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Health-related quality of life and health utility among patients with diabetes in Zabol, Southeast Iran

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Objectives The current study aimed to assess the factors associated with health-related quality of life (HRQoL) and health utility (HU) among patients with diabetes in Zabol, Southeast Iran.
Methods Among patients referred to Zabol city diabetes clinic, a total of 213 consecutive patients 18 years and older consent to participate in the study in 2015. The Persian version of EuroQol-5D-3L (EQ-5D-3L) using the UK preference weights was applied to derive HU. Logistic regression and ordinary least squares were used for data analysis. The STATA version 13 (StataCorp LP, College Station, TX, USA) was used for statistical analysis.
Results The highest and lowest proportions of "some or extreme problems" were seen in pain/discomfort (86.6%) and self-care (27.8%) dimensions of the EQ-5D-3L, respectively. About 33% of women and 14% of men rated their health worse than death (p=0.002). The mean EQ-5D-3L index score and visual analogue scale were 0.37 (95% CI: 0.31–0.42) and 51.6 (95% CI: 48.7–54.5), respectively. Older age at diagnosis, longer duration of diabetes, lower education, and history of macrovascular complications were associated with lower HRQoL and HU.
Conclusion This study highlights the importance of education and diabetes-related complications in HRQoL/HU of diabetes people. The findings suggest that urgent interventions are required to improve HRQoL/HU of diabetes patients in Zabol. Moreover, our results provide inputs for future economic evaluation studies among diabetes patients with similar socioeconomic status in Iran.
Keywords Diabetes, Health-related quality of life, Health utility, EQ-5D-3L, Iran.

Introduction

Diabetes mellitus is a chronic disease with a rising prevalence globally. The number of diabetic patients in 2011 was estimated to be around 366 million worldwide, and it is predicted that this figure will rise to more than 50% by 2030. A prevalence of 12.5% was estimated among people aged 20–79 years in Middle East and North Africa region.[1] For the Iranian population, prevalence has increased from 7.7% in 2005 to 10.3% in 2016.[2–4]

Diabetes elevates risk of a number of macro- and microvascular complications.[5, 6] A pooled analysis of 8.49 million person-years at risk, from 102 prospective studies, indicated that hazard ratios (HRs) of coronary heart disease, ischemic stroke and hemorrhagic stroke were 2, 2.27 and 1.56 for diabetic compared with non-diabetic peoples, respectively.[7] A population-based study in Iran found that HRs of having cardiovascular disease (CVD) were 3.30 and 1.90 for women and men with diabetes compared with people without diabetes, respectively.[8] The association between diabetes and complications causes both a shorter life expectancy[9, 10] and a poorer health-related quality of life (HRQoL) among the diabetic patients compared to those without diabetes.[11] Similarly, diabetic patients with diabetes-related complications have lower HRQoL compared to diabetic patients without any complication.[12–15]

There has been a growing interest in assessing HRQoL in patients with diabetes in Iran over the recent years. These studies have reported a negative impact of diabetes-related complications on HRQoL.[16–18] HRQoL is a multidimensional concept that includes domains related to physical, mental, emotional, and social functioning. It goes beyond direct measures of population health, life expectancy, and causes of death, and focuses on the impact health status has on quality of life, for example, for diabetic patients.[19] While, HRQoL is an important outcome in evaluating the effects of different health states and assessing the effectiveness of various interventions, it is patients' health utilities (HUs) which are the main interest in the context of economic evaluation.[20] Some approaches to economic evaluation in the health sector are: Cost of Illness Studies, Cost Benefit Analysis, Cost Effective Analysis (CEA), Cost Utility Analysis. In Cost Utility Analysis, an extension of CEA but enables comparisons of different treatments with quite different outcomes. This is especially when interventions cause differences in the quantity (survival) and quality of life. It does this through combining these in the common metric of the Quality Adjusted Life Year (QALY). The costs data for achieving a QALY mean that different interventions for the same illness/conditions can be compared as can interventions for other conditions. It can be used to assess whether drugs should be listed on PBS and to guide resource allocation decisions HUs are used to calculate QALYs, as a common outcome measure in cost–utility analyses.[21] HU is a measure of individual's preferences for different health outcomes. It is a cardinal value, usually between 0 and 1, covering different health states from the worst to perfect health.[20] These HU values are generally combined with survival estimates to generate QALY (e.g., 2 years with a HU value of 0.7 and 2 years with a HU value of 0.5 generate a QALY value of 2.9 for these 5years survival).[20] There are two main approaches to elicit the patients' HU: direct method such as standard gamble and time trade-off, and indirect method using preference-based measures such as

EuroQol-5D (EQ-5D)[22] and SF-6D.[23–25] Among generic instruments, EQ-5D, WHOQOL, Health Utility Index, Quality of Well-Being, and SF-36 have been used internationally. We selected EQ-5D because, among these instruments, it has the advantage of being able to calculate a single comprehensive scalar unit of values that can be compared among diseases and used for economic evaluation. EQ-5D is a preference-based HRQL questionnaire that was developed in Europe.[26] We measured HRQL in patients with diabetes using EQ-5D, one of the preference-based measures among HRQL instruments that enable calculation of the utility value.[27] To our knowledge, only one previous study measured HU among patients with type 2 diabetes using the EQ-5D in Iran (28). They found that while CVD and nephropathy had a negative impact on HU, there was positive association between having retinopathy and HU.[28]

The primary aim of the current study was to assess demographic, socioeconomic, and clinical correlates of HRQoL/HU among patients with diabetes in a deprived area of Iran. In addition, since event-specific effects on HU are more useful in conducting economic evaluation studies, our secondary aim was to evaluate the effect of macrovascular complications including myocardial infarction (MI), coronary heart disease and stroke as separate events, not pooled as CVD, on patients' HU.

Methods

Design and Subjects

A cross-sectional study was conducted among patients referred to a hospital-based diabetes clinic in Zabol in 2015, 213 of 254 consecutive patients (with either type 1 or type 2 diabetes) who visited the diabetes clinic met the inclusion criteria for the current study: (a) age 18 years or older, (b) consent to participate in the study. These were patients with confirmed diabetes by physicians in the clinic. This is the only diabetes clinic in Zabol. The study was approved by the Zabol University of Medical Sciences' ethical committee.

Explanatory Variables

A questionnaire was designed by the research team to collect the data on the variables required for the current study. The main variables included year of birth, year of diagnosis of diabetes, gender, resident place, household income, employment status, years of education, weight (kg), height (cm), and history of self-reported doctor's diagnosed macrovascular diabetes-related complications. Patients were asked if they visited a physician for any of the following complications during last year: stroke, MI, and coronary heart disease. A categorical variable using three quintiles of household income was used as the measure of socioeconomic status in this analysis.

Health-related quality of life and health utility assessment

The Persian version of EQ-5D-3L was used to assess HRQoL/HU in the study. The EQ-5D-3L is simple to use and have shown good performance among people with diabetes in previous studies.[29,30] The EQ-5D-3L is a multiattribute preference-based instrument which constitute of five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has three levels: no problems, some problems, and extreme problems,[22] which result in 243[35] potential health states. Responses to these dimensions are weighted based on the preference elicited from a sample of general population to compute an index score. The EQ-5D-3L index score ranges from less than 0 (negative values) for health states worse than death to 1 for full health. The EQ-5D-3L questionnaire also contains a visual analog scale (VAS) tool which entails respondent rates his/her current health state on a scale from 0, the worst imaginable health state, to 100, the best imaginable health state. In the current study, due to lack of preference weights for the Iranian population, the value sets for UK population[31] was used. Patients responded to the EQ-5D-3L questionnaire through a face-to-face interview, conducted by a trained interviewer. This questionnaire has been translated by the EuroQol Group into various languages, and for this study, after filling out a form about the current study method on the group's website, the translated and validated version was sent to the participants. The reliability and validity of the EQ-5D have been well-documented in different contexts for different diseases.[32–34]

Data Analysis

The continuous variables are shown as mean and standard deviation and the categorical as percentages. Responses to the EQ-5D-3L questions were merged for all five dimensions and a binary outcome as "no problem" or "some or extreme problem" was created. Then, χ^2 and Logistic regression were used to assess the associations between the explanatory variables and these binary variables. The STATA version 13 (Stata Corp LP, College Station, TX, USA) was used for statistical analysis.

The EQ-5D-3L index score and VAS were analyzed using *t*-test, analysis of variance (ANOVA) and ordinary least squares (OLS). Due to skewed nature of the EQ-5D-3L scores, several methods have been used in the literature to analyze the scores.[35–37] We chose the OLS with robust standard errors in the current study for two main reasons: first, only 5% the patients reported no problem in any dimensions of the EQ-5D-3L (i.e., an index score = 1.0) and 1% reported a VAS score of 100. It is shown that in this situation OLS works as well as other methods.[36] Second, when HU is the main interest of analysis, as in the current study, the OLS with robust standard errors is a valid approach.[37]

As education level is highly associated with employment and income, we excluded income and employment status from multivariate analysis to avoid any mediation bias. Years of education was categorized in two level: 8 years and less, and more than 8 years. Three patients with missing value on the year of diagnosis were excluded from the analysis. The design variables and residual plots were used to check the linearity of the continuous variables and continuous covariates were treated as mean-centered values. The STATA version 13 (Stata Corp LP, College Station, TX, USA) was used for statistical analysis. Participants were asked to participate on a voluntary basis. They were informed about the study objectives, procedures, risks, benefits, alternatives, their rights, and data anonymity and confidentiality. This information was included in the informed consent form signed by the participants.

Results

The mean (SD) age at diagnosis and duration of diabetes were 39.86 (±13.36) years and 9.73 (±7.10) years, respectively. Sixty three percent of the sample were male and 31% had a BMI ≥

30 (Table 1). The macrovascular complications were more common among men. "Some or extreme problems" in pain/discomfort dimension has the highest prevalence, with 86.6%, followed by anxiety/depression (84.5%). In total, 33.3% of women and 14.1% of men rated their health worse than death (i.e., EQ-5D-3L score < 0, *P*=0.002). The mean (95% CI) EQ-5D-3L index score and VAS scale were 0.37 (0.31–0.42) and 51.6 (48.7–54.5), respectively. The Spearman rank correlation between the EQ-5D index score and VAS scale was 0.65 ($P < 0.001$).

The univariate analysis showed that men and people diagnosed at age older than 25 years had lower problems on the EQ-5D-3L dimensions (Table 2). Better socioeconomic status was generally associated with lower frequency of the problems. The patients with a history of macrovascular events generally suffered from more problems, but this was not statistically significant for pain/discomfort and anxiety/depression dimensions. Patients who received combination of insulin and oral hypoglycemic agents (OHA) had statistically significantly more difficulties in doing their usual daily activities.

Table 1. **Demographic, socioeconomic and clinical characteristics of the sample, stratified by sex (N = 213)**

Variable	Men	Women
N	78	135
Age at diagnosis, years	39.87 ± 15.35	39.86 ± 12.12
Diabetes duration, years	10.70 ± 8.33	9.17 ± 6.24
BMI	26.08 ± 4.50	28.85 ± 4.57
Treatment		
OHA (%)	57.69	48.15
Insulin ± OHA (%)	42.31	51.85
History of MI (%)	7.69	11.11
History of coronary heart disease (%)	15.38	14.81
History of stroke (%)	5.13	12.59
Household income		
Low (%)	38.46	47.41
Middle (%)	26.92	31.11
High (%)	34.62	21.48
Employment		
Unemployed / housekeeper (%)	12.82	90.37
Employed (%)	38.46	5.93
Retired (%)	48.72	3.70
Education		
No education (%)	14.10	50.37
1–8 years (%)	33.33	34.07
9–12 years (%)	37.18	13.33
>12 year (%)	15.38	2.22

BMI: body mass index, OHA: oral hypoglycaemic agents, MI: myocardial infarct.

The results of logistic regression showed no gender difference in suffering from problems in the EQ-5D-3L dimensions (Table 3). Except for self-care, there was no statistically significant association between age at diagnosis and having problems in any EQ-5D-3L dimensions. Longer duration of diabetes and history of macrovascular complications were associated with higher odds of having problems. People with higher education had statistically significantly lower odds of having problems in all dimensions.

The results of OLS regression revealed that older age at diagnosis, longer duration of diabetes, lower education, and history of macrovascular complications were associated with lower EQ-5D-3L index scores (Table 4). A similar finding was observed when VAS scale was used as dependent variable, except for history of stroke which was no longer statistically significant.

Discussion

In order to support conducting economic evaluation of diabetes preventive or curative interventions in Iran, we have estimated HU scores for a range of factors, including demographic, socioeconomic, and clinical factors, among patients referred to a clinic in Southeast Iran. As one may expect, macrovascular complications' history was associated with lower HRQoL/HU among patients with diabetes. Among these complications, history of MI had the highest negative impact on EQ-5D-3L index score. In addition, higher education was associated with higher HRQoL/HU among patients with diabetes Similar to previous national and international studies,[28,38–40] people with diabetes had more commonly problem on pain/discomfort and anxiety/depression dimensions of the EQ-5D-3L and had least problem in self-care. In addition, physician, nurses, and other caregivers should pay more attention on these dimensions. Our findings on the association between education, age at diagnosis, and duration of diabetes with HRQoL/HU were in line with previous national and international studies.[13,30,41–43]. These findings have important clinical and policy-making implications since identifying the most affected dimensions of HRQoL and its determinant can guide toward a better management of the disease and improving HRQoL in these patients.

We found no significant association between treatment modality and HRQoL/HU. This might be due to poor sensitivity of the EQ-5D-3L to treatment modality in diabetes context as has been previously shown.[15,28,44] While the mean VAS score was closer to the value reported in the national survey of type 2 diabetes (51.5 vs. 56.8), the mean EQ-5D index score in the current study was significantly lower than the national survey (0.37 vs. 0.70).[28] There are several possible explanations for this disparity: first, our study included the patients who were referred to a clinic who might be potentially sicker than general diabetes population included in the national survey. Second, Zabol city located in Sistan & Baluchestan province that is considered as one of the most deprived provinces in the country. This poor socioeconomic status not only can directly affect the patients' HRQoL/HU, but also influences the quality and access to care and treatment for patients in this city. Third, we included both type 1 and type 2 diabetes patients while in the national survey only type 2 diabetes patients were included. Patients with type 1 diabetes are diagnosed in younger age, therefore have

Table 2. **Association of the dimensions of EQ-5D-3L and explanatory variables in analysis (N = 213)**

Variable		Mobility		Self-care		Usual activities		Pain/discomfort		Anxiety/depression		EQ-5D index	
		Percent	P-value	Percent	P-value	Percent	P-value	Percent	P-value	Percent	P-value	Mean (95% CI)	P-value
Gender	Women	69.63	0.001	34.07	0.012	53.33	0.023	90.37	0.046	86.67	0.252	0.31 (0.24–0.39)	0.016
	Men	47.44		17.95		37.18		80.77		80.77		0.46 (0.37–0.54)	
Age at diagnosis, years	≤25	37.04	0.003	7.41	0.032	18.52	0.004	74.07	0.078	62.96	0.017	0.67 (0.56–0.78)	<0.001
	26–35	53.19		21.28		46.81		82.98		91.49		0.37 (0.25–0.48)	
	36–45	79.03		35.48		62.90		95.16		87.10		0.26 (0.16–0.37)	
	46–55	60.34		31.03		43.10		87.93		84.48		0.36 (0.25–0.47)	
	≥56	63.16		42.11		52.63		84.21		89.47		0.28 (0.03–0.53)	
BMI	<25	55.74	0.078	22.95	0.051	42.62	0.235	81.97	0.402	80.33	0.522	0.43 (0.32–0.54)	0.185
	25–30	56.98		23.26		44.19		88.37		87.21		0.37 (0.29–0.46)	
	≥30	72.73		39.39		56.06		89.39		84.85		0.30 (0.19–0.40)	
Duration of diabetes, years	≤5	54.55	0.225	24.68	0.434	44.16	0.614	83.12	0.252	80.52	0.411	0.40 (0.30–0.50)	0.511
	5–10	66.10		30.51		45.76		93.22		84.75		0.32 (0.21–0.43)	
	10–15	58.70		23.91		47.83		82.61		84.78		0.41 (0.29–0.54)	
	>15	74.19		38.71		58.06		90.32		93.55		0.30 (0.17–0.43)	
Household income	Lowest quintile	64.89	0.220	31.91	0.503	50.00	0.050	90.43	0.209	87.23	0.619	0.32 (0.24–0.40)	0.189
	Middle quintile	65.08		26.98		55.56		87.30		82.54		0.36 (0.25–0.47)	
	Highest quintile	51.79		23.21		33.93		80.36		82.14		0.45 (0.34–0.57)	
Employment	Unemployed	68.94	0.004	33.33	0.077	54.55	0.150	91.67	0.024	87.88	0.182	0.30 (0.23–0.38)	0.013
	Employed	39.47		15.79		28.95		76.32		76.32		0.51 (0.39–0.63)	
	Retired	58.14		23.26		41.86		81.40		81.40		0.43 (0.30–0.56)	
Education	No education	81.01	<0.001	45.57	<0.001	63.29	<0.001	94.94	0.001	91.14	<0.001	0.18 (0.09–0.27)	<0.001
	1–8 years	62.50		26.39		55.56		90.28		88.89		0.34 (0.25–0.43)	
	9–12 years	38.30		6.38		17.02		72.34		63.83		0.64 (0.54–0.73)	
	>12 years	26.67		13.33		20.00		73.33		93.33		0.62 (0.44–0.80)	
History of MI	No	59.38	0.054	24.48	<0.001	44.79	0.020	85.94	0.231	83.85	0.426	0.40 (0.34–0.46)	<0.001
	Yes	80.95		61.90		71.43		95.24		90.48		0.07 (-0.13–0.28)	
History of coronary heart disease	No	59.12	0.089	22.10	<0.001	43.09	0.003	86.19	0.493	83.43	0.299	0.41 (0.35–0.47)	<0.001
	Yes	75.00		62.50		71.88		90.63		90.63		0.11 (-0.04–0.26)	
History of stroke	No	58.33	0.004	26.04	0.037	45.31	0.063	85.94	0.231	83.33	0.152	0.40 (0.34–0.46)	<0.001
	Yes	90.48		47.62		66.67		95.24		95.24		0.08 (-0.10–0.25)	
Treatment	OHA	59.09	0.455	25.45	0.363	40.91	0.049	87.27	0.852	85.45	0.693	0.39 (0.31–0.47)	0.450
	Insulin ± OHA	64.08		31.07		54.37		86.41		83.50		0.34 (0.26–0.43)	

Table 3. **The impact of demographic, socioeconomic, and clinical factors on EQ-5D-3L dimensions (N = 213)**

Variable		Mobility		Self-care		Usual activities		Pain/discomfort		Anxiety/ depression	
		OR	P-value	OR	P-value	OR	P-value	OR	P-value	OR	P-value
Men		0.58	0.147	0.57	0.217	0.96	0.913	0.68	0.398	0.92	0.854
Age at diagnosis		1.02	0.183	1.05	0.007	1.02	0.159	1.02	0.396	1.01	0.549
Diabetes duration		1.08	0.004	1.10	0.003	1.05	0.058	1.04	0.189	1.05	0.095
Body mass index		1.07	0.053	1.07	0.140	1.04	0.233	1.01	0.824	0.99	0.833
Education	≤8 years (ref)	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–
	>8 years	0.36	0.009	0.23	0.013	0.18	<0.001	0.30	0.013	0.32	0.015
Treatment	OHA (ref)	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–
	Insulin ± OHA	1.14	0.716	1.08	0.846	1.73	0.103	0.85	0.738	0.71	0.458
History of MI		2.84	0.090	6.64	0.003	3.20	0.043	2.77	0.318	1.58	0.549
History of coronary heart disease		1.87	0.193	7.00	<0.001	3.80	0.003	1.25	0.717	1.55	0.526
History of stroke		4.63	0.042	1.35	0.619	1.36	0.589	1.58	0.646	2.50	0.338

OR: odds ratio.

Table 4. **The impact of demographic, socioeconomic, and clinical factors on EQ-5D-3L index score and visual analog scale (N = 213)**

Variable		EQ-5D index score		Visual analog scale	
		Coefficient	P-value	Coefficient	P-value
Men		0.005	0.927	1.005	0.756
Age at diagnosis		–0.004	0.050	–0.279	0.012
Diabetes duration		–0.007	0.036	–0.567	0.003
Body mass index		–0.006	0.301	–0.285	0.356
Education	≤8 years (ref)	0.000	–	0.000	–
	>8 years	0.291	<0.001	11.498	<0.001
Treatment	OHA (ref)	0.000	–	0.000	–
	Insulin ± OHA	–0.021	0.682	–3.150	0.282
History of MI		–0.295	0.002	–12.099	0.011
History of coronary heart disease		–0.250	<0.001	–8.536	0.026
History of stroke		–0.188	<0.001	–1.425	0.688
Constant		0.376	<0.001	52.035	<0.001

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longer duration of diabetes and this might have caused lower HRQoL/HU in the current study. In addition, a previous study showed that diabetes-related complications have more negative impact on HRQoL among type 1 diabetes patients with younger age.

The range of HU decrement due to macrovascular complications was higher in our study than the estimates reported in previous studies.[45] This may reflect either poor access to secondary health care or low quality of care for patients with diabetes in such deprived area. In addition, such differences imply that the cost–utility analyses using estimates from previous national study might not be generalizable to diabetes patients in this deprived area of the country.

The results of the current study should be interpreted in light of a number of limitations. First, the sampling method was non-random, and this negatively affects representativeness of the patients and limits generalizability of the results presented here. Second, the data were self-reported, with risk of potential recall bias and measurement errors that might bias the results. Third, we used the preference weights from the UK population to calculate the EQ-5D-3L index score. Due to intercultural differences in health state preferences,[46–48] this might be problematic. Fourth, both type 1 and type 2 diabetes were included in the study, which may limit transparency and comparability of the results. Fifth, as this is a cross-sectional study, any causal inference from the results should be avoided.

Conclusion

The current study has estimated HU scores for a range of demographic and clinical features of diabetic patients in a deprived area of Iran. The findings showed that older age at diagnosis, longer duration of diabetes, lower socioeconomic status, and history of macrovascular complications were associated with lower HRQoL/HU. The findings also showed that the mean EQ-5D-3L index score in the sample of diabetes patients in the current study was lower than the Iranian diabetes general population, implying that specific interventions should be implemented to improve HRQoL of patients in this area. Using these estimates in conducting cost–utility analyses can assist informed decisions by policy-makers in Iran. Assessing the effects of microvascular complications on HRQoL/HU and evaluating the changes of HRQoL/HU over time in a larger sample size are topics for future research.

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Conflicts of interest

The authors declare that there is no conflict of interests.

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