Original article

Assessment of Quality of Life and Prevalence of Depression Among Type 1 Diabetic Patients at Prince Mansour Military Hospital, Taif, KSA

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Abstract

Background: Patients with diabetes were shown to report poor quality of life and significant depressive symptoms. Only a dearth of surveys was conducted to evaluate the extent of depression among Saudi patients with diabetes and how depression mediate the effect of diabetes on perceived quality of life. **_Method:_** The study is a cross sectional questionnaire-based observational investigation using a simple random sampling scheme. We utilized World Health Organization Quality of Life Brief Version (WHOQOL-BREF) and Primary Health Questionnaire PHQ-9 to evaluate depressive symptoms and quality of life. We used generalized linear regression and mediation analysis to estimate the effect of clinical and demographic variables on quality of life and the mediating effect for depressive symptoms. **_Results:_** (n = 203) agreed to be included in the study. The prevalence for severe depression was (11.3%), and for moderate depression was (18.7%) among the participating patients. Poor QoL was found in retired patients, prolonged duration of diabetes, depressive score, and experiencing DKA. Notably, we found significant interaction between duration of DM and HbA1c level in terms of their combined effect on quality of life. Among patients with prolonged diabetes duration HbA1c level was associated with poorer quality of life. However, paradoxically, among newly diagnosed diabetes patients the higher the HbA1c the better was the quality of life. Age effect was negative on the QoL, after adjusting for the HbA1c*DM duration interaction. We found that depression score significantly mediated the negative effect of age on quality of life among patients living with diabetes (Sobel test t = -2.851, p = 0.004); however, the depression-mediated effect on the path from duration of diabetes to quality-of-life score was statistically not significant (Sobel test t = -0.021, p = 0.984). **_Recommendations:_** Patients with diabetes should be screened and treated for symptoms of depression throughout the course of their illness, given their detrimental effect on their life quality. Older patients with diabetes require amelioration of depressive symptoms given their effect on life quality regardless of duration of diabetes or presence of complications.

Keywords: *Type 1 diabetes, depression, quality of life, mediation analysis, glycaemic control, Saudi Arabia.*

Introduction

Diabetes mellitus is a highly prevalence non-communicable condition that affects over 415 million individuals globally [Rwegerera et al., 2018]. It is projected to rise in prevalence significantly among developing countries by over 20% within the coming twenty years [Shaw et al., 2010].

Several studies have reported that QOL in diabetic patients is decreased in comparison with individuals without diabetes [Rubin and Peyrot, 1999; de Grauw et al., 1999] particularly in those who experience diabetes-related diabetic complications [Wexler et al., 2016].

Moreover, co-occurrence of depression and diabetes may even further decrease QOL.

Emotional stressors related to DM often negatively impact a Patient's mental and social well-being. There are several disease-related factors that have a notable influence on the psychological well-being of people with DM. These include, but not limited to, the stress from being diagnosed with a chronic condition, the cost of managing the DM, the effect of diabetes-associated complications, and medication side effects [Snoek and Skinner, 2006].

Several studies have reported that patients with DM have a poorer QOL in comparison with those without [16] particularly in those who experienced diabetes-related complications [De Visser et al., 2002; American Diabetes Association, 1999] and those with questionable adherence to management plan [Piette et al., 2002; Snoek and Skinner, 2006] and those with comorbid psychiatric illness [Rubin and Peyrot, 1999].

A chain of studies has recently investigated QOL and its relationship to depressive illness among patients with diabetes.

AlBuhairan et al. [2016] conducted a cross-sectional study among Saudi Arabian adolescents with T1DM to measure the HRQOL and the impact of the disease on the family. They found that adolescents reported a cumulative mean HRQoL score of 64.8, while parents reported notably lower scores of 60.3. The lowest scores reported by both adolescents and parents were for "Worry." Female gender and late adolescent age were predictors of lower HRQoL for adolescents with T1DM. The Family Impact module showed low scores for "Emotional functioning" and high scores for "Family relationships".

Al-Shehri et al [2014] attempted to assess potential correlates of poor QOL among four hundred Saudi patients with diabetes. He utilized the tool designed by Bradley et al. [1999] to report the staggering finding that 78.7% reported poor QOL. Women and married patients with poorly controlled type 2 diabetes who experienced at least one complication were particularly worse in terms of QOL.

Al Hayek et al. [2014] investigated nearly three hundred patinets with diabetes in Riyadh using the Short-Form 36-item survey (SF-36). Older patients, insulin-only users, complications were associated with worsening QOL.

In Kuwait, Al-Khaledi et al. [2018] conducted large-scale study that included over five hundred patients with diabetes using SF-12. Worse quality of life was reported among women and patients with diabetes complications.

In Oman, D'Souza et al. [2018] performed a cross-sectional study to explore predictors of HRQOL among individuals with T2DM. Revised Summary of Diabetes Self-Care Activities and Euro- QOL scales were utilized for data collection. Schooling and management skills were highly notable predictors of QOL among females in comparison with males. Age, prevention of daily activity, and management of diabetes were significant predictors of health state among females as compared to males. The study reported that the variance in the total QOL was 30.6% for females versus 35.7% for males.

In addition, Munkácsi et al. [2018] performed a case-control study to compare symptoms of mental health problems in one hundred and thirty children and youth with and one hundred and seventy-seven without type 1 diabetes. The study showed a notable difference could be reported in well-being and depressive symptoms. The children with T1DM could be described with notably higher mental health, but with less physical activity and lower levels of depression in comparison with the control group.

Besides, Anderson et al. [2018] carried out a cross-sectional study to characterize diabetes-specific HRQOL in a global sample of young adults with T1DM and to identify the main factors associated with QOL. The study included 5,887 participants who were attending diabetes clinics in twenty countries across five continents. Participants completed the PedsQL Diabetes Module 3.0 and were interviewed about family-related factors to estimate HRQOL. Specifics about treatment procedure and self-management were collected from medical records. The results reported that across all age groups, females showed notably lower HRQOL than males. The 19–25-year age group reported the lowest HRQOL. Multivariate linear regression analyses stated that HRQOL was notably associated with HbA1c; the lower the HbA1c, the better the HRQOL. Three diabetes-management behaviors were notably related to better HRQOL: advanced procedures utilized to measure food intake, frequent daily blood glucose monitoring, and daily physical activity.

In addition, Schram et al. [2009] carried out a systemic review in Europe to outline the knowledge on the relationship of depression with various aspects of QOL in patients with diabetes. The systematic literature search using MEDLINE, Psychinfo, Social SciSearch, SciSearch, and EMBASE was performed from January 1990 until September 2007. The researchers identified articles that compared the QOL between diabetic patients with and without depressive symptoms. Twenty articles were identified, including two longitudinal and eighteen cross-sectional studies. QOL was estimated as generic, diabetes-specific, and domain-specific QOL. All studies recorded a negative relationship between depression and at least one aspect of QOL in diabetic patients. Diabetic patients with depression also had a severely lower diabetes specific QOL. Generic and domain specific QOL were observed to be mild to moderately lower in the presence of depressive signs. Therefore, enhanced awareness and monitoring for depression are required within different diabetes care settings.

The primary goal of diabetes early diagnosis and treatment is to improve the quality of life.

WHO, furthermore, introduced QoL as an estimation of well-being as well as the measurement of health and the effects of health care. To the best of my knowledge, there is not enough data collected yet about the assessment of QOL and prevalence of depression and its relationship to QOL among patients with T1DM in Taif.

Objectives of the study

1. To determine the Prevalence of depression among type 1 diabetic patients in Taif.
2. To Assess the Quality of life among type 1 diabetic patients in Taif.
3. To study the relationship between depression and quality of life among type 1 diabetic patients in Taif.

Method

Study Design: This is a Cross sectional study.

Study Population: T1DM patients attending Diabetes and Endocrine Center at Prince Mansour Military Hospital in Taif.

Inclusion criteria: Adult patients with type one diabetes mellitus. Participants' aged 14 and above years old.

Exclusion criteria: Individuals who suffer from any other chronic diseases (for example, epilepsy, mental retardation, cancer, celiac, thyroid disease). Diabetic patients with insulin pump using less than 6 months. Patients diagnosed with type 1 diabetes less than 6 months.

Study Area The research took place in Taif city in western region of the kingdom of Saudi Arabia. Diabetes and Endocrine Center is located at Prince Mansour Military Hospital, the center serve adult and children with type 1 and 2 diabetes and contain different specialized clinic for diabetes care include: (foot care clinic, dietitians, diabetes education, insulin pump clinic, ophthalmology clinic, GDM clinic).

Sample size: The total number of diabetic patients with type 1, age more than 14 years registered in the center are 427 patients. By using the Raosoft software the sample size was calculated at 95 % Confidence level with margin of error 5% and response distribution of 50%, the sample size is (203).

Sampling technique: Patients medical record files were randomly selected using random number generator, patient data are store in

Diabetes and Endocrine Center as computer-based filing system. All patients who use insulin pump were selected in average not more than 50% of total sample size So, by computerized randomization 203 files were selected out of 427.

Data collection tools
Check list was used to collect the date from the medical records and medical history. The check list contain: age, gender, duration of diabetes, level of education, HbA1C, number of diabetic keto acidosis in last 6 months, the occurrence of diabetes complications and medications taken.

The World Health Organization Quality of Life Brief Version (WHOQOL-BREF): The World Health Organization Quality of Life Brief Version to assess the health Quality of life and is the brief version of the 100-item WHOQOL-100 quality of life measure. It was revealed that there were no significant mean differences between Arabic and English version questionnaires in Arab Cultures. Also, the reliability and validity of the WHOQOL have been demonstrated for both type 1 diabetes patients and type 2 diabetes patients. The WHOQOL is a self-administrated questionnaire consist of 26 items cover 4 domains: physical health (7 items), mental health (6 items), social relations (3 items), environmental health (8 items) and one item to measure the public health and another one to measure the overall quality of life. Each item is score from 1 to 5. the domain score is calculated by use the mean score of items within each domain. Mean scores are then multiplied by 4 in order to make domain scores comparable with the scores used in the WHOQOL-100. The higher Domain scores denote higher quality of life. Approval was taken from the Author of the Arabic version of WHOQOL -BREF questionnaire to use it in this research [Dalky et al., 2019].

The Patient Health Questionnaire (PHQ-9): The PHQ-9 is the 9-item depression module from the full PHQ. Major depression is diagnosed if 5 or more of the 9 depressive symptom criteria have been present at least "more than half the days" in the past 2 weeks, and 1 of the symptoms is depressed mood or anhedonia. The diagnostic validity of the PHQ has recently been established in 2 studies involving 3,000 patients in 8 primary care clinics and 3,000 patients in 7 obstetrics-gynecology clinics [Kroenke et al., 2001]. At 9 items, the PHQ depression scale (which we call the PHQ-9) is half the length of many other depression measures, has comparable sensitivity and specificity. The PHQ-9 has the potential of being a dual-purpose instrument that, with the same 9 items, can establish depressive disorder diagnoses as well as grade depressive symptom severity. As a severity measure, the PHQ-9 score can range from 0 to 27, since each of the 9 items can be scored from 0 (not at all) to 3 (nearly every day) [Adekkanattu et al., 2018].

Data Collection technique: After taking the Approval from Research committee at Armed forces medical services, the researcher was starting collecting the data using the Questionnaire by direct interviewing the patient in private room to ensure their privacy after taking their approval to participate in this study, the checklist then was used to draw the required data from medical records.

Study variables: *Dependent variable:* Quality of life of type 1 diabetic patients.

Independent variables were socio demographic data; age, gender, duration of diabetes, emergency room visits in last 6 months, HbA1c, Level of education, the occurrence of diabetes complication, and medications taken.

Depression PHQ-9 score were used to categorized depression into 'no depression' (0–4), 'mild' (5–9), 'moderate' (10–14) and 'severe depression' (≥ 15).

Data entry and analysis: The program was used is Statistical Package for the Social Sciences (SPSS) version 20. Significance: P –value < 0.05. Statistical test such as Chi square and T test and any appropriate test require were used. we used Poisson regression modelling to study the effect of clinical and demographic factors on QOL. We used mediation analysis using the concepts of Structural Equation Modelling techniques. Sobel test was used to test the null hypothesis that a composite parameter for the effect of duration of diabetes and PHQ-9 score on QOL is equal to zero. Similarly, for the composite effect of age and PHQ-9 score on QOL.

Pilot study/pretesting: Pilot study was carried out in same center on 10% of the total number which is 20 files. To evaluate appropriateness of data collection instrument, to identify the clarity and applicability of the tools, and to provide feedback about the questionnaire and standardize the data collection approach. The files reviewed in pilot study were excluded from the main study.

Ethical Considerations

Approval from Research committee at Armed forces medical services in Taif was taken before conducting the research. Approval from the Research committee at Armed forces medical services was taken to get permission to use patient's data.

All data that used during the research will be confidential and for the research purpose only.

At the end of the study, the results and recommendations will be submitted to the institute.

Results

The total number of patients included in the study was (n = 203) type 1 diabetes patients.

For a detailed account of demographic results see table (1) below. The mean QoL score was 83.7 points (SD= 16.7 points), ranging between 38 and 115 points. The median QoL score was 86 points.

Among those who agreed to participate, there were (n = 103, 50.7%) men and (n = 100, 49.3%) women. There was no significant difference in terms of QoL between male and female patients (t = 1.112, p = 0.2676).

The mean age among the participants was 25.9 years (SD = 9.7) the estimate for the effect of age was -0.003 (equivalent of odds = 0.997). This means that one year extra in age is associated with 0.3% decrease in QoL score (p = 0.0002). There were (n = 36, 17.7%) participant who reported at least one medical comorbidity in addition to diabetes. They scored an average of 74.8 in QoL (compared to a mean QoL score of 85.6 in those with no medical comorbidity). This difference was statistically significant (t = 3.622, p = 0.00037).

With regards to glycaemic control, the majority (n = 182, 89.7%) of participants were of poor control (i.e. over 7% HbA1c level), but they scored marginally lower in terms of quality of life (mean score was 83.4, compared to 86.2 among those with optimum glycaemic control readings). The difference was not statistically significant (t = 0.89692, p = 0.3774).

Moreover, there were (n = 30, 14.8%) participant who reported at least one diabetes-related complication. They scored an average of 76.2 in QoL (compared to a mean QoL score of 84.9 in those complication-free patients). This difference was statistically significant (t = 2.682, p = 0.00793).

The mean duration for diabetes was 12.1 years (SD = 6.9). The estimate for the unadjusted effect of duration of diabetes was -0.0048 (equivalent of unadjusted odds = 0.995). Hence, indicative of the fact that one year extra in living with diabetes is associated with 0.5% decrease in QoL score (p = 0.0000218).

In terms of experiencing DKA, there were (n = 23, 11.3%) participant who reported the same. They scored an average of 74.3 in QoL (compared to a mean QoL score of 84.9 in those who did not experience DKA). This difference was statistically significant (t = 2.612, p = 0.0146).

Table 1: Baseline demographics of the study participants and unadjusted effect on QoL

Factor	Count (n)/mean	Percentage /SD	Mean QoL score/ Estimate	Test statistic	P value
Age	μ = 25.9 years	SD = 9.7 years	-0.003	t = -3.737	0.0002
Gender					
Male	103	50.7%	82.4	t = 1.112	0.2676
Female	100	49.3%	85.0		
Hb A1c	μ = 9.2%	SD = 1.98	0.001	z = 0.1954	0.8451
Glycaemic control					
Good (HbA1c < 7)	21	10.3%	86.2	t = 0.89692	0.3774
Poor (HbA1c > 7)	182	89.7%	83.4		
Employment					
Employee	26	12.8%	80.7	F = 3.028	0.0117
Housewife	11	5.4%	85.9		
Professional	21	10.3%	90.8		
Retired	3	1.5%	61.7		
Student	71	35.0%	86.4		
Unemployed	71	35.0%	80.5		
Education					
Illiterate	4	2.0%	81.0	F = 0.537	0.709
Intermediate	11	5.4%	89.5		
Primary	19	9.4%	80.4		
Secondary	56	27.6%	84.1		
University	113	55.7%	83.5		
Occupation					
Employee	47	23.2%	85.2		
Retired	3	1.5%	61.7	F = 3.167	0.0255
Students	71	35%	86.4		
Unemployed	82	40.4%	81.2		
Medical Comorbidity					
No	167	82.3%	85.6	t = 3.622	0.00037
Yes	36	17.7%	74.8		
Marital Status					
Divorced	6	3.0%	82.0	F = 1.526	0.220
Married	52	25.6%	80.3		
Single	145	71.4%	84.9		
DM Complications					
Yes	30	14.8%	76.2	t = 2.682	0.00793
No	173	85.2%	84.9		
DM Duration	μ = 12.1 years	SD = 6.9 years	-0.0048	z = -4.2458	0.0000218
DKA					
Yes	23	11.3%	74.3	t = 2.6122	0.01463
No	180	88.7%	84.9		
DM Treatment					
Insulin injection	174	85.7%	82.7	t = 1.985	0.05456
Insulin pump	29	14.3%	89.5		

As per table 2, the prevalence for severe depression was (n = 23, 11.3%), and for moderate depression was (n = 38, 18.7%) among the participating patients. The severer the depressive symptoms the worse were the QoL scores, namely 95.9, 85.2, 76.1, 62.7 for no depression, mild depression, moderate depression, and severe depression, respectively (F= 36.89, p < 0.0001). Analysing PHQ-9 total score, we found the mean score was 8.5 (SD = 5.8 points). Odds = 0.978, indicating that a rise by one point in PHQ-9 score is associated with reduction of 2.2% in overall QoL score among our patients (p < 0.0001).

Table 2: Description of the unadjusted effects for depressive symptoms on QoL among diabetes patients

Factor	Count (n)/ mean	Percentage /SD	Mean QoL score/ Estimate	Test statistic	P value
PHQ-9 total	μ = 8.5	SD = 5.8	Odds = 0.978	z = -16.263	< 0.0001
Depression					
No depression	52	25.6%	95.9	F = 36.89	< 0.0001

Mild	90	44.3%	85.2		
Moderate	38	18.7%	76.1		
Severe	23	11.3%	62.7		
QoL	μ = 83.7	SD = 16.7	-	-	-

Regression analysis for the adjusted impact of clinical and sociodemographic factors

In terms of the adjusted impact for the various clinical and demographic factors on QoL score, as displayed in table 3, we notice that poor glycaemic control was associated with non-significant reduction in odds of QoL score (Odds = 0.985, p = 0.573). Also, being retired from work is associated with 20.7% reduction in QoL Score compared to those still in employment (Odds = 0.793, p = 0.007). Similarly, prolongation of diabetes duration by one year is associated with 0.3% reduction in QoL score (adjusted Odds = 0.997, p = 0.018). Contrary to the unadjusted age effect described earlier, when adjusted to other clinical and demographic variables, older age by a year is associated with 0.7% increase in QoL scores (odds = 0.7%, p < 0.001). Each one point extra in terms of PHQ-9 is associated with reduction in QoL score by 2.1% (odds = 0.979, p < 0.001). Moreover, experiencing DKA was associated with 8.1% reduction in QoL score (Odds = 0.919, p = 0.002).

Table 3: Adjusted impact of sociodemographic variables on the total QoL score among the study participants

	Odds	95% CI	P value
Sex: Male	0.975	0.943 to 1.009	0.148204
HBA1c (Poor control)	0.985	0.952 to 1.019	0.572530
Education: Intermediate	1.083	0.942 to 1.244	0.263474
Education: Primary	1.057	0.926 to 1.208	0.409828
Education: Secondary	1.089	0.961 to 1.233	0.180226
Education: University	1.076	0.953 to 1.215	0.235135
Employment: Housewife	1.060	0.971 to 1.158	0.192326
Employment: Professional	1.037	0.969 to 1.111	0.293959
Employment: Retired	0.793	0.670 to 0.938	0.006926 **
Employment: Student	1.033	0.967 to 1.105	0.335601
Employment: Unemployed	0.992	0.935 to 1.052	0.782295
Marital Status: Married	1.012	0.915 to 1.119	0.817247
Marital Status: Single	1.079	0.978 to 1.191	0.130308
Comorbidity	0.978	0.933 to 1.026	0.362992
DM Complications	0.953	0.904 to 1.005	0.077579
DM Duration	0.997	0.994 to 0.999	0.018235 *
Age	1.007	1.003 to 1.010	0.00007 ***
PHQ	0.979	0.976 to 0.982	<0.000001 ***
Treatment: Insulin pump	1.046	1.000 to 1.095	0.052373
DKA	0.919	0.871 to 0.970	0.002120 **

(*) indicates p < 0.05;(**) indicates p < 0.01; (***) indicates p < 0.001

Interaction effect analysis for the adjusted impact of Glycaemic control, age, and duration of diabetes on QoL

In order to further understand the impact of age, duration of diabetes, and glycaemic control on QoL, we proposed an interaction effect between HBA1c and diabetes duration and adjusted that interaction effect to the age of individuals. The results are displayed in table 4.

There was clear evidence for interaction effect between HbA1c and DM duration as they influence QoL (p = 0.047).

Notably, when the duration for DM was short, the higher the HbA1c the better was the quality of life. However, this relation reversed when the DM duration was prolonged, as QoL deteriorated substantially with higher readings of HbA1c. Age effect was negative, after adjusting for the HbA1c DM duration interaction, on the QoL as expected.

Table 4: Age-adjusted interaction effect between glycaemic control and diabetes on the total QoL score among the study participants

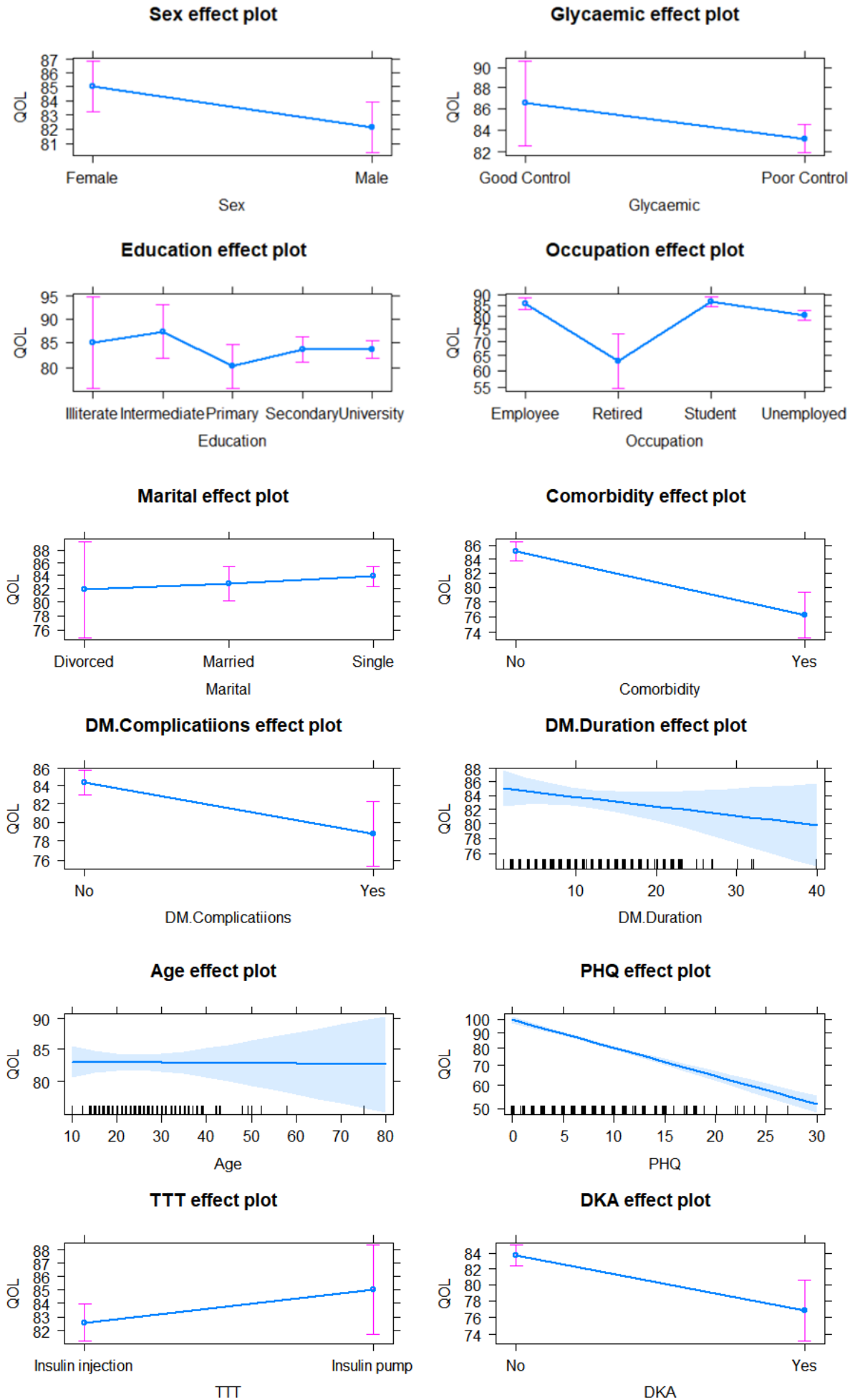| Factor	Estimate	SE	t value	p value
HBA1c	0.0113	0.0082	1.3832	0.16661
DM Duration	0.0076	0.0058	1.3191	0.18712
Age	-0.0021	0.0010	-2.1133	0.03458 *
HBA1c×DM Duration interaction	-0.0012	0.0006	-1.9849	0.04715 *

Figure 1: Estimates for the effects of clinical and demographic factors on QoL
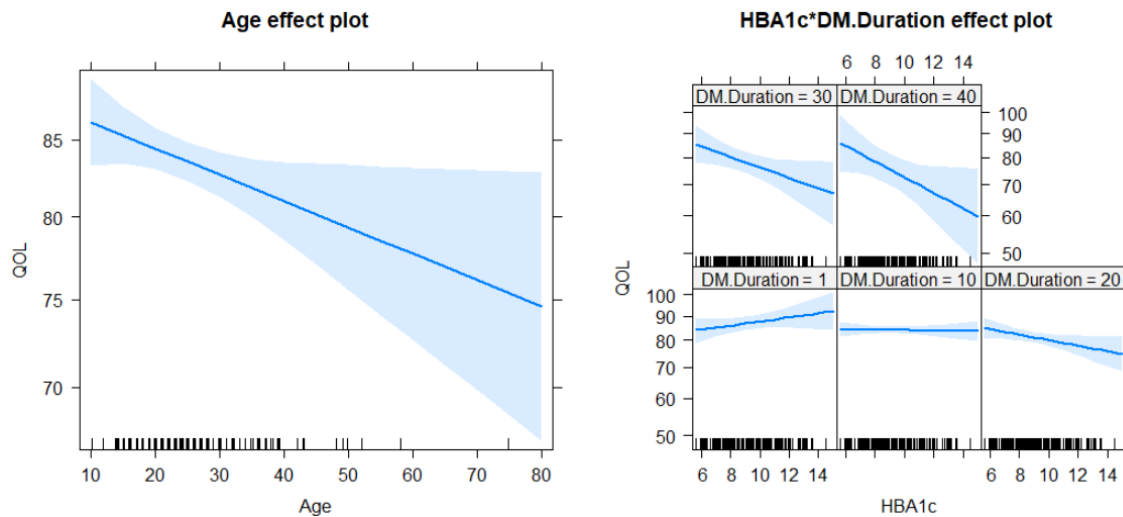
Figure 2: Estimates for the interaction effect of glycaemic control and DM duration on QoL

Notably, when the duration for DM was short the higher the HbA1c the better was the quality of life. However, this relation reversed when the DM duration was prolonged, as QoL deteriorated substantially with higher readings of HbA1c.

Mediation Analysis

In order to study if the PHQ score mediated between age and diabetes duration with Qol, we ran a tow-layered mediation analysis.

We examined and contrasted a direct path from age to QoL and from duration and QoL with an indirect path that passes from age through PHQ to Qol, and another indirect path from duration to PHQ to QoL.

We found that depression score (as measured through PHQ-9) significantly mediated the negative effect of age on quality of life among patients living with diabetes (Sobel test $t = -2.851$, $p = 0.004$); however, the depression-mediated effect on the path from duration of diabetes to quality-of-life score was statistically not significant (Sobel test $t = -0.021$, $p = 0.984$).
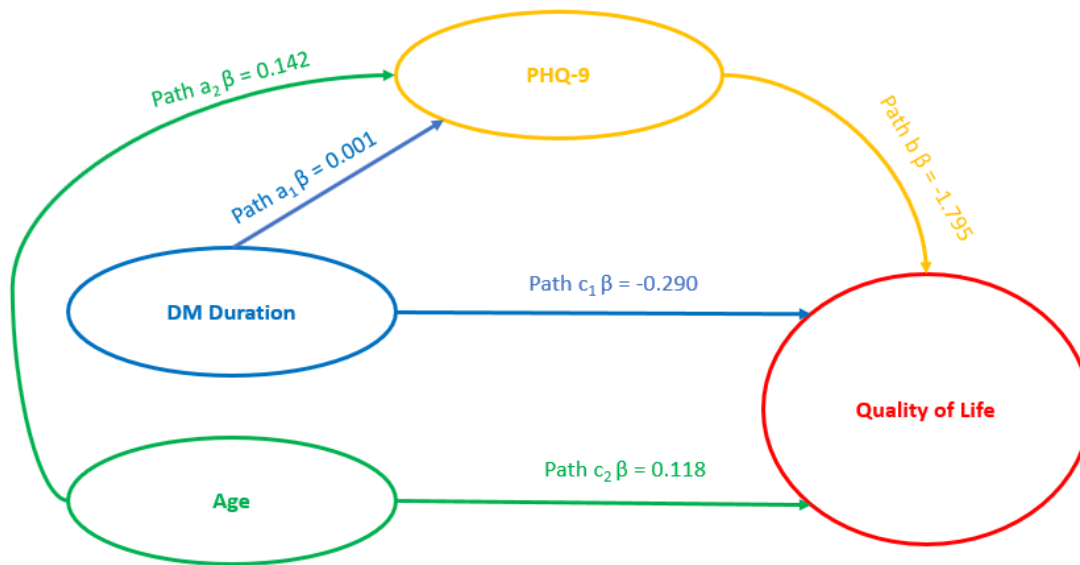

Figure 3: Estimates for the mediating effects of depression on the path between age and QoL and between duration of diabetes and QoL

Table 5: Full estimates for the mediation model of the PHQ score for the path between age and QoL and from DM duration and QoL score among the study participants

Regressions:				
	Estimate	Std.Err	z-value	P value
QoL ~				
Duration (c1)	-0.290	0.154	-1.883	0.060
Age (c2)	0.118	0.112	1.045	0.296
PHQscore ~				
Duration (a1)	0.001	0.067	0.021	0.984
Age (a2)	0.142	0.048	2.948	0.003
QoL ~				
PHQscore (b)	-1.795	0.160	-11.209	<0.001
Covariances:				
Duration ~~				

Age	35.226	5.314	6.628	<0.001
Variances:				
.QoL	166.948	16.571	10.075	<0.001
.PHQscore	32.062	3.182	10.075	<0.001
Duration	47.978	4.762	10.075	<0.001
Age	93.637	9.294	10.075	<0.001
Defined Parameters:				
a1b	-0.002	0.121	-0.021	0.984
a2b	-0.256	0.090	-2.851	0.004
total	-0.430	0.171	-2.520	0.012

Discussion

We investigated a sample of over two hundred patients with diabetes type 1 attending the Specialist Endocrinology Centre affiliated to the Armed Forces Hospitals in Taif Saudi Arabia. We attempted to evaluate depressive symptoms present among type 1 diabetes patients and how they influence their quality of life and mediate the effect of clinical and demographic factors.

Alarmingly, depression affected nearly three quarters of our participants. This highlights the extent of underdiagnosed depression among Saudi patients who has to live with diabetes. This resonates with global figures for the estimates for prevalence of depression among diabetes type 1 patients. Recent large-scale studies gave an estimate for the prevalence of depression for patients with diabetes as high as three times the prevalence among non-diabetes patients [Roy and Lloyd et al., 2012]. Although authors have proposed several direct biological links between diabetes and depressive disorder, including epigenetic and environmental factors, a range of psychosocial mechanisms were proposed to better explain the close association between the two [Bădescu et al., 2016], including the psychological burden of chronic illness and the heightened anxiety in managing the momentary and long-terms aspects of diabetes. Furthermore, among our participants, one in nine suffered severe depression and one in three reported severe or moderate depressive symptoms. This result mirrors the international figure for severe depressive symptoms among patients with diabetes, namely 10.6% [Lloyd et al., 2018].

Our data gives clear evidence to the detrimental effects for depressive score, retirement from employment and experiencing DKA in terms of worsening quality of life among patients with diabetes attending our centre in Saudi Arabia. Many previous studies have shown that depression was one of the main factors that worsened quality of life among patients with diabetes [Jing et al., 2018; Walker et al., 2015; Pan et al., 2013; Donald et al., 2013]. Anhedonia and inability to feel the enjoyable aspects of daily life activities are inherent parts of depressive illness and, thus, substantially suppresses patients' quality of life [Barthel et al., 2020]. Furthermore, depressive illness was found to be closely associated with diabetes complications [de Groot et al., 2001]. Several studies linked depressive symptoms in diabetes to poor quality of life given the detrimental effect of depressed mood and fatiguability in how patients with diabetes underrate their life quality experience [Verma et al., 2010; Wexler et al., 2006].

The effect for glycaemic control and diabetes duration and age was not straightforward though. Past research studies suggested that frequent checking of glucose (required for good glycaemic control) counter-affect quality of life for patients [Daher et al., 2015]. Other studies found that tight glycaemic control, however, is associated with better experience of life quality among patients with diabetes [Shim et al., 2012; U.K. Prospective Diabetes Study Group, 1999]. Our findings suggest that older age was associated with worsening in quality of life as we take account of significant interaction between glycaemic control and duration of diabetes. We found that when the duration for DM was short, i.e. among patients newly diagnosed with diabetes, the higher the HbA1c the better was the quality of life. This is difficult to explain. Probably, worry earlier during the course of the disease, which could lead patients to strive for tighter glycaemic control, worsens quality of life among those with low HbA1c readings [Daher et al., 2015]. Young patients with diabetes express distress in terms of stigma, daily practical management issues, navigating the healthcare services, and, more importantly, worries about prospects of marriage, pregnancy, and childbirth [Balfe et al., 2013]. However, as per our findings form the interaction model, this relation reversed when the DM duration was prolonged, i.e., among patients living with diabetes for considerable time duration, as QoL deteriorated substantially with higher readings of HbA1c. This can be explained in the light of worsening quality of life as a result of poor glycaemic control and higher susceptibility to depression and complications of diabetes [Stojanović et al., 2018; de Groot et al., 2001]. The results of studies that attempted to evaluate the crude effect of duration of diabetes on quality of life were, unfortunately, not consistent. A series of studies concluded that duration of living with diabetes tend not to have an impact on quality of life [Daher et al., 2015; Mikailiūkštienė et al., 2015]. Whereas other investigations clarified a negative, and intuitive effect for longer duration of diabetes on quality of life experienced by patients [Redekop et al., 2002; Glasgow et al., 1997] particularly in Saudi Arabia [Al Hayek et al., 2014]. Pooled results from a large recent meta-analysis suggest that duration of diabetes worsens quality of life [Jing et al., 2018]. We propose, in accordance with our clear findings, an interaction effect with glycaemic control. However, this requires further focused studies to reproduce our findings.

Interestingly, one study arrived at the counterintuitive conclusion that reaching a 'desired' glycaemic control was associated with poor quality of life [Daher et al., 2015]. That can be related to higher levels of anxiety and disruption of non-diabetes lifestyle. Indeed, elevated anxiety was shown to affect 40% of patients with diabetes [Grigsby et al., 2002]. Recent estimates were even higher for anxiety symptoms, over 90% of patients with diabetes were found to have some form of anxiety [Bulut A, Bulut, 2016]. Age effect was negative, after adjusting for the HbA1c DM duration interaction, on the QoL as expected. The effect for older age on poor quality of life was corroborated by recent research studies [Girma et al., 2020]. Limited physical activity and depression were proposed as mediators for old age effect on quality of life in chronic illness [McIntyre et al., 2019]. Our results pointed out age relation with poor life quality to be mediated by depression, more so than the duration of diabetes relationship to quality of life. Our results, uniquely, make clear distinction between effects of old age and duration of diabetes with regards to quality of life and depressive symptoms effects. This is also difficult to explain. Recent studies, nonetheless, gave an indicator that physical activity could ameliorate depressive symptoms in older adults with diabetes [Lee et al., 2020]. Many authors found association between diabetes duration and its

complications to be more compelling than age of patients [Wannamethee et al., 2011]. However, this remains an understudied are in terms of effect of depressive symptoms and quality of life.

There are several points of strength for the current study. We have a large sample size. We used robust analytical approach and we utilized well-validated psychometric tools. One significant limitation in the current research, however, is the cross-sectional design that gives only a snapshot of the relationships between different variables.

Future research should focus on the relationship between glycaemic control and quality of life in a longitudinal design to examine the behaviour of such relationship across the course of diabetes. Further studies should explore the distinctive effects of older age and longer duration of diabetes by including interaction effects between the two or adjusting for their simultaneous effects using robust statistical modelling techniques.

Recommendations

1. Patients with diabetes should be screened and treated for symptoms of depression throughout the course of their illness, given their detrimental effect on their life quality.

2. Early during the course of illness patients with diabetes should be supported psychologically and socially to prevent the shock effect of their diagnosis on the quality of life they experience

3. Future research should focus on the relationship between glycaemic control and quality of life in a longitudinal design to examine the behaviour of such relationship across the course of diabetes.

4. Older patients with diabetes require amelioration of depressive symptoms given their effect on life quality regardless of duration of diabetes or presence of complications.

References

[1] Adekkanattu P, Sholle ET, DeFerio J, Pathak J, Johnson SB, Campion TR Jr. Ascertaining Depression Severity by Extracting Patient Health Questionnaire-9 (PHQ-9) Scores from Clinical Notes. AMIA Annu Symp Proc. 2018 Dec 5;2018:147-156. PMID: 30815052; PMCID: PMC6371338.

[2] Al Hayek AA, Robert AA, Al Saeed A, Alzaid AA, Al Sabaan FS. Factors Associated with Health-Related Quality of Life among Saudi Patients with Type 2 Diabetes Mellitus: A Cross-Sectional Survey. Diabetes Metab J. 2014 Jun;38(3):220-9. doi: 10.4093/dmj.2014.38.3.220. Epub 2014 Jun 17. PMID: 25003076; PMCID: PMC4083029.

[3] Al Hayek AA, Robert AA, Al Saeed A, Alzaid AA, Al Sabaan FS. Factors associated with health-related quality of life among Saudi patients with type 2 diabetes mellitus: a cross-sectional survey. Diabetes & metabolism journal. 2014 Jun 1;38(3):220-9.

[4] AlBuhairan F, Nasim M, Al Otaibi A, Shaheen NA, Al Jaser S, Al Alwan I. Health related quality of life and family impact of type 1 diabetes among adolescents in Saudi Arabia. Diabetes research and clinical practice. 2016 Apr 1;114:173-9.

[5] Al-Khaledi M, Al-Dousari H, Al-Dhufairi S, Al-Mousawi T, Al-Azemi R, Al-Azimi F, Badr HE. Diabetes self-management: a key to better health-related quality of life

[6] Al-Shehri FS. Quality of life among Saudi diabetics. Journal of Diabetes Mellitus. 2014 Jul 31;2014.

[7] American Diabetes Association. Quality of life in type 2 diabetic patients is affected by complications but not by intensive policies to improve blood glucose or blood pressure control (UKPDS 37). UK Prospective Diabetes Study Group. Diabetes care. 1999 Jul 1;22(7):1125-36.

[8] Anderson BJ, Laffel LM, Domenger C, Danne T, Phillip M, Mazza C, Hanas R, Waldron S, Beck RW, Calvi-Gries F, Mathieu C. Factors associated with diabetes-specific health-related quality of life in youth with type 1 diabetes: the Global TEENs Study. Diabetes Care. 2017 Aug 1;40(8):1002-9.

[9] Bădescu SV, Tătaru C, Kobylinska L, Georgescu EL, Zahiu DM, Zăgrean AM, Zăgrean L. The association between Diabetes mellitus and Depression. J Med Life. 2016 Apr-Jun;9(2):120-5. PMID: 27453739; PMCID: PMC4863499.

[10] Balfe M, Doyle F, Smith D, Sreenan S, Brugha R, Hevey D, Conroy R. What's distressing about having type 1 diabetes? A qualitative study of young adults' perspectives. BMC Endocr Disord. 2013 Jul 25;13:25. doi: 10.1186/1472-6823-13-25. PMID: 23885644; PMCID: PMC3733731.

[11] Barthel AL, Pinaire MA, Curtiss JE, Baker AW, Brown ML, Hoeppner SS, Bui E, Simon NM, Hofmann SG. Anhedonia is central for the association between quality of life, metacognition, sleep, and affective symptoms in generalized anxiety disorder: A complex network analysis. J Affect Disord. 2020 Dec 1;277:1013-1021. doi: 10.1016/j.jad.2020.08.077. Epub 2020 Sep 2. PMID: 33065810; PMCID: PMC7575821.

[12] Bradley C, Todd C, Gorton T, Symonds E, Martin A, Plowright R. The development of an individualized questionnaire measure of perceived impact of diabetes on quality of life: the ADDQoL. Quality of Life Research. 1999 Jan 1;8(1-2):79-91.

[13] Bulut A, Bulut A. Evaluation of anxiety condition among type 1 and type 2 diabetic patients. Neuropsychiatr Dis Treat. 2016 Oct 11;12:2573-2579. doi: 10.2147/NDT.S105588. PMID: 27785034; PMCID: PMC5067063.

[14] Daher AM, AlMashoor SA, Winn T. Glycaemic control and quality of life among ethnically diverse Malaysian diabetic patients. Qual Life Res. 2015 Apr;24(4):951-8. doi: 10.1007/s11136-014-0830-5. Epub 2014 Oct 29. PMID: 25352036.

[15] Dalky HF, Meininger JC, Al-Ali NM. The Reliability and Validity of the Arabic World Health Organization Quality of Life-BREF Instrument Among Family Caregivers of Relatives With Psychiatric Illnesses in Jordan. J Nurs Res. 2017 Jun;25(3):224-230. doi: 10.1097/JNR.0000000000000146. PMID: 28481818.

[16] de Grauw WJ, van de Lisdonk EH, Behr RR, van Gerwen WH, van den Hoogen HJ, van Weel C. The impact of type 2 diabetes mellitus on daily functioning. Family practice. 1999 Apr 1;16(2):133-9.

[17] de Groot M, Anderson R, Freedland KE, Clouse RE, Lustman PJ. Association of depression and diabetes complications: a meta-analysis. Psychosom Med. 2001

Jul-Aug;63(4):619-30. doi: 10.1097/00006842-200107000-00015. PMID: 11485116.

[18] De Visser CL, Bilo HJ, Groenier KH, De Visser W, Meyboom-de Jong B. The influence of cardiovascular disease on quality of life in type 2 diabetics. Quality of Life Research. 2002 May 1;11(3):249-61.

[19] Donald M, Dower J, Coll JR, Baker P, Mukandi B, Doi SA. Mental health issues decrease diabetes-specific quality of life independent of glycaemic control and complications: findings from Australia's living with diabetes cohort study. Health Qual Life Outcomes. 2013;11:170. doi: 10.1186/1477-7525-11-170

[20] D'Souza MS, Venkatesaperumal R, Ruppert SD, Karkada SN, Jacob D. Health related quality of life among Omani men and women with type 2 diabetes. Journal of diabetes research. 2016 Jan 1;2016.

[21] Girma M, Wodajo S, Ademe S, Edmealem A, W/Silasie M, Mesafint G. Health-Related Quality of Life and Associated Factors Among Type Two Diabetic Patients on Follow-Up in Dessie Comprehensive Specialized Hospital, Dessie, North East Ethiopia, 2020. Diabetes Metab Syndr Obes. 2020 Nov 20;13:4529-4541. doi: 10.2147/DMSO.S279306. Erratum in: Diabetes Metab Syndr Obes. 2021 Feb 17;14:751. PMID: 33244250; PMCID: PMC7685383.

[22] Glasgow RE, Ruggiero L, Eakin EG, Dryfoos J, Chobanian L. Quality of life and associated characteristics in a large national sample of adults with diabetes. Diabetes Care. 1997 Apr;20(4):562-7. doi: 10.2337/diacare.20.4.562. PMID: 9096981.

[23] Grigsby AB, Anderson RJ, Freedland KE, Clouse RE, Lustman PJ. Prevalence of anxiety in adults with diabetes: a systematic review. J Psychosom Res. 2002 Dec;53(6):1053-60. doi: 10.1016/s0022-3999(02)00417-8. PMID: 12479986.

[24] Jing X, Chen J, Dong Y, Han D, Zhao H, Wang X, Gao F, Li C, Cui Z, Liu Y, Ma J. Related factors of quality of life of type 2 diabetes patients: a systematic review and meta-analysis. Health Qual Life Outcomes. 2018 Sep 19;16(1):189. doi: 10.1186/s12955-018-1021-9. PMID: 30231882; PMCID: PMC6147036.

[25] Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med. 2001 Sep;16(9):606-13. doi: 10.1046/j.1525-1497.2001.016009606.x. PMID: 11556941; PMCID: PMC1495268.

[26] Lee J, Callaghan T, Ory M, Zhao H, Bolin J. Difference in the risk of depressive symptoms associated with physical activity in persons with diabetes: Across age, gender, and race/ethnicity. J Affect Disord. 2020 May 15;269:108-116. doi: 10.1016/j.jad.2020.03.035. Epub 2020 Mar 19. PMID: 32250863.

[27] Lloyd CE, Nouwen A, Sartorius N, Ahmed HU, Alvarez A, Bahendeka S, Basangwa D, Bobrov AE, Boden S, Bulgari V, Burti L, Chaturvedi SK, Cimino LC, Gaebel W, de Girolamo G, Gondek TM, de Braude MG, Guntupalli A, Heinze MG, Ji L, Hong X, Khan A, Kiejna A, Kokoszka A, Kamala T, Lalic NM, Lecic Tosevski D, Mankovsky B, Li M, Musau A, Müssig K, Ndetei D, Rabbani G, Srikanta SS, Starostina EG, Shevchuk M, Taj R, Vukovic O, Wölwer W, Xin Y. Prevalence and correlates of depressive disorders in people with Type 2 diabetes: results from the International Prevalence and Treatment of Diabetes and Depression (INTERPRET-DD) study, a collaborative study carried out in 14 countries. Diabet Med. 2018 Jun;35(6):760-769. doi: 10.1111/dme.13611. Epub 2018 Mar 30. PMID: 29478265.

[28] McIntyre E, Lauche R, Frawley J, Sibbritt D, Reddy P, Adams J. Physical activity and depression symptoms in women with chronic illness and the mediating role of health-related quality of life. J Affect Disord. 2019 Jun 1;252:294-299. doi: 10.1016/j.jad.2019.04.057. Epub 2019 Apr 8. PMID: 30991257.

[29] Mikailiūkštienė A, Juozulynas A, Narkauskaitė L, Žagminas K, Sąlyga J, Stukas R. Quality of life in relation to social and disease factors in patients with type 2 diabetes in Lithuania. Med Sci Monit. 2013 Mar 6;19:165-74. doi: 10.12659/MSM.883823. PMID: 23462804; PMCID: PMC3628352.

[30] Munkácsi B, Papp G, Felszeghy E, Kovács KE, Nagy BE. The associations between mental health, health-related quality of life and insulin pump therapy among children and adolescents with type 1 diabetes. Journal of Pediatric Endocrinology and Metabolism. 2018 Oct 25;31(10):1065-72.

[31] Pan X, Hong Z, Xu R. Relationship between negative emotion and quality of life of type 2 diabetes patients. J Qilu Nur. 2013;19(21):38–39

[32] Piette JD, Wagner TH, Potter MB, Schillinger D. Health insurance status, cost-related medication underuse, and outcomes among diabetes patients in three systems of care. Medical care. 2004 Feb 1:102-9.

[33] Redekop WK, Koopmanschap MA, Stolk RP, Rutten GE, Wolffenbuttel BH, Niessen LW. Health-related quality of life and treatment satisfaction in Dutch patients with type 2 diabetes. Diabetes Care. 2002 Mar;25(3):458-63. doi: 10.2337/diacare.25.3.458. PMID: 11874930.

[34] Roy T, Lloyd CE. Epidemiology of depression and diabetes: a systematic review. J Affect Disord. 2012 Oct;142 Suppl:S8-21. doi: 10.1016/S0165-0327(12)70004-6. PMID: 23062861.

[35] Rubin RR, Peyrot M. Quality of life and diabetes. Diabetes/metabolism research and reviews. 1999 May;15(3):205-18.

[36] Rwegerera GM, Moshomo T, Gaenamong M, Oyewo TA, Gollakota S, Rivera YP, Masaka A, Godman B, Shimwela M, Habte D. Health-related quality of life and associated factors among patients with diabetes mellitus in Botswana. Alexandria journal of medicine. 2018 Jun 1;54(2):111-8.

[37] Schram MT, Baan CA, Pouwer F. Depression and quality of life in patients with diabetes: a systematic review from the European depression in diabetes (EDID) research consortium. Current diabetes reviews. 2009 May 1;5(2):112-9.

[38] Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes research and clinical practice. 2010 Jan 1;87(1):4-14.

[39] Shim YT, Lee J, Toh MP, Tang WE, Ko Y. Health-related quality of life and glycaemic control in patients with Type 2 diabetes mellitus in Singapore. Diabet Med. 2012 Aug;29(8):e241-8. doi: 10.1111/j.1464-5491.2012.03689.x. PMID: 22507291.

[40] Snoek FJ, Skinner TC. Psychological aspects of diabetes management. Medicine. 2006 Feb 1;34(2):61-2.

[41] Stojanović M, Cvetanović G, Anđelković Apostolović M, Stojanović D, Rančić N. Impact of socio-demographic characteristics and long-term complications on quality of life in patients with diabetes mellitus. Cent Eur J Public Health. 2018 Jun;26(2):104-110. doi: 10.21101/cejph.a5022. PMID: 30102498.

[42] U.K. Prospective Diabetes Study Group. Quality of life in type 2 diabetic patients is affected by complications but not by intensive policies to improve blood glucose or blood pressure control (UKPDS 37). U.K. Prospective Diabetes Study Group. Diabetes Care. 1999 Jul;22(7):1125-36. doi: 10.2337/diacare.22.7.1125. PMID: 10388978.

[43] Verma SK, Luo N, Subramaniam M, Sum CF, Stahl D, Liow PH, Chong SA. Impact of depression on health-related quality of life in patients with diabetes. Ann Acad Med Singap. 2010 Dec;39(12):913-7. PMID: 21274488.

[44] Walker RJ, Lynch CP, Strom Williams J, Voronca D, Egede LE. Meaning of illness and quality of life in patients with type 2 diabetes. J Diabetes Complicat. 2015;29(5):665–669. doi: 10.1016/j.jdiacomp.2015.04.006.

[45] Wannamethee SG, Shaper AG, Whincup PH, Lennon L, Sattar N. Impact of diabetes on cardiovascular disease risk and all-cause mortality in older men: influence of age at onset, diabetes duration, and established and novel risk factors. Arch Intern Med. 2011 Mar 14;171(5):404-10. doi: 10.1001/archinternmed.2011.2. PMID: 21403036.

[46] Wexler DJ, Grant RW, Wittenberg E, Bosch JL, Cagliero E, Delahanty L, Blais MA, Meigs JB. Correlates of health-related quality of life in type 2 diabetes. Diabetologia. 2006 Jul 1;49(7):1489-97.