

# Adherence to Antihypertensive Medications Among Patients with Chronic Kidney Disease in Saudi Arabia: A Single-Center Experience

Running title: Adherence to antihypertensive medications in chronic kidney disease patients

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## KEYWORDS

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## ABSTRACT

**Background:** Hypertension is highly prevalent among patients with chronic kidney disease (CKD), and is a leading cause of CKD progression, cardiovascular events, and mortality. Adherence to antihypertensive medications is important in maintaining blood pressure (BP) control, and reducing its related complications. **Objectives:** To assess the adherence to antihypertensive medication among patients with CKD, and to explore the reasons of nonadherence. **Material and methods:** This was a cross-sectional, retrospective study examining the rates and reasons of nonadherence to antihypertensive medication among adult patients with predialysis CKD at a large tertiary hospital in Saudi Arabia. Data were analyzed using SAS Version 9.2 by SAS Institute Inc., Cary NC, USA. **Results:** A total of 301 patients with pre-dialysis CKD and hypertension were included in this study. The mean age of the study population was  $53.5 \pm 16.6$ , and 55% were male. Out of the total 301 patients, 108 (36%) had controlled BP, while 194 (64%) had uncontrolled BP. Overall, 105 patients (35%) were adherent to antihypertension medications, while the remaining 195 (65%) were not adherent. The most common reason for nonadherence was having too many medications to take (65%), followed by forgetfulness (54%), and complex dosing schedule (46%). **Conclusion:** Adherence to antihypertensive medication is suboptimal among pre-dialysis CKD patients in Saudi Arabia, putting this population at higher risk of CKD progression and cardiovascular events. Large scale studies and quality improvement initiatives and interventions in Saudi Arabia are needed to tackle this problem in order to improve the outcomes of CKD patients with hypertension.

## 1. Introduction

Chronic kidney disease (CKD) is a major public health problem that pose huge challenges to patients, caregivers, and healthcare systems, given the highly associated morbidity, mortality, treatment costs, and decreased quality of life (1-4). The prevalence of CKD has increased over the last two decades by 29.3%, affecting 10-15% of worldwide population (5). In Saudi Arabia, the

prevalence of different risk factors for CKD such as diabetes mellitus (DM), hypertension (HTN), obesity, sedentary lifestyle, and smoking has substantially increased over the last years, resulting in higher risks of CKD in this part of the world (6-8).

Based on previous studies, it is estimated that 60-92% of CKD patients have HTN, resulting in higher risk for cardiovascular disease, which is by the far the leading cause of mortality in this group of patients (9-11). Blood pressure (BP) control is one of the most effective interventions to slow the progression of CKD, as well as to reduce the risk of cardiovascular disease and its related complications (12). However, previous studies have demonstrated that only small proportion of CKD patients achieve optimal BP control (13, 14).

Non-adherence to antihypertensive medications is one of the underestimated factors that is highly prevalent among CKD patients, which could contribute largely to the suboptimal control of BP. In fact, CKD patients are at higher risk of medications non-adherence given the large number of prescribed medications, with different studies demonstrating higher rates of medications non-adherence among CKD patients, with such non-adherence being associated with increased risk of hospitalization, morbidity, and mortality (15-17).

## **2. Objectives**

To investigate the prevalence of non-adherence to antihypertensive medications among CKD patients, and to explore the reasons for non-adherence in this group of patients.

## **3. Method**

This was a cross-sectional, retrospective study including 301 patients with HTN and pre-dialysis CKD who were following in the outpatient nephrology clinics at a large tertiary hospital in the eastern province of Saudi Arabia from the period of June 1 to November 30, 2024. Participants included patients who were 18 years or older, diagnosed with HTN and CKD for at least three months and who had not been undergoing dialysis. Patients with history of kidney transplantation were excluded from the current analysis. Demographic and clinical information including age, gender, comorbidities, body mass index (BMI), number of prescribed BP medications, and serum creatinine were obtained from patients' records. CKD was defined as a GFR less than 60 ml/min/1.73 m<sup>2</sup>. The estimated GFR was calculated from serum creatinine using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. To determine BP control, an average of the three most recent clinic BP measurements was used. BP measurements in our nephrology clinics are usually taken in a sitting position after 5 minutes of rest using validated automated sphygmomanometers. Blood pressure was defined as controlled if the mean of 3 recordings yielded < 140 mmHg systolic and < 90 mmHg diastolic. All the participants in this study had been provided an informed consent for being included in the study according to the declaration of Helsinki. Data were described using means  $\pm$  standard deviations (SD) for continuous variables and frequency distributions with percentages for categorical variables. Calculations were carried out using SAS Version 9.2 by SAS Institute Inc., Cary NC, USA.

## **4. Results**

### *Demographic and Clinical Characteristics*

A total of 301 patients met the inclusion criteria and were included in the present study. The patients' demographic and clinical characteristics are shown in table 1. The mean age of the study population was  $53.5 \pm 16.6$ , and 55% were male. Out the included patients, 69% had diabetes, and 22% were known to have ischemic heart disease. Obesity was common with 44.5% of the patients having BMI above 30 kg/m<sup>2</sup>. In terms of the stage of CKD, 15% had stage 3A, 25% stage 3B, 28% stage 4, and 32% stage 5. For HTN management, 11% were on one BP medication, 41% on two medications, 36% on three medications, and 9% on four medications or more (Table 1).

**Table 1. Patient characteristics**

Characteristics	N (%) Total=301
<b>Age, years (53.5±16.6)</b>	
18 – 39	27 (9%)
40 - 60	77 (25.5%)
>60	197 (65.5%)
<b>Gender</b>	
Male	166 (55%)
Female	135 (45%)
<b>Coexisting comorbidities</b>	
Diabetes mellitus	208 (69%)
Ischemic heart disease	66 (22%)
<b>CKD stage</b>	
3A	45 (15%)
3B	75 (25%)
4	84 (28%)
5	97 (32%)
<b>Body mass index (BMI)</b>	
<18.5	8 (2.5%)
18.5-24.9	57 (19%)
25-29.9	102 (34%)
30-39.9	113
≥40	(37.5%) 21 (7%)
<b>Number of BP medications</b>	
0	9 (3%)
1	33 (11%)
2	124 (41%)
3	108 (36%)
≥ 4	27 (9%)
<b>Controlled BP (&lt;140/90)</b>	
Yes	108 (36%)
No	193 (64%)

**BP Control and Adherence to Antihypertensive Medications**

Out of the total 301 patients with HTN and CKD, 108 (36%) had controlled BP, while 194 (64%) had uncontrolled BP (Table 1). Overall, 105 patients (35%) were adherent to antihypertension medications, while the remaining 195 (65%) were not adherent to their antihypertensive medications. Among those who here adherent to antihypertension medications, 63% had controlled BP, and 37% had uncontrolled BP. On the other hand, among the non-adheres group, 22% had controlled BP, and 78% had uncontrolled BP (Table 2).

**Table 2. Adherence level and blood pressure (BP) control**

*Reasons for non-adherence to BP medications*

Out of the 195 patients who were not adherent to antihypertensive medications, different reasons were identified. Of these reasons, “Too many medications to take” was the most frequent (65%), followed by forgetfulness (54%). Other reasons included: complex dosing schedule (46%), Fear of adverse effects (39%), poor knowledge of disease and long-term complications (22%), ran out of medications (17%), poor communication / insufficient instructions from the treating team (16%), and lack of social support (7%) (Table 3).

**Reasons for non-adherence to BP**

Reasons for non-adherence	Number (%)
Too many medications to take	127 (65%)
Forgetfulness	105 (54%)
Complex dosing schedule	90 (46%)
Fear of adverse effects	76 (39%)
Poor knowledge of disease and long-term complications	43 (22%)
Ran out of medications	33 (17%)
Poor communication / insufficient instructions from the treating team	31 (16%)
Lack of social support	14 (7%)

**medications (N=195)**

	Adherence to BP medications		Total
	Adherers	Non-adheres	
Controlled BP	66 (22%)	42 (14%)	108 (36%)
Uncontrolled BP	39 (13%)	153 (51%)	194 (64%)
Total	105 (35%)	195 (65%)	301

**5. Discussion**

The present study investigated the prevalence of nonadherence to antihypertensive medications among patient with pre-dialysis CKD in Saudi Arabia. We found that only 35% of the patients in this study were adherent to their antihypertensive medications, while the remaining majority (65%) were nonadherent. We also explored the reasons for nonadherence and found that the large number of medications, forgetfulness, complex dosing secludes, and fear of adverse events were the most frequently patient-reported reasons for nonadherence. Such findings are concerning given that medication nonadherence can usually results in uncontrolled hypertension, which is a leading cause of CKD progression and cardiovascular events. More efforts are needed in Saudi Arabia to tackle this problem in order to improve the outcomes of patients with CKD and hypertension.

Patients with CKD are at higher risk of medications non-adherence given the large number of medications and comorbidities in these group of patients. Different studies have demonstrated that medications non-adherence is common among CKD patients, and that it associates with increased risk of hospitalization, morbidity, and mortality (15-17). It is very important to address the reasons of nonadherence in order to plan different interventions to enhance such adherence. Specifically, nephrologists and health care providers should allocate more time for counselling the patients about medications adherence during every visit to the clinic. Moreover, more patient education is needed about lifestyle modifications, including salt restriction, weight reduction, and exercise given there important role in blood pressure control. This is even more important in CKD

population as obesity can accelerate the progression of CKD. The high prevalence of obesity in this study (44.5%) is noteworthy and further highlights the need for different interventions aiming to promote weight reduction in this group of patients.

Patients with CKD are at higher risk of several complications, including cardiovascular disease, which has remained the leading cause of death among patient on HD (18-20). Optimal BP control will not only reduce the risk of CKD progression but will also decrease the risk of cardiovascular events in these patients. In a previously published meta-analysis, lowering systolic blood pressure by 10 mmHg was found to be associated with 20% reduction in the risk of major cardiovascular events (12).

Although this study has provided an insight to the state of adherence to antihypertensive medication among patients with CKD in Saudi Arabia and its related reasons, we do acknowledge several limitations in this study. The use of office blood pressure readings (as opposed the gold standard 24-hour ambulatory blood pressure monitoring), and the observational, retrospective nature of the data in this single-center study are factors that may limit the generalizability of this study. Moreover, this study was confined to Saudi population, and such finding may not be generalizable to other countries with different populations and ethnicity backgrounds. Lastly, other factors that could affect BP control such as smoking, dietary habits and socioeconomic status were not assessed in present study. Further multi-center, large-scale prospective studies with in this region of the world are therefore needed.

In conclusion, adherence to antihypertensive medication is suboptimal among pre-dialysis CKD patients in Saudi Arabia, putting this population at higher risk of CKD progression and cardiovascular events. Large scale studies and quality improvement initiatives and interventions in Saudi Arabia are needed to tackle this problem in order to improve the outcomes of CKD patients with hypertension.

#### **Declarations**

#### **Competing interests**

The author declare that he has no competing interests.

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#### **Authors' contributions**

The manuscript was prepared by a single author, who analyzed and interpreted the data, and wrote the manuscript.

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