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RESEARCH

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# Clinical and biochemical features of hypokalemic paralysis: a study from rural Eastern India

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## Abstract

**Background** Hypokalemic paralysis is characterized by episodic attacks of flaccid muscle weakness of variable duration and severity associated with hypokalemia. Overall, there is a scarcity of data regarding hypokalemic paralysis from Indian subcontinent particularly from rural areas.

**Methods** A total of 50 consecutive patients of hypokalemic paralysis who were admitted in our hospital were recruited in this study.

**Results** Fifty patients of hypokalemic paralysis were admitted to our department over a period of 4 years. Forty-two (84%) patients presented with classic acute onset quadriparesis, while eight patients had atypical presentation. Five patients had paraparesis, two had hemiparesis and one patient presented with isolated neck muscle weakness without any limb weakness. Thirty-two patients had primary hypokalemic periodic paralysis (HoPP) and 18 had secondary hypokalemic paralysis. There was no significant difference in severity of weakness ($p=0.53$), number of episodes of weakness ($p=0.66$) and serum CPK levels ($p=0.36$) between primary and secondary hypokalemic paralysis. Secondary cases required significantly prolonged time for recovery as well as higher potassium supplements as compared to the primary HoPP. The severity of weakness of proximal muscles measured in MRC grading showed a significant correlation with serum potassium levels ($p=0.010$), but did not show any correlation with CPK Levels ($p=0.86$).

**Conclusion** Hypokalemic paralysis is an important cause of acute flaccid paralysis in the Emergency Room that often improves dramatically with potassium supplements. While secondary cases often require treatment of underlying etiology, primary hypokalemic paralysis often requires chronic treatment with acetazolamide and/or potassium-sparing diuretics.

## Key Message

Hypokalemic paralysis is an important differential diagnosis of acute flaccid paralysis that rapidly recovers with treatment. Most of the cases are primary, usually a calcium channel disorder (Type I) or very rarely a sodium channel disorder (Type II). However, secondary causes should be evaluated for and reasonably excluded before labeling the disorder as primary hypokalemic paralysis.

**Keywords** Periodic paralysis, Hypokalemia, Primary, Secondary

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## Introduction

Hypokalemic paralysis is an important cause of acute flaccid muscular paralysis in the Emergency Room and often shows a dramatic response to correction of potassium deficit [1]. Patients are classified as having either a primary hypokalemic periodic paralysis (primary HoPP) or secondary hypokalemic paralysis. Primary HoPP is a channelopathy due to calcium channel (Type 1) or sodium channel (Type 2) disorder [2]. Secondary hypokalemic paralysis is often due to potassium losses like diuretics, renal tubular acidosis, etc. Irrespective of the type, patients usually present with acute motor weakness without sensory and bowel/bladder disturbances with or without respiratory involvement [3]. However, the two types differ in etiology, severity of weakness, duration of weakness, biochemical parameters, arterial blood gas analysis and long-term management. There is scarcity of data regarding hypokalemic paralysis from Eastern India particularly from rural areas. The present study was thus done to determine the clinical and biochemical characteristics of hypokalemic paralysis and its outcome after potassium replacement therapy.

## Aims and objectives

1. To determine the clinical and biochemical features of hypokalemic paralysis in rural West Bengal.
2. To determine any differences between primary and secondary hypokalemic paralysis in this patient population.

## Materials and methods

This is a prospective single-center study done over a period of 4 years after ethical clearance was obtained from Institutional Ethics Committee (IEC). The study was done in the Department of Neurology, Burdwan Medical College, West Bengal, from May 2015 to April 2019. During this period, all patients admitted to our department with acute flaccid motor weakness were evaluated and patients who had hypokalemia as a cause of weakness were included in the study. This was confirmed by finding low serum potassium at the time of admission and resolution of weakness once serum potassium was corrected. Over this period, 50 patients of hypokalemic periodic paralysis were admitted in our department. A detailed clinical history including age, sex, residence, duration of weakness, pattern of weakness, temporal profile of symptoms, other neurological symptoms like sensory symptoms, bowel/bladder involvement, drug history, family history and history of consanguinity in parents was obtained. In addition, number of episodes of acute muscular weakness, time to improve, precipitating factors and for secondary causes, history of renal stone, bone pain, dry eye, fractures, thyroid disease, etc., were documented. A detailed general physical, systemic and neurological examination was done in all patients. Other causes of acute flaccid motor weakness like Guillain–Barre syndrome, acute myelitis, acute neuropathy or neuromuscular disorder were ruled out with proper history and clinical examination supplemented by investigations like nerve conduction studies, cerebrospinal fluid examination, spine MRI, etc. Hypokalemia was diagnosed as serum potassium of less than 3.5 meq/L. Hypokalemia was evaluated in all patients to rule out secondary causes. The following biochemical parameters were estimated: serum sodium, potassium, bicarbonate, chloride, creatine, calcium, phosphate, magnesium, albumin, and globulin, 24-h urinary calcium, phosphate, potassium and creatine. All the patients underwent thyroid function test, arterial blood gas analysis and 12-lead electrocardiogram (ECG). Serum aldosterone, plasma renin levels and CT of the adrenal gland were done in selected group of patients. The clinical and laboratory data of these patients were analyzed, and patients were categorized into primary hypokalemic periodic paralysis (primary HoPP) or secondary hypokalemic paralysis. A written informed consent was taken from the participants or their immediate family members before including into the study.

### Statistical analysis

Standard statistical procedures were used to analyze the data. Data were described as mean ± SD and percentages. Chi-square test was used for categorical data. Statistical Package for Social Sciences (SPSS version 23 IBM) and Microsoft Excel was used for data analysis. $p$ value of $< 0.05$ was taken as significant.

## Results

Out of the 50 patients in our study, 32 had primary hypokalemic paralysis and 18 had secondary hypokalemic paralysis. The mean age of presentation of studied subjects was 36.28 ± 15.90 (15–73) years. The mean age of primary hypokalemic paralysis subjects was 28.6 years, whereas the mean age of subjects having secondary paralysis was 49.5 years. ($p = 001$). 74% ($n = 37$) were men and 26% ($n = 13$) women. Sex, religion, ethnicity (tribal and non-tribal), type of worker and alcoholic habits did not have significant difference between primary and secondary hypokalemic paralysis patient groups. Hypertension was absent in all the patients in primary hypokalemic paralysis patients whereas it was present in 33% ($n = 6/18$) in secondary paralysis group ($p = 0.001$). Two patients of primary group had family history of similar illness thus diagnosed as familial primary

hypokalemic periodic paralysis whereas 30 patients of primary group had no family history thus diagnosed as sporadic primary hypokalemic periodic paralysis. None of the patients with secondary periodic paralysis had family history of similar illness. Figure 1 depicts the various underlying diagnoses in patients with secondary hypokalemic paralysis. Figure 2 shows various precipitating factors for weakness in each group. Heavy exertion was the significant ($p=0.032$) precipitating factor for weakness in primary hypokalemic paralysis, whereas weakness in secondary group occurred spontaneously in most of the patients. The maximum number of cases occurred in summer season (44%) followed by monsoon (28%) and then winter months (24%). 84% ($n=42/50$) presented with classic acute onset quadriparesis with or without neck muscle weakness. Lower limbs were weaker than upper limbs in patients having quadriparesis. Eight cases had atypical presentation out of which five patients had paraparesis, two cases had hemiparesis and one case presented with isolated neck muscle weakness without any limb weakness (Table 1). In patients with paraparesis contrast enhanced MRI of dorso-lumbar spine and nerve conduction studies were done to rule out acute myelopathy and paraparetic form of Guillain–Barre syndrome, respectively. Similarly in patients with hemiparesis MRI of brain and cervical spine was done to rule out stroke or any other pathology like demyelination. In patients with neck muscle weakness, neuromuscular causes of weakness were rule out by appropriate testing like electromyography, CPK and repetitive nerve stimulation tests. None of the cases in our series had the ocular or respiratory weakness. The pattern of weakness involvement within two groups did not differ significantly. Patients with isolated neck muscle weakness and hemiparetic variant were diagnosed to have primary hypokalemic paralysis. Duration of weakness in primary group was 72 h. or less and in secondary group 72 h or more (Fig. 3). The serum potassium concentration significantly correlated with the severity of weakness in both groups but did not have significant correlation with CPK levels (Table 2). Secondary group cases required significantly prolonged time for recovery ($p=0.016$) and more potassium requirements for recovery as compared to primary group.

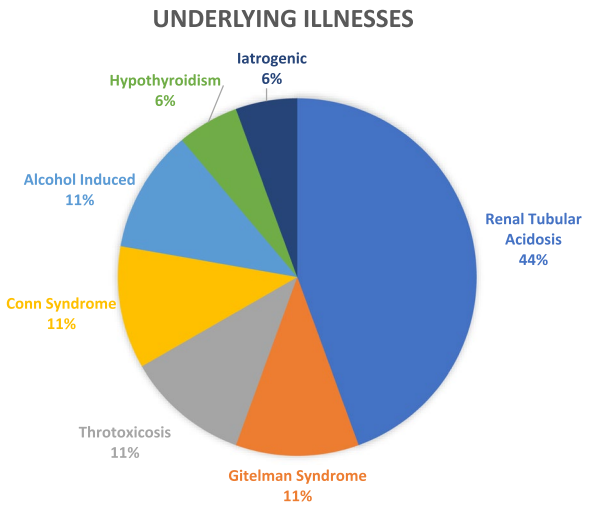


**Fig. 1** Underlying etiologies in secondary hypokalemic paralysis

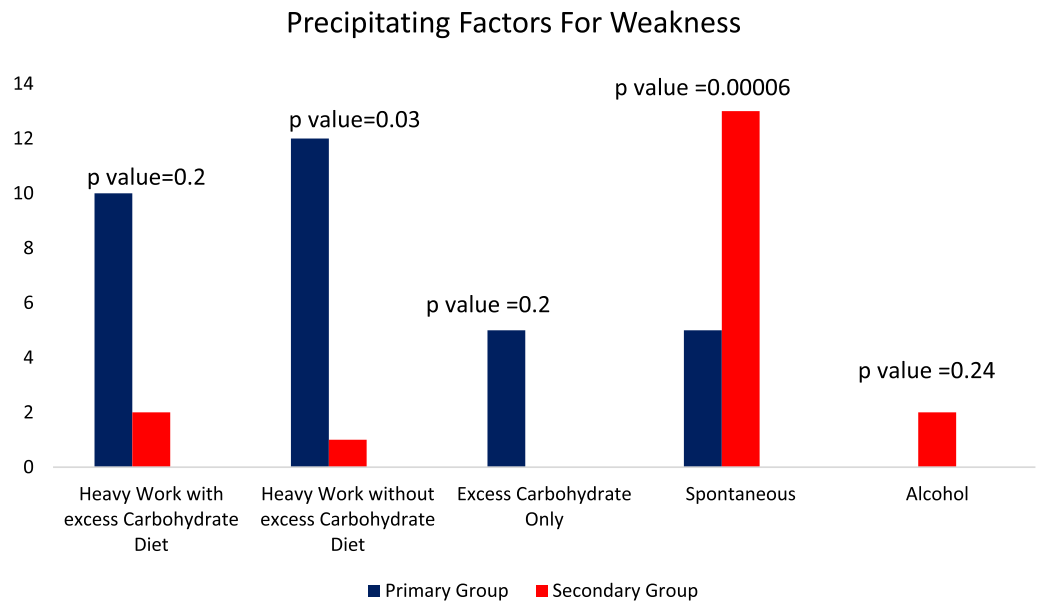


**Fig. 2** Precipitating factors for weakness in two groups

**Table 1** Table showing power grading, number of attacks, time taken to improve and serum CPK levels in two groups

| | Primary group (*n*) | Secondary group (*n*) | Total (*n*) | *p* value |
|---|---|---|---|---|
| **Power (MRC grading)** | | | | |
| 0/5 and 1/5 | 6 | 6 | 12 | 0.53 |
| 2/5 | 10 | 7 | 17 | |
| 3/5 | 11 | 2 | 13 | |
| 4/5 and more | 5 | 3 | 8 | |
| **Number of attacks** | | | | |
| Single | 8 | 2 | 10 | 0.66 |
| < 5 | 18 | 13 | 31 | |
| > 5 | 6 | 3 | 9 | |
| **Time taken to improve** | | | | |
| < 2 days | 18 | 2 | 20 | 0.018 |
| 2–5 days | 14 | 14 | 28 | |
| > 5 days | 0 | 2 | 2 | |
| **Serum CPK** | | | | |
| < 500 | 10 | 4 | 14 | 0.36 |
| 500–1000 | 14 | 6 | 20 | |
| > 1000 | 8 | 8 | 16 | |
| **Total** | 32 | 18 | 50 | |

**Table 2** Co-relation between serum potassium and CPK levels with degree of weakness

| Parameter | Muscle power (MRC grading) | | | Total | *p* value |
|---|---|---|---|---|---|
| | 0 and 1 | 2 and 3 | 4 and above | | |
| **CPK levels** | | | | | |
| < 500 | 2 | 10 | 2 | 14 | 0.86 |
| 500–1000 | 4 | 12 | 4 | 20 | |
| > 1000 | 6 | 8 | 2 | 16 | |
| **Serum potassium** | | | | | |
| 2.5–3.5 | 0 | 8 | 6 | 14 | 0.01 |
| 1.5–2.5 | 6 | 18 | 2 | 26 | |
| < 1.5 | 6 | 4 | 0 | 10 | |
| **Total** | 12 | 30 | 8 | 50 | |

## Discussion

Hypokalemic periodic paralysis is the best-known form of periodic paralysis and is characterized by hypokalemia occurring during the episode of muscle weakness. In the present hospital-based prospective study, 50 cases of hypokalemic paralysis were detected over a period of 4 years. The male:female ratio in our study was 2.84:1. The mean age of our patients was 36.28 ± 15.90 years with an age range of 03–73 years with a bimodal age distribution of 21–30 year and 41–50 years. Majority of the cases were from Burdwan district 7 cases from Birbhum, 7 cases from Bankura and 5 cases from Hooghly. Many studies from different parts of India have reported similar epidemiological patterns [4–6].

Classification of hypokalemic paralysis into primary and secondary is essential because the long-term management and prognosis differ [7]. Primary hypokalemic periodic paralysis is a channelopathy; either calcium channel (Type 1) or sodium channel (Type 2) is involved [8]. Alteration of serum potassium level is not the principal defect in primary periodic paralysis; instead the altered potassium metabolism is a result of the periodic

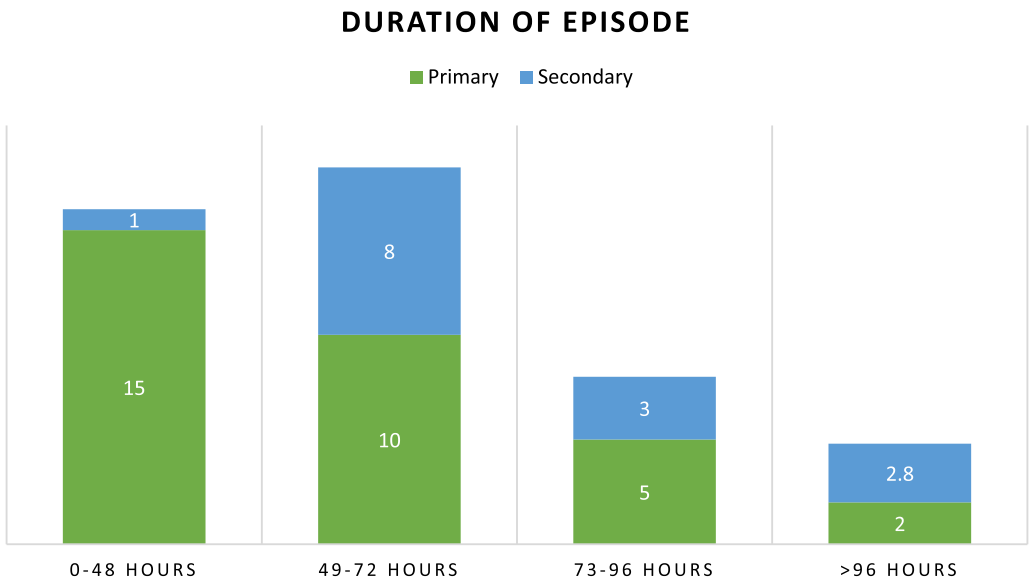


**Fig. 3** Duration of weakness episode in two groups

paralysis [9]. Besides primary periodic paralysis is usually associated with smaller changes in serum potassium whereas secondary hypokalemic paralysis is associated with marked changes in serum potassium. Overall primary hypokalemic paralysis is more common than secondary [10]. In our study, 36% of patients with hypokalemic paralysis had a secondary cause for their condition. Primary HoPP occurred in 64% of patients out of which 60% were sporadic and 4% familial. In the secondary group, RTA emerged as the most common cause (44%) followed by thyrotoxic periodic paralysis (11.1%), alcoholism (11.1%), primary hyperaldosteronism (11.1%) and hypothyroidism (5.6%). Among the secondary causes, alcoholism and hypothyroidism have rarely been reported as causes of hypokalemic weakness. Hypokalemia in alcoholism may be due to inadequate intake, inappropriate kaliuresis due to hypomagnesemia or alcoholic ketoacidosis [11, 12]. Although more commonly associated with thyrotoxicosis, hypokalemic paralysis has also been reported with hypothyroidism [13]. Our patient with hypokalemic weakness secondary to hypothyroidism had onset of illness after 40 years of age which makes the primary cause of hypokalemic paralysis less likely; also, the non-recurrence of episodes of paralysis after thyroid replacement during follow-up favors this association. There was a seasonal variation in the incidence of hypokalemic attacks with highest numbers of cases (44%) being symptomatic during the summer season in the months of April to June, when the average temperature in this region ranges from 20 to 40 °C. The cause of this seasonal variation is unclear; more dehydration and large consumption of sweetened drinks have been proposed to precipitate the attacks. However, our patients did not have any clinical evidence of dehydration on admission to hospital. Attacks of weakness in primary hypokalemic weakness are usually precipitated by high carbohydrate intake [14]. Carbohydrate intake causes insulin release from pancreas resulting in cellular shifts of potassium [15]. Rice is a staple food of West Bengal and people often consume rice three times a day. Besides, West Bengal is famous for sweets, another rich carbohydrate source. Although attacks were more common in patients with high carbohydrate intake in our study, the difference between primary and secondary group were not statistically significant. Attacks are also precipitated by strenuous exercise as shown in our study.

Patients of hypokalemic paralysis presented with acute, proximal more than distal, motor weakness often initially involving lower limbs followed by upper limbs. During an attack, there is often hyporeflexia and muscles appear swollen and tender [16]. In our study, 42 cases (84%) had quadriparesis with neck muscle weakness, 5 cases (10%) had paraparesis, 2 cases (4%) had hemiparesis and one patient presented with isolated neck muscle weakness. Atypical manifestations of hypokalemic weakness have been described in few reports [17, 18]. The muscle weakness was more pronounced in the secondary group compared to the primary group which is, however, statistically insignificant ($p=0.53$). In most of the cases the severity of weakness in the lower limbs was either greater than or equal to upper ($p=0.004$). Hypokalemic periodic paralysis is episodic rather than periodic. Recurrent attacks usually occur in patients not on chronic therapy and are more severe and prolonged in Type 1 HoPP than Type 2 HoPP. In our study, in primary group, single attack occurred in 8 cases (25%), 2 to 5 attacks in 19 cases (56.25%), more than 5 attacks in 6 cases (18.75%). In secondary group, single attack occurred in 2 cases (11.11%), 2–5 attacks in 13 cases (72.22%) and more than 5 attacks in 3 cases (16.67%). So, multiple attacks were more in secondary cases though statistically insignificant ($p=3.446$). Similar findings have been reported elsewhere [19]. The mean serum potassium concentration in secondary hypokalemic paralysis ($2.38\pm0.45$ meq/L) was lower than in those with primary hypokalemic paralysis ($2.41\pm0.63$ meq/L), though the difference was statistically insignificant ($p=0.855$). Although some studies have reported markedly lower serum potassium concentrations in secondary hypokalemic paralysis, not all studies support this finding [20, 21]. Hypokalemic paralysis is a myopathy associated with damaged to muscle membrane and thus is associated with elevated CPK levels [22]. In our study, the elevation of serum creatine kinase (CPK) occurred in 76% of the cases. Elevated CPK was significantly higher ($p=0.009$) in the secondary group (900.67 U/L $\pm$ 673.37U/L) compared to the primary group (507.84 U/L $\pm$ 345.91U/L). It is postulated that hypokalemia causes muscle ischemia, resulting in a rise in serum CPK with profound hypokalemia even leading to rhabdomyolysis [23]. ECG changes are frequent in hypokalemia ranging from PR prolongation, flattening of T waves, inversion of T waves to appearance of U waves. In our study, U wave was seen in 46% cases, T wave flattening was seen in 12% cases, T wave inversion in 10% cases, ST segment depression in 2% cases, prolonged PR interval in 6% cases, atrial fibrillation in 2% and normal ECG in 20% cases. In this study, recovery with potassium replacement therapy was seen in most of cases (96%). However, two secondary cases (RTA) died due to late presentation to the hospital. Acute attacks of hypokalemic paralysis are treated with potassium chloride supplementation (30 meq orally every 30 min till serum potassium normalizes). However, some recommend slower rates of administration

to minimize post-treatment hyperkalemia due to movement of potassium back out of the cells. Further attacks in primary hypokalemic paralysis can be prevented by non-pharmacological interventions like low carbohydrate diet and avoiding vigorous exercise. Pharmacological interventions for prevention of attacks include carbonic anhydrase inhibitors (acetazolamide 250 mg twice a day), dichlorphenamide (50 mg twice a day), potassium-sparing diuretics, etc. Patients with secondary hypokalemic paralysis need correction of underlying disease to prevent further attacks. In our study, the secondary group needed significantly longer time to recover compared to the patients with primary HoPP ($p = 0.003$). Patients with secondary hypokalemic paralysis have a significantly negative total body potassium balance, whereas in primary hypokalemic paralysis is associated with an intracellular shift of potassium. Therefore, patients with primary hypokalemic paralysis need smaller amounts of potassium shorter time to recovery compared to the secondary group.

This study was a hospital-based study, so it may not reflect the true picture of hypokalemic paralysis in the community. Epidemiological studies require community-based study for unbiased estimate. Further detailed study from different parts of West Bengal may be needed to find out the magnitude of the problem in this state.

## Conclusion

Hypokalemic paralysis is an important cause of acute flaccid paralysis in the Emergency Room of any hospital. Hypokalemia can cause significant respiratory and cardiac problems resulting in death of patients as seen in our study. Immediate treatment is beneficial as well as gratifying due to rapid recovery. Extensive evaluation to diagnose secondary causes is essential for successful prevention of relapses.

### Abbreviations

| | |
|---|---|
| HoPP | Hypokalemic periodic paralysis |
| MRCS | Medical Research Council Scale for Muscle Strength |
| CPK | Creatine phosphokinase |
| MRI | Magnetic resonance imaging |

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### Author contributions

AB collected the data, HG analyzed and interpreted the data and WD and AY prepared the manuscript and rechecked the paper and corrected for mistakes before submitting to journal. All authors read and approved the final manuscript.

### Funding

Not applicable.

### Availability of data and materials

Research data are available with the corresponding author and will be made available on the request of a qualified scientist.

## Declarations

### Ethical approval and consent to participate

The study was approved by the Institutional Ethics Committee and informed consent was taken from all patients before entering into study.

### Consent for publication

I, the corresponding author, on behalf of my other authors give consent to the journal to publish this paper.

### Competing interests

No author has any financial or non-financial competing interests.

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