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Cost effectiveness analysis of anti-hypertensive drugs used for chronic kidney disease patients

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ABSTRACT

Cost effectiveness analysis branch of pharmacoeconomics is a technique used to aid in decision making between alternatives. A prospective observational study would be conducted in the nephrology department at O.P, Patients with CKD with hypertension, with or deprived of diabetes are included in the study. Patients with drug-induced renal disease or unknown cause. Pregnant women with chronic kidney disease are excluded from the study. The research was conducted in 150 patients in which common are men. The mean age of the research people was found to be 51.2 ± 7.02 . It was observed that calcium channel blockers 127 (84.6%), diuretics 51 (34%), α agonists 33 (22%), β blockers 21 (14%), α blockers 17 (11.3%), $\alpha+\beta$ blockers 10 (6.6%), Angiotensin receptor blockers 3 (2%) and angiotensin-converting enzyme inhibitors 1 (0.6%) were the numerous antihypertensive drugs given to the study people. Incremental Cost-Effectiveness Ratio was assessed, and it was observed that Rs.31.80 was extra required while using diuretics than Calcium Channel Blockers for achieving respective maintenance value. The major classes of antihypertensive drugs prescribed in all of them are CCB+ α agonist was found most effective CCB+ Diuretics were the second most effective. Incremental Cost-Effectiveness Ratio was calculated, and it was found that Rs.4.40 was Extra needed to attaining essential upkeep of blood pressure. Pharmacoeconomic study shows that Calcium channel blockers were the utmost cost-effective antihypertensive in CKD patients when linked to other antihypertensive drugs. In two-drug combination therapy, CCB+ α agonist was found most effective.

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INTRODUCTION

Globally adult population was highly affected by hypertension (HTN), which is associated with the huge economic burden at entire populations ((CDC), 2011). The direct and indirect cost of the treatment for HTN was estimated at \$47.3 billion and \$39 billion, respectively. Moreover, HTN was a primarily self-determining risk factor for other expensive diseases (Benjamin *et al.*, 2017).

Chronic kidney disease (CKD) is distinct as the presence of kidney damage (i.e., pathological irregularities or markers of injury) for 3 months or further; and/or an projected glomerular filtration rate (eGFR) <60 mL/min/1.73 m² for 3 months

or lengthier, with or deprived of kidney damage (Aiyegbusi *et al.*, 2016). HTN usually develops concurrently with broadminded kidney problem with augmented risk. Diabetes and HTN are the foremost causes of CKD in all high-income nations and many low- and middle-income nations. CKD is related with the significant financial burden, disease development, augmented disease cruelty, and weakening of health upsurge the resource operation and escalated costs (Sood *et al.*, 2012).

Pharmacoeconomic analysis can afford valuable evidence for physicians in setting healthy needed populations. A number of pharmacoeconomic research of antihypertensive drugs was conducted in latest years have observed regulation of HTN to be cost-effective (Park *et al.*, 2017). Hence, the present research was commenced to assess the cost-effectiveness of anti-hypertensive treatments for CKD patients in a single center.

MATERIALS AND METHODS

A prospective observational study was conducted in the Nephrology division from September 2017 – February 2018. Data were collected from prescriptions and through medication history interview of the subjects included in the study at the outpatient department. Patients with CKD with HTN, with or without diabetes are included in the study. Patients with drug-induced renal disease or unknown cause and pregnant women with chronic kidney disease are excluded from the study. The subsequent patient details were documented as name, age, sex, outpatient number, diagnosis and applicable laboratory values. All the details of the medicines prescribed to the patients also documented. The cost-efficiency of antihypertensive medicines in patients getting a mono and combination drug (Two drug therapy) were calculated using the incremental cost-effectiveness ratios (ICER); where

ICER = Cost of Drug A – Cost of Drug B / Effect of Drug A – Effect of Drug B

Drug A= First Most Effective Therapy,

Drug B= Second Most Effective Therapy.

Cost-effective therapy was calculated as per the average maintenance of blood pressure by the mono and combination drug prescribed to the individual patient. This research was approved by the Institutional Ethics Committee of Rajiv Gandhi Institute of Medical Sciences College and Hospital, Kadapa, Andhra Pradesh, India. Microsoft Excel was used for recording and analyzing the data of recruited subjects. Descriptive statistical analysis, like mean, was used to calculate the average.

RESULTS AND DISCUSSION

The total study population was 150, in this 73.3% was male, and 26.6% was female patients. The age group of more number of patients were observed as 51-60 years. Out of 150 patients, 87 (58%) patients had hypertension, 7(4.6%) patients had diabetes, and 56 (37.3%) patients had both hypertension and diabetes. The results were present in Table 1.

In the present study, most of the patients (85.3%) received polytherapy with a minimum of five drugs. The mean number of drugs prescribed to the patients were 5.75 ± 1.57 . The prescription pattern of antihypertensive drugs were observed as 50.6% of the patient were received more than five drugs. 32% of the patients received a combination of antihypertensive and antidiabetic drugs. The results were present in Table 2.

CCBs 127 (84.6%), diuretics 51 (34%), α agonists 33 (22%), β blockers 21 (14%), α blockers 17 (11.3%), $\alpha+\beta$ blockers 10 (6.6%), Angiotensin receptor blockers 3 (2%) and ACE inhibitors 1 (0.6%) were the various antihypertensive drugs prescribed to the patients. CCBs are the uppermost and ACE inhibitors were the minimum prescribed class of antihypertensive drugs to the patients. The results were present in Figure 1.

In the present study, 64 (41.3%) patients were prescribed with single, 63 (42%) patients were prescribed with two, 19 (12.6%) patients were prescribed with three antihypertensive drugs, 4(2.6%) patients were prescribed with four antihypertensive drugs, 1 (0.67%) patients were prescribed with five and six antihypertensive drugs. The results were present in Figure 2.

The single antihypertensive drug was prescribed to 62 (41.3%) patients (87.09%); in this, 8.06% of the patients were received CCBs and diuretics. Nifedipine and furosemide was found to be the most prescribed drug, respectively. It is observed that α agonist (n=19) and diuretics (n=17) were most prescribed medicines along with CCBs in combination therapy.

Cost-effective analysis (CEA) was analyzed in a total of 62 CKD patients getting a monotherapy of HTN. The normal cost of each category of medicine was calculated in INR, and the average value of maintenance BP after getting the medicine was considered. Based on the calculation, it is observed that CCBs was most cost-effective antihypertensive drugs and diuretics were the subsequent most effective medicine. ICER was calculated, and it was observed that Rs.31.80 was extra required while using diuretics than CCBs for HTN treatment. The

Table 1: Demographic details of study populations (n=150)

Variables	Number of people	
	Values in Number	Values in Percentage (%)
Gender		
Males	110	73.3
Females	40	26.65
Age (Years)		
11-20	03	2
21-30	09	6
31-40	20	13.3
41-50	32	21.3
51-60	46	30.6
61-70	35	23.3
71-80	04	2.6
81-90	01	0.6
Family Income (INR per annum)		
<50,000	47	31.4
50,000-1,00,000	78	52
>1,00,000	25	16.6
Co morbidity's		
HTN	87	58
HTN+DM	56	37.3
DM	07	4.6

Table 2: Total number of drugs prescribed per patient in the study population (n=150)

Number of drugs	Patient with HTN (n=87)	Patients with HTN+DM (n=56)	Patients with DM (n=7)	No of pre- scriptions	Percent- age (%)
1	0	0	0	0	0
2-4	11	8	3	22	14.6
>5	76	48	4	128	85.3

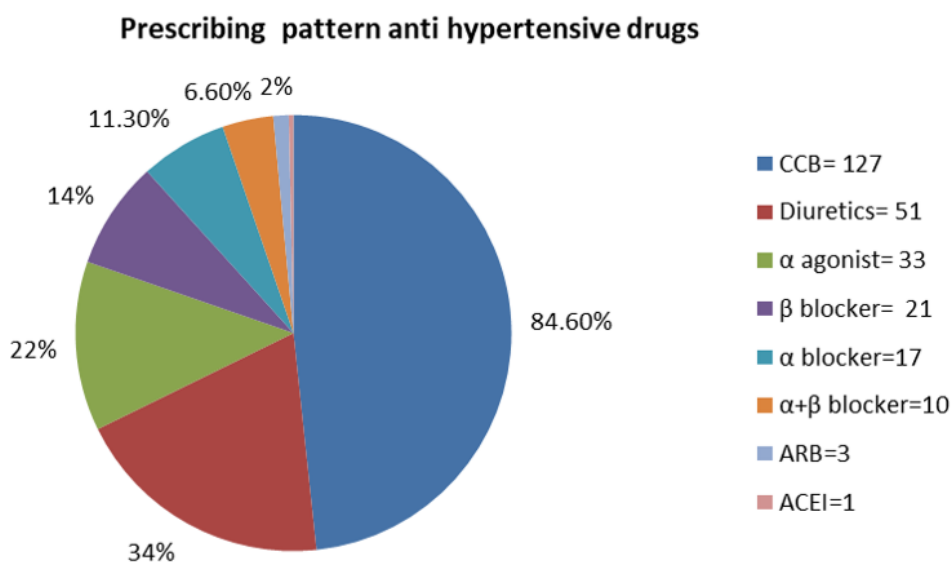


Figure 1: The use of anti-hypertensive drugs in study populations

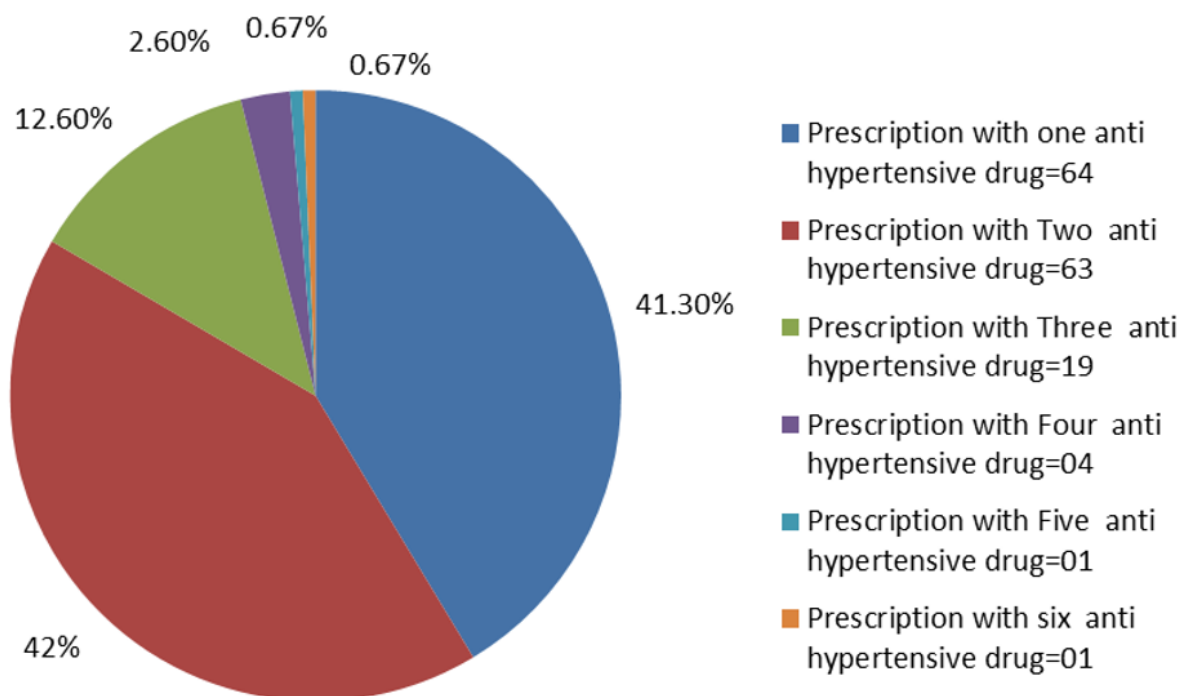


Figure 2: Prescription pattern of number of anti-hypertensive drugs per patient

Incremental Cost-Effectiveness Ratio of two anti-hypertensive drugs was calculated, and it was found that Rs.4.40 was extra needed to achieve required maintenance of blood pressure. The results were present in Tables 3 and 4.

Cost Effective analysis was carried out between monotherapy and combination therapy, where Combination therapy is the first most effective therapy, and monotherapy was the second most effective therapy. Incremental Cost-Effective Ratio was calculated; it was found that Rs. 96 extra needed for a subject to shift from monotherapy to combination therapy.

In the present study, CKD patients were more with male (73.3%) compare to female. A recent study reported that males are more likely to have CKD with an average of 70% (Karthikeyan *et al.*, 2004; Alwyn *et al.*, 2016). The mean age (51.2 ± 7.02) of the study population also similar with other studies indicate most of the early elderly population affected by the CKD (Alwyn *et al.*, 2016).

Assessment of prescription pattern of anti-hypertensive is one of the objectives of the present study. The study assessed that 41.3% of subjects received monotherapy, and 42% of subjects received two-drug combination therapy. Calcium channel blockers (CCBs) was mostly preferred drug class in monotherapy for the treatment of hypertension followed by diuretics, which resembles the report documented by others (Juno *et al.*,

2015; Priya and Basavanna, 2015; Vummareddy *et al.*, 2017). Among CCBs, Nifedipine was the most commonly used antihypertensive agent. The choice of CCBs to control the blood pressure influenced by its renoprotective effect and also CCBs effectively reduces the systemic blood pressure while maintaining the glomerular filtration rate and effective renal plasma flow (Juno *et al.*, 2015).

CCBs and α agonist were the most preferred combination drugs in the study population, which is contrary to the study conducted by Raju *et al.* (2016), where CCB+ β blockers are preferred. According to KKF KDOQI guidelines for CKD patients to maintain the blood pressure long-acting antihypertensive drugs should be preferred. The prescription pattern of antihypertensive drugs complies with the guidelines also. In CEA study, out of four prescribed drugs, CCBs were found to be most effective, and diuretics were the subsequent most effective antihypertensive drugs. The results was similar to the finding of (Alwyn *et al.*, 2016).

The Analysis of 150 prescriptions exposed that poly-drug therapy was more favored than monotherapy. CCBs were the most usually prescribed antihypertensive drug in CKD patients. Among the CCBs, Nifedipine is the mostly preferred drug. Among combination drug therapy CCB+ α agonist was mostly preferred. Pharmacoeconomic analysis of monotherapy shows that CCBs were the most cost-effective antihypertensive in CKD patients when associated to additional antihypertensive

Table 3: Cost-effective analysis of mono therapy of anti-hypertensive drugs

Antihypertensive class	No of prescriptions (N=60)	Cost of drugs per month (in Rs)	Maintenance of BP during Followups (mmHg)			Mean and S.D	Average of maintenance B.P (mmHg)
CCBs	54	91.5	142.8	140.8	138.2	140.6+2.3	140.6
Diuretics	5	15	137	152	140	143+7.9	143
ARBS	1	156	148	144	140	144+4.0	144

Table 4: Cost effective analysis of anti-hypertensive drugs for combination therapy

Anti-hypertensive class	Number of prescriptions (N=44)	Cost of drugs per month. (in Rs)	Maintenance of BP during Followups (mmHg)			Mean and S.D	Average value of maintenance B.P (mmHg)
CCBs+ α agonist	18	139.5	141.4	138.2	140.8	140.1+1.7	140.1
CCBs+ β blockers	9	159.7	148	145.1	136	143.03+6.2	143.03
CCBs+Diuretics	17	106.5	151	149.5	142	147.5+4.8	147.5

drugs. Cost effective analysis of two-drug combination therapy shows that CCB+ α agonist is the most cost-effective therapy. Cost analysis showed that Monotherapy to be more economical.

CONCLUSION

In our study, we observed that most of the patient's economic status is below one lakh and the patients with CKD are majorly with Polypharmacy condition so there may be an increased burden of cost, hence there is need of consideration of the economic status of patients before prescribing the drug therapy. Inadequate oral instructions by clinical pharmacist regarding the use of medications prone to decreased adherence of patients towards medications, so there is a need of improving the counselling process for better outcomes. Use of anti-hypertensive in CKD patients does not diverge from the guidelines given by NKF KDOQI.

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