Evaluation of factors associated with medication adherence and hypertension among diabetic patients in Pakistan

Ali Hassan-Gillani^{1,2,3*}, Amna Saeed^{1,2,3}, Farhat Khanum⁴, Muhammad Q. Uz-Zaman⁵, and Jamshaid Akbar⁶

¹Department of Pharmacy Administration and Clinical Pharmacy, School of Pharmacy Xi'an Jiaotong University, Shaanxi, China; ²Center for Drug Safety and Policy Research, Xian Jiaotong University, Xi'an, Shaanxi, China; ³Shaanxi Centre for Health Reform and Development Research, Xi'an, Shaanxi, China; ⁴Department of Pharmacy, Yusra Institute of Pharmaceutical Sciences Islamabad, Pakistan; ⁵Department of Pharmacy and Alternative Medicine, Islamia University Bahawalpur, Pakistan; ⁶Department of Pharmaceutical Sciences Superior University Lahore, Pakistan

Abstract

Introduction: Non-adherence to a drug regimen is an important issue for the management of diabetes, and it leads to therapeutic failure. Uncontrolled diabetes is a prime reason for other complications, specifically hypertension (HTN). Thus, we evaluated the factors associated with therapeutic adherence to diabetes medication and factors associated with HTN among a population with diabetes in Punjab, Pakistan. **Materials and methods:** A descriptive cross-sectional study was conducted from December 2015 to March 2016. Systemic sampling technique was adopted to recruit patients. The eight-item Morisky Medication Adherence Scale-8 was used to evaluate adherence. Descriptive statistics were used to elaborate on the variables, bivariate, and multivariable analyses. These were conducted to classify factors independently associated with moderate-high adherence to medication therapy and factors associated with HTN. **Results:** A total of 299 people completed the study, with a mean age $\pm$ standard deviation, 48.8 ± 14.6 years. One hundred and sixty-nine (56.5%) participants were men, 270 (90.3%) were married. High adherence was found in 85 (28.4%), moderate in 69 (23.1%), and low in 145 (48.5%) patients. Patients who were taking help from the family members in taking medicine correctly and patients who believe that drug therapy caused side effects were showing reduced moderate-high adherence (adjusted odds ratio [AOR] = 0.562; 95% confidence interval [CI] = 0.328, 0.961) and (AOR = 0.349; 95% CI = 0.192, 0.635), respectively. A total of 44.4% of patients had HTN as a comorbidity. Family history of HTN (AOR = 23.42; 95% CI = 9.655, 56.853; $p < 0.001$), and abnormal cholesterol levels (AOR = 23.401; 95% CI = 10.195, 53.765; $p = 0.01$) were significantly associated with a hypertensive status of diabetic patients in our population. **Conclusions:** Patients who were depending on family members to take medication correctly at a proper time, and the patients who believed that drugs caused side effects were showing a reduced level of adherence to our study group. The risk factors of HTN (i.e., abnormal cholesterol levels) were prevalent among the patients of diabetes; these must be monitored and controlled.

Key words: Diabetes. Compliance. Hypertension. Risk factors.

Correspondence:

*Ali Hassan-Gillani

E-mail: hassangillaniali@yahoo.com

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Introduction

Diabetes mellitus (DM) is one of the most common non-communicable diseases. In recent years, DM has been escalating at a drastic rate and has become a global threat¹. The prevalence of DM has been found to be 6.9% in Pakistan². This surge in DM prevalence is attributable to urbanization and socioeconomic development, which ultimately alter traditional lifestyles³. To achieve desired therapeutic outcomes and disease management, patients must comply with drug therapy. The World Health Organization (WHO) defines compliance as “the extent to which a person’s behavior (taking medication, following a diet and/or executing lifestyle changes) corresponds with agreed recommendations from a health-care provider”^{4,5}. Lower adherence level to prescribed medication is the reason for 30-50% treatment failure and, in result, leads to organ failure⁶. The prevalence of hypertension (HTN) among people with diabetes is relatively high (ranging from 32% to 82%) compared with people who do not have diabetes. Risk factors for the development of HTN in the general population include older age, male sex, sedentary lifestyle, smoking, abnormal body mass index (BMI), family history of HTN, and dyslipidemia⁷. The presence of type 2 diabetes, duration of DM, and poor control is also factors that contribute to the development of HTN⁷⁻⁹.

Comprehensive diabetes care and management depend on effectual diabetes education, enhanced knowledge, attitudes, and skills that eventually lead to better control of the disease¹⁰. The burden on health-care systems can be reduced by intervening to motivate and guide the patient in the right direction¹¹. Several factors can hamper adherence, which can be classified as the patient, therapy, health-care system, socioeconomic, and disease-related factors; accessibility falls into the category of health-care facility-related factors¹². Furthermore, the previous studies showed that other factors, such as improper scheduled time and low patient education, increased medication non-adherence. Furthermore, medication adherence has been influenced by local culture and religious affiliations that influence individual medication behavior^{13,14}. Despite giving due recognition to DM as one of the most important health concerns in the middle and old aged, it demands the gathering of related information on medication-taking patterns and factors associated thereof. Although a study was performed by Nazir et al., which evaluated the relationship between medication adherence and glycated hemoglobin (HbA1c) level¹⁵, the studies on

factors affecting medication adherence are very rare in Pakistan. This study was designed to assess the adherence to medication therapy, confounding factors that affect adherence and the prevalence of predictors of HTN status among patients with DM in southern Punjab, Pakistan.

Materials and Methods

Study design and site

A descriptive and cross-sectional study was conducted among patients with DM from December 2015 to March 2016. The study site was southern Punjab, Pakistan. The target districts were Bahawalpur, Multan, and Rahim Yar Khan.

Study population and study setting

All those had been diagnosed as diabetics according to the measuring standards of American Diabetes Association (taking the diabetes medication for at least or more than a year) on oral hypoglycemic or insulin therapy; of any age, sex, religion, and socioeconomic status; and willing to participate in the study. Both type 1 and type 2 patients were captivated. The participant’s name and contact or any other personnel information were not collected. Patients who had been diagnosed with DM within the last year, and those who were unwilling or unable to participate (mentally compromised, and unconscious) were excluded from the study. The diabetes treatment is accessed by medical records of hospitalized patients and prescription records of outpatients, and further asking patients if they are taking any additional medication for diabetes. Among all Primary Health Care Centers (PHCC) and private clinics in the study districts, three PHCC and three private clinics were selected. We chose those clinics that included diabetes management and family practice/general medicine/internal medicine and those with a higher patient volume.

Study instrument

The study instrument consisted of descriptive as well as dichotomous and multiple-choice questions. The descriptive portion queried patient demographics, comorbidities, laboratory test results, and drug therapy; the quantitative portion consisted of dichotomous and multiple-choice questions. Other study variables included possible reasons for non-adherence, such as type

of medication therapy, affordability, poly-pharmacy, use of a glucometer (GM), and help with medication from family members, accessibility, beliefs about side effects of drug therapy, and beliefs about the benefits of drug therapy. The comorbidities were assessed by the description in the medication charts of the inpatients and prescriptions of outpatients. At least 30 min of walking 5 days a week was considered to be the minimum parameter for exercise compliance or physical activity^{16,17}. Any patient who reported cigarette smoking of any kind and in any quantity during the past 12 months was considered a current smoker¹⁷. Questions were closed-ended in yes/no format. An eight-item Morisky Medication Adherence Scale (MMAS)-8 is the tool widely used for the assessment of adherence to different conditions¹⁸⁻²⁰. The Urdu version of the MMAS-8 scale was available, which was translated and validated by Saleem et al. in the study²¹. The rest of the questionnaire was designed in English and translated into Urdu. To ensure that the original meaning of the questionnaire items was maintained, the Urdu version was translated back into English by a researcher acquainted with both languages. The Urdu version of the questionnaire was pretested on 30 diabetic patients outside of the study area, and minor changes were made as needed.

Adherence with medication (both oral medication and insulin) was assessed by the MMAS-8. Responses were summed, with the total possible MMAS-8 score ranging from 0 to 8. Adherence was high if the mean score was 8, moderate if the mean score was ≥ 6 -< 8, and low if the score was < 6²². Dichotomization was done based on the given criteria. Patients with score > 6 were characterized as moderate-high adherent and all others as low-adherent²³.

To evaluate participants' HTN status, the researchers measured each patient's blood pressure using a standard mercury sphygmomanometer. According to the WHO criteria, patients were considered to have HTN with systolic blood pressure 160 mmHg or more and/or diastolic blood pressure 95 mmHg or more, or if under ongoing treatment with antihypertensive drugs. BMI was calculated using a standard formula (weight in kg, divided by the square of the height in m²). BMI < 18.5 is classified as underweight, 18.5-24.9 as normal, 25-29.9 as overweight (pre obesity), and ≥ 30.0 is considered obese²⁴. Lipid profile (LP) and blood glucose level (BGL) were assessed by testing participant blood samples. Officially recommended by ADA, the normal BGL for a normal person is 140 mg/dl and for diabetic, its < 180 mg/dl²⁵. The capillary tube whole blood method

was used, with a cholesterol lipid analyzer to measure LP. Dyslipidemia was considered present with total cholesterol > 5.60 mmol/L.

Training of data collectors and quality management of data

Six data collectors were designated to collect data simultaneously in six different territories. The training involved the following aspects: (1) presenting a brief introduction of the study purpose to patients; (2) conducting face-to-face patient interviews; and (3) coping with patient lack of cooperation or other difficulties during the interview. The training was carried out for 3 days, with a demonstration given by the prime researcher. Trainees then conducted a pilot study in each of their respective districts and were observed for their interviewing skills.

Sample size

The sample size was calculated based on the prevalence of the disease. Assuming the prevalence of disease as 6.9% in Pakistan², 3% as precision rate, and 95% confidence interval (CI), a total of 282 sample size was calculated.

Study sampling

No diabetes registry or computerized database of DM patients was available in the study districts; therefore, systematic random sampling in the study settings (centers and clinics) was used to select potential participants in the study. Patients attending the private clinics were listed before visiting physicians. The list contains the medical complaints to the attending physician, diabetes status and some other variables. Every third DM patient who was listed as diabetic and visited any of the participating centers and clinics was chosen; a total of almost 900 individuals were approached from hospitals and private clinics. Only 398 of the total responded, of whom 299 completed the study. Three hundred and seventy-three approached patients were unwilling to participate (due to either time limitations or disinterest in the study); 129 patients were mentally compromised or seriously ill and excluded from the study.

Data analysis

Questionnaires with responses for more than 95% of questions were considered well completed and were

Table 1. The demographics of respondents

Demographic characteristics	Respondents n (%)
Age (48.8 ± 14.6)	
< 25	17 (5.7)
26-40	71 (23.7)
41-55	116 (38.7)
More than 55	95 (31.8)
Locality	
Urban	196 (65.5)
Rural	103 (34.5)
Gender	
Male	169 (56.5)
Female	130 (43.5)
Monthly income (PKR)	
< 15,000	68 (22.7)
15,000-30,000	134 (44.8)
More than 30,000	97 (32.4)
Marital status	
Married	270 (90.3)
Single	29 (9.7)
Education	
Less than primary	124 (41.5)
Primary-Middle	65 (21.7)
Matric	71 (23.7)
Graduate	39 (13.1)
Family history of diabetes	
Positive	208 (69.6)
Negative	91 (30.4)
Family history of hypertension	
Positive	97 (32.4)
Negative	202 (67.6)

PKR: Pakistani rupee.

included in the statistical analysis. Data were entered into EpiData 3.1.0 software and double-checked by the researchers. SPSS for Windows, Version 18.0 (SPSS Inc., Chicago, IL, USA) was used for data analysis. Demographic characteristics were illustrated using descriptive analysis. Percentages were used for categorical variables whereas continuous variables were expressed by mean ± standard deviation. Relationships between the proposed predictors and moderate-high adherence with DM medication therapy and that between predictors and HTN were assessed using logistic regression. To determine variables independently associated with medication adherence and HTN, variables with $p \leq 0.25$ in the bivariate analysis were selected for multivariable logistic regression. We base this on the Wald test from logistic regression and p value cutoff point of 0.25. More traditional levels such as 0.05 can fail in identifying variables known to be important^{26,27}. The statistical significance of associations among the

Table 2. Clinical characteristics of DM patients

Variable	n (%)
Duration of diabetes (years) (9.36 ± 6.9)	
1-5	100 (33.4)
6-10	109 (36.5)
11-15	47 (15.7)
More than 15	43 (14.4)
Smoker	
Yes	46 (15.4)
No	253 (84.6)
Total cholesterol	
High (> 5.60 mmol/L)	116 (39.2)
Normal ($\leq$ 5.60 mmol/L)	180 (60.8)
BMI	
Underweight	47 (15.7)
Normal	192 (64.2)
Overweight	60 (20.1)
Exercise compliance	
Yes	176 (58.9)
No	123 (41.1)
BGL	
Normal	187 (62.7)
High	111 (37.3)

BGL: blood glucose level; BMI: body mass index; DM: diabetes mellitus.

variables was accessed using 95% CIs with a respective odds ratio (ORs) with the moderate-high adherence (not with low-adherence). $p < 0.05$ was used as the cutoff point for statistical significance. Variables with 10% missing values were excluded from the analysis.

Results

Demographic and clinical characteristics

Out of the total approached patients, 398 initially agreed to participate in the study (response rate, 44.3%), while only 299 of them completed the questionnaires. Age of respondents was 48.8 ± 14.6 years; 169 (56.5%) participants were men, 270 (90.3%) were married, 103 (34.5%) were rural residents, and 68 (22.7%) had income < 15,000 Pakistani rupee (PKR). There was a positive family history of DM for 204 (69.6%) respondents, and 97 (32.4%) had a positive family history of HTN (Table 1).

The mean duration of diabetes was 9.36 ± 6.9 years. About 15.4% were current smokers, and 176 (58.9%) were compliant with exercise. Most respondents were in the normal BMI range (64.2%); BGL was normal in 187 (62.7%) participants, and 180 (60.8%) had normal cholesterol levels (Table 2).

Table 3. Questions related to patients adherence with medication*

Questions	Yes (%)	No (%)
Do you sometimes forget to take your medicine?	33 (11.0)	266 (89.0)
People sometimes miss taking medicine for reason other than forgetting. Thinking over the past 2 weeks, were there any days when you are not taking your medicine?	76 (25.4)	223 (74.6)
Have you ever cut back or stop taking your medications without telling your doctor because you felt worse when you took it?	121 (0.5)	178 (59.5)
When you travel or leave home, do you sometimes forget to bring along your medication?	44 (14.7)	255 (85.3)
Did you take your medications yesterday?	271 (90.6)	28 (9.4)
When you feel like your diabetes is under control, do you sometimes stop taking your medications?	78 (34.1)	221 (73.9)
Taking medication every day is a real inconvenience for some people; do you ever feel hassled about sticking to your treatment plan?	34 (11.4)	265 (88.6)
How often do you have difficulty remembering to take all your medicines? Never/Rarely 125 (41.8) Once in a while 35 (11.7) Sometimes 33 (11.0) Usually 38 (12.8) All the time 68 (22.7)		

Table 4. The different levels of adherence

Adherence level	n	%
Low adherence	145	48.5
Moderate adherence	69	23.1
High adherence	85	28.4

Adherence rate with medications

A total of 85 (28.4%) were showing high adherence (MMAS-8 score 8), 69 (23.1%) were showing moderate, and 145 (48.5%) were showing low adherence. A total of 154 (51.5%) patients were in the range of moderate to high adherence. The mean score for the compliance was 5.89 ± 1.780 (Tables 3 and 4).

The trend is showing the adherence decreased with age (70.6% in age < 25 vs. 44.2% in > 55 years). The rural population tends to demonstrate less moderate-high adherence as compared to urban residents (46.6% vs. 54.1%). Similarly, the increase in income and education showed an increasing trend in the moderate-high adherence of patients. About 42.6% of patients of income < 15,000 Pkr showed moderate-high adherence, which is considerably less as compared to those having income more than 30,000 Pkr (59%).

In terms of clinical characteristics influence on the adherence, it decreases with the increase in the

duration of diabetes, those with the duration of more than 15 years have moderate-high adherence rate of 44.2% which is low as compared to moderate-high adherence rate shown by patients with duration 1-5 years (52.0%). Similarly, an increase in the number of comorbidities decreases the rate of adherence.

Patients who were helped by family members to take their medicine at the right time showed considerable high adherence (60.8% vs. 46.7%). Similarly, those patients who had their own GM (57.0%) were showing more adherence as compared to those without GM (46.5%).

Factor related to medication compliance

The association between predictors and moderate-high adherence was investigated using univariate and multivariate analyses. Predictors showing an association with moderate-high adherence ($p \leq 0.25$ in the univariate analysis) were selected as candidate variables for multivariable logistic regression analysis. Relying on help from family members to take their medication correctly and fear that medicine will cause side effects significantly decrease compliance (Adjusted OR [AOR] = 0.562; 95% CI = 0.328, 0.961 and AOR = 0.349; 95% CI = 0.192, 0.635, respectively). Both of these variables had significant associations with therapeutic moderate-high adherence ($p = 0.035$ and 0.001 , respectively) (Tables 5 and 6).

Table 5. Demographic characteristics and factors affecting compliance

Demographic characteristics	n (299)	Medication adherence n (%)				
		Low-adherent (145) n (%)	Moderate-high adherent (154) n (%)	p value	AOR (95% CI)	p value
Age						
< 25	17	5 (29.4)	12 (70.6)	0.180	1	
26-40	71	33 (46.5)	39 (53.5)		2.092 (0.614, 7.127)	
41-55	116	55 (47.4)	61 (52.6)		1.149 (0.580, 2.274)	
More than 55	95	53 (55.8)	42 (44.2)		1.060 (0.583, 1.925)	
Locality						
Urban	196	90 (45.9)	106 (54.1)	0.219	1	
Rural	103	55 (53.4)	48 (46.6)		0.608 (0.358, 1.032)	
Gender						
Male	169	83 (49.1)	86 (50.9)	0.808		
Female	130	62 (47.7)	68 (52.3)			
BMI						
Underweight	47	26 (62.9)	21 (37.1)	0.261		
Normal	192	95 (49.5)	97 (50.5)			
Overweight	60	24 (40.0)	36 (60.0)			
Monthly income						
< 15,000	68	39 (57.4)	29 (42.6)	0.085	1	
15,000-30,000	134	67 (50.0)	67 (50.0)		0.759 (0.328, 1.753)	
More than 30,000	97	39 (40.2)	58 (59.8)		1.098 (0.468, 2.574)	
Marital status						
Married	270	134 (49.6)	136 (50.4)	0.26		
Single	29	11 (38.0)	18 (62.0)			
Education						
Less than primary	124	55 (44.4)	69 (55.6)	0.111	1	
Primary-middle	65	39 (60.0)	26 (30.0)		0.914 (0.405, 2.060)	
Matric	71	36 (50.7)	35 (49.3)		0.508 (0.210, 1.231)	
Graduate	39	15 (38.5)	24 (61.5)		0.698 (0.296, 1.644)	
Family history of diabetes						
Positive	208	106 (51.0)	102 (49.0)	0.197	1	
Negative	91	39 (42.9)	52 (57.1)		1.585 (0.906, 2.772)	
Duration of diabetes (years)						
1-5	100	48 (48.0)	52 (52.0)	0.745		
6-10	109	52 (47.7)	57 (52.3)			
10-15	47	21 (44.6)	26 (55.4)			
More than 15	43	24 (55.8)	19 (44.2)			
Smoker						
Yes	46	23 (50.0)	23 (50.0)	0.824		
No	253	122 (48.2)	131 (51.8)			
Co-morbidities						
No	42	18 (42.9)	24 (57.1)	0.460		
1	40	17 (42.5)	23 (57.5)			
More than 1	217	110 (50.7)	107 (49.3)			
Medications						
Single therapy (OHG or insulin)	249	122 (48.9)	127 (51.1)	0.699		
Combination therapy (OHG+ Insulin)	50	23 (46.0)	27 (54.0)			
Polypharmacy						
Yes	66	31 (47.0)	35 (53.0)	0.779		
No	233	114 (49.0)	119 (51.0)			
Do you take help of family member in taking medication at the right time?						
Yes	197	105 (53.3)	92 (46.7)	0.000	0.562 (0.328, 0.961)	0.035
No	102	40 (39.2)	62 (60.8)		1	

(Continues)

Table 5. Demographic characteristics and factors affecting compliance (*Continued*)

Demographic characteristics	n (299)	Medication adherence n (%)				
		Low-adherent (145) n (%)	Moderate-high adherent (154) n (%)	p value	AOR (95% CI)	p value
Do you believe drug therapy cause side effect to you?						
Yes	74	51 (68.9)	23 (31.1)	0.000	0.349 (0.192, 0.635)	0.001
No	225	94 (41.8)	131 (58.2)			
Do you believe drug therapy is beneficial to you?						
Yes	269	129 (48.0)	140 (52.0)	0.576		
No	30	16 (53.3)	14 (46.7)			
Is your medicine affordable for you?						
Yes	189	83 (44.5)	105 (55.5)	0.066	1.334 (0.704, 2.52)	
No	110	71 (64.6)	39 (35.4)			
Do you face any difficulty in getting medicine?						
Yes	95	46 (48.4)	49 (51.6)	0.986		
No	204	99 (48.5)	105 (51.5)			
Do you have your own glucometer?						
Yes	142	61 (43.0)	81 (57.0)	0.068	1.820 (0.911, 3.635)	
No	157	84 (53.5)	73 (46.5)			
Do you sometimes feel confused with the drug regimen?						
Yes	148	83 (56.0)	65 (44.0)	0.009	0.760 (0.444, 1.3)	
No	151	62 (41.0)	89 (59.0)			

*Hosmer and Lemeshow is 0.847 for medication adherence.

Correlation between BGL and medication adherence

Possible relationships between BGL and medication adherence were demonstrated by the Spearman's rank-order correlation coefficient. The criteria for defining correlation were as follows: a correlation coefficient of 0-0.25 was considered weak correlation, 0.25-0.5 fair correlation, 0.5-0.75 good correlation, and greater than 0.75 excellent correlation²⁸. A weak, insignificant correlation was seen between medication adherence and BGL ($r = 0.029$, $p = 0.631$).

The prevalence of HTN and its risk factor in diabetics

Among 299 patients, 133 (44.4%) were diagnosed with HTN. The prevalence of HTN found to be highest among diabetics older than 55 (61%) as compared to those aged < 25 (17.7%). Urban residents show more prevalence (47.0%) as compared to the rural population (39.0%). Those who had a positive family history of HTN had a significantly high prevalence of HTN ($p < 0.001$). Taking into consideration the clinical outcomes

increasing BMI increases the chances of being hypertensive, i.e., those who were overweight had a prevalence of 50.0%, and those who were underweight had 36.2%.

Predictors that were included in multivariate logistic regression ($p \leq 0.25$ in bivariate analysis) were age, residence location, sex, monthly income, marital status, family history of HTN, duration of HTN, smoking, cholesterol level, and exercise compliance. Multivariate logistic regression analysis of HTN variables revealed that family history of HTN (AOR = 23.42; 95% CI = 9.655, 56.853; $p < 0.001$), and abnormal cholesterol levels (AOR = 23.401; 95% CI = 10.195, 53.765; $p = 0.01$) were significantly associated with HTN (Table 6).

Discussion

Avoiding complications and achieving optimal health are the primary goals of DM management. This requires a combined effort from health-care officials and patients to improve adherence. Diabetes itself is a major influencing factor in the development of HTN. In this cross-sectional study, we measured the proportion of therapeutic adherence and prevalence of risk factors

Table 6. The prevalence of risk factor of hypertension in diabetic patients

Variables	n	Absence of HTN n (%)	Presence of HTN n (%)	p value	AOR (95% CI)	p value
Age (48.8±14.6)						
< 25	17	14 (82.3)	3 (17.7)	0.1	1	
26-40	71	54 (76.0)	17 (24.0)		0.604 (0.086, 3.103)	
41-55	116	61 (52.5)	55 (48.5)		0.149 (0.046, 4.830)	
More than 55	95	37 (39.0)	58 (61.0)		0.676 (0.246, 1.35)	
Locality						
Urban	196	104 (53.0)	92 (47.0)	0.238	1	
Rural	103	62 (61.0)	41 (39.0)		0.654 (0.291, 1.467)	
Gender						
Male	169	100 (59.1)	69 (40.9)	0.147	1	
Female	130	66 (50.7)	64 (49.3)		1.757 (0.795, 3.883)	
Monthly income (PKR)						
< 15,000	68	44 (64.7)	24 (35.3)	0.186	1	
15,000-30,000	134	73 (54.4)	61 (44.6)		0.779 (0.276, 2.203)	
More than 30,000	97	49 (50.5)	48 (49.5)		1.351 (0.578, 3.159)	
Marital status						
Married	270	146 (54.0)	124 (46.0)	0.125	1	
Single	29	20 (69.0)	9 (31.0)		0.727 (0.207, 2.548)	
Education						
Less than primary	124	71 (57.2)	53 (42.8)	0.468		
Primary-Middle	65	31 (47.7)	34 (52.3)			
Matric	71	43 (60.5)	28 (39.5)			
Graduate	39	21 (53.8)	18 (46.2)			
Family history of diabetes						
Positive	208	116 (55.7)	92 (44.3)	0.895		
Negative	91	50 (54.9)	41 (45.1)			
Family history of HTN						
Positive	97	15 (15.5)	82 (84.5)	< 0.001	23.42 (9.655, 56.853)	< 0.001
Negative	202	151 (74.7)	51 (25.3)		1	
Duration of diabetes (years) (9.36±6.9)						
1-5	100	65 (66.0)	35 (34.0)	0.008	1	
6-10	109	64 (58.7)	45 (42.2)		0.643 (0.135, 1.635)	
11-15	47	20 (42.5)	27 (57.5)		0.667 (0.17, 0.800)	
More than 15	43	17 (39.5)	26 (60.5)		1.032 (0.244, 2.017)	
Smoker						
Yes	46	22 (47.8)	24 (52.2)	0.24	1.532 (0.537, 4.366)	
No	253	144 (56.9)	109 (43.1)		1	
Total cholesterol						
High	116	23 (19.8)	93 (80.2)	< 0.001	23.401 (10.195, 53.765)	0.001
Normal	180	142 (78.8)	38 (21.2)		1	
BMI						
Underweight	47	30 (63.8)	17 (36.2)	0.351		
Normal	192	106 (55.2)	86 (44.8)			
Overweight	60	30 (50.0)	30 (50.0)			
Exercise compliance						
Yes	176	104 (59.0)	72 (41.0)	0.137	0.781 (0.359, 1.7)	
No	123	62 (50.4)	61 (49.6)		1	
Diabetes medication adherence						
Moderate-high	154	89 (57.8)	65 (42.2)	0.415		
Low	145	77 (53.1)	68 (46.9)			
BGL						
Normal	187	105 (56.1)	82 (43.9)	0.725		
High	111	60 (54.0)	51 (46.0)			

Hosmer and Lemeshow value was 0.634 for predictors of HTN.

AOR: adjusted odds ratio; BGL: blood glucose level; CI: confidence interval; HTN: hypertension; PKR: Pakistani rupee.

for HTN among DM patients in South Pakistan for the first time. The study population showed poor adherence to medication therapy. These results are in line with the previous studies conducted worldwide²⁹, whereas the results of another study contradicted our results³⁰. The difference in results may be attributed to different study periods, study locations, and study tools.

After adjustment for other factors in multivariable logistic regression, two factors were significantly associated with moderate-high adherence. DM patients who had family help or social support to take their medication correctly were less moderate-high adherent than those who do not have such support. The motivation for the self-management of diabetes is a pillar component in adherence. This attitude negates the need for dependence on primary care and thus strongly influences compliance. These results are in line with those of the previous studies^{31,32}; however, some studies found positive associations between family or social support and adherence as such support reduces negative attitudes, improves motivation, and helps with remembering how to correctly take medication³³.

Similarly, a study made in France demonstrated that the patients who were dependent on the family support showed significance high rate of good adherence than those who did not depend on the family support (29.2 vs. 2.4% $p = 0.0002$)³⁴. Those patients who believed that drug therapy caused them side effects were less likely to adhere to therapy. This factor can substantially affect patient compliance, as previous studies have showed^{35,36}.

Adherence to treatment increased with age in our study. Patients aged 26-40 years were showing more moderate-high adherence than those < 25 years of age. This study result was in line with a report in the United States (USA) showing that age < 24 years was a significant predictor of non-adherence to treatment³⁷. Younger people are less concerned about the detrimental effects of DM and less interested in the importance of adherence. They are, therefore, more careless about their treatment. Rural populations demonstrated lower moderate-high adherence than urban ones (54.1% vs. 46.6%). Rural areas lack basic health-care facilities and proper health education, and rural residents have low socioeconomic status, which all affect treatment adherence. Our population of income more than 30,000 PKR were (59.8%) more likely to be moderate-high adherent than those with monthly incomes under 15,000 PKR (46.2%). A study in France suggested that poor adherence was directly proportional to financial hardship. Those patients who do not have any

financial burden were showing good adherence (20.3%) than those who had some financial hardship (proper compliance 5.6%) ($p < 0.05$)³⁴. In this study, participants with higher education than matric (10th-11th high school) graduation were likely to be more adherent (61.5%) as compared with those who had less than primary level educations (55.6%). These results are in accordance with the previous studies³⁸.

In our study, patients who could afford the cost of therapy were 1.334 times more likely to be adherent. The previous studies conducted in the US showed that the high cost of medication was a reason for lack of adherence, and a study in France associated poor adherence with the affordability of treatment^{34,39}. A negative attitude or lack of motivation is another factor that hinders adherence. Patients in our study who felt confused or irritated by their drug regimen were less likely to be moderate-high adherent than those who did not. This effect was also seen in the previous studies showing that irritable temperament decreased adherence significantly³⁰. A study in France showed that those patients who do not face difficulty in taking medications alone had a significantly high level of good adherence³⁴. Another study in China reported that patients with type D personality were more likely to have poor adherence⁴⁰. A total of 57% of patients who owned and used their own GM were moderate-high adherent which is a bit higher than those who did not own GM (46.5%). The reason might be that proper glycemic monitoring keep patients motivated to stick with therapy. A study in Ethiopia found that patients who owned a GM were significantly less low-adherent, i.e., 15% those patients who had their own GM were low-adherent which is less as compared to those who do not own a GM (42.8% non-adherent)⁴¹, and results of another study in the US demonstrated the positive response of self-monitoring blood glucose on sitagliptin treatment adherence⁴².

HTN is a silent killer that often accompanies DM. This was supported by the fact that 133 (44.4%) participants with DM in our study were diagnosed with HTN; similar findings have been reported worldwide⁷. However, in one study conducted in India, the HTN prevalence was < 17.7%⁴³. After adjusting the other factors, such as age, family history of HTN, and cholesterol level, were significantly associated with the presence of HTN. Multivariate logistic regression analysis demonstrated that patients in the age group of 26-40 years were less likely to have HTN than those < 25 years of age, although this contradicts previous reports. There is a significantly increased likelihood of developing HTN with increasing age⁴³. The chances of having HTN among patients

with a positive family history of HTN were 23.42 times greater than among those with no family history of HTN. There have been no studies correlating the relationship between family HTN history and HTN risk in populations with DM; however, a significantly increased risk of developing HTN with a positive family history has been reported previously in India⁴³. HTN was 23.4 times more common among patients with high cholesterol levels than in those with a normal cholesterol level. The previous studies have not investigated cholesterol as a risk factor of HTN among diabetes patients; however, studies conducted among patients with HIV have demonstrated high cholesterol levels to be a risk factor for the development of HTN⁴⁴, with similar results reported in a US study⁴⁵.

Limitations

First, the response rate of the population in our study was very low due to the hasty environment and disinterest in the activity. Second, the comparisons of adherence were made against the BGL which is not the parameter used to represent the disease management outcome. HBA1c comparisons instead provide a proper understanding of one's disease management. However, resources did not allow calculating the HBA1c measurements, so the previous comparisons were made. Third, the selection process was based on systemic random sampling which cannot give the actual representativeness of the sample. However, this problem could be reduced by the selection of a large sample size, which was difficult due to a low response rate. Finally, recall biases may be present due to the face to face interview. This limitation was minimized by cross-checking as many variables as we could.

Conclusions

Dependence on the family for diabetes management and a belief that drug treatment is causing side effects is risk factors for moderate-high adherence with DM treatment. This situation can be rectified by improving health education and proper counseling. Health-care providers should focus on educating, motivating, and improving the skills of DM patients, which will ultimately improve their adherence. The prevalence of risk factors for HTN was high among DM patients. These must be monitored regularly and controlled to prevent HTN.

Ethics approval and informed consent

The study followed the tenets of the Declaration of Helsinki and was approved by the Ethics Committee for Medical Research of Xi'an Jiaotong University in Shaanxi, China (Ref # DIAB-16-19). This study was further approved by the Ethics Committee of Islamia University Bahawalpur. Written approval was also obtained from the medical superintendent of the respective study hospitals and physicians at private clinics. Willing literate patients were then asked to sign the consent form approved by the Ethics Committee. Illiterate patients were clarified about the contents of the written consent form, and the data collector asked permission to sign the consent form on their behalf.

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We acknowledge the participation of all the respondents. We do also acknowledge the help of data collectors. The MMAS (8-item) content, name, and trademarks are protected by US copyright and trademark laws. Permission for the use of the scale and its coding is required. A license agreement is available from Donald E. Morisky, ScD, ScM, MSPH, 14725 NE 20th St. Bellevue, WA 98007, USA; dmorisky@gmail.com.

Conflicts of interest

The authors disclose no conflicts of interest.

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Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

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