



Hypokalemia in dengue fever: A Descriptive Study

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Abstract

Background and Objectives: Dengue fever has become a major public health problem with high morbidity and mortality. Its clinical profile is changing with appearance of more neurological manifestations. It is vital to recognise at the earliest the signs, symptoms and alterations in biochemical parameters in dengue patients to reduce mortality. Among these hypokalemia is one of the possible manifestations of dengue fever, not widely recognised. This study was conducted at Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar to evaluate the prevalence of hypokalemia and its association with neurological manifestations.

Methodology: Primary data was collected from 350 cases of dengue admitted in Chalmeda Hospital fulfilling inclusion and exclusion criteria. They were screened for any neurological or any other abnormal clinical manifestations and serum potassium was evaluated at the time admission.

Results: Severe dengue was seen in 11.2% of all dengue cases with 18% of total cases were found to have hypokalemia, majority presenting as mild hypokalemia. 2.3% cases had neurological manifestation with 50% of them, significantly associated with hypokalemia.

Conclusion: Dengue fever is associated with hypokalemia which is associated with neurological manifestations and if not screened for, can be missed. Hence, screening of hypokalemia is as important to decrease morbidity and mortality of dengue fever.

Keywords: Dengue; Hypokalemia; Neurological manifestations

Introduction

Dengue fever is an arthropod borne viral fever acquiring epidemic proportion in tropical and sub-tropical climate including Telangana. It has become a major public health problem with high morbidity and mortality. Clinical presentation varies from a severe flu to a potentially lethal haemorrhagic fever and dengue shock syndrome.

It is vital to recognise at the earliest the signs, symptoms and alterations in biochemical parameters in dengue patients to reduce mortality. Among these hypokalemia is one of possible manifestations of dengue fever, not widely recognised. Hypokalemia is defined as a plasma K⁺ concentration below 3.5 mmol/L^[1]. Patients with hypokalemia often have no symptoms, particularly when the disorder is mild (3.5-3 mEq/L). With more severe hypokalemia, nonspecific symptoms, such as generalized weakness, lassitude, and constipation, are more common. In severe hypokalemia, muscle necrosis can occur, and at serum concentrations of less than 2.0 mmol per litre, an ascending paralysis can develop, with eventual impairment of respiratory function^[2].

The clinical profile of dengue is changing, and the neurological manifestations are reported more frequently. Neurological manifestations include encephalitis, aseptic meningitis, neuropathies, Guillain-Barre syndrome, myelitis, intracranial haemorrhage and thrombosis. Some of these manifestations are associated with hypokalemia. Prevalence study of hypokalemia in dengue is rarely reported. Awareness of this and screening for potassium levels will help the physician to keep the possibility of hypokalemia in dengue patients and manage its possible complications of paresis and eventual impairment of respiratory function.

Also this study will underline the importance of using potassium rich fluids as replacement fluid in management

of dengue fever.

Aim and Objectives

- To study hypokalemia in dengue fever

Materials and Methods

Source of data
Primary observed data of Dengue cases admitted as inpatient to Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar during the period of November 2021 to November 2022.

Method of collection of data (Including sampling procedure if any)

The data is collected from subjects fulfilling inclusion and exclusion criteria and admitted as inpatients in CAIMS, Karimnagar.

Sample size: 350

Sampling method: Descriptive study

Inclusion criteria

Subjects with clinical features suggestive of dengue infection, later on confirmed by dengue serology will be included in study.

Exclusion criteria

1. Subjects with mixed infections.
2. Subjects taking any medication causing hypokalaemia.
3. Subjects with renal insufficiency.

Method of Study

All those who are going to get admitted as inpatients in Chalmeda Hospital, Karimnagar with symptoms suggestive of Dengue fever i.e. fever, severe headache, joint pains, retro orbital pain, bleeding manifestation and shock are investigated with dengue serology. Those found positive for either of the tests are included in study and informed consent is taken from all patients. A detailed clinical history is taken from all patients followed by thorough clinical examination of all systems. After conducting physical examination, venous blood sample (by using appropriate anticoagulant i.e. EDTA for CBC and heparin for serum electrolyte estimation) was obtained. They are further investigated with all biochemical, microbiological, haematological and radiological investigations mentioned in study protocol.

Serum potassium levels are checked at the time of admission.

Estimation of Serum electrolytes (By Electrolyte Analyzer using the principle of Ion Selective Electrode)

The Normal Reference Range of potassium used in the present study as per our laboratory guidelines are

- Serum Potassium (K^+): 3.5-5.0 mEq/L

Investigations

1. Complete haemogram
2. Dengue serology for IgG, IgM, NS-1 Antigen
3. Serum electrolytes, blood urea, serum creatinine
4. Random blood sugar
5. Urine routine
6. Malarial parasite (QBC) and Widal test
7. Liver function test
8. ECG, ultrasound abdomen, chest x-ray

Following investigation will be done whenever necessary

1. Blood culture, urine culture
2. HbsAg, anti HCV, Leptospira IgM antibody

Statistical Methods

- Descriptive statistics(mean standard deviation,proportion)
- Chi square test/z test of proportion, multiple Bar and Piechart.
- Contingency coefficient.

Related statistical techniques using SPSS version 17.0 (forwindows 7.1)

Results

Distribution of subjects according to the age group Among the 350 subjects chosen for the study, majority of the subjects were distributed in the age group of 21 – 30years (23.7%), 31-40 years (22.9%) with maximum number

from 41-50 age groups (25.1%).

Table 1: Age distribution

Age (years)	Number of subjects	Percentage of subjects
<20	16	4.6
21-30	83	23.7
31-40	80	22.9
41-50	88	25.1
51-60	49	14.0
61-70	28	8.0
>71	6	1.7

Distribution of subjects according to sex

Among the total 350 subjects, 191 subjects were males (54.6%) and remaining 159 subjects were females (45.4%).

Table 2: Sex distribution

Sex	Number of subjects	Percentage of subjects
Female	159	45.4%
Male	191	54.6%

Dengue serology

Among the total subjects, around 56% were tested positive for NS-1 antigen as compared to IgM (53.1%) and IgG(44%).

Table 3: Pattern of dengue serology

		Number of subjects	Percentage of subjects
IgG	Negative	196	56.0%
	Positive	154	44.0%
IgM	Negative	164	46.9%
	Positive	186	53.1%
NS1	Negative	154	44.0%
	Positive	196	56.0%

Severity of dengue

Among the total 350 subjects who were tested positive for dengue, 39 subjects (11.2%) were found to have severe dengue of which 5 subjects (1.4%) had Dengue Hemorrhagic Fever (DHF) and 34 subjects (9.7%) had Dengue Shock Syndrome (DSS).

Table 4: Distribution as per dengue severity

		Number of subjects	Percentage of subjects
Severe Dengue	No	310	88.8%
	Yes	39	11.2%

Table 5: Distribution of different types of dengue

	Number subjects	Percentage of subjects
None	311	88.9%
DHF	5	1.4%
DSS	34	9.7%
Total	350	100.0%

Neurological manifestations

Of all the 350 patients, 2 patients showed signs of encephalitis and 4 patients were diagnosed with paraparesis of which one was diagnosed as Guillian-Barre syndrome and three were diagnosed with hypokalemic paraparesis which was reversible with potassium replacement and 2 patients had quadriparesis later diagnosed to have myositis.

Table 6: Neurological manifestations

		Number subjects	Percentage
Neurological manifestations	Encephalitis	2	.6%
	Paraparesis	4	1.1%
	None	342	97.7%
	Quadriparesis	2	.6%

Other manifestations

Four patients had presented with arrhythmias of which one had died and three others had reversible ECG changes secondary to decrease in potassium. 42 patients had features suggestive of polyserositis.

Table 7: Other manifestations

	Number subjects	Percentage
Cardiac arrhythmias	4	1.1%
Polyserositis	42	12.0%

Hematological and metabolic parameters

Mean platelet count was about 46 thousand and mean hematocrit was 40.70. Among metabolic parameters, mean sodium was about 140 mEq/l and mean potassium was 4 mEq/l with minimum up to 1.60 mEq/l.

Table 8: Hematological and metabolic parameters

	Mean	Standard Deviation	Median	Minimum	Maximum
Plateletcount	46523.96	25908.17	39000.00	6000.00	98000.00
Hematocrit	40.70	4.97	40.15	36.0	54.50
Serum Sodium	139.95	8.11	139.40	109.20	169.20
Serum Potassium	4.01	.68	3.90	1.60	6.10

Hypokalemia

Among all the 350 cases, 18% were found to have hypokalemia.

Table 9: Distribution of hypokalemia

		Number of subjects	Percentage of subjects
Hypokalemia	No	287	82.0%
	Yes	63	18.0%

Severity of hypokalemia

Of 63 hypokalemic patients, 43 had mild hypokalemia (3- 3.5mEq/l) and 14 had moderate (2.5-3mEq/l) and 6 patients had severe (<2.5mEq/l) hypokalemia

Table 10: Table Severity of hypokalemia

		Number of subjects	Percentage of subjects
Severity of Hypokalemia	None	287	82.0%
	Mild	43	12.3%
	Moderate	14	4.0%
	Severe	6	1.7%

Association of hypokalemia with Severity of dengue

As seen in the table, there is not much difference in the association of mild hyperkalemia with severe dengue fever but there is significant difference in the presence of moderate and severe hyperkalemia in severe dengue.

Table 11: Association of hypokalemia with severity of dengue

		Severe Dengue			
		Absent		Present	
		Total no.	Percentage	Total no.	Percentage
Severity of Hypokalemia	Normal	259	83.5%	27	69.2%
	Mild	38	12.3%	5	12.9%
	Moderate	9	2.9%	5	12.8%
	Severe	4	1.3%	2	5.1%

Chi-square test, p value= 0.006

Association of severe dengue with other parameters

There was no significant difference (at 5% significance level) in mean platelet count (p value= 0.4) in classical dengue fever (47,000) and severe dengue (43,400) and similarly no significant difference in serum sodium between the two groups (p value= 0.7).

But there was statistically significant difference in hematocrit (p value= 0.04) and potassium levels (p value= 0.04) between classical dengue and severe dengue.

Table 12: Association of severe dengue with other parameters

	Severe Dengue						p value
	Absent			Present			
	Mean	Standard Deviation	Median	Mean	Standard Deviation	Median	
Platelet count	46938.04	25909.24	39000.00	43388.89	26413.50	39000.00	0.4
Hematocrit	40.44	4.77	40.05	42.60	6.03	45.20	0.04
Serum Sodium	139.89	7.74	139.40	140.42	10.76	142.20	0.7
Serum Potassium	4.04	.66	3.90	3.80	.79	3.80	0.04

Association of hypokalemia with neurological symptoms Hypokalemia was present in half of the patients diagnosed with neurological symptoms and 17.3% of dengue patients with no neurological symptoms. P value was calculated to be as 0.038 which suggests a significant relation between hypokalemia and neurological symptoms.

Table 13: Association of hypokalemia with neurological symptoms

		Neurological symptoms			
		Absent		Present	
		Total no.	Percentage	Total no.	Percentage
Hypokalemia	No	283	82.7%	4	50.0%
	Yes	59	17.3%	4	50.0%

Chi-square test, p value= 0.038

Association of neurological symptoms in dengue with other parameters

There was significant relation between platelet count (p value= 0.02) and serum potassium (p value= 0.03) with presence of neurological symptoms unlike hematocrit (p value= 0.7) and serum sodium (p value= 0.3).

Table 14: Association of neurological symptoms in dengue with other parameters

	Neurological symptoms				p value
	Absent		Present		
	Mean	Standard Deviation	Mean	Standard Deviation	
Platelet count	45954.14	25606.02	67750.00	29979.76	0.02
Hematocrit	40.68	4.94	41.44	6.33	0.7
Serum Sodium	140.02	8.02	136.95	11.36	0.3
Serum Potassium	4.02	.67	3.34	.73	0.03

Discussion

The clinical profile of dengue is changing, and the neurological manifestations are reported more frequently. Some of these manifestations are associated with hypokalemia. Prevalence study of hypokalemia in dengue is rarely reported. Hence the present study was taken up and conducted at CAIMS. We included 350 cases of dengue.

Age and Sex

Dengue affects humans of all age groups worldwide. In some parts of the world, it is mainly a pediatric health problem. A study done by Gurdeep S.D *et al.* in 81 cases of dengue fever 53 were males (65.4%) and 28(34.5%) were females ^[3].

In the study by Abin Varghese *et al.*, among 100 patients 71 (71%) were males and 29 (29%) were females. Most of the patients were adults (79%), and only 21 (21%) were children (< than 12 years) ^[4].

In the current study we have selected totally 350 subjects diagnosed having dengue fever. More number of dengue cases was found in the age group of 41-50 years. Among them, 191 subjects were males (54.6%) and remaining 159 subjects were females (45.4%). Thus, the present study shows male preponderance in dengue fever.

Type of Dengue Fever

Among the 350 dengue cases included in our study, 311 were classical dengue fever and 39 were severe dengue cases of which 5 subjects (1.4%) had Dengue Hemorrhagic Fever (DHF) and 34 subjects (9.7%) had Dengue Shock Syndrome (DSS). Among the total subjects, around 56% were tested positive for NS-1 antigen as compared to IgM (53.1%) and IgG (44%).

Neurological Manifestations

Neurological complications of dengue infection have been observed more frequently in the recent past and some studies highlighted varied neurological complications arising in the course of dengue illness. But the true incidence of these manifestations is not clearly mentioned in the literature. The reported papers are mainly hospital-based studies and also neurological complications arising due to dengue fever is recently observed more frequently. In one study, 41 cases of neurological complications arising due to dengue fever have been reported. These patients had both central and peripheral neurological complications. Misra *et al.* included 17 patients of neurological complications in his prospective hospital-based study ^[5]. Reported six patients of neurological manifestations and Solomon *et al.* mentioned nine patients of encephalitis associated with dengue fever ^[6]. In our study, we report two cases of encephalitis. Patient A had presented with complaints of acute fever with altered sensorium and one patient also had multiple episodes of GTCS. CSF analysis showed pleocytosis and positive dengue serology. Verma *et al.* recently reported a case of epilepsia partialis continua in a young woman suffering from dengue encephalitis. She presented with encephalitic syndrome of headache, vomiting, altered sensorium and intractable seizures ^[7]. In a study from Thai hospital, 18% children with encephalitis were found to have a positive dengue serology ^[8]. Misra *et al.* gave the description of 11 patients of encephalopathy with dengue infection ^[5]. Solomon *et al.* reported nine patients of dengue encephalitis. The diagnosis was based on positive antibody to dengue infection in sera and clinical presentation of focal neurological deficits, seizures and cerebrospinal fluid pleocytosis ^[6].

We also report 4 cases of paraparesis with dengue fever. Out of these, one case had presented to us with history of fever and ascending paralysis later was diagnosed to be Guillain Barre Syndrome. Guillain Barre Syndrome has been infrequently reported related to dengue fever. Soares *et al.* discussed about seven cases of Guillain Barre Syndrome associated with dengue-positive IgM antibody in serum, with minimal clinical symptomatology. According to the authors, dengue infection should be routinely looked for in Guillain Barre Syndrome cases in an endemic zone ^[9].

Other three cases were diagnosed to have hypokalemic periodic paralysis. All three patients had significant low serum potassium values and improved dramatically with potassium supplementation. Gupta *et al.* ^[10] reported that dengue fever can precipitate the attack of hypokalaemic periodic paralysis; however, dengue fever causing pure motor quadriplegia due to hypokalaemia was only occasionally reported.

Various studies mentioned about involvement of the musculature leading to proximal weakness associated with dengue fever. Misra *et al.* in their study reported six patients of pure motor quadriplegia related to dengue fever diagnosed as acute viral myositis. All patients showed improvement on therapy ^[5]. In a recently published study from a tertiary center of north India, seven patients of acute dengue viral myositis have been reported, in which authors highlighted that acute dengue viral myositis can present with fulminant variety requiring ventilatory support. They concluded that early respiratory involvement, severe myalgia and elevated serum creatine phosphokinase levels are indicators of severe acute dengue viral myositis ^[10]. We had two patients of dengue myositis who presented to us as high grade fever with quadriplegia and muscle tenderness with elevated creatinine phosphokinase.

Other atypical manifestations

The clinical spectrum of dengue is vast and the newly incorporated expanded dengue syndrome introduces a wide range of presentations that are rarely observed and appreciated but nevertheless have the potential to cause significant morbidity and even mortality. Cardiac involvement in dengue is one such example.

Arrhythmias are the commonest abnormality found in cardiac involvement in dengue and sinus tachycardia is probably the most frequently seen phenomenon. Occurring either during the febrile phase or when developing Dengue haemorrhagic fever with fluid leakage. This may or may not be due to cardiac involvement. Other manifestations include T wave abnormalities, ST segment depressions and elevation, sinus pauses, ectopics that are either atrial or ventricular in origin, ventricular trigeminy, atrial fibrillation, heart blocks such as first-degree block and Mobitz type I second-degree AV block, bundle branch blocks [12-14].

In our study, four patients had presented with arrhythmias. One had come with ventricular tachycardia and died. Others had ECG changes suggestive of hypokalemia which were reversible with potassium replacement.

Serum Electrolytes

In our current study, the mean serum potassium level in dengue patients is found to be 4.01 ± 0.68 mEq/L. Among the 350 cases, 63(18%) of the patients had Hypokalemia (<3.5 mEq/L) with majority having mild hypokalemia (12.3% of total 350 cases). In another retrospective study done on clinical data from 1342 patients with dengue fever seen from 2002 to 2006 in Guangzhou, Ying R.S. *et al.* observed prevalence of hypokalemia in up to 28% of cases [15]. The causes of hypokalemia in this condition may be due to poor intake and an increase in renal excretion due to activation of renin, angiotensin and aldosterone system secondary to volume depletion.

Hypokalemia was also significantly associated with the presence of neurological manifestations seen in dengue fever. Thus, it is important to monitor potassium levels in all patients with neurological symptoms as it can have both prognostic and therapeutic role in managing such patients.

Severity of the disease

We also observed in our study that there is a significant difference in the presence of moderate and severe hyperkalemia in severe dengue but there is not much difference in the association of mild hyperkalemia with severe dengue fever

Severe dengue was significantly associated with higher hematocrit value than classical dengue but there was no significant difference in platelet count in both the groups. So it underlies the importance of monitoring hematocrit in dengue fever more than platelet count.

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Conflict of Interest

None

Funding Support

Nil

Conclusion

Hence, the results of our study implies the usefulness and prognostic value of identifying and correcting electrolyte disturbances and hematological alterations in dengue fever, leading to early relief of muscle fatigue and recovery. It also implies the use of treating electrolyte imbalance than just prescribing non-steroidal anti-inflammatory (NSAID) drugs to relieve myalgia. There are very less studies in this area, this shows need for more studies in this area to throw light on significant alteration in serum electrolyte, hematocrit and CBC in dengue.

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Conflict of Interest

None

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