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Predictors of Iranian Patients' Medication Adherence After Coronary Angioplasty

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Abstract

Objectives: Poor medication adherence (MA) is a significant concern in patients with cardiovascular disease (CVD) in low and middle-income countries. Thus, understanding the factors affecting this concern is the first step in designing effective interventions in such societies. In this regard, the purpose of this study was to investigate MA in a sample of Iranian patients after coronary angioplasty and to identify prediction factors based on the World Health Organization framework.

Materials and Methods: This descriptive-correlational research was conducted on 203 patients post carotid artery (CA) who were recruited from the Cardiology Clinics of Tabriz between November 2016 and February 2017. Data were collected based on socio-demographic characteristics and the Persian version of the Morisky Medication Adherence Scale (MMAS), and the Charlson comorbidity index was used as well. Finally, the multiple linear regression method was applied to identify the significant predictors of MA.

Results: The mean (standard deviation) MMAS score was 5.85 (±1.83). A multivariable model (adjusted R^2=0.136) predicted adherence using experienced medication side effects (B=-1.094, a 95% confidence interval (CI)= -1.700–-0.489, P<0.001) and having a recall (B=0.658, 95% of CI=0.153-1.163, P=0.011) and hospitalized history due to current disease (B=-0.537, 95% of CI=-1.031–-0.043, P=0.033).

Conclusions: The results of this study provide a better conception of the role of patients' experiences about medication side effects and the presence of a recall member in the family for MA after angioplasty. Patients' problems and concerns related to the side effects of medications must be resolved to improve MA.

Keywords: Medication adherence, Coronary angioplasty

Introduction

Cardiovascular disease (CVD) is the major cause of mortality in the world, substantially in low- and middle-income countries (1). However, the disease process can be remarkably slowed by cardioprotective medications and lifestyle changes (2) Sub-optimal medication adherence (MA) is a significant concern in patients with chronic illnesses (3), particularly in those suffering from CVD (4). MA relegates to the extent to which a patient operates in accordance with the prescribed interval and dose. While poor MA is associated with increased patient morbidity (5), mortality (4-6), healthcare costs (7), and increased risk of cardiovascular events (8,9), including myocardial infarction (4) and fatal stroke (6), it has been found that high adherence to the prescribed medication contributes to a decrease in cardiovascular events in the future, low readmission rates, and reduction in health care costs and morbidity and mortality (3,6,10).

Adherence to secondary medication is crucial in patients who have undergone carotid artery (CA) and stenting (11). According to the results of previous research, there is a strong relationship between discontinuing antiplatelet drugs and development of thrombosis post coronary stenting (5).

In general, adherence to long-term medication is approximately 57% in CVD (12). Based on the data from Iran, as a middle-income country, the use of secondary prevention medications was estimated to be less than 20% (13).

Several studies have attempted to investigate the reasons for medication non-adherence and reported multiple factors (4,9) such as patient, condition, therapeutic, socioeconomic, and system-related factors. The awareness of these factors may inform efforts to improve adherence rates (2,14). Non-adherence can propel to the inappropriate effects of treatment and poor outcomes (15). Therefore, identifying and subsequently addressing the barriers are important in improving MA, which could lead to improved patient outcomes and reduced health care costs (16).

The World Health Organization (WHO) suggests the consideration of macro- and micro-level factors including the health care system, medical conditions of the patient, and therapeutic and socioeconomic factors when studying

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Key Messages

- Factors related to patients, disease, treatment, and health care systems can have an impact on MA in patients.
- For MA improvement, the focus should be on consulting patients and decreasing their concerns about the prescribed medication (e.g., using patient-centred communication for determining and resolving these concerns).
- Patients concerned about the side effects of medications should be regularly assessed and resolved by nurses and physicians.
- The use of recall systems will be effective in promoting MA. Even this service can be provided by a family caregiver.
- Convenient and low-cost access to the drug does not guarantee its use in patients after angioplasty, but support for these patients is necessary through follow-up programs.
- The findings are useful for providing targets to individualize adherence support if patients' experiences on the side effects of their prescribed medications and family support to recall medication are related to adherence and can be intervened upon.

MA. This framework has improved our understanding of the factors that take part in non-adherence (17). Several studies have evaluated adherence to medication in different patient groups in Iran in order to understand the factors affecting MA in Iranian patients (18-21). In these studies, age, higher education, the complexity of regimen, forgetfulness, side effects, and fasting have been associated with non-adherence (18-20). However, to the best of our knowledge, no study has so far focused on MA in Iranian patients post angioplasty. Most studies of MA in patients with coronary artery disease or coronary interventions have constraints that reduce the efficiency of their findings. These studies commonly failed to use a theoretical model for the selection of variables predicting MA (22-24) Using such an approach, it is difficult to distinguish independent predictors of MA.

Therefore, this study aimed to ascertain MA and related factors in a sample of Iranian patients post angioplasty using the WHO framework.

Materials and Methods

This was descriptive-correlational research. The study sample consisted of a convenience sample of 203 patients who had undergone CA in the preceding month and attended the outpatient Cardiac Clinic of Shahid Madani Hospital in Tabriz (Iran) for a follow-up check. The participants of the study were older than 18 years old, and thus it was necessary to obtain their informed consent. Using 19 selected predictor variables to run a multiple regression method, this study needed a minimum sample size of 187 subjects to achieve 90% power and a medium effect size (0.15) at $\alpha = 0.05$. For considering a 10% attrition rate, 206 eligible patients were entered into the study, and finally, the data of 203 fully completed questionnaires underwent investigation.

Measurements

Data related to MA were collected in the second 6 months of 2018 by the Persian version of the Morisky Medication Adherence Scale (MMAS) through face-to-face interviews. The MMAS-8 (25) is a self-report measure of medication-taking behavior. It was developed from a formerly validated four-item scale (26) and supplemented with four other items addressing the circumstances surrounding adherence behavior. In addition to its authors, Gupta and Goren (27) provided evidence of adequate psychometric properties of the scale.

Response choices are "Yes" or "No" for items 1 to 7 of MMAS-8. Question No. 8 is a Likert-type question. The total score ranges from 0 to 8. Scores less than 6, $6 < 8$, and equal to 8 indicate low, moderate, and high adherence, respectively. The internal reliability of the Persian version of this scale was already confirmed (Cronbach's $\alpha = 0.697$) by (28).

The WHO framework for studying MA guided the selection of independent variables for the current study. A checklist was designed by the authors to gather these variables including demographics, patient's medical conditions, treatment and prescribed drugs, accessibility to the health care system, and socioeconomic factors. This framework is described in detail as follows.

1. Factors related to the patient included particular characteristics of each person, including demographic characteristics, abilities, and awareness of the disease, attitudes, opinions, and the patient's expectations of treatment (29).
2. Factors related to the patient's medical condition encompassing disease-related symptoms, the level of disability, the severity of the disease, and the associated depression (29). The Charlson comorbidity index was used to score the coexistence of several medical disorders. Accordingly, myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular accident, dementia, lung disease, connective tissue disorders, stomach ulcers, liver disease, and diabetes were scored 1. Complications caused by diabetes, paraplegia, kidney disease, and cancer received a score of 2, the presence of metastatic cancer and severe liver disease were scored 3, and finally, AIDS received a score of 6. The minimum and maximum scores on this scale were zero and 30, respectively (30).
3. Factors related to treatment included those caused by drug prescription, including drug regimen complexity, drug side effects, duration of antibiotic use, the required time for the effectiveness of drugs, changes in the treatment regimen, and the patient's previous experience of treatment (29).
4. Factors related to the health care system included the relationship between the patient and health care providers, access to medicines, patient education, time allocated to counseling, medical expenses,

insurance coverage, the complexity of the health system (bureaucracy), and medication uptake monitoring (29).

5. Socioeconomic factors were related to the economic and social situations of the patient (e.g., occupation, religion, education, social support, financial situation, cost of drugs, cultural beliefs, the presence of a person in the patient's family as a reminder, and distance from the health center).

Data Analysis

To analyze the data, SPSS statistical software (version 14) was applied, and a $P<0.05$ was considered statistically significant. The data were analyzed in three steps. In the first step, the correlation between each independent variable and MA scores was assessed using an independent *t* test. The analysis of variance and Pearson correlation coefficient were applied for categorical and quantitative variables, respectively. Independent variables showing a *P* value of less than 0.20 (31) with MA in bivariate analysis were included in multiple linear regression.

Hierarchical multiple regression with backward entry was used to identify significant predictors of MA. Data examination represented no problems with multicollinearity. The investigation of the scatter plots of pairs in independent and dependent variables revealed no violation of the linearity assumption, and the examination of partial regression plots demonstrated no violation of the assumption of homoscedasticity. Five regression models were separately constructed with entries into patient, condition, treatment, healthcare system, and socioeconomic related factors as independent variables, and MA was considered as a dependent variable. In the final step, an overall regression analysis was conducted to test the predictive value of a model that included only independent variables indicating significant contributions to MA in the above tested models.

Results

The mean age of the study participants was 55.62 ± 7.30 years, and the majority of participants were males (82.3%). Nearly half of the participants (48.8%) reported having hypertension and 29.1% of them suffered from diabetes. Only 36% of patients reported having no comorbidities. Of a total of 203 participants, 60% had undergone angioplasty with stent implantation. The bivariate correlations of the MMAS score with each participant's characteristics were tested before multivariate analysis (Table 1).

The internal consistency reliability of MMAS was assessed by calculating Cronbach's α coefficient, which

Table 1. Demographic and Clinical Characteristics of Participants and Bivariate Relationship Results

Characteristics	n (%) or Mean (SD)	Mean (SD) of MA	*P* Value[a]
Gender			
Male	167 (82.3)	5.79 (1.85)	
Female	36 (17.7)	6.13 (1.69)	0.310
Hypertension history			
Yes	99 (48.8)	5.75 (1.75)	
No	104 (51.2)	5.95 (1.90)	0.451
Diabetes history			
Yes	59 (29.1)	5.89 (1.71)	
No	144 (70.9)	5.84 (1.87)	0.838
Hospitalization history due to CAD			
Yes	82(40.4)	5.52 (1.84)	
No	121 (59.6)	6.08 (1.79)	0.033
Comorbidity (n=200)			
Yes	127 (62.6)	5.66 (1.75)	
No	73 (37.4)	6.15 (1.94)	0.074
Experienced side effects of medications (n=200)			
Yes	40 (19.7)	4.87 (1.52)	
No	160 (80.3)	6.08 (1.83)	<0.001
Presence of a reminder (n=200)			
Yes	128 (63.1)	6.13 (1.81)	
No	72 (36.9)	5.33 (1.77)	0.003
Age	55.62 (7.30)	5.85 (1.83)	0.257
Number of stents	1.62 (.93)	5.85 (1.83)	0.467
Frequency of the doctor's visit in a year	2.88 (1.03)	5.85 (1.83)	0.349
Expenditure of drugs (Rial)	805250 (434603)	5.85 (1.83)	0.117
Number of daily used drugs	2.79 (.50)	5.85 (1.83)	0.062
Time to access a health center (min)	11.01 (3.97)	5.85 (1.83)	0.082

Note. MA: Medication adherence; SD: Standard deviation; CAD: Coronary artery disease.

[a]Independent samples *t* test and Pearson correlation coefficient used for categorical and quantities variables, respectively.

indicated satisfactory internal consistency (Cronbach's α = 0.721).

Table 2 presents the levels of MA in the study sample. The mean of MA for patients in the sample was 5.85 ± 1.83. Only 32% of patients had high adherence to their prescribed cardiac medications while 45.8% of them were found to have low adherence.

The results of regression analysis (Table 3) revealed that among the patient-related factors, no variable could significantly predict MA ($P > 0.05$). Among the condition-related factors, comorbidities (B = -0.937, 95% of CI = -1.809 – -0.065, $P = 0.035$) and hospitalization due to the current disease (B = -0.669, 95% of CI = -1.229 – -0.109, $P = 0.020$) significantly predicted MA. Among treatment-related factors, the side effects of medications (B=-1.288, 95% of CI = -1.907 – -0.669, $P<0.001$), and among socioeconomic factors, recall (B = 0.863, 95% of CI = 0.299-1.427, $P = 0.003$) had significant effects on the models. Among health care system-related factors, no variable could significantly predict MA ($P > 0.05$). The adjusted R^2 values for the five described models were 2.8, 2.7, 12.2, 2.4, and 4%, respectively.

The overall regression model showed that the side effects of medications (B = -1.094, 95% of CI = -1.700 – -0.489,

Table 2. Medication Adherence Levels in Participants

Medication Adherence Level	Frequency	Percent
High adherence (score = 8)	65	32
Moderate adherence (6 to < 8)	45	22.2
Low adherence (<6)	93	45.8

Table 3. Predictors of Medication Adherence Using a Multidimensional Adherence Model in Participants

	B	95% CI for B		Beta	*P* Value	Explained Variance
		Lower Bound	Upper Bound			
Patient-Related Factors Predicted Medication Adherence						
Age	0.020	-0.017	0.057	0.079	0.293	0.028
Gender	-0.292	-0.983	0.399	-0.061	0.405	
Alcohol	1.154	-0.153	2.460	0.0123	0.083	
Narcotic	-2.286	-4.879	0.306	-0.124	0.084	
Regular visits	0.775	-0.221	1.772	0.111	0.126	
Marital status	-0.745	-2.864	1.374	-0.049	0.489	
Condition-related Factors Predicted Medication Adherence						
Family history of hypertension	0.142	-0.625	0.908	0.030	0.716	0.027
Comorbidity	-0.937	-1.809	-0.065	-0.244	0.035	
Hospitalize history due to CAD	-0.669	-1.229	-0.109	-0.176	0.020	
Number of stents	0.205	-0.098	0.507	0.101	0.183	
Percutaneous coronary intervention	-0.460	-3.043	2.123	-0.026	0.726	
Diabetes	0.581	-0.105	1.266	0.141	0.096	
HTN	0.319	-0.507	1.145	0.086	0.447	
Treatment-related Factors Predicted Medication Adherence						
Beta blockers	0.535	-0.058	1.127	0.125	0.077	0.122
Anti-platelet	0.219	-0.131	0.570	0.085	0.218	
Nitrate	0.214	-0.338	0.767	0.054	0.445	
ACEI	-0.160	-0.738	0.419	-0.038	0.587	
PPI	-0.382	-1.010	0.247	-0.098	0.233	
Calcium channel blockers	0.088	-0.603	0.779	0.017	0.802	
Side-effects of medications	-1.288	-1.907	-0.669	-0.281	<0.001	
Drugs number used daily	-0.432	-1.036	0.173	-0.119	0.161	
Health Care System-related Factors Predicted Medication Adherence						
Time to access health center	0.045	-0.026	0.117	0.098	0.213	0.04
Time to access pharmacy	0.041	-0.027	0.110	0.124	0.237	
Existence of a pharmacy nearby	0.475	-0.395	1.344	0.113	0.283	
Affordability	-0.017	-1.140	1.106	-0.002	0.976	
Time to visit the doctor	0.125	-0.141	0.391	0.071	0.354	
Cost	4.093	0.000	0.000	0.097	0.209	
Socioeconomic-Related Factors Predicted Medication Adherence						
Recall	0.863	0.299	1.427	0.226	0.003	0.024
Location	0.446	-0.197	1.089	0.106	0.173	
Continuing medications in Ramadan	-0.106	-1.274	1.062	-0.013	0.858	
Using alternative medicine	0.325	-0.352	1.002	0.067	0.345	
Moderate income	0.560	-1.091	2.212	0.103	0.504	
High income	0.684	-1.142	2.510	0.115	0.461	
Literacy under diploma	-0.124	-0.785	0.537	-0.034	0.712	
Literacy diploma and over	-0.063	-0.872	0.746	-0.015	0.878	

Note. CAD: Coronary artery disease; HTN: Hypertension; ACEI: Angiotensin-converting enzyme inhibitor; PPI: Proton pump inhibitor.

Table 4. Overall Predictors of Medication Adherence in Participants

Predictors	B	95% CI for B		Beta	*P* Value	Explained Variance
		Lower Bound	Upper Bound			
Comorbidity	-0.375	-0.878	0.128	-0.099	0.143	0.136
Hospitalization history due to current disease	-0.537	-1.031	-0.043	-0.144	0.033	
Side effects of medications	-1.094	-1.700	-0.489	-0.239	<0.001	
Recall	0.658	0.153	1.163	0.172	0.011	

$P<0.001$), recall (B = 0.658, 95% of CI = 0.153-1.163, $P=0.011$), and hospitalization history due to the current disease (B = -0.537, 95% of CI = -1.031 – -0.043, $P=0.033$) significantly explained 13.6% of the total variance for MA (Table 4). Beta coefficients demonstrated that the two predictors of side effects and hospitalization history have a negative effect whereas recall has a positive effect on MA (Table 4).

Discussion

Most prescribed cardiovascular drugs should be taken for a long time to improve symptoms and prevent subsequent cardiac events (32). However, evidence from a wider literature suggests that adherence to cardiac medications decreases over time (33). In the current study, only 32% of patients with post angioplasty highly adhered to their prescribed cardiovascular medications, which is in accordance with the findings of previous similar studies. For instance, Bansilal et al reported that MA to cardiovascular drugs in a long time was 34% in patients with myocardial infarction or atherosclerotic disease (6). Similarly, a meta-analysis by Chowdhury et al estimated the rate of MA to cardiovascular medications about 40.% (3). However, the adherence rate in our study is higher than that of the previously reported one (20%) in an international epidemiological study (13). This difference can be related to variations in the samples, study tools, and assessment time. In our study, patients had undertaken angioplasty within the preceding month, and evidence from wider literature shows that patients are more likely to adhere to their medications in the acute phase of their disease (34).

In addition, the number of comorbidities significantly contributed to the prediction of MA. Confirming the findings of the current study, Wong et al reported a significant relationship between the number of comorbidities and medication poor adherence (35). However, in a study by Gholamaliei et al, there was no significant relationship between the number of comorbidities including hypertension and MA in patients with diabetes (18).

In our study, the number of previous hospitalizations was another predictor of non-adherence. It is stated that poor adherence can lead to rehospitalisation (4) thus patients with poor adherence are more likely prone to hospitalization.

In the current study, there was a significant relationship between the side effects of drugs and MA, which is consistent with the findings of Momary et al, demonstrating that the experience of bloodshed adversely affects patients' adherence to clopidogrel (36).

In this study, having a family member to remind patients to take their medicine contributed to MA, which corroborates with the results of previous research (37). According to a review of qualitative studies, patients stated that having family support has a positive role in MA (38). In another study, patients receiving no help in their tasks had a barrier to MA (16). Forgetfulness was reported as the most common cause of non-adherence to medications by patients in Iran (39). Considering that forgetfulness is an unintentional reason for medication non-adherence (9), some practical and affordable interventional strategies such as sending short texts or involving the family in patient care can be effective in improving MA in patients after angioplasty (40).

The findings of this study should be interpreted in the context of some limitations. First, this study used a non-random sampling method, leaving the potential for bias. However, the results of our study mainly resonate with the findings of other studies conducted in Iran. Eventually, this study was based on self-reported data from study participants, which may be incomplete or inaccurate.

Conclusions

In general, adherence to cardiac medications is low in post-CA patients, including patients from Iran. The side effects of medications, the presence of a family member as the reminder, and the number of previous hospitalizations were factors that significantly and independently predicted MA in Iranian patients post CA. These results suggest that interventions for improving MA in patients post angioplasty should focus on patient education and consult them for detecting and decreasing concerns about the prescribed medication and use approaches for consumption recall. Considering the multifactorial nature of adherence problems, future studies are needed to identify the effect of manipulating these factors on MA in controlled trials.

Authors' Contribution

AA: concept and design; AG and FJ: data collection and interpretation of the data. RN and SO: performing of the study and writing of the draft. All authors read and approved the study.

Conflict of Interests

Authors have no conflict of interests.

Ethical Issues

This study was approved by the Ethics Committee of Tabriz University of Medical Sciences (license number: IR.TBZMED.REC.1395.432) and written informed consent was provided by participants prior to the study.

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