ORIGINAL ARTICLE

Potassium Disorders in Diabetic Patients with Chronic Kidney Disease and Poor Glycemic Control Associated with Hyperkalemia: A Single Center Cross-sectional Study

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ABSTRACT

Objective: To determine the incidence of hyperkalemia in diabetic patients with chronic kidney disease (CKD). Also, to establish the effect of blood sugar control and duration of DM and CKD on the development of hyperkalemia in this group of patients.

Study Design: Cross-sectional study.

Place and Duration of Study: The study was conducted at Nephrology Outpatient Department (OPD), Liaquat National Hospital Karachi, Pakistan over one year from January 2022 to December 2022.

Methods: Data were collected from endocrine and nephrology outpatient departments. Blood analysis was performed for serum potassium, HbA1C level, and serum creatinine level. SPSS version 21 was used to analyze the data.

Results: One hundred and fifty-six (156) patients were included in this study. Ninty (90) patients were males & 66 patients were females. Hyperkalemia was noted in ninety patients (57.6%) with a serum potassium level of 5.8±0.1 mg/dl in these patients and was seen predominantly in male patients. The mean HbA1c level was 9.288±1.185%. However, no significant relationship between the duration of diabetes and hyperkalemia was found. Most patients had stage IV CKD. Also, hyperkalemia is most commonly seen in stage IV CKD followed by stage V CKD. No significant relationship between the duration of CKD and hyperkalemia was found. Sixty-five percent (65%) of patients were taking medications that could lead to hyperkalemia and ACE/ARB were the most commonly used drugs followed by NSAIDs and diuretics.

Conclusion: Patients with diabetes mellitus with CKD were found at significantly increased risk of hyperkalemia importantly, patients with stage IV &V CKD and those who had poor glycemic control.

Keywords: *Arrhythmia, Chronic Kidney Disease, Diabetes Mellitus, Hyperkalemia, Hyperglycemia, Serum Potassium.*

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Introduction

As per US death certificates in 2010, Diabetes mellitus was reported as the sixth most common cause of death, and in Pakistan, more than 7.2 million people are affected by DM.[1,2] Similar to diabetes, Chronic kidney disease (CKD) has been emerging as a health challenge across the world.[3] Both DM and CKD are independently associated with an increased risk of hyperkalemia and cardiovascular diseases.[4,5] When two conditions exist together, the risk of hyperkalemia and sudden cardiac death potentiates. Certain factors of DM and CKD are associated with the risk of hyperkalemia including the uncontrolled

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status of diabetes and others. We aimed to report the incidence of hyperkalemia in this group of patients and to establish factors related to DM and CKD so that those factors can be addressed. Determining the incidence will help in reducing mortality in the mentioned population.

Methods

Study population and data source

This is a single-center, cross-sectional study of diabetic patients that included only those patients who had established chronic kidney disease. The study was performed at Liaquat National Hospital Karachi, Pakistan having a diabetes center and a large nephrology unit as well. Data were collected for patients coming to both endocrine and nephrology outpatient (OPD) departments. The study was conducted over 1 year from January 2022 to December 2022 after taking approval from the Ethical Review Committee on dated 2nd January 2022 vide letter no: App#0845-2022-LNH-ERC. Data regarding age, sex, presence or absence of diabetes, duration of diabetes, presence or absence of chronic kidney disease, and duration of CKD were obtained through verbal interviews of patients coming to endocrine OPD as well as nephrology OPD by a principal investigator. To know about the sugar control of patients we followed HbA1C. To establish the stage of CKD, we measured serum creatinine and creatinine clearance. We measured serum potassium levels to determine the presence or absence of hyperkalemia. All data were safely recorded on a pre-designed questionnaire. History regarding drug therapy was taken care of and also recorded on the same questionnaire.

Potassium measurement in serum

To measure serum potassium concentration, venous samples were taken using a vacuum technique with a lithium heparin solution container by trained nursing staff. These samples were analyzed by a trained laboratory technician at the central biochemistry lab of the hospital using a Communauté d'agglomération du Bassin d'Arcachon Sud with an acronym ' COBAS' 501 analyzer based on the spectrophotometric method. Results were obtained through the electronic database system of the central laboratory. Values are enrolled on an Excel sheet by a principal investigator. Hyperkalemia was defined as a serum potassium concentration greater than approximately 5.2 mEq/L as per the local laboratory reference range.

Determining sugar control of diabetic patients

To measure the HbA1C level in the blood, venous samples were taken using a vacuum technique with a lavender-top 3ml (K2 EDTA) tube by trained nursing staff. These samples were analyzed by a trained laboratory technician at the central biochemistry lab of the hospital using ion-exchange high-performance liquid chromatography (HPLC). Results were obtained through the electronic database system of the central laboratory. Values are enrolled on an Excel sheet by a principal investigator. Uncontrolled Diabetes: HbA1c > 7.0% were labeled as uncontrolled diabetes.

Creatinine measurement in serum and determining the stage of CKD

Creatinine was measured in serum by techniques similar to those described for potassium. The Cockcroft-Gault formula was applied to determine the stage of CKD.

Statistical Analysis: Data was entered on SPSS version 25. Mean± standard deviation was calculated for age, duration of CKD, HbA1c level, serum potassium level, and duration of DM. Frequency and percentages were calculated for gender, stage of CKD, and hyperkalemia (yes/no). The primary endpoint was to get the incidence of raised potassium in diabetic patients with CKD and the secondary endpoint was to evaluate the relationship between the duration of diabetes, the uncontrolled status of diabetes, the duration of CKD, and the stage of CKD with hyperkalemia. The Chi-square test was applied and $P < 0.05$ was taken as significant.

Results

A total of one hundred and fifty-six (156) patients with diabetes mellitus and chronic kidney disease (CKD) were included in this study. The mean age of patients was 59.7+8.87 years (Table- 1). Ninety patients were males & sixty-six patients were females. Hyperkalemia was noted in 90patients (57.6%) with a serum potassium level of 5.8±0.1 mg/dl in these patients. All patients were diabetic and the mean duration of DM was 11.1+6.18 years.

All patients had uncontrolled diabetes with a mean HbA1c level was 8.088+1.185%. However, no

Table-1: Baseline Characteristics

Serial Number	Mean	Standard Deviation (SD)
Age	59.77	8.8
Serum Potassium (mg/dl)	5.8	0.1
Duration of Diabetes (years)	11.1	6.18
Duration of CKD (months)	9.28	1.18
HbA1C level (%)	8.08	1.1

significant relationship between the duration of diabetes and hyperkalemia was found. All patients were CKD. The mean duration of CKD was 25.19±24 months in our patients. The stage of CKD was II in twenty-two (22) patients, III in twenty seven (44%) , IV in thirty-five (50%) , and V in forty (40). Most patients had stage IV CKD. Also, hyperkalemia is most commonly seen in stage IV CKD (33.9%) followed by stage V CKD (28.1%). However, hyperkalemia was also seen in stage II and stage III CKD at (13.5%) and (26.2%) respectively. Furthermore, no significant relationship between the duration of CKD and hyperkalemia was found. Hyperkalemia was seen predominantly in males (39.7%). (Figure.1). Sixty-five percent of patients were taking medications that can lead to hyperkalemia and were including ACE/ARB, NSAIDs, and diuretics. The majority of our patients were taking a combination of these drugs. The most common combination was ACE/ARB with diuretics.

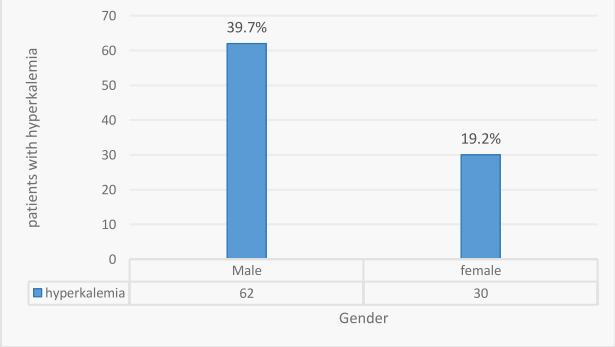

Fig.1: The frequency of hyperkalemia according to gender

Discussion

Diabetes mellitus (DM) is a worldwide pandemic and it affects a wide variety of populations across the world. Literature review reveals that diabetes mellitus when uncontrolled has many complications, including chronic kidney disease (CKD).[6] Diabetic patients frequently have CKD as a combined co-morbidity.[7] Type 2 diabetes is accountable for approximately half of end-stage kidney disease (ESKD) burden worldwide.[8] It has many metabolic effects; hyperkalemia is one among the others and a higher prevalence of hyperkalemia has been reported in diabetic patients with CKD.[9] There are multiple proposed mechanisms through which hyperkalemia can occur in diabetes including renin-angiotensin system (RAS) independent and RAS-dependent mechanisms.

Deranged renal function is a well-established risk factor for raised potassium.[10] As in our study, 57.6 % of patients had hyperkalemia. We found it remarkably high since the reported incidence of hyperkalemia in diabetic patients with CKD is 17.3%.[11] Both diabetes and CKD are conditions that have a suppressed RAS pathway under various pathophysiological effects. Diabetes is a hyporeninemic hypoaldosteronism condition. On the other hand, the distal renal tubular dysfunction in CKD results in impaired potassium (K+) excretion via a similar mechanism. Autonomic neuropathy, and afferent arteriolar hyalinosis due to Injury to the juxtaglomerular apparatus are other complications that result in raised potassium in these patients.[12] One important factor that affects the RAS pathway is drug therapy.[13] Worth important to mention is use potassium-sparing diuretics. The use of both steroidal and non-steroidal mineralocorticoid receptor blockers in the setting of CKD and diabetes is of growing interest to reduce proteinuria and to achieve blood pressure control.[14,15] Sixty-five percent of the patients in our study were using drugs that cause hyperkalemia. Among various drugs including ACE/ ARB and/or NSAIDs and/or diuretics, ACE/ARB was the most commonly used medication followed by diuretics and various combinations of the mentioned drugs. Various large trials have reported hyperkalemia in diabetic patients was related to

certain drug therapies. Aliskiren Trial in Type 2 Diabetes Using Cardio renal Endpoints (ALTITUDE) and Veterans Affairs Nephropathy in Diabetes (VA NEPHRON-D), both of these trials were conducted on diabetic patients with CKD and targeted renin-angiotensin system (RAS) blocked but both were terminated before completion because of safety concerns of hyperkalemia.[16] Potassium levels should be monitored in diabetic patients with CKD and special consideration should be paid to the medications of a diabetic patient to minimize the risk of hyperkalemia.

Good glycemic control is a challenge in CKD patients. There are various reasons for altered glycemic control in the CKD population and these patients encounter both hypoglycemia and hyperglycemia very frequently.[17] Poor glycemic control contributes to hyperkalemia as seen in our patients (poor glycemic control was revealed by mean HbA1c of 9.288+1.185%). However, the role of hemoglobin A1c in assessing glycemic control in CKD patients has limitations due to measurement bias either to the low or high range.[17] Diabetes is a hyperosmolar condition that results in the transcellular shift of water to the outside of the cell and that accompanies the extrusion of potassium from the cell to the interstitium resulting in hyperkalemia.[18] Hyperglycemia in diabetes mellitus causes hypertonicity due to extracellular solute (glucose) gain.[19] The Hypertonic effect of hyperglycemia is marked in patients with reduced renal function.[20,21] Insulin deficiency in diabetes also results in the transcellular shift of potassium and thus hyperkalemia.[22] In CKD there is abnormal insulin metabolism, altered gluconeogenesis, increased red blood cell (RBCs) glucose uptake during hemodialysis, and malnutrition. Continuous glucose monitoring in CKD patients is suggested for better glycemic control. Apart from the mentioned facts, we could not establish any relationship between the duration of diabetes and the duration of CKD with hyperkalemia.

A direct relationship between the severity of renal failure and the incidence of hyperkalemia has been found.[23] We in this perspective found that hyperkalemia was present in all stages of CKD however, the incidence of hyperkalemia was most common in stage IV & V CKD. A meta-analysis from more than 1.2 million individuals has reported that CKD offers various risk factors for hyperkalemia, while the drop in GFR has been found the strongest factor of hyperkalemia among all.[24] Another interesting fact revealed from the literature review is that hyperkalemia is more prevalent in males as compared to females.[25] We also reported similar findings and in our study 67 out of 90 male patients had hyperkalemia. This figure was comparatively lower for female patients. However, further studies to understand the gender-based risk for hyperkalemia are suggested.

Conclusion

Diabetic patients with CKD were found at significantly increased risk of hyperkalemia importantly, patients with stage IV &V CKD and those who had poor glycemic control. Special consideration should be given to the medications of diabetic patients with CKD and good glycemic control should be assured to minimize the risk of hyperkalemia. Further, we recommend monitoring serum potassium levels in diabetic patients with CKD who are using drugs that potentially can cause hyperkalemia.

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Conflict of Interest: The authors declare no conflict of interest

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Authors Contribution

MQ: Data collection, data analysis, results and interpretation, manuscript writing and proofreading
KN: Data collection, manuscript writing and proofreading
SR: Idea conception, data collection
MQ: Study designing, data collection
FN: Study designing, data collection, manuscript writing and proofreading
SB: Data collection, data analysis, results and interpretation