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Original Article

Impacts of Diuretic Use in Pre-Dialysis Chronic Kidney Disease Patient in a Tertiary Care Hospital

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ABSTRACT

Background: CKD is a global health concern with an estimated prevalence of 13.4%. Blood pressure can be a cause or consequence of CKD. In patients with Chronic Kidney Disease (CKD), hypertension is a common illness that contributes to the progressive loss of renal function towards end stage renal disease as well as cardiovascular events including heart attacks and stroke. Salt and water retention are caused by decreased kidney function, which finally causes volume expansion and elevated blood pressure. Diuretics therapy has been a cornerstone of care for CKD patients, especially for fluid excess and hypertension. In addition to their beneficial effects, diuretic usage is linked to negative renal outcomes. **Objectives:** The main aim of the study was to evaluate the association between diuretic use in Chronic Kidney Disease (CKD) progression and onset of end stage renal disease. **Materials and Methods:** A prospective observational study was conducted for 6 months among 107 patients of either sex those who underwent treatment for the pre dialysis chronic kidney diseases were included in the study. All the data were collected, documented and analysed based on standard protocol. Data collected were entered into Microsoft Excel. Statistical analysis was done by using Microsoft Excel. **Results and Discussion:** Out of 107 populations diagnosed with kidney disease, the study contains 71% males and 28% females. In this study kidney disease were seen commonly among age group of 27 to 91 years, showing that males were predominant for the development of chronic kidney disease. Commonly prescribed diuretics are Torsemide (100%), Furosemide (8.4%), and Aldactone (10.3%), Metolazone (37.4%). Torsemide is the drug that is most frequently prescribed. There is high burden of CKD among patients with type 2 DM and Hypertension. Majority of the patient have fluid overload and pulmonary oedema. There is a statistically significant reduction in weight and BMI in those patients who are on diuretics. The use of diuretics has not associated with any worsening of the renal function. Rather there was an improvement in the eGFR in those patients who was started on diuretics and whose fluid overload status was brought down to euvolemic status. The most widely used medications are beta blockers such Bisoprolol, Metoprolol, Carvedilol, and Nebivolol. The use of diuretics, including thiazide and loop diuretics, is not related with deteriorating eGFR; nevertheless, beta blockers have shown an improvement in eGFR that is statistically significant, pointing to a renoprotective impact. Since most of our patients were on metoprolol, we believe that metoprolol has a renoprotective effect on CKD patient but metoprolol in isolation has failed to improve eGFR. The beta blockers class themselves when analyzed against eGFR shows statistically improvement effect. **Conclusion:** The diuretics has not worsened eGFR but rather improvement was noted in the eGFR of patients who were on diuretics. Therefore, this study suggests diuretics does not have any deteriorating effect on the renal function but may contribute to improvement of eGFR if used. In our study, commonly prescribed medications did not impair eGFR function or impair renal function. Beta blockers, however, exhibit a renoprotective effect. Other drugs have failed in statistical terms to prove the renoprotective effect. Since most of our patients were on metoprolol, we believe that metoprolol has a renoprotective effect on CKD patients. But metoprolol in isolation has failed to improve eGFR. The beta blocker class themselves when analyzed against eGFR shows statistically improvement effect.

Keywords: Chronic kidney disease, Diuretics, eGFR, Renoprotective, Beta blockers.

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INTRODUCTION

Chronic kidney disease refers to kidney structural and functional abnormalities that develop over months or years, impacting overall health. It is recognized as a significant global public health concern. The estimated worldwide prevalence of chronic kidney disease is 13.4% (ranging from 11.7% to 15.1%), with approximately 4.902 to 7.083 million patients requiring renal replacement therapy due to End-Stage Kidney Disease (ESKD).[1] The primary causes of chronic kidney disease include Type1 or Type2 diabetes, high blood pressure, glomerulonephritis, inherited diseases, kidney and urinary tract abnormalities present from birth, autoimmune diseases like systemic lupus erythematosus, polycystic kidney disease, vesicoureteral reflux, and others.[2]

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Diuretics are medications that promote the excretion of water and salt from the body by increasing urine output. They are commonly used to treat a variety of medical conditions, including hypertension, edema, and heart failure. Diuretics act on the kidneys, which play a crucial role in maintaining fluid and electrolyte balance in the body.[3]

It is important to note that diuretics should be used cautiously in CKD patients with electrolyte imbalances, low blood pressure, and impaired kidney function. The dose and frequency of diuretics may need to be adjusted based on the patient's kidney function and response to treatment. Regular monitoring of kidney function, electrolytes, blood pressure, and fluid status is crucial in CKD patients receiving diuretic therapy.[4]

In general, diuretics are effective in managing fluid overload and blood pressure in predialysis CKD patients. This can lead to an improvement in symptoms like edema, shortness of breath, and fatigue. Additionally, diuretics may aid in slowing down the progression of CKD by reducing the workload on the kidneys and decreasing interstitial fibrosis.[5]

While diuretics are generally considered safe and effective, they can have negative effects on kidney function in certain patients. Chronic use of diuretics may result in electrolyte imbalances, especially hypokalemia (low potassium levels), which can cause muscle weakness, cramping, and cardiac arrhythmias. Furthermore, diuretics can decrease blood flow to the kidneys and impair renal function in individuals with pre-existing kidney disease.[6]

Therefore, the administration of diuretics to predialysis CKD patients should be carefully assessed and monitored by a healthcare professional. The benefits and risks of using diuretics should be carefully evaluated based on the patient's specific characteristics and clinical outcomes. Proper dosing and close monitoring of electrolyte levels can help minimize the risk of adverse effects and ensure the best possible therapeutic results.[7]

MATERIALS AND METHODS

This is a prospective observational study conducted at a tertiary-level Multi speciality Hospital, Kannur, Kerala, after the approval of the institutional ethical committee. The study was conducted in the Department of Nephrology.

Study criteria

The Patients above 18 years of age with chronic kidney disease of either gender, patients undergoing treatment for the long term, patients with co-morbidities and outpatients are included for the study. The pregnant and lactating women and patients who are already on diuretics are excluded and the study duration was six months.

Methodology

All chronic kidney disease patients who visited the nephrology department, initiated on diuretics, and not undergoing dialysis were included in this study. Detailed information about the study was provided to the patients, and informed consent for their participation was obtained. A designed Performa was used to collect data, including patient demographics, socioeconomics, lifestyle, medications, and lab parameters. The information was gathered from electronic medical records and direct patient interviews.[8,9]

The patients enrolled in the study were followed for 6 months, during which variations in lab parameters and clinical data were recorded. Those who did not complete the 6-month follow-up were excluded from the study analysis.[10]

Clinical and laboratory data were collected and entered into a standard Excel sheet format. The data was analysed using SPSS software version 21. Descriptive statistics were used for continuous or numerical variables such as age (presented as mean and standard deviation), and categorical variables like gender were represented in frequencies and percentages. Inferential statistics, such as the chi-square test, were used to determine associations between categorical variables. Fisher's exact test was employed when more than 20% of the cell values had an expected cell value of less than 5. The significance of differences between means was assessed using the Paired' *t*-test. A *p*-value of less than 0.05 was considered statistically significant.[11,12]

Ethical considerations

Informed consent was obtained from all patients, and their confidentiality was maintained throughout the study. Data collection began only after obtaining clearance from the Ethics Committee. The study received approval from the Institutional Human Ethical Committee under Ref No. 004/2022/CCOPS/IEC. The permission to conduct the study was obtained from the chairperson of the Institutional Human Ethical Committee.

RESULTS

A prospective observational study was conducted for a period of 6 months in the Department of Nephrology in a Tertiary Care Hospital, Kannur. A total of 107 patients satisfying the inclusion criteria were included in the study.

Characteristics of sample

Out of 107 patients, the age range of the sample population was found to be between 21 to 91 years. Of these, 76 (71.03%) were male, and 31 (28.97%) were female. Thus, chronic kidney disease was more prevalent among males than females. The most commonly observed comorbidities among the subjects were as follows: 90 (84.1%) had hypertension, 73 (68.2%) had diabetes mellitus, 25 (23.4%) had dyslipidemia, 6 (5.6%) had

cerebrovascular accident (CVA), 30 (28%) had coronary artery disease, 10 (9.3%) had Chronic Obstructive Pulmonary Disease (COPD), and 2 (1.9%) had cancer (Table 1). The mean weight and BMI at baseline and after 6 months are depicted in Table 2.

Serum electrolytes

The mean difference between baseline and after 6 months of serum electrolytes like Sodium, chloride, calcium, magnesium, and phosphorous shows that it's statistically significant (Table 3).

Different types of diuretics used in CKD

Commonly prescribed diuretics are Torsemide (100%), Furosemide (8.4%), and Aldactone (10.3%), Metolazone (37.4%). Torsemide is the drug that is most frequently prescribed. The other common drugs in CKD patients are summarized in Table 4.

eGFR changes

Among the subjects, 72 (67.29%) had Improved eGFR and 35 (32.71%) had Worsened eGFR after 06 months period of study.

Table 1: Baseline information.

Variable	All Patients (*n*=107)
General condition	
Age (years, median)	67
Male (%)	71%
Female (%)	29%
BMI (mean)	27.76
Weight (mean)	69.15
Comorbidities	
Hypertension	90
Diabetes	73
COPD	10
CAD	30
CVA	6
Dyslipidaemia	25
Cancer	2
Addictions (%)	
Smoker	11.21%
Alcohol	4.67%
Pan chewing	2.80%

eGFR Changes with drugs

eGFR was worsened in 44.8% of the subjects with Beta Blockers which is lower compared to 55.2% among those with improved eGFR and the difference was statistically significant. But other drugs failed to prove statistical significance (Table 5).

DISCUSSION

Among the 107 patients, 31 (28.97%) were female, and 76 (71.03%) were male, indicating a male predominance for the development of chronic kidney disease. Compared to women, men had a higher rate of all-cause and cardiovascular mortality, an increased risk of CKD progression, and a steeper decline in eGFR. This result aligns with the study by Oskar Swartlings *et al.*[13]

The majority of the patients (age group 21-91 years) in our study may be due to the incidence of CKD increasing with advancing age. The probability of CKD regression and mortality exceeded the risk of progression or kidney failure. Similar results were obtained in studies conducted by Ping Liu *et al.*[14]

In our study, 90 (84.1%) patients had hypertension, and 73 (68.2%) had diabetes mellitus. CKD burden was high among patients with type 2 diabetes mellitus and hypertension. Increasing age, systolic blood pressure, low educational status, and longer duration of hypertension were significantly associated with CKD. This result is consistent with the study by Elliot K, Tanner MD *et al.*[15]

The majority of patients (19.63%) had fluid overload, and 16.82% had pulmonary edema. A statistically significant (Paired't' test: *p*-value less than 0.05) reduction in weight and BMI was observed in patients taking diuretics. This was due to the initial BMI recorded during fluid overload, and once the diuretic optimized the fluid status, the patients' BMI improved, indicating a favorable effect on CKD over the long term. The use of diuretics effectively reduced weight by eliminating excess fluid. A similar study was conducted by Yi-Chun Tsai *et al.*[16]

The use of diuretics resulted in a reduction in pulse rate, possibly due to reduced cardiac overload and concurrent use of beta-blockers. However, there was no statistically significant impact on systolic and diastolic blood pressure with diuretic use for fluid overload conditions. This result is consistent with the study by Rina Oba *et al.*[17]

Table 2: Anthropometry.

	Group	N	Mean	S.D.	Mean Diff.	Paired 't' test *p* value
Weight	Baseline	107	69.15	11.77	2.00	0.001
	After 6 months	107	67.16	11.67		
BMI	Baseline	107	27.76	5.15	0.79	0.001
	After 6 months	107	26.97	5.10		

Table 3: Serum electrolytes comparison baseline and after 6 months.

	Group	N	Mean	S.D.	Mean Diff.	Paired '*t*' test *p* value
Sodium	Baseline	107	136.52	3.98	-2.14	0.000
	After 6 months	107	138.66	4.79		
Chloride	Baseline	107	102.97	6.34	-1.92	0.008
	After 6 months	107	104.89	5.70		
Potassium	Baseline	107	4.50	0.65	-0.09	0.147
	After 6 months	107	4.60	0.72		
Calcium	Baseline	107	8.17	1.04	-0.29	0.000
	After 6 months	107	8.46	0.94		
Magnesium	Baseline	107	1.73	0.29	-0.18	0.000
	After 6 months	107	1.91	0.34		
Phosphorus	Baseline	107	5.18	1.40	-0.27	0.003
	After 6 months	107	5.46	1.15		
Random Blood Sugar	Baseline	107	174.72	76.66	7.06	0.328
	After 6 months	107	167.66	90.70		

Table 4: Other drugs used in CKD patients.

Drugs	Frequency	Percentage
Beta-blockers		
Bisoprolol	12	11.21%
Metoprolol	16	14.95%
Carvedilol	5	4.67%
Nebivolol	4	3.74%
Calcium channel blockers		
Nifedipine	7	6.54%
Amlodipine	6	5.61%
Azelnidipine	4	3.74%
Benidipine	1	0.93%
Cilnidipine	59	55.14%
Oral anti hypoglycemics		
Sulfonyl Ureas	36	33.64%
Diamicron	29	27.10%
Glimepiride	9	8.41%
Gliptines	26	24.30%
Vildagliptin	1	0.93%
Linagliptin	26	24.30%
Metformin	2	1.87%
Insulin		
Insulin Aspart	3	2.80%
Lantus Catridge	5	4.67%
Mixtard	27	25.23%
Human Actrapid	13	12.15%

Our study statistically proved that the effect of dyselectrolytemia due to diuretics at 6 months is not significant. There was no major hyponatremia, hypochloremia, hypocalcemia, or hypophosphatemia noted in our calculations, even after 6 months of continued diuretic therapy. Therefore, when diuretic therapy is administered under supervision, the effect of dyselectrolytemia at 6 months is negligible. Our study has statistically proved that the hyponatremia, hypochloremia, hypocalcemia, and hypophosphatemia are negligible in patients who are under supervised administration of diuretics.

Metformin use did not result in worsening of eGFR in any patient, even though metformin is not recommended in low eGFR settings. This is because we did not use metformin in cases of advanced renal failure; it was used or continued only in patients with eGFR above 45. Our study suggests that metformin, when used in high eGFR stages, has no detrimental effect on renal function. This result is consistent with the study by De Broe M.E *et al.*[18]

Among the subjects, all 107 (100%) had diuretics, 47 (43.9%) had multiple diuretics, 107 (100%) had Torsemide, 9 (8.4%) had Furosemide, 11 (10.3%) had Aldactone, and 40 (37.4%) had Metolazone. Torsemide was commonly given to hospitalized patients. The use of diuretics was not associated with any worsening of renal function. On the contrary, there was a statistically significant improvement in eGFR in patients who started diuretics and achieved a euvolemic state. Diuretics did not worsen eGFR; rather, statistically significant improvement was noted in the eGFR of patients who were on diuretics (Table 6). Therefore, diuretics do not have any detrimental effect on renal function but may contribute to an improvement in eGFR if used statistically (Chi sq. test: *p*-value less than 0.05).

Table 5: Diuretics.

Diuretics	Frequency	Percent
Diuretics	107	100.00%
Multiple Diuretics	47	43.93%
Torsemide	107	100.00%
Furosemide	9	8.41%
Aldactone	11	10.28%
Metalazone	40	37.38%

Table 6: eGFR Change.

eGFR change	Frequency	Percent
Worsened	35	32.71
Improved	72	67.29
Total	107	100.00

Table 7: eGFR Changes with drugs.

Drugs	eGFR change		Chi sq. p-value	Odds ratio
	Worsened	Improved		
Multiple Diuretics	16 (34%)	31 (66%)	0.159	1.11 (0.49-2.51)
Beta Blockers	13 (44.8%)	16 (55.2%)	0.050	2.07 (0.86-5)
CCB	22 (32.4%)	46 (67.6%)	0.168	0.96 (0.41-2.21)
Sulfonyl Ureas	13 (36.1%)	23 (63.9%)	0.148	1.26 (0.54-2.93)
Insulin	16 (37.2%)	27 (62.8%)	0.119	1.4 (0.62-3.18)
Metformin	0 (0%)	2 (100%)	0.451	0.05 (0.02-11.39)
Prazosin	3 (33.3%)	6 (66.7%)	0.285	1.03 (0.24-4.39)
Telmisartan	2 (16.7%)	10 (83.3%)	0.129	0.38 (0.08-1.82)
Hydralazine	2 (28.6%)	5 (71.4%)	0.319	0.81 (0.15-4.41)
Clonidine	7 (46.7%)	8 (53.3%)	0.107	2 (0.66-6.05)

Among the subjects, 29 (27.1%) had beta-blockers, 12 (11.2%) had Bisoprolol, 16 (15%) had Metoprolol, 5 (4.7%) had Carvedilol, and 4 (3.7%) had Nebivolol. The drugs showed a favorable response on eGFR. The use of diuretics, whether thiazide or loop diuretics, was not associated with worsening eGFR, but beta-blockers demonstrated a statistically significant improvement in eGFR, suggesting a renoprotective effect. Since most of our patients were on metoprolol, we believe that metoprolol has a renoprotective effect on CKD patients, but metoprolol in isolation failed to show statistical significance. The beta-blocker class as a whole, when analyzed against eGFR improvement, showed statistical significance (Chi sq. test: *p*-value less than 0.05) (Table 7). This is similar to the study conducted by Peter D Hart *et al.*[19]

CONCLUSION

Out of the 107 individuals diagnosed with kidney disease in this study, 71% were male and 28% were female. The study revealed that kidney disease was most commonly observed among individuals aged 27 to 91 years, indicating a male predominance in the development of chronic kidney disease.

The most commonly prescribed diuretics were Torsemide (100%), Furosemide (8.4%), Aldactone (10.3%), and Metolazone (37.4%). Torsemide was the drug most frequently prescribed.

Patients taking diuretics experienced a statistically significant decrease in weight and BMI, primarily due to the reduction of excess fluid. This demonstrates a positive effect on CKD over an extended period. Additionally, the use of diuretics led to a reduction in pulse rate, which may be attributed to concurrent use of beta-blockers along with diuretics.

The use of diuretics did not lead to a decline in renal function; instead, patients who initiated diuretic therapy and achieved a euvolemic state experienced improvements in their eGFR.

At 6 months, there was no significant effect on dyselectrolytemia due to diuretic use. No significant hyponatremia, hypochloremia, hypocalcemia, or hypophosphatemia were observed in our study even after 6 months of sustained diuretic therapy.

Metformin use did not result in worsening of eGFR in any of the patients, despite the fact that metformin is not recommended in low eGFR settings.

Our study demonstrated that diuretics did not worsen eGFR; in fact, it was associated with an improvement in the eGFR of patients who were on diuretics. Therefore, this study suggests that diuretics do not have any detrimental effect on renal function but may contribute to the improvement of eGFR if used.

In our study, commonly prescribed medications did not impair eGFR or renal function. However, beta-blockers exhibited a renoprotective effect. Other drugs did not show a statistically significant renoprotective effect. Given that most of our patients were on metoprolol, we believe that metoprolol has a renoprotective effect on CKD patients. However, metoprolol in isolation failed to improve eGFR. When analyzed against eGFR, the beta blocker class as a whole showed statistically significant improvement.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

CKD: Chronic kidney disease; **ESKD:** End-stage kidney disease; **GFR:** Glomerular filtration rate; **eGFR:** Estimated Glomerular Filtration Rate; **KDIGO:** Kidney disease improving global outcome; **RRT:** Renal replacement therapy; **CHF:** Congestive heart failure; **BMI:** Body mass index; **CVA:** Cerebrovascular accident**; COPD:** Chronic obstructive pulmonary disease; **HTN:** Hypertension; **BP:** Blood pressure; **CCB:** Calcium channel blocker.

SUMMARY

The study findings indicate that diuretics did not exacerbate the decline in estimated glomerular filtration rate (eGFR). On the contrary, individuals taking diuretics showed an enhancement in eGFR. This suggests that diuretics may not adversely affect renal function and could potentially contribute to an improvement in eGFR when used.

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