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RESEARCH ARTICLE

Determinants of Medication Adherence among Jordanian Patients with End-Stage Kidney Disease

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Abstract:

Background:

End-stage kidney disease (ESKD) requires complex medical management. To ensure the success of the management plan, the patient's adherence to medication is fundamental. However, adherence to medication is challenging for patients with ESKD.

Objective:

This study aimed to describe adherence to medication and identify demographic and clinical determinants in Jordanian patients with ESKD.

Methods:

Cross-sectional correlational design was employed using a sample of 188 patients with ESKD who attended hemodialysis units at five hospitals in Amman between March and June 2021. Medication adherence was measured using Morisky Medication Adherence Scale (MMAS).

Results:

The mean age of the participants was 50.9 years (SD=15.64), more than half of the participants 109 (58.0%) were males and a total of 115 (61.2%) participants were non-smokers. The mean score of the MMAS was 5.18 (SD=2.024), which indicates a high prevalence of inadequate adherence to medication. Younger age, longer duration of hemodialysis, and higher number of medications were risk factors for inadequate adherence to medication among patients with ESKD.

Conclusion:

ESKD patients who are younger, have a longer duration of hemodialysis, and use a higher number of medications should be targeted as they face medication adherence challenges. Those patients should be taken into consideration when planning and developing interventions to enhance medication adherence in patients with ESKD.

Keywords: Medication adherence, End stage kidney disease, Jordanian patients, Medication, Hemodialysis, Cognitive impairment.

Article History

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1. INTRODUCTION

Chronic kidney disease (CKD) is one of the leading causes of mortality worldwide. In 2017, CKD caused 1.2 million deaths globally, with an increment of 41.5% from 1990. CKD is a highly prevalent condition worldwide, with a prevalence of 9.1% in 2017 with 0.041% of CKD patients in End-stage kidney disease (ESKD) [1].

ESKD requires complex medical management, including hemodialysis, fluid and dietary restrictions, and a complex medication regimen [2]. To ensure the success of the management plan, patient's adherence to medication is fundamental. However, adherence to medication is challenging for patients with ESKD [3] due partly to the high pill burden and the complexity of the medication regimen in patients with ESKD [4].

Medication adherence is defined as "the extent to which a person's behaviour (taking medication) corresponds with agreed recommendations from a health care provider" [5].

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Patients with ESKD who are on hemodialysis usually receive an average of 16 different medications daily [6]. Such a high pill burden is significantly associated with inadequate adherence to medication [7]. The prevalence of non-adherence to medication ranges between 18.8% to 78% [7 - 9]. Non-adherence to medication among patients with ESKD is associated with less control of blood pressure [10], greater phosphorus levels [11], greater risk for CKD progression [12], and higher mortality rates [13].

Older age, lower level of education, and poor literacy were associated with non-adherence to medication [7]. On the contrary, others found that older age, moderate level of education, and being married were associated with better adherence to medication. Other factors that were found to negatively influence adherence to medication were female gender, older age, African American race, and low income [14].

Psychosocial factors were also found to influence medication adherence. Evidence showed that anxiety, depression, and cognitive impairment were significantly associated with medication non-adherence [15, 16]. However, findings regarding cognitive impairment are controversial. While some findings showed that lower cognitive impairment is associated with non-adherence [17], other findings showed no association between cognitive impairment and non-adherence to medication among patients with ESKD [15]. Therefore, the relationship between cognitive impairment and adherence to medication entails further investigations to increase our understanding of this relationship, which, in turn, may enhance patients' adherence to medications.

Non-adherence to medication is a multifactorial phenomenon that needs to be understood before interventions can be developed to enhance medication adherence [4, 16]. However, studies that address the demographic and clinical determinants of medication adherence are scarce in developing countries [16]. Without such studies, interventions aimed at enhancing medication adherence are unable to target those most likely to benefit. Thus, this study aimed to describe adherence to medication and identify demographic and clinical determinants (age, gender, educational level, smoking habits, hemodialysis duration, number of medications that the patient takes, hemodialysis vintage, serum calcium level, serum potassium level, hemoglobin level, Urea reduction rate (URR), and Kt/V) in Jordanian patients with ESKD.

2. METHODS

2.1. Study Design

A quantitative, correlation, cross-sectional design was used to describe adherence to medication and identify demographic and clinical determinants in Jordanian patients with ESKD.

2.2.1. Setting

Patients were enrolled from hemodialysis units at five hospitals in Amman, representing the main healthcare sectors in Jordan: two public hospitals, two private hospitals, and one university-based program hospital.

2.2. Participants

Non-randomized convenient sampling was used. A convenience sample of ESKD patients who attended the hemodialysis units between March and June 2021 were approached and asked to participate. The eligibility criteria for the participants were (1) primarily diagnosed with ESKD on hemodialysis for at least 6 months, (2) 18 years or older, (3) and able to read and write Arabic. Patients were excluded if they have (1) auditory or a visual impairment, (2) a language barrier, (3) and psychiatric illnesses, as these conditions are known to affect cognitive functions.

The sample size was estimated using G* power software on the following statistical parameters for Pearson product-moment correlation: a medium effect size of 0.25, a power level of 0.80, and an alpha level of 0.05. The required sample size was 159 participants. To handle the problem of missing data, an extra 41 participants were included in the final sample size to have at least 200 participants with ESKD.

2.3. Instruments

Demographic information, including age, gender, educational level, medical history, and duration of dialysis, was collected using a self-report questionnaire. Clinical data, including the number of missing hemodialysis sessions, hemodialysis vintage, serum calcium level, serum potassium level, hemoglobin level, URR, and Kt/V, were collected from the patient's medical records.

Medication adherence was assessed using the Morisky Medication Adherence Scale (MMAS) [18]. The MMAS is an 8-item self-reported measure of medication adherence. Each item evaluates a specific medication-taking behaviour with 7 questions using yes/no responses, and one question uses a 5-point Likert scale. Participants summated scores can range from 0 to 8; a higher score indicates better adherence. Medication adherence can be categorized into 3 levels: high adherence (= 8 points), medium adherence (6 -7 points), and low adherence (< 6 points). The reliability of the Arabic version of the MMAS has been supported with adequate internal consistency ($\alpha = 0.70$), and the known-group validity was established (Cramer V statistic ($\phi_c = 0.34$)) [19].

Cognitive function was tested using the Mini-Mental Status Examination (MMSE) [20]. The MMSE is a set of 30 questions that measures orientation, attention, memory, language, and visual-spatial skills. Each correct response is given one point. The maximum score for the MMSE is 30; scores of 25-30 are considered normal; scores of 21-24 are considered mild cognitive impairment; scores of 10-20 are moderate cognitive impairment, and <10 is severe cognitive impairment. The Arabic version of the MMSE was found to be reliable Chronbach's α (0.73) with sufficient validity for measuring cognitive impairment among Arabic clients [21, 22].

2.4. Ethical Consideration

The study was approved by the ethical research committee at the Applied Science Private University and the Institutional Review Boards of the targeted hospitals. Prior to data collection, the study was clearly explained, and informed

consent was obtained by the researchers. Patients were assured that their participation was anonymous, their medical treatment would not be affected by their participation, and they had the right to withdraw from the study at any time. A pilot study was carried out to ensure clarity and understandability of the instruments before being introduced to participants, as well as to assess the feasibility of the study. The pilot study revealed the feasibility of the study procedure and instruments. Data were collected within the last hour of the hemodialysis session, with the assumption that this time participants were most likely least uremic and most cooperative. All tests were given, timed, and scored by the researchers according to the guidelines that are described by the MMSE test manual for administration and scoring. The researchers provided each participant with a blank paper and a pencil to complete the last part of the test. Every participant took about thirty minutes to complete the MMSE test and MMAS questionnaires.

2.5. Statistical Analysis

Statistical analyses were conducted using Statistical Package for the Social Science software (SPSS), version 21; SPSS Inc., Chicago, IL, USA. Descriptive statistics, including mean scores, standard deviations, and frequencies, were used to describe participants' demographic and clinical characteristics. In addition, inferential statistics, including

Pearson product-moment correlation, Spearman's Rho correlation, and Point-Biserial correlation, were used to test the correlations between medication adherence and the level of cognitive status, demographic, and clinical variables.

3. RESULTS

Among 200 patients with ESKD invited to participate in the study, 188 (85%) patients completed the study's questionnaires. The mean age of the participants was 50.9 years (SD=15.64). More than half of the participants 109 (58.0%) were male and 115 (61.2%) participants were non-smokers. The participants had received hemodialysis for an average period of 7.5 years (SD=6.6) and received an average of 4.89 medications daily (SD=2.132). The majority of the participants (94.7%, n=178) did not miss their dialysis sessions in the last month. The MMSE scores indicated that about half of the participants 44.2% (n=83) had no cognitive impairment, while 32.4% of the participants (n=61) had mild cognitive impairment, 22.8% (n=43) had moderate cognitive impairment, and one patient had severe cognitive impairment, 0.5% (n=1). Almost two-thirds of the participants have a low level (primary or secondary) of education (71.8%, n = 135) and were unemployed (77.7%, n=146). The participants' demographic and clinical characteristics are presented in Table 1.

Table 1. Frequency distributions of participants' demographic characteristics (N=188).

Variable	N%	M±SD
Gender		-
Male	109(58%)	
Female	79(42%)	
Smoking		-
Yes	73(38.8%)	
No	115(61.2%)	
Vascular access types		-
Fistula	113(60.1%)	
Graft	35(18.6%)	
Central venous access	40(21.3%)	
Age (years)	-	50.91±15.676
Hemodialysis vintage	-	7.571±6.6782
Educational level (years of formal education)	-	11.49±3.185
Categories of educational level		-
Primary school	69 (36.7)	
Secondary school	66 (35.1)	
University degree and higher	53 (28.2)	
Occupation		-
Employed	42 (22.3)	
Unemployed	82 (43.6)	
Retired	64 (34.1)	
Calcium level	-	8.71±1.138
Potassium level	-	4.898±0.993
Hemoglobin level	-	10.559±8.133
Urea Reduction Rate	-	0.407±0.234
Kt/v	-	1.388±0.481

Table 2. Descriptive statistics for individual items of the Morisky Medication Adherence Scale.

Question	Yes	No
1. Do you sometimes forget to take your pills?	86 (45.7%)	102 (54.3%)
2. People sometimes miss taking their medications for reasons other than forgetting. Thinking over the past 2 weeks, were there any days when you did not take your medicine?	69 (36.7%)	119 (63.3%)
3. Have you ever cut back or stopped taking your medication without telling your doctor because you felt worse when you took it?	56(29.8)	132(70.2)
4. When you travel or leave home, do you sometimes forget to bring along your medication?	59 (31.4%)	129 (68.6%)
5. Did you take your medicine yesterday?	38 (20.2%)	150 (79.8%)
6. When you feel like your ESKD is under control, do you sometimes stop taking your medicine?	45 (23.9%)	143 (76.1%)
7. Taking medication every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?	76 (40.4%)	112 (59.6%)

3.1. Adherence to Medication among the Participants

Results demonstrated that the total MMAS scores had a slightly negatively skewed distribution, with a skewness of -0.469 and a kurtosis of -0.555. The mean score of the total MMAS was 5.18 (SD=2.024). Based on MMAS categories, more than half of the participants were low adherent to medication (n=97, 51.6%) with MMAS score < 6, more than one-third of the participants (n= 66, 35.1%) were moderate adherent to medication with MMAS between 6-7, and 25 patients (13.3%) were high adherent to medication with MMAS of 8. The majority of the participants (79.8%, n = 150) did not take their medications the day before coming to the dialysis unit, while (40.4%, n = 76) reported that they felt hassled about sticking to their treatment plan. Further details are presented in Table 2.

The results showed that there was no significant difference in medication adherence between males (M=5.16, SD=1.982) and females (M=4.97, SD=2.000); $t(186) = 0.750, P=0.454$, and there was no difference in medication adherence between smokers (M=4.95, SD=1.943) and non-smokers (M=5.33, SD=2.068); $t(186) = -1.274, P=0.204$. One-way ANOVA was conducted to compare the effect of types of vascular dialysis access on adherence to medication; the results showed no significant difference in medication adherence among patients with different vascular dialysis access [$F(2, 185) = 1.31, P=0.27$]. To compare the impact of employment status on medication adherence, one-way ANOVA was used, and a statistically significant difference in medication adherence among employed and unemployed participants ($F(2, 185) = 10.681, p < 0.001$) was found. Post hoc comparisons using

Tukey's HSD test revealed that the mean MMAS score was significantly different among participants in the employment status categories. The mean score for the MMAS was significantly lower in the employed group compared to (M= 4.29, SD=2.33) MMAS mean score in the unemployed group (M= 5.00, SD=1.89) and retired group (M= 6, SD=1.66). This indicates that employed ESKD patients have worse adherence to medication, while retired ESKD patients have better medication adherence.

3.2. Correlates of Medication Adherence

Pearson product-moment correlation was used to examine the relationship between medication adherence (the total score of MMAS) and demographic and participants' clinical variables. The analysis showed that medication adherence was significantly correlated with age ($r=3.00, P < .001$), hemodialysis duration ($r=-0.183, P=0.012$), and the number of medications taken ($r=-0.303, P < .001$). Further details are shown in Table 3. However, no significant correlation was found between medication adherence and the number of years of ESKD ($r=0.072, P=0.323$) and cognitive impairment ($r=-0.007, P=0.922$). Regarding the clinical characteristics, the analysis showed that none of the clinical variables were significantly correlated with medication adherence. Spearman's Rank Order Correlation and Point-Biserial Correlation Coefficient were conducted to measure the relationship between categorical and nominal variables, including gender, smoking, vascular access types, missing dialysis sessions, and medication adherence. The results showed that gender, smoking, vascular access, and missing dialysis sessions were not significantly correlated with medication adherence.

Table 3. Correlation between medication adherence and demographic and clinical characteristics.

Demographic and Clinical Characteristics	Spearman rho	Pearson R	P value
1. Age	-	3.000**	0.001
2. hemodialysis duration (years)	-	-0.183*	0.012
3. Number of medications taken	-	-0.303**	0.001
4. Educational level	-	0.89	0.226
5. Number of years of ESKD	-	0.072	0.323
6. MMSE	-	0.007	0.922
7. Serum calcium level	-	0.102	0.16
8. Serum potassium level	-	0.12	0.11
9. Hemoglobin level	-	-0.04	0.59

(Table 3) contd.....

Demographic and Clinical Characteristics	Spearman rho	Pearson R	P value
10. Kt/V	-	0.24	0.29
11. URR (Urea reduction rate)	-	-0.15	0.13
12. Gender	-0.023	-	0.75
13. Smoking	0.11	-	0.14
14. Type of vascular access	0.02	-	0.79
15. Missing dialysis sessions	0.045	-	0.542

Note: P*significant at 0.05, **significant at 0.01.

4. DISCUSSION

The aim of this study was to describe adherence to medication and identify demographic and clinical determinants in Jordanian patients with ESKD. Our study revealed that the prevalence of inadequate adherence to medication is high. The high prevalence of inadequate adherence to medication represents a threat to patients’ health outcomes as well as overall healthcare costs [13]. The prevalence of inadequate adherence to medication in the current study (89.7%; n=163) was higher than that found by Ahlawat *et al.*, 2016 (78%; n=117), Alkatheri *et al.*, 2014 (71.91%; n = 64), and Daniels *et al.*, 2018 (20.2%; n=95) [7, 8, 23]. This necessitates further investigations to identify the possible causes for the high prevalence of inadequate adherence to medication among Jordanian patients. While our findings showed that inadequate adherence to medication was high among our sample, others found that adherence to medication was high among patients with ESKD [24]. The inconsistency evidenced in the studies regarding medication adherence is partly attributed to the diverse methods used to measure medication adherence and the inconsistent definition of medication adherence [25]. Consistent with others’ findings, this study showed that ESKD patients who were employed were less adherent to medications compared to unemployed patients [26, 27]. However, some authors found that unemployment was associated with non-adherence [28], and others found no significant difference in medication adherence between employed and unemployed patients [29]. As research findings are controversial, further research is needed to better understand the impact of employment status on medication adherence in patients with ESKD.

Since inadequate adherence to medication is linked to various poor outcomes [13], it is important to identify the variables that may hamper patients’ adherence to medication. Research findings showed that numerous factors play a role in inadequate adherence to medication among patients with ESKD. The current study showed that younger age is associated with inadequate adherence to medication; this finding is congruent with the findings of other studies [29]. However, other researchers found that inadequate adherence to medication was higher among older patients [7]. The authors attributed poor adherence among older patients to the complex treatment regimen, as elders have many comorbidities.

Another factor that was found to be associated with adherence to medication is the duration of hemodialysis; patients having a longer duration of hemodialysis are less adherent to medication. This could be attributed to the lack of motivation caused by the complex medical management regimen that disturbs patients’ daily lives [30]. The literature

regarding the relationship between medication adherence and the duration of hemodialysis is inconclusive. Ozen and colleagues (2019) found that patients with a longer duration of hemodialysis were less likely to have inadequate adherence to their medications [31]. In contrast, others found no association between medication adherence and the duration of hemodialysis [8, 23]. The indecisive research findings necessitate further investigations of the relationship between the duration of hemodialysis and adherence to medications among patients with ESKD.

The results of this study showed a strong association between the number of medications used and inadequate adherence to medication; the higher the number of medications taken, the higher the inadequate adherence among patients with ESKD. This result was congruent with others [3, 32]. On the contrary, Ghimire *et al.* (2016) found no association between inadequate adherence and medication regimen complexity [29]. Notably, Ghimire *et al.* include the number of medications taken in addition to dosage frequency in defining medication regimen complexity.

Cognitive impairment has been shown to be related to medication adherence [17], but in this study, cognitive impairment was not significantly associated with medication adherence. In our study, about half of the participants had no cognitive impairment, and more than two-thirds of the participants had mild cognitive impairment. This lack of variability in patients’ cognitive impairment scores may be one reason for our failure to find a relationship between cognitive impairment and medication adherence. Our finding is similar to Alosaimi and colleagues [15]. They also failed to find a significant relationship between cognitive impairment and adherence to medical management in patients with ESKD.

Our finding could not detect any significant association between medication adherence and clinical indicators (serum calcium level, serum potassium level, hemoglobin level, Kt/V, URR) in our patients. Similarly, Naalweh *et al.* [33] failed to detect significant associations between medication adherence and serum potassium and phosphate levels in patients with ESKD. This suggests that assessing medication adherence needs to be examined using longitudinal designs to examine its dynamic effects on clinical indicators.

This study has some limitations. A cross-sectional design was used. Therefore, causal relationships among the variables could not be examined. The use of a self-report questionnaire is subjected to recall and social desirability biases. However, validated and reliable instruments were used to reduce these biases. Despite its limitations, this study highlighted some important findings that need further investigations using qualitative designs to determine barriers to medication

adherence from patients' perspectives.

In summary, in this study, we found that medication adherence was quite poor in Jordanian patients with ESKD. Specific demographic and clinical characteristics were found to be associated with medication adherence. These findings can help healthcare providers target those patients with ESKD expected to have medication adherence challenges. Further studies are needed to identify what other factors are associated with inadequate adherence to medications and examine methods of improving medication adherence.

CONCLUSION AND IMPLICATIONS TO NURSING PRACTICE

This study revealed that inadequate adherence to medication is highly prevalent among Jordanian patients with ESKD. Assessing patients' obstacles that hinder their adherence to medication is the first step in implementing any intervention to improve medication adherence. Younger employed patients with ESKD, those with a longer duration of hemodialysis, and taking a higher number of medications should be considered at high risk for medication non-adherence.

LIST OF ABBREVIATIONS

CKD	=	Chronic Kidney Disease
ESKD	=	End Stage Kidney Disease
URR	=	Urea Reduction R
MMAS	=	Morisky Medication Adherence Scale
MMSE	=	Mini Mental Status Examination

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was reviewed and approved by the Institutional Review Boards of the targeted hospitals. Participants were screened for eligibility prior to enrolment.

HUMAN AND ANIMAL RIGHTS

No animals were used in this research. All procedures performed in studies involving human participants were in accordance with the ethical standards of institutional and/or research committees and with the 1975 Declaration of Helsinki, as revised in 2013.

CONSENT FOR PUBLICATION

Informed consent was obtained from all participants.

STANDARDS OF REPORTING

STROBE guidelines were followed.

AVAILABILITY OF DATA AND MATERIALS

The authors confirm that the data supporting the findings of this study are available within the manuscript.

FUNDING

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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