

Clinical and biochemical spectrum of hypokalemic paralysis in North: East India

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Abstract

Background: Acute hypokalemic paralysis, characterized by acute flaccid paralysis is primarily a calcium channelopathy, but secondary causes like renal tubular acidosis (RTA), thyrotoxic periodic paralysis (TPP), primary hyperaldosteronism, Gitelman's syndrome are also frequent. **Objective:** To study the etiology, varied presentations, and outcome after therapy of patients with hypokalemic paralysis. **Materials And Methods:** All patients who presented with acute flaccid paralysis with hypokalemia from October 2009 to September 2011 were included in the study. A detailed physical examination and laboratory tests including serum electrolytes, serum creatine phosphokinase (CPK), urine analysis, arterial blood gas analysis, thyroid hormones estimation, and electrocardiogram were carried out. Patients were further investigated for any secondary causes and treated with potassium supplementation. **Result:** The study included 56 patients aged 15-92 years (mean 36.76 ± 13.72), including 15 female patients. Twenty-four patients had hypokalemic paralysis due to secondary cause, which included 4 with distal RTA, 4 with Gitelman syndrome, 3 with TPP, 2 each with hypothyroidism, gastroenteritis, and Liddle's syndrome, 1 primary hyperaldosteronism, 3 with alcoholism, and 1 with dengue fever. Two female patients were antinuclear antibody-positive. Eleven patient had atypical presentation (neck muscle weakness in 4, bladder involvement in 3, 1 each with finger drop and foot drop, tetany in 1, and calf hypertrophy in 1), and 2 patient had respiratory paralysis. Five patients had positive family history of similar illness. All patients improved dramatically with potassium supplementation. **Conclusion:** A high percentage (42.9%) of secondary cause for hypokalemic paralysis warrants that the underlying cause must be adequately addressed to prevent the persistence or recurrence of paralysis.

Key Words

Hypokalemia, paralysis, secondary causes

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Introduction

Hypokalemic paralysis is a form of metabolic myopathy, which represents a heterogeneous group of disorder characterized by hypokalemia, acute flaccid paralysis, and potentially fatal episodes of muscle weakness through the involvement of the respiratory muscles, and life-threatening cardiac arrhythmias. Hypokalemic periodic paralysis (HPP) can be a primary disorder, which may be familial with autosomal-dominant inheritance or sporadic, or it may be secondary with causes like renal tubular acidosis (RTA), thyrotoxic periodic paralysis (TPP), primary hyperaldosteronism, Gitelman syndrome, barium poisoning, and diarrhea.^[1] Familial periodic paralysis

(FPP) is the commonest cause of HPP in Caucasians, and TPP is the leading cause in Asian population.^[2,3] Although the clinical manifestation may be similar in both types, the severity and the long-term management may be different and, therefore, it is imperative for physicians to find out the cause of hypokalemic paralysis. Failure to make a distinction between these two types may result in mismanagement, which can be even fatal.

Hypokalemic paralysis has been underreported in neurological practice. The present study was undertaken to know the etiology of hypokalemic paralysis, its varied presentations, and the clinical outcome after potassium replacement therapy of this easily treatable metabolic disorder.

Materials and Methods

The present study is a prospective single-center study done over a period of 24 months from October 2009 to September 2011. All patients with acute flaccid weakness due to hypokalemia (serum $K^+ < 3.5$ mmol/l) involving two or more limbs who did not have objective sensory signs were included in the study. Patients with other causes of acute flaccid weakness on further

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evaluation and those on diuretic therapy were excluded. A detail medical history including any previous episodes of weakness, thyroid disease, drug intake, diarrhea, vomiting, hypertension, and renal disease was noted. Any history of similar disease in the family was enquired about and recorded. The examination included detailed systemic examination and complete neurologic examination including assessment of muscle tone, muscle power using the Medical Research Council (MRC) scale, and deep tendon reflexes. Facial and bulbar weakness was noted.

The investigations including serum levels of sodium, potassium, calcium, magnesium, renal function tests, serum CPK, thyroid function tests, urine pH, arterial blood gas analysis, and 12 lead electrocardiogram (ECG) were done in all cases. Serum electrolytes were measured using ion-selective electrode method; thyroid function test was done using chemiluminescent assays for TSH, triiodothyronine (T3), and thyroxine (T4). Arterial blood gas (ABG) analysis was done by blood gas analyzer (Nova Phox Plus C). In selected cases, 24 hour urine calcium, USG and radiography of abdomen, serum renin and aldosterone levels, serum parathormone (PTH) levels were done, where it was indicated.

Patients with hyperchloremic metabolic acidosis with normal anion gap in the absence of gastrointestinal loss and a fasting urine pH > 5.5 were regarded as having renal tubular acidosis (RTA).^[4] The diagnosis of distal RTA was supported by nephrolithiasis on abdominal USG or radiography. In patients with RTA, tests for anti-nuclear antibody (ANA), anti-dsDNA, and rheumatoid factor were carried out to find out any secondary cause.

The presence of metabolic alkalosis (serum bicarbonate >29 mmol/l) with hypokalemia, hypomagnesemia (serum magnesium <1.8 mg/dL /<0.74 mmol/L), hypocalciuria (urinary calcium <0.05 mmol/kg/24 hours or <100 mg/24 hours), and elevated PTH (normal range: 14.0 – 72.0 pg/ml) were considered as indicative of Gitelman syndrome.^[5] Patients with hypertension, hypokalemia, and metabolic alkalosis mimicking hyperaldosteronism but with low renin (normal range - standing: 1.31 - 3.9 ng/ml/hr; supine: 0.15 - 2.33 ng/ml/hr) and aldosterone (normal range-standing: 40.0 ng/ml/supine: 10.0 - 160.0 ng/ml) levels were diagnosed as Liddle's syndrome.^[6] Patients with hypertension and hyperaldosteronism were diagnosed as primary hyperaldosteronism, and CT abdomen was done to diagnose adrenal adenomas or hyperplasia.^[7]

All patients were treated with potassium supplementation - oral (25 mEq at 6 h interval) or intravenous (10 mEq /hour), based on their serum potassium level (cut off level 1.5 mmol/l) and severity of clinical manifestations (extreme weakness, arrhythmia). Patients with thyrotoxicosis were treated with carbimazole and propranolol, and those with RTA were treated with oral potassium citrate. Patients with Gitelman syndrome were treated with spironolactone (25-100 mg/day). The patients with idiopathic periodic paralysis who were having recurrent attacks were started with acetazolamide (250 mg 3 times daily), and dose was titrated as required. Patients were also advised to modify their lifestyle, including avoidance of precipitating factors.

Data analysis was done with SPSS version 17.0. Where possible; all values were expressed as mean \pm SD. Independent t test was used to compare means assuming unequal variance. A *P* value < 0.05 was considered statistically significant, and a *P* value < 0.01 was considered statistically highly significant.

Result

The study included 56 patients with hypokalemic paralysis whose mean age was 36.76 \pm 13.72 years (range 15-92) years, the male: female ratio being 2.73:1. Five patients had a family history of a similar illness. Thirty-one patients (55.35%) presented with history of recurrent attacks in the past. Recurrent attacks were more common in the primary group compared to secondary group (59.3% vs. 29.1%).

Precipitating factor included heavy exertion in 11 patients, heavy carbohydrate meal in 6, fasting in 3, ethanol abuse in 3 and gastroenteritis in 2 patients. Twenty-three patients had myalgia, out of which 13 (56.52%) were in the secondary group, more so in ethanol abusers. Complaints of paresthesia were reported by 6 patients. All patients, except one patient with isolated bilateral asymmetric episodic finger drop, reported symmetrical weakness of both upper and lower limbs; respiratory paralysis was present in 2 patients on presentation. A total of 11 cases had atypical presentation in the form of neck muscles weakness (4 cases), bladder involvement (3 cases), finger drop and foot drop (1 case each), tetany (1 female of Gitelman syndrome), and calf hypertrophy (1 case) [Table 1]. No patient had weakness of jaw muscles. Deep tendon reflexes were absent in 18 patients (32.15%), diminished in 18 (32.15%) and normal in 20 (35.75%) patients. None had sensory, ocular problems or cranial nerve abnormalities on examination.

Thirty-two (57.1%) patients were diagnosed as primary hypokalemic periodic paralysis, out of which 27 (48.2%) cases of hypokalemic paralysis were diagnosed as sporadic periodic paralysis (SPP) and 5 (8.9%) of the cases were diagnosed as familial periodic paralysis (FPP) on the basis of positive family history of similar illness. Twenty-four (42.9%) of cases had secondary cause for their hypokalemic paralysis [Figure 1].

The secondary HPP included distal RTA in 4 patients (7.14%), of which 1 was found to have Sjogren syndrome on further evaluation. Renal calcinosis was present in 3 patients with distal RTA [Figure 2]. Gitelman syndrome was diagnosed in 4 cases (7.14%) with hypomagnesemia and hypocalciuria in all 4 patients, and hypocalcemia with raised serum PTH in 2 patients. Thyrotoxic periodic paralysis was diagnosed in 3 patients (5.35%) and hypothyroidism as a cause of paralysis in 2 patients (3.57%). One patient (1.78%) had primary hyperaldosteronism with elevated serum aldosterone level and low plasma renin activity. He presented with isolated, alternating, asymmetric episodic finger drop. He had bilateral adrenal hyperplasia on abdominal CT imaging. Two patients (3.57%) with hypertension, hypokalemia, and metabolic alkalosis with low renin and aldosterone levels were diagnosed as Liddle's syndrome. One patient (1.78%) developed hypokalemic paralysis following dengue fever, 2 patients (3.57%) post-gastroenteritis, and 3 patients (5.35%) had their

attacks precipitated by alcohol intake. Antinuclear antibody positivity was detected in 2 (3.57%) of cases.

The muscle weakness was significantly more pronounced in the secondary group compared to the idiopathic group on MRC grade. The muscle power in secondary hypokalemia group was 1.66 ± 0.96 and in the idiopathic group was 2.71 ± 0.99 ; $P = 0.002$.

Serum potassium ranged between 1.3 - 3.46 mmol/l (mean - 2.38 mmol/l ± 0.556). Severe hypokalemia (<1.5 mmol/l) was present in 4 patients. The serum potassium concentrations were lower in patients with secondary hypokalemic paralysis (Mean \pm SD -2.34 \pm 0.59 meq/L) than in those with primary hypokalemic paralysis (Mean \pm SD -2.41 \pm 0.52 meq/L) though the difference was statistically not significant ($P = 0.624$). Other electrolyte abnormalities included hypocalcemia in 12 and hypomagnesemia in 4 patients. ABG analysis showed acidosis in 4 and alkalosis in 7 cases.

The serum CPK was raised in 68% of the cases. Mean CPK was 662.35 ± 813.83 with a range of 53 - 3520. The serum CPK was also significantly higher in the secondary group compared to the primary (944.20 ± 899.24 vs. 450.968 ± 693.37 ; $P = 0.023$). Electrocardiograms showed U wave in 13 cases, prolonged PR interval in 6 cases, and sinus bradycardia in 1 case [Figure 3].

All patients had recovery with potassium replacement therapy. The secondary group needed significantly longer time (3.25 ± 0.84 days vs. 2.56 ± 0.75 days; $P = 0.002$) to recover compared to the patients with primary hypokalemic paralysis. Among the secondary group, the recovery time was longer in alcoholics (mean - 5 days vs. 3.25 days). The biochemical parameters in the patients with secondary hypokalemic periodic paralysis are shown in [Table 2]. Comparison of clinical and biochemical parameters (mean \pm SD) in idiopathic and secondary hypokalemic paralysis are shown in [Table 3].

Discussion

The first known description of periodic paralysis was given by Musgrave in 1727.^[8] Since then, hypokalemic paralysis has been reported from different parts the world. In one of the largest study on HPP from Taiwan by Lin *et al.*,^[3] a total of 97 cases of hypokalemic paralysis were reported over a period of 10 years. Various series of HPP cases has been reported from different parts of India also; however, this is the first series of hypokalemic paralysis from North-Eastern part of the country. Agrawal *et al.*^[9] has reported 40 cases of hypokalemic periodic paralysis in a period of 23 years. In an earlier series reported by Arya *et al.*,^[10] a total of 22 cases of hypokalemic paralysis were reported over 30 years. In retrospective study from South India by Rao *et al.*,^[11] 31 patients were detected over a period of 6 years. A recent prospective study from North India by Maurya and colleagues^[12] reported 30 patients of HPP over a period of 3 years.

In the present study, 56 cases of hypokalemic paralysis were detected over a period of 24 months. Our study has significantly higher number of cases over a short duration of time compared to previous studies from India, which means probably we come across a higher number of cases of hypokalemic paralysis in

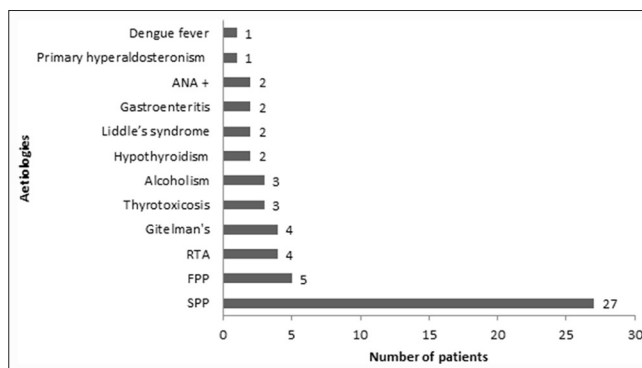


Figure 1: Frequency of different etiologies of hypokalemic paralysis



Figure 2: Radiograph of abdomen revealing nephrocalcinosis (arrow) in case of distal RTA

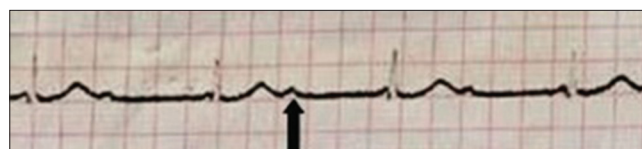


Figure 3: ECG showing bradycardia and U wave (arrow) in a patient with hypothyroidism who had recurrent flaccid quadriplegia with serum potassium of 1.96 mmol/l

Table 1: Atypical presentation in cases

Atypical presentation	Number of cases
Neck muscles weakness	4
Bladder involvement	3
Finger drop	1
Bilateral foot drop	1
Tetany	1
Calf hypertrophy	1

this region compared to other parts of the country.

There was a seasonal variation in the incidence of hypokalemic attacks; highest numbers of cases (32.14%) were symptomatic during the summer season in the month from April to June, when the average temperature in this region ranges from

Table 2: Biochemical changes in the patients with secondary hypokalemic paralysis

Age	Sex	S. K ⁺ (mmol/l)	S. Na ⁺ (mmol/l)	HCO ₃ ⁻ (mmol/l)	S. Cl ⁻ (mmol/l)	Urine pH	Blood pH	CPK IU/L	Others	Diagnosis
42	M	3.0	136	22.60	112.0	6.50	7.37	2740	T3-217.9 ng/dl;T4-19.7 µg/dl TSH<0.01 µIU/mL	TPP
59	M	2.9	144	21.7	110.0	7.00	7.42	101	T3-2.219 ng/dl;T4-170.47 µg/dl TSH-0.08 µIU/mL	TPP
28	M	2.8	139	19.0	96.0	6.50	7.44	178	T3-407 ng/dl;T4-292 µg/dl TSH<0.01 µIU/mL	TPP
49	M	2.2	144	24.2	98.0	6.5	7.46	190	Plasma renin-0.02 ng/ml S. Aldosterone-465.2 ng/l CT Abdomen-B/L adrenal hyperplasia	PHA
40	M	2.1	143	15.4	111.0	6.00	7.21	378	CT Abdomen-B/L Renal calculi	Distal RTA
35	M	2.7	142	20.2	108.0	7.5	7.22	216	USG Abdomen-B/L Nephrocalcinosis	Distal RTA
20	F	2.9	134	18.0	110.0	7.0	7.26	138	ANA+Anti SSa +/Anti SSb +	Distal RTA (Sjogren's syndrome)
62	M	2.0	139	18.9	108.6	6.5	7.18	3133	USG and X-ray Abdomen-Right Renal calculi	Distal RTA
45	F	2.4	138	29.2	83.90	6.5	7.50	412	24 hour urinary calcium-99 mg/24 hrs S. PTH-178.6 pg/ml, S. Mg ⁺⁺ -1.0 mg/dl	Gitelman's syndrome
35	F	1.7	141	37.4	104.0	7.0	7.46	833	24 hour urine Ca ⁺⁺ -97.5 S. PTH-67.2 pg/ml, S. Mg ⁺⁺ -1.3 mg/dl	Gitelman's syndrome
47	F	1.3	139	45.5	97.6	7.0	7.58	526	24 hour urine Ca ⁺⁺ -61 mg/24 hrs S. PTH-72.3 pg/ml S. Mg ⁺⁺ -1.2 mg/dl,	Gitelman's syndrome
59	M	1.3	139.0	22.5	101.3	6.0	7.49	104	24 hour urinary calcium-92.7 mg/24 hrs S. PTH-190.8 pg/ml, S. Mg ⁺⁺ -1.6 mg/dl	Gitelman's syndrome
50	M	2.6	148	36	103	6.0	7.547	742	Plasma Renin-0.13 ng/ml/hr S. Aldosterone<10.0 ng/L CT Abdomen-WNL	Liddle's syndrome
30	F	1.9	145	38	98.9	7.0	7.48		Plasma Renin-<0.03 ng/ml/hr S. Aldosterone-4.5 ng/L CT Abdomen-WNL	Liddle's syndrome
42	M	1.96	139.8	26.8	108.7	6.5	7.4	1727	T3 - 37.9 ng/dl;T4 - 2.7 µg/dl TSH-13.53 µIU/mL	HT
54	M	2.93	145.6	28.4	112.9	7.0	7.43	977	T3-45.2 ng/dl;T4-3.4 µg/dl TSH-12.16 µIU/mL	HT
20	F	2.0	143.0	30.0	98.6	5.50	7.34	86	ANA (+) Speckled pattern 2+1:40 ANA (+) HPP dilution DS DNA (-)	
35	F	3.4	141	28.00		7.00	7.41	286	ANA (+) Speckled pattern 4+1:160 dilution DS DNA (-)	ANA (+) HPP
40	M	2.80	133.20	22.70	98.90	5.00	7.39	1353		Alcoholism
45	M	2.4	137.0	26.90	103.00	6.00	7.38	1479		Alcoholism
48	M	2.7	138.0	33.90	110.7	7.5	7.40	2390		Alcoholism
35	M	1.4	132.0	18.90	86.0	7.0	7.33	778		GE
92	F	1.6	133.0	21.20	96.8	7.5	7.29	556		GE
21	F	2.3	136.0	99.0	110	6.5	7.35	1863	Anti Dengue IgG and IgM antibody positive	Dengue fever

PHA=Primary hyperaldosteronism, TPP=Thyrotoxic periodic paralysis, RTA =Renal tubular acidosis, GE=Gastroenteritis, HT=Hypothyroidism

Table 3: Comparison of clinical and biochemical parameters (mean±SD) in idiopathic and secondary hypokalemic paralysis

Parameters	Type of periodic paralysis		P value
	Primary (Mean±SD) (n=32)	Secondary (Mean±SD) (n=24)	
Weakness (MRC grade)	2.71±0.99	1.66±0.96	0.002
Time to improve (days)	2.56±0.75	3.25±0.84	0.002
Serum K ⁺ (mmol/l)	2.41±0.52	2.34±0.59	0.624
Serum CPK U/L	450.968±693.37	944.20±899.24	0.023

19-31°C. However, these patients did not have any clinical evidence of dehydration on admission to hospital. With the 'humid subtropical climate,' Assam is a temperate region and experiences heavy rainfall with an average humidity of 75%. This can be the one of the factor of high prevalence of cases of hypokalemic paralysis in the summer month. Also, rice is the staple food of the region, which is high in carbohydrate content and thus can be a precipitating factor for HPP. These findings in our study are consistent with an earlier Indian study, which had also shown high prevalence of cases of hypokalemic paralysis in the summer season.^[13] Male preponderance was observed in the present study, which has earlier been documented in the Indian literature.^[11,12]

In this study, 42.9% of patients with hypokalemic paralysis had a secondary cause for their condition. Primary hypokalemic periodic paralysis occurred in 57.1% of patients, out of which 48.2% of total cases were sporadic while 8.9% were familial.

In this study, distal RTA was one of the leading cause of secondary hypokalemic paralysis and this was found in 7.14% of cases. The diagnosis of distal RTA in our study was supported by nephrolithiasis on abdominal USG or radiography. An earlier study from Kashmir has reported 21 cases of hypokalemic paralysis secondary to distal RTA over a period of 8 years.^[14] Most of the cases in this study had distal RTA of sporadic nature. In the South Indian study, RTA was the cause in 13 out of 31 (42%) cases of HPP.^[11] In the study by Maurya *et al.*,^[12] RTA was the cause of HPP in 4 out of 30 (13.3%) cases; 3 cases were of distal RTA and only 1 case had proximal RTA. One of our patients had distal RTA secondary to Sjogren's syndrome. Hypokalemic paralysis in Sjogren's syndrome may precede the more classic clinical findings and serves as a clinical marker for this diagnosis.^[15]

Gitelman syndrome, which we diagnosed in 7.14% of cases, was the other leading cause of secondary HPP. Gitelman syndrome has been reported in earlier Indian studies with a varying incidence rate ranging from 3.2% to 13.3%.^[11,12] One of the female with Gitelman syndrome presented with tetany, which may be attributed to exacerbation of alkalosis and consequent low ionized plasma calcium in presence of hypomagnesemia.

In this study, thyrotoxic periodic paralysis was the cause in 5.35% of the cases of HPP. Asians are more often affected by this condition, with one study showing that Polynesians were at 159-fold higher risk compared to white Europeans.^[16] The Lin

et al.^[3] study had TPP in 40.2% as the etiology of hypokalemic paralysis. The earlier Indian studies has shown variable incidence of TPP, ranging from 6.4%^[11] to 16.7%.^[12]

We had 2 cases of Liddle's syndrome in the current study. Patients with Liddle's syndrome usually present with hypertension, often hypokalemia (in most cases), and metabolic alkalosis, similar to that seen in mineralocorticoid excess.^[6] Patients mostly present at a young age though, occasionally, cases may not be detected until well into adulthood.^[17] Periodic paralysis as a presenting symptom has been infrequently reported in patients with Liddle's syndrome. However, muscle weakness associated with hypokalemia (especially in lower limbs) has been described, though rarely, in elderly patients with Liddle's syndrome.^[18]

In our series, 1 patient (1.78%) had primary hyperaldosteronism as the secondary cause of HPP. The patient presented with isolated episodic, asymmetric alternating finger drop and was finally diagnosed as primary hyperaldosteronism, secondary to bilateral adrenal hyperplasia. Periodic paralysis as a presentation of primary hyperaldosteronism is commonly reported among the oriental races.^[19,20] In a series of 50 patients with primary hyperaldosteronism from Taiwan, 42% presented with periodic paralysis, although all 50 had hypokalemia.^[19] In another oriental series, 21 of 43 cases (49%) of primary hyperaldosteronism presented with muscular paralysis as the initial symptom.^[20] In the study by Rao *et al.*,^[11] secondary HPP was due to hyperaldosteronism in 13 out of 31 (42%) of patients. However, the study was undertaken in a tertiary care endocrinology practice, which may reflect the higher percentage of hyperaldosteronism and RTA as the etiology of HPP as compared to our study.

In our study, we had a case of hypokalemic paralysis following dengue fever, without any similar episode of weakness in the past. The pure motor quadriplegia in this patient had dramatic recovery after potassium supplementation. The patient was also investigated to exclude other causes of hypokalemia, but no other secondary cause was detected. Hypokalemia, in association with infectious diseases, dengue fever in particular, have been reported and documented in up to 28% of serologically-proven cases of dengue infection.^[21] Indian studies have recently reported serologically confirmed cases of dengue infection with acute, pure motor, reversible quadriplegia due to hypokalemia.^[22,23] Hypokalemia occurring in dengue fever can be secondary to re-distribution of potassium into the cells, transient renal tubular abnormalities leading to increased urinary potassium wasting and increased catecholamine levels secondary to infections and secondary insulin resistance leading to intracellular shift of potassium.^[22]

Two of the female patients had positive antinuclear antibody (Speckled pattern) in greater than 1:40 dilution, with negative dsDNA, but they did not have any acid-base disorder and on investigation, no other secondary cause can be found to suggest any specific connective tissue disorder. We could not establish the significance of this finding in our study. It may be incidental or may be causally related in some unknown way.

Two of our cases were detected as hypokalemic paralysis secondary to hypothyroidism. There are rare case reports of association of hypokalemic paralysis with hypothyroidism.^[24] Both of our cases had onset of illness after 40 years of age, which makes the primary cause of HPP unlikely, also the non-recurrence of episodes of paralysis after thyroid replacement during short follow-up favors this association.

Three patients had hypokalemic paralysis following heavy alcohol intake, 1 of them having past history of recurrent episodes of weakness on alcohol intake. They did not have prior history of similar illness without alcohol intake or positive family history suggestive of periodic paralysis. All the 3 patients had severe myalgia, and they took longer time to recover in comparison to other secondary disorders.

Occurrence of recurrent attacks was more in primary hypokalemic periodic paralysis as compared to secondary hypokalemic periodic paralysis.

The muscle weakness was also more pronounced in the secondary group compared to the primary group, and the difference was statistically highly significant ($P = 0.002$). One of the earlier study has also shown similar results; however, the difference in power between patients with primary and secondary hypokalemic paralysis in the study was non-significant.^[12]

Atypical presentation in the form of bladder involvement, early neck muscle weakness, and finger drop, which we found in our study, has also been reported in earlier Indian studies.^[13,25] It is likely that these atypical manifestations are a result of failure of transmission of nerve impulses at the synaptic junctions as a result of hypokalemia.^[26]

In our study, the serum potassium concentrations were lower in patients with secondary hypokalemic paralysis than in those with primary hypokalemic paralysis though the difference was statistically insignificant ($P = 0.624$). Our finding is similar to the previous study, which also showed no significant difference in potassium values between patients of primary and secondary hypokalemic paralysis.^[3] But, in the study by Maurya and colleagues,^[12] the serum potassium concentrations were significantly lower in patients of secondary hypokalemic paralysis than in those with primary hypokalemic paralysis.

In our study, the elevation of serum CPK in 68% patients is an indirect evidence of damage to muscle membrane. This has also been infrequently reported in earlier Indian studies.^[13] Serum CPK was also significantly higher ($P = 0.023$) in the secondary group compared to the primary group. It is postulated that hypokalemia causes muscle ischemia, resulting in a rise in serum CPK. Higher than normal levels of this enzymes during the recovery phase can be used to identify symptomatic patients, in whom serum potassium becomes normal after or during hypokalemic paralysis.

In contrast to the primary group patients, an acid-base disorder was present only in the secondary group (Acidosis in 4 and Alkalosis in 7 cases). Distal RTA was the diagnosis in cases with metabolic acidosis, while cases with metabolic alkalosis

had Gitelman syndrome, Liddle's syndrome, or primary hyperaldosteronism as the final diagnosis. This has been reported in earlier studies also.^[3] So, in cases with an acid-base disorder, a secondary cause of HPP should be suspected and investigated.

In this study, recovery with potassium replacement therapy was seen in all cases. The secondary group needed longer time to recover compared to the patients with primary HPP, and the difference in recovery time was found to be statistically significant ($P = 0.002$). This feature has been documented in the literature.^[3,12] This delay in recovery can be attributed to a significantly negative total body potassium balance in patients with secondary hypokalemic paralysis. Among the secondary group, the recovery time was longer in alcoholics (mean-5 days vs. 3.25 days). This delay in recovery can be because of co-existent hypomagnesemia with hypokalemia in alcoholics as reported in earlier case reports.^[27]

There was no mortality during the entire period of this study, thereby suggesting that a timely intervention can be life-saving in this easily treatable but potentially fatal disease.

Conclusions

In this series of hypokalemic paralysis from North-East India, 56 cases of hypokalemic paralysis were detected in a short span of time of 2 years, making it comparatively larger study in comparison to previous Indian studies. This may also reflect higher prevalence of the condition in this region. We have also seen both varied presentations and a wide variety of secondary causes in comparison to previous Indian studies. Our study also highlights some of the unusual causes of HPP like hypothyroidism, which has been previously reported only in isolated case reports, and association of HPP with alcoholism has also not been frequently reported.

Finally, we can conclude that HPP is an important cause of acute flaccid paralysis, and early recognition and prompt management of this condition will give gratifying result and prevent further attacks in some cases.

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