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ORIGINAL ARTICLE

TOXICOLOGICAL ASSESSMENT, MEDICATION ADHERENCE AND NON-ADHERENCE IN CHRONIC KIDNEY DISEASE PATIENTS: A CROSS-SECTIONAL STUDY

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ABSTRACT

Introduction: *Chronic kidney disease (CKD) poses significant global and national health challenges, with high prevalence, morbidity, mortality, and healthcare costs. Its management is complicated by co-morbidities and patient non-adherence to treatment regimens, compounded by toxicological issues such as medication side effects and drug interactions.*

Materials and methods: *This study, conducted at the Universal College of Medical Sciences and Teaching Hospital, involved 170 randomly selected patients. Data from medical records and interviews focused on adherence and toxicological concerns, with the 8-item Morisky Medication Adherence Scale assessing adherence. Toxicological effects were evaluated through patient self-reports and record reviews, with SPSS version 20.0 used for data analysis.*

Results: *The study showed that 85% of hypertensive patients were on non-ACEI regimens, while 25% with both diabetes and hypertension managed with insulin plus non-ACEI regimens. Only 32.9% adhered to prescribed regimens, citing high medication costs (51%) and toxicological concerns (12%) as primary reasons for non-adherence. Younger patients, specific occupations (e.g., teachers), and higher education levels correlated with better adherence.*

Conclusion: *The study highlights the prevalence of medication use and adherence in CKD patients, emphasizing the need for cost-effective strategies and toxicological monitoring to improve adherence and patient outcomes.*

Keywords: *Chronic Kidney Disease, Management Practice, Medication Adherence, Non-Adherence, Toxicology*

INTRODUCTION

Chronic Kidney Disease (CKD) is a significant global health concern, affecting millions of individuals and imposing substantial burdens on healthcare systems. Managing CKD requires a comprehensive approach, including lifestyle modifications, medication adherence, regular monitoring, and addressing toxicological concerns to slow disease progression and prevent complications.[1] Tertiary care hospitals play a critical role in providing specialized care to CKD patients, offering advanced treatments and interventions tailored to individual needs. The prevalence of CKD in the population is a considerable social and economic problem worldwide, and one that is increasing.[2] It often goes undetected and undiagnosed until kidney function is down to 25% of normal. Globally, 10% of the population is affected by CKD, and millions die each year due to the high economic cost of treatment.[3]

While previous studies have explored various aspects of CKD management, there is limited research focusing on the specific practices, adherence levels, and toxicological challenges among patients in tertiary care settings.[4] This gap hinders the development of targeted strategies that address the unique challenges faced by this population. Despite the availability of effective management strategies, adherence to prescribed regimens remains a challenge among CKD patients. Non-adherence can lead to worsening of the disease, increased hospitalizations, higher mortality rates, and toxicological complications from improper medication use.[5] Understanding the factors influencing adherence and non-adherence, including toxicological concerns, is crucial for developing interventions that improve patient outcomes and optimize healthcare resources.[6]

This research aims to investigate the management practices, adherence rates, toxicological challenges, and factors contributing to non-adherence among CKD patients at a tertiary care hospital. By identifying key barriers and facilitators, the study seeks to inform the design of effective interventions that enhance adherence, improve toxicological safety, and enhance the quality of care for CKD patients.

MATERIALS AND METHODS

Study Design and Settings:

The study was conducted in the Universal College of Medical Sciences and Teaching Hospital, Ranigaun, Bhairahawa, Nepal. The hospital-based cross-sectional study was conducted on data collected over a period of 9 months from April 2019 to December 2019.

Research Materials:

Data were collected using a structured questionnaire and data abstraction format to extract information from the patients and medical records. The questionnaire for the interview contained socio-demographic characteristics. The 8-item Morisky Medication Adherence Scale (MMAS-8), a validated scale, was utilized to collect information required to assess medication adherence and reasons contributing to non-adherence, including toxicological effects. The MMAS-8 scale is used to classify patients on medication as "poor" (a patient who scored >2), "moderate" (patients who scored 1 or 2), and high (patients who scored 0 for MMAS-8) on motivation and knowledge domains.[7,8] Additionally, data abstraction format was used to extract information about management practices and toxicological events, which was pre-developed and validated.

Toxicological Assessment:

Toxicological data were gathered from patient self-reports and medical record reviews. Reports of adverse drug reactions, drug interactions, and other toxicological effects were documented and analyzed.

Sample Size and Sampling Method:

A random sampling method was used to collect the data. The sample size is calculated using a single population proportion formula.[9]

$n=(Z^2\ P(1-P))/d^2$

Where,

n = Desired sample size.

Z = Standard normal distribution usually set as 1.96 (which corresponds to 95% confidence).

P = Expected prevalence 21.22% (obtained from a pilot study) and negative prevalence = 1 −0.106 = 0.894.

d = Degree of accuracy desired (marginal error is 0.066); then the sample size is:

$n=(1.96^2\times0.212(1-0.106))/0.066^2 =169.5\approx170$

Inclusion Criteria:

- All CKD patients on medications for more than 3 months irrespective of the stages of CKD.
- Patients aged 18 years and above.
- Patients who are willing to participate and give consent.

Exclusion Criteria:

- Patients who refused to participate in the study.
- Patients with cognitive impairment.

Study Procedure:

First, the study was approved by the institutional ethical committee. Then, consent forms were obtained from patients who were willing to participate in the study. Data were collected randomly from a sample of 170 patients from the in-patient, out-patient department, and hemodialysis/nephrology unit. The required details/data were collected using structured questionnaires to extract information from the patients, and disease-related data abstraction format was used to extract information from medical records, medication cardex, patients' OPD cards, and direct interviews of the patients at the same time.

Statistical Analysis:

All data were entered into SPSS version-20 statistical software for analysis. Descriptive statistics were used to describe patients' baseline characteristics. The chi-square test was used to determine P-values. The P-value was used to determine the statistical significance, i.e., association between medication adherence, toxicological events, and independent variables (socio-demographic of patients). A p-value ≤ 0.05 (5%) was considered statistically significant.

RESULTS

Socio-Demographic Characteristics:

Table 1 indicates males comprised the majority of the sex category, i.e., 110 (64.7%). Table 2 shows the majority of the population was in the age group of less than 65 years, accounting for 84.7%. Table 3 shows the

marital status, with the majority of the population being married, comprising 85.9% of the marital status category. Table 4 shows housewives comprised the majority of the population, accounting for 25.9%. Table 5 shows the majority of the population/patients were unable to read and write, comprising 56.5% of the patients. Table 6 shows the average family income (1-5 lakh) per year was in the majority of the population, accounting for 61.2%.

Table 1: Sex distribution of population.

Sex	Number of patients	% of patients
Male	110	64.7
Female	60	35.3

Table 2: Age distribution of population.

Age	Number of patients	% of patients
≤65	144	84.7
>65	26	15.3

Table 3: Marital status of population.

Marital Status	Number of patients	% of patients
Single	18	10.6
Married	146	85.9
Widowed	6	3.5

Table 4: Occupation of population.

Occupations	Number of Patients	% of patients
Government employee	10	5.9
Farmer	24	14.1
Merchant/trade	6	3.5
Daily labourer	30	17.6
House wife	44	25.9
Retired	40	23.5
Others	16	9.4

Table 5: Education status of population.

Education status	Number of patients	% of patients
Higher education	16	9.4
Secondary education	18	10.6
Primary education	40	23.5
Cannot read and write	96	56.5

Table 6: Yearly family income of population.

Yearly family income	Number of patients	% of patients
No income	10	5.9
Low income(≤1 lakh)	54	31.8
Average income(1-5 lakh)	104	61.2
Above average (5-10 lakh)	2	1.2

Duration of CKD in Years:

From Figure 1, the majority of participants having 1-5 years of CKD duration comprised 48.55%.

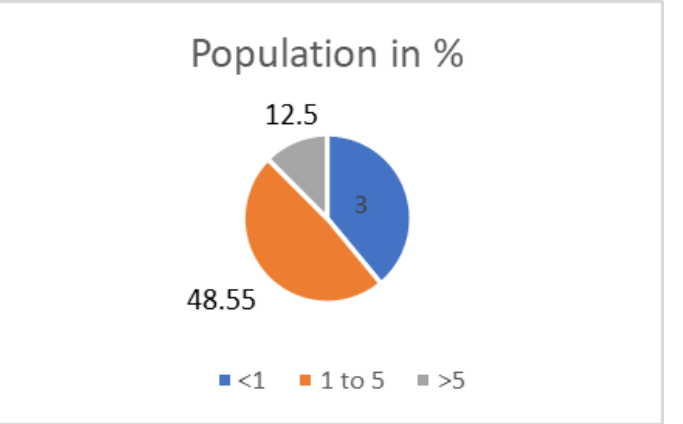

Figure 1: Duration of CKD of population.

Level of Medication Adherence:

Assessment of patient's response to the 8-item Morisky Medication Adherence Scale showed that 56 (32.9%), 40 (23.5%), and 74 (43.5%) patients exhibited high, medium, and poor adherence to the prescribed regimens, respectively.

Reasons for Medication Non-Adherence:

Upon evaluation of the reasons for CKD medication non-adherence, high medication costs (51%) and toxicological concerns (12%) were the main reasons. Additionally, forgetfulness (47%), complex regimens (15%), and experiencing side effects (12%) were reasons for non-adherence. Feeling well without medication, lack of trust in the efficacy of medications, and physicians' mode of approach were the least common reasons for medication non-adherence.

Association of Socio-Demographic Characteristics with Medication Adherence:

Variables such as sex, age, occupation, education status, and yearly family income were included in the chi-square analysis. Based on the results, only age (P=0.001), occupation (P=0.000), and education status (P=0.002) of patients had a significant association with CKD medication adherence. The age group of ≤ 65 adhered more to medications than those above 65. Patients in occupations like teaching adhered more than retired patients and other occupations. Retired patients were less adherent. Patients who were educated had a significant association with their medication adherence and adhered more than those who cannot read/write.

Table 7: Chi-square test analysis for association between socio-demographic and adherence.

Variables	Level of Medication Adherence				
	Poor adherence	Medium adherence	High adherence	Chi-square test	P-value
Sex					
Male	48 (64.9%)	38 (45%)	44 (78.6%)	5.75	0.056
Female	26 (35.1%)	22 (55%)	12 (21.4%)		
Age in years					
≤65	52 (70.3%)	38 (95%)	56 (100%)**	13.41	0.001*
>65	22 (29.7%)**	2 (5%)	0		
Occupation					
Farmer	16 (21.6%)	4 (10%)	4 (7.1%)	35.26	0.000*
Govt. empoyee	2 (2.7%)	2 (5%)	6 (10.7%)		
Merchant/ trade	0	2 (5%)	4 (7.1%)		
Daily labourer	10 (13.5%)	8 (20%)	12 (21.4%)		
Housewife	16 (21.6%)	16 (40%)	12 (21.4%)		
Retired	30 (40.5%)**	8 (20%)	2 (3.6%)		
Others***	0	0	16 (28.6%)**		
Education status					
Can't read &write	56 (75.7%)**	24 (60%)	16 (28.6%)	21.14	0.002*
Primary	12 (16.2%)	12 (30%)	16 (28.6%)**		
Secondary	6 (8.1%)	2 (5%)	10 (17%)		
Higher Edu.	0	2 (5%)	14 (25%)		
Income(in years)					
No income	4 (5.4%)	4 (10%)	2 (3.6%)	6.27	0.393
Low(≤ 1akh)	24 (32.4%)	18 (45%)	12 (21.4%)		
Average(1-5lakh)	46 (62.2%)	18 (45%)	40 (71.4%)		
Above average	0	0	2 (3.6%)		

Note: *Statistically significant at P≤0.05, ***driver,teachers and students.

Co-Morbidities and Complications:

From the table, 158 (93%) of the participants had CKD co-morbidities, and 146 (86%) had CKD complications. Hypertension was the most common co-morbidity, present in 142 (84%) participants. Additionally, 64 (38%) participants had anaemia, and 80 (47%) had other CKD complications.

Table 8: Presence of co-morbidities and complications among CKD patients.

Variables	Frequency	Percentage
Co-morbidities		
Absent	12	7%
Present	158	93%
Specific Co-morbidities(n=79)		
Hypertension	142	84%
Diabetes mellitus	58	34%
Ichemic heart Disease	0	0%
Dyslipidemia	12	71%
Peripheral Vascular Disease	2	1%
Others*	12	71%
Complications		
Absent	24	14%
Present	146	86%
Specific Complications(n=73)		
CVD/Heart disease	4	2%
Osteodystrophy	32	19%
Anaemia	64	38%
Hyperkalaemia	24	14%
Fluid buildup/Edema	14	8%
Others**	80	47%

Note: * = Hypothyroidism, and COPD, ** = Gout, UTI, Hyperphosphatemia, pneumonia, AGE, Pulmonary edema, BPH, TB.

Management Practices for Co-Morbidities and Complications:

Pharmacological treatment for the management of CKD co-morbidities and complications was analyzed, focusing on toxicological safety and effectiveness.

Profile of Prescribed Medication:

Table 9 shows that calcium channel blocker, amlodipine, is prescribed in the majority of patients, accounting for 136 (80%). Diuretics, such as furosemide, were prescribed in 132 (78%) of patients. Antihypertensive beta-blocker (atenolol) was used in 86 (51%) of patients. Among haematinics, iron and folic acid were prescribed in 54

(32%) patients, and erythropoietin was used in 32 (18%) of patients. Insulin was used in 32 (18%) of patients. Analgesics, such as acetaminophen, were prescribed in 90 (53%) of patients.

Table 9: List of prescribed medication.

SN	Variables	Frequency	Percentages (%)
1	Angiotensin converting enzyme inhibitors	0	0%
2	Calcium channel blockers		
	Amlodipine	136	80%
	Nifedipine	8	5%
3	Diuretics		
	Furosemide	132	78%
	Torsemide	36	21%
4	Beta-blockers		
	Atenolol	2	1%
	Metoprolol	20	12%
	Carvedilol	16	9%
5	Angiotensin receptor blockers		
	Losartan	12	7%
6	Alpha-blockers		
	Prazosin	56	31%
7	Anti-diabetic		
	Insulin	52	31%
8	ASA (aspirin)	2	1%
9	Antibiotics	50	29%
10	Iron	110	65%
11	Erythropoietin	24	14%
12	Calcium formulation/supplements*	92	54%
13	Statins/Atorvastatin	12	7%
14	Febuxostat	24	14%
15	Others*	72	42%

Note: * = Sodium valporate, glicazide, linagliptin, metolazone, clopodogrel, levothyroxin sodium, clonidine, vitamin B6, propranolol, alfuzosin, salmetrol, theophylline, tamsulosin, sodium bicarbonate, sevelamer HCl, vitamin D, labetalol, lanthanum carbonate. Antibiotics; pyrazinamide, isoniazide, rifampicin, cefixime, ethambutol, cotrimazole, levofloxaxin, piperacillin & tazobactum, linezolid. Calcium supplements*: calcium + vitamin D & calcium formulations.

Adverse Drug Reactions and Toxicological Concerns:

Of the 170 patients, 42 reported experiencing at least one adverse drug reaction. Gastrointestinal disturbances, dizziness, and headaches were the most commonly reported adverse effects. Eight patients experienced potential drug interactions, emphasizing the need for careful medication management.

DISCUSSION

In the present study, different medications were used in the management of co-morbidities and complications of CKD. Amlodipine and furosemide were prescribed in 80% and 78% of CKD patients, respectively. Anti-hypertensive therapy remains the most effective strategy for slowing the progression of chronic kidney diseases. Some studies and various clinical guidelines stated the use of ACEIs and ARBs as the mainstays of hypertension treatment in CKD. But based on co-morbidities status, on-ACEI based combination were the most commonly used treatment regimens in the management of hypertension alone, which is in agreement with my study where highly non-ACEIs regimens were used.[10] There were no used of ACEIs based regimens in my study this might be because of the absence of concurrent albuminuria (albumin excretion > 300 mg/d), high potential risk of hyperkalaemia, and moreover it is not effective in the high blood pressure control.[11] Calcium channel blockers commonly amlodipine is used in combination as blood pressure control with or without diabetes mellitus in non-proteinuria patients.[12] Diuretics are frequently used as part of combination drug therapy in CKD and offer antihypertensive and cardio protective effects,also helps to decrease the fluid or volume overload.

The study assessed medication adherence in CKD patients, focusing on toxicological challenges. The majority of patients were on calcium channel blockers and diuretics, with amlodipine and furosemide being the most commonly prescribed drugs. Adherence rates were suboptimal, with only 32.9% of patients exhibiting high adherence. High medication costs, toxicological concerns, and complex regimens were significant barriers to adherence. Adverse drug reactions and potential drug interactions were identified, highlighting the need for improved medication management and toxicological monitoring.

The study's findings align with previous research, indicating that medication adherence in CKD patients is often suboptimal due to various factors, including high costs, complex regimens, and side effects. However, this study uniquely emphasizes the importance of toxicological considerations in adherence and management practices. To enhance adherence and minimize toxicological risks, healthcare providers should consider interventions such as patient education, simplified medication regimens, and regular monitoring for adverse effects. Addressing

high medication costs through financial support programs may also improve adherence.

CONCLUSIONS

The study highlights significant challenges in CKD management, including suboptimal medication adherence, toxicological concerns, and high costs. Addressing these issues through targeted interventions may improve patient outcomes and reduce the burden of CKD on healthcare systems.

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CONFLICT OF INTEREST: No

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