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## Assessment Of Chronic Kidney Disease Patients Treatment Pattern In A Tertiary Care Teaching Hospital.

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### ABSTRACT

CKD (chronic kidney failure) is described as the gradual loss of kidney function. Based on e-GFR, CKD failure is classified under 5 stages. Hence Pharmacist can contribute in the management and rational drug usage management by providing general awareness to the clinicians regarding the importance of dose adjustment and usage in CKD patients Assessment of CKD patient's treatment pattern. This is a retrospective, prospective, & observational study conducted in CKD patients over a period of 6 months. The relevant information were collected in a structured data collection form and data were analyzed by using descriptive statistics. A total of 125 patients cases have been analyzed. The age group was between 21-90 years, 69.6% were males and 30.4% were females; mean [Standard deviation(SD)] urea level was 107.14mg/dL, mean (SD) creatinine level was 5.51 mg/dL; 58.4% were in stage 5. The most commonly seen co-morbidities were HTN, followed by T<sub>2</sub>DM, ANEMIA, IHD. The most commonly prescribed drugs were antihypertensive (183), diuretics (121), anti-ulcers (98) and antibiotics (97). 64 drug interactions were found and 20 dose adjustments were intervened. This study clearly showed that there were significant medication related problems such as drug interactions, dose adjustment requirements and presence of more than 1 of co-morbidities were observed. This study also focused that the Pharmacist contributions become importance in promotion of rational use of drugs.

**Keywords:** chronic kidney disease (CKD), hypertension (HTN), Diabetes mellitus(DM), GFR: Glomerular filtration rate

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## INTRODUCTION

Chronic kidney disease is one of the most common public health problem occurring worldwide.[1] CKD clinical practice guidelines (2012) defined as “abnormalities of kidney structure or function present for >3 months”. Even in the developing countries CKD has been the major cause of morbidity and mortality which was considered as a health problem and in India and the burden of CKD cannot be estimated precisely. Based on eGFR CKD is classified into 5 stages 1.Stage 1,eGFR  $\geq 90$ ml/min/1.73m<sup>2</sup> 2. Stage 2,eGFR 60-89 ml/min/1.73m<sup>2</sup> 3. Stage 3,eGFR 30-59ml/min/1.73m<sup>2</sup> 4. Stage 4,eGFR 15-29ml/min/1.73m<sup>2</sup> 5. Stage 5,eGFR <15 ml/min/1.73m<sup>2</sup>. [2,3]

CKD in 3-4 Stage is considered as the optimal stage for consultation and limitations for the available diagnostic test. CKD undiagnosed and treated insufficiently leads an opportunities for further worsening . [4,5,6] High rates of morbidity, hospitalization mortality are most common among CKD patients. Progression of CKD to ESRD increase the financial burden for further renal transplantation and increase the risk factor and in both developed and developing countries. The incidence of ESRD is 150-200 population per million and of CKD is 800 per million population approximately. [3]

The rate of progression of CKD varies depending on etiology and pathophysiology of disease. As the age progression above 40 years the reduction in renal flow mass and glomerular sclerosis can be commonly observed (eGFR may fall by about 0.75 ml/min/1.73m<sup>2</sup> per year). The majority of the patient's ages above 60 were in the CKD category. Therefore difficulty to differentiate age related loss of kidney function and renal disease. Patient above and below 65 years with 45-59 eGFR almost show identical risk for ESRD. Hence the laboratory tests support early detection of CKD. [5]

CKD Assessment is mainly carried out based on repeated sample of serum creatinine within 2-3 months to be sure of renal disease chronicity. Appropriate interpretation and markers and stages of CKD are essential for optimal management. [2,3]

Co-morbidities are common for CKD patients. Patients over the age of 65 years, four to five Co-morbidities are common in 64% of the patients. The Co-morbidities include higher tension diabetes, Hypertension, cardiovascular disease, infections etc. Individuals with Co-morbidities, elderly and family history of renal disease increased the risk of developing CKD. and needs greater health care. So the co- morbidities should be strictly considered in the disease management. [5,7,8]

Evidence shows that cardiovascular disease, kidney failure, premature death is the serious outcome of the CKD . Progressive kidney damage leads to end stage renal disease. The improved clinical care from early stage first to third stage CKD may reduce risk for progression towards ESRD. To survive ESRD patients require kidney transplantation and dialysis [5]

Hence it is important to study the prescribed trend in CKD patients as they take drug for life long and it should be studied on a regular basis, traditionally the health programs for CKD mainly focus on the management of hypertension, diabetes and cardiovascular disease. DM is considered as one of the major cause of ESRD next to that of renal vascular disease including hypertension. [6,8]

Strict BP control may reduce the relative risk of death in CKD . A blood pressure goal should be at least less than 140/90mmHg in CKD and a target of 130/80 mmHg in patient with proteinuria. [9,10]

Hence, the current study was planned to evaluate the drug use pattern among CKD patients with the objective, 1.To understand the incidence of comorbidities in the patients, 2 To know the drug drug interactions and its management 3. To helps in contributing the rational promotion of drugs by creating general awareness to the clinicians regarding the need/ importance of dose adjustment and to find out the cost of the commonly used drugs.

## METHODOLOGY

A Retrospective (2016-2017) & Prospective study”( 2017-2018) observational study was conducted in Adichunchanagiri Hospital and Research Centre, from October 2017 to march 2018 .The Institutional Ethics

Committee approval was obtained before carrying out of this study(NO.AIMS/IEC/1633/2017-18). The inclusion criteria include 1.Patients with CKD admitted to medicine department 2. Dialysis patients i.e., both outpatients and inpatients. The exclusion criterion includes pediatric patients and who are not willing to participate in the study (Prospective cases only).

The consented patients details were collected in data collection form, which consist of demographic details along with patient medication chart, interaction chart with its severity, presence of co morbidities and other necessary details. The obtained data was subjected to descriptive statistics.

### RESULTS

Out of 50 prospective cases, majority of the patients were under the age group of 61-70(30 %) followed by 41-50& 51-60 were (22%)21-30 &71-80 were (8%) 31-40 were (6%) 81-90 were (2%) in which the females were 24% , rest were male patients. The BMI showed 72 % were normal, whereas 28 % were overweight patients. 44 were non-alcoholic (88%) and rest 6 were alcoholic (12%).16% account for smokers and rest 84% were non –smokers . Out of 50 patients studied ,29 patients belong to stage 5 CKD (58%),13 belongs to stage 4 CKD(26%),7 belongs to stage 3 CKD (14%) and remaining 1 to stage 2 CKD(2%).

In the 75 retrospective cases majority were at the age of 51-60 years (26.6%), followed by 41-50(24%) , 61-70(22.6%) and 71-80(16%) years, 31-40 years(5.3%) ,21-30 years & least were 1- 10 years. 49 (65.33)were males and 26 were female patients. 89% does not have any alcohol habits and 82.6% were non-smokers. More than 2 co-morbidities out of which HTN, T2DM, were predominantly seen both in prospective cases & retrospective (6 %; 2% .16%; 14.7%). (figure1 & figure2) . The mean Number of days stayed in the hospital of prospective and retrospective cases was 5.2+2.01; 5.32+2.27.

Figure 1 Distribution of co-morbidities (prospective)

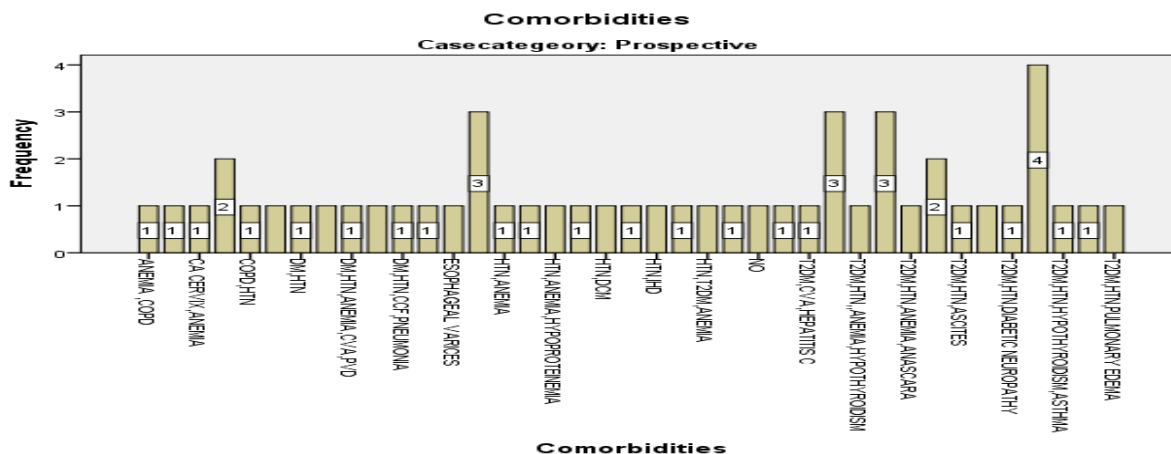
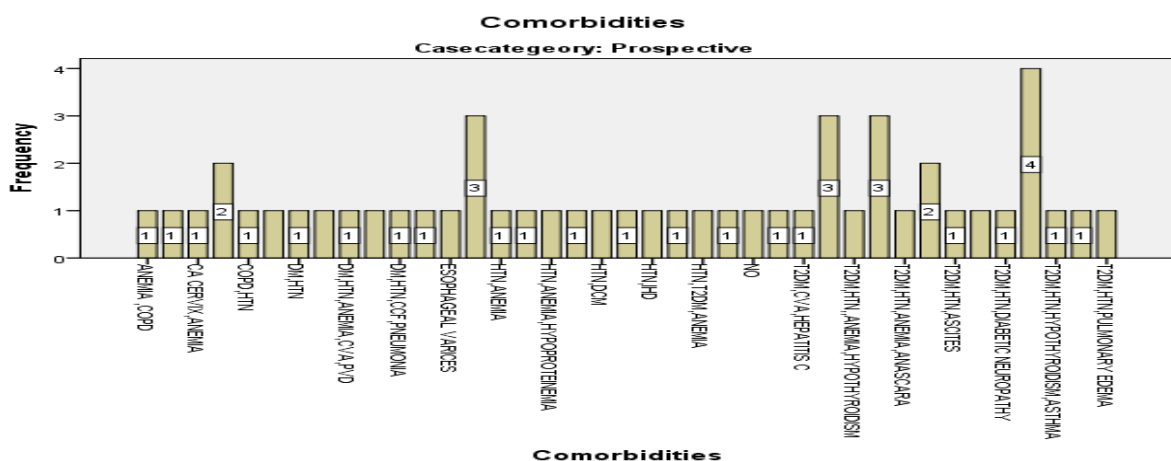


Figure 2 : Distribution of co-morbidities (Retrospective)



The major co –morbidity are summarized in figure 1 & 2. Two to three co-morbidity were most commonly found in patients, out of which HTN,T<sub>2</sub>DM, Anemia ,IHD account for the largest part, other co-morbidity like Asthma, COPD, Hypothyroidism, Infections were in the next category. In the prospective cases, the mean urea and serum creatinine value are 102.84±50.46; 5.21±3.00. In the retrospective cases the Mean BP in systolic is 151.48 ± 41.45. The mean BP Diastolic is 88.12 ± 18.68

In the retrospective cases, the mean urea and serum creatinine value is 111.44±56.58; 5.81±3.81 respectively. The Mean systolic BP is 154.88±37.59. The mean Diastolic BP is 90.30 ±17.20

The drugs most frequently prescribed drugs are summarized in table 1. The most commonly prescribed drugs were anti- hypertensive (183), diuretics (121), anti-ulcers (98) and antibiotics (97) followed by anti emetics, anti-platelets, vitamin & iron supplements, anti diabetes, corticosteroids. Renal protectants (33) like renosave (n-acetyl cysteine) were also prescribed.

**Table 1 : Distribution of drugs among CKD patients prospective and retrospective cases.**

S.no	Type of drug	Prospective N (%)	Retrospective N(%)
1.	Cefoperazone	11	30
2.	Levofloxacin	3(6)	5(6.7)
3.	Meropenam	3(6)	0
4.	Azithromycin	2(4)	7(9.3)
5.	Moxifloxacin	1(2)	1(1.3)
6.	Vancomycin	1(2)	1(1.3)
7.	cefotaxime	1(2)	4(5.3)
8.	Amoxicillin+clavulanic acid	5(10)	5(6.7)
9.	Piperacillin+tazobactam	6(12)	12(16)
10.	Carvedilol	5(10)	5(6.66)
11.	Metoprolol	9(18)	11(14.6)
12.	Labetalol	2(4)	4(5.3)
13.	Cilnidipine	24(48)	37(49.3)
14.	Nifedipine	3(6)	5(6.66)
15.	Amlodipine	6(12)	12(16)
16.	Clonidine	10(20)	21(28)
17.	Prazosin	9(18)	19(25.3)
18.	Ramipril	1(2)	0
19.	Furosemide	35(70)	47(62.6)
20.	Torseamide	11(22)	9(12)
21.	Metolazone	5(10)	12(16)
22.	Spiranolactone	2(4)	0
23.	Anti-platelet	23(46)	28(37.3)
24.	Vitamin supplement	15(30)	28(37.3)
25.	Iron supplement	13(26)	10(13.3)
26.	Anti-diabetic	26 (52)	12(16)

27.	Anti-ulcer	40(80)	58(77.3)
28.	Anti-emetic	18(36)	35(46.6)
29.	Corticosteroids	18(36)	22 (29.3)
30.	Renal Protectant	19(38)	14(18.6)
31.	Bronchodilator	22(44)	14(18.6)

Antibiotics were administered to manage the various infections of CKD were Cefoperazone ,amoxicillin + clavulanic acid, levofloxacin were most frequently prescribed. cefoperazone was the antibiotic prescribed with highest percentage(32.8%). A total of 183 anti-hypertensive was used in 125 patients ,among which Cilnidipine (48.8%) a calcium channel blocker followed by metoprolol were most commonly prescribed . 74.4% of CKD patients were prescribed with diuretics of which 65.6% were administered with furosemide. The most commonly used five drugs/ drug classes were diuretics, calcium channel blocker, antibiotics, proton pump inhibitors and anti –platelets.

**Table2: Distribution of Number of DDI in prospective cases**

Case category	Stage of CKD	Number of DDI	Frequency	Percent
Retrospective	Stage 3 EGFR>30-59 ml/min	0	4	26.7
		1	6	40.0
		2	4	26.7
		4	1	6.7
		Total	15	100.0
	Stage 4 EGFR 15-29 ml/min	0	11	68.8
		1	4	25.0
		2	1	6.3
		Total	16	100.0
	stage 5 EGFR >15 ml/min	0	20	45.5
		1	16	36.4
		2	7	15.9
		3	1	2.3
		Total	44	100.0

Table 2& 3 summarizes the potential drug interactions in the study.A total of 64 drug interactions were found among 125 subjects within a period of 6 months.

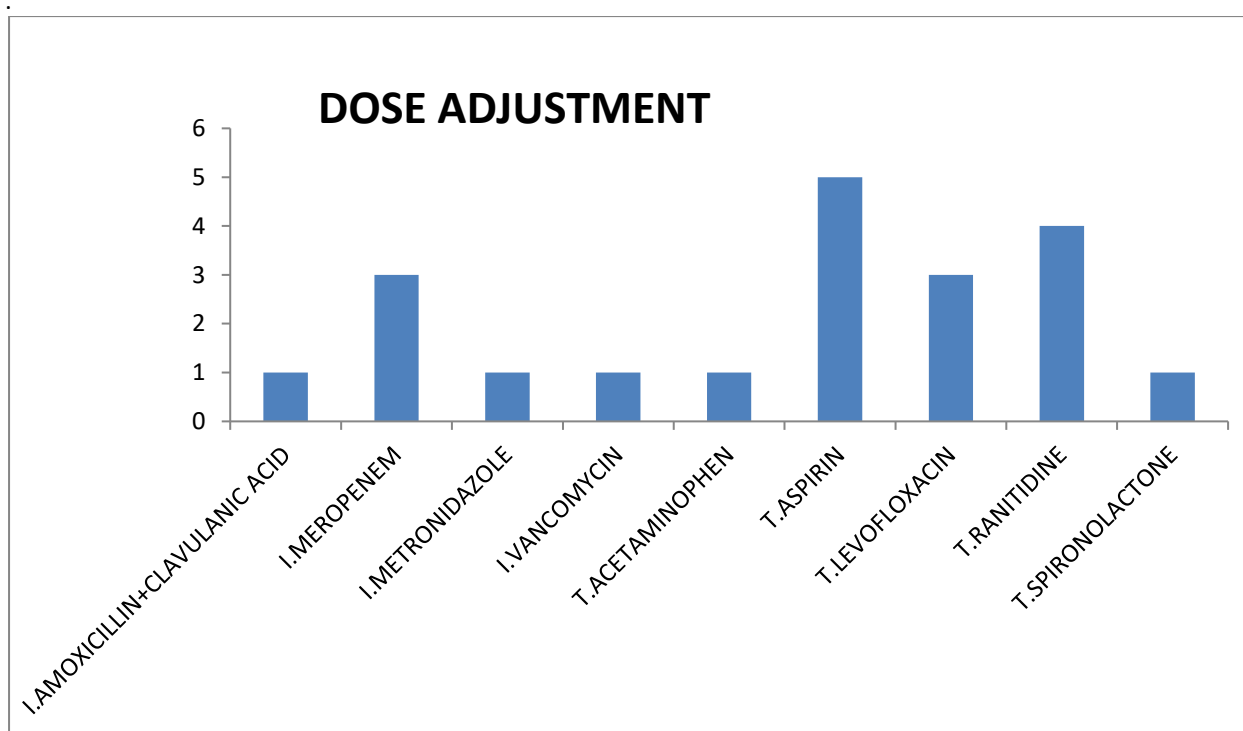
**Table 3: Distribution of the Number of interactions**

Casecategory	Stageof CKD	No of inteactions	Frequency	Percent
Prospective	stage2 EGFR 60-89 ml/min	0	1	100.0
	Stage 3 EGFR>30-59 ml/min	0	4	57.1
		1	1	14.3
		2	1	14.3
		3	1	14.3
		Total	7	100.0
	Stage 4 EGFR 15-29	0	9	69.2

	ml/min	1	2	15.4
		2	2	15.4
		Total	13	100.0
stage 5 EGFR >15 ml/min		0	11	37.9
		1	8	27.6
		2	5	17.2
		3	4	13.8
		4	1	3.4
		Total	29	100.0

The maximum no of interactions were found in stage 3&stage 5 CKD patients.

**Figure 3 : Distribution of drugs requiring dose adjustment**



Dose of drugs like aspirin ,ranitidine ,meropenem,levofloxacin require dose adjustment in CKD patients.The figure 3 depicted drugs with their adjusted dose,a total of 20 dugs dose were adjusted. Meropenem. aspirin. ranitidine, levofloxacin, spironolactone, amoxicillin+clavulanic acid ,acetaminophen ,vancomycin,metronidazole were identified as the drugs which need dose adjustment in study participants

**Table 4: Distribution of total drug cost in CKD patients.**

S. NO	Drug	Total Cost prospective Mean ±SD	Total Cost Retrospective Mean ±SD
1.	Beta blockers	25.62+85.38	20.20+48.91
2.	Calcium channel blockers	41.88+45.24	41.02+41.68
3.	Diuretics	59.08+108.70	48.60+69.53
4.	Antiplatelets	8.48+12.82	7.56+16.90
5.	Vitamins	17.2+43.44	19+42.52
6.	Antidiabetics	319.72+396.74	204.26+322.11
7.	Anti -ulcers	12.30+28.70	22.54+42.07

The table gives the total cost of drugs that are commonly prescribed for CKD patients, most expensive drug was found to be anti-diabetic in both retro and prospective cases while anti –platelet was least among the drugs prescribed.

### DISCUSSION

This study revealed male predominance (69.6%) is more and average age is > 50 years. In this study out of 125 cases majority of patients were presented with 3-4 co-morbidities, HTN, T2DM, ANEMIA, IHD, Hypothyroidism were found most common. This study was found similar to that conducted by Wouters J, Donoghue J.D, Ritchie J, Kanavas G.P and Narvasa in which 64% patients had 4-5 co-morbidities. Based on the calculated eGFR values, 58.4% of study participants belongs to stage 5 of CKD. (5) Polypharmacy has been defined as the use of 5 or more medications to one patients. Most of the patients were prescribed with antihypertensive, antibiotics, diuretics, anti-platelets, anti-diabetes, vitamin, mineral and iron supplements. Assessing the 125 CKD patients, most commonly prescribed class of anti-hypertensives were calcium channel blocker (clonidine) and Metoprolol, of diuretics was furosemide, which was similar to study conducted by Abhishek.P.A, Panda.R, Mohapatra.J, Mohapatra.N, Mohanty.S, in which they showed that most commonly prescribed antihypertensives among the CKD patients was calcium channel blockers followed by beta-blockers. (11)

To manage various infectious condition present in CKD patients antibiotics like Cefoperazone, amoxicillin+clavulanic acid, piperacillin+tazobactam, levofloxacin were prescribed commonly. Cefoperazone was the antibiotic prescribed with highest percentage. Anemia, one of the most common co-morbidity among CKD patients, iron vitamin and mineral supplements were co-administered to manage this condition. Antiplatelets like aspirin, clopidogrel and their combination drugs, insulin was administered in patients to manage associated co-morbidities. During our study period, no ADR's were reported among the patients. Moderate drug interactions were the commonest and mainly seen in stage 5 CKD patients. Guidelines for the dose adjustment in renal patients suggest that aspirin should be avoided in ESRD patients, in renal impaired patients it was identified that the dose of drugs like aspirin, ranitidine, meropenem were to be adjusted.

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