ASSESSMENT OF HEALTH RELATED QUALITY OF LIFE, HRQOL OF DIABETIC PATIENTS USING EURO-QOL-5D INSTRUMENT IN QUETTA, PAKISTAN

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Abstract:
Objective: The study intends to determine Health Related Quality of Life of diabetes out-patients by using EQ-5D scale.
Methodology: A questionnaire based, cross sectional study design was used to evaluate the HRQoL of diabetic patients in different outpatient clinics of Quetta, Pakistan. A convenience sampling technique was used to collect the data. A sample of 332 diabetic patients was selected for participation in the study. Euro-QoL-5D instrument was used to measure HRQoL of diabetes patients. Coded data was entered in SPSS version 20. Inferential statistics (Mann–Whitney U test and Kruskal Wallis tests, p < 0.05) were used to assess the significance among study variables. Multiple regression analysis was used to investigate how well clinical characteristics initially statistically significant variables predict health status measured by EQ-5D scores or how much each variable affect health state.
Results: The mean age of study subjects was 53.8±11.9 with majority had matriculation as their education status. The cohort was predominantly represented by Type 2 Diabetes mellitus patients 321(96.7%) with uncontrolled diabetes 191 (57.5%) and with an average of their diabetes duration of 8.38±6.66 years. All demographic and disease characteristics were found to be statistically significant to affect HRQoL whereas upon regression educational status, type of therapy and glucose control were influencing factors.
Conclusion: The study concluded treatment types, complications and glucose control have been some important factors in predicting the low health related quality of life of diabetic patients. It is recommended to change treatment modalities towards single and/or oral anti-diabetic drugs and without insulin therapy to make better the patients' quality of life. Measures regarding the prevention of blood glucose control should be educated to patients to avoid the complications in future life of diabetic patients and it would enhance their health related quality of life.
Key words: *Health Related Quality of Life, Diabetes Mellitus, out-patients, Pakistan, EQ-5D.*

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INTRODUCTION:

Diabetes Mellitus is rendered as a syndrome with heterogeneous group of diseases characterized by impaired glucose regulation as a consequence of chronic hyperglycemia [1, 2]. Diabetes Mellitus is most commonly classified as Type 1 diabetes mellitus/Insulin Dependent Diabetes Mellitus; Type 2 diabetes mellitus Non-insulin Dependent Diabetes Mellitus/ and Gestational diabetes mellitus diabetes, a type which occurs during pregnancy [2-4]. Worldwide increase in prevalence of diabetes mellitus, with or without being associated with other chronic diseases leads to increased consumption of health care resources; impairing health related quality of life and therefore diabetes has been rendered as an international public health problem [5]

International Diabetes Federation stated 1 in 11adults have diabetes and there were over 415 million people suffering from Diabetes Mellitus in 2015, and by 2040 this number will increase up to 642 million [6] . In Pakistan, the prevalence of diabetes among adults is 6.9% and 86,364 adults died due to diabetes [6] and not only its prevalence is imposing a burden its high cost also places the burden on society and also on an individual patient which may affect person's quality of life.

Health related quality of life, being a type of quality of life [7] is defined as an individual's perceived quality of life representing satisfaction in the areas likely to be affected by health status [8]. HRQoL is measured by many different scales of which few kinds are generic scales; function specific scales, population specific scales and disease specific scales [9]. HRQoL is one of the patient reported outcomes and needs to be assessed as it influences patient self-care behavior and their other treatment outcomes and if HRQoL is not improved it may cause disease complications [4].

HRQoL is adversely affected by chronic degenerative diseases and diabetes is one of the topmost disease which leads to complications if blood glucose is not controlled. Being chronic it may reduce HRQoL of patients but considerably less than other diseases and if complications occur then it may have adversely affect QoL of diabetics [5, 8]. The main rationale behind determining the Patients Quality of Life is to determine their medication related needs and to determine treatment related problems which would pave the way for better therapeutic understanding or a relationship between health care provider and patient to achieve better outcomes.

Within this context HRQoL is underreported in Pakistan especially for diabetes patients therefore the current study aims to determine Health Related Quality of Life of diabetes out-patients by using EQ-5D scale.

METHODOLOGY:

Study Design and Settings
A questionnaire based, cross sectional study design was used to evaluate the HRQoL of diabetic patients in different outpatient clinics of Quetta, Pakistan.

Sampling Technique
A convenience sampling technique was used to collect the data.

Sample Size
A population based sample of 385 diabetic patients was selected for participation in the study as was prescribed. In order to attain the required sample size 450 questionnaires were distributed among diabetic patients out of which complete data was achieved by 332 diabetic patients.

Inclusion and Exclusion Criteria
Patients having confirmed diagnosis of Diabetes from at least three months or more, and understands Urdu (National language of Pakistan) were included in the study. Pregnant ladies diagnosed with gestational diabetes mellitus, immigrants from other countries and diabetics who did not consent to participate were excluded from the study.

Ethical Considerations
This research was conducted according to National Bioethics Committee Pakistan's guidelines [10] according to which written followed by oral consent was taken from the patients and they were given assurance about the confidentiality of their responses and they were informed about their right to leave the questionnaire at any time.

Study Instrument
Euro-QoL-5D instrument was used to measure HRQoL of diabetes patients. European Quality of Life Scale (EQ-5D) [11] is a highly used, self-administered validated generic instrument, consists of five dimensions named mobility, self-care, usual activities, pain/discomfort, and anxiety/ depression. Each domain is categorized into three levels of severity i.e. no problem/some problem/extreme problems. Responses to these five items are used to obtain the weighted EQ-5D index score, which demonstrate health state with a possible range from -0.594 to 1.0. Second portion of questionnaire is EQ-5D visual analogue scale (VAS), on which patients' present-day health is to be rated on a scale which ranges from 0 (worst imaginable health state) to 100 (best imaginable health state). Higher scores on the index score and VAS denoted better health state. Urdu version of EQ-5D was adopted and its internal consistency determined by Cronbach's alpha value

was 0.785. The study has been registered with the Euro-QOL group.

Statistical analysis

All statistical analysis were carried out in SPSS version 20 [12]. Descriptive statistics were used to determine the demographic and disease characteristics of the study population. The variables with categories were measured as frequency and percentages whereas the variables which were continuous were expressed as mean ± standard deviation.

Inferential statistics (Mann–Whitney U test and Kruskal Wallis tests, $p < 0.05$) were used to assess the significance among demographic and disease variables.

Multiple regression analysis was used to investigate how well clinical characteristics initially statistically significant variables predict health status measured

by EQ-5D scores or how much each variable affect health state. The health status was not categorized into poor and good health state instead the scores (continuous variables) were used in relation to other variables due to which standard multiple regression was applied.

RESULTS AND DISCUSSION

Demographic Characteristics

The demographic characteristics of study participants are represented in Table 1 which described the mean age of study subjects as 53.8±11.9. Ethnicity distribution was equal for Pakhtoons and Punjabi 107 (32.2%) and they were majority married 314 (94.6%). Education status was also almost equally distributed with matriculation 77 (23.2%) followed by graduated 64 (19.3%) and intermediate 62 (18.7%).

Table 1: Demographic Characteristics of the respondents

Characteristics	Frequency N=332	Percentage (%)
Age (53.8±11.9)years		
<30	13	3.9
31-40	37	11.1
41-50	85	25.6
51-60	104	31.3
61-70	69	20.8
>70	24	7.2
Gender		
Male	171	51.5
Female	161	48.5
Marital status		
Unmarried	18	5.4
Married	314	94.6
Ethnicity		
Baloch	79	23.8
Pakhtoon	107	32.2
Punjabi	107	32.2
Sindhi	14	4.2
Others	25	7.5
Educational Status		
No education	25	7.5
Only Religious Education	16	4.8
Primary	41	12.3
Matriculation	77	23.2
Intermediate	62	18.7
Graduation	64	19.3
Higher Education	47	14.2
Occupation		
Student	5	1.5
Unemployed	16	4.8
Retired	41	12.3
Employee	80	24.1
Self employed	62	18.7
House Wife	128	38.6

Disease Characteristics of Diabetics

Disease characteristics of study population are displayed in Table 2. The cohort was predominantly represented by Type 2 Diabetes mellitus patients 321(96.7%) with uncontrolled diabetes 191 (57.5%) and with an average of their diabetes duration of 8.3±6.6 years. Majority of diabetic patients used 2 anti-diabetic medications 124 (37.3%) and their cost of treatment was in the range of 1000 to 3000PkRs. Hyperglycemia 129 (23.2%), followed by retinopathy 122 (21.9%) and diabetic foot syndrome 87 (15.6%) were the highly reported complications of diabetes. Large number of patients also followed diet therapy 264 (34.2%) and 262 (33.9%) patients used oral anti diabetic medications for the treatment of diabetes.

Table 2: Disease characteristics of respondents

Disease characteristics	Frequency N=332	Percentage (%)
Duration of Diabetes mellitus (8.3±6.6)years		
<1year	13	3.9
1-6	152	45.8
7-12	86	25.9
13-18	50	15.1
19-24	25	7.5
>25	06	1.8
Number of Diabetes Medications		
No medication	16	4.8
1	117	35.2
2	124	37.3
3	55	16.6
4	18	5.4
5	02	0.6
Cost of treatment of diabetes (3543±2729.0)		
No cost	26	7.8
PkRs1000-3000	176	53
3001-6000	68	20.5
6001-9000	48	14.5
>9000	14	4.2
Bearer of expenses of treatment of diabetes		
Oneself	164	49.4
Family	141	42.5
Government	27	8.1
Glucose control		
Glucose test not performed	05	1.5
Controlled	136	41.0
Uncontrolled	191	57.5
Type of treatment		
Diet therapy only	264	34.2
Pills	262	33.9
Insulin injection	149	19.3
Pills and insulin	98	12.7
Complications		
No complications	61	18.4
Hyperglycemia	129	23.2
Hypoglycemia	55	9.9
Retinopathy	122	21.9
Neuropathy	44	7.9
Nephropathy	65	11.7
Diabetic Foot syndrome	87	15.6
Others	54	9.7

EQ-5D HEALTH STATUS
Out of two forty three health states seventy EQ-5D health states were reported by the diabetes patients with majority 36 (10.8%) having no problem in first three dimensions i.e., mobility, self-care and performing usual daily activities and some problem in their mental health state and had moderate pain as demonstrated in Table 3. First most frequently twenty health states have been demonstrated in a table 3.

The mean EQ-5D descriptive score and EQ-VAS obtained were 0.39±0.39 and 57.7±16.1, respectively. 165 (49.7%) patients reported some problem in walking around i.e. first domain however, 211 (63.6%) participants had no problem in taking their self-care. An almost equal distribution between no problem 152 (45.8%) and some problem 154 (46.2%) in performing usual activities was found among diabetics as shown in the table 4.

Table 3: Self-Reported EQ-5D Health States

S.No	EQ-5D state	Frequency	Percentage
1	11122	36	10.8
2	22222	26	7.8
3	11121	20	6.0
4	11111	19	5.7
5	21222	18	5.4
6	22223	18	5.4
7	22233	17	5.1
8	11123	14	4.2
9	21122	11	3.3
10	11112	08	2.4
11	11122	08	2.4
12	11132	07	2.1
13	21221	07	2.1
14	21232	07	2.1
15	21121	05	1.5
16	21233	05	1.5
17	33333	05	1.5
18	11131	02	0.6
19	11212	02	0.6
20	11233	02	0.6

Table 4: EQ-5D Domains

EQ-5D dimensions	Frequency	Percentage
Mobility		
No problem in walking around	144	43.4
Some problem in walking about	165	49.7
Confined to bed	23	6.9
Self-care		
No problem in self-care	211	63.6
Some problem in washing and dressing myself	109	32.8
Unable to wash or dress myself	12	3.6
Usual activities		
No problem in performing usual activities	152	45.8
Some problem in performing usual activities	154	46.4
Unable to perform usual activities	26	7.8
Pain and Discomfort		
No pain or discomfort	46	13.9
Moderate pain or discomfort	196	59.0
Extreme pain or discomfort	90	27.1
Anxiety and Depression		
Not anxious or depress	72	21.7
Moderately anxious or depress	162	48.8
Extremely anxious or depress	98	29.5

Association of Demographic characteristics and EQ-5D scores and EQ-VAS
The relation between demographic characteristics and EQ-5D and VAS scores was determined by applying Kruskal Wallis test and Mann-Whitney U tests.

Statistically significant difference with EQ-5D and VAS scores was found among all demographic variables except ethnicity which show p-value of 0.162 greater than 0.05 with VAS score as shown in Table 5.

Table 5: Association of Demographic characteristics and EQ-5D scores and EQ-VAS

Characteristics	Frequency	EQ-5D Score (0.39±0.39)	EQ-VAS (57.7±16.1)
Age (53.8±11.9)[**2]			
<30	13	0.58±0.28	65.2±11.9
31-40	37	0.42±0.44	59.2±19.7
41-50	85	0.39±0.39	56.4±16.0
51-60	104	0.45±0.39	60.7±16.7
61-70	69	0.30±0.38	52.7±13.1
>70	24	0.27±0.39	57.9±14.0
Gender[**1]			
Male	171	0.47±0.37	60.8±14.9
Female	161	0.31±0.41	54.5±16.7
Marital status[**1]			
Unmarried	18	0.57±0.35	65.2±13.7
Married	314	0.38±0.39	57.3±16.1
Ethnicity*[2]			
Baloch	79	0.35±0.41	58.9±15.4
Pakhtoon	107	0.35±0.39	56.1±14.8
Punjabi	107	0.48±0.36	59.8±18.2
Sindhi	14	0.22±0.51	47.3±17.4
Others	25	0.45±0.39	57.6±11.0
Educational Status[**2]			
No education	25	0.03±0.46	45.4±19.1
Only Religious Education	16	0.27±0.47	58.4±17.0
Primary	41	0.32±0.37	56.5±15.9
Matriculation	77	0.35±0.38	57.9±14.1
Intermediate	62	0.43±0.35	55.7±13.8
Graduation	64	0.48±0.37	61.1±16.8
Higher Education	47	0.60±0.31	62.8±16.2
Occupation[**2]			
Student	05	0.57±0.32	67.0±8.3
Unemployed	16	0.31±0.59	53.3±14.6
Retired	41	0.45±0.32	56.4±12.9
Employee	80	0.53±0.35	61.6±16.9
Self employed	62	0.46±0.35	60.4±15.2
House Wife	128	0.27±0.41	54.6±16.7

* Statistically significant with EQ-5D scores.
‖ statistically significant with EQ-VAS scores.
** Statistically significant with both EQ-5D scores and EQ-VAS.
1 Mann Whitney Test
2 Kruskal Wallis Test
 p-value<0.05

Association of Disease Characteristics with EQ-5D scores and EQ-VAS
Table 6 demonstrates that all disease characteristics were found statistically associated with EQ-5D and VAS scores.

Table 6: Association of Disease Characteristics with EQ-5D scores and EQ-VAS

Disease characteristics	Frequency	EQ-5D score (0.39±0.39)	EQ-VAS (57.7±16.1)
Duration of Diabetes mellitus[**2]			
<1year	13	0.62±0.46	70.0±19.6
1-6	152	0.51±0.34	60.5±16.6
7-12	86	0.29±0.39	53.5±14.7
13-18	50	0.25±0.42	55.1±15.7
19-24	25	0.18±0.39	52.4±9.8
>25	06	0.67±0.33	65.0±15.1
Number of Diabetes Medications[**2]			
No medication	16	0.63±0.44	76.2±19.0
1	117	0.46±0.32	59.8±15.9
2	124	0.35±0.42	55.7±15.5
3	55	0.38±0.4	55.7±12.4
4	18	0.24±0.48	50.5±16.6
5	02	0.33±0.37	40.0±14.1
Cost of treatment of diabetes[**2]			
No cost	26	0.44±0.43	55.7±18.2
PKR1000-3000	176	0.48±0.36	60.9±16.7
3001-6000	68	0.28±0.41	55.1±13.5
6001-9000	48	0.29±0.38	52.6±13.1
>9000	14	0.19±0.5	52.5±18.4
Bearer of expenses of treatment of diabetes[**2]			
Oneself	164	0.49±0.35	60.2±16.3
Family	141	0.28±0.42	55.1±15.1
Government	27	0.39±0.41	56.3±18.5
Glucose control[**2]			
Glucose test not performed	05	0.47±0.36	56.0±15.2
Controlled	136	0.52±0.36	63.6±15.4
Uncontrolled	191	0.31±0.40	53.6±15.5
Type of treatment[**1]			
Single therapy	235	0.48±0.36	60.5±16.0
Multiple therapy	97	0.18±0.40	51.1±14.5
Complications[**1]			
No complications	61	0.64±0.33	70.0±16.7
Complications	271	0.34±0.39	55.0±14.6

* *Statistically significant with EQ-5D scores.*
∥ *statistically significant with EQ-VAS scores.*
** *Statistically significant with both EQ-5D scores and EQ-VAS.*
1 Mann Whitney test
2 Kruskal Wallis test

Table 7: Effect of Demographic and Disease characteristics on HRQoL

Model Summary			
R	R^2	Adjusted R^2	SE of estimates
0.576	0.332	0.304	0.3327

Multiple Regression				
Variables	Standardized Coefficients	p values	95% C.I for EXP(B)	
	Beta		Lower	Upper
Age	-0.009	0.875	-0.038	0.033
Gender	0.006	0.927	-0.095	0.104
Marital Status	-0.025	0.651	-0.231	0.145
Ethnicity	0.073	0.122	-0.007	0.059
Educational Status	**0.273**	**0.000**	0.040	0.088
Occupation	-0.037	0.531	-0.047	0.024
Duration of diabetes	-0.105	0.074	-0.064	1.384
Number of medications	0.059	0.292	-0.030	-0.061
Cost of treatment	-0.105	0.071	-0.095	0.000
Bearer of treatment cost	-0.110	0.061	-0.196	-0.072
Glucose control	**-0.205**	**0.000**	-0.236	-0.092
Type of treatment	**-0.212**	**0.000**	-0.304	-0.101
Presence of complications	-0.146	0.004	-0.252	-0.061

Impact of Demographic and Disease Characteristics on Health status

Multiple regression analysis was used to investigate how well clinical characteristics initially statistically significant variables predict health status measured by EQ-5D scores or how much each variable affect health state. The health status was not categorized into poor and good health state instead the scores (continuous variables) were used in relation to other variables due to which standard multiple regression was applied.

All clinical characteristics and demographic characteristics were added collectively into the regression analysis model in order to conclude which factors influence the patients' quality of life more and also indicating not any possibility of multicollinearity and singularity by Tolerance and VIF values which are more than 0.1 and less than 10, respectively. By applying the enter method, a significant model occurred ($F_{13, 318}$ = 12.143, P < 0.001). Type of therapy, glucose level and education level was found as the influencing factors on HRQoL as shown in the table 7

The study conducted with an objective of determining or evaluating health related quality of life using a generic measure i.e. EQ-5D. It was revealed from the study that patients living with diabetes were living a lower quality of life (QOL). These study findings correspond significantly with the other similar studies conducted in other regions of

Pakistan with and without using the same questionnaire i.e. Sargodha and Karachi [8, 13, 14].

The study findings not only correspond with the studies conducted in Pakistan but with the other studies [15-18] as well which have been conducted elsewhere in the world and they all reported lower quality of life of diabetes patients. While these studies which indicated poor QOL in their diabetic population their EQ-5D scores were remarkably higher than the scores of Pakistan diabetic population. These were the developed countries and the quality of life of healthy population in those countries is even higher than a developing country like Pakistan so this could be a rationale behind the higher EQ-5D scores of diabetic population who had reported a poor/bad quality of life.

The current study also demonstrated that patients perceive their health differently from the scores of their health status obtained. Majority had reported some problem in first three domains and moderation in their pain and anxiety. These same findings were also confirmed by other similar studies [15, 18, 19]. Whereas some mixed results have also been reported by a study conducted on Dutch diabetic population where they showed some problem in mobility and pain more frequently than in self-care [16]. Diabetic patients in all these studies have shown no or nearly less problems in self-care which could be an indicative of their self-efficacy and self-management in regarding to their disease as well.

The current study also found that old age, female gender, illiteracy, being married is linked with the low quality of life. Nearly alike results have also been stated by other studies which used Euro-QoL or other generic QoL measures. Female gender is strongly associated with low QoL in previous studies and in the current study as well and previous studies also reported females with some problems in all dimensions of Euro-QoL [16, 18] and dimensions of physical activities of other generic measures [13]. Unemployment followed by gender is also associated with low QoL as observed in other studies [18, 20] which are in line with the findings of the current study. The studies conducted in Iran [18] have almost similar results to the current study in case of all demographic characteristics' association with quality of life. This finding could be useful in confirming the low quality of life of diabetic patients in Asian countries. Regarding association of clinical characteristics to the quality of life of diabetes patients the current study found all characteristics associated with low quality of life.

It has also been observed in the study findings that people with higher education have controlled glucose levels and showed better quality of life as compared to those with low level of education. These results give insight to a fact that highly educated people are more concerned about their health and they tend to maintain their good health. Therefore they take steps to keep their glucose levels controlled which would definitely leads to good quality of life.

In addition to high education and glucose levels type of therapy also influenced quality of life of the studied population. Within the context it is demonstrated that single therapy be it oral anti-diabetic agents or insulin injections only, leads to better quality of life rather than using both type of treatments simultaneously. This also seems logical as patients compliance to their treatment does improve when they are given a single therapy for treatment so this may lead to their blood glucose control and hence improves QoL.

When compared these findings with the similar studies mixed results have been obtained. Insulin therapy have also been a factor for low quality of life among almost all diabetic patients of every region [16, 18] but opposite results were seen in another study which was conducted in Korea which reported no statistically significant relationship between treatment type and health related QoL. Similarly duration of diabetes had a relationship with low quality of life in Iranian study and study conducted on Dutch population and duration was not associated with quality of life in Korean diabetic patients. Presence of diabetes complications does affect quality of life as reported in other diabetic populations [16, 17, 21]. Solli et al. reported that out of all complications the complications which are strongly associated with problems in mobility were neuropathy and ischemic heart disease and foot ulcers were associated with anxiety and depression [21].

Keeping in view all these results from the current study and from the previous studies it is concluded that female gender, old age, treatment types, complications, unemployment, illiteracy, diabetes duration, complications and glucose control have been some important factors in predicting the low health related quality of life of diabetic patients.

CONCLUSION:

The study concluded female gender, old age, treatment types, complications, unemployment, illiteracy, diabetes duration, complications and glucose control have been some important factors in predicting the low health related quality of life of diabetic patients. It is recommended to educate the patients by suitable educational methods and special consideration should be given to female and less educated diabetic patients in improving their self-esteem so that their quality of life could be improved. Treatment modalities should be more oriented towards single and oral anti-diabetic drugs and without insulin therapy to improve quality of life. Processes regarding the prevention of complications and blood glucose control should be educated to patients to avoid the complications in future life of diabetic patients and it would enhance their health related quality of life.

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