

# Evaluation of medication adherence and predictors of sub-optimal adherence among pre-dialysis patients with chronic kidney disease

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## Abstract

**Background:** Multiple medications are required to effectively manage chronic kidney disease (CKD) and associated complications, posing the risk of poor medication adherence.

**Objectives:** To measure medication adherence levels and to investigate the potential predictors of sub-optimal medication adherence in pre-dialysis patients with CKD.

**Methods:** A prospective study was conducted in the medical and nephrology outpatients' clinics in Maiduguri. Non-dialysis patients with CKD stages 1–4 aged 18 years and above were recruited through their physicians. The level of medication adherence was determined using Morisky Medication Adherence Scale. Descriptive statistics were used to summarize patients' background characteristics. Multivariate binary logistic regression analyses were performed to investigate the significantly potential predictors of sub-optimal medication adherence at a  $p < 0.05$ .

**Results:** There were 107 participants (48.6%) who had high medication adherence, while 97 (44.1%), and 16 (7.3%) of them had moderate adherence, and low adherence, respectively. The univariate analysis revealed that medication adherence level differed significantly with the number of medications taken daily by patients ( $p < 0.05$ ). Multivariate logistic regression analyses did not reveal a significant independent predictor of sub-optimal medication adherence.

**Conclusion:** A majority of the participants reported sub-optimal medication adherence. The independent variables considered did not significantly predict sub-optimal medication adherence in the study population. Nevertheless, the study findings highlight the importance of clinical pharmacists' CKD management supportive care to help improve medication adherence.

## Keywords

Chronic kidney disease, end-stage renal disease, medication adherence, Nigeria, pharmacists

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## Introduction

Chronic kidney disease (CKD) is a growing threat to global public health with increasing incidence and prevalence worldwide. It is reported that 10.0% of the world population is affected by this disease.<sup>1</sup> The overall prevalence of CKD in Africa is between 10.7% and 15.8%,<sup>2,3</sup> while that of Nigeria range from 10.0% to 13.2%.<sup>4</sup> CKD is a debilitating disease with poor health-related quality of life (HRQoL) as one of the adverse health outcomes.<sup>5–8</sup> A high number of medications are required to effectively manage this disease and associated complications, posing the risk of poor medication adherence.

Adherence to medication is defined as ‘the extent to which the patient’s behaviour matches agreed recommendations from the prescriber’.<sup>9</sup> Medication adherence is a key component of effective CKD management.<sup>10,11</sup> The ultimate goals of medication are to retard CKD progression and control its associated complications and comorbidities while treating the underlying ailments.<sup>11</sup> A recent study reported that good medication adherence rates in the pre-dialysis patients with CKD ranged from 33.0% to 87.7%.<sup>12</sup> Varied good medication adherence rates have been reported in some developed countries, such as the United States (33%–75.6%),<sup>13</sup> Canada (87.7%)<sup>14</sup> and Australia (57.4%).<sup>15</sup> Similarly, different adherence rates have also been reported in resources-constrained countries such as Brazil (73.2%),<sup>16</sup> Ethiopia (61.3%),<sup>17</sup> and Kenya (84.5%).<sup>18</sup>

Adherence to medications remains a major issue among patients with CKD because routine management of multiple medications is a challenging task. Hence, patients with CKD may miss their medications, intentionally or unintentionally.<sup>9</sup> Condition-related factors (such as advanced CKD), patient-related factors (misconception about medication and lack of perceived self-efficacy in medication use), therapy-related factors (such as polypharmacy), health system-based factors (such as loss of confidence in physicians) and socio-economic factor (poor social support and lower education level) have been reported to be responsible for poor medication adherence in pre-dialysis patients with CKD.<sup>12</sup>

Poor medication adherence has varying degrees of impact on patient prognosis and progression. It poses a major obstacle to achieving treatment goals and ultimately increases the risk of morbidity, hospitalization, and mortality.<sup>11,19</sup> Some studies conducted in resources-constrained countries such as India, Thailand, and Nigeria highlighted that poor medication adherence leads to negative clinical outcomes.<sup>20–22</sup> Hence, optimizing medication adherence in patients with CKD is a priority issue for healthcare providers.

Addressing poor medication adherence requires identification of the predictors, so that stronger emphasis can be placed on such specific factors or a select group of patients to improve adherence. This strategy may help in eliminating or minimizing the associated factors to non-adherence and decrease morbidity, hospitalization, and mortality burden of the disease.

Studies that evaluate medication adherence among patients with CKD in Nigeria are scarce. The paucity of such evidence among pre-dialysis patients with CKD in Nigeria justifies the need for this study. This study was, therefore, conducted to measure medication adherence level and to investigate the potential predictors of sub-optimal medication adherence in pre-dialysis patients with CKD. This type of study is apt in resource-limited countries, including Nigeria where the outcomes of poor medication adherence in CKD could be graver compared to developed economies.

## Methods

### Study design and settings

A baseline prospective, hospital-based study was conducted in the medical and nephrology outpatients’ clinics of major secondary and tertiary hospitals in Maiduguri, Borno State, Nigeria.

### Sample size calculation

The sample size was estimated using Raosoft® online sample size calculator,<sup>23</sup> assuming CKD prevalence of 13.2% in the state with an estimated population size of 6,713,792 people,<sup>24</sup> at a 5% margin error and 95% confidence interval. The minimum sample size for the study was 177 patients.

### Participants

The study population comprised all patients with CKD that received care at the study settings from November 2019 to February 2020. The inclusion criteria were patients aged 18–85 years at CKD stages 1–4 (based on a single estimated glomerular filtration rate (eGFR) values of 90–15 mL/min/1.73 m<sup>2</sup> for 3 months prior to enrolment) and not receiving renal replacement therapy, agreed to provide informed consent and absence of cognitive deficit.

The exclusion criteria included acute kidney injury diagnosis, patients currently receiving dialysis, refusal to participate in the study, presence of cognitive impairment, and CKD stage 5. Patients with CKD stage 5 were excluded because this preliminary study was designed to inform interventional study with a view to optimize medication adherence and halt or retard CKD progression. The eGFR values were determined using the online eGFR calculator developed by the National Kidney Foundation based on the modified diet for renal disease (MDRD) study equation.<sup>25</sup>

### Study instrument

The study instrument used was Morisky, Green, and Levine (MGL) Medication Adherence Questionnaire.<sup>26</sup> Permission to use the MGL Medication Adherence Questionnaire was obtained from the developers. This instrument has high

reliability and validity for assessing patient adherence. Response categories were dichotomized ('yes' or 'no') for each item. The questionnaire was itemized to determine forgetfulness behaviour in taking medications, carelessness in medication-taking, stopping medication when feeling better, and if a patient stops taking the medication when feeling worse. The response was scored as follows: a 'yes' response was scored 1 point and 0 to a 'no' response. The total score ranged from 0 to 4. Adherence levels were then categorized into three based on the total score. A score of 0, 1–2, and 3–4 were classified as high adherence, moderate adherence, and low adherence, respectively.

### Ethical approval and informed consent

The Health Research and Ethics committee of the University of Maiduguri Teaching Hospital and Ethics committee of the State Specialist Hospital granted ethical approval for the study with approval numbers UMTH/REC/18/234 and SSH/GEN/641/Vol. I. Prior to data collection, all potential participants were informed about the study objectives, assured of confidentiality and anonymity of information collected, and their right to refuse to participate in the study. Those who agreed to participate in the study provided written informed consent.

### Data collection

The study instrument (MGL Medication Adherence Questionnaire) was used to collect data in the clinic after patients' consultations with the physicians over a 4-month period. The study instrument was administered to those proficient in English language by a research assistant, while interviewer-assisted administration in the Hausa language was used by two research assistants for those with informal or without any form of education. The data collected included socio-demographics, the number of drugs taken, co-morbidities, blood pressure (BP) values, creatinine values, and medication adherence information.

### Data analysis

Data were summarized using descriptive statistics (frequency, percent, mean and standard deviation). Chi-square was used to determine variables associated with sub-optimal medication adherence. The point-biserial correlations ( $r_{pb}$ ) were used to evaluate the strength of relationships between independent variables and adherence scores.

Categorical variables were coded thus: age (<65 years=0 and  $\geq$ 65 years=1); gender (male=0 and female=1), marital status (single=0 and married=1), occupation (unemployed=0 and employed=1); religion (Islam=0 and Christianity=1); health insurance coverage (no=0 and yes=1); educational status (uneducated=0 and

educated=1); BP level (<130/80 mmHg=0 and  $\geq$ 130/80 mmHg=1); CKD stage (stages 1–2=0 and stages 3–4=1); comorbidities (absent=0 and present=1); number of daily medications (<5=0 and  $\geq$ 5=1) and adherence levels (high adherence=0 and sub-optimal adherence (low and moderate adherence)=1).

All variables with  $p$  values less than 0.2 in the univariate analysis were included in the multivariate logistic regression analysis using the enter method to investigate the potential predictors of sub-optimal medication adherence. A  $p$ -value of less than 0.05 was considered statistically significant. Statistical analyses were performed using SPSS version 21 (IBM Corp., Armonk, NY, USA).

## Results

Of the 230 eligible patients that were invited to participate in the study, 220 (95.7%) of them agreed to participate and were subsequently recruited. The mean age of the participants was  $52.7 \pm 12.4$  years, ranging from 19 to 81 years. Of these participants, 135 (61.4%) were females and 186 (84.5%) were married. A majority (66.8%,  $n=147$ ) of them were of Islamic faith, and at CKD stages 3–4 (95.0%,  $n=209$ ). The mean BP value was  $137.9 \pm 21.7$  mmHg systolic and  $84.7 \pm 12.9$  mmHg diastolic, while the average number of medications taken daily by a participant was  $5 \pm 1.1$ . Hypertension (77.7%,  $n=171$ ) was the most predominant comorbidity among the study population. The detailed background information of the participants is presented in Table 1.

Overall, 51.4% of participants reported sub-optimal medication adherence as shown in Figure 1.

Table 2 shows that the medication adherence level differed significantly with the number of medications taken daily by patients ( $p < 0.05$ ).

The results of the correlation analysis showed negative relationships between BP level ( $r_{pb} = -0.029$ ,  $p = 0.674$ ), CKD stage ( $r_{pb} = -0.073$ ,  $p = 0.281$ ), comorbidities ( $r_{pb} = -0.044$ ,  $p = 0.958$ ), the number of daily medications taken by a patient ( $r_{pb} = -0.069$ ,  $p = 0.311$ ) and adherence score, though none of these independent variables reached statistically significance level (Table 3).

The multivariate logistic regression analysis shows that females (adjusted odds ratio (AOR): 1.53; 95% confidence interval (CI): 0.88–2.68) and Christian patients (AOR: 1.62; 95% CI: 0.91–2.90) were more likely to be non-adherent compared to males and Islamic patients. Although no significant association was achieved (Table 4).

## Discussion

The sub-optimal medication adherence rate obtained in our study demonstrates that a huge proportion of the participants were struggling with medication adherence. Contrary to our results, a lower rate of 32.9% was reported in the

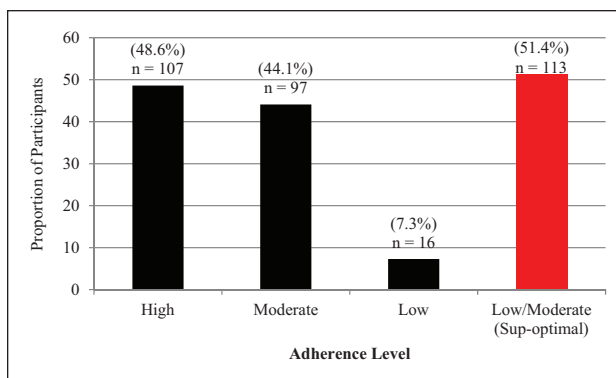
**Table 1.** Background information of the participants (n = 220).

Variable	n (%)
Age (years)	
<65	182 (82.7)
≥65	38 (17.3)
Gender	
Male	85 (38.6)
Female	135 (61.4)
Marital status	
Single	34 (15.5)
Married	186 (84.5)
Occupation	
Unemployed	78 (35.5)
Employed	142 (64.5)
Religion	
Islam	147 (66.8)
Christianity	73 (33.2)
Educational level	
Uneducated	66 (30.0)
Educated	154 (70.0)
Health insurance coverage	
No	190 (86.4)
Yes	30 (13.6)
Blood pressure level (mmHg)	
≤130/80	101 (46.0)
>130/80	119 (54.0)
CKD stage	
1–2	11 (5.0)
3–4	209 (95.0)
Comorbidities	
Hypertension	171 (77.7)
Diabetes mellitus	7 (3.2)
Asthma	3 (1.4)
Chronic pyelonephritis	2 (0.9)
Prostate hyperplasia	2 (0.9)
Congestive heart failure	1 (0.5)
Hyperthyroidism	1 (0.5)
Peptic ulcer disease	1 (0.5)
Seizure disorder	1 (0.5)
Sickle cell disease	1 (0.5)
Number of drugs taken daily	
<5	83 (37.7)
≥5	137 (62.3)

CKD: chronic kidney disease.

United States among pre-dialysis CKD patients,<sup>27</sup> while 38.7% was reported among all ambulatory patients with CKD in Ethiopia.<sup>17</sup> In addition, an Indian study reported a much higher baseline sub-optimal medication adherence rate of 91.4% among patients with CKD stages 3–5.<sup>28</sup>

Similarly, studies conducted in India that enrolled both pre-dialysis and dialysis CKD patients also reported much higher sub-optimal medication adherence rates ranging from 78.0% to 98.5%.<sup>16,29–32</sup> Variation in the methods of assessments, study populations, level of information or education received from healthcare personnel and other patient-related factors could account for this difference.

**Figure 1.** Distribution of participants according to medication adherence level.

Studies have shown that sub-optimal medication adherence is associated with heightened risk for CKD progression.<sup>27</sup> This underscores the need for appropriate interventions by renal healthcare providers, especially clinical pharmacists to improve medication adherence in this high-risk group of patients.

Comparing our results with that of the dialysis CKD population revealed that high proportions of patients on dialysis exhibited much higher sub-optimal medication adherence.<sup>33,34</sup> These much higher sub-optimal medication adherence rates in the dialysis CKD population might be connected with polypharmacy, because some of these patients may take as high as 19 medications daily.<sup>35</sup> It is worthy to note that higher sub-optimal medication adherence rates than the results of the current study have been reported in other disease conditions, such as psychiatric illness,<sup>36</sup> gout,<sup>37</sup> diabetes mellitus,<sup>38</sup> and hypertension.<sup>39</sup> Cognitive impairment of patients with psychiatric illnesses and self-perceived mildness of other disease conditions could be responsible for these higher rates.

Furthermore, the multivariate analysis of the association between medication adherence level and independent variables revealed no significantly negative associations. These findings suggest that gender, religion, BP level, number of comorbidities, and the number of medications did not have a substantial effect on a patient's medication adherence. In agreement with the findings of some previous studies that enrolled pre-dialysis patients with CKD,<sup>15,16</sup> increasing number of medications were not associated with worse adherence.

In summary, our study results suggest that pre-dialysis patients with CKD generally have sub-optimal medication adherence and socio-demographic factors, comorbidities, and medication regimen did not affect their ability to adhere to their medications.

### Limitations

The main limitation of the current study was that self-report as a tool for measuring medication adherence has been associated with over-estimation of adherence. Therefore, further study using a multi-method approach that combines feasible

**Table 2.** Association between medication adherence level and participants' characteristics (n = 220).

Variable	Adherence level, n (%)		p value
	High (n = 107)	Sub-optimal (n = 113)	
Age (years)			
<65	89 (83.2)	93 (82.3)	0.863
≥65	18 (16.8)	20 (17.7)	
Gender			
Male	46 (43.0)	39 (34.5)	0.197
Female	61 (57.0)	74 (65.5)	
Marital status			
Single	18 (16.8)	16 (14.2)	0.585
Married	89 (83.2)	97 (85.8)	
Occupation			
Unemployed	35 (32.7)	43 (38.1)	0.408
Employed	72 (67.3)	70 (61.9)	
Religion			
Islam	78 (72.9)	69 (61.1)	0.062
Christianity	29 (27.1)	44 (38.9)	
Health insurance coverage			
No	95 (88.8)	95 (84.1)	0.308
Yes	12 (11.2)	18 (15.9)	
Educational level			
Uneducated	34 (31.8)	32 (28.3)	0.576
Educated	73 (68.2)	81 (71.7)	
BP level (mmHg)			
≤130/80	44 (41.1)	57 (50.4)	0.166
>130/80	63 (58.9)	56 (49.6)	
CKD stage			
1–2	5 (4.7)	6 (5.3)	0.829
3–4	102 (95.3)	107 (94.7)	
Comorbidities			
Absent	19 (17.8)	26 (23.0)	0.334
Present	88 (82.2)	87 (77.0)	
Number of drugs taken daily			
<5	33 (30.8)	50 (44.2)	0.040*
≥5	74 (69.2)	63 (55.8)	

BP: blood pressure; CKD: chronic kidney disease.

\*Chi-square test significant at  $p < 0.05$ .

**Table 3.** Correlation analysis of the independent variables and medication adherence score.

Variable	Age	Gender	Marital status	Occupation	Religion	Insurance coverage	Education	BP	CKD stage	Comorbidities	Number of daily medications
Adherence											
Point-biserial correlation ( $r_{pb}$ )	0.004	0.043	0.046	0.010	0.089	0.035	0.027	-0.029	-0.073	-0.044	-0.069
p value	0.958	0.528	0.494	0.887	0.190	0.609	0.695	0.674	0.281	0.513	0.311

BP: blood pressure; CKD: chronic kidney disease.

self-reporting and reasonable objective measurement of adherence behaviour should be carried out. In addition, only

two centres were used for the study, so the study findings cannot be generalized to other settings.

**Table 4.** Multivariate logistic regression analyses results of predictors of sub-optimal medication adherence.

Independent variable	AOR (95% CI) <sup>a</sup>	p value
Gender		
Male	1.00	
Female	1.53 (0.88–2.68)	0.136
Religion		
Islam	1.00	
Christianity	1.62 (0.91–2.90)	0.103
Blood pressure (mmHg)		
< 130/80	1.00	
≥ 130/80	0.93 (0.47–1.82)	0.822
Number of daily medications		
< 5	1.00	
≥ 5	0.60 (0.30–1.20)	0.150

Dependent variable = medication adherence. AOR: adjusted odds ratio; CI: confidence interval.

<sup>a</sup>Sub-optimal (low + moderate adherence = 1 vs. high adherence = 0).

## Conclusion

The study shows that a majority of the participants self-reported sub-optimal adherence to their medications. This finding highlights the heightened need for clinical pharmacists to be encouraged to provide CKD management supportive care to build rapport with patients with sub-optimal medication adherence to optimize their medication adherence and avert adverse renal outcomes.

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## Authors' contributions

R.N.O has full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Acquisition and analyses were done by R.N.O. Interpretation of the data was performed by I.U., J.D.O., S.I.Y., M.O.A., and M.J.O. Supervision was performed by M.O.A and M.J.O. Drafting of the manuscript was performed by R.N.O. Study concept, design, and critical revision of the manuscript for important intellectual content were performed by all authors. All authors read and approved the final manuscript.

## Availability of data and materials

The data set generated and/or analysed during the current study is available from the corresponding author upon reasonable request.

## Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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