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PREVALENCE AND PREDICTORS OF NON-ADHERENCE TO MEDICATION AMONG PATIENTS ON HEMODIALYSIS IN A TERTIARY CARE HOSPITAL, TAIF, KINGDOM OF SAUDI ARABIA

[1]**Majed Qalil Al-Orabi; (Pharm D)** [2]**Nader NajiAlshalawi; (Pharm D)** [3]**Mohmmed M. Alotaibi; (Pharm D)**
[4]**Mustafa Awad A Abdallah** [5]**Prof. Yousif MA** [6]**Dr. Abubaker Ibrahim Elbur***

[1]Clinical Pharmacy Department; College of Pharmacy, Taif University, KSA.
[2]Pharmacy Department; Al –Hada Armed Forced Hospital, Taif; KSA.
[3]Pharmacy Department; King Abdul Aziz Specialized Hospital; Taif; KSA.
[4,5]Pharmacy Practice Research Unit; College of Pharmacy;Taif University.
[6]Pharmacy Practice Research Unit; College of Pharmacy; Taif University P.O. Box: 888; 21974, Al-Haweiah, Taif; Kingdom of Saudi Arabia.

*Correspondence for Author: Dr. Abubaker Ibrahim Elbur
Pharmacy Practice Research Unit; College of Pharmacy; Taif University P.O. Box: 888; 21974, Al-Haweiah, Taif; Kingdom of Saudi Arabia.

ABSTRACT
Background: Adherence to medication among patients on hemodialysis is an important issue for the delivery of optimum health care. **Objectives:** This study was conducted to measure the prevalence and to identify predictors of patients' non-adherence to drug therapy among patients on hemodialysis. **Methods:** A cross-sectional study was conducted at the Kidney Center at King Abdul Aziz Specialized Hospital;Taif;Saudi Arabia; during the September –November 2013. All adult patients on hemodialysis were included. Logistic regression analysis was performed. P value of < 0.05 was considered to be statistically significant. All statistical tests were conducted using the Statistical Package for Social Sciences (SPSS) version 21. **Results:** A total of 259 patients was included in the study. Males were 65.6%. The mean age was 48 ± 16 years and > 60 years old patients were 26.6%. Nearly half of the patients (49.0%) had mild depression. Overall, 27.8% of the patients were found to be adherent to treatment. Multivariable analysis identified only three predictors that significantly associated with non- adherence to treatment, namely; younger age (< 50 years), ($P<0.001$), being a Saudi citizen ($P = 0.001$) and had no or minimal depression (P=0.025). **Conclusions:** Adherence to drug therapy among patients on hemodialysis was low. The identified predictors of non- adherence should be considered in any future interventions designed to improve patients' adherence to medications.

KEYWORDS: Prevalence, Predictors Adherence, Medication, Hemodialysis.

INTRODUCTION
In Saudi Arabia the prevalence and incidence of End Stage Kidney Disease (ESKD) increased markedly during the last 30 years.[1] Major contributory factors that lead to this rise are rapid change in lifestyle, urbanization, fast increase in life expectancy beside the increase in population growth.[1] Statistics published in the year 2010 showed that there were 176 dialysis centers in the country with 4,264 machines catering for 10,928 patients. These services were provided majorly by the Ministry of Health together with the contribution of the private sector as well.[2]

Understanding the factors that may influence the treatment outcomes among patients on hemodialysis are important for the delivery of optimum health care. Adherence to medication is one of the most important factors since most of the patients at this stage suffer from one or more other concomitant illnesses. As a consequence, these patients have highest burdens of daily pill intake that may reach 20 pills per day, according to the type of co-morbidities.[3]

Low level of adherence is prevalent among patients on hemodialysis and many factors that influence patients' compliance were reported in the literature. A systematic review reported rates of non-adherence to the oral medications in a range of 3 - 80%.[4] A recent study conducted among patients ESKD undergoing online-haemodiafiltrationto measure the prevalence of self-reported medication non-adherence.[5] Non-adherence to medications was found to be low in that study and the patient's age and depression status are important factors associated with non-adherence to medication. The intake of a larger number of daily pills was found to be a significant contributory factor to non-adherence.[6] In contrast, patients on long-term hemodialysis were found to be more knowledgeable and more complaints to

treatment.[7] Elderly patients were found to be more adherent than their younger counterparts who significantly made more dosing errors and missed taking their medication.[8] Higher educational level was found to be significantly associatedwith better adherence to medical treatment.[9] Chan *et al*[10] identified poor knowledge, insufficient self-efficacy skills, forgetfulness to take medication as important barriers to patients' adherence. In contrast, other researchers concluded that patients'demographics, medical history and the type of treatment did not adequately explain non-adherence behavior.[11]

To the best of our knowledge, there was no research conducted in Saudi Arabia to measure non- adherence to medications and to Identify its predictors among patients on hemodialysis. Therefore, this study was conducted to measure patients' adherence to drug therapy and to identify predictors of non- adherence to medication with special emphasis on the impact of the severity of depression on non-adherence among other factors.

METHODS
A cross-sectional study was conducted at the Kidney Center in King Abdulaziz Specialized Hospital; Taif; Saudi Arabia during the period of three months (September –November 2013). Convenience method of sampling was adopted, Whereby all adult (>18 years) patients with ESRD who were on hemodialysis were included. Patients <18 years old, patients refused to participate in the study and patients with cognitive impairment were immediately excluded. Verbal consent was obtained. Data was collected by the researchers in association with nursing supervisor working in females section of the center. Data was collected through face-to-face interview method using a structured-questionnaire, which was designed in three sections. The first section was about patients' demographics and background characteristics (gender, age in year, nationality, residence, educational level, occupation, monthly income, presence of other disease/s, duration of hemodialysis, previous history of kidney transplantation and the number of currently used medications). Section two was an instrument to measure the degree of depression; Patient Health Questionnaire-9 (PHQ-9).[12] PHQ-9 is 9-item instrument with structured four responses to each item (not at all, several days, more

than half of the days and nearly every day). The patients were questioned over the last 2 weeks, how often has he/she has been bothered by any of the listed problems in the instrument presented in table (2).The instrument was translated into Arabic language using forward-backward translation method. A scoring system was developed to measure the severity of depression, which was classified as "No depression, minimal, mild, moderate, moderately severe, and severe depression". The last part was designed to measure patient adherence to treatment using the 4-item Moriskey Scale[13], which assesses patients' forgetfulness about taking medications, carelessness about taking medications, stopping medication when feeling better and stopping medication when feeling worse. Questions were recorded as 'yes' and 'no' and scored one point for 'yes' and zero point for a 'no' response. Scores were summed to give total score, ranging from 0 to 4.Non-adherence was defined as a score greater than zero. Ethical approval was obtained for the conduction of the study from Pharmacy Practice Research Unit (PPRU), College of Pharmacy, Taif University, Kingdom of Saudi Arabia.

Percentages and means were used to describe the variables. A multivariate model was developed to identify predictors of adherence to drug therapy. Crude logistic regression analyses were performed as initial steps of qualifying covariates to be included in multivariate logistic regression analyses. All covariates with p-values $<= 0.25$ were included in the model. P value of < 0.05 was considered to be statistically significant. All statistical tests were conducted using the Statistical Package for Social Sciences (SPSS) version 21.

RESULTS
Background characteristics
A total of 259 patients was included in the study, of them 170(65.6%) were males The mean age was 48 ± 16 years and > 60 years old patients were 69 (26.6%) . Saudi participants were 217 (83.8%) and 219 (84.6%) were living in the city. Participants who were living with other co-morbidities were 183 (70.1%), of them 158 (86.3%) had hypertension and 66 (36.1%) suffered from diabetes. Patients' background characteristics were presented in table (1).

Table (1): Patients' demographic characteristics.

Background characteristics	Frequency	Percent
Gender		
Male	170	65.6
Female	089	34.4
Age in year		
$\leq$50	132	51.0
>50	127	49.0
Nationality		
Saudi	217	83.8
Non- Saudi	42	16.2

Residence		
Urban	219	84.6
Rural	040	15.4
Educational level		
Secondary & above	95	36.7
Below secondary	164	63.3
Employment status		
Working	65	25.1
Not - working	194	74.9
Monthly income (SR)		
$\leq$5000	202	78.0
>5000	057	22.0
Presence of other disease/s		
Yes	183	70.7
No	076	29.3
Duration of heamodialysis		
$\leq$5 years	136	52.5
>5 years	123	47.5
Previous kidney transplantation		
Yes	25	9.7
No	234	90.3
No of medications		
$\leq$5	166	64.1
>5	93	35.9
Total	259	100

Severity of depression

Patients' response to individual items of Patient Health Questionnaire-9 were shown in table (2). The results showed that nearly half of the patients 127 (49.0%) had mild depression, while 60 (23.2%), 30 (11.6%), 21 (8.1%) and only 4 (1.5%) had minimal depression, moderate depression, moderately severe and severe depression respectively.

Adherence to treatment

Responses to Morisky scale showed that 104 (40.2%) admitted that they forgotten to take medicines, 101 (39.0%) were careless at times about taking medicines, 63 (24.3%) stopped medicines when feel worse and 64 (24.7%) did the same action when feel better. Overall, 27 (27.8%) were found to be adherent to treatment.

Table (2): Patients' responses to the items of Patient

No	Item	Not at all	Several days	More than half of the days	Nearly every day
1	Little interest or pleasure in doing things	95(36.7%)	123(47.5%)	22(8.5%)	19(7.3%)
2	Feeling down, depressed, or hopeless	118(45.6%)	114(44%)	12(4.6%)	15(5.8%)
3	Trouble falling or staying asleep, or sleeping too much	82(31.7%)	98(37.8%)	32(12.4%)	47(18.1%)
4	Feeling tired or having little energy	60(23.2%)	127(49%)	24(9.3%)	48(18.5%)
5	Poor appetite or overeating	98(37.8%)	104(40.2%)	22(8.5%)	35(13.5%)
6	Feeling bad about yourself — or that you are a failure or have let yourself or your family down	144(55.6%)	82(31.7%)	16(6.2%)	17(6.6%)
7	Trouble concentrating on things, such as reading the newspaper or watching television	142(54.8%)	98(37.8%)	9(3.5%)	10(3.9%)
8	Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	127(49%)	85(32.8%)	92(11.2%)	18(6.9%)
9	Thoughts that you would be better off dead or of hurting yourself in some way	217(83.8%)	31(12%)	5(1.9%)	6(2.3%)

Health Questionnaire-9.

Predictors of adherence to drug therapy
Univariable analysis
Univariable analysis showed significant difference in adherence to drug therapy between female and male patients (18.0% vs. 32.9%), (P = 0.012). Older patients were more committed to their treatment plan than younger ones (40.2% vs. 15.9%), (P < 0.001). Non-Saudi patients were more adherent compared to Saudi ones (52.4% vs. 23.0%), (P <0.001) and participants had

another disease/s were complying more than those suffered from renal disease only 31.7% vs.18.4% (P= 0.032). Non- adherence to treatment was proportionally more in patients classified with mild, moderate and severe depression compared to those with no to minimal depression(78% vs. 54.4%), (*P* = 0.002). The results of the univariable analysis was presented in table (3).

Table (3): Univariable analysis.

Characteristics	Comparison	Univariable analysis	
		OR (95% CL)	P value
Gender	Female vs. male	2.2 (1.2-4.2)	0.012
Age in year	$\leq$50 vs. >50	0.3 (0.2-0.5)	<0.001
Nationality	Saudi vs. non- Saudi	0.3 (0.1-0.5)	<0.001
Residence	Rural vs. urban	1.2 (0.5-2.5)	0.668
Educational level	Below secondary vs. secondary & above	1.2 (0.7-2.2)	0.456
Employment status	Not - working vs. working	1.3 (0.7-2.5)	0.349
Monthly income (SR)	>5000 vs. $\leq$5000	0.9 (0.5-1.7)	0.699
Comorbidity	Absence vs. presence of disease/s	2.1(1.1-4.0)	0.032
Duration of heamodialysis	$\leq$5 years vs. >5 years		
kidney transplantation	**Previous** kidney transplantation vs. none	1.0(0.4-2.5)	0.981
No of medications	$\leq$5 medications vs. >5	1.3(0.7-2.2)	0.41
Severity of depression	Non to minimal vs. mild to severe	2.5(1.4-4.5)	0.002

Multivariable analysis
Multivariable analysis identified only three predictors that significantly associated with non- adherence to treatment, namely; younger age (< 50 years), (*P*<0.001),

being a Saudi citizen (*P* = 0.001) and had no or minimal depression (*P* = 0.025) as shown in table (4).

Table (4): Multivariable analysis.

Variable	Adjusted odd ratio	95% Confidence interval	P value
Age in year	0.3	0.1-0.5	< 0.001
Nationality	0.3	0.1-0.6	0.001
Severity of depression	2.1	1.1-4.1	0.025

DISCUSSION
The background and demographic characteristics of the recruited patients more or less resemble the characteristics of similar patients published in other studies. Males were predominating in this study. A meta-analysis of 68 studies contained a total of 11,345 patients to evaluate the effect of gender on the progression of non-diabetic chronic renal disease.[14] The final results of this meta- analysis indicated that men with chronic renal disease of various etiologies show a more rapid decline in renal function with time than do women. Factors may be involved in this gender dissimilarity may include diet, kidney and glomerular size, differences in glomerular hemodynamics, and the direct effects of sex hormones.[15]

Elderly (> 60 years old) constituted 27% of the interviewed sample. Age-related increase in the annual incidence of CKD was documented in Europe.[16] The incidence rate among patients aged more than 75 years was almost seven times that of patients aged 20–39 years

and it was more than twice that of patients aged 40–59 years.

Low socioeconomic status is consorting with an increased risk of chronic renal failure.[17] The educational level and monthly income significantly varied in patients with ESRF. In the present study, participants with lower educational levels and monthly income were proportionally more than others. In conforming to the previously mentioned results; a study in Denmark demonstrated the relationship between education level and income and renal replacement therapy (RRT), as patients had a low educational level and income had higher incidence of RRT.[18]

A high percentage of non-working patients was documented in this study as three quarters of the interviewed patients were either jobless or pensioners. This finding is in agreement with the results of another study which showed that the unemployment rate among working-age patients with chronic kidney disease and

end-stage renal disease (ESRD) is high compared with that in the general population (71% versus 9.9%).[19] This also accords with earlier study, which showed changes in employment status in ESRD during their first year of dialysis. Within 1 year, the percentage of employed patients fall from 31% to 25% of hemodialysis patients.[20] Nearly 60% of the recruited patients were taking > 5 medications. This finding attributed to the increased number of concomitant diseases with ESRD as 73% of them were suffering from other diseases. Couchoud*et al*[21] found that at least one comorbid condition was reported for 85%, and three or more for 36% with a high comorbidity rate (85%).Hypertension and diabetes were identified as the most prevalent illnesses among the interviewed patients.Long-standing diabetes and/or hypertension are considered as the primary contributors to kidney disease.[22]

Approximately half of the interviewed patients had "Mild depression". This result was consistent with the finding of another study that suggested CKD patients on dialysis were more likely being depressed than those on the pre-dialysis period with a frequency of depressive symptoms of 34.5% for dialysis patients versus 13.3% in pre-dialysis patient.[23] No single patients' background characteristics was found to be associated with severity of depression. However, in another research conducted among hemodialysis patients, depression was found to be associated with a low body mass index and an increased number of comorbid physical illnesses.[24] Numerous researches have studied the adherence rates to drug therapies in patients with CKD or on dialysis and poor drug adherence was found to be the predominating practice.[25] Unfortunately, the results of the study showed a low rate of adherence among the participants with younger age and being a Saudi citizen as independent factors for non-adherence. Berman*et al*[26] found a strong association between adherence and older age.

In addition, the results showed that the severity of depression was found to be a strong predictor of non-adherence to medications. This finding is in agreement with the result of a meta-analysis of 31 studies which indicated that depression is associated with poor adherence to medication across a wide range of chronic diseases.[27]

Substantial efforts are needed at this center to improve adherence to medications among patients on hemodialysis. Despite the fact that no single strategy has been approved to improve patients adherence,healthcare providers should adopt a patient-centered approach. This approach may focus on removal of barriers to adherence, improve patient- healthcare provider communication, continuous education, and simplification of drug therapy.[28]

This study was not without limitations. Firstly, it was conducted in only one dialysis center in one hospital in the country, this may limit the generalizability of the results to all patients. Future research on the same topic can be conducted as multi-center studies to enroll patients from different hospitals or centers. Secondly, patient self-report method was used to measure adherence to treatment. This limitation can be overcome in the future by combining more than one method to exactly measure patients' adherence.

CONCLUSIONS
A considerable number of patients on hemodialysis at this center were found to be non –adherent to medication, with important predictors that should be considered when interventional programs are designed in the future to improve the level of adherence to medication. Multidisciplinary efforts from providers in the center and social support from families are needed to motivate the patients to better comply with their treatment regimen. Periodic assessment of patients' depression status is also mandatory.

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