European Journal of Molecular & Clinical Medicine (EJMCM)
ISSN: 2515-8260 Volume 09, Issue 03, 2022

Original research article

A Study of Clinical and Etiological Spectrum of Hypokalemic Flaccid Paralysis

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Abstract

Background: There is very little information on the clinical and etiological characteristics of hypokalemic individuals in developing nations. Very few studies have taken a methodical, approach to address the etiology of hypokalemia. This study was done to examine the clinical and etiological profile of individuals with hypokalemia, keeping in mind the nature and prevalence of hypokalemia in this area.

Methods: This hospital-based cross-sectional study was conducted in the Department of General Medicine of Owaisi hospital attached to Deccan College of Medical Sciences, Hyderabad, Telangana state. Based on the inclusion and exclusion criteria during the study duration, we found n=32 patients who were admitted with hypokalemic flaccid paralysis in all the medical units and neurology wards.

Results: Among the participants maximum of 46.9% had Distal Renal Tubular Acidosis (dRTA) followed by 21.9% who had Gitelman syndrome. Only 15.6% had Idiopathic periodic paralysis, 6.3% had GI potassium loss, and at least 3.1% had primary hyperaldosteronism. N=22(68.75%) had severe hypokalemia and n=10(31.25%) had moderate hypokalemia but none had mild hypokalemia. In the cases of the study based on the etiology and age groups, we found in most of the cases were with secondary hypokalemia and only n=5(15.6%) with idiopathic hypokalemia.

Conclusion: The common causes were secondary causes like dRTA followed by Gitelman's syndrome followed by idiopathic or sporadic periodic paralysis. The age of onset of idiopathic or sporadic paralysis is lesser than due to secondary causes. ECG changes seen in hypokalemia were independent of serum potassium levels. Measurement of urinary potassium excretion and acid-base parameters provide valuable clues for diagnosis.

Keywords: Hypokalemia, Flaccid Paralysis, Gitelman's Syndrome, Hyperaldosteronism

Introduction

Potassium is the most abundant cation in the body. Total body potassium ranges between 37 and 52 mmol/kg body weight out of which 98 percent is found within cells. The normal range of potassium concentration in serum is from 3.5 to 5.0 mmol/l. The ratio of intracellular to extracellular potassium concentration is a critical determinant of cellular resting membrane potential and thereby of the function of excitable tissues, particularly the nerves and muscles. The maintenance of the intracellular to extracellular gradient is largely dependent on the ubiquitous Na^+, K^+ -ATPase enzyme, which pumps two potassium ions into the cell for every three sodiumions extruded. The mechanisms of potassium homeostasis can be considered in termsof internal balance (the relationship between intracellular and extracellular potassium concentration) and external balance (which determines total body potassium) [1] Hypokalaemia is defined as serum potassium concentration<3.5 mmol/l and isthe commonest electrolyte abnormality seen in clinical practice, found in up to 20 percent of patients in the hospital. Clinical manifestations mainly involve the musculoskeletaland cardiovascular systems. Hence, the physical exam should focus on identifying neurologic manifestations and cardiac dysrhythmias. [1] Symptoms of hypokalaemia do not become evident until the serum potassium level is less than 3 mmol/L unless there is a precipitous fall or the patient has a processthat is potentiated by hypokalaemia. The severity of symptoms also tends to be proportional to the degree and duration of hypokalaemia. Symptoms resolve with correction of the hypokalaemia. Symptoms may include feeling tired, leg cramps, weakness, and constipation. [2] Low potassium also increases the risk of an abnormal heart rhythm which is slow and can cause cardiac arrest. Hypokalaemia is graded into Mild, Moderate, and severe depending upon the levels of potassium. It is graded as mild hypokalemia if levels are between 3.0 – 3.5 mmol/L, moderate if the levels are between 2.5 – 3.0 mmol/L, and severe if the levels are below 2.5 mmol/L. Studies in this field have found the overall prevalence of hypokalemia from 6.7% to 21%. [3-6] It is also known as Familial Hypokalemic Periodic Paralysis (FHPP) [7] which isa rare autosomal dominant channelopathy characterized by muscle weakness or paralysis when there is a fall in potassium levels in the blood. Secondary hypokalemic flaccid paralysis is secondary to renal losses as in the usageof drugs like diuretics, amphotericin band acetazolamide or renal tubular acidosis, Gitelman's syndrome, Bartter's syndrome, and hyperaldosteronism. Secondaryto extra renal losses as in profuse vomiting or nasogastric drainage or surreptitious vomiting and diarrhea. It can be either due to the redistribution of potassium into thecells in a setting of normal total body potassium in conditions such as insulin excess andbeta-agonist usage and thyrotoxic periodic paralysis etc., In one study done to know the prevalence of hypokalaemia in hospitalized patients it was found to be 23%. [3] Overall, the prevalence of hypokalaemia was foundto be in a range of 6.7%-21% [4-6] As Hypokalaemia is the commonest electrolyte ion imbalance that presents to the clinic with Muscle weakness and is the most common reversible causeof paralysis when adequate treatment is given on time. The main objective of the current study was to understand the cause of hypokalemia and the application of appropriate therapy so that the quality oflife of patients can be improved as well the disability-adjusted life year (DALY'S) lost can be reduced.

Material and methods

This hospital-based cross-sectional study was conducted in the Department of General Medicine of Owaisi hospital attached to Deccan College of Medical Sciences, Hyderabad, Telangana state, India. Institutional Ethical approval was obtained for the study. Written consent was obtained from all the patients in this study. The Total duration of the study was for 18 months from May 2020 to November 2021.

Inclusion criteria

1. Patients aged 18 years to 44 years.
2. Males and Females
3. Patients who presented with acute flaccid paralysis with proven hypokalemia
4. Patients who have given informed consent for participating in the study

Exclusion criteria

1. Patients with abnormal thyroid functions or other endocrinal diseases
2. Those on therapy with Beta-2 agonists, theophylline, chloroquine, steroids, insulin, diuretics, and laxatives.
3. Patients with known myopathic and polyneuropathic illnesses such as Guillen Barre syndrome
4. Pregnant females
5. Devastated and debilitated persons with mental illness, physical disability, and medical illnesses

Based on the inclusion and exclusion criteria during the study duration, we found n=32 patients who were admitted with hypokalemic flaccid paralysis in all the medical units and neurology wards. A questionnaire was designed for data collection after a systematic review of published studies. Validation of questionnaire was done after incorporation of the received inputs the questionnaire was pilot tested, thereafter further modifications were done. The questionnaire was initially designed in English and then was translated into the local language (Urdu) the final version of the questionnaire consisted of 4 different parts:

I. Socio-demographic profile.
II. History of chief complaints, Present history, Past history, and Family history.
III. General examination and systemic examination
IV. Lab investigations

The lab investigations included Complete blood count, Serum electrolytes, Serum creatinine and BUN, Serum osmolality, Serum Magnesium and calcium, Urinary PH, osmolality, creatinine, electrolytes, chloride and calcium, ABG, Thyroid profile, Serum Aldosterone levels.

ECG changes: Hypokalemia leads to characteristic ECG changes (PR prolongation, ST-segment and T-wave depression, U-wave formation). The earliest electrocardiographic findings, associated with hypokalemia, are decreased T wave height. Then, ST depressions and T inversions appear as serum potassium levels reduce further.

Patients were assessed clinically, with symptomatology and precipitating factors being evaluated. Precipitating factors and recurrence of attacks of paralysis in the same individual and frequency of attacks were taken into consideration for all the patients. The clinical diagnosis of hypokalemic paralysis was suspected and was subjected to general and systemic examination followed by investigations to confirm the diagnosis. Any levels above or below were considered abnormal and have been recorded. The blood and urine analyses were done with special emphasis on serum electrolytes and urine potassium. Arterial blood gas analysis was done. In all cases, an electrocardiogram was taken, and the changes were studied. The response of therapy with oral potassium chloride is studied in all the above n=32 cases and also after starting intravenous (IV) potassium chloride (KCl) therapy was studied and the levels of K+ were recorded pre and post-treatment, as well as the clinical wellbeing, was checked.

Statistical analysis: The data entry responses were coded and thereafter data were entered into Microsoft Excel version 2013. At a later stage, all the data was transferred to SPSS version

20.0 for statistical analysis. Descriptive summary using frequencies, proportions, graphs, and cross tabs were used to display study results. Significance between various factors was determined using the Chi-Square test and P<0.05 is considered significant.

Results

Out of n=32 cases n=14(43.75%) were females and n=18(56.25%) were males. Among study cases, a maximum of 43.75% were between 18-25 years of age and a minimum of 18.75% were among the 36-44 years of age group and the mean age was found to be 29.19 ± 5.5 years. And lowest age of 18 years and the highest age recorded was 44 years. The maximum of 25% were males seen in the age group of 18-26 years followed by 21.9% were females seen in 27-35 years age group and least was 3.1% of females seen in 36-44years of age group details have been depicted in table 1.

Table 1: Distribution of participants according to age group and gender

Age groups (yrs)	*Females*	*Males*	*Total*	*Percentages*
18-26	6(18.8%)	8(25%)	14	43.75%
27-35	7(21.9%)	5(15.6%)	12	37.5%
36-44	1(3.1%)	5(15.6%)	6	18.75%
Total	14(43.8%)	18(56.2%)	32	100%

Among the cases in the study, the maximum number of cases34.4% presented with only Fever followed by 25% who presented with vomiting, 9.4% presented with fever and vomiting, and only 3.1% with diarrhea.28% had no clinical history (table 2).

Table 2: Distribution of participants according to Clinical history

Clinical history	*Frequency*	*Percentage*
Diarrhea	1	3.1
Fever only	11	34.4
Fever and vomiting	3	9.4
Vomiting's	8	25
No clinical history	9	28.1
Total	32	100

In the cases of the study, we found n=7(21.9%) of cases with the presence of paraparesis and n=25(78.1%) cases with the absence of paraparesis. In the cases of the study, quadriparesis was found to be present in 78.1% and bulbar weakness was found in 15.6% of cases. In the majority of cases 75% there were no predisposing factors discovered while the carbohydrate-rich meal was the predisposing factor in 9.4% followed by strenuous activity in 9.4% of cases depicted in table 3.

Table 3: Distribution of patients based on clinical observation and etiology

	Frequency	*Percentage*

Paraparesis		
Yes	7	21.9
No	25	78.1
Total	32	100
Quadriparesis		
Yes	25	78.1
No	7	21.9
Total	32	100
Bulbar weakness		
Yes	5	15.6
No	27	84.4
Total	32	100
Predisposing factors		
Carbohydrate-rich meal	5	15.6
Strenuous activity	3	9.4
Nil	24	75
Total	32	100

Among the participants maximum of 46.9% had Distal Renal Tubular Acidosis (dRTA) followed by 21.9% who had Gitelman syndrome. Only 15.6% had Idiopathic periodic paralysis, 6.3% had GI potassium loss and at least 3.1% had primary hyperaldosteronism given in table 4.

Table 4: Distribution of patients according to Etiological factors

Etiology	*Frequency*	*Percentage*
Barters Syndrome	2	6.3
dRTA	15	46.9
GI potassium loss	2	6.3
Gitelman syndrome	7	21.9
Idiopathic periodic paralysis	5	15.6
Primary hyperaldosteronism	1	3.1
Total	32	100

Among the participants, n=15 patients 46.9% had dRTA, of which n=4(12.5%) had Sjogren's syndrome. All n=4 patients were female and were presented with severe hypokalemia with varied clinical manifestations.

The ECG recordings showed n=12(7.5%) cases with sinus rhythm and n=20(62.5%) with ECG changes. Among the changes in the ECG observed were flat T waves in n=6(18.75%), ST depression in n=4(12.5%), T wave inversion in n=7(21.87%), and prolonged QT interval in n=3(9.37%) given in Figure 2.

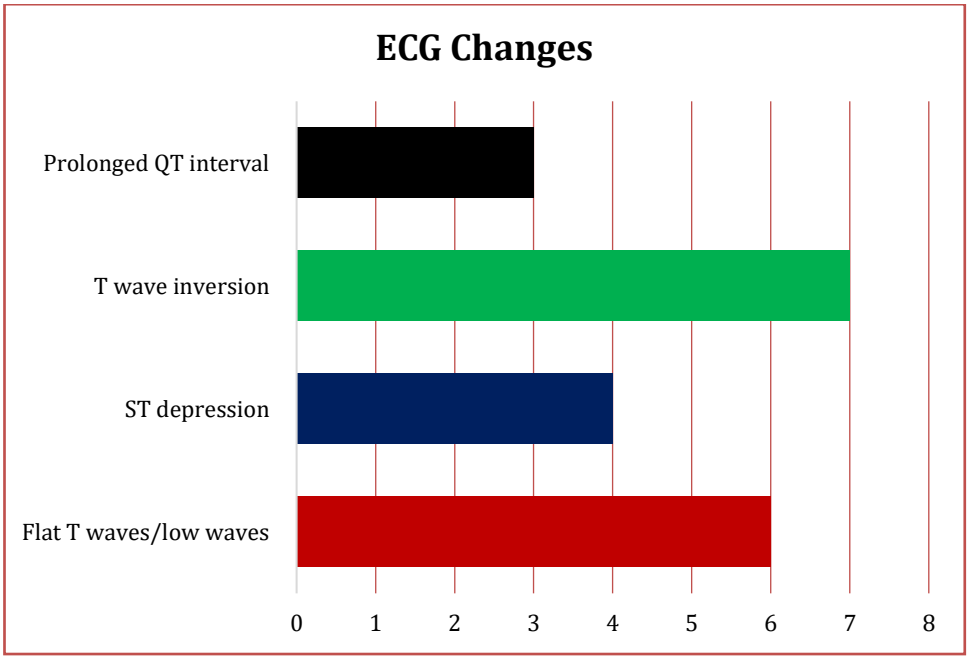

Figure 2: ECG changes observed in the cases of the study

Among the cases, a maximum of n=22(68.75%) had severe hypokalemia and n=10(31.25%) had moderate hypokalemia but none had mild hypokalemia. In the cases of the study based on the etiology and age groups, we found in most of the cases were with secondary hypokalemia and only n=5(15.6%) with idiopathic hypokalemia. however, this difference was not found to be significant as the P-value is 0.13. The details have been depicted in table 5.

Table 5: Distribution of cases based on age groups and etiology

Age groups	*Idiopathic*	*Secondary*	*Total*
18-26 years	4(12.5%)	10(31.2%)	14(43.8%)
27-35 years	0(0.00%)	12(37.5%)	12(37.5%)
36-44 years	1(3.1%)	5(15.6%)	6(18.8%)
Total	5(15.6%)	27(84.4%)	32(100%)

It was observed that as the age increases the number of cases decreases and the maximum number of cases n=11(34.4%) cases were seen of dRTA in the age group of 18-26 years. From table 6 it can be said that the maximum number of patients who presented with severe hypokalemia had dRTA and the maximum number of patients who had moderate hypokalemia had Gitelman syndrome. The Maximum number of patients who had moderate hypokalemia presented with paraparesis and this was found to be significant with a p-value of 0.004. This confirms the correlation between the severity of weakness and serum potassium levels. Similarly, patients who had severe hypokalemia presented with Quadriparesis, and this correlation was found to be significant with a P-value of 0.004. This confirms that the magnitude of the muscle weakness correlates with serum potassium levels. Among the patient's maximum of 53.1% presented with metabolic acidosis followed by 28.1% with metabolic alkalosis and only 18.8% of patients had normal findings on arterial blood gas (ABG) analysis.

Table 6: Showing relation between Severity of hypokalemia and Etiology.

Etiology	*Grading of hypokalemia*		*Total*
	Moderate	Severe	
Barters syndrome	0%	2(6.2%)	2(6.2%)
dRTA	2(6.2%)	9(28.1%)	11(34.4%)
Sjogrens syndrome	0(6.2%)	4(12.5%)	4(12.5%)
GI potassium loss	0(0%)	2(6.2%)	2(6.2%)
Gitelman syndrome	5(15.6%)	2(6.2%)	7(21.9%)
Idiopathic periodic paralysis	2(6.2%)	3(9.4%)	5(15.6%)
Primary hyperaldosteronism	0(0%)	1(3.1%)	1(3.1%)
Total	9(28.1%)	23(71.9%)	32(100%)

Discussion

In this study, we found a maximum number of 43.75% of patients between 18-25 years of age, and the mean age was found to be 29.19 ± 7.7years. PL Rahmawati et al., [8] in their study found that the mean age was 35.6 years ranging from 21 to 77 years. KM Jeyabalaji et al., [9] in a similar study found that the mean age of presentation was 37 years, and most of the patients were in the age group between 20-30 years that is 18 patients constituting 39.13% which was in contrast to our study. Dungdung et al., [10] found in their study that the mean age was 28 years and was ranging between 26-35 years of the age group which was similar to this study. In the current study, it was found that a maximum of 56.25% are Males and 43.75% were Females. PL Rahmawati et al., [8] in a similar study found the majority of the patients were male n=10 that is 58.8% which is similar to our study. KM Jeyabalaji et al., [9] in their study found that n=26 were males which constitutes 56.52% and n=20 were females which are about 43.47% which is also similar to observations of this study. The present study found that a maximum of 34.4% presented with Fever followed by 25% presented with vomiting, 9.4% presented with fever and vomiting, and only 3.1% with diarrhea, and 28% had no clinical history. Among the patients n=7(21.9%) presented with paraparesis but a maximum of n=25(78.1%) presented with Quadriparesis. 84.4% did not have any bulbar weakness and only 15.6% had a bulbar weakness. MR Kumar et al., [10] in their study found that all the patients had weakness in all four limbs without cranial nerve involvement. N=16 patients had muscle pain and five patients had muscle cramps at the time of presentation. In this study, it was found that among the patients only 15.6% had a carbohydrate-rich meal and 9.4% had strenuous activity but 75% had no such predisposing factors. M Yogendhra et al., [11] in their study found that taking fermented rice (bassi) in diet (n=51, 98%) and (n=27, 51.9%) twice a day. When studied about other precipitating factors for Hypokalemic Periodic Paralysis reveals that the majority (n=39, 51%) of the patients had no precipitating event, n=9 patients (17%) had a heavy meal before this episode, followed by n=4 patients out of which n=2 patients (3.8%) had diarrhea and exertion. Sung CC et al., [12] found that among patients with low urinary K (+) excretion (n = 17), chronic alcoholism, remote diuretic use, and anorexia /bulimia nervosa were the most common causes. PL Rahmawati et al., [8] in their study found that n=4 patients (23.52%) with primary hypokalemic periodic paralysis (PP) and n=13 (76.48%) with secondary hypokalemic periodic paralysis. The secondary causes of hypokalemic PP were gastrointestinal potassium loss (n=3 patients, 17.64%), Kidney loss (n=5 patients, 29.41%), thyroid disease (n=4 patients, 23.52%), and hyperinsulinemia (n=1 patient, 5.88%). Hence it was concluded that a larger proportion of the presenting cases was secondary hypokalemic PP similar to this study. Chandramohan G et al., [14] in their study found that the most common

secondary cause was distal renal tubular acidosis (RTA) (n = 75, 36%), followed by Gitelman syndrome (n = 39, 18%), thyrotoxic paralysis (n = 8, 4%), hyperaldosteronism (n = 7, 3%), and proximal RTA (n = 6, 4%). In this study, it was found that the mean K^+ Level is 2.2 ± 0.4 and the mean value of Na^+ is 137.91± 5.04. General Random Blood Glucose (GRBS) mean value was found as 103.50 ± 41.46. Serum Creatinine means level was found to be 1.03 ± 0.17 and Blood Urea levels were found as 30.91±6.8. maximum of 22(68.75%) had severe hypokalemia and 10(31.25%) had moderate hypokalemia but none had mild hypokalemia. Yogendra M et al., [11] in their study found that severe hypokalemia was found in n=6(11.3%), moderate hypokalemia was found in n=42(80.7%) whereas sodium levels were less than 135 meq/l in n=16 (30.7%), serum urea was >45mg% in n=4(7.5%) which was in contrast to this study. SA. Malik et al., [15] in their study found that Hypokalemia was mild in n=24 patients (17%), moderate in n=82 (57%) patients, and severe in n=37 (26%) patients. in mild hypokalemia patients 12% were symptomatic, in moderate hypokalemia patients 22% were symptomatic and in severe hypokalemia 35% were symptomatic. In this study, it was found that 62.5% had ECG changes like flat T waves, U waves, ST depressions, etc. 37.5% of patients showed normal sinus Rhythm. N=20 patients who showed abnormal ECG changes it was found that a maximum of 35% had T wave inversion followed by n=6 patients (30%) who had Flat T waves and n=4 patients (20%) had ST depressions and n=3 patients (15%) had prolonged QT interval. Jeyabalaji et al., [9] found in their study that the earliest ECG change noted was T wave flattening which was present in 100% of the patients, and their mean serum potassium value was 1.92 mEq/L. The next change in ECG that was noted was the appearance of a U wave (shorter than a T wave) that occurred in 52.17% of patients whose mean serum potassium value was 2.06 mEq/L. In this study, it was found that a maximum of 53.1% presented with metabolic acidosis followed by 28.1% with metabolic alkalosis, and only 18.8% of patients had normal findings on ABG. Among them, the maximum was in the age group of 18- 26 years. Jeyabalaji et al., [9] in their study found that a total of 65.21% of patients in this study had normal anion gap metabolic acidosis (NAGMA). Most of them had early morning urine pH values of >5.5 and were diagnosed with Distal RTA. A total of 21.7% of patients had metabolic alkalosis similar to this study.

Conclusions

Within the limitations of the present study, we found the common causes were secondary causes like dRTA followed by Gitelman's syndrome followed by idiopathic or sporadic periodic paralysis. The age of onset of idiopathic or sporadic paralysis is lesser than due to secondary causes. ECG changes seen in hypokalemia were independent of serum potassium levels. Measurement of urinary potassium excretion and acid-base parameters provide valuable clues for diagnosis. It is essential to correct hypokalemia before alkali therapy in patients with metabolic acidosis and to correct hypomagnesemia along with correction of hypokalemia in patients with metabolic alkalosis.

References

1. Palmer BF. Regulation of Potassium Homeostasis. Clin J Am Soc Nephrol. 2015; 10(6):1050-60.
2. Soar J, Perkins GD, Abbas G, Alfonzo A, Barelli A, Bierens JJ, et al. European Resuscitation Council Guidelines for Resuscitation 2010 Section 8. Cardiac arrest in special circumstances: Electrolyte abnormalities, poisoning, drowning, accidental hypothermia, hyperthermia, asthma, anaphylaxis, cardiac surgery, trauma, pregnancy, electrocution. Resuscitation. 2010; 81(10):1400-33.

3. Widodo D, Setiawan B, Chen K, Nainggolan L, Santoso WD. The prevalence of hypokalemia in hospitalized patients with infectious diseases problems at Cipto Mangunkusumo Hospital, Jakarta. Acta Med Indones. 2006; 38(4):202-05.
4. Paice BJ, Paterson KR, Onyanga-Omara F, Donnelly T, Gray JM, Lawson DH. Record linkage study of hypokalaemia in hospitalized patients. Postgrad Med J. 1986; 62(725):187–191.
5. Lippi G, Favaloro EJ, Montagnana M, Guidi GC. Prevalence of hypokalaemia: the experience of a large academic hospital. Intern Med J. 2010;40(4):315–316.
6. Liamis G, Rodenburg EM, Hofman A, Zietse R, Stricker BH, Hoorn EJ. Electrolyte disorders in community subjects: prevalence and risk factors. Am J Med. 2013;126(3):256–263.
7. David B. Mount. Fluid and Electrolyte Disturbances. Harrison's principles of Internal Medicine. 20th Edn. New York: McGraw-Hill Education. August 2018; p. 304-308.
8. Rahmawati PL, Arimbawa IK, Laksmidewi AAAP. Profile of Patients with Hypokalemic Periodic Paralysis. Int J Med Rev Case Rep. 2021; 5(4): 26-32.
9. KM Jeyabalaji, K Manoj Kumar. Clinical and Etiological Profile of Patients presenting with Hypokalemic Periodic Paralysis. A Single Centre Study from South India, International Journal of Scientific Research 2021;10(4):59-62.
10. Dungdung A, Jalawadi VM, Yadav UP. Study of incidence and prevalence of hypokalemic periodic paralysis. Int J Res Med Sci 2019; 7:810-14.
11. Kumar MR, Bharath R, Rammohan P, Agrawal A. Clinical Profile in Hypokalemic Periodic Paralysis Cases. Eur J Gen Med. 2014;11(1):6-9.
12. Yogendra Malhotra, Harshlata Sahu. A Study of Clinical & Biochemical Profile of Patients with Periodic Paralysis with Special Reference to Hypokalemic Periodic Paralysis. IOSR Journal of Dental and Medical Sciences 2019;18(1): 05-08
13. Sung CC, Cheng CJ, Chiang WF, Chau T, Hsu YJ, Yang SS, Lin SH. Etiologic and therapeutic analysis in patients with hypokalemic nonperiodic paralysis. Am J Med. 2015; 128(3):289-96
14. Chandramohan G, Dineshkumar T, Arul R, Seenivasan M, Dhanapriya J, Sakthirajan R, Balasubramaniyan T, Gopalakrishnan1 N. Spectrum of hypokalemic paralysis from a tertiary care center in India. Indian J Nephrol 2018; 28:365-69.
15. Suhail A. Malik, Mosin S. Khan, Syed Mudassar, Parvaiz A. Koul. Clinical and Etiological Profile of Hypokalemia: A Prospective Study in a Tertiary Care Hospital. 2017; 107-112.