INTRODUCTION

In physiology, the primary ions of the electrolytes are sodium (Na+), potassium (K+), calcium (Ca2+), chloride (Cl), hydrogen phosphate (HPO4 2-), and hydrogen carbonate (HCO3-) [1]. Potassium is one amongst those which is the most abundant cation in the body, with estimated total-body stores of 3,000 to 4,000 mmol. About 98% of potassium is seen within the intracellular compartment, and the remaining 2% is distributed within the extracellular compartment. The Sodium-Potassium adenosine triphosphate (Na+-K+-ATPase) pump located in the cell membrane is responsible for the compartmentalization of Potassium. This pump is an active transport system that maintains increased intracellular stores of potassium by transporting Sodium out of the cell and Potassium into the cell at a ratio of 3:2. Consequently, the pump maintains higher concentration of potassium inside the cell. Potassium plays a main role in the transmission of nerve impulse, contraction of muscles and maintenance of fluid balance in the body [2].

The normal value of serum potassium is 3.5-5.0 mmol/L. Hypokalemia is an electrolyte imbalance and is indicated by a low level of Potassium in the blood. Hypokalemia is divided into three categories based on serum potassium levels: mild 3.0-3.5 mmol/L, moderate 2.5-3.0 mmol/L and severe<2.5 mmol/L. Up to 21% of hospitalized patients have serum potassium levels lower than 3.5mmol/L with 5% of patients exhibiting potassium levels lower than 3 mmol/L [3][4]. Hypokalemia is defined as serum potassium concentration greater than 5.0mmol/L. It is less common than hypokalemia. Hyperkalemia is divided into three categories based on serum electrolytes; mild 5.1-5.5 mmol/L, moderate 5.6-6.0 mmol/L and severe>6 mmol/L. The incidence of hyperkalemia in hospitalized patients has been estimated to be 1.4-10% [4].

One of the most common electrolyte complications are Potassium abnormalities in hospitalized patients. Potassium is one of the critical electrolytes involved in various cellular activities. Potassium loss in the body affects the quality of life of the patient and increases morbidity and mortality. So, it is very important to monitor the potassium levels, initiate the standard treatment immediately and normalize them [5]. Hence in this study, we aimed to capture the data regarding the potassium abnormalities in the hospital setting and understand the causes and their management strategies.

MATERIALS AND METHODS

The present study was a prospective and observational study conducted at Apollo Hospitals, Jubilee Hills, Hyderabad, India. This study was approved by the institutional ethical committee (No: SVC/2015/28). Case records of the inpatients who are above or equal to 18 y with abnormal potassium values were included and outpatients are excluded from the study. The data was collected regarding patient's demographics such as age, family history, co-morbid conditions, abnormal potassium values, dose, frequency, lab parameters such as serum electrolytes values (Sodium, Calcium, Magnesium and Chlorides), Serum Creatinine (S. Cr), complete blood picture, electrocardiogram (ECG), liver function tests like albumin, globulin, and alkaline phosphatase were recorded. Statistical analysis is done by using descriptive statistics and CI of mean. Descriptive analysis was used to report the findings of continuous data and Categorical data, potassium abnormalities was analyzed by confidence intervals of their respective means.

RESULTS AND DISCUSSION

A total of 200 in-patients who have abnormal potassium values were considered for the study, of which the majority were males (53%). Higher percentage of our study population belonged to the age group of 51-60 y (27%), as it is known that risk of cardiovascular disease (Hypertension, Coronary artery diseases) and renal disease (Chronic kidney disease and Acute kidney injury) are significantly higher in this age (table 1). Blood pressure increases with age and lifetime risk of developing cardiovascular diseases among those of 55 y age and older was observed to be 90% [6,7].

Majority of our study population were found to be overweight and obese with an average body mass index (BMI) of 27.4 kg/m². Obesity is
characterized by a marked insulin resistance which involves an abnormal regulation of Potassium uptake and metabolism (table 1). The disease induced hypokalemia 87 (55.06%) cases and hyperkalemia 19 (51.35%) cases, and the drug-induced hypokalemia 71 (44.93%) cases and hyperkalemia 18 (48.65%) cases, were observed among 158 cases of hypokalemia (The 95% confidence interval extends from 0.7281 to 0.8410) and37 cases of hyperkalemia (The 95% confidence interval extends from 0.1370 to 0.2449) respectively (table 2).

Chronic kidney disease (CKD), diabetes mellitus (DM), hypertension (HTN), coronary artery disease (CAD) and urinary tract infections (UTI) are the conditions where potassium abnormalities were seen to a larger extent. In our study we noted that Lactulose, furosemide, methylprednisone, nonadrenaline, actrapid, perindopril, enalapril, irbesartan, telmisartan, aspirin, and combinational drugs like furosemide +lactulose, non-steroidal anti-inflammatory drugs and angiotensin-converting enzyme inhibitors (NSAIDS+ACEI), β-blockers, angiotensin receptor blockers and beta blockers(ARB+β-blockers) are the drugs causing potassium abnormalities (table 3).

Among disease induced hypokalemia, nephrotic disorders are the prime reasons, it can be because of increased water intake and increased reabsorption of sodium chloride and water offer to sustain the edemas, while aldosterone promotes renal excretion of K+ and H+ leads to develop hypokalemia and alkalosis [8, 9].

Table 1: Patient demographics (N=200)

| Gender | No of cases (%) |
|--------|-----------------|
| Females| 94 (47%)        |
| Males  | 106 (53%)       |

Table 2: Details of Potassium abnormalities in the study population (N=200)

| Potassium abnormality | Hypokalemia | Hyperkalemia | Subsequent K+ abnormality |
|-----------------------|-------------|--------------|---------------------------|
| Serum K⁺ value < 3.5 mmol/l | 158* (80%) | -            | 05 (3%)                   |
| > 5.0 mmol/l          | -           | 37 **(17%)   | -                         |
| Severity              | Mild        | Moderate     | Severe                    |
|                       | 118 (74.6%) | 35 (22.15%)  | 05 (3.16%)                |
|                       | 22 (59.45%) | 10 (27.02%)  | 05 (13.15%)               |
| Etiology              | Disease induced | Hyperkalemia | Subsequent potassium abnormality |
|                       | 87 (55.06%) | 19 (51.35%)  | 05 (100%)                 |
| Drug induced          | 71 (44.93%) | 18 (48.65%)  | -                         |

| ECG Changes (n=17) | Sinus Tachycardia | Disease induced |
|--------------------|-------------------|-----------------|
| Hypokalemia        | Drug-induced      | Disease induced |
|                    | 10 (71%)          | 4 (29%)         |
| Hyperkalemia       | 1 (33.3%)         | 2 (66.7%)       |

*95%CI 0.7281 to 0.8410**95% CI 0.1370 to 0.2449

Table 3: Common drugs in dosing potassium abnormalities (N = 200)

| Drugs causing potassium abnormalities | Laxatives | Loop diuretics | Corticosteroids | Catecholamine | Insulin | Combination | Hyperkalemia (n=37) |
|--------------------------------------|-----------|----------------|-----------------|---------------|---------|-------------|---------------------|
| ACEIs*                               | Lactulose | Furosemide     | Methyl prednisone | Nor adrenaline | Actrapid | Furosemide + Lactulose | 02 (11.11%)         |
| ARBs*                                | Perindopril | Enalapril      | Irbesartan      | Telmisartan   | 02 (11.11%)         |
| NSAIDs*                              | Aspirin   | 02 (11.11%)    | 01 (5.55%)      | 02 (11.11%)   |
| Combinations                         | NSAIDS+ACEIs, | β-blockers + NSAIDS+ACEIs | ARBs+β blockers | NSAIDS+ACEIs, | β-blockers + NSAIDS+ACEIs | ARBs+β blockers | 02 (11.11%)         |

ACEI’s: Angiotensin Converting Enzyme Inhibitors, ARB’s: Angiotensin Receptor Blockers, NSAIDS: Non-Steroidal Anti-Inflammatory Drugs
Management of Hypokalemia and Hyperkalemia:

The Serum Potassium levels in hypokalemia patients were normalized with 10ml (13.3mEq) of Potassium chloride syrup, which was administered three times a day in 27 (17%) cases, which showed a 0.5mmol/l increase in Serum Potassium. Injection potassium chloride (KCl) was given in 28 (17.7%) cases and were managed with 40mEq given twice a day, which showed an increase of 0.3mmol/l Serum potassium (table 4).

Potassium citrate and magnesium citrate (Potrate M) was also given for the management of hypokalemia when there was an abnormality of magnesium in metabolic alkalosis patients. Potrate M was given in 4 (2.5%) cases with 15 ml twice a day, showed an increase of 0.5mmol/l serum potassium. In our study, combination therapy was given for the management of hypokalemia. Syrup potassium chloride (Potrate) 20ml and injection Potassium chloride 10 mEq, stat was given in 8 (5%) cases, which showed an increase of 0.4 mmol/l (table 4).

For the management of hyperkalemia, parenteral, nebulizers and oral dosage forms were prescribed. Calcium gluconate, Insulin, Potassium bind was given as injections and as nebulizers and subcutaneous Insulin 16 units once a day was given in 1 (2.7%) case which showed decrease of 0.2mmol/l serum potassium respectively (table 4).

Hyperkalemia was also managed using more than one drug. In our study the combination drugs were inj. Calcium gluconate 10 ml stat and Salbutamol 2 cc nebulizer three times a day was given in 2 (5.4%) cases Which showed a decrease of 0.1 mmol/l serum potassium (table 4).

In a few cases extra supplementation of potassium led to hyperkalemia and upon treatment, it subsequently resulted in hypokalemia. Such kind of Potassium abnormalities was found to be 5 (3%) cases in our study. In subsequent hypokalemia and hyperkalemia, mild and severe cases were seen in 3 and 2 cases respectively, which are found in both disease and drug induced Potassium abnormalities (table 2).

Patients with longer duration of hospital stay were observed to be with subsequent hypokalemia and hyperkalemia as these patients require continuous monitoring. The initiation of potassium supplements was influenced by the duration of stay in these patients. Naranjo’s causality scale was used to assess the causality of potassium abnormalities. In our study, we found that about half of the cases of drug induced hypokalemia and the drug induced hyperkalemia were possible (table 5).

| Drug | Dose | No of cases | Route | Frequency | Average increase in K+ value (mmol) |
|------|------|-------------|-------|-----------|-----------------------------------|
| Syrup | 10 ml | 41 | PO | OD 01 | 0.1 |
| Potassium chloride | 40 meq | 28 | IV | BD 28 | 0.3 |
| Inj. Potassium chloride | 15 ml | 07 | PO | BD 04 | 0.5 |
| Potassium citrate and Magnesium citrate | 20 ml | 08 | PO | Stat | 0.4 |
| Inj. Potassium chloride | 20 meq | 10 | IV | | |

Table 4: Management of potassium abnormalities in the study population (N=200)

| Drug | Dose | No of cases | Route | Frequency | Average decrease in K+ value (mmol) |
|------|------|-------------|-------|-----------|-----------------------------------|
| Calcium gluconate | 10 ml | 03 | IV | Stat | 0.2 |
| Furosemide | 20 mg | 01 | PO | BD | 0.2 |
| Potassium Bind Sachet | 15 ml | 02 | PO | OD | 0.1 |
| Salbutamol + Ipratropium Bromide | 2 cc | 02 | Neb | QID | 0.1 |
| Salbutamol | 1 cc | 01 | Neb | QID | 0.1 |
| Sodium bicarbonate | 500 mg | 02 | PO | BD | 1.1 |
| Insulin | 16U | 01 | SC | HS | 0.2 |
| Calcium gluconate | 10 ml | 02 | IV | Stat | 0.3 |
| Salbutamol | 2 cc | | Neb | TID | |

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Table 5: Causality assessment

| Naranjo's scale (n=89) | Hypokalemia (71) | Hyperkalemia (18) |
|------------------------|------------------|------------------|
| Probable (5-8) | 25 | 06 |
| Possible (1-4) | 30 | 09 |
| Definite (≥9) | 14 | 03 |
| Doubtful | 02 | 00 |

LIMITATIONS

Difficulty in accessing data in ICU and Hemodialysis department. Since, data collected was from inpatient only, the status of improvement in potassium levels after discharge was unavailable.

CONCLUSION

From our study, we observed that hypokalemia was the most common potassium abnormality. The common causes of the abnormalities were because of diseases. However, they were mild in...
nature and were treated with no negative outcome. Regular monitoring is required to prevent further complications and to improve the quality of life.

ACKNOWLEDGMENT

It is a pleasant task to express our thanks to all those who contributed in many ways to the success of this study. We are thankful to the Principal Dr. M. Bhagavan Raju and Management of Sri Venkateshwara College of Pharmacy, Apollo Hospitals, Jubilee hills for their support in carrying out this project. Funding: None.

AUTHORS CONTRIBUTIONS

Vidya Maheshwaram, Sahitya K, Srujana K and Naveen Kumar V, Pharm D students collected the data. Dr Rawheena Mayee research guide, Dr Aparna Yerramilli, Dr Sanjeev Sharma-guides of this study contributed in the design of the study, protocol process, data analysis and manuscript writing.

CONFLICT OF INTERESTS

The author(s) declare(s) that they have no conflicts of interest to disclose.

REFERENCES

1. Olubunmi CO jo, Modupe F Asaolu. Status of plasma electrolytes, urea, creatinine, and c-reactive protein in cancer patients. Asian J Pharm Clin Res 2018;11:268-70.
2. Lawrence J Appel, David H Baker Potassium. Dietary reference intakes for water, sodium, chloride, and sulfate. Washington, dc: the national academies Press; 2005. p. 186-268.
3. Robert J Luft, Friedrich C Shirley. Pathophysiology and management of hypokalemia: a clinical perspective. National Rev Nephrol 2011;10:2010-75.
4. Marjorie J Arca, Brian Kenney. The management of hyperkalemia in the emergency department. J Accident Emergency Med 2010;17:181-92.
5. Cohn JN, Kowey PR, Wheeler PK, Prisant LM. New guidelines for potassium replacement in clinical practice a contemporary review by the national council on potassium in clinical practice. Arch Intern Med 2000;160:2429-36.
6. Matsui H, Shimosawa T, Ueda Y, Wang H, Ogura S, Kaneko T, et al. Protective effect of potassium against the hypertensive cardiac dysfunction: association with reactive oxygen species reduction. Hypertension 2006;48:225-31.
7. Krauss RM, Eckel RH, Howard B, Appel LJ, Daniels SR, Deckelbaum RJ, et al. Dietary guidelines. Revision 2000: a statement for healthcare professionals from the Nutrition Committee of the American Heart Association. Stroke 2000;31:2751-66.
8. David B Mount. Fluid and electrolyte disturbances. In: Jameson Fauci, Braunwald, Kasper. editors. Harrison's principles of internal medicine. 20th ed. New York: McGraw-Hill, Medical Pub. Division; 2005;46:281-96.
9. Harikesh Maurya, Tirath Kumar. A review on comprehensive overview in the management of nephrotic disorders. J Critical Rev 2016;3:34-43.