



## ASSOCIATION OF MEDICATION ADHERENCE WITH COGNITIVE STATUS IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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### ABSTRACT

Chronic kidney disease is emerged as a new risk factor of cognitive impairment. A cross-sectional, observational, questionnaire based study was conducted at Nephrology department of Govt. Medical College, Calicut. Morisky medication adherence questionnaire was used to assess medication adherence and Montreal Cognitive Assessment Questionnaire was used to assess cognitive status. Patient's divided into 5 groups depending on stage of chronic kidney disease. Estimated glomerular filtration rate was calculated using Modification of diet in renal disease equation. Results found as 51.4% are highly adherent to therapy, followed by 38.1% with medium adherence and 10.5% with low adherence. 53.8% have mild cognitive impairment and 46.2% have normal cognitive status. Medication adherence with cognitive status was found to be statistically significant ( $P=0.000$ ). We concluded that there is a significant association between medication adherence and cognitive status. Patients with higher medication adherence have less cognitive impairment.

**KEYWORDS:** *Chronic kidney disease, Cognitive impairment, Medication adherence*



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## INTRODUCTION

Chronic kidney disease (CKD) is defined as progressive loss of kidney function occurring over several months to years. It is characterized by gradual replacement of normal kidney architecture with interstitial fibrosis, reduction in the glomerular filtration rate (GFR) and/or urinary abnormalities or structural abnormalities of the renal tract<sup>1,2</sup>. CKD is a worldwide public health problem<sup>3</sup>. It is emerging to be an important chronic disease globally. Recent studies estimated that the age-adjusted incidence rate of ESRD in India is about 229 per million population and >100,000 new patients enter renal replacement programs annually. Only 10% of the Indian ESRD patients receive renal replacement therapy because of scarce resources<sup>4</sup>. CKD is associated with alteration in physiologic and metabolic functions<sup>5</sup>. Impairment of cognitive functions occurs frequently in chronic kidney disease (CKD). The conditions most associated with this decline are depression, delirium, mild cognitive impairment (MCI) and dementia. The mechanisms behind the cognitive decline is not established yet, but some factors, as neuronal damage by uremic toxins, cerebrovascular ischemic lesions, oxidative stress, chronic inflammation, anemia, hyperhomocysteinemia, the endothelial dysfunction may play a critical role. The diagnosis of cognitive decline in patients with CKD may have an important impact on the management and prognosis<sup>6</sup>. Medication adherence is defined as the extent to which individuals follow instructions they are given for prescribed treatments. Non-adherence reduces health benefits of drug therapy and augments advancement of CKD to end-stage renal disease<sup>7</sup>. Measurement of medication adherence is challenging because adherence is an individual patient behavior. Adherence is a key factor associated with the effectiveness of all pharmacological therapies but is particularly critical for medications prescribed for chronic conditions. Poor adherence to medical treatment severely compromises patient outcomes and increases patient mortality<sup>8</sup>. High medication adherence and early detection of MCI helps to control the further progression of CKD. Previous studies focused on medication adherence and cognitive impairment in CKD patients. But the results remain conflicting. Several studies suggest that cognitive impairment depends on stage of CKD. Some studies reveal that, cognitive impairment occurs only in dialysis patients. Medication adherence is a key factor to control the progression of CKD. Several factors lead to medication non adherence. It is depends on the population acceptance towards medicine. This study focuses on determination of medication adherence, cognitive status and relation between medication adherence and cognitive status in CKD patients. There are no studies available to assess the

relation between medication adherence and cognitive status among CKD populations. The objective of the study is to determine the association of medication adherence with cognitive status in chronic kidney disease patients. The incidence of CKD as well as cognitive impairment associated with CKD is increasing among the whole population. The early diagnosis and management of cognitive status plays an important role in prevention of progressive loss of kidney function. In most patients kidney disease progressed into chronic stage because of poor diagnosis as well as low medication adherence. Identification of adherence to medications in chronic diseases will help to manage the progression of disease and other complications associated with that.

## MATERIALS & METHODS

Cross-sectional observational study was carried out at the Nephrology department of Govt. Medical College, Calicut after obtaining research ethical committee approval. The inclusion criteria was age between 19-79 years and patients with CKD (stage 3-5) with minimum 3 months of disease duration. Patients meeting eligibility criteria were briefed about the study and informed consent obtained from those willing to participate were enrolled in to the study. Patients with Psychiatric disorders, Neurological disorders, Pregnant and lactating patients, Blind patients, Severe diabetic complication, Patients below 18 years and above 80 years, Renal transplant patients and Patients with acute kidney disease were excluded from the study. This study was conducted over a period of 6 months from February 2016 to July 2016. Patient data collection form was prepared and the information was collected from the patient by interviewing the patient and also from the case records. Medication adherence was assessed by Morisky Medication Adherence Questionnaire (8-item) and Cognitive status was assessed by Montreal Cognitive Assessment Questionnaire (Questionnaires are used with permission).

### *Glomerular filtration rate by modification of diet in renal disease (MDRD) equation*

MDRD equation is more accurate as an estimator of kidney function. The working group of the National Kidney Foundation's (NKF) Kidney Dialysis Outcomes and Quality Initiative (K/DOQI) has developed a CKD classification system based on the presence of structural kidney damage and/or functional changes in glomerular filtration rate (GFR) present for a period of 3 months or more. CKD is categorized by the level of kidney function (as defined by GFR) into stages 1 through 5, with each increasing number indicating a more advanced stage of the disease.<sup>3</sup>

Stage 1 includes GFR  $\geq$  90 mL/min, Stage 2 includes GFR 60–89 mL/min, Stage 3a includes GFR 45–59 mL/min, Stage 3b includes GFR 30–44 mL/min, Stage 4 includes GFR 15– 29 mL/min and Stage 5 includes GFR < 15 mL/min

Formula used was;

$$eGFR \text{ (mL/min/1.73m}^2\text{)} = 186 \times [S_{cr} \text{ (}\mu\text{mol/L)/88.4}]^{-1.154} \times \text{Age}^{-0.203} \text{ (for males)}$$

$$eGFR \text{ (mL/min/1.73m}^2\text{)} = 186 \times [S_{cr} \text{ (}\mu\text{mol/L)/88.4}]^{-1.154} \times \text{Age}^{-0.203} \times 0.742 \text{ (for female)}$$

**Morisky medication adherence questionnaire (8-item)**

Adherence was checked by interviewing the patient with Morisky 8-item medication adherence questionnaire. Scores were given according to the answers given by the patient. For each question there were two possible answers-yes or no.

Adherence score for these two answers were set as yes=0 and no=1

<6 - Low adherence, 6 to <8 - Medium adherence, 8 - High adherence

**Montreal cognitive assessment questionnaire**

Cognitive status was checked by interviewing the patient with Montreal cognitive assessment questionnaire. It assesses different cognitive domains: attention and concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking,

calculations and orientation. Time to administer the MoCA is approximately 10 minutes. The total possible score is 30 points. Add one point for an individual who has 12 years or fewer of formal education, for a possible maximum of 30 points. Score of 26 or above is considered as normal.

**STATISTICAL ANALYSIS**

PASW Statistics version 18, 2009 software was used for statistical analysis. Data collected were analyzed using descriptive (Frequency and Percentage) statistics. The association of medication adherence with cognitive status was determined by using Pearson chi-square method. P value of less than 0.05 was considered as significant.

**RESULTS**

Total 210 patients were enrolled in this study.

**Table 1**  
**Baseline characteristics of the population**

Features	Number of patients	Percentage
<b>Gender</b>		
Male	140	66.7
Female	70	33.3
<b>Age range (in years)</b>		
31-40	25	11.9
41-50	52	24.8
51-60	81	38.6
61-70	49	23.3
71-80	3	1.4
<b>Educational Qualification</b>		
Lower Primary (1-4)	40	19
Upper Primary (5-7)	61	29
High School (8-10)	87	41.5
Pre-degree/Degree (>10)	22	10.5
<b>Stage</b>		
3a	31	14.8
3b	48	22.9
4	45	21.3
5ND	59	28.1
5D	27	12.9
<b>Medical history of co-morbidities</b>		
Nil	25	11.9
DM	31	14.8
HTN	57	27.1
DM+HTN	49	23.2
Others	23	11
DM + HTN + Others	25	11.9

**DM: Diabetes Mellitus, HTN: Hypertension, ND: Non dialysis, D: Dialysis**

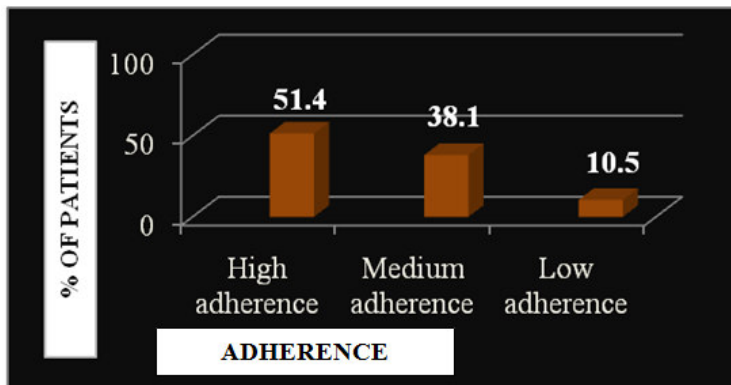
Out of 210 patients, 140 (66.7%) were males and 70 (33.3%) were females. The majority of patients diagnosed with chronic kidney disease (CKD) were in the age group of 51-60 (38.6%) and the least number of patients were under the age group of 71-80 (1.4%). The minimum and maximum age included in the study was 31 and 76 years respectively. 87 (41.5%) patients in this study have high school educational level followed by 61 (29%) having upper primary educational level, 40 (19%) having lower primary educational level and only 22

(10.5%) having pre-degree or degree educational level. 59 (28.1%) were in stage 5 (nondialysis). Remaining patient population were in 3b (22.9%), 4 (21.3%), 3a (14.8%) and dialysis stage (12.9%). Among the total sample of 210 patients, 25 (11.9%) have CKD alone and 185 (88.1%) have co-morbidities along with chronic kidney disease. 57 (27.1%) have CKD along with hypertension, 31 (14.8%) patients have CKD along with DM, 49 (23.2%) have CKD+HTN+DM and 23 (11%) have other diseases as co-morbidity.

**Table 2**  
**Patient medication adherence**

Adherence	MMAS score	No of patients	Percentage
High adherence	8	108	51.4
Medium adherence	6 to <8	80	38.1
Low adherence	<6	22	10.5
<b>Total</b>		<b>210</b>	<b>100</b>

*MMAS: Morisky Medication Adherence Scale*



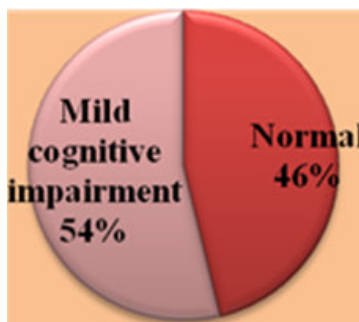
108 (51.4%) patients are highly adherent, followed by 80 (38.1%) patients are medium adherent and only 22 (10.5%) patients are low adherent.

**Figure 1**  
**Patient medication adherence**

**Table 3**  
**Patient cognitive status**

Cognitive status	MoCA score	No of patients	Percentage
Normal	≥26	97	46.2
Mild cognitive impairment	<26	113	53.8
<b>Total</b>		<b>210</b>	<b>100</b>

*MoCA: Montreal Cognitive Assessment*

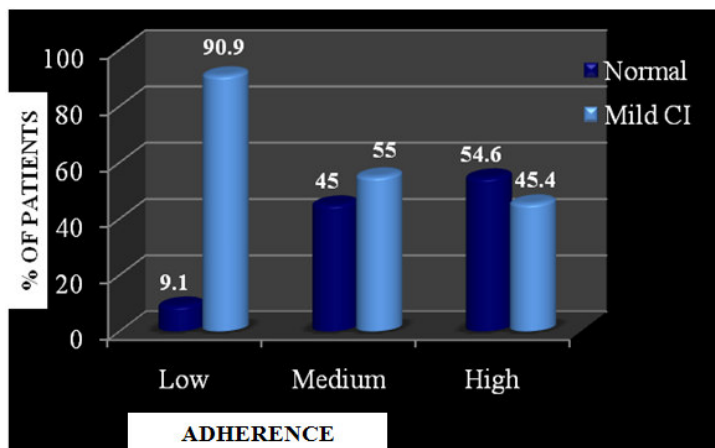


113 (53.8%) have mild cognitive impairment and 97 (46.2%) have normal cognitive status.

**Figure 2**  
**Patient cognitive status**

**Table 4**  
**Association of medication adherence with cognitive status**

Adherence	Cognitive status				Total	p value
	Normal		Mild cognitive impairment			
	No of Patients	percentage	No of Patients	percentage		
Low	2	9.1	20	90.9	22	0.000
Medium	36	45	44	55	80	
High	59	54.6	49	45.4	108	
<b>Total</b>	<b>97</b>	<b>46.2</b>	<b>113</b>	<b>53.8</b>	<b>210</b>	



*Chi-square value of medication adherence with cognitive status was statistically significant ( $P=0.000$ ). The majority of patients with cognitive impairment 20 (90.9%) were low adherent, followed by 44 (55.0%) with medium adherence and 49 (45.4%) with high adherence. Patients with higher medication adherence have less cognitive impairment.*

**Figure 3**

**Association of medication adherence with cognitive status**

## DISCUSSION

Out of 210 patients, 66.7% were males and 33.3% were females. This result was concordant with the nationwide survey of ESRD by the Japanese Society for Dialysis Therapy, revealed a higher incidence and prevalence in men than in women<sup>9</sup>. Manju et al study results also similar to the results, i.e. men are more prone to develop chronic kidney disease (CKD) and progress to end-stage renal disease than are women<sup>10</sup>. The majority of patients diagnosed with chronic kidney disease (CKD) were in the age group of 51-60 (38.6%) and the least number of patients were under the age group of 71-80 (1.4%). This finding is consistent with Odagiri G et al study. The prevalence of CKD was high in elderly population and patients showed a higher prevalence of cognitive impairment in older groups (50 years and older)<sup>11</sup>. Among the total sample of patients, 11.9% have CKD alone and 88.1% have co-morbidities along with chronic kidney disease. 27.1% have CKD along with hypertension, 14.8% patients have CKD along with DM, 23.2% have CKD+HTN+DM and 11% have other diseases as co-morbidity. A study by Salini et al also showed similar results that 34.18% patients were hypertensive, 22.78% were diabetics, 5.06% were dyslipidemic and 21.52% of patients had combination of hypertension and diabetes<sup>12</sup>. 51.4% are highly adherent, followed by 38.1% patients are medium adherent and only 10.5% patients are low adherent. This finding is concordance with the finding of Firdous SS et al study, which revealed the following adherence levels: high adherence 51.3%, medium adherence 29.7% and low adherence 19%<sup>13</sup>. 53.8% have mild cognitive impairment and 46.2% have normal cognitive status. Studies by Khatri M et al<sup>14</sup>, Madan P et al<sup>15</sup>,

Williams UE et al<sup>16</sup> and Sander D et al<sup>17</sup> etc showed similar results with the study.

## CONCLUSION

There is a significant association between medication adherence and cognitive status. The majority of patients with mild cognitive impairment were low adherent, followed by medium adherent and high adherent. Patients with higher medication adherence have less cognitive impairment. So in order to improve the cognitive status of chronic kidney disease patients, the adherence to the prescribed drugs are to be improved. Health care professionals should actively participate in educational programmes like counseling to increase medication adherence. This type of study should be planned in large sample size so that the health care policy makers will get the better insight in to the present scenario and can provide the way to optimize the medication adherence and cognitive status of CKD patients. One of the limitations of this study is not determined the reason for medication adherence. The actual cause of non adherence determination helps to increase the medication adherence and to control the progression of CKD.

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## CONFLICT OF INTEREST

Conflict of interest declared none.

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