

## Impact of Depression on Health Related Quality of Life in Patients with Diabetes

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### Abstract

**Introduction:** Diabetes mellitus (DM) is a serious chronic illness that has a major impact on the quality of life of the individuals. Our aim was to examine the determinants of health-related quality of life (HRQOL) in patients with DM. **Materials and Methods:** Adult outpatients attending a Diabetes Centre were recruited on consecutive basis between August 2006 and February 2007. Clinical data were collected from interviews with the subjects and from medical records. Assessment of depressive symptoms was done using the Center for Epidemiologic Studies Depression Scale (CES-D) and HRQOL using the Short Form 36 Health Survey (SF-36). A two-step regression analysis was conducted for identifying factors affecting patients' quality of life. **Results:** Five hundred and thirty-seven patients participated in the study. The mean (SD) age of the participants was 54.7 (13.3) years and 315 (58.7%) were males. The prevalence of depressive symptoms was 31.1% (n = 167). After adjusting for other variables, the effects of depressive symptoms persisted for all the 8 domains of SF-36 ( $P < 0.001$  for all). The medical factors that were negatively associated with HRQOL were a diagnosis of Type 1 DM, duration of the illness of more than 10 years, HbA1c levels of  $\geq 7\%$ , and comorbidity of stroke and retinopathy. Being male and a regular exerciser had a positive effect on HRQOL. **Conclusion:** These findings highlight the importance of detecting and treating comorbid depression in DM.

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**Key words:** CES-D, Diabetes mellitus, SF-36

### Introduction

Diabetes Mellitus (DM) is a serious chronic illness that imposes significant morbidity and mortality and has a major impact on the quality of life of the individuals suffering from this illness.<sup>1-3</sup> Singapore, a multi-ethnic country in Southeast Asia, with Chinese, Malay and Indian as the three main ethnic groups,<sup>4</sup> has one of the highest rates of DM in the world. In the 2004 National Health Survey, the crude prevalence of DM among adult Singaporeans was 8.2%. There is also ethnic variance in the rates of DM: it is most common amongst Indians with a prevalence of 15.3%, followed by Malays with 11.0%, and Chinese with 7.1%.<sup>5</sup>

In public health and in medicine, the concept of health-related quality of life refers to a person's or group's

perceived physical and mental health over time. Physicians have often used health-related quality of life (HRQOL) to measure the effects of chronic illness in their patients to better understand how an illness interferes with a person's day-to-day life. Similarly, public health professionals use health-related quality of life to identify subgroups with poor physical or mental health and this can help guide policies or interventions to improve their health. The HRQOL deficits reported by patients with DM are generally attributed to the disease itself, its restrictive treatment regimens and its associated comorbidities. The UK Prospective Diabetes Study (UKPDS) found that the complications of diabetes affect quality of life more than the overall treatment intensity.<sup>6</sup> Similarly, a study conducted in Singapore reported that HRQOL was significantly lower in patients

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with DM than those without DM and the comorbidities had an additive detrimental effect on HRQOL.<sup>7</sup> Besides medical comorbidities, older age,<sup>8</sup> socio-economic factors,<sup>9</sup> and the burden of the treatment regimen<sup>10</sup> are some of the other factors that have been found to have significant association with HRQOL.

The comorbidity of depression in DM has been well established, a meta-analysis found that the odds of depression in patients with diabetes is nearly double that of non-diabetic population.<sup>11</sup> We have recently reported that the prevalence rate of depressive symptoms, as measured by Center for Epidemiologic Studies Depression Scale (CES-D), in 537 patients with DM was 31.1%.<sup>12</sup> Depression has been found to be associated with poor compliance to treatment,<sup>13</sup> poor glucose control<sup>14</sup> as well as other physical complications of diabetes.<sup>15</sup> Thus, the presence of comorbid depression in patients with DM would have a further deleterious effect on HRQOL. There have been a few studies that have examined the impact of depression on HRQOL and these were designed as population-based surveys. Pawaskar and colleagues<sup>16</sup> in their prospective cohort survey of elderly patients with type 2 DM found that impairments in daily activities and lower HRQOL were predictors of depressive symptomatology. Another study that compared HRQOL and depression among individuals with type 2 DM and those at low or high risk for DM found respondents with type 2 DM and even those at high risk had decreased HRQOL and increased depression than those with lower cardiometabolic risk.<sup>17</sup>

The aims of our present study were to examine the association between depression and HRQOL in patients with DM as well as to understand the effects of socio-demographic, medical and emotional factors on HRQOL through a cross-sectional assessment of patients attending a specialised diabetes clinic. Our hypothesis was that the presence of depressive symptoms would have a significant and negative impact on HRQOL.

## Materials and Methods

Adult outpatients (aged 21 years and above) attending the Alexandra Hospital Diabetes Centre who had their annual screen performed within the previous 6 months were invited to participate in the study. The annual screen is a detailed medical examination that included a clinical examination by a physician and laboratory tests to assess for diabetic control and complications. Glycosylated haemoglobin (HbA1c) was measured using high-performance liquid chromatography.

Patients with other significant medical illnesses that were not related to DM such as asthma, chronic obstructive pulmonary disease (COPD), current psychiatric disorders other than depression, and current history of substance abuse

(including alcohol) were excluded in order to minimise the confounding effects of other chronic conditions on HRQOL. Written informed consent was obtained from all subjects and the study was approved by the Institutional Ethics Committee.

Socio-demographic and clinical data were collected by a research assistant from interviews with the subjects as well as from the medical records. The diagnoses of medical complications were made by the attending physicians using ICD-10 diagnostic criteria. Information on the level of exercise was obtained from the patients and this was graded into 3 categories. Category 1: no exercise i.e. no sporting activity at all. Category 2: irregular exercise i.e. 3 or less than 3 occasions of sporting activity lasting at least 30 minutes per week. Category 3: regular exercise i.e. 3 or more than 3 occasions of sporting activity per week.

Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression Scale (CES-D)<sup>10</sup> which is a self-report 20-item questionnaire and has been shown to effectively predict depressive symptoms in diabetic populations in clinic settings.<sup>11</sup> We have validated the CES-D in an earlier study in the same population, and found that a cut-off score of 16 or more has a high negative predictive value of more than 90% in the 3 major ethnic groups.<sup>18</sup> We have accordingly defined those with a score of more than 16 as suffering from clinically significant depressive symptoms.

HRQOL was assessed using the Short Form 36 Health Survey (SF-36). The SF-36 is a widely used generic health-related quality of life measure. It consists of 36 items which measure HRQOL in the past 4 weeks in 8 domains, namely, physical functioning (PF), role limitations due to physical problems (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role limitations due to emotional problems (RE), and mental health (MH). Eight SF-36 scores (range, 0 to 100), one for each life domain, can be generated with higher scores indicating better HRQOL. In Singapore, the English and Chinese versions of SF-36 have demonstrated good psychometric properties in a population survey.<sup>19</sup> In this study, the English, Chinese, Malay, and Tamil versions of the SF-36 (version 2)<sup>20</sup> for Singapore were used.

## Statistical Analyses

For describing the study sample, frequency was calculated for categorical variables and mean and standard deviation (SD) were calculated for continuous variables. The SF-36 scores of the patients were compared with Singaporean population norms after the adjustment of age, gender, ethnicity, and survey language using one-sample t-tests. Patients with and without depressive symptoms as measured by the CES-D were compared using two-sample t-tests.

Based on our previous study,<sup>18</sup> a CES-D score of 16 points or higher indicates the presence of clinically significant depressive symptoms. For identifying factors affecting patients' quality of life, a two-step regression analysis was conducted for each SF-36 score. First, univariate analysis was performed for each demographic, health-related, and clinical variable for each of the SF-36 scores. Second, those significant factors in the first step were included in a multiple linear regression model for each SF-36 score to identify the factors with adjustment of possible confounding effects.

All statistical analyses were performed with SAS for Windows (Version 9.1). All tests were two-sided with a *P*-value of <0.05 were considered significant.

## Results

A total of 537 patients participated in the study. The mean (SD) age of the participants was 54.7 (13.3) years and the mean (SD) duration of illness 10.2 (8.5) years. Two hundred and twenty-two (41.3%) were females, 390 (72.6%) were Chinese, 58 (10.8%) Malays, 74 (13.8%) Indians and 15 (2.8 %) were of other ethnicity. The mean score on CES-D was 12.2 (10.3), and prevalence of depressive symptoms as defined by the CES-D score of  $\geq 16$  was 31.1% (*n* = 167) (Table 1).

When the mean scores on SF-36 for the 8 domains were compared to the general Singapore population norms,<sup>21</sup> patients' HRQOL was significantly lower than the general Singaporean population in domains like RP, BP, GH, VT, and SF, with other dimensions similar to the population norms (Table 2). We also compared the mean scores on SF-36 in patients with DM with and without depressive symptoms. Patients with depressive symptoms had significantly worse HRQOL than those without depressive symptoms in all SF life domains (Table 3).

Linear regression analyses identifying factors associated with HRQOL scores are shown in Table 4. In summary, the results show that after adjusting for other variables, the effects of depressive symptoms persist for all the 8 domains of SF-36 (*P* < 0.001). Being  $\geq 65$  years of age had a significant negative effect on PF (*P* < 0.01) and a positive effect on GH (*P* < 0.01). Compared to other ethnicities, Indians were most likely to report poorer HRQOL in the domain of MH (*P* < 0.05). Being unemployed or retired had significant negative effect on PF (*P* < 0.01) and being separated or divorced had a negative effect on RE (*P* < 0.01). Male gender had a positive effect on the following domains of HRQOL: PF (*P* < 0.01), BP (*P* < 0.05) and VT (*P* < 0.05). Another important factor that had a positive effect on HRQOL was "regular exercise". Those who exercised regularly, compared to those who never exercised, had significantly better HRQOL for the following domains: PF (*P* < 0.01), BP (*P* < 0.05), VT (*P* < 0.001), and MH (*P* < 0.05).

Table 1. Socio-demographic and Clinical Characteristics of Patients with DM in the Sample

	n	%
<b>Sex</b>		
Female	222	41.3
Male	315	58.7
<b>Ethnicity</b>		
Chinese	390	72.6
Malay	58	10.8
Indian	74	13.8
Other	15	2.8
<b>Education</b>		
Primary or lower	183	34.3
Secondary	206	38.7
Tertiary	144	27.0
<b>Marital Status</b>		
Single	67	12.5
Married	409	76.2
Separated/divorced	16	3.0
Widowed	45	8.4
<b>Working Status</b>		
Employed	256	47.9
Unemployed	83	15.5
Homemaker/housewife	87	16.3
Retired	109	20.4
<b>Exercise Level</b>		
None	282	52.5
Irregular	125	23.3
Regular	130	24.2
<b>Type of DM</b>		
Type I	19	3.6
Type II	518	96.5
<b>Treatment of DM</b>		
Diet only	368	68.5
Oral medication	136	25.3
Insulin	33	6.2
<b>HbA1c, %</b>		
< 7	123	22.9
$\geq 7$	414	77.1
< 16 (without depression)	370	68.9
$\geq 16$ (with depression)	167	31.1

With regards to the medical factors and other comorbidities, having Type 1 DM had a negative effect on RP (*P* < 0.01) and a duration of the illness of more than 10 years had a negative effect on VT (*P* < 0.05). HbA1c levels of  $\geq 7\%$  was a significant negative predictor of the domains RP (*P* < 0.01), SF (*P* < 0.05) and RE (*P* < 0.01).

Table 2. SF-36 Scores of Patients as Compared with Singapore Population Norms

SF-36 sub-scale	Mean	SD	Singaporean population norms*	P-value (one-sample t-test)
Physical functioning (PF)	75.0	23.9	81.1	0.2775
Role physical (RP)	78.9	25.1	82.5	0.0226
Bodily pain (BP)	73.9	25.4	79.9	0.0004
General health (GH)	60.4	21.8	68.3	<0.0001
Vitality (VT)	59.1	21.4	63.7	0.0004
Social functioning (SF)	79.1	24.6	82.5	0.0287
Role emotional (RE)	81.7	23.8	80.8	0.4635
Mental health (MH)	72.7	20.2	72.8	0.5038

SD: Standard Deviation. \*Adjusted for age, gender, ethnicity and survey language.

Table 3. SF-36 Scores of Patients with and without Depressive Symptoms

SF-36 sub-scale	Patients without depressive symptoms (CES-D <16) (n = 259)		Patients with depressive symptoms (CES-D ≥16) (n = 121)		P-value (two-sample t-test)
	Mean	SD	Mean	SD	
Physical functioning (PF)	84.5	17.6	70.1	25.2	<0.0001
Role physical (RP)	86.7	18.8	64.7	27.1	<0.0001
Bodily pain (BP)	80.4	22.2	64.5	26.1	<0.0001
General health (GH)	64.7	20.5	47.9	20.0	<0.0001
Vitality (VT)	67.4	17.3	43.8	18.8	<0.0001
Social functioning (SF)	88.2	17.8	61.8	25.4	<0.0001
Role emotional (RE)	90.6	16.2	62.6	25.6	<0.0001
Mental health (MH)	80.6	14.4	53.9	19.0	<0.0001

Having a diagnosis of stroke had a significant negative impact on PF ( $P < 0.001$ ) and retinopathy had a negative effect on RP ( $P < 0.05$ ).

## Discussion

Our finding that patients with DM had poorer HRQOL compared to the general population was not unexpected. It was also not surprising to find the negative association between medical complications of stroke and retinopathy with the PF and RP domains of HRQOL. Similar findings have been reported in previous studies.<sup>1,22</sup> Having HbA1c level of  $\geq 7$  is indicative of poor glycemic control and possibly implies a more severe illness, with patients needing more intensive and restrictive medical management. All this could have led to the deleterious effect on the role functioning both due to physical as well as emotional problems as found in our study.

But by far the most significant negative impact on all the domains of HRQOL was due to the presence of depressive symptoms. The high prevalence rates of depressive symptoms in chronic diseases particularly DM has been well

documented.<sup>11,23</sup> The presence of this comorbidity has been shown to be responsible for poorer treatment outcomes<sup>14,24,25</sup> and greater disability<sup>26</sup> and can result in a poorer quality of life. Similarly, the need to follow strict dietary regime, go for regular glucose monitoring and presence of disabling complications, can have a significant impact on HRQOL, and can be a major stressor for depression. There have been few studies that have looked at this complex interaction between depression and DM and its impact on HRQOL. When investigators compared depressed diabetics and depressed non-diabetics as well as those with combined depression and DM in an Australian population study, they found that the effect of depression on HRQOL was greater than the effect of DM, but when depression was added to DM, the effect for the physical dimensions of HRQOL was more than additive.<sup>27</sup> Similar findings were reported in a study conducted by the World Health Organisation (WHO) involving 245,404 participants across 60 countries that looked at the effect of depression and chronic diseases. The investigators found that comorbid state of depression with diabetes caused even greater decrements in health than

Table 4. Linear Regression Analysis of SF-36 Scores

	Regression coefficient (P-values) <sup>§</sup>							
	PF	RP	BP	GH	VT	SF	RE	MH
<b>R-square (adjusted)</b>	0.31	0.20	0.19	0.19	0.33	0.19	0.28	0.41
<b>Age (reference: &lt;45 years)</b>		NS	NS		NS	NS	NS	
45-64 years	-5.9			5.3				2.3
≥65 years	<b>-14.1†</b>			<b>10.0†</b>				3.3
<b>Male (reference: female)</b>	<b>8.4†</b>	NS	<b>7.0*</b>	NS	<b>5.4*</b>	NS	NS	NS
<b>Race (reference: Chinese)</b>				NS	NS			
Malay	-5.5	6.3	-7.1			-2.3	1.7	1.9
Indian	-6.5	-4.1	-4.5			-2.8	-6.5	<b>-6.6*</b>
Other	1.9	-6.6	-12.4			-0.02	3.4	2.4
<b>Marital status (reference: single)</b>		NS	NS			NS		
Married	8.5			1.7	3.6		5.8	4.1
Separated/divorced	14.2			-3.9	7.7		<b>24.6†</b>	8.7
Widowed	8.0			1.5	4.8		1.8	2.3
<b>Educational level (reference: primary)</b>		NS	NS	NS		NS	NS	NS
Secondary	2.1				2.0			
Tertiary	-2.8				-4.4			
<b>Working status (reference: employed)</b>		NS		NS		NS	NS	NS
Unemployed	<b>-8.2*</b>		-1.1		-4.0			
Homemaker/housewife	-4.0		-7.3		-1.3			
Retired	<b>-10.4†</b>		-0.01		-2.5			
<b>Exercise level (reference: none)</b>		NS						
Irregular exerciser	3.8		1.5	4.7	0.01	0.8	2.1	2.4
Regular exerciser	<b>9.5†</b>		<b>8.8*</b>	4.5	<b>9.6‡</b>	4.4	0.4	<b>5.6*</b>
<b>Type 1 diabetes (reference: type 2)</b>	NS	<b>-25.0†</b>	NS	NS	NS	NS	NS	NS
<b>Duration of diabetes (reference: 0-4 yrs)</b>	NS	NS	NS	NS		NS	NS	NS
5-9 yrs					-2.6			
10+ yrs					<b>-6.1*</b>			
Coronary artery disease (yes)	NS	NS	NS	NS	NS	7.0	NS	NS
Retinopathy (yes)	NS	<b>-5.6*</b>	NS	NS	NS	NS	NS	NS
Stroke (yes)	<b>-18.1‡</b>	NS	NS	NS	NS	NS	NS	NS
HbA1c ≥7%	-2.0	<b>-10.6†</b>	-3.8	NS	NS	<b>-8.1*</b>	<b>-7.9†</b>	-3.4
With depressive symptoms	<b>-12.6‡</b>	<b>-18.3‡</b>	<b>-17.9‡</b>	<b>-18.1‡</b>	<b>-22.0‡</b>	<b>-20.0‡</b>	<b>-24.1‡</b>	<b>-25.6‡</b>

\* $P < 0.05$ , † $P < 0.01$ , ‡ $P < 0.001$ , § Adjusted for all other variables in the table except for those marked with "NS". NS – Not significant in univariate analysis thus not included in the linear regression for the quality of life score. PF: Physical functioning; RP: Role limitations due to physical problems; BP: Bodily pain; GH: General health; VT: Vitality; SF: Social functioning; RE: Role limitations due to emotional problems; MH: Mental health

the addition of the 2 conditions separately. This finding is suggestive of an interactive effect between depression and DM that causes an extra negative effect on health beyond the simple addition of each of the 2 conditions.<sup>28</sup> Findings from a National Health Epidemiological study from the US suggested that although the main effects of depression were comparable with arthritis, hypertension and DM on HRQOL, patients with insulin-dependant diabetes appeared to have significantly stronger effects on HRQOL than depression. But consistent with other studies, they also

found that depression and chronic medical illnesses interact to amplify the effects of the medical illness, causing a significant impact on the HRQOL.<sup>29</sup> Unfortunately, much of the focus in the treatment of DM is geared towards achieving optimum glycemic control as well as the treatment of associated medical complications. But given the fact that 31.1% of the patients in this study had significant depressive symptoms and these were significantly related to not only their emotional but also their physical health, this calls for an urgent need to proactively screen patients with DM for

depression and refer them for treatment that is based on a multidisciplinary team approach and attends to the medical and psychological needs of the patients.

Another intervention that could also help improve the HRQOL of patients would be one that is targeted towards exercise and physical fitness. Our study showed that patients who exercised regularly reported significantly better quality of life in the domains of physical functioning, bodily pain, vitality as well as mental health. A recent study by Williamson et al<sup>30</sup> tested the efficacy of a weight management programme for improving HRQOL in overweight adults with DM by randomly assigning them to 2 treatment arms: intensive lifestyle intervention (ILI) and diabetes support and education (DSE). The findings of this study support the hypothesis that participation in a lifestyle modification intervention was associated with significant improvement in HRQOL.

Previous population-based studies have reported a higher prevalence of DM,<sup>31</sup> as well as depression,<sup>32</sup> in the Indian ethnic group in Singapore. Our research group has recently reported a higher prevalence of depression in patients with DM.<sup>12</sup> Hence, the finding of poorer HRQOL in MH domain among the Indians does suggest that compared to Chinese or Malays, they are more vulnerable to the comorbidities of DM and depression and this has a significant impact on their HRQOL. Our finding that older patients reported better general health than younger patients was somewhat surprising, but in a study of the general population in Singapore using the SF-36, self-perceived general health was found to be stable with increasing age.<sup>33</sup> The association between divorce and better RE was also unusual. This could be due to sampling bias as there were only 19 divorced patients in the study and we may have recruited those divorced patients whose role functions had been previously affected by emotional problems with their partners and were less affected after they divorced.

This study has some limitations. Some patients who were approached did not consent to the study. However, the non-participation rate was low (6.1%) and analysis of available limited data on these subjects indicated that this group was not different in terms of age, gender and ethnic composition from study participants (data not shown) and hence, was unlikely to have introduced a systematic error. Another major limitation was that the cross-sectional design did not allow us to ascertain the temporal and potentially complex relationship between depression and HRQOL. However, the findings from this study draw our attention to the fact that HRQOL that looks at health from an individual's perspective is truly multi-faceted and simple measures to detect and treat depression can go a long way towards reducing the burden of the illness and the disability.

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