ORIGINAL ARTICLE

DRUG NON-ADHERENCE IN TYPE 2 DIABETES MELLITUS; PREDICTORS AND ASSOCIATIONS

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Background: Diabetes being a serious health issue faced by developing countries with drug adherence having pivot role for recommended glycaemic target. This study aims to determine drug non-adherence in type 2 diabetics and its predictors and associations. **Methods:** This cross sectional study was conducted after ethical approval at Medicine Dept. Rawal Institute of Health Sciences Islamabad over 10 months duration. Demographic details, duration of diabetes, education, socioeconomic class, glycaemic control, mode of anti-diabetic therapy, number of medications and other modes of therapy documented. Michigan Diabetes Knowledge Questionnaire applied with outcome as good, acceptable and poor knowledge. Drug adherence was assessed by Morisky Medication Adherence Scale (non-adherence at <6 points). Data analysed via SPSS version 17 with significant *p*-value <0.05. **Results:** Among 183 diabetics there were 43 (23.5%) males and 140 (76.5%) females. Mean age was 56.6±10.6 years and mean duration of diabetes 8.4±6.57 years. One hundred and fourteen (62%) cases were non-adherent. Diabetes knowledge was poor in 76 (41.5 %), acceptable in 76 (41.5 %) and good in 31 (16.9%). Un-satisfactory glycaemic control present in 149 (81.4%). Non-adherence was found to be associated with poor glycaemic control, poor dietary adherence, poly-pharmacy, illiteracy, practicing other modes of therapy and poor diabetes knowledge (p<0.05). **Conclusion:** Non-adherence to medication in type 2 diabetics needs to be addressed. Suggested contributory factors are illiteracy, practicing other modes of therapy, poor diabetes knowledge and poly-pharmacy. Public awareness programs, self-monitoring of blood sugars, regular follow-up visits with focus at patient education may improve glycaemic control and diabetes related complications.

Keywords: Diabetes mellitus, drug adherence, diabetes knowledge, glycaemic control, poly-pharmacy

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INTRODUCTION

As per IDF Diabetes Atlas 2013, 382 million people globally are suffering from diabetes with numbers expected to rise to 592 million by 2035.[1] The prevalence of diabetes mellitus in Pakistan has been documented to be 8.6%; 11.1% in Baluchistan & NWFP and 13.9% in Sindh.[2] Pakistan belongs to high prevalence area for diabetes, currently having 6.9 million people affected. This figure is expected to double by 2025 and affect 11.5 million people.[1,3]

Diabetes mellitus has been associated with spectrum of metabolic derangements that cause secondary pathophysiologic changes in multiple organ systems thus imposing a tremendous burden on individuals with diabetes mellitus and healthcare system. Achievement of appropriate glycaemic control is the primary aim in patients with diabetes and selection of appropriate mode of therapy along with life style and dietary modifications are the mainstay of management in diabetes.[4]

Adherence to the medication imposes important therapeutic and economic implications in diabetics.[5] Drug adherence is defined as the extent to which patient takes the medications being prescribed by his health care provider.[6] Certain patterns of non-adherence are defined as primary non-adherence, non-persistence and non-compliance.[7] Primary non-adherence refers to those patients who receive prescription but fail to obtain medications from the beginning. Its incidence has been reported to be 4–31%.[8,9] However, non-persistent are those patients who stop taking medicines altogether and poor executers are those who do continue medication but don't follow the prescribed dose and schedule regularly.[10]

Multiple factors have been studied to influence medical adherence in diabetics. In addition to demographic and clinical factors; certain factors like social, economic, cultural, regional beliefs, aging process and cognition impairment, knowledge about disease and medications being responsible for regional variations in adherence to medication.[11] Several studies have analysed the barriers associated with reluctance of patients for initiation of insulin therapy. However certain studies have proven that these barriers are faced not only to initiate the insulin but also other anti-diabetic therapies as well.[12,13]

The knowledge and insight of disease is associated with medication adherence as well as glycaemic control that is one of the main targets to be achieved in diabetics.[14] The efficacy of therapy has been found to be reduced along with increased risk of

hospitalization and mortality in type 2 diabetics with persistent non-adherence to medication.[14] Also the non-compliance or refusal to take medications is associated with diabetes related complications that ultimately have medical and financial implications. Certain psychosocial factors have also been studied to have role in drug compliance; psychological counselling and training sessions are suggested for diabetics to improve compliance.[16]

The objective of this study was to assess the non-adherence to anti-diabetic medications in diabetics from our region and to study the factors responsible for non-adherence. The results will be helpful to health care providers to take measures for improving adherence to medication in our diabetics.

MATERIAL AND METHODS

This cross sectional study conducted from November 2014 to August 2015 at Department of Medicine Rawal Institute of Health Sciences Islamabad after ethical approval from institutional committee. One hundred and eighty-three outdoor cases of type 2 diabetes mellitus were selected by convenience sampling and informed consent obtained. Sample size was calculated with 95% confidence interval, 5% precision and 15% estimated prevalence of non-adherence.[17,18]

Patients on dietary control alone, type 1 diabetes mellitus cases, having no record of the prescribed medications, critically ill patients and those with mental or physical condition that could interfere with their capability to understand or answer the questionnaire were excluded. Demographic details, socioeconomic status, education, duration of diabetes, dietary adherence and use of other modes of therapy was documented. Dietary adherence assessed by Perceived Dietary Adherence Questionnaire (PDAQ).[19] Record of fasting and random blood sugars reviewed and HbA1c advised. Satisfactory glycaemic control was labelled at HbA1c ≤7% as per recommendation of American Diabetic Association (ADA).[4]

Knowledge of diabetes was assessed by a Michigan Diabetes Knowledge Test (MDKT) based on 24 questions developed by Michigan Diabetes research and training Centre (MDRTC).[20] Questionnaire includes basic information about diabetes (10 questions), glycaemic control (7 questions) and complications of diabetes (7 questions). Each question has 3 options; yes, no and doesn't know. One mark given for correct answer and zero for wrong answer or doesn't know. The knowledge level was labelled as low (0–40%), medium (41–60%) and high (>60%).[21]

Drug adherence was assessed by Morisky Medication Adherence Scale (MMAS-8 score) based on 8 questions. The total score is obtained by adding points for eight questions that ranges from 0–8 points. Patients were categorized as having low (<6), medium (6 and <8) or high (8) adherence. Non-adherence was labelled at <6 points.[22,23]

SPSS version 17 was used for data analysis. Frequencies and percentages calculated for descriptive variables (socioeconomic class, glycaemic control, educational status, dietary adherence, glycaemic control and poly-pharmacy). Mean and standard deviation evaluated for quantitative variables (age and duration of diabetes). Chi-square test applied to study association of drug non-adherence with glycaemic control and other risk factors. *p*-value <0.05 is considered as statistically significant.

RESULTS

Among 183 patients with diabetes mellitus type 2, mean age was 56.6±10.6 (36–86) years. Mean duration of diabetes was 8.4±6.57 (1–35) years. Glycaemic control was un-satisfactory in 149 (81.4 %). Ninety (i.e., 49.4%) patients were illiterate and 73 (39.8%) patients were below poverty line (Table-1).

Mode of therapy was oral hypo-glycaemic in 136 (74.3%), insulin in 20 (10.9%) and combination therapy in 27 (14.7%). Poly-pharmacy (i.e., the number of medicines used >4) in 90 (49%) cases. Fifty-three (29 %) patients gave history of following other modes of therapy; i.e., homeopathic treatment in 16 (8.7 %), herbal medicine in 12 (6.6%) and *hikmat* in 25 (13.7 %) for diabetes. Dietary adherence was un-satisfactory in 89 (48.6%).

Drug adherence was low in 114 (62%), medium in 64 (35%) and high in 5 (2.7%). One hundred and fourteen (62%) patients were labelled as non-adherent (MMAS-8 score <6) and 69 (37.7%) were adherent (MMAS-8 score ≥6). 49 % diabetics said they sometimes forget to take medicines and 51% missed their doses during the last 2 weeks period; 32% used to stop taking medicines due to worsening of symptoms or side effects of medicines without informing their doctor; 45% patients didn't take medicines along with them while leaving home; 17% missed the dose day before hospital visit; 16% had history of stopping medicines when they started feeling better and 79 % felt hassled to follow their treatment plan (Table-2).

Diabetes knowledge according to DKQ-24 questionnaire was poor in 76 (41.5%), acceptable in 76 (41.5%) and high in 31 (16.9%) diabetics (Table-3). Non-adherence was found to be associated with poor diabetes knowledge (p<0.0001). Non-adherence was also found to be associated with illiteracy, poor glycaemic control, poly-pharmacy and use of other modes of therapy (p<0.05). However non-adherence wasn't found to be associated with age, gender, duration of diabetes and mode of treatment.

Table-1: Demographic features and risk factors for Non-adherence in type 2 diabetics

Variable	n (%)	Comparison with Drug Non-adherence		
		Adherent n=69	Non-adherent n=114	*p*-value
Age (mean±SD) years	56.6±10.6	55.7±8.76	57±11.6	0.397
Duration of diabetes(mean±SD) years	8.4±6.57	7.48±5.88	9.02±6.87	
• **<10 years**	100 (54.6%)	42 (42%)	58 (58%)	0.188
• **≥10 years**	83 (45.3%)	27 (32.5%)	56 (67.5%)	
Gender n (%)				
• Male	43 (23.5 %)	18 (42%)	25 (58 %)	0.57
• Female	140 (76.5 %)	52 (37%)	88 (63 %)	
Education n (%)				
• Illiterate	86 (47%)	17 (20%)	69 (80%)	
• Literate	97 (53%)	52 (54%)	45 (46%)	
o Primary	31 (17%)	17 (55%)	14 (45%)	<0.0001*
o Middle	12 (7%)	8 (66%)	4 (33%)	
o Matric	32 (17%)	16 (50%)	16 (50%)	
o Higher Secondary	13 (7%)	7 (54%)	6 (46%)	
o Graduation and above	9 (5%)	4 (44%)	5 (56%)	
Socioeconomic class n (%)				
• Below poverty line	73 (39.8%)	31 (42.5%)	42 (57.5)	0.339
• Above poverty line	110 (60%)	39 (35.5%)	71 (64.5%)	
Anti-diabetic therapy n (%)				
• Oral hypoglycaemics	136(74.3%)	51 (37.5%)	85 (62.5%)	
• Insulin	20 (10.9%)	10 (50%)	10 (50%)	0.47
• Combination therapy	27 (14.7%)	9 (33.3%)	18 (66.7%)	
Other modes of therapy				
• **None**	130 (71%)	56 (43%)	74 (57%)	
• **Yes**	53 (29%)	14 (26.4%)	39 (73.6%)	
• Homeopathic	16 (8.7%)	2 (12.5%)	14 (87.5%)	0.035*
• Herbal	12 (6.6%)	4 (33%)	8 (67%)	
• Hikmat	25 (13.7%)	8 (32%)	17 (68%)	
Dietary adherence				
• Satisfactory	94 (51.4%)	49 (52%)	45 (48%)	<0.0001*
• Unsatisfactory	89 (48.6%)	21 (23.6%)	68 (76.4%)	
Glycaemic control				
• Satisfactory	34 (18.6%)	20 (58.8%)	14 (41.2%)	0.006*
• Un-satisfactory	149 (81.4%)	50 (33.6%)	99 (66.4%)	
Poly-pharmacy				
• Yes	90 (49%)	27 (20%)	63 (70%)	0.034*
• No	93 (51%)	42 (45%)	51 (55%)	

Table-2: Drug Adherence in type 2 diabetes in view of Morisky Drug Adherence (MMAS-8) Scale

Drug adherence in diabetes - mmas-8 score			Correctly answered n (%)
MMAS-8 Questions	1.	Forgets to take medicines sometimes (No=1, Yes=0)	93 (51%)
	2.	During last 2 weeks forgot to take medicines at some days (No=1, Yes=0)	90 (49%)
	3.	Stops when feels unhealthy after taking (No=1, Yes=0)	125 (68%)
	4.	Forgets to take medicines while leaves home (No=1, Yes=0)	101 (55%)
	5.	Took medicines yesterday (No=0, Yes=1)	151 (83%)
	6.	Stops medicines when feels healthy (No=1, Yes=0)	136 (74%)
	7.	Feeling hassled about sticking to treatment plan (No=1, Yes=0)	38 (21%)
	8.	Difficulty in remembering to take medicines	
		Never/rarely (4)	54 (30%)
		Once in a while (3)	68 (37%)
		Sometimes (2)	21 (12%)
		Usually (1)	9 (5%)
		All the time (0)	0 (0%)
		(Divide the score by 4)	
MMAS-8 Score	**High Adherence**	(Score =8)	5 (2.7%)
	Medium Adherence	(Score =6 and <8)	64 (35%)
	Low Adherence	(Score <6)	114 (62%)

Table-3: Drug non-adherence in relation to level of diabetes knowledge; based on DKQ-24 questionnaire

Diabetes Knowledge			Adherent	Non-adherent	*p*-value
Level of Knowledge	**DKQ-24 score**	n (%)	n=69	n=114	
1. Good	>80 %	31 (16.9%)	22 (32%)	9 (7.8%)	
2. Acceptable	61–80 %	76 (41.5%)	25 (36%)	51 (44.7%)	<0.0001*
3. Poor	<60%	76 (41.5%)	22 (32%)	54 (47%)	

(Chi-square test; *Significant *p*-value <0.05)

DISCUSSION

In this study, drug adherence and diabetes related knowledge was assessed in a selected sample of type 2 diabetes mellitus patients. This study found a high prevalence of non-adherence in our diabetics. A regional study recently conducted by Imtiaz *et al* in Multan on indoor diabetics' shows 36% to be non-compliant.[24] Another study conducted by Riaz *et al* in Karachi shows even higher level of non-compliance (88%) to insulin in diabetics.[25] A study conducted in Uganda shows comparatively better compliance levels, i.e., 29% approximately. There are regional variations in compliance showing wide spectrum of results from as low as 36% to a very high value of 93% in certain regions.[17] Thus, pointing to need of such studies for chronic diseases to compare regional data and determine the contributory factors.

Almost 2/3rd of the participants were females. Females had comparatively higher non-adherence (63%) as compared to males (58%) but there was no significant association between gender and non-adherence. A French population-based study by Tiv M *et al*[26] and regional study by Imtiaz *et al*[24] also found no significant association between gender and non-adherence in diabetics. Comparatively high non-adherence among females in current study could be result of low diabetes knowledge and literacy rate among females. Also, most of the females in our country are dependent on males for financial support, outdoor tasks and approach to health care facility.

Most of the patients presenting to medical outdoor were elderly having age above 55 years. This can be explained by the improved health care facilities and increased life expectancy in diabetics. The knowledge score has been found to decline with age in several studies. A study conducted by Westberg *et al* demonstrated that knowledge score decreases by 3% with every 10 years increase in age.[27] Current study shows no significant association between age and non-adherence**.**

A large number of our diabetics (39.8%) belong to lower socioeconomic class, i.e., below poverty line. This possibly indicates inability to bear expenses of consultation and medication. Pakistan being a developing country needs to improve health care system to face the challenges of rising burden of non-communicable chronic diseases. Authors suggest that physician should decide the plan of management in view of international recommendations, patient preferences and financial background of the patient.

Studies have suggested that non-adherence rates are highest during the initial first year of treatment and almost half of the diabetics have non-adherence up to 80% during this time period.[28] A total of 54.6% of our diabetics were having diabetes for less than ten years duration. Non-adherence was comparatively higher in >10 years duration (67.5%) of diabetes as compared to ≤10 years duration (58%), however the difference was not statistically significant.

Certain factors like diabetes knowledge, beliefs and myths, other modes of therapy (i.e., *hikmat*, homeopathic, herbal therapy) being practiced in the region are responsible for tendency to avoid and delay the medical treatment. A total of 39% of our patients had history of use of these modes of therapy. And non-adherence was significantly more in patients following other modes of therapy (73.7%) as compared to those who didn't (57%) (p=0.035). Contrary to this, a study conducted at Uganda didn't find significant association between non-adherence and use of alternative medicine.[29] A regional study by Rafique G *et al* suggests that in view of misguidance and claims of cure by certain quacks, discussion about effects of such therapies should be a part of education of diabetics.[30]

Un-satisfactory glycaemic control was observed in 81.4% diabetics. Regional study has shown un-satisfactory glycaemic control in up to 75% of diabetics.[31] HbA1c <7% (recommended by ADA) has been found to reduce the incidence of micro-vascular disease and neuropathy in diabetics.[5] Poor glycaemic control was found to be associated with non-adherence in current study. Thus, indicating the importance of drug compliance to attain the target goal of HbA1c in diabetics. Lau *et al* demonstrated that type 2 diabetics who fail to take 80% of the oral hypoglycaemic have higher risk of subsequent hospitalization in the year ahead.[32]

Dietary adherence (assessed by PDAQ)[19] was un-satisfactory in 48.6% patients; i.e., significantly associated with drug non-adherence (p<0.0001). Riaz *et al* found similar results of dietary non-adherence in 58% diabetics.[27] In the management plan of diabetes, dietary modification has an important role. Educating the patients about importance of dietary modification, counselling by dietician and provision of diet charts in local language may help diabetics adhere to dietary plan.

Current study found non-adherence to be associated with poly-pharmacy. Most of the diabetics have to take multiple medications in addition to anti-diabetic medications. The reason is high prevalence of co-morbid conditions like hypertension, ischemic heart disease and nephropathy in diabetics. Sweileh *et al* found weak association between poly-pharmacy and drug non-adherence, the major contributing factors suggested were beliefs and disease related knowledge among diabetics in that study.[33] Contrary to this, our study demonstrated high non-adherence in diabetics taking >4 medications (p=0.034). Hence,

those with poly-pharmacy should be considered at high risk of non-adherence. Adjusting the timings of medications according to need and comfort of patients and timely omitting the medication no longer required may help the patients follow the prescriptions well.

By applying the 24 item DKQ to our patients, the results show that 41.5% of our patients had poor knowledge of diabetes. An Indian study by Dussa *et al*[35] found low mean DKQ-scores indicating poor knowledge in diabetics. Similarly an Ethiopian study found good knowledge in only 44% diabetics.[35] DKQ questionnaire is inexpensive, simple, quick and effective way to assess the knowledge level of diabetics. The reading level of this questionnaire is of 6th grade level. However as most of our patients were illiterate so the physician himself asked them the particular questions and documented the replied answers. Also at the end of interview patients were explained about the wrongly answered questions and relevant guidance along with written literature was provided. Hence, it was a good opportunity to educate and council the diabetics presenting to hospital. Poor diabetes knowledge was found to be associated with non-adherence (p<0.0001). There is need to educate diabetics about diabetes and its complications.

Forty seven percent of our patients were illiterate and 80% of these were non-adherent. This suggests that Illiteracy has impacts beyond socioeconomic implications. Imtiaz *et al* also found association between illiteracy and drug non-adherence.[24] Thus we can conclude that the literate patients possibly have better diabetes knowledge and awareness and hence better drug compliance than illiterate.

Most of the patients (79%) mentioned that they felt hassled about the treatment plan and 49% showed forgetfulness to take medicines. Also a significant number of patients took medicines the day before hospital visit**.** Thus, indicating that regular follow up visits, counselling sessions suggesting the means to reduce forgetfulness, i.e., use of pill boxes, supervision by a family member and addressing the problems faced by the patient may lead to better compliance. Jimmy B *et al* concluded that identification of these barriers in individual case and adaptation of suitable techniques may lead to better drug-adherence.[36]

Few regional studies have addressed the factors contributing to non-adherence in diabetics Current study has utilized reliable tools like MMAS-8 score and Michigan diabetes knowledge questionnaire, i.e., cost effective, widely used, time tested and proven. This will provide the figures that can be compared to the available regional and international data. Better understanding of these factors by our health care providers will be helpful to adapt the measures to improve drug adherence and increase the awareness about its importance and implications.

There are certain limitations of this study. We were unable to include the contribution of physical or visual morbidity. Authors recommend the assessment of insulin injection technique in future studies as despite of adherence, the erroneous technique may be responsible for inability to achieve the desired treatment outcome. Also, larger sample size is recommended for future studies. There might be an underestimation of drug non-adherence in our population as patients attending clinic and coming for follow ups are the ones actually concerned about their health as compared to those who don't attend the clinics and results of this study should be interpreted carefully.

CONCLUSION

Non-adherence to medication in patients with type 2 diabetes mellitus needs to be addressed. The suggested contributory factors are illiteracy, other modes of therapy, poor knowledge of diabetes and poly-pharmacy. Public awareness programs, self-monitoring of blood sugars, regular follow-up visits to health care facility and ensuring the drug compliance by inquiring and educating the patient and a responsible family member may not only improve the glycaemic control but also reduce the diabetes related complications.

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AUTHOR'S CONTRIBUTION

NS and SA contributed to data acquisition, study design, statistical analysis and manuscript writing. NK, WA and FS contributed to data acquisition, preparation of manuscript and literature review.

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