

Medication non-adherence in chronic kidney disease patients using Modified Morisky Adherence Scale (MMAS-8)

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ABSTRACT

Background: Chronic kidney disease (CKD) requires long-term medication to slow disease progression and prevent complications; however, treatment complexity, polypharmacy, socioeconomic factors, and disease-related factors can contribute to poor medication adherence. This study assessed medication adherence among patients with CKD and its relationship with selected demographic and clinical variables using the 8-item Modified Morisky Medication Adherence Scale (MMAS-8).

Methods: This Descriptive Cross-Sectional Study was performed in Nephrology Department of Khyber Teaching Hospital, Peshawar. One hundred and fifty-one patients with diagnosed CKD, aged 17-60 years were recruited by consecutive sampling. Demographic and clinical data, such as sex, age, education, income status, CKD stage, diabetes mellitus, hypertension, and the number of medications taken per day was collected. The MMAS-8 medication adherence questionnaire was used to determine medication adherence. Data were analyzed using SPSS version 20. Descriptive statistics, Chi-square/Fisher's exact tests, Mann-Whitney U tests and binary logistic regression analyses were conducted.

Results: 151 people participated, 93 (61.6%) were classified as medication non-adherent and 58 (38.4%) were adherent. There was a significant association of medication non-adherence with hypertension ($p=0.027$). The number of medications taken per day was the most significant correlate of non-adherence ($p<0.001$). Medication burden was found to be a significant predictor of medication non-adherence when logistic regression analysis was performed ($OR=1.57$; $p<0.001$).

Conclusion: Patient non-compliance with medications is a well-recognized issue with CKD patients. Adherence screening, counselling with the patient, and optimizing medication regimens might help improve adherence and aid in better management of CKD and clinical outcomes.

Keywords: Medication Adherence, Patient Compliance, Polypharmacy, Renal Insufficiency

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Introduction

Chronic kidney disease (CKD) is a significant public health problem because of the high morbidity, mortality and healthcare burden,

along with progressive clinical course and increasing prevalence in the world. CKD is defined as abnormalities of kidney structure or function that last for at least three months, and is linked to other health problems that occur over a long time. The prevalence of CKD has also been on the rise, affecting millions of people across the world, including the

majority of the world's population in low and middle-income countries where there is often a delay in diagnosis and limited access to renal care, which leads to poor outcomes of the disease (1,2). Loss of kidney function, which is often measured by estimated glomerular filtration rate (eGFR), has a strong correlation with worsening cardiovascular morbidity, hospitalization, end-stage kidney disease (ESKD) and early death (3).

There is a need for comprehensive and sustained care of CKD including pharmacologic intervention, diet changes, and lifestyle changes, management of blood pressure, glycemic control, and periodic review with a health care provider. Of these, medication compliance is deemed to be critical in slowing disease progression and minimizing complications. Good medication adherence will ensure optimal management of hypertension, diabetes, proteinuria and other risk factors for CKD, which minimizes the risk of worsening of renal function and the requirement for renal replacement therapy⁴. Although the management of CKD has improved, there is still a major problem with medication compliance and adherence in patients with CKD (5).

Medication non-adherence is defined as the non-compliance of patients with their medications according to the physician's prescriptions and/or instructions on dosage, time, or frequency. Failure to adhere to treatment in CKD patients can have detrimental impacts on treatment efficacy, disease progression, emergency room visits, and health care expenditure. Multiple medications are usually prescribed for CKD and must be taken for an extended period of time, making it difficult to adhere to treatment. Some of the causes of medication adherence are polypharmacy, adverse drug effects, socioeconomic problems, insufficient

education of patients, no knowledge about disease severity, psychological problems and poor access to healthcare (5,6). Recent studies have shown that non-adherence to medications is still a significant problem in CKD patients and that the early identification of non-adherent patients and the creation of effective strategies to improve adherence are important (7).

Therefore, evaluating adherence to medication is an important aspect of CKD care. A variety of strategies have been devised for assessing adherence, such as electronic monitoring systems, pharmacy refill records, and patient-reported questionnaires. Objective methods are useful, but are often costly and not readily available in day-to-day clinical practice. Self-reported adherence tools are still common, as they are easy to use, inexpensive and feasible for hospital-based studies⁸. Of these tools, the Morisky Medication Adherence Scale (MMAS-8), which has 8 items, is one of the most commonly used scales to evaluate medication-taking behavior in people with chronic conditions such as CKD (9).

The MMAS-8 measures various aspects of medication taking behavior, such as medication forgetting, carelessness, medication interruption, and medication adherence problems. It is easy to use and has a clear scoring system to help healthcare professionals identify patients who may be low adherers and act to support them. In the last few years, the reliability and validity of MMAS-8 have been assessed in various populations, thus reinforcing its potential as an adherence assessment tool for practical use (10). Although no gold standard tool is currently accepted, a recent systematic review of medication adherence measurement tools among CKD patients indicated that MMAS-8 is one of the most common methods for

measuring adherence because of its feasibility and acceptable psychometric properties (11). Medication adherence has been growing in research interest in the context of CKD. Inadequate adherence can lead to reduced management of the complications of the disease, and higher healthcare utilization. Moreover, understanding those factors that challenge adherence can help the clinician tailor a special intervention such as patient education, medication counseling, and better follow-up plans (12). The recent studies show that combining information from patient-reported adherence measures with other clinical parameters might give a more comprehensive picture of the patients' adherence to the treatment (13).

Diabetes mellitus, hypertension, lack of awareness and difficulty in providing access to specialized renal service are the factors which have made CKD an emerging problem in health care in Pakistan. The adherence to treatment is important when considering treatment success, as patients presenting at tertiary care centers will often be poly pharmacological and have numerous comorbidities. However, there are scarce local data on medication non-adherence measured by the commonly used medication adherence assessment tool, the MMAS-8, in patients with CKD. Because of this, knowledge of the prevalence and associated factors of medication non-adherence in this population could assist the health care provider in developing an appropriate strategy to increase medication adherence and patient outcomes (14,15).

Hence, the present study was designed to evaluate medication adherence in patients suffering from chronic kidney disease by Modified Morisky Medication Adherence Scale-8 (MMAS-8). The proportion of CKD patient that are non-adherent to medication

will be determined and its relationship with other selected demographic and clinical variables. The results of this research will help identify patients' medication-taking habits and can help guide patient counselling, treatment adherence strategies, and overall management of patients with CKD in the clinical setting (16).

Hence, the current study was undertaken to evaluate the adherence to the medication among the chronic kidney disease patients with Modified Morisky Medication Adherence Scale-8 (MMAS-8). The objectives of the study were to find out the prevalence of non-adherence to medication among the CKD patients and to correlate the non-adherence with some demographic and clinical factors such as age, gender, education, socioeconomic status, stage of CKD, presence of comorbidities, and number of the medications taken per day. The results from this study could help to understand the behaviour regarding medication use by those with CKD and guide healthcare workers to find out the challenges of adherence and to create personal counselling sessions and help improve long-term management of the disease and patient outcomes.

Methods

The department of Nephrology Khyber Teaching Hospital, Peshawar was selected for this study which was descriptive cross-sectional study based in hospital. The aim of the study was to evaluate the level of adherence to medication among patients with chronic kidney disease (CKD) using Modified Morisky Medication Adherence Scale-8 (MMAS-8). This study was carried out with the approval of relevant institutional ethical committee and also the relevant authorities. All participants gave informed consent. All participant information was treated as

confidential and data collected were only used for research purposes.

This study took place for six months following ethical approval (Ref: 995/DME/KMC). Patients who were eligible and attending the nephrology department were assessed and enrolled during the study period according to the pre-defined eligibility criteria.

The sample size calculation method used was the WHO. Based on the previously reported prevalence of medication non-adherence among patients with CKD of 74% and a 95% confidence interval of 7%, the number of participants for the study was calculated to be 151. The population was sampled using non-probability consecutive sampling technique. The patients who attended nephrology OPD at the study period and fulfilled the eligibility criteria were consecutively recruited until the sample size of the study was reached.

The patients attending the Department of Nephrology, Khyber teaching hospital, Peshawar with diagnosis of chronic kidney disease were studied. Chronic kidney disease was labelled as kidney abnormality and/or function abnormality that lasts for more than three months and has effects on health. Clinical history, previous medical records and laboratory investigations, including estimation of glomerular filtration rate, confirmed a diagnosis of CKD.

Patients who met the predetermined inclusion criteria were included in the study. The study population included patients with diagnosed chronic kidney disease (CKD) based on the operational definition. Patients aged 17-60 years, both male and female, were included. Those who met the inclusion criteria and gave informed consent were included in the study. Patients were excluded if they had a condition that would interfere with assessing adherence or completion of the study questionnaire. Those who had a history of Alzheimer's

disease, previous stroke, bipolar disorder and major depression were excluded. Patients who had a terminal illness or palliative care were also excluded. In addition, patients with severe malnutrition, amputation, paraplegia were excluded.

After obtaining ethical approval, written informed consent was obtained from all participants before data collection. Each participant was informed about the purpose and procedure of the study and confidentiality. Information was gathered on a proforma which was structured to include demographic, clinical and medication-related information. Demographic factors were age, gender, educational status, and the monthly income, and clinical factors were body weight, height, body mass index (BMI), blood pressure, diabetes mellitus status, hypertension status, and number of drugs taken per day. Patients' history, medical records and investigations confirmed CKD status. All participants completed a Modified Morisky Medication Adherence Scale-8 (MMAS-8) and answers were noted using the modified scoring system.

The Modified Morisky Medication Adherence Scale-8 (MMAS-8) was used to measure medication adherence. The scale includes 8 questions to assess medication-taking behavior, such as forgetfulness, disturbance of medication adherence, inconvenience due to treatment and problems of maintaining medication adherence. The total MMAS-8 score was determined by the scoring guidelines. Patients with an MMAS-8 score above 3 were considered as medication non-adherent and those with a score below 3 were considered adherent.

The main dependent variable in the study was the patient's compliance with drug therapy in CKD. Independent variables were demographic and clinical variables: age, sex,

educational status, monthly income, weight, BMI, hypertension, diabetes mellitus, and number of medicines per day. The association between these variables and the medication adherence status was evaluated.

Data were entered and analyzed using Statistical Package for the Social Sciences (SPSS), version 20. The normality of continuous variables was assessed using the Shapiro-Wilk test. Normally distributed continuous variables were presented as mean $\pm$ standard deviation (SD), while non-normally distributed variables were presented as median with interquartile range (IQR). Categorical variables were presented as frequencies and percentages. The Chi-square test or Fisher's exact test was used, as appropriate, to assess associations between medication non-adherence and categorical demographic and clinical variables. The Mann-Whitney U test was used to compare continuous variables between adherent and non-adherent groups. Binary logistic regression analysis was performed to identify independent predictors of medication non-adherence, with results expressed as odds ratios (ORs). A p-value ≤ 0.05 was considered statistically significant. Results were presented in tables and appropriate graphical representations.

Results

Demographic and clinical features of 151 CKD patients included in the study are shown in Table 1. The mean age of participants was 38.9 ± 12.4 years reflecting the presence of younger and middle aged CKD patients. There were a slightly higher number of males than females in the study population. This suggests possible socioeconomic problems among CKD patients as more than 50% of the participants had an educational level below matriculation and were among the lower

income category. In terms of clinical features, the highest prevalence of the disease level was observed in Stage 3 CKD, followed by Stage 4 and Stage 5 CKD. Hypertension was the most common comorbidity and around half had diabetes mellitus. The mean number of meds taken daily indicated a high medication burden for CKD patients, which can make it harder for patients to adhere to their meds.

Table 1. Baseline Characteristics of Study Participants

Variable	Category	n (%) / Mean $\pm$ SD
Age (years)	Mean $\pm$ SD	38.9 ± 12.4
Gender	Male	85 (56.3%)
	Female	66 (43.7%)
Education level	Matric or above	68 (45.0%)
	Less than matric	83 (55.0%)
Monthly income	<50,000 PKR	98 (64.9%)
	>50,000 PKR	53 (35.1%)
CKD stage	Stage 3	68 (45.0%)
	Stage 4	53 (35.1%)
	Stage 5	30 (19.9%)
Diabetes mellitus	Yes	73 (48.3%)
	No	78 (51.7%)
Hypertension	Yes	94 (62.3%)
	No	57 (37.7%)
Weight (kg)	Mean $\pm$ SD	66.3 ± 11.7
BMI (kg/m ²)	Mean $\pm$ SD	24.5 ± 4.2
Daily medications	Mean $\pm$ SD	5.1 ± 1.9
MMAS-8 score	Mean $\pm$ SD	3.8 ± 1.6

Table 2 shows the distribution of medication adherence status of the CKD patients according to MMAS-8 classification. Of 151 patients, 93 (61.6%) were considered to be medication non-adherent, while 58 (38.4%) patients were considered to be adequately adherent to their medications. The results showed that the adherence rate to medications was very high among CKD patients, which means that a large number of patients might have difficulties in taking medications

regularly. In conclusion, the high level of non-adherence among patients indicates that it is essential to regularly assess and intervene with those who do not adhere to treatment in a CKD setting.

Table 2. Prevalence of Medication Non-Adherence According to MMAS-8

Medication adherence status	Frequency	Percentage
Adherent	58	38.4%
Non-adherent	93	61.6%
Total	151	100%

As shown in Figure 1, there are more patients with good adherence than those with poor adherence. As illustrated in the figure, there was a higher prevalence of medication non-adherence than adherence, with around 66% of the participants being classified as medication non-adherent. The result suggests that adherence to medication-taking is still a

big problem in patients with CKD who need long-term treatment.

Table 3 shows the association between demographic and clinical features and non-adherence to medication in patients with CKD. The only variable that had a statistically significant association with the assessed variables was hypertension, which was associated with a higher likelihood of having medication adherence difficulties ($p=0.027$). There was no statistically significant association found between educational level, monthly income, gender, stage of the CKD, and diabetes mellitus and medication adherence. There was, however, a tendency for the association between CKD stage and diabetes mellitus, which indicates that disease severity and burden of disease may be associated with medication adherence. These results suggest there are many clinical and social factors which have an interactive effect on adherence to medication.

Table 3. Association of demographic and clinical factors with medication non-adherence

Variable	χ^2	p-value	Crude OR (COR)	95% CI	Adjusted OR (AOR)	95% CI	p-value
Gender	1.018	0.313	0.72	0.38–1.36	0.63	0.30–1.32	0.248
Education level	2.346	0.126	0.61	0.33–1.14	0.47	0.21–1.03	0.061
Monthly income	1.095	0.295	0.78	0.41–1.49	0.82	0.39–1.73	0.604
CKD stage	5.339	0.069	—	—	—	—	—
Stage 3			Reference		Reference		
Stage 4			0.58	0.29–1.17	0.46	0.19–1.10	0.086
Stage 5			1.21	0.53–2.77	1.75	0.57–5.36	0.332
Diabetes mellitus	2.962	0.085	0.59	0.31–1.11	0.44	0.19–1.02	0.052
Hypertension	4.870	0.027	0.50	0.26–0.95	0.43	0.19–0.97	0.045
Age (years)	—	—	1.00	0.98–1.03	0.999	0.97–1.03	0.974
BMI (kg/m ²)	—	—	1.01	0.96–1.06	0.997	0.95–1.05	0.945
Daily medications	—	<0.001	1.48	1.22–1.80	1.57	1.25–1.97	<0.001

Note: OR, odds ratio; COR, crude odds ratio; AOR, adjusted odds ratio; CI, confidence interval; BMI, body mass index; CKD, chronic kidney disease. Reference categories are indicated. COR represents univariable logistic

regression estimates, whereas AOR represents estimates from the multivariable binary logistic regression model.

Continuous variables were compared between adherent and non-adherent CKD

patients and are shown in Table 4. The analysis showed that patients identified as being medication non-adherent have significantly more number of medications to take daily ($p<0.001$). This indicates that higher medication burdens could adversely affect adherence behavior, and make the regimen more complex, as well as decreasing the patient's ability to keep up with medication schedules. There were no significant differences in age and BMI between adherence groups. As predicted, there was a significant difference between the MMAS-8 scores for the two groups ($p<0.001$), supporting the validity of classification using the adherence classification method.

Table 4. Comparison of Continuous Variables between Adherent and Non-Adherent Groups

Variable	Mann-Whitney U	p-value
Age	2527.0	0.786
BMI	2684.5	0.982
Daily medications	1574.0	<0.001
MMAS-8 score	0.0	<0.001

The distribution of CKD stages among participants is shown in figure 2. Most patients were in stage 3 (44%), stage 4 (39%) and stage 5 (20%) of the disease. The presence of patients in all stages of advanced CKD suggests that many patients needed multiple treatment regimens, which could lead to increased medication burden and adherence issues.

The distribution of MMAS-8 adherence scores for study participants is shown in Figure 3. The distribution shows there is variation in medication-taking behaviour, with a significant proportion of patients having higher MMAS-8 scores, indicating poorer adherence. The results reveal an individual adherence pattern imbalance, and indicate the importance of individualized adherence improvement strategies.

The logistic regression analysis to determine independent predictors of medication non-adherence was conducted and is displayed in table 5. The analysis showed that number of medications per day ($p<0.001$, $OR=1.57$) was a significant predictor of medication non-adherence. This means that for every extra drug taken there was a higher chance that the person would engage in poor adherence behaviour. Medication non-adherence was also significantly associated with hypertension ($OR=0.43$, $p=0.045$). The following factors were not statistically significant independent predictors: age, BMI, gender, CKD stage, diabetes mellitus, and education. These findings underscore the complexity of the medications as an important factor affecting adherence in patients with CKD.

The MMAS-8 scores for each number of daily medications are shown in Figure 4. As there is an upward trend, a greater number of medications taken tended to be associated with poorer adherence behavior, as measured by MMAS-8 scores. This discovery validates the hypothesis that polypharmacy and treatment complexity may be significant factors hindering adherence to treatment among CKD patients.

The odds ratio of various factors associated with the non-adherence to medications is presented in figure 5. Figure shows that the highest association with poor adherence behavior was medication burden. Other clinical parameters such as hypertension, diabetes, and educational status had different degrees of association. The results highlight the need for considering treatment complexity and patient characteristics to design intervention to enhance medication adherence.

Discussion

Adherence to medications is an important factor in the successful treatment of chronic kidney disease (CKD) because the progression of this condition and its complications can be controlled with long-term pharmacological therapy. The aim of the present study was to use the Modified Morisky Medication Adherence Scale-8 (MMAS-8) to assess medication non-adherence in patients with CKD. The results showed that a significant number of patients were found to be medication non-adherent and indicated that the issue of patients taking their medications optimally remains a big problem in CKD population. The percentage of patients not taking medication, as observed, is similar to what is found in previous studies of medication adherence among patients with kidney disease. An umbrella review published recently stated that CKD patients have a significant medication-related burden because of complex medication regimens, the presence of multiple comorbidities, and the need for long-term treatment. Non-adherence to medicines is a central theme in the review as it plays a role in suboptimal disease control, greater health service use, and poorer health outcomes (17). Likewise, Wu et al. reported that there was a high level of non-adherence to medications among patients with CKD and factors associated with medication non-adherence included socioeconomic factors and patient-related barriers and medication burden (18). The results of this study reinforce the need to routinely evaluate medication adherence in nephrology care.

Medication non-adherence was significantly related to the number of medications in the present study. The clinical relevance of this finding is that there are multiple drugs that are used for controlling blood pressure, managing diabetes, providing cardiovascular

protection, managing anemia and managing mineral bone disorder in patients with CKD. Prescribing more medicines can make things more complicated, which can cause problems with remembering to take medicines, confusion about which medicines and how much to take and when, and lower morale to take medicines for a long time. Polypharmacy has been previously shown as an important factor affecting adherence to medications among those with CKD (17,19). Hence, interventions like medication reconciliation, medication regimen simplification and pharmacist-led counselling could enhance adherence of patients with complex medication regimens. The current study used the MMAS-8 questionnaire to assess medication adherence. Because of ease of use and feasibility in clinical research, the MMAS-8 is one of the more widely used adherence assessment tools in CKD research. A recent systematic evidence searches showed that MMAS-8 is still one of the most widely used instruments to assess medication adherence in patients with CKD, although none of them is the recognized gold standard (20). The ongoing adoption of MMAS-8 for clinical studies highlights its utility, especially in environments with limited resources, where adherence monitoring through electronic systems or pharmacists might not be feasible. Another finding from the analysis was that there was an association between the point of hypertension status and medication adherence. Hypertension is a highly prevalent comorbidity of CKD and is a chronic condition that needs ongoing treatment to decrease cardiovascular and renal complications. Noncompliance in the care of people with hypertension and chronic kidney disease may lead to suboptimal blood pressure management and even faster kidney function loss. Previous studies have

emphasized the need to provide more support to the adherence to medications among CKD patients with multiple chronic conditions as the complexity of the disease and the required treatment can affect medication adherence (18,21). The results of this study can have implications to clinical practice, especially in tertiary care nephrology clinics. Non-adherence should be part of the routine care of CKD. While it is essential that healthcare providers prescribe the right medications, it is equally crucial to be aware of barriers that may exist for patients, such as treatment complexity, socioeconomic factors, and insufficient knowledge of the disease. There are recent intervention studies indicating that medication therapy management, assisted by a pharmacist, and structured patient education program can enhance self-management and adherence to medications among KD patients (22). This study is limited in some aspects, although they have been useful. The cross-sectional design precludes the ability to draw causal conclusions on relationships between factors and medication adherence. Moreover, MMAS-8 is a self-report scale, and it could be subject to recall bias or socially desired response. MMAS-8 is a useful and well-tested strategy to assess adherence-related issues in a clinical setting, though (20,23). Longitudinal studies conducted across multiple centers should be able to capture more information about medication-taking behavior of CKD populations in the future and include objective adherence measures. To sum up, medication non-adherence is a significant problem in the group of CKD patients and is related with treatment complexity and clinical features. Standardized screening tools, like the MMAS-8, can be used to identify patients who are not adherent, which can help guide targeted interventions, optimize disease management, and help

lower the likelihood of complications related to CKD.

Conclusion

Chronic kidney disease (CKD) requires long-term treatment and adherence to multiple medications. This study found that medication non-adherence remains common among CKD patients, with a higher daily medication burden being a significant predictor of non-adherence. The MMAS-8 provided a simple and practical method for identifying patients with adherence difficulties who may benefit from counselling, medication education, and regimen simplification. A patient-centered approach addressing clinical, behavioral, and social barriers may improve medication adherence and CKD management. Although the cross-sectional design limits causal inference, these findings highlight the need for routine adherence assessment. Larger multicenter longitudinal studies using objective adherence measures are recommended.

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All the authors agree to take responsibility for every facet of the work, making sure that any concerns about its integrity or veracity are thoroughly examined and addressed.	