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"Alteration of electrolyte balance with severity of Chronic Kidney Disease"

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Abstract-

Introduction

Electrolytes play a vital role in maintaining homeostasis in the body. Hyperkalemia and dysnatremia occurs most often in chronic renal failure due to compromised renal water regulation. Even in end stage renal failure hyperkalemia may lead to life threatening condition. There may be some secondary mechanisms apart from reduced renal function that could contribute to hyperkalemia in patients with Chronic renal failure.

CKD patients are at additional risk of hyponatremia due to compromised capacity to dilute or concentrate urine. Furthermore, various drugs and limited nutritional solute intake can contribute to the Sodium derangements.

Thus, in this study we aim to compare the sodium potassium derangement in Chronic renal failure patients grouped on the basis of Glomerular filtration rate (GFR).

Study objectives

1. To evaluate the alteration of sodium potassium levels in Chronic Renal Failure patients.

2. Comparison of sodium potassium levels in different stages of Chronic Renal Failure patients.

Study design

Prospective Observational study

Materials and methods

This study was conducted at Shyam Shah Medical College, Rewa. Chronic Renal Failure patients were identified from the Medicine outdoor and indoor units.

Results- 86.16 % patients were hyponatremic, 2.51 % patients were hypokalemic. There was a positive correlation between e GFR and sodium and negative correlation with potassium.

Conclusion- Hyperkalemia is seen predominantly as compared to hyponatremia as CKD progresses from mild to severe form, most probably due to low numeric reference range of potassium. Attention of electrolyte levels is to be given not only in late stages of CKD, but also in early stages.

Key words- Hyperkalemia, Hypernatremia, Electrolyte imbalance, chronic kidney disease, eGFR, MDRD equation.

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Introduction

Electrolytes play a vital role in maintaining homeostasis in the body. They help to regulate heart and neurological function, fluid balance, oxygen delivery, acid–base balance. [1,2] The kidney is a principally responsible organ for retention and excretion of electrolytes and fluid in healthy individuals. [3] The GFR (Glomerular filtration rate) is one component of excretory function, but is widely accepted as the best overall index of kidney function because it is generally reduced after widespread structural damage and most other kidney functions decline in parallel with GFR in CKD.

Chronic kidney disease (CKD) is defined as the presence of kidney damage or an estimated glomerular filtration rate (eGFR) less than 60 ml/min per 1.73 square meters, persisting for 3 months or more. [4,5,6]

Hyperkalemia and dysnatremia occurs most often in chronic renal failure due to compromised renal water regulation. Even in end stage renal failure hyperkalemia may lead to life threatening condition. There may be some secondary mechanisms apart from reduced renal function that could contribute to hyperkalemia in patients with Chronic renal failure. These include high dietary intake of potassium, trans cellular shift of potassium, and drugs that inhibit renal excretion of potassium. [7,8,9]

CKD patients are at additional risk of hyponatremia due to compromised capacity to dilute or concentrate urine. Furthermore, various drugs and limited nutritional solute intake can contribute to the Sodium derangements.

Thus, in this study we aim to compare the sodium potassium derangement in Chronic renal failure patients grouped on the basis of Glomerular filtration rate (GFR).

Aim & objectives

1. To evaluate the alteration of sodium potassium levels in Chronic Renal Failure patients.

2. Comparison of sodium potassium levels in different stages of Chronic Renal Failure patients.

Study design

Cross sectional study

Materials and methods

Study design and setting

Institutional ethical approval was obtained before the commencement of study. This study was done at a tertiary care center. The study duration was from September 2021 to August 2022.

Study participants and size

The study population comprised of 300 patients diagnosed with chronic kidney disease between age group 16 to 60 years of age. Subjects suffering from liver disease, ischemic heart disease and on anti- hypertension drugs were excluded from the study. Informed written consents were taken from patients. 6ml blood was drawn by venous puncture. Serum was separated and used for the assay.

To compute the sample size, following parameters were used:

(1) a significance level (or type I error rate) [5%]

(2) power [90%]

(3) the sample size ratio of all five groups

(4) the true (allowable) difference in mean outcome parameter between groups [0%]

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(5) SD [from previous studies, it is assumed to be 10% in this study]

(6) clinically meaningful difference [a difference of 5% change of outcome is considered as the clinically meaningful difference]

$$\text{Sample size}(n) = \frac{(Z\alpha/2)^2\ p * q}{d^2}$$

Z is the confidence level (99%), *p* is the prevalence of CKD, *d* is the degree of freedom (0.05)

Data collection and variables

Demographics (age, gender, income, education, marital status, employment, income range) data was collected at the time of enrollment. Anthropometric measurements (height, weight, waist and hip circumference) of all the individuals were measured wearing light clothes without shoes and hat. Height was measured to the nearest 0.1 cm using a portable stadiometer. Weight was measured to the nearest 0.1 g using calibrated platform scales. Medical history (h/o any chronic illness, any type of medication taken, h/o any type of allergy) family history (h/o any disease in family members) h/o alcohol consumption, smoking, use of tobacco products was taken at the time of enrollment. Blood pressure was measured by mercury sphygmomanometer using standard recommended procedures.

Blood sample collection and biochemical analysis

Under aseptic precautions 6ml of blood was collected from the antecubital vein using aseptic precautions in a plain vacutainer. Serum was separated and used for the assay. BA -400 Autoanalyzer and Sensa core Electrolyte Analyzer was used for the assay. Serum was obtained through centrifugation at 3000 rpm for 5 min using centrifuge in thermostable condition. Standard operating procedures were followed in pre-analytic, analytic and post-analytic phases to maintain quality control of the laboratory analysis. The serum was assessed for urea, creatinine, uric acid, GFR and electrolytes -sodium, potassium.

Assay of electrolytes- Na^+, K^+

Serum electrolyte was analyzed based on the ion-selective electrode method. Different electrodes were used in the analyzer: pH/Na^+/Cl^-, K^+ and a reference electrode. Each electrode has an ion-selective membrane that interacts specifically with the corresponding ions contained in the sample. The procedure was started by switching on the Sensa Core ion selective electrolyte analyzer, a brief countdown began. After countdown was completed, the prompt 'Open Sample Door Introduce Sample' was displayed. The door is lifted and 100 µl of serum sample is aspirated. then sample door is closed, and the electrolyte result is displayed.

The reference interval for sodium concentration level in the blood is136–145millimole per liter (mmol/L) and those study subjects whose serum sodium concentration level below 135 mmol/L and greater than 145 mmol/L were considered to be hyponatremic and hypernatremia respectively.

The reference interval for potassium concentration levels in the blood is 3.5–5.1 mmol/L. Those study subjects whose serum potassium concentration level below 3.5 mmol/L and greater than 5.1 mmol/L was considered to be hypokalemic and hyperkalemic respectively.

Serum creatinine was assessed by modified Jaffe's kinetic method. [10] Blood urea was estimated by GLDH method.[11,12] Serum uric acid estimated by Uricase method. [13,14]

GFR analysis

In recent years, a number of new equations have been developed for use with standardized serum creatinine assays and gained worldwide acceptance for implementation into clinical practice as a "first test" for assessing GFR in

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adults. Here, we focus on the Modification of Diet in Renal Disease (MDRD) Study equations because it was developed using rigorous methods and recommended by clinical practice guidelines.

GFR was estimated using modified MDRD (modification of diet for renal disease) equation. [15-18]

GFR= 175x Sr Cr-1.154 x age-0.203 x 1.212 [if black] x 0.742 [if female]

According to KIDGO classification, chronic kidney disease is defined as abnormalities of kidney structure or function, present for >3months, with one or more criteria, albuminuria, electrolyte abnormalities or decreased GFR < 60ml/min/1.73m^2 [19]

Chronic kidney disease grading based on Glomerular filtration rate (GFR) [20]

G1	Normal or high	GFR ≥ 90
G2	Mildly decreased	GFR 60-89
G3a	Mildly to moderately decreased	GFR 45-59
G3b	Moderately to severely decreased	GFR 30-44
G4	Severely decreased	GFR 15-29
G5	Kidney failure	GFR <15

Statistical analysis and Result-

Socio-demographic

In this study, 60.66 % were males and 40 % were female subjects. 5.7% were hypertensive who were not on any anti-hypertensive drugs and 15% were smokers.

Percent of patients with low sodium levels were 86.16%

Percent of patients with high potassium levels were 2.51%

Sodium in different stages of CKD (Fig 1)

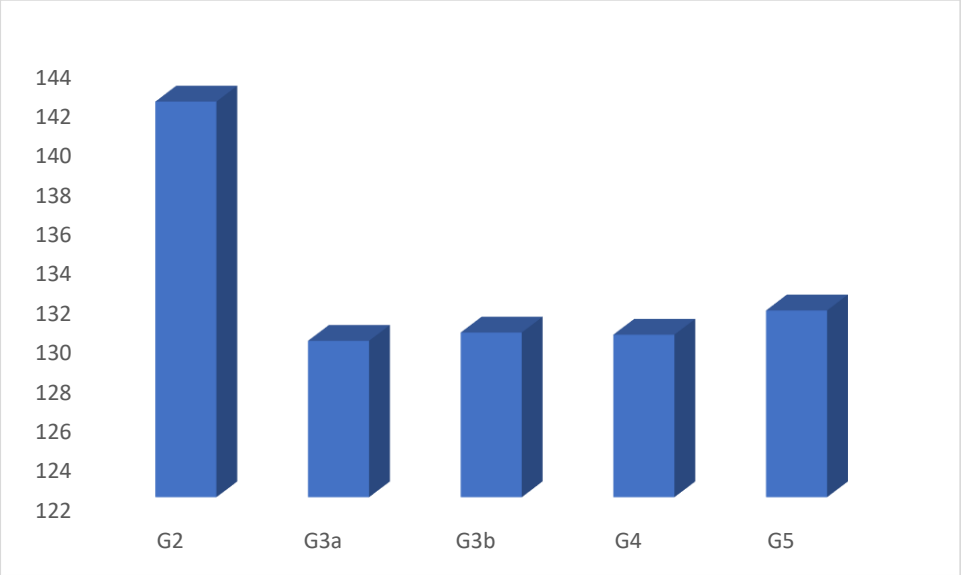

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Fig 1 Mean sodium in different stages of CKD

Mean-132.59

SD-8.012

P value-0.000013

F value-10.469

Potassium in different stages of CKD (Fig 2)

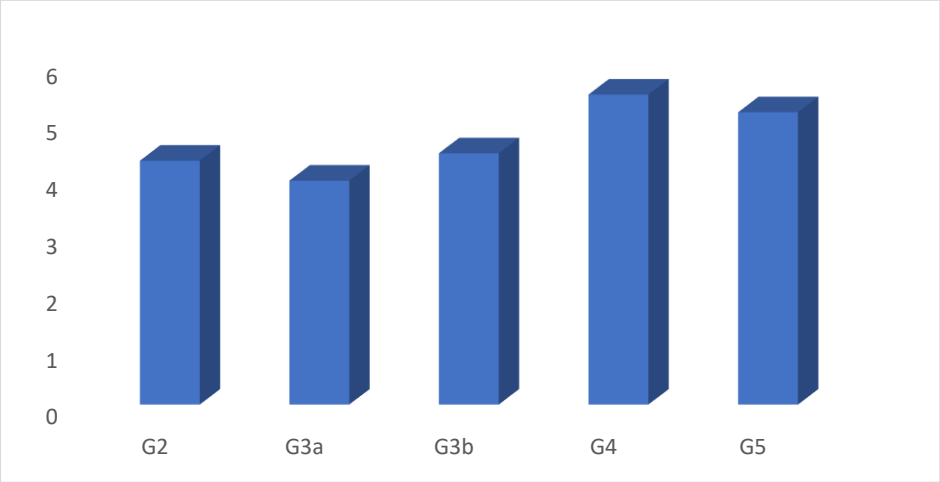

Fig 2 Mean Potassium in different stages of CKD

Mean-4.78

SD-1.087

P value-0.000

F value-8.668

Correlation between eGFR and sodium is 0.543. The scatter plot shows a strong, positive association between serum sodium and e GFR. There don't appear to be any outliers in the data. (P= 0.000) **(Fig 3)**

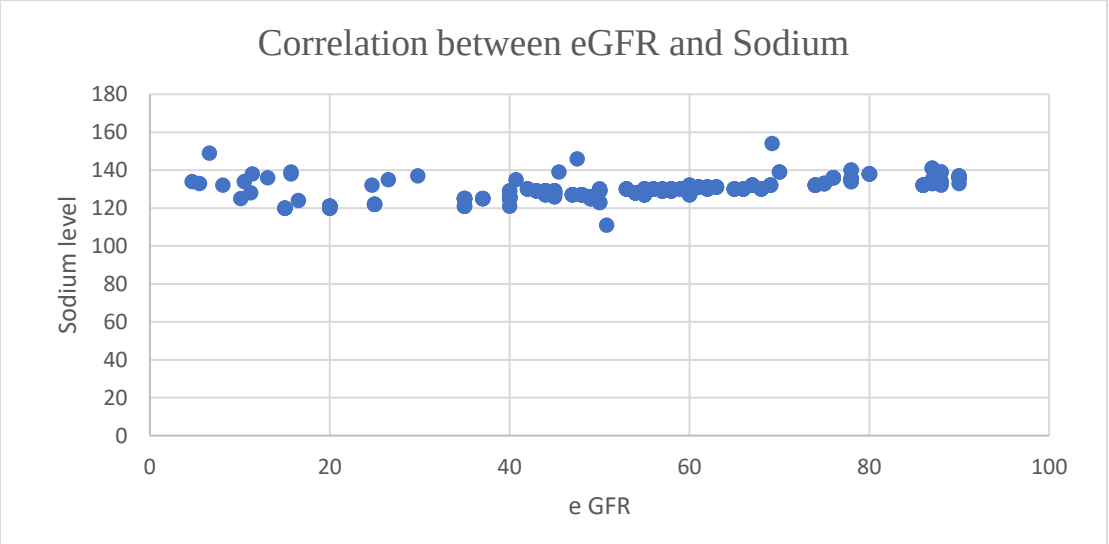

Fig 3 Correlation between eGFR and Sodium level

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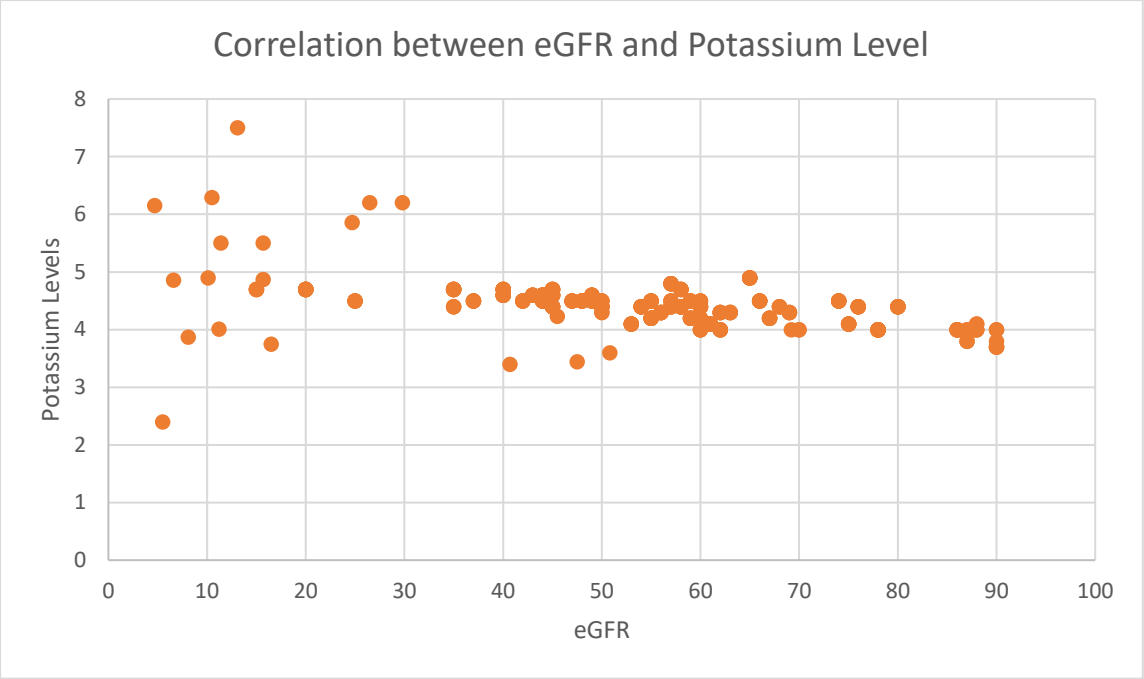

Fig 4 Correlation between eGFR and Potassium level

Correlation between eGFR and potassium is -0.516. The scatter plot shows a strong, negative association between serum potassium and e GFR. There don't appear to be any outliers in the data. (P= 0.000) **(Fig 4)**

Discussion- Chronic kidney disease results from various etiologies and lead to gradual loss of kidney function. Kidneys remove waste material and extra fluid from our body. It also maintains healthy balance of water and other electrolytes in body. So, in CKD electrolyte imbalance is built up and variates according to stages.

Once patient is diagnosed with CKD main aim becomes to slow down its effects as kidney damage is irreversible. In this study, we have evaluated the serum sodium and potassium levels in CKD patients and compared them with their GFR levels. At different levels of GFR, which also indicates stages of chronic kidney disease, serum sodium and potassium levels have positive and negative correlation respectively. The clearance concept was important not only to study formation of urine or kidney physiology but it also provided simple tool to measure glomerular filtration rate in the form of creatinine. Later, various equations were developed to measure eGFR. Of those, we have used MDRD equation for calculation of eGFR in this study. The inclusion of the automatic calculation of GFR in the laboratory on the basis of creatinine constitutes a useful tool for daily practice in clinical laboratory.

Serum sodium represents water balance and is the primary determinant of serum osmolality. Changes in serum osmolality drive fluid in and out of cells and affect cell volume and function. In this study, 86.16 % of CKD patients were having hyponatremia (Na <135 m Eq/L). This may be due to volume overload, increase in extra cellular fluid volume or diuretic usage. Fig 1 shows mean sodium levels in different stages of CKD. [21]

In CKD the kidney function to dilute or concentrate urine is compromised. In mild hyponatremia, body shows no symptoms. When it becomes severe, body starts showing symptoms. In this study, hyponatremia is positively correlated with values of e GFR (Fig No 3). Salt and water retention plays important role in development of hypertension in chronic kidney disease. Reduced GFR in CKD causes disorder in water homeostasis.

Hyperkalemia is mostly seen in CKD patients and in this study also percent of patients with high potassium levels were 51.1% and statistical analysis showed a strong, negative association between serum potassium and e GFR (Fig No 4). Hyperkalemia manifests clinically as muscle weakness, paralysis, cardiac arrhythmias. CKD is often associated with diabetes mellitus, hypertension, heart disease. Drugs used for such treatment also contribute to increased potassium levels by inhibition of Na K ATPase.

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The values of GFR are numerically high, hence has more error tolerance as compared to serum creatinine. [22] Similarly, sodium (135-145 m Eq/L) has high numeric reference range when compared to potassium (3.5-5mEq/L). This might be a cause why potassium variation is seen significantly as compared to sodium at low GFR values.

The significance of the risk score of abnormal electrolytes in predicting the prognosis of the patient is very high.

Conclusion- Electrolyte imbalance is undoubtedly present in chronic kidney disease and degrades as glomerular filtration rate decreases. Hyperkalemia is seen predominantly as compared to hyponatremia as CKD progresses from mild to severe form, most probably due to low numeric reference range of potassium. Attention of electrolyte levels is to be given not only in late stages of CKD, but also in early stages.

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Conflict of interest- The authors declare that there is no conflict of interest.

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