Neurology Asia 2016; 21(1) : 23 – 32

Hypokalemic paralysis associated with dengue fever: Study from a tertiary centre in North India

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Abstract

Objective: Dengue associated hypokalemic paralysis (DHP) is an unusual neurological complication of dengue fever. This was a retrospective study of patients with DHP compared with idiopathic hypokalemic paralysis (IHP) seen in a tertiary centre in North India. *Methods:* Dengue was diagnosed by positive nonstructural protein (NS) 1 antigen and dengue-IgM antibody. Various clinical and laboratory parameters were compared between patients with DHP and IHP. *Results:* DHP was seen in 18 out of 489 (3.7%) dengue patients seen in the 4-years study period. Complications of bulbar weakness or respiratory failure developed in 6/18 (33.3%) of DHP patients. DHP patients with complications had higher hematocrit ($p<0.001$), lower platelet count ($p=0.002$), lower serum potassium ($p=0.007$) and higher creatinekinase (CK) ($p<0.001$) as compared to those without complications. When compared to IHP, DHP patients had fever at admission ($p<0.001$); myalgia ($p<0.001$); no past episodes ($p=0.032$); greater disability ($p=0.02$); lower serum potassium ($p=0.0338$); higher CK ($p=0.001$); and nerve conduction abnormalities ($p=0.035$).
Conclusions: DHP should be suspected in patients who present with acute onset muscle weakness associated with fever. Predictors of complications in DHP include high hematocrit, low platelet count, low serum potassium and raised CK.

INTRODUCTION

Dengue is a mosquito borne arboviral disease caused by dengue virus, which belongs to the *Flaviviridae* family. It causes a febrile illness, which is usually self-limiting; but occasionally may have serious complications. The disease is rapidly spreading to become endemic in many developing countries worldwide, so that about half of the global population is presentlyat risk of dengue infection. According to World Health Organization (WHO) estimates, there are currently 50–100 million dengue infections worldwide every year.[1] Dengue outbreaks are being constantly reported from various parts of India. The case fatality rate for dengue fever in India ranges from 1.5 to 10.9%.[2] The most severe complications of dengue include dengue hemorrhagic fever and dengue shock syndrome. Neurological complications of dengue are being increasingly recognized in recent years. These complications include encephalitis, encephalomyelitis, opsoclonus-myoclonus, brachial neuritis, Guillain-Barré syndrome, myositis and hypokalemic paralysis.[3,4]

Hypokalemic paralysis is flaccid generalized weakness associated with reduction in serum potassium levels, either spontaneously or due to triggers such as insulin or glucose administration. Hypokalemic periodic paralysis is a channelopathy, which is of two types, type 1 due to mutation in CACNL1A3 calcium channel gene, and type 2 due to mutation SCN4A sodium channel gene.[5] Periodic paralysis associated with low serum potassium may also be observed in conditions such as thyrotoxicosis, primary hyperaldosteronism and Sjogren syndrome with distal renal tubular acidosis.[6-8]In India, other than the above mentioned etiology, dengue, Gitelman syndrome, Liddle syndrome, alcoholism, and gastroenteritis are the other reported causes.[9,10] Dengue as an etiology of hypokalemic paralysis was observed in 13.7% and 1.7% cases.[9,10]There is no previous study comparing the clinical and laboratory features along with outcome of DHP with IHP, which is the purpose of the current study.

METHODS

This retrospective observational study was conducted in King George's Medical University, Lucknow; which is a leading tertiary care hospital in North India. The study was approved by

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Institutional Ethics Committee of King George's Medical University, Lucknow, India. We traced the case records of patients with diagnosis of hypokalemic paralysis admitted in our institution, over a period of four years from August 2010 to July 2014. We also reviewed the case records of all dengue patients admitted during this period to determine the prevalence of hypokalemic paralysis in dengue fever. The records of these patients with hypokalemic paralysis were examined for demographic features such as age, gender, residence, details of fever, headache, body ache, rash, nausea, vomiting, diarrhea, weakness of limbs, neck weakness, cranial nerve complains, sensory complains, autonomic features, lymphadenopathy, hepatosplenomegaly, bleeding tendencies and details of the clinical neurological examination. The laboratory investigations included hemoglobin, hematocrit, red blood cell count, total leukocyte count, differential leukocyte count, platelet count, peripheral blood smear, serum electrolytes including sodium, potassium, calcium and magnesium, blood urea, serum creatinine, serum bilirubin, liver enzymes, serum proteins, blood sugar, arterial blood gas analysis (blood pH, bicarbonate, anion gap), urine electrolytes, thyroid profile, IgM for dengue repeated twice one week apart, non structural protein (NS) 1 antigen for dengue, chest radiograph, electrocardiograph and nerve conduction study were extracted. Bulbar weakness was said to be present if patient had symptoms of dysphagia, nasal regurgitation of fluids, hoarseness of voice and weak or absent gag reflex. Respiratory weakness was said to be present if any of following was observed in patients: use of accessory muscles of respiration, paradoxical breathing, inability to count to 20 in single breath, hypoxemia (paO2<60 mm of Hg), hypercarbia (paCO2>45 mm of Hg) or respiratory acidosis on arterial blood gas analysis. The baseline disability of the patients were assessed by Guillain-Barré syndrome disability (GBSD) score (Table 5) and modified Barthel index. The patients were evaluated on a daily basis till their recovery. The GBS disability score and Barthel index in recovered patients were estimated at the time of discharge. Serum electrolytes were repeated daily.

We studied patients with DHP (Group I) and IHP (Group II). The diagnosis of dengue in Group I was made on the basis of positive NS1 antigen and two positive dengue IgM, at least one week apart. Patients were diagnosed as IHP if the investigations for dengue were negative and no cause of hypokalemic paralysis could be ascertained. We compared patients in these two groups for clinical features, disability status, laboratory investigations and outcome.

Statistical analysis

Categorical variables were presented as numbers and percentages. Continuous data were evaluated for normal distribution by Shapiro Wilk test. Continuous variables were expressed as mean (standard deviation) if normally distributed and as median (range) if not normally distributed. Pearson's chi square test was used for comparison of categorical data between different groups. Fisher's exact test was used for small numbers. Continuous data were compared between different groups by two-tailed t-test for independent samples, if the variables were normally distributed. Man Whitney U test was used to compare continuous data between different groups, if

Table 5: Guillain-Barré syndrome disability scale

0	Healthy
1	Minor symptoms or signs of neuropathy but capable of manual work/capable of running
2	Able to walk without support of a stick (5m across an open space) but incapable of manual work/running
3	Able to walk with a stick, appliance or support (5m across an open space)
4	Confined to bed or chair bound
5	Requiring assisted ventilation (for any part of the day or night)
6	Death

Hughes RA, Newsom-Davis JM, Perkin GD, Pierce JM. Controlled trial prednisolone in acute polyneuropathy. *Lancet* 1978; 2:750-3.

the variables were not normally distributed. Multivariate analysis of various parameters between the two groups was performed using binary logistic regression. P value <0.05 was considered as significant. Statistical analysis was performed using the Statistical Software for Social Sciences (SPSS) version 16.0 for windows platform.

RESULTS

During the study period, 58 patients of hypokalemic paralysis were admitted in our institution. The etiologies of these patients were as follows: thyrotoxicosis in 6 (10.3%) patients, renal tubular acidosis in 3 (5.2%) patients, Gitelman syndrome in 2 (3.4%) patients, gastroenteritis in 4 (6.9%) patients, dengue in 18 (31.0 %) and IHP in 25 (43.1%) patients. There were thus 18 DHP patients in Group I and 25 IHP patients in Group II (Figure 1).

There were 489 patients admitted for dengue fever during the study period. Of these, 18 patients developed hypokalemic paralysis. Thus the prevalence of hypokalemic paralysis among dengue fever patients was 3.7%. The mean (SD) age of these patients was 34.7 (14.0) years, range 16- 65 years. The male: female ratio was 2.6: 1 (13 males and 5 females). None of the patients had preexisting co-morbidities such as diabetes mellitus, hypertension, or cardiac, renal and hepatic diseases. Out of the 18 patients, 10 (55.5%) patients had fever at the time of admission. The remaining 8 (44.4%) patients had

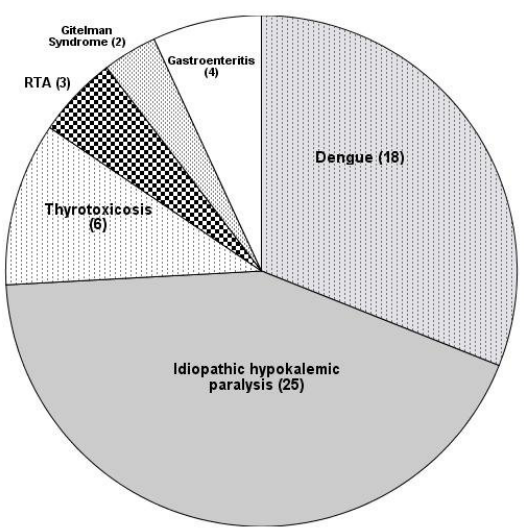

Figure 1. Etiology of hypokalemic paralysis in 58 patients. Numbers in bracket indicate number of patients.
RTA, renal tubular acidosis

fever in the preceding days, but it had subsided at the time of admission. Six (33.3%) patients had chills and rigors, 13 (72.2%) patients had nausea and 6 (33.3%) patients had vomiting. Abdominal pain was complained by 8 (44.4%) patients, but none of these patients had diarrhea or constipation. Arthralgia was present in 13 (72.2%) patients and 16 (88.8%) patients complained of myalgia. Petechial rash was present in 3 (16.6%) patients. None of the patients had ecchymoses or mucosal bleeds. Mean (SD) pulse rate on admission was 101.3 (22.3) per minute. Mean (SD) systolic blood pressure at admission was 116 (16.1) mmHg. Hypotension (systolic blood pressure < 100 mmHg) was present in three (16.6%) patients. Tachypnea (respiratory rate> 20/ minute) was present in five (27.7%) patients at admission. Mean (SD) serum potassium level in DHP patients was 2.1(0.4) mEq/L while in patients with dengue fever without hypokalemic paralysis it was 4.3(0.6) mEq/L. Hypokalemia was observed in 57 (12.1%)patients of dengue fever without paralysis.

The neurological disability was pure motor quadriparesis in all patients. The neurological disability occurred with fever in 10 (55.5%) patients and following fever in 8 (44.4%) patients. The weakness started in lower limbs in 15 (83.3%) patients and upper limbs in 3 (16.6%) patients. Mean (SD) duration of onset to peak weakness was 25.1 (11.6) hours, range 9-48 hours. Involvement of both proximal and distal muscles was most common, seen in 13 (72.2%) patients. Involvement of predominantly proximal muscles was seen in four (22.2%) patients and predominantly distal muscle weakness was seen in one (5.5%) patients. Involvement of lower limb muscles was more severe than upper limbs in all cases. Deep tendon reflexes were normal in 5 (27.7%); hypoactive in 9 (50%) and absent in 4 (22.2%) patients. Plantar response was flexor in all patients. Neck muscle weakness was noted in 3 (16.6%) patients; whereas bulbar weakness was present in 4 (22.2%) patients. Respiratory involvement was seen in 5 (27.7%) patients. Respiratory failure was managed by noninvasive mechanical ventilation in 4 patients while one patient was managed conservatively. None of the patients had facial weakness, diplopia or visual complains. Bowel or bladder involvements were not present in any patient. No patient had family history of weakness or history of similar weakness in the past. We could not find precipitating factors of hypokalemia in any patient. Mean (SD) GBSD score was 4 (0.6); mean (SD) Barthel index was 5.8 (1.6) and mean

(SD) modified Rankin scale score was 4.2 (0.4). Serum potassium was corrected by intravenous route in 7 (38.8%) patients administered in a dose of 40 mEq every 4 hours in 20% mannitol as slow infusion. The indications for intravenous potassium correction were serum potassium level <2 mEq/L; respiratory or bulbar weakness and inability to take oral fluids. Remaining 11 (61.1%) patients received oral potassium correction in a dose of 20-25 mEq every 6 hours. Rebound hyperkalemia occurred in 5 (27.7%) patients. No patient required platelet transfusion. Mean (SD) recovery time was 26.8 (18.2) hours, range 6-64 hours. Recovery was complete in all patients. The mean (SD) duration of hospitalization was 3.7 (1.7) days. The demographic, clinical and laboratory profile of these patients is shown in Tables 1 and 2.

Out of 18 patients with DHP, complications developed in 6 (33.3%) in the form of bulbar weakness or respiratory distress. We compared clinical and laboratory features between patients with complicated and uncomplicated hypokalemic paralysis associated with dengue (Table 3). DHP patients had significantly higher hematocrit ($p<0.001$), lower platelet count ($p=0.002$), lower serum potassium ($p=0.007$) and higher serum CK level ($p<0.001$). These parameters were also associated with DHP patients, as indicated by GBS disability score. (Figure 2)

We compared various parameters between patients with DHP (Group I) and IHP (Group II), which is shown in Table 4.

Table 1: Clinical features of patients with dengue associated hypokalemic paralysis

Clinical features / Patient No.	Age	Sex	Fever at admission	Duration from onset to peak weakness (hours)	Neck weakness	Bulbar weakness	Respiratory weakness	GBSD score	Recovery time (hours)
1	28	M	Yes	9	No	No	No	4	12
2	31	F	No	17	Yes	Yes	No	4	42
3	54	M	Yes	40	No	No	Yes	5	48
4	23	F	No	12	No	No	No	4	24
5	19	M	Yes	48	No	No	No	3	18
6	39	M	No	21	Yes	Yes	Yes	5	56
7	36	M	Yes	10	No	No	No	4	30
8	22	M	Yes	18	No	No	Yes	4	48
9	43	M	No	36	No	No	No	3	24
10	30	F	Yes	16	No	No	No	4	8
11	65	M	Yes	26	No	Yes	Yes	5	64
12	27	M	No	32	No	No	No	4	10
13	16	F	Yes	39	No	No	No	3	12
14	34	M	No	24	No	No	No	4	18
15	56	M	Yes	15	No	No	No	4	6
16	38	M	No	22	Yes	Yes	Yes	5	40
17	47	F	No	28	No	No	No	3	10
18	17	M	Yes	40	No	No	No	4	14

M, Male; F, Female; GBSD, Guillain-Barré syndrome disability

Table 2: Laboratory features of patients with dengue associated hypokalemic paralysis

Lab Features / Patient No.	Hemoglobin (mg/dL)	Platelet count (x10^3/cumm)	Serum K+ (meq/L)	Serum CK (IU/L)	Blood pH	Urinary pH	ECG	Motor NCS
1	14.4	140	2.9	124	7.45	7.0	normal	normal
2	11.8	58	1.9	410	7.36	6.0	U wave	decr. CMAP
3	13.6	38	1.6	545	7.41	6.7	Flat T	decr. CMAP
4	9.8	130	2.8	208	7.49	6.9	normal	normal
5	12.6	110	2.6	258	7.44	6.1	Flat T	normal
6	11.2	79	1.3	490	7.38	7.0	U wave	decr. CMAP
7	15.6	36	3.4	395	7.37	6.2	normal	decr. CMAP
8	14.2	32	1.7	510	7.35	7.5	Flat T	normal
9	13.9	98	3.0	110	7.38	7.6	normal	decr. CMAP
10	8.9	84	1.8	140	7.37	6.8	Flat T	normal
11	10.4	42	2.1	520	7.31	7.3	U wave	decr. CMAP
12	14.3	108	2.7	228	7.42	6.5	normal	normal
13	12.1	57	3.2	260	7.45	7.8	normal	normal
14	9.5	125	2.0	310	7.34	7.1	normal	decr. CMAP
15	15.2	135	2.5	225	7.32	7.4	normal	decr. CMAP
16	11.3	46	2.4	490	7.39	6.5	Flat T	normal
17	10.5	178	2.3	160	7.44	7.1	normal	decr. CMAP
18	8.4	124	3.1	185	7.46	7.2	Flat T	decr. CMAP

CK, Creatinekinase; decr. CMAP, decreased amplitude of compound muscle action potential; ECG, Electrocardiograph; NCS, Nerve conduction study.

DISCUSSION

Hypokalemic paralysis is a rapidly progressive acute muscle weakness, in association with reduced serum potassium concentration. The temporal course and clinical presentation of hypokalemic paralysis resemble those of Guillain-Barré syndrome in many cases. Timely diagnosis and early treatment of hypokalemic paralysis are essential, as the weakness is completely reversible with treatment; and may be life threatening if left untreated. Primary hypokalemic paralysis is a genetic disorder which is caused by defect in ion channels. The most common cause of hypokalemic periodic paralysis is due to mutation in calcium channel gene, and the other cause is mutation in the sodium channel gene. The secondary hypokalemic paralysis is due to reduction in serum potassium concentration as a result of many conditions. In our study, the etiologies of hypokalemic paralysis were thyrotoxicosis, renal tubular acidosis, dengue, Gitelman syndrome, gastroenteritis, diabetic ketoacidosis and idiopathic hypokalemic paralysis. The causes are similar to those reported in previous studies from India.[6,9,10]

We found that hypokalemic paralysis occurred in 3.7% of patients with dengue. In a previous study, hypokalemic paralysis was seen in 3 out of 26 patients with various neurological complications of dengue.[4]We did not study other neurological manifestations of dengue. As for pathophysiology of hypokalemia in dengue, plasma leakage through vascular wall is considered to be central pathology in dengue. Unlike other hemorrhagic viral infections, there is

Table 3: Comparison of various parameters between patients with complicated and uncomplicated dengue associated hypokalemic paralysis

Features	Complicated dengue associated hypokalemic paralysis (n=6)	Uncomplicated dengue associated hypokalemic paralysis (n=12)	P value	Test statistics
Presence of fever at onset of weakness	3 (50%)	7 (58.3%)	1	-
Vomiting	4 (66.7%)	2 (16.7%)	0.107	-
Abdominal pain	4 (66.7%)	4 (33.3%)	0.321	-
Arthralgia	3 (50%)	10 (83.3%)	0.268	-
Myalgia	6 (100%)	10 (83.3%)	0.289	$\chi^2 = 1.125$
Rash	2 (33.3%)	1 (8.3%)	0.245	-
Mean (SD) systolic BP in mmHg	117.7 (19.2)	115.1 (15.2)	0.767	95% C.I.= -15.07 to 20.07
Mean (SD) duration from onset to peak weakness [in hours]	24 (8.5)	25.7 (13.3)	0.775	95% C.I.= -14.49 to 10.99
Mean (SD) hematocrit [in %]	45.2 (3.5)	36.9 (2.5)	**<0.001**	95% C.I.= 5.2 to 11.3
Mean (SD) platelet count [x 10^3/cumm]	49.2 (17)	110.4 (38.2)	**0.002**	95% C.I.= -96.33 to -26.17
Mean (SD) serum K in mEq/L	1.8 (0.3)	2.3 (0.3)	**0.007**	95% C.I.= -0.88 to -0.16
Mean (SD) Serum Ca [in mEq/L]	9.1 (0.6)	9.0 (0.7)	0.98	95% C.I.= -0.69 to 0.71
Mean (SD) serum CK [IU/L]	494.2 (46.1)	216.9 (82.2)	**<0.001**	95% C.I.= 199.97 to 354.52
ECG changes	6 (100%)	3 (25%)	0.009	-
Reduced CMAP in motor NCS	4 (66.7%)	6 (50%)	0.638	-

C.I., Confidence interval; SD, Standard deviation; ECG, Electrocardiograph; CK, Creatinekinase; CMAP, Compound muscle action potential; NCS, Nerve conduction study.

lack of overt endothelial damage and cytopathic effects on endothelial cells in dengue infection.[11] The endothelial damage in dengue is thought to result from multiple factors including antibodies secreted by B lymphocytes and cytokines involved in the cell mediated immunity, such as tumor necrosis factor- alpha (TNF-α), interferon- gamma (IFN-γ), interleukins IL-2, IL-6, IL-1β, and IL-8.[12-14] This inflammatory response is further enhanced by the activation of endothelial cells, which then overexpress various chemokines and vascular endothelial growth factor (VEGF).[11] The endothelial dysfunction leads to loss of fluid and electrolytes out of vascular compartment and decrease in serum potassium levels. Impairment of renal function, due to glomerular, tubular, interstitial or vascular endothelial damage may be the second factor causing hypokalemia in dengue. In a study from India, it was observed that 10.8% patients with dengue fever developed acute kidney injury, of which 5.4% were mild, 3.1% moderate, and 2.2% severe.[15] In another study from Taiwan,

Table 4: Comparison of various parameters between patients with dengue associated hypokalemic paralysis and idiopathic hypokalemic paralysis

Features	Dengue associated hypokalemic paralysis [Group I] (N=18)	Idiopathic hypokalemic paralysis [Group II] (n= 25)	P value	Test statistic
Mean (SD) age in years	34.7 (14.02)	27.2 (7.5)	**0.028**	95% C.I.= 0.84 to 14.2
Male: female)	13:5	17:8	0.766	$\chi^2 = 0.088$
Presence of fever at admission	10 (55.6%)	0 (0%)	**<0.001**	$\chi^2 = 18.09$
Presence of precipitating factors	0 (0%)	9 (36%)	**0.004**	$\chi^2 = 8.195$
Mean (SD) duration from onset to peak weakness [hours]	25.2 (11.7)	28 (12.7)	0.454	95% C.I.= -10.54 to 4.79
Myalgia	16 (88.9%)	7 (28%)	**<0.001**	$\chi^2 = 15.595$
Absent deep tendon reflexes	4 (22.2%)	6 (24%)	1.0	-
Predominantly proximal weakness	4 (22.2%)	7 (28%)	0.736	-
Both proximal and distal weakness	13 (72.2%)	16 (64%)	0.57	$\chi^2 = 0.322$
Predominantly distal weakness	1 (5.6%)	2 (8%)	1.0	-
Neck muscle weakness	3 (16.7%)	2 (8%)	0.634	-
Bulbar weakness	4 (22.2%)	1 (4%)	0.144	-
Respiratory involvement	5 (27.8%)	1 (4%)	0.067	-
History of past episodes of weakness	0 (0%)	6 (24%)	**0.032**	-
Family History	0 (0%)	2 (8%)	0.502	-
Median (range) GBS disability score	4 (3-5)	4 (3-4)	**0.02**	Z = -2.319
Median (range) Barthel index	6 (4-8)	7 (5-9)	**0.036**	Z= -2.1
Median (range) Modified Rankin scale (MRS) score	4 (4-5)	4 (4-5)	**0.028**	Z = -2.19
Mean (SD) serum K [mEq/L]	2.1 (0.4)	2.4 (0.3)	**0.038**	95% C.I.= -0.48 to -0.01
Features	**Dengue associated hypokalemic paralysis [Group I] (N=18)**	**Idiopathic hypokalemic paralysis [Group II] (n= 25)**	**P value**	**Test statistic**
Mean (SD) serum CK [IU/L]	309.3 (151.9)	182.1 (76)	**0.001**	95% C.I.= 56.15 to 198.27
ECG changes of hypokalemia	9 (50%)	6 (24%)	0.078	$\chi^2 = 3.114$
Reduced CMAP in NCS	10 (55.6%)	6 (24%)	**0.035**	$\chi^2 = 4.46$
Intravenous potassium treatment	8 (44.4%)	7 (28%)	0.264	$\chi^2 = 1.246$
Rebound hyperkalemia during treatment	3 (16.7%)	2 (8%)	0.634	-
Mean (SD) recovery time (hours)	26.9 (18.3)	23.6 (12.2)	0.477	95% C.I.= -6.04 to 12.69
Median (range) duration of hospitalization (days)	3.5 (2-7)	3 (2-6)	0.378	Z= -0.881

C.I., Confidence interval; SD, Standard deviation; ECG, Electrocardiograph; CK, Creatinekinase; CMAP, Compound muscle action potential; NCS, Nerve conduction study; GBS disability score, Guillain-Barré syndrome disability score.

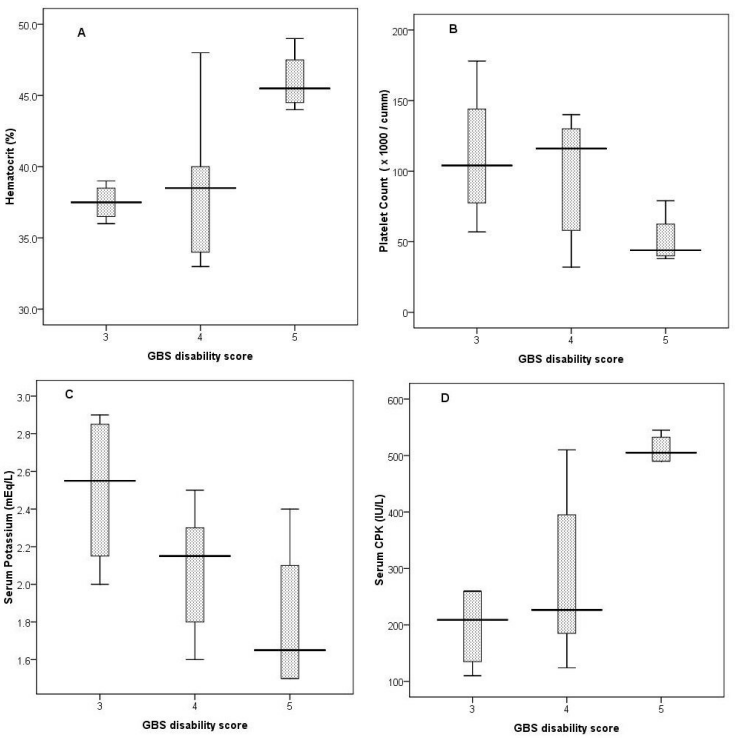

Figure 2: Correlation of hematocrit, platelet count, serum potassium and serum creatinekinase with disability of patients with dengue associated hypokalemic paralysis measured by GBS disability score.

dengue fever was complicated by acute kidney injury in 21(4%) of 519 patients.[16] However, there are very few studies describing histopathological findings of renal pathology in dengue fever. Dengue virus and dengue RNA weredemonstrated in kidney samples of 12 cases with fatal dengue hemorrhagic fever in Cuba.[17] In another case of severe dengue infection, the renal biopsy showedhemorrhage on glomerular capillaries and proximal convoluted tubules; along with mononuclear infiltrate around the collectingducts, with hemorrhagic foci, interstitial edema andvascularcongestion.Immunostaining with specific DENV-3immunoperoxidase demonstrated the viral antigen on endothelium and inflammatory cellsin the renal medulla.[18] Nephrotic range proteinuria, suggesting glomerular injury has been demonstrated in dengue hemorrhagic fever.[19] Acute tubular necrosis has been demonstrated by kidney biopsy in a patient with non-hemorrhagic dengue fever.[20] A combination of techniques using immunohistochemistry and in situ hybridization demonstrated dengue viral antigens and RNA in kidney samples from patients with dengue fever.[21] Thus, there is enough data to demonstrate renal impairment in dengue, which may be due to inflammatory response by a combination of antibodies, lymphocytes, mononuclear cells and cytokines. Damage of renal tubules probably leads to inability to retain potassium by the kidneys, resulting in loss of serum potassium. It has also been postulated that stress due to dengue infection leads to release of catecholamines and hyperinsulinemia, which may result in shift of potassium from extracellular to intracellular compartment.[22]

The mean age of DHP patients in our study was 34.7 years, compared to 27.2 years in IHP patients. In a previous study, the mean age of IHP patients was 23.07 years.[9] The younger age at presentation of IHP patients may be due to inclusion of patients with hypokalemic periodic paralysis, which is a channelopathy known to presents at an earlier age.[23] There was no significant difference in sex ratios between the two groups. On comparing clinical and laboratory features between DHP patients and IHP patients, it was observed that there was no significant difference between the two groups in the duration from onset to peak weakness, pattern of weakness, absent deep tendon reflexes, neck muscle weakness, bulbar weakness, respiratory involvement, ECG changes, need of intravenous potassium therapy, rebound hyperkalemia, recovery time and duration of

hospitalization. However, DHP patients had fever at admission, significant myalgia, greater disability as measured by GBS disability score, Barthel index and MRS score, significant nerve conduction abnormalities, significantly lower serum potassium and higher serum CK levels. On the other hand, IHP patients had precipitating factors at onset of weakness and history of past episodes of weakness, which were not seen in the dengue group. The greater disability and lower potassium levels in dengue group is consistent with higher risk of complications and poor outcome in this group of patients. Hence dengue should be suspected as a probable etiology in any patient in endemic region with hypokalemic paralysis, especially in presence of fever. Prompt potassium correction is necessary in such patients to prevent or treat further complications like respiratory paralysis and bulbar weakness.

The finding of increased CK level in the dengue group demonstrates greater muscle damage in dengue patients compared to IHP patients. The low serum potassium levels, if left uncorrected may lead to rhabdomyolyis.[24,25] Myositis has been described to occur in dengue fever. Inflammatory infiltrates have been demonstrated in muscle biopsy samples of these patients.[4,26] However, it may be clinically difficult to differentiate between hypokalemic paralysis and myositis in a dengue patient with generalized weakness. Reversal of weakness on potassium supplementation favors a diagnosis of hypokalemic paralysis, whereas myositis may be suggested by higher CK level and confirmed by muscle biopsy demonstrating inflammatory infiltrate.

We also found that dengue patients with complicated hypokalemic paralysis (those with respiratory or bulbar weakness) had significantly higher hematocrit, lower platelet count, lower serum potassium and higher serum CK levels. Higher hematocrit and lower platelet count have been shown to be associated with severe infection and poor outcome in dengue infection.[27]This may indicate more immunological and metabolic derangements in these patients.

In conclusion, hypokalemic paralysis is an important neurological complication of dengue infection, seen in 3.7% patients with dengue fever. It should be suspected in patients from endemic areas who present with acute muscle weakness with fever. DHP differs from IHP by absence of history of previous episodes of weakness, presence of fever, myalgia, greater disability along with lower serum potassium and higher creatinekinase levels. Dengue associated hypokalemic paralysis is complicated by respiratory and bulbar weakness in 33.3% patients. The predictors of complications in these patients include higher hematocrit, lower platelet count, lower serum potassium and higher serum creatinekinase levels.

The limitations of this study were the limited number of patients. The small sample size and retrospective design of our study makes generalization of the results difficult. We also did not perform muscle biopsies in our patient. The patients with IHP were not subjected to genetic testing due to lack of resources. There is a need of prospective studies with larger sample size for better understanding of DHP.

DISCLOSURE

Financial support: None

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