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Prevalence and Predictors of Medication Non-Adherence in Patients of Chronic Kidney Disease: Evidence from A Cross Sectional Study

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Abstract

Introduction: A high level of adherence to prescribed medication is essential to obtain the desired outcomes in patients of chronic kidney disease (CKD). Non-adherence to medication leads to increased morbidity and mortality. Non-adherence to medication has not been studied extensively in patients of CKD in India.

Objective: To study the prevalence and predictors of medication non-adherence in patients of CKD.

Method: Medication non-adherence was studied with the help of Morisky 8-item Medication Adherence Scale (MMAS-8) through a cross sectional study. Patients, aged 18 yrs or more, diagnosed with CKD according to Kidney Disease: Improving Global Outcomes (KDIGO) definition, and willing to participate in the study were included. On the basis of MMAS-8 scores, patients were classified to have high, medium and low adherence. Binary logistic regression was used to determine the various factors affecting adherence to drug therapy in CKD patients.

Results: A total of 150 patients were included in study. Only 22% of the patients had high adherence to medications. Of all, 55% and 23% of the patients belonged to low and medium adherence, respectively. Adherence to drug therapy was found significantly different in different stages of CKD, gender, Body Mass Index (BMI) categories, hemodialysis status, co-morbidities, treatment funding and in patients of different socioeconomic status.

Forgetfulness was found to be most common reason for non-adherence, while maximum non-adherence were reported for antihypertensive medications. Pill burden, age, literacy, reimbursement, medication by caregivers was found to significantly affecting the medication adherence.

Conclusion: Medication non adherence was found to be highly prevalent in patients of CKD.

Keywords Medication adherence; Compliance; Non-adherence; Chronic kidney disease; India

Introduction

Chronic kidney disease (CKD) is a major metabolic disorder responsible for the increased global morbidity due to non-communicable disease. The prevalence of CKD in different parts of India has been known to vary from 0.78%-1.4% [1-4].

Diabetes and hypertension are the major risk factors and most common co-morbidities in CKD [5]. The number of CKD patients is continuously increasing over time. The major goal of drug therapy in CKD patients is to slow down the progression of disease along with correcting the associated co-morbidities.

Non-adherence to chronic drug therapy is known to significantly increase the disease burden in developing economies. The major predictors of the poor adherence include cost of medication, missed appointments, side effect(s) of medication, psychological problems, treatment complexity, asymptomatic disease, inadequate follow up, poor patient provider relationship, patients' lack of insight in illness, patients' lack of belief in benefit of treatment and barrier to access the healthcare facilities. Pill burden is one of the most common reasons for medication non-adherence in patients of CKD [6-10].

Adherence to medication using indirect methods is performed using questionnaire, self-reports, pill count, and prescriptions refilling [11,12]. Adherence to drug therapy in CKD patients globally varies from as low as 38 to as high as 83% [13-17].

This study was carried out to estimate the prevalence of medication non-adherence using (MMAS-8) in CKD patients at a tertiary care hospital and to evaluate the factors affecting it.

Methods

This cross-sectional study was carried out for a period of six months, i.e., June 2015 to December 2015 at the renal clinic of the medicine OPD at a tertiary care public teaching hospital, Chandigarh. The study protocol was approved by the Human Ethics Committee of Government Medical College and Hospital (GMCH), Chandigarh. Permission to use MMAS-8 was obtained.

Patients willing to participate and ready to give informed consent for participation were included in study.

Patients aged 18 years or above, diagnosed with CKD as laid down in Kidney Disease: Improving Global Outcomes (KDIGO) were included in study [18]. Patients having known cognitive impairment or unable to complete interviews were excluded from study. The patients were recruited for study only after obtaining a written informed consent for participation.

Patient's demographic and anthropometric details were collected from patients OPD record(s) and through interview. The records were used for collecting clinical details.

Modified Kuppuswamy's scale was used to assess the socioeconomic status [19]. According to this scale patients were classified in to five socioeconomic classes on the basis of total score. The total score were calculated from the patient's education, occupation and family income per month.

The patients were classified, into different stages of CKD, on the basis of glomerular filtration rate (GFR) and albuminuria [18]. Creatinine clearance (CrCl) was calculated using the Cockcroft-Gault equation [20].

World Health Organization Global database on Body Mass Index was used to classiffy the patients on the basis of body weight as underwight, normal, overweight, pre-obese and obese [21].

Adherence to medication were measured using the 8-item Morisky Medication Adherence Scale (MMAS-8), which is a validated scale. This scale included 7 items with yes/no response options and 1 item with a 5-point Likert scale response option.

The items in the scale provide information regarding barriers to medication adherence such as forgetting to take medications, not taking medications when one feels worse, and difficulties in sticking to a treatment plan. The scores for the 8 items were pooled to obtain an overall adherence score with a range of 0-8; higher scores indicating better adherence.

Based on this overall score, patients were classified as having poor, medium, or good adherence (Morisky score < 6, 6–7.9 and 8 respectively). MMAS-8 had a good reliability with a Cronbach's alpha value of 0.83 and a good predictive validity [12].

Further, patients were interviewed to identify the medication towards which patients were non-adherent and the specific reason for non-adherence.

Mean with standard deviation (SD) and numbers with percentages, were used for data representation whereas applicable. Chi-square test was used to determine the association between two categorical variables. Student t-test (unpaired) was used to find out the difference between mean of Independent categorical variable and dependent continuous variable.

Multivariate binary logistic regression analysis was used to assess the different predictors of medication non-adherence, such as age, sex, medication by caregivers, duration of CKD, number of medication, education, hemodialysis, and treatment reimbursement. Medication non-adherence was predicted by odds ratios (OR) with 95% confidence interval (CI). Patients with MMAS-8 score less than six were considered as non-adherent. A p-value less than 0.05 were considered statistically significant. IBM SPSS Statistics vary 20.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

Results

A total of 190 CKD patients were screened during the study period. Of this, 40 patients were excluded; 2 due to cognitive impairment, 14 were unable to complete interview, 18 were underage, and 6 were unwilling to participate in the study. These results, therefore, are based upon data obtained from 150 patients.

The average age of the patients was 53.8 (6.4) yrs. Of all, 32% of the patients were above 60 yrs. On the basis of Kuppuswamy scale, 40% of the patients belonged to lower middle class. Of all the patients, 81% of the patients were paying out of pocket for treatment (Table 1).

Over half of the patients had hypertension as a comorbidity followed by anemia, diabetes (55%, 47% and 33% respectively). 44% of the patients were in G5 stage of CKD. 40% of the patients were found to be overweight. The percentage of pre-obese and obese patients was 30% and 10%, respectively. Only 29% of the patients were found to be on hemodialysis (Table 1).

Variable	Total (N = 150)	Low (N = 82)	Medium (N = 35)	High (N = 33)	P-value
Gender					
Male	81 (54)	39 (48.3)	25 (30.8)	17 (20.9)	0.048
Female	69 (46)	43 (62.3)	10 (14.4)	16 (23.3)	
Age					
≤ 60 year	102 (68)	56 (54.9)	24 (23.4)	22 (21.5)	0.79
> 60 year	48 (32)	26 (54.2)	11 (22.9)	11 (22.9)	
SES status					
Upper	8 (6)	4 (50.0)	2 (25.0)	2 (25.0)	0.041
U. middle	34 (22)	19 (55.8)	8 (23.3)	7 (20.5)	
L. middle	61 (40)	33 (54.2)	14 (22.9)	14 (22.9)	
U. Lower	40 (27)	22 (55.0)	9 (22.5)	9 (22.5)	

Lower	7 (5)	4 (57.2)	2 (28.6)	1 (14.2)	
Habits					
Habits (Smoking)	36 (24)	20 (55.6)	8 (22.2)	8 (22.2)	0.891
No habit	114(76)	62 (54.4)	27 (23.7)	25 (21.9)	
Funding					
Out of pocket	121 (81)	66 (54.5)	28 (23.2)	27 (22.3)	< 0.001
Employer	29 (19)	16 (55.2)	7 (24.1)	6 (20.7)	
CKD stages					
CKD I-III	44 (29)	24 (54.5)	11 (25.0)	9 (20.5)	< 0.001
CKD IV	40 (27)	22 (55.0)	9 (22.5)	9 (22.5)	
CKD V	66 (44)	36 (54.5)	15 (22.8)	15 (22.7)	
Comorbidities					
Hypertension	83 (55)	45 (54.2)	20 (24.1)	18 (21.7)	0.052
Diabetes	50 (33)	27 (54.0)	12 (24.0)	11 (22.0)	
Anemia	71 (47)	39 (54.9)	17 (23.9)	15 (21.2)	
Hemodialysis	43 (29)	24 (55.8)	10 (23.3)	9 (20.9)	< 0.001
No dialysis	107 (71)	58 (54.2)	25 (23.4)	24 (22.4)	
BMI					
Underweight	39 (26)	21 (53.8)	9 (23.1)	9 (23.1)	0.041
Normal range	51 (34)	28 (54.9)	12 (23.5)	11 (21.6)	
Overweight	60 (40)	33 (55.0)	14 (23.3)	13 (21.7)	

Table 1: Characteristics of patients based on MMAS-8 score. Values are n (% of row total), P < 0.05-Significant, P < 0.001-Highly significant, BMI-Body Mass Index.

The medication adherence was categorized into 'low', 'medium', and 'high' on the basis of MMAS-8 score. Higher the score in MMAS-8, better is the adherence to medication. Among all the enrolled patients, 55% and 23% showed 'low' and 'medium' medication adherence, respectively; only 22% showed 'high' medication adherence. 78% of the patients were 'non-adherent' to the drug therapy (Table 1).

The level of medication adherence was found to be significantly associated with sex, socioeconomic status, treatment funding, stages of CKD, dialysis, and among different stages of BMI (Table 1).

Among the reasons for non-adherence, forgetfulness in 28% of the patients was found to be most common reason followed by high cost of medication, lack of information, complex dosing schedule, and others (Table 2).

The maximum number of patients were found non-adherent towards antihypertensive medication (24%), followed by oral anti-diabetic medication (21%), Insulin (19%) and iron injection (11%), steroids (9%), erythropoietin injection (7%), 'other medication' (7%), and drugs for thyroid disorders (2%). 'Other medication' included phosphate binders, vitamins and minerals.

#	Factor	%
1	Forgetfulness	28
2	High medication cost	23
3	Lack of information	19
4	Complex dosing schedule	15
5	Injection inconvenience	6
6	Missed appointment	4
7	Uneasy feeling	3
8	Poor access to medication	2

Table 2: Factors evaluated for non-adherence. *Non-adherence-MMAS-8 scores less than six.

Different predictors of medication non-adherence were studied using multivariate binary logistic regression. The likelihood of non-adherence to drug therapy was significantly higher in patients over 60 yrs (OR 1.36, 1.11-2.51; p < 0.05). Non-adherence was found to be

associated with more than 5 medication (OR 1.72, 0.86-3.42; p < 0.05), out-of-pocket expenditure (OR 1.67, 1.32-2.46; p < 0.05), self-administration (OR 2.21, 0.98-6.23; p < 0.05) and illiteracy (OR 3.51, 1.45-7.65; p < 0.05) (Table 3).

Variable	Adjusted Odds ratio (95% confidence interval)	P-value
Gender		
Male	1 (reference)	
Female	0.97 (0.32-1.5)	0.561
Age		
≤ 60 year	1 (reference)	
> 60 year	1.36 (1.11-2.51)	0.041
Funding		
Employer	1 (reference)	
Out of pocket	1.67 (1.32-2.46)	0.023
CKD stages		
CKD I-IV	1 (reference)	
CKD IV-V	1.12 (0.26-2.45)	0.655
Hemodialysis		
Yes	1 (reference)	
No	1.24 (0.56-2.14)	0.342
No. of medication		
≤ 5	1 (reference)	
> 5	1.72 (0.86-3.42)	0.041
Medication by caregivers		
Care givers	1 (reference)	
Self	2.21 (0.98-6.23)	0.032
Duration of CKD		
≤ 2 yr	1 (reference)	
> 2 yr	1.8 (0.98-4.53)	0.923
Education		
Literate	1 (reference)	
Illiterate	3.51 (1.45-7.65)	0.045

Table 3: Predicators of medication non-adherence. P < 0.05-Significant.

Discussion

In this study, the medication adherence among the CKD patients using the MMAS-8 and various factors affecting it were evaluated.

World Health Organization defines adherence as "the extent to which a person's behaviour – taking medication, following a diet, and / or executing lifestyle changes, corresponds with agreed recommendations from a health care provider" [22].

Adherence to drug therapy is a major problem in chronic illness especially in developing country where patients have to spend out of pocket as there was no-cover by insurance mechanism. Non-adherence to medication in developing countries significantly increased the disease burden, and severely decreased the patient quality of life [23]. The reasons for non-adherence to medication in CKD patients could be multiple [11]. There are a few evidences on non-adherence to drug therapy in CKD patients all over the world [13,15,16,24-26]. Assessment of adherence helps in identifying the various associated

risk factors and developing the intervention to improve the medication adherence. The lack of such evidence in Indian CKD patients is one of the drivers for this study.

This study has used the MMAS-8 for estimation of medication adherence. The measure of adherence to drug therapy in different studies using different tools varies from 38-83% [13-16,25].

Prevalence of non-adherence (78%) in the present study was higher than that reported by Neri et al. (52%; n= 1238) and Sánchez Gili et al. (26%; n = 94) using same tool [14,15]. One of the possible reasons for high prevalence of non-adherence could be unavailability of insurance for majority of the population because of which patients have to pay out of pocket for their expenditure.

Weng et al., using self-reported adherence using the Immunosuppressive Therapy Adherence Scale (ITAS), reported that out of 252 patients, 41% of the kidney transplant recipients were non-adherent [25].

Chiu et al. reported non-adherence in 62% of the participants (n = 1154) using to a pill count method [13]. Adherence was found lower than the present study. This could be due to differences in the tools and study disease condition [25].

Varleta et al. reported forgetfulness as the most common factor responsible for non-adherence in 67% of the patients (n = 310) using Morisky Green questionnaire; the present study finds this only in 28% of the patients [27].

CKD has a high cost of illness [28]. High cost of medication was found as one of the most common reasons for non-adherence to drug therapy in present study (23%). Frankenfield et al. has also reported that cost is a major factor for non-adherence in 23% of the ESRD patients [24].

Missed appointment was found to be responsible for non-adherence in 4% of the CKD patients in the present study. Missed appointment was found to be one of the responsible for poor medication adherence according to van Servellen et al. [7].

More than 5 pills and drug administration were found to be significant risk factors in present study. Magacho et al. also reported more than 5 pills as a major contributing factor for non-adherence (n = 149; CKD patients not on dialysis) [16].

According to Moreira et al., pill burden (≥ 4) was statistically significantly associated with non-adherence [29]. Self-administration was found to be associated with non-adherence on comparison to medication by caregivers in present study.

Medication adherence was found to be low in the elderly patients. The possible reasons for this low adherence in elderly are complex therapeutic regimen, forgetfulness, and lack of insight into disease. Adherence in elderly patients could be increased by simpler medication regimen that is easy to remember. Other than this adherence can be further improved by involving the caregivers. Gerbino et al. also reported low adherence in elderly patients [26].

Literacy of the patients leads to significantly higher medication adherence in comparison to the illiterate. This could be due to better awareness about the harms of non-adherence to prescribing regimen on the disease conditions. They are also able to understand the importance of timely medication. Very few patients know about the correct timing of medication.

Medical adherence was found to be significantly higher in patients receiving medical reimbursement. Most of the patients in present study belonged to lower socioeconomic status class; affordability of treatment remains a major issue for these patients. This type of non-adherence can be decreased by increasing the universal insurance coverage for CKD patients.

From the above findings, it appears that pill burden decreases the medication adherence. However, the number of medications in CKD patients cannot be reduced. Therefore, other strategies have to be explored to increase the medication adherence. One can decrease the frequency of drug by using the long acting medications. One can also decrease the frequency of insulin by using the long acting one, by prescribing the drug combinations for antihypertensive and drugs for treating anaemia. But, it is not possible to reduce the frequency of phosphate binders with currently available phosphate binders [30].

Medication by care-givers is a better option to increase the medication adherence. Further, the caregivers should be explained about the importance of regular medication, about the use of medication, and possible side effects to improve the medication adherence.

Conclusion

Non adherence to drug therapy is highly prevalent among CKD patients in India; 78% of the patients were non-adherent. Patient's age, educational status, medical reimbursement mechanism, and medication by caregivers are some of the factors that affected medication adherence in this study.

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