Medication Adherence in Greek Hemodialysis Patients: The Contribution of Depression and Health Cognitions

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Abstract

Background Several studies have shown that non-adherence is a common and increasing problem among individuals with chronic illnesses, including hemodialysis patients.

Purpose The present study aimed to investigate the influence of depression and health cognitions on medication adherence among patients undergoing hemodialysis.

Method A sample of 168 participants was recruited from six general hospitals in the broader area of Athens, consisting of patients undergoing in-center hemodialysis. Measurements were conducted with the following instruments: the Medication Adherence Rating Scale, the Center for Epidemiologic Studies Depression Scale (CES-D), and the Multidimensional Health Locus of Control (MHLC) scale.

Results The results indicated that medication adherence was associated positively with the dimensions of internal and doctor-attributed health locus of control, measured by the MHLC. It was also related negatively to depression, measured by the CES-D.

Conclusions The present study demonstrates the importance of depression in understanding the medication adherence of hemodialysis patients, as well as the contribution of heath cognitions.

Keywords Adherence · Medication · Hemodialysis · Depression · Health cognitions

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Introduction

Patients suffering from chronic kidney disease (CKD) have to cope with many adversities, e.g., physical symptoms, limitations in food and fluid intake, changes in their body image, work and economic status, social roles, activity levels, self-image, health status, and normal routines, while their control over treatment cannot always be predicted [1–3]. Such constraints are expected to affect the patients' lives and their physical and social functioning, leading them to reconsider their personal and professional goals within the context of living with a chronic illness [4–6].

Further, patients with CKD who receive dialysis are generally prescribed an average of 10 different medications that they must take several times daily [7]. This represents a large pill burden. A recent study found the median number of daily pills for hemodialysis (HD) patients to be 19 [8]. Consequently, effective CKD control requires regular preventive medication and a response to that medication. Poor receptiveness to CKD medication can be related to individual variability in the dose needed to achieve a response, as well as to low-adherent behavior in relation to the CKD medication regimen [9].

Adherence to medications and treatments has been defined in several ways for patients with CKD who receive dialysis. One definition of adherence includes a person's behaviors concerning taking medication, following a diet, and making changes in lifestyle in accordance with health professional recommendations [10]. Another common definition is the extent to which people follow the instructions they are given for prescribed treatments [11]. The National Kidney Foundation Dialysis Outcome and Quality Initiative considers non-adherence to include missed or shortened dialysis treatments, interdialytic weight gain, treatment

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adequacy (Kt/V), and measures of serum albumin and serum phosphorus [12].

Health psychology offers a number of models that seek to help us understand the factors which influence an individual's adherence to a medical regime. One such model is Leventhal and colleagues' self-regulatory model, which suggests that cognitive factors influence a range of illness-coping behaviors and outcomes among people experiencing illness or disease. The related concept of patient self-management involves care planning, collaborative problem solving, and decision making to manage kidney disease and treatment, including medications [13].

Therefore, a factor which contributes to the patient's self-management and hence medication adherence is health cognitions. Heath cognitions reflect individuals' beliefs regarding the extent to which they are able to control or influence health outcomes. They are based on personal experience. They are also expected to develop and change over the course of illness, and hence the experience of different treatments is likely to influence them [13]. Regarding the role and the importance of health cognitions, it has been recognized recently that internal health locus of control, that is the patient's preference to focus on his/her personal control on the disease management, is significantly and positively related to physical and social functioning, bodily pain, general health perception, and the physical component score of the SF-36 in HD and peritoneal dialysis patients [13]. A higher personal control is also associated with lower emotional response, better understanding on behalf of the patient of his/her disease, and higher medication adherence [14]. The findings suggest that by identifying patients' beliefs about an illness and its treatment, it might be possible to obtain more insight into their (mal-)adaptive responses to the illness [14].

Finally, it has been indicated that better health-related quality of life in dialysis patients is associated with higher control beliefs, lower illness and treatment disruptiveness, lower consequences, and fewer symptoms [14, 15]. In general, it is evident that an individual with internal locus of control may be more willing to follow treatment recommendations as he or she believes that the path of disease progression may be controlled via personal ability and action; action in this sense referring to adherence [16]. The positive reinforcement maintaining behavior is derived from the belief that hard work and ability lead to desired positive outcomes [17]. In contrast, individuals who believe that their fate is determined largely by chance or by other persons and not by their own actions may less likely to adhere to therapy, because they feel that their actions may not appreciably affect outcomes [17]. These individuals would attribute advances or declines in health to natural remission or progression of disease.

Past studies have shown that non-adherence is a common and increasing problem by those with chronic illnesses, including hemodialysis patients. These studies tended to examine non-adherence as a whole, including diet, fluid restriction, skipping treatments, and medications. Because of the multiple medications that hemodialysis patients need on a daily basis, a study of non-adherence directly related to medication-taking behavior was thought to be important for this population. Although a considerable number of articles on CKD have been published, few studies have examined the relation of medication adherence to depression or to health cognitions in patients on maintenance dialysis. Also, studies of health cognitions and adherence have produced mixed findings. Consequently, the assessment of this relation needs to be better understood and addressed more fully in CKD patients.

The purpose of the present study is (a) to examine the association of medication adherence with mental health and health cognitions in CKD patients, and (b) to determine whether sociodemographic and clinical factors are involved in these patients' medication adherence.

Our central hypothesis is that a high level of medication adherence is related to better mental health, indicated by fewer symptoms of depression, and to internal and doctor-attributed health locus of control. Further, we hypothesize that chance or other attributed locus of control are associated with lower level of medication adherence.

Method

Participants

A cohort of 171 patients was recruited from six general hospitals in the broader area of Athens, undergoing in-center HD. From this cohort, 168 patients provided full data on the variables studied, while the remaining three patients were excluded, having incomplete data, because they decided during the interview to discontinue their participation. Selection criteria included: (a) >18 years of age; (b) ability to communicate in Greek; (c) diagnosed with CKD; (d) dialysis treatment for at least a year; (e) adequate level of cooperation and perceived ability.

The rate of response was very high, reaching 99 %. Thus, the total sample includes almost all patients of these six units, consisting of 105 men (62.5 %) and 63 women (37.5 %). Participants were, on average, 62 years old. With regards to the variable of marital status, 112 patients (66.7 %) were married, 35 (20.8 %) were single, and 21 (12.5 %) divorced or widowed. Further, concerning educational level, the majority of patients (41.7 %) had university education, 33.3 % had secondary, and 25 % had elementary education. Regarding work status, 126 patients (75 %) were

retired or housewives, 28 (16.7 %) were employees, and 14 (8.3 %) were freelancers. Mean length of HD treatment in years was 6.38±5.41. Patients who participated in the present study were undergoing current dialysis for a varied period of time, and were categorized into two distinct groups regarding current treatment: (a) HD patients who recently commenced treatment (<4 years) and (b) HD patients on long-term treatment (>4 years). A cut-off period of 4 years of treatment was agreed upon because it was considered that a period of 3–4 years is required for patient adjustment to the diagnosis and treatment of a chronic illness [1]. Ninety-eight patients (58.3 %) had recently commenced treatment, while 70 (41.7 %) were in long term treatment.

Participants were Greek adults having signed a consent form for participation. All subjects had been informed of their rights to refuse or discontinue participation in the study according to the ethical standards of the Helsinki Declaration. Ethical permission for the study was obtained from the scientific committees of the participating hospitals. The study took place between October 2007 and June 2008.

Procedure

Measurements were conducted with the following instruments:

(1) The Medication Adherence Report Scale (MARS) was developed to measure adherence to a wide range of medication regimens [18]. The five statements comprising the scale are: "I forget to take my diabetes medicines", "I alter the dose of my diabetes medicines", "I stop taking my diabetes medicine for a while", "I decide to miss out a dose of my diabetes medicine", and "I take less diabetes medicine than instructed". The MARS was scored in accordance with standard practice with a maximum score of 25 by summing the score from the five questions, each with a five-point response scale (from "always true" to "never"; scored 1–5) [18]. The higher the score, the better is the adherence [18]. A cut-off point of <20 indicates an abnormal pattern of medication adherence while scores above 20 indicate a normal pattern of medication adherence among patients [19]. The MARS has previously been used in samples with chronic disease and has shown good internal reliability [19, 20]. In the present study, the above questionnaire was used in order to assess patients' adherence to medication that they take as a result of the hemodialysis treatment.

(2) The Center for Epidemiologic Studies Depression Scale (CES-D) [21, 22] is a 20-item self-report measure of depression. Scores range from 0 to 60, with higher scores indicating more symptoms of depression.

CES-D scores 0–15 are considered indicative of no depressive symptomatology, 16–26 are indicative of mild depression, and scores of 27 or more are indicative of severe depression [23, 24].

(3) The Multidimensional Health Locus of Control (MHLC) is a self-report tool measuring a patient's beliefs about control over health outcomes. Health locus of control is one of the widely used measures of individuals' health beliefs and has been designed to determine whether patients are internalists or externalists. It includes three orthogonal dimensions (internal, chance, and powerful others). A revised form of the MHLC further subdivides the powerful others scale into two separate scales: doctors and others [25]. Briefly, the theory holds that health locus of control is the degree to which individuals believe that their health is controlled by internal or external factors. Whether a person is external or internal is assessed by a series of statements. The statements are scored and summed to find the above. "Externals" refer to the belief that one's outcome is under the control of powerful others (i.e., doctors) or is determined by fate, luck or chance. "Internals" refers to the belief that one's outcome is directly the result of one's own behavior [25, 26]. The four categories are not mutually exclusive. Higher scores indicate stronger presence of the specific dimension of beliefs. In the present study, the above questionnaire was used in order to assess patients' locus of control related to CKD.

Statistical Analysis

Kolmogorov–Smirnov tests were performed in order to check whether the values of the sample fell within a normal distribution. Statistical analyses were also performed with the use of independent samples t test and one-way ANOVA in order to investigate potential effects of sociodemographic factors on medication adherence. Finally, independent samples t test analysis was used in order to examine differences between patients who recently commenced treatment (<4 years) and those on long term treatment (>4 years). A p value of 0.05 or less was considered to indicate statistical significance. All analyses were performed with the statistical package for the social sciences (SPSS 13.0 for Windows).

Results

The values of the total cohort were found to pass the normality distribution test. Full descriptive clinical data of the sample are presented in Table 1.

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Table 1 Clinical characteristics of the sample (*N*=168).

	HD patients
Pattern of adherence (M ± SD)	(22.58±2.70)
Normal (20–25 score) (M ± SD)	126 (75.0 %) (24.00±1.16)
Abnormal (<20 score) (M ± SD)	42 (25.0 %) (18.33±0.95)
Degree of depression (M ± SD)	(28.66±8.24)
No depression (0–15)	0 (00.0 %)
Mild depression (16–26)	70 (41.7 %)
Severe depression (>26)	98 (58.3 %)
Health Locus of Control dimensions	
Internal (M ± SD)	(27.25±3.06)
Chance (M ± SD)	(23.83±5.96)
Doctors (M ± SD)	(15.91±2.50)
Others (M ± SD)	(12.91±3.55)

HD Haemodialysis

The results of investigating the differences between HD patients with a normal and those with an abnormal pattern of medication adherence indicated that patients who were more adherent to medication showed less *depressive* symptoms. They also presented higher scores on *internal* and *doctors* locus of control as well as lower scores on *others*-attributed locus of control (Table 2).

Further, *t* test analysis of the differences between patients who present mild depression and those with severe depression indicated that patients with severe depression were less adherent to medication and less focused on *doctors* and *others*-attributed health locus of control (Table 2).

Concerning the differences between the two categories of duration of treatment, patients with more than 4 years of treatment presented higher scores of *depression* and a more *internal*-attributed locus of control (Table 2).

In order to assess the associations between adherence, locus of control, depression, and duration of treatment, intercorrelations were used. Medication adherence was associated positively with *internal* locus of control as well as *doctors*, and negatively with *depression* and duration of treatment (Table 3). Further, duration of treatment was related positively to *internal* locus of control and *depression*, and negatively to the dimension of *others* locus of control (Table 3). Partial correlation analyses showed that the positive relation between adherence and *internal* locus of control as well as *doctors* and the negative association with the dimension of *others* became even higher whether *depression* is controlled for (Table 4).

Regarding the effects of sociodemographic and clinical variables on medication adherence, the results indicated that younger patients (<45 years) were significantly (*p*<0.01)

Table 2 Mean scores ± SD of depression, medication adherence and health locus of control dimensions

	(*N*=42) HD patients with an abnormal pattern of adherence (<20) M ± SD	(*N*=126) HD patients with a normal pattern of adherence (20–25) M ± SD	*p* value
CES-D - Depression	35.66±6.09	26.33±7.53	*p*<0.01
Health Locus of Control dimensions			
Internal	25.00±3.30	28.00±2.59	*p*<0.01
Chance	23.00±2.18	24.11±6.75	0.11
Doctors	14.33±2.90	16.44±2.12	*p*<0.01
Others	13.66±1.26	12.66±4.01	0.02
	(N=98) HD treatment (<4 years) M ± SD	(N=70) HD treatment (>4 years) M ± SD	*p* value
CES-D - Depression	25.43±5.03	33.20±9.65	*p*<0.01
Health Locus of Control dimensions			
Internal	26.57±3.64	28.20±1.61	*p*<0.01
Chance	24.00±7.38	23.60±3.03	0.63
Doctors	15.85±2.48	16.00±2.55	0.72
Others	14.14±2.60	11.20±4.00	*p*<0.01
	(*N*=70) HD patients with mild depression (16–26) M ± SD	(*N*=98) HD patients with severe depression (>26) M ± SD	*p* value
MARS - Medication Adherence	23.60±1.36	21.85±3.15	*p*<0.01
Health Locus of Control dimensions			
Internal	27.00±2.20	27.42±3.55	0.37
Chance	23.20±6.96	24.28±5.11	0.25
Doctors	16.40±1.63	15.57±2.93	0.03
Others	13.80±2.33	12.28±4.11	0.01

Independent samples *t* test showing differences between patients with an abnormal and normal pattern of adherence, the two categories of duration of treatment as well as patients with mild and severe depression. *N*=168

Table 3 Intercorrelations between medication adherence, health locus of control dimensions, depression & duration of HD treatment

	MARS - Medication Adherence	MHLC - Internal	MHLC - Chance	MHLC - Doctors	MHLC - Others	CES-D - Depression	Duration of HD treatment
MARS - Medication Adherence	–	0.44**	0.03	0.24**	−0.08	−0.44**	−0.44**
MHLC - Internal	–	–	−0.29**	0.42**	−0.11	0.12	0.21**
MHLC - Chance	–	–	–	0.41**	−0.03	0.00	−0.05
MHLC - Doctors	–	–	–	–	0.26**	0.06	0.06
MHLC - Others	–	–	–	–	–	−0.25**	−0.21**
CES-D - Depression	–	–	–	–	–	–	0.43**
Duration of HD treatment	–	–	–	–	–	–	–

$N=168$

**$p<0.01$

more adherent (24.50±0.51) than older patients (>45 years) (22.20±2.79). Also, married patients presented significantly ($p<0.01$) higher scores of medication adherence (23.36± 2.08) than singles (22.60±2.27) or divorced/widowed patients (18.38±2.42). Concerning work status, those who were not working indicated significantly ($p<0.01$) less adherence (21.88±2.77) than patients who were working (24.66±0.47). There was no statistically significant relation with regards to the variables of gender and level of education. Finally, patients on long term HD treatment (>4 years) presented significantly ($p<0.01$) lower scores of medication adherence (21.60±3.02) than those who recently commenced treatment (<4 years) (23.28±2.19).

Discussion

The present study shows strong associations of medication adherence with depression as well as health locus of control in CKD patients.

Concerning the relation between the dimensions of health locus of control and the variable of medication adherence in the total sample, HD patients who focus on themselves in order to face their problems related to the disease present a higher level of medication adherence. These results correspond to previous findings showing that a higher personal

Table 4 Partial correlations between Medication Adherence and Health Locus of Control dimensions with the control of depression

	Health Locus of Control dimensions			
MARS	Internal	Chance	Doctors	Others
Medication Adherence	0.55**	0.04	0.30**	−0.22**

$N=168$

**$p<0.01$

control is associated with better understanding of CKD as well as higher adherence to medication [13]. Most studies that have used the MHLC questionnaire have observed significant associations between adherence and high internal locus of control (LOC) [27]. Individuals who believe that, in general, their actions play a large role in determining their circumstances may tend to adhere to the prescribed treatment regimen because they believe that they can affect their own health [17].

With respect to the relation of medication adherence to external LOC, high powerful-others scores have been shown to be independently related to better adherence [28]. In a study of renal dialysis patients, those who reported high powerful-other LOC had the best adherence [29]. Azlin et al. have shown in their research regarding LOC among non-adherent hypertensive patients undergoing pharmacotherapy that respondents with external locus of control ("doctors") have better drug adherence [30]. In our study, HD patients who are more adherent focus on the medical staff and less on other people.

It is obvious that adherence emphasizes not only the need for agreement but also the extent to which the patient's behavior matches the agreed recommendations from the prescriber and the prescription.

Other studies have shown that patient-related factors, i.e., personality traits, are associated with medication adherence. Personality traits are defined as "dimensions of individual differences in tendencies to show consistent patterns of thoughts, feelings, and actions". Specifically, patients with low conscientiousness, cynical hostility, or lacking self-control present decreased phosphate binder adherence in four of eight studies to examine personality [31].

As far as depression is concerned, the findings have demonstrated a negative association between level of medication adherence and depressive symptoms. Patients with depressive symptoms report greater feelings of hopelessness, compromising cognitive abilities. Hopelessness, cognitive distortions,

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and fatigue produce negative expectations of the future that may affect individual ability to carry out prescribed therapies and lead to inadequate fluid and dietary adherence behaviors [9]. Akman et al. found double likelihood of dietary non-adherence in depressed CKD patients when compared to patients without depression [32].

Also, based on the results of the present study, patients with severe depression are less focused on external factors with regards to locus of control. These findings are in agreement with the findings of other studies which have shown that belief in powerful others is associated with lower scores of depression in older people [33]. Further, Meyers has indicated in a study concerning religiosity and health locus of control as predictors of depression and anxiety in women with breast cancer that a significant negative correlation was found between powerful others locus of control and level of depression [34].

Regarding sociodemographic features and specifically the relation between age and medication adherence, findings are controversial. While some investigators have found older patients to have better adherence, others have shown younger patients to be more successful adherers [35]. In this study, there was a significant association between age and adherence, with the majority of the respondents of the older age group (45 years and above) was noted to be non-adherent to the prescribed medication. This could be explained by the fact that in advanced age, health problems are different and multiple. Older people take a greater number of medications, making non-adherence more likely [36]. Moreira et al. [36] observed that the average number of daily pills in older patients and the more advanced stages of CKD were statistically associated with non-adherence to drug therapy. Further, elderly people are more likely to have memory problems, to have complex drug regimens, and to experience more medication side effects [36].

Further, marital status might influence patients' adherence to medication positively [3]. In our study, patients who are married seem to adhere better than the singles and the divorced or widowed. This is a finding which is in agreement with other studies' results [37]. The help and support from a spouse could be the reason why married patients are more adherent to medication. Other studies have shown that divorced/widowed patients undergoing hemodialysis, compared to singles and married, indicate a more compromised quality of life (QoL), reporting poorer physical health and social relations, more negative perception of their environment, as well as poorer overall QoL/health. On the basis of these findings, married patients seem to experience a better QoL. Similar evidence in the literature indicates that the status of marriage in these patients may be significantly correlated to an enhanced physical and emotional well-being as well as better medication adherence [3, 37].

Further, findings have demonstrated that pensioners and housewives are less adherent to medication treatment. Perhaps, this relates to the fact that the pensioners are also older patients. This finding may also be associated with pensioners' as well as housewives' lower income in comparison to the income of those patients who have paid work. Cost is a crucial issue in patient's adherence, especially for patients with chronic disease, as the treatment period could be life-long [38]. Healthcare expenditure can be a large portion of living expenses for patients suffering from chronic disease. Healthcare cost should not be a big burden if the patient has a relatively high income or health insurance, but a number of studies found that patients who had no insurance cover [39], or who had low income [40], were more likely to be non-adherent to treatment. This is a specific problem in Greece, where health insurance organizations do not cover the whole cost of the very expensive medications that HD patents must take [41].

With respect to the variable of duration of treatment, acute illnesses are associated with higher adherence than chronic illnesses [42]. Longer duration of the disease and a longer duration of treatment period may both compromise patients' adherence [43]. In one trial that compared 6-month and 9-month treatment of tuberculosis, adherence rates were 60 % and 50 % for the two regimes, respectively [44]. In another study comparing preventive regimes of 3, 6, and 12 months, adherence rates were 87, 78, and 68 % for the three regimes, respectively [45]. Other studies have indicated that HD patients on long term of treatment had increased deficits in physical, social and environmental QoL, mental health, as well as medication adherence [1].

The limitations in our study should be mentioned. First, there is a need for future research to use prospective and longitudinal study designs to examine the interaction between adherence to medication and mental health as well as health cognitions in patients with CKD. Another methodological issue relates to the sample representativeness. Studies on the broader CKD population and recruiting even larger samples to enable effective multi-group analysis should be pursued in future research.

Further, measuring medication adherence in the CKD population can be impacted by numerous other factors besides medications (such as adherence to diet and dialysis), residual renal function, comorbid conditions, nutritional status, or type of dialysis treatment. In future studies, the above variables should be examined using in this way consistent and standardized measures of adherence.

Despite its limitations, the present study demonstrates the importance of psychosocial factors in understanding medication adherence of patients with CKD. It is important for renal health professionals to identify and attempt to remove their patients' barriers to medication self-management and optimal medication adherence. Staff in the dialysis unit can

impact patient satisfaction with care and include patients as active team members in order to identify barriers to medication adherence and to create individualized care plans for patients.

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