approved for publication.
5	**Atiya Anwar:** Literature review, data analysis, critical revisions, approved for publication.