

Does adherence to the therapeutic regimen associate with health related quality of life: Findings from an observational study of type 2 diabetes mellitus patients in Pakistan

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Abstract: Patient adherence with a therapeutic regimen predicts successful treatment and reduces the severity of negative complications. The purpose of this work was to find the relationship between general Health Related Quality of Life (HRQoL) and compliance to the treatment among type 2 diabetes mellitus patients (T2DM) in Sargodha, Pakistan. The research was planned as a cross-sectional survey. T2DM patients attending a tertiary care institute in Sargodha, Pakistan were targeted for the study. The Urdu version of the Morisky Medication Adherence Scale (MMAS-Urdu) and EuroQol Quality of Life Scale were employed to evaluate adherence to treatment regimen and HRQoL correspondingly. Descriptive statistics were used for the elaboration of socio-demographic characteristics. The Spearman rank order test was employed to determine the relationship between medicine adherence and HRQoL. $P < 0.05$ was considered statistically significant. A total of 392 patients were selected for the survey. Most participants were males ($n=222$, 56.6%) with 5.58 ± 4.09 years of history of T2DM. Majority of respondents ($n=137$, 34.9%) were categorized in age group of 51 to 60 years with mean age of 50.77 ± 9.671 years. The present study highlighted that individuals with type 2 diabetes mellitus had decreased HRQoL (0.4715 ± 0.3360) and poor medication adherence (4.44 ± 1.8). Significant, yet weak positive correlations were observed between medication adherence and HRQoL ($r=0.217$ and 0.136 for EQ-5D and EQ-VAS respectively). Although the association between adherence to therapeutic regimen and HRQoL in the present study cohort was significant, it was rated as weak, hence failed in producing an overall impression on quality of life. The study highlights the need of identifying other individual factors affecting HRQoL among T2DM patients in Pakistan.

Keywords: Medication adherence, health related quality of life, association, diabetes mellitus type 2, Pakistan.

INTRODUCTION

Adherence to the treatment regimen and general Health Related Quality of Life (HRQoL) are two distinct concepts. Medication adherence has been defined as the active, voluntary and collaborative involvement of the patient in a mutually acceptable course of behavior to produce a therapeutic result (Meichenbaum and Turk, 1987). On the other hand, HRQoL refers to the physical function, psychological state, and social dimensions of health that are influenced by a person's experiences, beliefs, expectations and perceptions (Hume, 1989, Testa and Simonson, 1996). Both adherence and HRQoL are two different outcomes that represent different opinions following the processes of pharmaceutical care. Where adherence is an intermediate outcome, HRQoL is an ultimate consequence of the therapeutic plan (Revicki *et al.*, 2000). The only attribute common to the both notions is the relationship with patients and hence are important variables while assessing the success or failure of pharmacotherapy (Côté *et al.*, 2003).

During the process of pharmaceutical care, it is believed that patients who are adhered to the therapeutic regimen

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had experienced an improved HRQoL, especially in the case of chronic conditions (Lars Osterberg and Terrence Blaschke, 2005). Within this context, type 2 diabetes mellitus (T2DM) is a complex syndrome, which needs continual attention to food, blood glucose checking, and medicine consumption for control of blood glucose (WHO, 2003). For optimal glycemic control, the most important factor is the adherence to the treatment plan (Revicki *et al.*, 2000). However, in real practice, non-adherence to medication is a major issue in achieving ideal blood glucose levels (Saaddine *et al.*, 2002; Kerr *et al.*, 2004). In addition to the increased prevalence of diabetes-associated complications, a decrease in the overall HRQoL is also observed among patients with T2DM (Abolhasani *et al.*, 2005; Lewis, 1997). Although, it has been recommended that adherence to therapeutic regimen and HRQoL are linked, the available literature reports contradictory results from various parts of the world ((Côté *et al.*, 2003; Pippalla *et al.*, 1997; Sung *et al.*, 1998; Holzemer *et al.*, 1999; Billups *et al.*, 2000). Due to the paucity of studies examining the correlation between HRQoL and adherence to recommended therapies in Pakistani population, the current study was directed to assess the association between HRQoL and adherence to therapeutic regimens in patients with T2DM.

Methodology

Design and settings of study

A cross sectional questionnaire based survey was carried out between October 2014 and January 2015 at a public sector teaching hospital in the city of Sargodha, Pakistan. This hospital is generalised in nature and provides medical services to major population of the region.

Ethical considerations

No approval is required for cross sectional studies in Pakistan (Anonymous). However, approval from the relevant medical superintendent of the hospital was obtained to conduct the survey. Prior to data collection, informed consent was obtained from all participants before participation in the study. All participants were assured of confidentiality, and were required to sign an informed consent document before the data collection process.

Participants and sampling criteria

A prevalence based approach was used to identify the required sample for this study. It is estimated about 12% the population in Pakistan is affected by T2DM (Shera *et al.*, 1995); as a result, 392 patients were recruited for the study (Daniel, 1999).

Inclusion and exclusion criteria

Adult aging 18 years and above, with confirmed diagnosis of T2DM and ability to understand and write Urdu (official language of Pakistan) were recruited for the survey. Pregnant women, participants with Type 1 Diabetes Mellitus, having severe diabetic complications, psychiatric disorder, and foreign nationals were excluded from this survey.

Study variables and data collection

The survey instruments consisted of demographic data form, Morisky Medication Adherence Scale Urdu version (MMAS-U) and EuroQOL EQ-5D.

Assessment of medication adherence

The MMAS-U was employed for the evaluation of adherence to recommended therapies. The MMAS-U is a validated and reliable questionnaire which has been often used to measure patients' adherence to recommended medicines. The MMAS-U comprises of seven yes/no questions and one question answered on a five-point Likert type scale (Fahad *et al.*, 2012). The Morisky Medication Adherence Scale had three dimensions including forgetting, arbitrary stopping-medication, and difficulty in taking daily medication. A score of 8 was grouped as high adherence, score 6<8 was grouped as medium adherence and a score of <6 was categorized as low adherence (Morisky *et al.*, 2008; Krousel-Wood *et al.*, 2009).

Assessment of HRQOL

HRQOL in patients with T2DM was assessed by using EQ-5D, a generic measure of health status that provides a

simple descriptive profile and a single index value that can be used in the clinical and economic evaluation of health care and in population health surveys (Rabin *et al.*, 2001; EuroQoL Group, 1990). EQ-5D comprises of visual analog scale (VAS), which enables the respondent to provide a self-rating of his or her own health on a VAS graduated scale (0-100). The 'best imaginable health state' is set at 100 and 'worst imaginable health state' is set at zero. It likewise also includes EQ-5D self-classifier, a descriptive system that enables the participant to classify his/her health according to five dimensions. These dimensions define health in terms of mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension is divided into three levels, i.e., no problem/some or moderate problems/extreme problems. The resulting health state can therefore be defined by a 5-digit number by combining one level from each of the five dimensions. Potentially 245 health states can be defined according to this classification, and the information gathered can be used in a variety of ways (Shaw *et al.*, 2005). The research was registered with Euro QOL and EQ-5D Urdu version was provided by Euro QOL upon request.

STATISTICAL ANALYSIS

Descriptive statistics were employed to depict the socio-demographic variables of the participants. Continuous variables were expressed as mean and standard deviation and categorical variables as percentages and frequencies. The EQ-5D preference weight for each health state was not available for Pakistani population. Therefore, the states were derived from time trade-off (TTO) tariff of preference weights of the UK general population (Dolan *et al.*, 1995). Medication adherence was calculated according to the scoring system of the MMAS-U (Fahad *et al.*, 2012). The Spearman rank order correlation was employed to assess the relationship between medicines adherence and HRQoL. The compiled data were analyzed by using the Statistical Package for Social Sciences (SPSS) software version 21.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

392 T2DM subjects were recruited for the survey. table 1 represents the socio-demographic information and scores of HRQoL of study participants. The average age (SD) of the subjects was 50.77 (9.671) years, with 56.6% males and 90% of respondents were married. The average (SD) duration of disease was 5.58 (4.09) years. Eighty-three (21%) had matriculation level of education with 137 (34.9%) were house wives/house makers. Nearly 58% (n=226) had monthly income of more than Pakistan rupees (PKR) 15000 *(1.00 PKR=0.0098USD) with 71.9% (n=282) had urban residences. The mean EQ-5D score was 0.4715±0.3360 and EQ-VAS score was 64.77± 6.566.

Eighty-eight different health states were reported by the study participants whereby 43(11.0%) respondents pointed out no problem in 1st, 2nd & 3rd domain while moderate problem in 4th & 5th domain and 33 respondents (8.4%) stated moderate problems in all five areas. Even not a single participant reported no problem in all five domains and one respondent who reported extreme problems in all areas as shown in table 2.

Adherence scores

Table 3 presents the reported adherence to medication in

the current research. Among all the participants, 282 (71.9 %) were categorized as low-adherers and 97 (24.7%) were medium adherers. Only 3.32 of the patients answered were considered adherent to the therapies. The most frequently endorsed reasons for non-adherence were forgetting (61.2%) and carelessness (48.0%).

DISCUSSION

The goal of the present work was to test the correlation between HRQoL and treatment adherence among T2DM

Table 1: Characteristics of survey respondents and description of HRQOL scores

Description	N	Mean EQ-5D Score	Std Deviation	Mean EQ-VAS Score	Std Deviation
<i>Age (50.77 ±9.671)</i>					
30-40	69	0.4920	0.34134	66.6	13.583
41-50	131	0.4542	0.37430	66.4	16.247
51-60	137	0.4924	0.32265	64.4	14.925
61-70	55	0.4702	0.35672	63.6	12.121
<i>Gender</i>					
Male	222	0.5418	0.31859	68.6	14.660
Female	170	0.3889	0.36593	60.99	13.894
<i>Marital Status</i>					
Married	353	0.4797	0.34099	65.422	14.744
Unmarried	18	0.5013	0.37728	70.53	11.534
Widow	21	0.3983	0.43537	59.05	16.779
<i>Education</i>					
Illiterate	52	0.3665	0.37618	57.2	16.805
Primary	37	0.3833	0.37875	63.4	14.532
Middle	17	0.5244	0.33374	66.8	16.099
Matriculation	83	0.4303	0.36466	63.95	14.834
Intermediate	73	0.5227	0.29553	67.83	13.914
Graduate	75	0.5149	0.36634	68.3	14.249
Masters	55	0.5774	0.27322	68.4	11.472
<i>Occupation</i>					
Private Job	63	0.4655	0.35740	67.75	16.201
Government Job	76	0.5911	0.30786	68.68	13.399
Business Man	80	0.5259	0.31331	69.64	13.552
House Wife / House Maker	137	0.3789	0.36064	59.56	14.067
Retired	36	0.5046	0.35083	65.97	14.383
<i>Monthly Income (PKR)*</i>					
Nil	124	0.3762	0.35859	59.3	14.229
5000-10000	11	0.3798	0.38497	60	21.564
10000-15000	31	0.4266	0.38361	60.6	16.266
>15000	226	0.5414	0.32124	60.5	13.139
<i>Location</i>					
Urban	282	0.4794	0.34273	65.44	14.914
Rural	110	0.4655	0.36204	64.9	14.574
<i>Duration of Disease (5.58 ± 4.09)</i>					
< 1 Year	40	0.4966	0.27855	68.5	11.379
1-3 Years	59	0.4806	0.35790	67.4	14.397
3-5 Years	134	0.4842	0.35828	67.2	14.430
> 5 Years	159	0.4629	0.35267	60.95	14.672

*1.00 PKR = 0.0098USD

Table 2: Frequency of self-reported (EQ-5D) health states

Health State	*F	%	Health State	*F	%	Health State	*F	%	Health State	*F	%
11112	31	7.9	12221	2	0.5	21233	8	2	22333	4	1
11121	17	4.3	12222	5	1.3	21312	1	0.3	23221	1	0.3
11122	43	11	12223	6	1.5	21322	2	0.5	23222	1	0.3
11123	3	0.8	12233	3	0.8	22111	2	0.5	23223	2	0.5
11132	1	0.3	12311	1	0.3	22112	1	0.3	23321	1	0.3
11133	1	0.3	12323	1	0.3	22121	2	0.5	23322	2	0.5
11211	1	0.3	12332	1	0.3	22122	5	1.3	31111	1	0.3
11212	7	1.8	12333	1	0.3	22131	1	0.3	31121	1	0.3
11213	1	0.3	13131	1	0.3	22132	1	0.3	31122	1	0.3
11221	9	2.3	21111	3	0.8	22211	3	0.8	31222	3	0.8
11222	15	3.8	21112	2	0.5	22212	2	0.5	31332	1	0.3
11223	5	1.3	21121	7	1.8	22213	1	0.3	31333	1	0.3
11231	1	0.3	21122	18	4.6	22221	5	1.3	32222	2	0.5
11232	3	0.8	21123	2	0.5	22222	33	8.4	32232	3	0.8
11233	1	0.3	21132	1	0.3	22223	6	1.5	32322	3	0.8
11322	2	0.5	21211	4	1	22232	7	1.8	32332	2	0.5
12111	1	0.3	21212	2	0.5	22233	6	1.5	32333	2	0.5
12112	2	0.5	21213	1	0.3	22321	1	0.3	33222	2	0.5
12121	1	0.3	21221	13	3.3	22322	4	1	33232	1	0.3
12122	2	0.5	21222	23	5.9	22323	1	0.3	33233	2	0.5
12133	1	0.3	21223	8	2	22331	1	0.3	33322	1	0.3
12211	1	0.3	21232	4	1	22332	3	0.8	33333	1	0.3

Within 88 different health states, the majority (n = 43, 11%) stated no problems/difficulties in the first, second and third domain while moderate problems/difficulties in fourth and fifth domain* respectively. *Mobility, self-care, usual activities, pain/discomfort and anxiety/depression) domains of HRQoL in order; *Frequency

Table 3: Self-reported medication adherence behavior of study participants (MMAS)

Item	Yes (n, %)	No (n, %)
Do you sometimes forget to take your anti-diabetic pills?	240 (61.2)	152 (38.7)
Over the past two weeks, were there any days when you did not take your anti-diabetic medicine?	154 (39.2)	238 (60.7)
Have you ever cut back or stopped taking your medication without telling your doctor because you felt worse when you took it?	139 (35.4)	253 (64.5)
When you travel or leave home, do you sometimes forget to bring along your medications?	164 (41.8)	228 (58.1)
Did you take your anti-diabetic medicine yesterday?	317 (80.8)	75 (19.1)
When you feel like your blood glucose is under control, do you sometimes stop taking your medicine?	129 (32.9)	263 (67.1)
Do you ever feel hassled about sticking to your anti-diabetic treatment plan?	188 (47.9)	204 (52.0)
How often do you have difficulty remembering to take all your anti- diabetic medication?		
Never	236 (60.2)	
Almost Never	81 (20.6)	
Sometimes	49 (12.5)	
Quite often	24 (6.1)	
Always	2 (0.5)	

patients in Sargodha, Pakistan. This cross-sectional, observational study demonstrated that HRQoL was severely impaired and demonstrated a weak positive correlation with treatment adherence. Earlier conducted studies evaluating the correlation between HRQoL and

treatment adherence have produced conflicting results (Côté *et al.*, 2003; Sung *et al.*, 1998; Trivedi *et al.*, 2008). The correlation between treatment adherence and HRQoL may be twofold. The effect of treatment adherence on HRQoL might be a consequence of the effectiveness of

Table 4: Correlation coefficient (Total adherence score and EQ-VAS score)

Spearman's Rho	Adherence score	EQ-VAS score	EQ-5D Score
Correlation Coefficient	1.000	0.136	0.217
Sig. (2-tailed)*	-	0.007	0.000
N	392	392	392

*Correlation significant at the 0.05 level

therapy and the negative effects (i.e., side effects, daily life limitation of therapy, social stigma) that it can generate. Adherence to the therapeutic regimen is an important factor in disease state management. Treatment adherence is a key component linked to the effectiveness of all pharmacological therapies and foremost important for medicines prescribed for chronic disorders (Osterberg and Blaschke, 2005). According to WHO, improving adherence to medical treatment for chronic conditions can significantly produce health and economic benefits. Non-adherence to treatment recommendations is often frustrating and a crucial problem in the management of patients with chronic disease like diabetes. Sabaté (2003); Honish *et al.*, (2006) and Wattana *et al.* (2007) reported that good adherence with dietary control, exercise, and medication use were positively associated with HRQoL. In another study, Glasgow and colleagues (Glasgow *et al.*, 2006) highlighted that regular education of patients with T2DM is an important strategy that may lead to improved adherence and better HRQoL. Furthermore, Cukor and colleagues (Cukor *et al.*, 2008) found that higher levels of depression are correlated with missing medication doses. According to the literature, poor adherence affects the clinical outcomes and HRQoL causing increased mobility, mortality and healthcare costs (Pittman, 2010). However, the impact of treatment adherence on the HRQoL of T2DM patients is less clear. HRQoL is an important psycho-social characteristic which may impact an individual's ability to manage his/her chronic disease. Within this context, many health professionals believe that side effect profiles in adherents may reduce the HRQoL. One study conducted in Italy demonstrated that more than 25% AIDS patients stopped their therapy within the first year because of toxicity and other side-effects (D'Arminio *et al.*, 2000). In another survey, Kasper and colleagues (2000) demonstrated that 37% of their participants either discontinued or altered their medications because of the side effects. Another study showed that in diabetic patients, HRQoL is affected when there are complications (Anonymous, 1999) and in relation to their treatment, the use of insulin is negatively associated with their HRQoL (Redekop *et al.*, 2002). The negative correlation between adherence to the recommended therapeutic regimen and HRQoL is attributed to self-regulatory model. In self-regulatory approach, individuals will assess the outcomes of being adherent to medications and then make a decision to continue to be adherent or make changes to their regimen. In most of the cases, the patient notices their own behavior and assesses how this behaviour affects their

existing health condition. On the other hand, in social-cognitive models, beliefs that the medications may improve health and the importance of pleasing others who think you should take your medications are important considerations (Cote *et al.*, 2003). Previous studies indicated that T2DM patients have linked HRQoL to factors identified as precursors to adherence to therapeutic regimen, including patients' beliefs that they are capable to carry out behavior (self-efficacy) (Williams *et al.*, 2009), their attitudes and knowledge about the treatment of disease (Rose *et al.*, 2002), their perceived level of competence (Williams *et al.*, 2009) and their overall outlook on life (optimism).⁴¹ Additionally, there are other multi-factorial reasons for lower HRQoL among T2DM patients. Diabetic patients are more likely to be elder, obese, less likely to exercise, and more potential to have other chronic and serious health conditions such as high blood pressure, ischemic heart disease, high cholesterol (Myers *et al.*, 2013) and are more likely to have complications such as, damage to the blood vessels of the retina, damage to peripheral nerves, kidney disease, upper GI symptoms, erectile dysfunction, amputations, high blood sugar, and abnormally low level of blood sugar (Daniele *et al.*, 2013). In summation, the monetary value of managing diabetic patients is high as treating non-diabetic patients; mainly due to the high costs linked with management of diabetic complications (Mikailiukstiene *et al.*, 2013).

Few studies also illustrated that women with diabetes mellitus seemed to have worse HRQoL and mental well-being than men with T2DM (Mikailiukstiene *et al.*, 2013; Unden *et al.*, 2008). The current study also highlighted that female with T2DM appeared to have poorer HRQoL than their counterpart. Another study showed that low socioeconomic status and patients with a high school education or less had negative effect on HRQoL (Eljedi *et al.*, 2006). The present study also confirms that patients with a low economic status and high school education or less had poor HRQoL. Furthermore, another study revealed that T2DM has the relationship between longer duration of disease and poor HRQoL (Glasgow *et al.*, 1997). The current findings also demonstrated a correlation between duration of diabetes and HRQoL whereby longer duration of diabetes is linked with poor HRQoL.

The current study showed a small positive correlation between adherence to treatment and HRQoL among T2DM patients. Such a correlation was also found in a study conducted in Brazil (Miranzi *et al.*, 2008). The most

frequently endorsed reasons for non-adherence were forgetting (61.2%) and carelessness (48%). However, adherence behavior and HRQoL are very complex and multifaceted phenomenon and success or failure of treatment and overall health status are not dependent on a single factor.

CONCLUSION

Although the association between adherence to therapeutic regimen and HRQoL in the present study cohort was significant, it was rated as weak, hence failed in producing an overall impression on HRQoL. The study, highlights the need to identify other individual factors affecting HRQoL among T2DM patients in Pakistan.

Limitations

The study was conducted with a small number of T2DM patients who were selected from the outpatient clinic of public sector teaching (tertiary care) hospital situated in Sargodha, Pakistan. The study findings might not be generalized to the entire T2DM population of the country. Furthermore, the use of self-reporting methods are inferior and recall bias is always linked with self-reporting.

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