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Research Article

Glycemic Control of Type 2 Diabetics and Associated Depressive Disorders Spectrum - Descriptive Comparative Study in Ismailia City - Egypt

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Abstract

Background: Depressive disorders are highly prevalent in the general population worldwide. Evidence suggests a longitudinal reciprocal bi-directional relationship between depression and type 2 diabetes. This study aimed at detecting the relationship between glycemic control and the spectrum of depressive disorders among patients with type II diabetes attending the health insurance outpatient clinics of medical complex, Ismailia city between January and March 2022, Ismailia city, Egypt.

Methods: This study recruited 105 patients with type II diabetes randomly selected from patients attending the specialized endocrinology and diabetes center clinics in the medical complex, health insurance Ismailia city and matched on a regular basis with another 105 non-diabetic individuals randomly selected from new patients attending for general medical checkup and covered in the comprehensive medical insurance pilot run currently in Egypt. Brief medical history and examination was carried out for all participants including, duration of type 2 DM diagnosis, presence of diabetic complications, and smoking status, and BMI recording, followed by interview for self-completion of the "Beck Depression inventory II scale". A venous blood sample, in a non-fasting state, was drawn for measuring HbA1C% from all participants.

Results: The mean HbA1c% in diabetic group was 8.7% ± 2.1, compared with 5.3 ± 0.44 in non-diabetic group. Assessment of prevalence and the grades of depression in the two study groups, showed a highly statistically significant difference between the two groups with 55 subjects representing 52.4% in the diabetic group, compared with 11 subjects, representing 10.5% in the non-diabetic group. The grades of severity of depression between the two groups showed also a highly statistically significant difference with 33.3%, 15.2%, and 3.8% respectively for mild, moderate, and severe depression in the diabetic group, compared with 8.6%, 1.9%, and 0% respectively for mild, moderate, and severe depression in the non-diabetic group. High statistically significant difference in Beck 'depression inventory Score (BDI-II) was shown between the two groups with mean score of 14.2 ± 7.6 in the diabetic group, compared with 9.8 ± 3.3 in the non-diabetic group. A linear positive correlation was shown between HbA1c%, and BDI-II score in all of the study participants. In the diabetic group a moderate positive correlation was shown between BDI-II and HbA1c% with r coefficient 0.37 that was highly statistically significant ($P < 0.001$). The results of binary regression analysis model for prediction of depression, showed among several independent factors selected, that smoking, and presence of diabetic complications were statistically significant predictors ($P = 0.016$, and 0.013, respectively), and glycemic control (HbA1c%) was highly statistically significant predictor ($P < 0.001$).

Conclusion: In this study, poor glycemic control reflected in high glycosylated hemoglobin percent (HbA1c%), was shown to be closely related to higher percentages of all grades of depressive disorders as assessed by BDI-II scale (Beck Depression inventory II scale) when comparing type 2 diabetic and non-diabetic patients, and among the type 2 diabetic patients. A positive linear correlation was shown between the glycemic control level and BDI-II scale score. Glycemic control was shown to be the strongest predictor of depressive disorders, followed by presence of diabetic complications, and smoking.

Keywords: Glycemic Control; Spectrum of Depressive Disorders, and Predictors

Introduction

Depression is projected to become the leading cause of disability and was the second leading contributor to the global burden of disease by 2020 [1]. World Health Organization (WHO) ranked depression the fourth global burden of disease and found it to be the largest non- fatal burden of disease, with nearly 12% of total years lived with disability [2]. Diabetes is a global health concern due to its increasing prevalence which was projected to rise from 2.8% in 2000 (171 million adults) to 4.4% in 2030 for all age-groups [3]. (366 million adults). There were over 7.8 million cases of diabetes in Egypt in 2015 [4]. Diabetes has been associated with an increased risk of certain psychiatric disorders, particularly depression and anxiety disorders [5]. The complex interactions of biological, psychological, social and genetic factors that contribute to the association between diabetes and depression remain uncertain. Type II diabetic patients with poor glycemic control were more likely to have depression than those with good diabetic control. A conclusion that was confirmed across different cultural and ethnic groups [6]. while others found no correlation between HbA1c and depressive disorders [7]. It is currently unclear how and when depression develops after diagnosis of type II diabetes and results are equivocal. Recent studies have shown that coexisting depression increases synergistically the risk of death among people with diabetes [8]. Data suggest a bidirectional relationship; depression symptoms predict the onset of type 2 diabetes, and the diagnosis of type 2 diabetes is associated with increased depressive symptoms over time, with the first directional effect appearing to be more robust than the second. The presence of psychiatric comorbidity especially depression has been associated with medications non-adherence, suboptimal glycemic control, and the development of diabetes -related complications [9]. Accordingly, in this study, we tried to study the relationship between depressive disorders in all grades of severity and status of glycemic control, and what factors can predict the occurrence of depressive disorder among a sample of type 2 diabetic patients attending the specialized endocrinology and diabetes center in Ismailia Medical Complex, Ismailia, Egypt.

The Aim of this Work

This study aimed at studying the relationship between degree of glycemic control in type 2 diabetics mellitus and the spectrum of depressive disorders prevalence among controlled and uncontrolled type 2 diabetics compared with non- diabetic patients.

Subjects and Methods

Sample size calculation: The power of the study was estimated using G*Power 3.1.9.4, with a 95% confidence level (Z-score = 1.96), and a margin of error (confidence interval) of +/- 5%. Based on the study of Kalantari., *et al*. [10] that reported the prevalence of depression in adult patients with diabetes mellitus to be 37.8% compared with a prevalence of 16% in non-diabetic subjects, the sample size was estimated to include 105 subjects in each group of the study.

Subjects

105 patients with type II diabetes mellitus were randomly selected from patients attending the specialized endocrinology and diabetes center clinics of the Medical Complex of Health Insurance, Ismailia City, and matched on a regular basis for another 105 non-diabetic individuals randomly selected from new patients attending for general medical checkup offered in the comprehensive medical insurance pilot in Ismailia Governorate, Egypt.

Inclusion criteria

Type 2 diabetic/non-diabetic adults attending the outpatient clinics and given their informed consent to participate in the study.

Exclusion criteria

Previous history or currently receiving treatment of any psychiatric conditions.

- History of or on treatment for any non-diabetic co-morbid diseases.

Methods

Brief medical history and examination was carried out for all participants including, duration of type 2 DM diagnosis, presence of diabetic complications, and smoking status, and BMI recording. Measurement of glycosylated haemoglobin percent (HbA1c%). was done by collecting non-fasting 5 ml of venous blood sample in EDTA tube by ion-exchange high-performance liquid chromatography (HPLC) for the automatic separation of HbA1c. EDTA blood is sampled directly from the primary tube, diluted in hemolyzing buffer and pumped via a pre-filter to the ion-exchange column. A series of three buffers are used to elute the hemoglobin from the column and the peak measurement achieved by dual wavelength detection. Quantitation is two-point calibrators. blood sample takes 3 minutes to elute and there is no pretreatment of the sample [11]. The method was applied systematically for all of the study participants. This was followed by interview with all subjects for completion of the "Beck Depression inventory II scale" (BDI-II). The BDI-II scale is a scale that measures the existence and severity of symptoms of depression, it is self-administered questionnaire consists of 21 items that include 2 subscales, 13 items for somatic and 8 items for affective symptoms. Each item is scored on a scale of 0-3 in a list of four statements arranged in increasing severity about a particular symptom of depression, with 2 items 16 and 18, there are seven options to indicate either increase or decrease of appetite, and sleep. Total score of 0-13 is considered minimal range, 14-19 is mild, 20-28 is moderate, and 29-63 is severe. The BDI-II was proven a relevant psychometric instrument, showing high reliability, capacity to discriminate between depressed and non-depressed subjects with improved concurrent, content, and structural validity, and internal consistency was described as around 0.9 and the retest reliability ranged from 0.73 to 0.9. The BDI-II can be viewed as cost- effective questionnaire for measuring the severity of depression, with broad applicability for research and clinical practice worldwide. Substantial overlap between measures of depression and anxiety was reported [12].

Statistical analysis

The raw data coded and entered SPSS system files (version 22), the following statistical measures were used when appropriate; Descriptive statistics including frequency, distribution, mean, median with interquartile range (IQR) and standard deviation to describe different characteristics. Univariate analyses, including Student t test, χ^2 test, and Mann Whitney test, were used to test the significance of results of quantitative variables. Spearman's rank correlation coefficient or Spearman's rho was used to assess how well the relationship between two variables can be described using a monotonic function. Binary regression analysis model was used to predict different biosocial variables that predict change in BDI-II score.

Results

Comparison of the sociodemographic characteristics between the two study groups showed no statistically significant difference in any of sociodemographic data compared. The mean age of participants in diabetic group was 52 years, and 53 years in non-diabetic group. Female patients represented 54% in diabetic group, and 53% in non-diabetic group (Table 1). Statistically significant difference in the means of glycosylated hemoglobin percent (HbA1%) was evident between the two study groups, with a mean 8.7% $\pm$ 2.1 in diabetic group, compared with 5.3 $\pm$ 0.44 in non-diabetic group (Figure 1). The mean duration of disease in diabetic group was 5.7 $\pm$ 3 year. Twenty patients in the diabetic group, representing 19% have been previously diagnosed with diabetic complications, and 18 patients representing 17.1% was controlled, while 87 patients representing 82.9% was uncontrolled (Table 2).

Characteristics	Group 1 N= 105	Group 2 N= 105	Test	P
Age (years)				
Mean ± SD	52.1 ± 12.2	53.6 ± 11.8	t =0.9	0.37
Gender: N (%)				
Male	51 (48.6)	52 (49.5)	χ^2 = 0.19	0.89
Female	54 (51.4)	53 (50.5)		
BMI (kg/m^2)				
Mean ± SD	29.5 ± 4.8	30.9 ± 4.7	t = 0.66	0.51
Smoking: N (%)				
Yes	14 (13.3)	12 (11.4)	χ^2 = 0.18	0.68
Education level: N (%)				
Illiterate	15 (14.3)	16 (15.2)	χ^2 = 2.1	0.71
Primary	16 (15.2)	20 (19)		
Secondary	40 (38.1)	44 (41.9)		
University	29 (27.6)	22 (21)		
Post graduate	5 (4.8)	3 (2.9)		

Marital status: N (%)				
Married	66 (62.9)	73 (69.5)	$\chi^2 = 1.7$	0.64
Single	4 (3.8)	2 (1.9)		
Divorced	21 (20)	20 (19)		
Widowed	14 (13.3)	10 (9.5)		
Parental consanguinity: N (%)				
Yes	38 (36.2)	43 (41)	$\chi^2 = 0.5$	0.48
Employment: N (%)				
Employed	44 (41.9)	42 (40)	$\chi^2 = 3.9$	0.27
Unemployed	25 (23.8)	34 (32.4)		
Retired	19 (18.1)	20 (19)		
Housewife	17 (16.2)	9 (8.6)		
Residence: N (%)				
Urban	73 (69.5)	78 (74.3)	$\chi^2 = 0.59$	0.44
Rural	32 (30.5)	27 (25.7)		

Table 1: Sociodemographic characteristics of the study groups.

Group 1: Diabetic group, group 2: non-diabetic group, χ^2: Chi-square test, t: student-t test.

Characteristics	Diabetic group N= 105	Non-diabetic group N= 105	Test	P
Diabetes complications: N (%)s				
Neuropathy	6 (5.7)	--	--	--
Retinopathy	8 (7.6)	--		
Nephropathy	4 (3.8)	--		
Diabetic foot	2 (1.9)	--		
Disease duration (years)				
Mean ± SD	5.7 ± 3	--	--	--
HbA1c (%)				
Mean ± SD	8.7 ± 2.1	5.3 ± 0.44	U =3155	<0.001*
Median (IQR)	8.8 (7.4-10)	5.4 (5-5.6)		
Mode of treatment: N (%)				
Oral antidiabetics	82 (78.1)	--	--	--
Insulin	23 (21.9)	--		
DM control: N (%)				
Controlled	18 (17.1)	--	--	--
Uncontrolled	87 (82.9)	--		

Table 2: Comparison of type 2 diabetes mellitus related data in the study groups.

U: Mann-Whitney, *: Statistically significant at $p \leq 0.05$.

Figure 1: HbA1c (%) in the study groups.

Comparing the sociodemographic characteristics between controlled and uncontrolled patients in the diabetic group showed no statistically significant differences in all variables compared including, educational level, and employment status. The mean age was 51.7 years in controlled diabetic patients versus 52.2 years in uncontrolled diabetic patients, BMI (mean ± SD) was 28.7 ± 4.6 in controlled patients, versus 29.7 ± 4.8 in uncontrolled patients (Table 3).

Characteristics	Controlled DM (HbA1c% <6.5) N = 18	Uncontrolled DM (HbA1c% >6.5) N = 87	Test	P
Age (years)				
Mean ± SD	51.7 ± 15.5	52.2 ± 11.5	t =0.16	0.88
Gender: N (%)				
Male	12 (66.7)	39 (44.8)	$\chi^2 = 2.85$	0.09
Female	6 (33.3)	48 (55.2)		
BMI (kg/m^2)				
Mean ± SD	28.7 ± 4.6	29.7 ± 4.8	t = 0.81	0.42
Smoking: N (%)				
Yes	4 (22.2)	10 (11.5)	$\chi^2 = 1.49$	0.22
Education level: N (%)				
Illiterate	1 (5.6)	14 (16.1)	$\chi^2 = 4.4$	0.35
Primary	5 (27.8)	11 (12.6)		
Secondary	7 (38.9)	33 (37.9)		
University	5 (27.8)	24 (27.6)		
Post graduate	0 (0)	5 (5.7)		
Marital status: N (%)				

Married	13 (72.2)	53 (60.9)	$\chi^2 = 6.1$	0.12
Single	1 (5.6)	3 (3.4)		
Divorced	0 (0)	21 (24.1)		
Widowed	4 (22.2)	10 (11.5)		
Parental consanguinity: N (%)				
Yes	5 (27.8)	33 (37.9)	$\chi^2 = 0.67$	0.42
Employment: N (%)				
Employed	7 (38.9)	37 (42.5)	$\chi^2 = 2.6$	0.46
Unemployed	6 (33.3)	19 (21.8)		
Retired	4 (22.2)	15 (17.2)		
Housewife	1 (5.6)	16 (18.4)		
Residence: N (%)				
Urban	12 (66.7)	61 (70.1)	$\chi^2 = 0.08$	0.77
Rural	6 (33.3)	26 (29.5)		

Table 3: Comparison of sociodemographic characteristics between controlled and uncontrolled diabetics patients.

χ^2: Chi-square test, t: student-t test.

Assessment of depression prevalence in the study groups, showed a high statistically significant difference between the two study groups, with 55 subjects representing 52.4% in the diabetic group, compared with 11 subjects, representing 10.5% in the non-diabetic group. A High statistically significant difference in Beck 'depression inventory Score (BDI-II) was shown between the two study groups, with mean score of 14.2 ± 7.6 in the diabetic group, compared with 9.8 ± 3.3 in the non-diabetic group. The grades of severity of depression between the two groups showed also a highly statistically significant difference with 33.3%, 15.2%, and 3.8% respectively for mild, moderate, and severe depression in the diabetic groups, compared with 8.6%, 1.9%, and 0% respectively for mild, moderate, and severe depression in the non-diabetic groups (Table 4). Moderate and severe depression constituted 19% in the diabetic group, compared with 1.9% in the non-diabetic groups (table 4, Figure 2).

The comparison between patients with controlled and uncontrolled glycemia in the diabetic group regarding clinical data, showed no statistically significant difference between the groups including occurrence of diabetic complications, means of disease duration that was 5.2± 2.7 years in the controlled patients versus

Characteristics	**Diabetic group N = 105**	**Non-diabetic group N = 105**	**Test**	**P**
BDI-II score				
Mean ± SD	14.2 ± 7.6	9.8 ± 3.3	U = 3153	<0.001*
Median (IQR)	13.8 (9.6-17)	9.5 (7.6-11.3)		
Depression: N (%)				
Yes	55 (52.4)	11 (10.5)	$\chi^2 = 42.8$	<0.001*
No	50 (47.6)	94 (89.5)		
Depression grades: N (%)				
No/Minimal	50 (47.6)	94 (89.5)	$\chi^2 = 43.7$	<0.001*
Mild	35 (33.3)	9 (8.6)		
Moderate	16 (15.2)	2 (1.9)		
Severe	4 (3.8)	0 (0)		

Table 4: Assessment of depression in the study groups.

χ^2Chi- U: χ^2: Chi-square test Mann-Whitney, *: Statistically significant at p ≤ 0.05.

Figure 2: BDI-II scores in the study groups.

5.7 ± 3.1 in the uncontrolled patients and mode of treatment, where, 77.8% on oral antidiabetics and 22.2% on insulin therapy in the controlled patients versus 78.3% on oral antidiabetics and 21.8% on insulin therapy in the uncontrolled patients, while HbA1c% levels were highly statistically significantly different between the two groups with a mean (SD) 5.6 ± 1.1, representing 17% in the controlled patients, compared with a mean (SD) of 9.4 ± 1.6, representing 83% in the uncontrolled patients (Table 5, Figure

3). Based on BDI-II score, depression was diagnosed in 22.2% in the controlled diabetic patients, compared with 58.6% in the uncontrolled patients, that was statistically significant (P < 0.022), with the mean score of BDI-II, 11.2 ± 5.7 in the controlled patients, compared with a score of 14.8 ± 7 in the uncontrolled patients, that was statistically significant difference (P < 0.033). The percentages of severity grades of depression in the controlled, compared with uncontrolled group was alike highly statistically significantly different with percentages 16.8%, 5.6%, and 0%, respectively for mild, moderate, and severe depression in the controlled patient, compared with percentages 36.8%, 17.2%, and 4.6%, respectively for mild, moderate, and severe depression in the uncontrolled group (Table 5, Figure 4).

Characteristics	Controlled DM N = 18	Uncontrolled DM N = 87	Test	P
Diabetes complications: N (%)				
Neuropathy	1 (5.6)	5 (5.7)	χ^2 = 0.001	0.98
Retinopathy	2 (11.1)	6 (6.9)	χ^2 = 0.38	0.54
Nephropathy	2 (11.1)	2 (2.3)	χ^2 = 3.2	0.08
Diabetic foot	0 (0)	2 (2.3)	χ^2 = 0.42	0.52
Disease duration (years)				
Mean ± SD	5.2 ± 2.7	5.7 ± 3.1	--	--
HbA1c (%)				
Mean ± SD	5.6 ± 1.1	9.4 ± 1.6	U =145	<0.001*
Median (IQR)	6 (5.6-6.4)	9.3 (8.1-10.3)		
Mode of treatment: N (%)				
Oral antidiabetics	14 (77.8)	68 (78.2)	χ^2 = 0.21	0.9
Insulin	4 (22.2)	19 (21.8)		
BDI-II score (%)				
Mean ± SD	11.2 ± 5.7	14.8 ± 7	U = 532.5	0.033*
Median (IQR)	11.3 (6-14)	14 (10.2-17.7)		
Depression: N (%)				
Yes	5 (27.8)	50 (57.5)	χ^2 = 5.27	0.022*
No	13 (72.2)	37 (42.5)		
Depression grades: N (%)				
No/Minimal	14 (77.8)	36 (41.4)	χ^2 = 43.7	<0.001*
Mild	3 (16.8)	32 (36.8)		
Moderate	1 (5.6)	15 (17.2)		
Severe	0 (0)	4 (4.6)		

Table 5: Comparison between patients with controlled and uncontrolled DM regarding clinical data.

χ^2: Chi-square test, U: Mann-Whitney, *: Statistically significant at p ≤ 0.05.

Figure 3: HbA1c (%) in the diabetic group according to the DM control.

Figure 4: BDI-II score in the diabetic group according to the DM control.

The correlation between BDI-II score and data of the study participants showed a moderate correlation with HbA1c% with r coefficient 0.37 that was highly statistically significant (P < 0.001) (Table 6). A linear correlation manner was shown between HbA1c%, and BDI-II score in all of the study participants (Figure 5).

Patients parameters	BDI-II score	
	r	p
Age (years)	-0.06	0.37
BMI (kg/m^2)	-0.03	0.7
Duration of disease (years)	0.1	0.3
HbA1c (%)	0.37	<0.001*

Table 6: Correlation between BDI-II score and the study participants' data.

r: Pearson coefficient, *: Statistically significant at p ≤ 0.05.

Figure 5: Correlation between HbA1c (%) and BDI-II in the study participants.

The results of binary regression analysis model for variables that predict depression in all of the study participants, showed among several independent factors selected that, smoking, and diabetic complications were statistically significant (P = 0.016, and 0.013, respectively), and HbA1c%, and DM control was highly statistically significant (P < 0.001) (Table 7).

	B	SE	P-value
Age (years)	-0.009	0.12	0.49
Gender	0.12	0.8	0.63
BMI	-0.05	0.03	0.1
Smoking	1.9	0.79	0.016*
Education level	0.04	0.49	0.93
Marital status	-0.36	0.56	0.58
Parental consanguinity	-0.14	0.31	0.66
Employment	0.2	0.36	0.58
Residence	0.16	0.33	0.63
Diabetes complications	1.02	0.4	0.013*
Disease duration	0.04	0.07	0.5
HbA1c	0.44	0.08	<0.001*
Mode of treatment	0.013	0.47	0.97
DM control	2.20	0.35	<0.001*

Table 7: Binary logistic regression analysis for the prediction of presence of depression.

B: Regression coefficient; SE: standard error; * Significant.

Discussion

In our study, we found high prevalence of depressive disorders including all grades of severity in 52.4% of the diabetic group while

only 10.5 %of the non-diabetic patients had depression. It was mild in 33.3% moderate and severe in 19% of the diabetic group, compared with moderate and severe in 1.9% of the non-diabetic group. Comparing the findings of our study with others, in an Egyptian study carried out in 2012 to estimates the prevalence of depression among a sample size of 303 type 2 diabetics attending family health centers in Alexandria using Hamilton Depression Rating Scale (HAM-D), moderate to severe depression was present in 39.1% and 40.7% in males and females respectively, compared with 19% in the present study [13]. In a cross-sectional Iranian study 2019 that included 514 type 2 diabetics patients, and used Beck Depression Inventory II scale to assess depression, depression was found in 46.3% of the study population, and there was no significant association between glycemic control expressed as HbA1c level and depression (OR: 1.11 95% CI: 0.87-1.57), by contrast , sex (OR: 2.03, 95% CI: 1.03-3.99), residence (OR: 1.92, 95% CI:1.28-2.91), and sexual complications (OR: 5.54, 95% CI: 1.07-27.87) have a significant statistical association with depression [14]. In a Tunisian study 2017 that recruited 100 type 2 diabetic patients to study the prevalence of depression using validated Arabic version of Hospital Anxiety and Depression Scale (HAD), the prevalence of depression was 31%, and poor glycemic control, presence of macro-angiopathy, irregular follow up, and poor treatment adherence were more common in depressed compared with no depressed patients [15].

In a descriptive study 2018 carried out in Northern Greece to investigate the role of self- efficacy, depression and glycemic control in a convenience sample of 170 adults with type 2 diabetes mellitus who completed the General Health Questionnaire-28 (GHQ-28), and the Diabetes Empowerment Scale- short form (DES) questionnaire, the overall rates of diabetic patients showing psychological distress was 50.6%, adults with low to moderate income compared with high economical status, and adults who graduated elementary education compared with those with a higher educational level, experienced higher levels of depression and anxiety. There was negative correlation between Body mass index (BMI), and self-efficacy scale, and negative correlation between depression and self-efficacy [16].

Comparing our findings with other studies done in other Arabic countries showed variable results, in a Bahraini study 2009 surveyed 264 type 2 diabetic patients using Beck Depression Inventory scale (BDI), 33.3% of the study participants showed score of 16 or more on BDI, with no significant association was found between BDI score and metabolic control, duration of diabetes, and presence of diabetic complications [17]. In a Saudi study 2019 carried on 450 adults with T2DM to study the prevalence and predictors of depression, anxiety, and stress, using a validated depression, Anxiety, and Stress Scale (DASS-21), the prevalence of depression, anxiety, and stress was 33.8%, 38.3%, and 25.5% respectively, major predictors of psychological distress were age, sex, the presence of comorbidities, duration since t2DM diagnosis, and serum level of A1c [18]. In another Saudi observational study carried on 267 adults patients with type 2 diabetes seen at King Abdulla Medical City in Mecca, using the Arabic version of the Patients Health Questionnaire -9 (PHQ-9) to asses prevalence of depression, 73% suffered from different degrees of depression;36%, 19.9%, 8.6%, 5.2%, and 3.4% of the participants were suffering from minimal, mild, moderate, moderately severe, and severe depression, respectively, and only neuropathy was a significant risk factors of depression (odds ratio = 2.87, 95% CI 1.18-6.97. P = 0.02) [19].

The longitudinal, and reciprocal relation between depression and glycemic control has been investigated by some studies. In a prospective study carried out in Taiwan 2019 on a nationally representative sample of 398 patients with type 2 diabetes, followed for 3 years, and applied statistical method (cross -lagged structural equation model) to examine the reciprocal relationship between depressive symptoms and glycemic control, and the moderation effects of perceived family support, a stronger association was noted for higher depressive symptoms scores predicting worse glycemic control (B = 0.22, critical ratio 3.0), as opposed to worse glycemic control predicting depressive symptoms scores, in patients wit low family and friend support , more depressive symptoms at baseline were associated with subsequent worse glycemic levels (B = 0.36, critical ratio 4.03) [20]. In a systematic review and meta-analysis study included 37 eligible studies, six investigated the longitudinal association between self-reported depressive symptoms and HbA1c, and five the reverse longitudinal association, with a combined sample size of 48793 and mean follow up of 2 years, The pooled effect estimates were reported as partial correlation coefficients (rp) or odds ratio (OR), the study concluded that higher levels of baseline depressive symptoms were

associated with subsequent higher levels of HbA1c (partial r = 0.07 (95% CI 0.03-0.12), whereas higher baseline HbA1c values were also associated with 18% increased risk of (probable) depression (OR = 1.18 (95% CI 1.12- 1.25) [21].

Depression itself has been associated with high levels of HbA1c in individuals with T2DM, the association between diabetes and depression suggests the usefulness of determining HbA1c as a biological marker of depressive symptoms as shown in a Meta-analysis of 34 studies with 68,398 participants to determine HbA1c levels in individual with T2DM with vs. without depression. Investigators used rigorous methodology to ensure the quality assessment using the Newcastle-Ottawa Assessment Scale (NOS), and the cut-off point of the studies included was determined with scores of six or higher on collected data up to January 2020 [22]. The Meta-analysis used the ''d'' statistic and 95% confidence interval (95% CI) to estimates the mean difference in HbA1c levels, and the pooled weighted mean difference with 95% CI was calculated thereafter, the heterogeneity among studies was evaluated using the Cochran Q test and inconsistency index (I^2), that considered $p < 0.10$ as significant and indicative of heterogeneity, and the values of $I^2 < 25$ were considered as absence of heterogeneity. The results showed that individuals with T2DM with depression showed significantly increased levels of HbA1c in comparison to individuals with T2DM without depression (d= 0.18, 95% CI: 0.12-0.29, p(Z) < 0.001; $I^2 = 85.00$) , HbA1c levels also remained elevated in individuals with T2DM with depression who were taking talking hypoglycemic drugs, in individuals with less than 10 years of evolution, and in individuals with complications of the disease. The study postulates that there is a diabetes-HbA1c-depression connection, linked to negative moods and a greater risk of diabetes complications in general. These findings may be more or less consistent with the findings of our study.

The prevalence of mental disorders in Egypt has been estimated in back dated national household survey in 2009 including 14,600 adults aged 18-64 years in 5 regions in Egypt, the overall prevalence was estimated at 16.93% of the studied population, the main problems were mood disorders, anxiety disorders, and multiple disorders in 6.43%, 4.75%, and 4.72%, respectively. The effectiveness of antidepressant acceptance, and adherence in type 2 diabetics have been investigated in a study carried in Egypt between 2013-15, and recruited 196 diabetics scored more than 20 on screening for Major Depression Inventory (MDI), of them, 86 (43.9%) accepted and were adherent to treatment with fluoxetine for 8 weeks, and decliners were matched as control via diabetologist visits, in comparison with control, there was reduction from baseline in MDI, fasting and glycosylated hemoglobin levels (p for all comparisons < 0.001) [24]. The effectiveness of non-pharmacological interventions, like cognitive behavioral therapy (CBT) on glycemic control and psychological outcomes in adults with type 1, and 2 diabetes mellitus was investigated in a systematic review and meta- analysis of 12 RCTs in 2017, CBT was shown effective in reducing short term and medium term glycemic control, although no significant effect was found for long term glycemic control, it was also effective in improving short term and medium term anxiety and depression, and long-term depression, while mixed results were found for diabetes related distress and quality of life, although the findings were inconclusive [25].

These findings emphasize the important role played BY Family physicians in dealing with the complexity of chronic illnesses encountered in very day practice and the importance of working in multidisciplinary teams.

The limitations of the study

are mainly related to the type of design adopted, as cross-sectional studies do not establish a cause-and-effect relationship, more controlled studies including prospective and clinical randomized trials are needed. Despite these limitations, the results contribute to the expansion of knowledge regarding the bidirectional relationship between DM and depressive symptoms and add to growing evidence regarding glycemic control and HbA1c level use as biomarker for depression screening in type 2 diabetics.

Conclusions

This study concluded that depressive disorders in all grades of severity were much common in type 2 diabetics compared with non-diabetics, and in uncontrolled diabetics compared with controlled patients. factors that were shown to predict depression in regression analysis model used were smoking, presence of diabetic complications, and the status of glycemic control, and the later was the strongest predictor of depressive disorders. A positive linear correlation was shown between the glycemic control level and BDI-II scale score. Family physicians have a crucial role in

caring for diabetic patients by the virtue of the holistic approach they utilize with patients and their families incorporating elements of life style counselling like weight control, smoking cessation and exercise advice, improving family support and self-efficacy to help control glycemic status and associated high rates of depressive disorders.

Ethical Approval and Consent to Participate

Approval for conducting the study was officially obtained from the Medical Research Ethics Review Board of Ministry of Health and Population (DOHP) authorities, an informed consent was obtained from all subjects/ and or their legal guardian(s) in case of illiterate participants in the study. All methods were carried out accordance with relevant guidelines and regulations.

Availability of Data and Materials

All Raw data generated or analyzed during this study are available on request from the corresponding author.

Consent to Publish

All authors of this study are consenting for publishing of this research and the participants as well were consenting for scientific publication of the research following appropriate explanation and assured informed consent.

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Conflict of Interest

No competing or conflicting interests in any form were involved in this research.

Author Contribution

Dr. Seham A. Ibrahim; reviewed the results of the study, shared in editing of discussion part, and the final conclusions of the study. Dr. Hassan A. Shora; wrote the protocol of this study, was responsible data collection and integrity for the statistical analysis. Dr Ashraf Eltantawy; done the subjects and methods section, gave his guidance, expertise for research in psychiatry. Dr. Ismail Dahshan; done the commentary on the results part of the study, did the literature review, and shared in editing the discussion part, and the final review and preparation for this research submission.

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