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Depression and glycemic control in a sample of patients with type 2 diabetes

Abstract

Background: Diabetes mellitus is a serious public health burden, accounting for substantial morbidity, disability, mortality, and health care cost; in addition to impaired physical health. Patients with diabetes frequently have comorbid affective illness; they are twice likely to be depressed as people without chronic diseases. Depression may be a risk factor for poor metabolic control in diabetes, however some investigators have found moderate to strong association between depression and glycemic control, although others have found no relationship.

Purpose of the study: The purpose of this study was to investigate the association of comorbid depression and glycemic control in a clinical sample of adult Saudi patients with type 2 diabetes.

Methods: The sample included 172 type 2 diabetes mellitus adult patients regularly followed in diabetes clinic at Saudi airlines medical center in Jeddah, western Saudi Arabia. We assessed depression by beck depression inventory II (BDI-II), and clinical diagnosis according to DSM IV TR by an expert psychiatrist, and assessed diabetic control by hemoglobin A1c (HbA1c), and fasting blood glucose (FBG). The association between depression and diabetic control was analyzed cross-sectionally, and controlled for demographics (age, sex, employment, education), and clinical variables (smoking, BMI, duration of DM, diabetes medications, medical comorbidities, lipid profile, and renal functions). We used student t-test for group comparison, X2 for baseline association between categorical baseline variables, one-way analyses of variant (ANOVA), Pearson correlation coefficient to examine univariate associations between continuous baseline variables, and multiple regression analyses to adjust for the demographic and clinical potentially confounding factors.

Results: Unadjusted analyses revealed a significant positive relationship between BDI scores and HbA1c (r=0.17, p=0.02), this relationship was evident throughout the entire range of BDI scores. Also the comparison between clinically depressed and non-depressed groups of patients using t-test revealed that HbA1c is significantly higher in the depressed group with P value (0.01). After adjustment for demographic variables, BDI scores, and clinical depression remained associated with HbA1c changes, but after full adjustment for all demographic and clinical variables, fully adjusted analyses revealed that duration of diabetic illness is the strongest factor which predicts higher HbA1c (p=0.00), and only clinically diagnosed major depressive disorder (MDD), and probable severe depression (BDI score>25), - but not the entire range of BDI scores- was less significant predictors of higher HbA1c [P=(0.034) and (0.046) respectively].

Conclusion: patients with diabetes and comorbid sever depressive symptomatology or clinical major depressive disorders are associated with poor glycemic control in type 2 diabetes. However, to study the persistence of this relation prospectively, to explore the factors that could mediate this relation, as well as the study of impact of treating depression on glycemic control may be an interesting areas for further research.

Keywords: depression, MDD, depressive disorder, diabetes, diabetic control, HbA1c

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Hesham Abuhegazy,[1] Heba Elkeshishi,[2] Hesham Farrag,[3] Noha Saleh[4]

[1]Al-Azhar University faculty of medicine, Department of psychiatry and behavioral sciences, Egypt
[2]El-menia University faculty of arts, Department of psychology, Egypt
[3]Zagazig University faculty of medicine, Department of internal medicine, Egypt
[4]Alexendia University institute of public health, Biostatistics department, Egypt

Correspondence: Hesham Abuhegazy, Al-Azhar University faculty of medicine, Department of psychiatry and behavioral sciences, Cairo, Egypt, Tel 966530107236, Email abuhegazy@gmail.com

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Abbreviations: HbA_1c, hemoglobin A_1c; BDI-II, beck depression inventory ii; FBG, fasting blood glucose; DM, diabetes mellitus; BMI, body mass index; DSMIV, diagnostic and statistical manual of mental disorders; ECG, electro cardio gram; LDL, low density lipoprotein

Introduction

Diabetes mellitus is a serious public health burden, accounting for substantial morbidity, disability, mortality, and health care cost.[1] Evidence from large randomized clinical trials indicates that good glycemic control as evidenced by low hemoglobin A_1c (HbA_1c) scores, is associated with decreased complications, decreased mortality, and improved quality of life.[2] People with diabetes are twice likely to be depressed as people without chronic diseases.[3] Current epidemiological evidence suggests that at least one third of adults with diabetes suffer from clinically relevant depressive disorders.[4–6] Comorbid depression in adults with diabetes is associated with higher complication rates, increased health care use and cost, diminished quality of life, increased disability, and increased risk of death,[2] as well depression may be a risk factor for poor metabolic control in diabetes, however some investigators have found moderate

to strong association between depression and glycemic control, although others have found no relationship.[7] The lack of reporting of sociodemographic and clinical variables in most studies is a significant limitation, as analyses of the association between depression and diabetes severity and HbA_1c have often not controlled for potentially important confounding variables.[8] The purpose of this study was to investigate the association of comorbid depression and glycemic control after controlling for demographic and clinical characteristics.

Methods

Patients

The adult patients (18-65 years old) diagnosed with type-2 diabetes and regularly followed through the outpatient diabetes clinic in Saudi Arabian airline medical center in Jeddah, Saudi Arabia were asked to participate in the study, with assuming that effect size is 0.3,[4–6] alpha error 5%, and power 80%, the sample size should be not less than 143 (according to G power 3.1.3), we approached 224 patients, only 21 of them refused participation, while all others accepted to participate and gave informed consent., persons who declined participation, and participants were not significantly different in terms of age, and sex. Out of potential participants, 31 patients were excluded because they fulfill one or more of the following exclusion criteria:

a. Type of diabetes is indeterminate from the medical records and/or consultation with the physician

b. There is History of stroke, brain surgery, closed head injury, dementia, pregnancy, or illness that could affect glucose control.

c. They are unable to independently complete BDI questionnaire (Arabic version) because of visual disability or primary language other than Arabic.

Participants who included were male and female patients between ages of 18- 65 years with definite diagnoses of type-2 diabetes mellitus.

Measures

Depressive symptoms were assessed by use of Arabic version of beck depression inventory II (the psychological corporation, Orlando, FL). BDI-II has been shown to have high reliability and validity,[9] furthermore BDI has been validated as a tool for measuring depression in diabetic patients, it is also widely used to assess depression in both community, and clinical samples.[10–12] BDI has been translated into Arabic by Ahmed Abdelkhalek and shown high reliability and validity as well. Scores of 16 and above were used as a cut off point for probable depression, and 25 and above for confirmed depression.[13] Clinical depression has been assessed by direct interview performed by a consultant psychiatrist, with proper experience, and patients been diagnosed according to DSMIV-TR classification. Glycemic control was assessed by both fasting blood glucose, and HBA_1c, an accepted index of average glucose level over the previous 12-16 weeks.

Procedures

After informed consent, patients who included in the study were interviewed to collect personal and demographic information patients were asked to complete the BDI-II in the interview. All patients undergoes an interview with the diabetes physician where vital signs including pulse, temperature, blood pressure, height, weight, BME, have been assessed, all data about his/her illness were reviewed and completed including duration of diabetes, types of medications, periods of refill, as well physician assessed the presence of hypoglycemic, or hyperglycemic symptoms, diabetic complications, medical comorbidities, recent infections, other medical conditions, or medications which may affect glucose control.

All patients undergoes ECG, and echocardiogram to assess ejection fraction and left ventricular hypertrophy, fundus examination to assess retinopathy, and full laboratory make up (either obtained from medical records if performed within 3 months, or newly requested) including fasting blood glucose, HBA1c, serum creatinin and urea, 24 hours protein, and full lipid profile. All patients have interviewed by consultant psychiatrist, history of psychiatric illnesses and psychotropic medications was taken, mental state examination, and diagnosis according to DSMIV-TR was performed, (the psychiatrist was unaware about the BDI scores). Proper action was done for all patients found having clinical depression, or other psychiatric morbidities. All procedures were approved by the research and ethics committee of Saudi airlines medical center.

Statistical analysis

Data were analyzed using the software SPSS 16.0 for Windows (SPSS Inc, Chicago, Ill). Firstly, the data were tested for normal distribution using Kolmogrov and Smirnov test. We used Two-tailed *t*-tests or x^2 tests to examine difference between patients with depression and those without depression regarding sociodemographic, and clinical variables. Pearson's correlation, ANOVA and *t*-tests were used to determine significant associations between the possible covariates, BDI score and HbA_1c. Statistical significance was declared for $p \leq 0.05$. To detect the significant predictors of HbA_1c all the significantly associated variables in univariate analysis were included in multiple hierarchical regression models.

Prior to conducting a hierarchical multiple regressions, the relevant assumptions of this statistical analysis were tested. Firstly, an examination of correlations revealed that no independent variables were highly correlated except for cholesterol level and LDL. Also, the collinearity statistics (i.e., Tolerance and VIF) for both variables were high beyond the accepted limits. So cholesterol and LDL were excluded from the regression model. Correction was done for multiple testing through a three stage hierarchical multiple regression conducted with HbA_1C as the dependent variable. Sociodemographic variables (sex and education) was entered at stage one of the regression to control for their effect. The clinical variables were entered at stage two, and finally depression variables (Clinical diagnosis and BDI score) were entered at stage three as dummy variables.

Results

Patients' characteristics

0ut of 224 eligible patients approached, 203 approved to participate, and only 172 patients were enrolled. The study sample comprised of 172 type 2 diabetic patients, 69.8% of them were males, mean age was 51.3 (SD=6.2) years, the majority had intermediate education (60.9%), more than half were employed (51.2%) and 42.4% of them were smokers, 93% were receiving oral diabetic medications, Regarding their clinical assessment data, mean BMI was 31.9 (SD=5.8), mean duration of diabetes was 10.7 (SD=3.5) years, mean FBS was 176.9 (SD=7.4) and mean HbA_1C was 8.7(SD=2. and ranged from 5.5 to 14.8) (Table 1). BDI score ranged from 0 to 43 with a mean of 14.8 (SD=8.9), depression was evidenced in 46.5% of the patients; with 16.3% of the patients were diagnosed with MDD while 30.3% were diagnosed with other depressive disorders. 14% receiving multiple antidepressants and 14% had psychiatric co-morbidity (Table 2).

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Table 1 Descriptive statistics of the study sample according to DSMIV diagnosiss

Characteristics	All sample N=172	Not depressed N=92	Depressed N=80	P value
Mean Age in Years±SD	51.3±6.2	51.7±6.4	51.8±5.8	0.323
Mean BMI±SD	31.9±5.8	31.5±5.3	31.7±6.6	0.907
Mean Duration of Diabetes±SD	10.7±3.5	10.7±8.1	10.9±7.4	0.926
Mean FBS±SD	176.9±7.4	162.1±5.4	200.3±6.8	0.000*
Mean HbA1C±SD	8.7±2.1	8.4±2.2	9.1±2.1	0.010*
Mean Cholesterol±SD	171.1±46.3	166.5±43.2	176.5±43.1	0.169
Mean Triglyceride±SD	141.1±86.9	131.9±67.5	153.9±74.9	0.004*
Mean HDL±SD	48.5±15.2	47.96±13.9	48.9±15.2	0.698
Mean LDL±SD	99.6±38.4	91.5±35.5	102.6±39.8	0.105
Mean Serum Creatinine±SD	1.9±0.9	1.01±0.30	0.90±0.19	0.005*
Mean Serum Urea±SD	14.9±4.1	15.3±4.9	14.4±2.5	0.158
Mean Protein Creatinine Ratio±SD	0.86±0.5	1.1±0.7	0.34±0.3	0.002*
Gender (%)				
Male	120 (69.8)	72 (78.3)	48 (60.0)	0.009*
Female	52 (30.2)	20 (21.7)	32 (40.0)	
Level of Education (%)				
Illiterate	4 (2.6)	4 (4.3)	0 (0)	
Read and Write	12 (7.9)	0 (0)	12 (15.0)	
Intermediate	112 (60.9)	56 (60.9)	56 (70.0)	0.000*
High	44 (28.5)	32 (34.8)	12 (15.0)	
Employment (%)				
Non	84 (48.8)	48 (52.2)	36 (45.0)	0.348
Employed	88 (51.2)	44 (47.8)	44 (55.0)	
Smoking (%)				
No	87 (57.6)	52 (56.5)	40 (50.0)	0.392
Yes	64 (42.4)	40 (43.5)	40 (50.0)	
Medication for Diabetes (%)				
Insulin	12 (7.0)	4 (4.3)	8 (10.0)	0.147
Oral	160 (93.0)	88 (95.7)	72 (70.0)	
Ejection Fraction (%)				
50% and More	160 (93.0)	88 (95.7)	72 (90.0)	0.147
Less than 50%	12 (7.0)	4 (4.3)	8 (10.0)	

*Significant P value of x2 or t–test≤0.05

Factors associated with depression

The comparison between clinically depressed diabetic patients and non depressed ones (Table 1) revealed that depressed patients were more females (p=0.009), less educated (p=0.000), with higher fasting blood glucose (p=0.000), HbA_1c (p=0.010), and triglycerides (p=0.006). Patients reporting high BDI score (more depressive symptoms) – as shown in table 3- were mostly females (P=0.006), less educated (P=0.021), with higher fasting blood sugar (r=0.327, P=0.000), cholesterol (r =0. 328, P=0.000), and LDL (r=0.340, P=0.000), they were more insulin users (P=0.000), had a longer duration of psychiatric illness (r=0. 258, P=0.000), more psychiatric co morbidity (P=0.000), and they were using multiple antidepressants (P=0.000).

Factors associated with glycemic control

Patients with poor glycemic control (higher HbA_1c) were mostly females (p=0.000), less educated (P=0.012), had more hyperglycemic, less hypoglycemic symptoms (p=0.000, and 0.001), less medical co morbidities (p=0.003), poorer ejection fraction (p=0.000), longer duration of diabetes (p=0.000), longer duration of psychiatric illness (p=0.025), and higher levels of laboratory investigations (FBS, cholesterol, triglycerides, LDL and serum urea). Some covariates are correlated with both BDI score and HbA_1c as sex, education, FBS, cholesterol, LDL /and duration of psychiatric illness (Table 3)

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Table 2 Psychological assessment of study sample

Psychiatric diagnosis (%)	
Not Depressed	92 (53.3)
Depressed	80 (46.5)
MDD	28 (16.3)
Mixed Depression and Anxiety	12 (6.9)
Dysthymia	40 (23.3)
Psychotropic medication (%)	
Non	132 (76.7)
One Drug	16 (9.3)
Multiple Drugs	24 (14.0)
Psychiatric co-morbidity (%)	
Non	148 (86.0)
Yes	24 (14.0)

Unadjusted correlation between depression and glycemic control: Showed that there was a significant linear correlation between BDI scores and HbA_1C (r=0.173, P=0.021), and between BDI scores and fasting blood sugar (r=0.327, p=0.000) indicating that depression is associated with poor glycemic control. The scatter plot in (Figures 1 & 2) showed a linear relationship between them.

Predictors of glycemic control

The hierarchical multiple regression (Table 4) revealed that Sociodemographic factors contributed significantly to the regression model, (F=8.4, p=0 .000) and accounted for 8% of the variation in HbA_1c. Adding the clinical variables to the model explained an additional 65.5% of variation in HbA_1c and this change in R^2 was significant, (F=28.07, p=0 .000). Finally, the addition of clinical depression and BDI score to the regression model both explained an additional 67.8% of the variation in HbA_1c and this change in R^2 square was also significant, (F=22.2, p=0.000). When all independent variables were included in stage three of the regression model, clinically diagnosed major depressive disorder (MDD) - but not other depressive diagnoses (p=0.034)-, and probable severe depression (BDI score>25), - but not the entire range of BDI scores- (p=0.046) was significant predictors of higher HbA_1c.other predictors of HbA_1c were duration of diabetes which was the most important predictor of HbA_1c (B=0.52, p=0.000), hyperglycemic symptoms (B=0.20, p=0.000), abnormal ejection fraction (B=0.27, p=0.000), and higher fasting blood sugar (B=0.20, p=0.014) were also significant predictors of higher HBA_1c. (Table 4) Illustrated data about the actual relation between depressive symptoms and HbA_1c where all other covariates were controlled.

Table 3 Factors associated with BDI score and HBA1c

Factors	**BDI Score**		**HbA_1c**	
	Correlation coefficient	**P value**	**Correlation coefficient**	**P value**
Age	r=-0.143	0.056	r=-0.001	0.991
BMI	r=0.103	0.17	r=-0.014	0.854
Duration of Diabetes	r=0.164	0.104	r=0.368	0.000*
Duration of Psychiatric Illness	r=0.258	0.000*	r=0.167	0.025*
FBS	r=0.327	0.000*	r=0.674	0.000*
Cholesterol	r=0.328	0.000*	r=0.236	0.001*
Triglyceride	r=0.079	0.294	r=0.335	0.000*
HDL	r= -0.025	0.734	r=-0.142	0.057
LDL	r= 0.340	0.000*	r=0.331	0.000*
Serum Creatinnine	r=-0.013	0.866	r=0.021	0.785
Serum Urea	r=0.064	0.393	r=0.183	0.014*
Protein Creatinine Ratio	r=-0.025	0.74	r=0.120	0.109
	Mean±SD	**P Value**	**Mean±SD**	**P Value**
Gender				
Male	13.7±8.8	0.006*	7.8±1.7	0.000*
Female	17.7±8.6		9.10±2.1	
Level of education				
Illiterate	14.8±6.8		9.1±1.7	
Read and Write	22.0±6.7		8.9±1.9	
Intermediate	13.7±8.5	0.012*	8.4±2.3	0.012*
High	8.0±0.05		5.5±0.5	
Employment				
Non	14.1±7.1	0.253	8.7±2.3	0.898
Employed	15.5±10.3		8.8±1.8	

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Table Continued...

Factors	BDI Score		HbA_1c	
	Correlation coefficient	P value	Correlation coefficient	P value
Smoking				
No	15.2±8.9	0.467	8.5±2.1	0.083
Yes	14.3±9.1		9.1±2.2	
Medication for diabetes				
Insulin	20.1±1.5	0.000*	8.4±1.8	0.562
Oral	14.5±9.1		8.8±2.1	
Hyperglycemic symptoms				
No	14.3±9.1	0.254	7.7±1.3	0.000*
Yes	15.8±8.5		10.4±1.9	
Hypoglycemic symptoms				
No	14.1±9.5	0.056	9.02±2.1	0.001*
Yes	15.8±9.5		8.04±1.6	
Hypertension				
No	13.8±5.9	0.08	8.8±2.1	0.611
Yes	16.2±1.8		8.6±1.9	
Co-morbidity				
No	15.2±9.4	0.684	8.9±2.2	0.003*
Yes	16.2±9.6		7.8±1.2	
Ejection Fraction				
50% and More	14.6±9.1	0.295	8.4±1.8	0.000*
Less than 50%	17.6±3.2		12.1±2.4	
Psychiatric co-morbidity				
No	14.2±9.3	0.000*	8.7±1.9	0.699
Yes	19.0±4.5		8.9±2.9	
Antidepressant medications				
No*	13.2±4.8	0.000*	8.6±2.4	0.129
One Drug	19.5±5.7		8.4±1.6	
Multiple Drug	21.2±9.8		8.7±2.03	

*Significant P value of pearson correlation coefficient or t-test or ANOVA test≤0.05

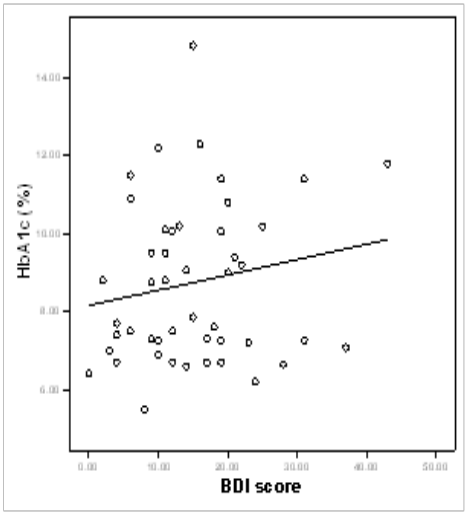

Figure 1 Relationship of BDI scores and HA1c.

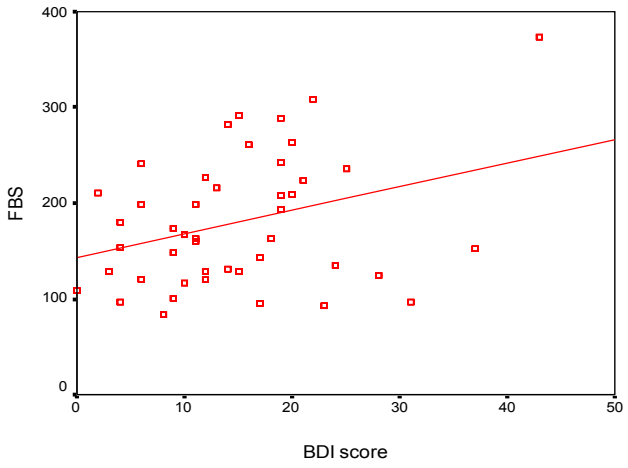

Figure 2 Relationship of BDI scores and fasting blood sugar.

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Table 4 Hierarchical Regression Analysis for Variables predicting HbA_1c

Variable	β	t	P-Value	R	R^2	Adjusted R^2
Step1				0.302	0.091	0.08
Socio-demographic						
Education	-0.05	0.68	0.492			
Gender	0.31	4.01	0.000*			
Step 2				0.824	0.679	0.655
Socio-demographic						
Education	-0.07	1.03	0.185			
Gender	0.06	0.797	0.427			
Clinical parameters						
Duration of Diabetes	0.42	5.6	0.000*			
Duration of Depression	0.04	0.81	0.417			
Hyperglycemic Symptoms	0.3	4.1	0.000*			
Hypoglycemic Symptoms	0.05	1.07	0.283			
Left Ventricular Hypertrophy	0.01	0.124	0.901			
Ejection Fraction	0.24	4.2	0.000*			
Co-morbidity	0.01	0.223	0.824			
Fasting Blood Sugar	0.16	2.09	0.004*			
Triglyceride	0.06	1.2	0.215			
Serum Urea	0.05	0.9	0.365			
Step 3				0.843	0.71	0.678
Socio-demographic						
Education	0.08	1.5	0.121			
Gender	o.13	1.6	0.099			
Clinical parameters						
Duration of Diabetes	0.52	6.5	0.000*			
Psychological Duration	0.14	1.9	0.051			
Hyperglycemic Symptoms	0.2	3.6	0.000*			
Hypoglycemic Symptoms	0.07	1.3	0.189			
Left ventricular Hypertrophy	0.1	1.1	0.264			
Ejection fraction	0.27	4.8	0.000*			
Co-morbidity	0.05	0.91	0.362			
Fasting Blood Sugar	0.2	2.5	0.014*			
Triglyceride	0.003	0.57	0.955			
Serum Urea	0.04	0.64	0.521			
Clinical depression						
Mixed Anx & Dep	0.01	0.26	0.789			
Dysthymia	0.03	0.36	0.178			
MDD	0.15	2.1	0.034*			
BDI score						
BDI Score 17-25	0.009	0.11	0.907			
BDI Score>25	0.12	2.2	0.046*			

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Discussion

This study of adults with type-2 diabetes demonstrates a significant relationship between depression weather measured as a continuous variable (BDI scores), or as a dichotomous variable (depressed/not depressed according to DSM-IV), and glycemic control as measured by HbA_1c, the study shows that depressed diabetic patients have HbA_1c levels significantly higher than their non depressed counterparts (p=0.01), and that there is significant correlation between BDI scores and HbA_1c (r=0.173, p=0.021). The unadjusted observed relationship between depressive symptoms and glycemic control is linear throughout the complete range of observed BDI scores. This come in concordance with numerous cross sectional studies,[14–17] as well as a meta-analysis of 30 studies found depression is associated with suboptimal glycemic control with moderate effect size.[18]

Although there many demographic, and clinical variables could influence glycemic control, the adjustment of this observed relationship for various demographic and clinical variables had weakened the relation but not eliminate it, after full adjustment only the major depressive disorder (MDD), and BDI scores higher than 25, but not the full range, were significant predictors for higher HbA1c (p= 0.034, and 0.046 respectively), which come in concordance with IDEA Tel study on elderly patients which found a significant correlation between depression and HbA1c at base line and a trend for depression to predict HbA1c when other factors were controlled.[7] this adjusted results stands between the studies who found positive relation between depression and glycemic control[6,13] and those don't found such like relation,[3,19] and as well goes consistent with the findings of the large meta-analysis[18] which found that the association between depression and glycemic control was larger when standardized interviews and diagnostic criteria rather than self-report questionnaires were used to assess depression (ES 0.28 vs. 0.15). Perhaps because this relationship might be stronger in patients with clinical rather than subclinical depression. Self-report inventories are also less specific measures of depression, as elevated scores may be produced not only by depression but also by anxiety, general emotional distress, or medical illness. Like many other studies[6–8,20] we have found patients with more depressive symptoms mostly females, less educated, with higher FBG, HbA_1c, more disturbed metabolic profile, and more insulin users. however age, smoking, longer duration of diabetes, and diabetic related complications which have been found as risk factors for depression in diabetic patients,[6] don't be confirmed through our findings.

It is worth mentioned to notice that prevalence of depressive disorders in this study reaches 16.3% for MDD, and 30% for other depressive diagnoses (dysthymia, and mixed depression and anxiety disorder); many cross sectional studies located in Saudi Arabia found similar prevalence rates of depression among clinical samples of type-2 diabetic patients., researchers who used BDI as screening tool found prevalence ranges 34%, 41.9%, and 62.5% respectively,[21–23] while those who used other screening tools found prevalence rates of 37.9%, 45.8, and 49.6% respectively.[24–26] this finding goes in concordance with a large meta-analyses of prevalence of depression in adults with diabetes by Anderson et al.[27] which included 42 studies that found prevalence of depression in clinical samples is 32.7%, decreases by using structured interviews to 14.2%, and increases by using self-report instruments up to 34.9%, and earlier study by Gavard et al.[28] which found that major depression was present in 14.7%, and elevated depression symptoms in 26% of diabetic patients.

The study has some limitations, first: clinical sample of depressed patients may not resemble general population sample due to changes in help seeking behavior. Second: is the cross sectional design of the study. And third: the influence of confounding factors cannot be fully accounted for. However the relation between depression and HbA1c level is repeatedly found, it remains unclear if some other factors as changes in self care behavior, poor adherence to diabetes education programs, oral hypoglycemic medications and dietary interventions, or counter regulatory hormones[3,29] mediate the relation between depression and glycemic control. Although this was not the focus of present study, it needs to be examined in future studies. The associations observed in this study are likely valid, however future studies need to validate our findings in different patient populations, and with prospective study design.

Conclusion

This study on adults with type 2 diabetes has demonstrated that sever depressive symptomatology, as well as major depressive disorder (MDD) are significantly associated with poorer glycemic control as measured by higher HbA_1c. We recommend to screen for depression among poorly controlled diabetic patients.

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Conflict of interest

The author declares no conflict of interest.

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