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# ASSESSMENT OF CLINICAL AND ECONOMIC IMPACT OF PHARMACIST INTERVENTION IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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**Abstract :** Chronic kidney disease shows worldwide health events epidemically. s part of a multidisciplinary patient care strategy, clinical pharmacy services have led to improvements in patient care. Pharmacists play an important role in the renal MDT by minimizing drug-related problems, optimizing therapy, laboratory monitoring, determining drug dosage adjustments, developing monitoring plans, avoiding nephrotoxic drugs, managing complications of kidney disease, patient education, and establishing effective medication management programs. Pharmacists represent an essential component of the team through their medication expertise in pharmacotherapy, helping to manage comorbid conditions, slow kidney disease progression, and provide a positive impact on improving the care of kidney patients.

**KEYWORDS:** Chronic kidney disease, Renal function, Pharmacist management.

## I. INTRODUCTION

II. Chronic kidney disease (CKD) is a progressive disease of declining kidney functions where the nephrons of the kidney are damaged and/or stop functioning and this process is spread over a long period, maybe several months to years. In CKD, the reduction in kidney function is irreversible with a progressive decrease in the glomerular filtration rate, which eventually ends in end-stage renal disease (ESRD). Renal replacement therapies (RRTs) like haemodialysis (making use of an artificial kidney), peritoneal dialysis (using the peritoneal membrane to remove accumulated waste from blood), and renal transplantation are the means of survival once ESRD sets in (1). It is estimated that 750 million persons across the globe are affected by kidney disease making it a global public health problem (2). The burden of kidney disease and its detection and management differs worldwide based on socio-economic setting and is influenced by local cultural and political factors (2). Though several countries have established national data collecting systems like registries for CKD & ESRD, there are inconsistencies in collected data particularly from low- and middleincome countries. High quality data with respect to patients with CKD and not on any mode of renal replacement therapy is limited (2). World Health Organization‟s (WHO) Global burden of disease 2015 study estimates

that reduced glomerular filtration rates directly contributed to over a million deaths, and close to twenty million disability-adjusted life-years (DALYs) and loss of life years of about 18 million from cardiovascular diseases (3).

The growing number of people with CKD, the number of people progressing to end stage, and the resulting financial load of managing the disease in both first world as well as emergent nations has thrown light upon preventing occurrence of CKD and minimizing the risk factors. According to a National Health and Nutrition Examination Survey (NHANES) report, in the United States, overall prevalence of CKD (stages 1- 5) gradually increased from 14.2% (2001-2004) to 14.8% (2013-2016) and CKD stage 3 is most prevalent (4). In Europe, CKD prevalence varied from 4.1% reported in a Swiss study (Swiss Bus Santé study) to 25.5% in a German study (the Northeast German SHIP study) (5). Quality of data from Africa being poor, exact estimates are not reported. A systematic review from Africa reported CKD prevalence from 2-42% from the community-level studies, 11-90% in patients with diabetes, and 13-51% in patients with hypertension (6). In India, a population-based survey has reported an incidence of 151 per million population in Central India (8), reduced GFR was found in 13% of population (9), other studies report between 0.8% to 4.8% of reduced GFR (10,11). According to an Indian CKD registry report published in 2012, among approximately fifty-two thousand registered CKD patients, 48% had ESRD, 16% had CKD of undetermined etiology, hypertensive nephrosclerosis and glomerulonephritis were causes of CKD in 13% and 14% of CKD patients respectively, and the most common cause was diabetic nephropathy (31% of patients) (12). A 5 year follow-up epidemiological study observed that kidney disease patients progressed to ESRD at yearly rates of 23% for those with polycystic kidney disease, 10% for those with glomerulonephritis and 12% for those with diabetic nephropathy, but the risk of death before ESRD was 2-fold higher among diabetic nephropathy patients than those with cystic kidney disease (13).

CKD is a complex disease with multiple comorbidities and attendant complications. Evidence has accumulated over the years and we now know that the disease is associated with significant morbidity and mortality risks. What makes the disease deadlier is that the metabolic complications associated with it that include mineral and electrolyte imbalance, metabolic acidosis, anemia, and renal osteodystrophy among others may remain asymptomatic for a long time. It is proven now that these complications can significantly affect the physical, and emotional health of a person.

**(I). Risk Factors of CKD**

Risk factors for CKD are classified into three categories.

Susceptibility factors, which are associated with an increased risk of developing CKD, but are not directly proven to cause CKD. These factors are generally not modifiable by pharmacologic therapy or lifestyle modifications.

Initiation factors, which directly cause CKD. These factors are modifiable by pharmacologic therapy.

Progression factors, which result in a faster decline in kidney function and cause worsening of CKD. These factors may also be modified by pharmacologic therapy or lifestyle modifications to slow the progression of CKD.

**Susceptibility factors**

- Advanced age
- Reduced kidney mass
- Low birth weight

**Initiation Factors**

- Diabetes mellitus
- Autoimmune disease
- Polycystic kidney disease

**Progression factors**

- Hyperglycemia: Poor blood glucose control (in patients with diabetes)
- Hypertension: Elevated blood pressure
- Proteinuria
- Tobacco smoking

## NEED OF THE STUDY.

Chronic kidney disease is an expensive condition to manage due to the morbidities associated with disease progression. It has also become a concern for preventive medicine due to its increasing prevalence, multiple out-patient visits as well as emergency and hospital admissions. This has also placed a huge burden on the medical staff as well as healthcare resources. Patients with CKD are also prescribed with multiple medications to manage the disease as well as associated comorbidities that can lead to drug related problems in practice. It is also well-known that CKD can progress to ESRD, in which case renal replacement therapy by dialysis or renal transplantation is the sole management process. In the present scenario, it is estimated that close to two million CKD patients across the world require renal replacement therapy (39). This number is set to increase due to the increasing aging population, as well as increasing incidences of diabetes and hypertension among the general population.

## AIM AND OBJECTIVES

### Primary Objectives

To evaluate the clinical and economic impact of pharmacist-initiated drug therapy changes on disease control and health -related outcomes in patients with Chronic Kidney Disease

### Secondary Objectives

I. To study the rate and pattern of occurrence of drug related problems in CKD patients

II. To assess the impact of pharmacist-initiated changes to drug therapy on disease control and health-related quality of life.

III. To determine the predictors of impaired health-related quality of life.

IV. To assess the impact of pharmacist's intervention on cost of drug therapy in chronic kidney disease patients.

## RESEARCH METHODOLOGY

### Study hypothesis:

Pharmacist-provided healthcare services to chronic kidney disease patients will have positive impact on disease control and better health-related outcomes in patients with chronic kidney disease.

### Study Design

Randomized, controlled, prospective, open labelled, interventional study

Retrospective studies have limitations in terms of completeness of data, and so a prospective study is a good choice. Among analytical studies, since the study population consisted of patients with chronic kidney disease, a case-control study and cohort study were not suited. Also, since the study required some kind of intervention by way of pharmacist providing pharmaceutical care services, and to really assess the impact of these services there was a need for two groups, an experimental and a comparison group, an interventional study design was chosen. Since randomization eliminates bias when grouping patients, a randomized, controlled, interventional study was chosen.

**Study Site:** the study will conduct at nephrology department in tertiary care hospital in Jaipur.

### Sample Size Calculation

Choosing paired t-test as a suitable statistical test to investigate research question, the sample size was calculated. Assuming a standard deviation value of 2, keeping the level of significance at 1%, power of the study at 90%, and minimum detectable significance between two groups as 1, a sample size of 52 for each group was obtained.

When comparing two means in a study the formula is as follows:

$$n = \frac{2\left[(a+b)^2\sigma^2\right]}{(\mu_1-\mu_2)^2}$$

Where

σ- standard deviation

Zα - Z value for α error

Zβ - Z value for β error

d – clinically meaningful difference

Considering α error as 0.01 then Zα= 2.33 ; Considering βerror as 0.10 Zβ =1.28

Assuming standard deviation, σ= 2 (obtained from health-related outcomes studies in CKD), and d = 1, we get

$N= 2^2 *2(2.33+1.28)^2 /1^2 = 104$

Since we have 2 groups, so, 104/2= 52 in each group

**Study Criteria**

- Patients admitted to nephrology, medicine, surgery, and orthopedics wards of a selected tertiary care hospital
- Patients who were diagnosed with chronic kidney disease of any stage and etiology
- Patients of any age and gender
- Patients who gave consent to participate in the study

**Exclusion criteria:**

- Patients diagnosed with cancer, undergoing chemotherapy or undergone organ transplantation.
- Patients visiting nephrology outpatient's department except those visiting haemodialysis unit
- Patients with current or planned pregnancy
- Patients diagnosed with anemia other than anemia of chronic kidney disease
- Patients with significant liver disease as evidenced by ChildPugh grades B & C
- Patients with alcohol dependence as defined by the American Medical Association.
- Patients diagnosed with substance abuse disorders

## RESULTS AND DISCUSSION

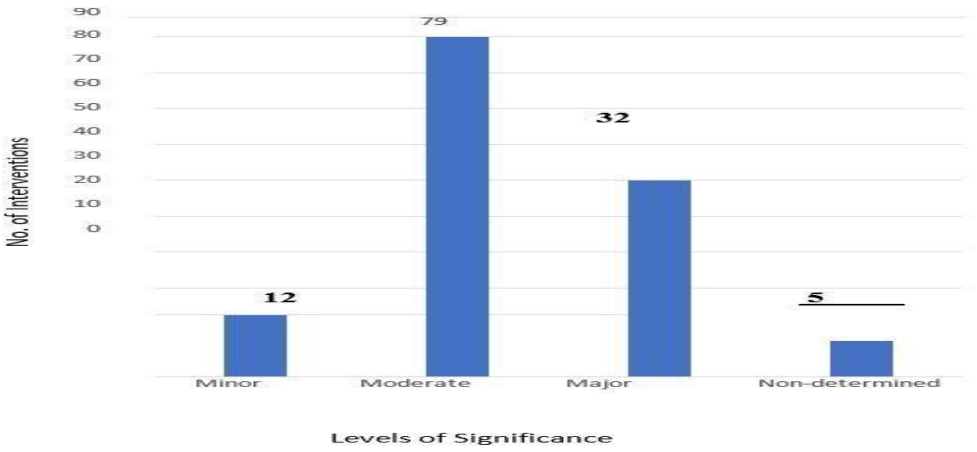
**Demographic Details of Study Population**

Among 104 patients (52 in Test group and 52 in Control group) included for analysis, 98.5% were inpatients and 1.5% were ambulatory patients on maintenance haemodialysis.
There were more males in the study population (56%), and majority (40%) of patients belonged to age group 50-59 years followed by age group 30-49 years (37%) The average age of the study group was 53 years (range:16-91) Study patients received an average of 7 medications per patient and majority of them (30%) had middle or high-school education Diabetes and Hypertension were most commonly observed co-morbidities, followed by hypothyroidism, COPD, and IHD.

**Assessment of Drug Related Problems**
A total of 45 DRPs were identified from patients.
The rate of occurrence of DRP was 1.05 per patient.
ADRs (28%) were the most common DRP followed by untreated indication and therapeutic duplication (10% each).
Too many drugs for indication, drug use without indication (9% each) and potential Drug interactions (8%) were the next most common DRPs in the study population.
Most common cause of DRPs were drug dose requiring adjustments 11.7%, drug interactions 7.85%, followed by therapeutic duplication 6.94%.
Most commonly implicated drug in treatment effectiveness was piperacillin + tazobactum , followed by pantoprazole, ceftazidime + tazobactum, and clopidogrel

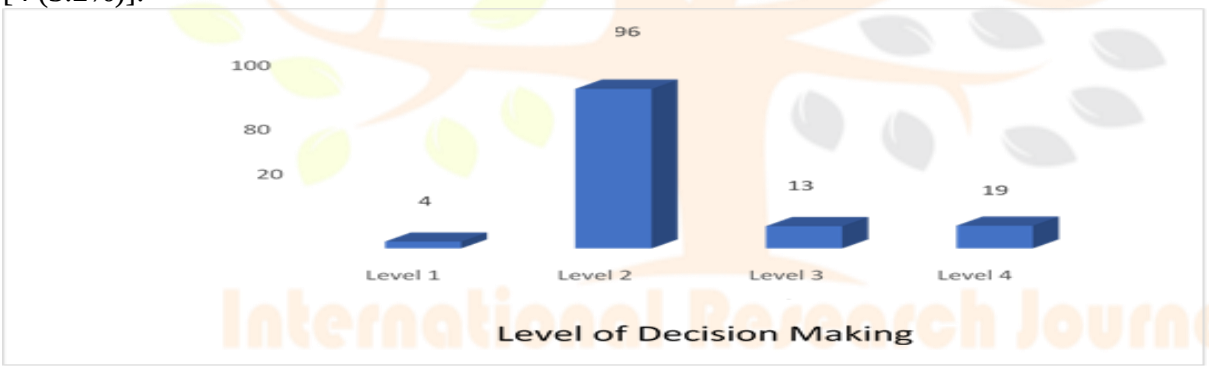
**Significance of Pharmacist Interventions**

A total of 53.6 % of interventions were found to have moderate significance, 35% to have major significance, and 8% to have minor significance. Effect of interventions on morbidity, treatment costs or hospital stay could not be determined for about 4% of interventions.




**Level of Decision making by pharmacist for interventions**

Level of Decision making by pharmacist for interventions was categorized based on level of involvement. It was seen that majority of the interventions [96 (75.3%)] belonged to Level 2 Corrective, while few of them were Level 3 Consultative [13 (10.5%)] and Level 4 Proactive [19 (10.8%)]. A small number were annotative [4 (3.2%)].




**Impact of Pharmacist Intervention on Health-related Quality of Life**

HRQoL values of 102 patients with ESRD on MHD were selected for analysis. Among these, 52 patients were in the test group and 50 patients were in the control **group. Total HRQoL scores and scores of different HRQoL domains among subjects in the test group at baseline, 3 months and 6 months are shown** .

When baseline values were compared with those at 3 months significant difference (p=0.015) was found in Burden of Kidney Disease subscale. No significant differences were found when baseline values and values at

| Scale (number of items in scale) | HRQoL Scores (Mean ± SD) | | | P values | |
|---|---|---|---|---|---|
| | Baseline | 3 months | 6 months | Baseline-3 months | Baseline- 6 months |
| Symptom/problem list (12) | 49.98 ± 17.41 | 52.82 ± 18.65 | 48.45 ± 18.60 | 0.38 | 0.642 |
| Effects of kidney disease (8) | 51.75 ± 13.05 | 51.47 ± 13.18 | 49.83 ± 12.96 | 0.907 | 0.420 |
| Burden of kidney disease (4) | 61.44 ± 10.89 | 62.71 ± 9.43 | 62.27 ± 10.41 | 0.496 | 0.670 |
| SF-12 Physical Health Composite (12) | 43.56 ± 6.15 | 43.08 ± 6.20 | 42.06 ± 5.33 | 0.671 | 0.156 |
| SF-12 Mental Health Composite (12) | 43.57 ± 8.34 | 42.56 ± 6.90 | 44.29 ± 5.08 | 0.471 | 0.569 |
| Total Score | 49.80 ± 5.83 | 50.53 ± 5.93 | 49.38 ± 6.45 | 0.497 | 0.708 |

Total HRQoL scores and scores of different HRQoL domains of test and control groups obtained at 6 months were compared. The results are depicted in Table 6.12. There was significant difference in Symptoms domain (p=0.035), Physical composite (p=0.031), and Mental composite (p=0.033) between test and control groups that was in favour of test group. Total scores in the test group was higher than control group though not significant.

| Scale (number of items in scale) | HRQoL Scores (Mean ± SD) | | P value |
|---|---|---|---|
| | Test (n=52) | Control (n=50) | |
| Symptom/problem list (12) | 55.65 ± 15.93 | 48.45 ± 18.60 | 0.035* |
| Effects of kidney disease (8) | 48.21 ± 14.64 | 49.83 ± 12.96 | 0.554 |
| Burden of kidney disease (4) | 59.06 ± 11.84 | 62.27 ± 10.41 | 0.146 |
| SF-12 Physical Health Composite (12) | 44.60 ± 6.36 | 42.06 ± 5.33 | 0.031* |
| SF-12 Mental Health Composite (12) | 46.32 ± 4.53 | 44.29 ± 5.08 | 0.033* |
| Total Score | 50.30 ± 6.35 | 49.38 ± 6.45 | 0.466 |

**Impact of pharmacist intervention on cost of drug therapy**

The total cost of pharmacist interventions was found to be INR 3321621 [Median - 1200, IQR 300-3010]. The direct costs of pharmacist interventions performed in the study population were tabulated in Table 6.15. Interventions that led to an increase in cost amounted to INR 1300751 and those that decreased cost amounted to 1614960. There was a net cost saving of INR 314209 for pharmacist interventions. Cost saving per intervention was approximately INR 252.37, and cost saving per patient was found to be INR 271.80. Details of cost descriptions for different types of interventions are provided.

## CONCLUSION

CKD is a complex disease with multiple comorbidities, multiple prescribed medications, and attendant complications that can affect the physical and emotional health of the individual The research project aimed to evaluate clinical and economic consequences of clinical pharmacist intervention in CKD patients The study found that clinical pharmacist interventions can significantly improve disease control measures, improve health related quality of life, and reduce costs of drug therapy. Employing clinical pharmacists in hospitals is beneficial.

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