THE POTENTIAL ROLE OF eGFR IN DIFFERENTIATING BETWEEN TRUE AND PSEUDOHYPERKALEMIA AT A TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: To determine the potential role of eGFR in differentiating between true and pseudohyperkalemia at a tertiary care hospital.

Material and Methods: Cross-sectional study conducted in department of Chemical Pathology, Sheikh Zayed Hospital, Rahim Yar khan from January 1, 2022 to August 31, 2022. A total of 101 study subjects satisfying the inclusion criteria were included in study. Included specimen were analysed for serum creatinine level and estimated glomerular filtration rate (eGFR) was calculated by using chronic kidney disease-Epidemiology Collaboration (CKD-EPI) creatinine equation.

Results: Of the total 101 study subjects, 59(58.4%) were male and 42(41.65%) were females. Mean age of study subjects was 45.28±12.265 years. Of the total 101 study samples, 75(74.3%) were classified as true hyperkalemia while 26(25.7%) were classified as pseudohyperkalemia with statistically significant difference of eGFR between two groups (*P* value: 0.00).

Conclusion: Serum electrolytes are one of the most frequently requested diagnostic tests; thus, errors in these readings may alter the course of treatment for patients. As shown in our study that true hyperkalemia is very rare in patients with normal kidney function. So, estimated GFR can be taken as useful tool to differentiate between true and pseudohyperkalemia.

Key Words: Pseudohyperkalemia, True hyperkalemia, Estimated GFR, CKD

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INTRODUCTION

Hyperkalemia is very common electrolyte abnormality in clinical medicine leading to severe complications [1]. To prevent the detrimental outcome, hyperkalemia should be treated on urgent basis. One of the major cause of true hyperkalemia is renal dysfunction [2]. Pseudohyperkalemia is false elevation of serum or plasma potassium level in which measured value of serum potassium is above the upper reference limit when the actual concentration is within the reference range [3].

Pseudohyperkalemia can result from fist clenching during blood sample collection due to release of potassium from muscles, thrombocytosis, leukocytosis and erythrocytosis especially in context of hematological malignancies that render the abnormal blood cells fragile [4]. Other causes of pseudohyperkalemia may include increased tension due to tourniquet and mechanical lysis of red blood cells by inverting tubes too rigorously [5,6].

In order to investigate the cause of true hyperkalemia, assessment of kidney function is essential as the excretion of majority of potassium is through the kidneys [7]. Abnormal potassium level is very common manifestation in patients with chronic renal dysfunction with decreased renal clearance [8, 9. It is essential to determine the cases of pseudohyperkalemia to prevent the administration of unnecessary and potentially harmful therapy to patients [10,11].

Estimated glomerular filtration rate evaluate the kidney function and it has major role in monitoring the stages of kidney disease. There is no direct method for estimation of eGFR, however, the rate is measured by estimating other substances in the blood such as creatinine. Different formulas are being used for calculation of eGFR and low eGFR is considered as most important risk factor associated with hyperkalemia [12,13].

The aim of the study is to recognize and evaluate the raised potassium level so that immediate treatment can be administered for the best interest of the patients. The potential role of eGFR in differentiating between true and pseudohyperkalemia can prevent the administration of unnecessary and potentially harmful therapy to the patients.

MATERIAL AND METHODS

Cross-sectional study conducted in Chemical pathology department, Sheikh Zayed Hospital, Rahim Yar khan from January 1, 2022 to August 31, 2022.

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Non-probability consecutive sampling technique was used. Both genders between 20-70 years of age with clear serum samples and potassium >5.5mmol/L were included in study. Following subjects were excluded on the basis of history and medical record. Hemolysed specimen, thrombocytosis, leukocytosis, suspected EDTA contaminated sample, history of solid organ or bone marrow transplant, leukemia, history of multiple blood transfusion, Addison disease, Sickle cell disease, HIV. After taking ethical approval from institutional review board, informed consent was taken. A total of 101 study subjects satisfying the inclusion criteria were included and data was collected. Specimen with serum potassium with a repeat within 7 days were included and results were followed retrospectively to label them as true or pseudohyperkalemia on the basis of reference change value. eGFR cut point 90ml/min/1.73m^2 was used to differentiate the true and pseudohyperkalemia. Estimated glomerular filtration rate (eGFR) was calculated by using chronic kidney disease-Epidemiology Collaboration (CKD-EPI) creatinine equation. Weight of the patients was also taken to calculate eGFR. Serum potassium and serum creatinine were estimated on automated chemistry analyzer (Atellica CH930) based on principle of spectrophotometry and indirect potentiometry. All results were recorded on a predesigned proforma. Data was entered and analysed using SPSS 23. Shapiro Wilk Test was used to check the normality of data. Normally distributed quantitative variables were presented in terms of mean & SD while non-normally distributed quantitative variables were presented in terms of median & IQR. Qualitative variables presented in terms of frequency and percentages. Variables controlled through stratification and post-stratification, Chi square test was used for analysis of significance. P value <0.05 was taken as significant.

RESULTS

Of the total 101 patients, 59 (58.45%) were male and 42(41.6%) were females with mean age 45.28±12.265 years (Table-I). Mean serum creatinine was 4.392±2.3526mg/dl with 30(29.7%) results in ≤4.0mg/dl subgroup and 71(70.3%) results in >4.0mg/dl subgroup (Table-I). Mean serum potassium was 5.848±0.2685mmol/L while repeat serum potassium mean was 5.802±1.2635 mmol/L (Table-I). Mean eGFR calculated was 37.79±46.375 ml/min/1.73m^2 with 75 (74.3%) patients having ≤90ml/min/1.73m^2 and 26 (25.7%) patients having >90ml/min/1.73m^2 (Table-I). Of the total 101 patients, 75 (74.25%) were having true hyperkalemia and 26 (25.74%) were having pseudohyperkalemia. 28 (37.33%) patients having true hyperkalemia were between 20-40 years of age and 47 (62.66%) were between 41-70 years of age (Table-II). 21 (80.76%) patients having pseudohyperkalemia were between 20-40 years of age and 5 (19.23%) were between 41-70 years of age (Table-II). Mean age in true hyperkalemia was 48.85±11.343 years while in pseudohyperkalemia was 34.96±8.478 years (Table-II). Mean serum creatinine in true hyperkalemia was 5.664±1.0473 mg/dl while in pseudohyperkalemia was 0.723±0.1986mg/dl (Table-II). Mean serum potassium in true hyperkalemia was 5.853±0.2910 mmol/L while in pseudohyperkalemia was 5.831±0.1934 mmol/L with no statistically significant difference (*p* value: 0.714) (Table-II). Repeat serum potassium mean in true hyperkalemia was 6.476 ± 0.4893 mmol/L while in pseudohyperkalemia was 3.858 ± 0.6185 mmol/L with statistically significant difference (*p* value: 0.000). Mean eGFR in true hyperkalemia was 27.96 ± 39.211 ml/ min/ 1.73m^2 while in pseudohyperkalemia was 66.15 ± 54.083 ml/min/ 1.73m^2 with statistically significant difference (p value: 0.000) (Table-II). All patients in true hyperkalemia (n=75) were having eGFR ≤90 ml/min/1.73m^2 while all patients in pseudo-hyperkalemia (n=26) were having eGFR >90 ml/min/1.73m^2 (Table-II).

Table-I: Distribution of study subjects with respect to age, gender, serum creatinine, serum potassium, repeat serum potassium and eGFR (n=101).

Variable (mean±SD)	Sub groups	Frequency	Percentage
Age (45.28 ± 12.265) years	20-40	49	48.5%
	41-70	52	51.5%
	Total	**101**	**100%**
Gender	Male	59	58.45
	Female	42	41.6%
	Total	**101**	**100%**
Serum Creatinine (4.392 + 2.3526) mg/dl	4.0	30	29.7%
	4.0	71	70.3%
	Total	**101**	**100%**
Serum Potassium (5.848+0.2685)	<6.0	69	68.3%
	≥6.0	32	31.7%

mmol/L	Total	101	100%
Repeat Serum Potassium (5.802+1.2635) mmol/L	<6.0	31	30.7%
	≥6.0	70	69.3%
	Total	**101**	**100%**
eGFR (37.79+46.375) ml/min/1.73m2	≤90	75	74.3%
	>90	26	25.7%
	Total	**101**	**100%**

Table-II: Distribution of Age, Gender, serum creatinine, serum potassium, Repeat serum potassium and eGFR subgroups with respect to true and pseudohyperkalemia (n=101).

Variable	Subgroups	Hyperkalemia		Total	*P* value
		True hyperkalemia	Pseudohyperkameia		
Age (Years)	**20-40**	28(37.33%)	21(80.76%)	49(48.51%)	0.000
	41-70	47(62.66%)	5(19.23%)	52(51.48%)	
	Total	75(74.25%)	26(25.74%)	101(100%)	
	mean±SD	48.85±11.343	34.96±8.478		
Gender	**Male**	47(62.66%)	12(46.15%)	59(58.41%)	0.144
	Female	28(37.33%)	14(53.84%)	42(41.58%)	
	Total	75(74.25%)	26(25.74%)	101(100%)	
Serum Creatinine (mg/dl)	**≤4.0**	4(5.33%)	26(100%)	30(29.70%)	0.000
	>4.0	71((94.66%)	0(0.00%)	71(70.29%)	
	Total	75(74.25%)	26(25.74%)	101(100%)	
	mean+SD	5.664+1.0473	0.723+0.1986		
Serum Potassium (mmol/L)	**<6.0**	50(66.66%)	19(73.07%)	69(68.31%)	0.714
	≥6.0	25(33.33%)	7(26.92%)	32(31.68%)	
	Total	75(74.25%)	26(25.74%)	101(100%)	
	mean±SD	5.853±0.2910	5.831±0.1934		
Repeat serum potassium (mmol/L)	**<6.0**	5(6.66%)	26(100%)	31(30.69%)	0.000
	≥6.0	70(93.33%)	0(0.00%)	70(69.30%)	
	Total	75(74.25%)	26(25.74%)	101(100%)	
	mean±SD	6.476±0.4893	3.858±0.6185		
eGFR (ml/min/1.73m^2)	**≤90**	75(100%)	0(0.00%)	75(74.25%)	0.000
	>90	0(0.00%)	26(100%)	26(25.74%)	
	Total	75(74.25%)	26(25.74%)	101(100%)	
	mean±SD	27.96±39.211	66.15±54.083		

DISCUSSION

The study conducted to investigate the role of eGFR in differentiating between true and pseudohyperkalemia. On the basis of our study, it was observed that true hyperkalemia is more prevalent in patients with decline renal function while pseudohyperkalemia was more prevalent in patients with normal renal function. Of the total 101 patients, 75(74.25%) were having true hyperkalemia while 26 (25.74%) were having pseudohyperkalemia. Morris *et al* demonstrated in their study that of the total 60 patient samples with serum potassium ≥6.5mmol/L, 30(50%) were classified as true hyperkalemia and 30(50%) were classified as pseudohyperkalemia [14].

Of the total 101 patients, 49 (48.5%) were between 20 to 40 years of age while 52(51.5%) were between 41-70 years of age with mean age 45.28 ± 12.265 years (Table-I). Of the total 75 patients with true hyperkalemia, 28 (37.33%) were between 20-40 years of age while 47(62.66%) were between 41-70 years of age with mean age in true hyperkalemia 48.85 ± 11.343 years. While in patients with pseudo-hyperkalemia, 21(80.76%) were between 20-40 years of age while 5 (19.23%) were between 41-70 years of age with mean age in pseudohyperkalemia subgroup 34.96 ± 8.478 years. The difference of true and pseudohyperkalemia with respect to age was statistically significant (*p* value: 0.000) (Table-II) Morris *et al* demonstrated in their study that the patients with true hyperkalemia had median age 74.0 years while in patients with pseudohyperkalemia, median age was 68.0 years which shows that the patients with true hyperkalemia were older than the patients with pseudohyperkalemia [14]. Kovesdy CP *et al* demonstrated in their study that mean age was 55±16 years with average EGFR 83 ± 23 mL/min/1.73m^2 and mean baseline potassium calculated was 4.2 ± 0.4 mmol/L [15].

Of the total 101 patients, 59(58.45%) were male while 42(41.6%) were females (Table-I). Of the total 75 patients with true hyperkalemia, 47(62.66%) were male while 28(37.33%) were females (Table-II). Of the total 26 patients with pseudohyperkalemia, 12(46.15%) were male and 14(53.84%) were females (Table-II). The difference of true and pseudo-hyperkalemia with respect to gender was not statistically significant (*p* value: 0.144) (Table-II). Morris *et al* demonstrated in their study that there is

no statistical difference between true/ pseudohyperkalemia with respect to gender [14].

Of the total 101 patients, 30(29.79%) were having serum creatinine ≤4.0mg/dl while 71(70.3%) were having serum creatinine >4.0mg/dl with mean serum creatinine 4.392±2.3526mg/dl (Table-I). Of the total 75 patients with true hyperkalemia, 4(5.33%) were having serum creatinine ≤4.0mg/dl while 71((94.66%) were having serum creatinine >4.0mg/dl with mean serum creatinine 5.664 ± 1.0473 mg/dl in true hyperkalemia (Table-II). Of the total 26 patients with pseudohyperkalemia, all patients (100%) were having serum creatinine ≤4.0 mg/dl with mean serum creatinine 0.723 ± 0.1986 mg/dl in pseudohyperkalemia (Table-II). The difference of true and pseudohyperkalemia with respect to serum creatinine was statistically significant between two groups (*p* value: 0.000) (Table-II). Morris *et al* demonstrated that true hyperkalemia is not associated with normal renal function [14]. Drawz PE *et al* demonstrated in their study that kidneys play a vital role in potassium homeostasis with chronic renal dysfunction being an important risk factor for hyperkalemia. [16]Einhorn LN *et al* and Fleet JL *et al* demonstrated in their study that risk of hyperkalemia is more in patients with chronic kidney disease than in general population [17, 18].

Of the total 101 patients, 69(68.3%) were having serum potassium <6.0mmol/L while 32(31.7%) were having serum potassium ≥6.0 mmol/L with mean serum potassium 4.392 ± 2.3526mmol/L (Table-I). Of the total 75 patients with true hyperkalemia, 50 (66.66%) were having serum potassium <6.0mmol/L while 25 (33.33%) were having serum potassium ≥6.0mmol/L with mean serum potassium 5.853 ± 0.2910 mmol/L in true hyperkalemia (Table-II). Of the total 26 patients with pseudohyperkalemia, 19 (73.07%) were having serum potassium <6.0mmol/L while 7 (26.92%) were having serum potassium ≥6.0mmol/L with mean serum potassium 5.831±0.1934mmol/L in pseudohyperkalemia (Table-II). The difference of true and pseudohyperkalemia with respect to serum potassium was not statistically significant (*p* value: 0.714) (Table-II). Dewey J *et al* demonstrated in their study that mean serum potassium level in true hyperkalemia was 7.5mmol/L in the absence of hemolysis and EKG changes [1]. Of the total 101 patients, 31(30.7%) were having repeat serum potassium <6.0mmol/L while 70 (69.3%) were having ≥6.0mmol/L repeat serum potassium with mean 5.802 ± 1.2635 mmol/L (Table-I). Of the total 75 patients with true hyperkalemia, 5(6.66%) were having repeat serum potassium <6.0mmol/L while 70 (93.33%) were having repeat serum potassium ≥ 6.0mmol/L with mean repeat serum potassium 3.858 ± 0.6185 mmol/L in pseudo-hyperkalemia (Table-II). The difference of true and pseudohyperkalemia in repeat serum potassium was statistically significant (p value: 0.000) (Table-II). Of the total 101 patients, 75(74.3%) were having eGFR ≤90 ml/min/1.73m^2 while 26 (25.74%) were having eGFR >90 ml/min/1.73m^2 with mean eGFR (37.79 + 46.375) ml/min/1.73m^2. Of the total 75 patients with true hyperkalemia, all patients (100%) were having eGFR ≤90 ml/min/1.73m2 while out of total 26 patients with pseudo-hyperkalemia, all patients (100%) were having eGFR >90 ml/min/1.73m2 (Table-II).The difference between two groups with respect to eGFR was statistically significant (p value: 0.000) (Table-II). Study conducted by Morris *et al* shows the median eGFR in patients with true hyperkalemia was 33.0ml/min/1.73m2 while in patients with pseudohyperkalemia was 79.5 ml/min/1.73m^2. Morris *et al* demonstrated that at an initial potassium value of >6.5 mmol/L, the sensitivity of eGFR at 90 ml/min/1.73m2 in differentiating true and pseudohyperkalemia is 100% [14]. Coresh J *et al* and Mills KT *et al* demonstrated in their study that careful assessment of abnormal potassium level in patients with chronic renal dysfunction is important to prevent the complications due to worldwide increase prevalence of chronic kidney disease [19,20]. Grams ME *et al*, James MT *et al* and Hallan SI *et al* determined the cross sectional association of serum potassium level with renal function by categorizing the values of eGFR. The relationship of the kidney function was determined with abnormal serum potassium level with respect to age, gender, race and diabetic status [21,22,23].

CONCLUSION

True hyperkalemia is uncommon in patients with normal renal function making the eGFR a useful tool in predicting true from pseudohyperkalemia especially when K ≥ 6.4 mmol/L. Laboratories can develop strategies to identify and triage specimens with suspected pseudohyperkalemia.

CONFLICT OF INTEREST

None

AUTHOR CONTRIBUTION

Syeda Sabahat Haider: Manuscript concept, study design. Literature review, editing

Rukhsana Tumrani: Sample collection, Data analysis
Mehvish Sana and Ume Farwa: Literature review, results and review
Samreen Akhter and Rabiya Mehmood: Specimen, data collection and analysis

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