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THE ASSOCIATION BETWEEN DEPRESSIVE SYMPTOMS AND GLYCEMIC CONTROL IN TYPE 2 DIABETIC PATIENTS

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ABSTRACT

Diabetes mellitus is a significant risk factor for depression. However, there is significant controversy over if depression in patients with diabetes is associated with poor glycemic control. To find out the relationship between depressive symptoms and glycemic control in patients with type 2 diabetes mellitus…, a cross-sectional descriptive study was conducted among patients who attend PSMMC Alwazarat primary care health clinic with a laboratory and clinical evidence of diabetes mellitus. Two hundred and forty patients with type 2 diabetes were enrolled in this study. Zung Self-Rating Scale for Depression (ZSDS) was used to measure their depressive symptoms and HbA1c blood level was used to measure their glycemic control. Statistical analysis was applied to determine the relationship between the glycemic control and the depressive symptoms. Both patients with and without depression were similar in age. Statistical analysis revealed no significant relationship between ZSDS scores and HbA1c level. Depressive scores were significantly higher in diabetic patients with hypertension (P=0.008) and on insulin treatment (P=0.04). There was a significant positive relationship between ZSDS scores and disease duration ($P < 0.05$). The findings of this study showed that there was no significant association between the level of depressive symptoms and HbA1c in patients with type 2 diabetes.

INTRODUCTION

Diabetes mellitus is a significant risk factor for depression. Recent prevalence studies suggested that approximately 15% of all patients with diabetes suffer from clinical depression, and even a greater percentage (about 30%) suffer from some sort of psychiatric disturbances [1]. However, there is significant controversy over if depression in patients with diabetes is associated with poor glycemic control.

Some investigators have found moderate to strong associations between depressive symptoms and hemoglobin (HbA1c) [2-3], although others have found no relationship [4-5]. A study found that there is statistically significant association between depression and hyperglycemia in both type 1 and type 2 diabetes [6]. Some other cross-sectional studies have found a significant positive association between depressive symptoms and HbA1c in patients with Type 1 diabetes but not in type 2 diabetes [7-8]. Since there are few reports about the association between a well-standardized measure of depressive symptoms and an established index of glycemic control in Saudi Arabia, this study was conducted to examine the rate of current depressive symptoms in a sample of individuals with type 2 diabetes.

According to the American Diabetes Association (ADA) guidelines, patients with diabetes should maintain low levels of glycated hemoglobin (A1C), blood pressure and low-density lipoprotein [9]. However, only 10% of the patients meet all those three goals simultaneously [10]. As a consequence, the control of the disease is inadequate, leading to an increase of the morbidity and mortality [11].

Several factors may account for an unsatisfactory metabolic control of DM. Among them it is important to emphasize the relevance of the occurrence of a psychiatric comorbidity. The presence of depression in a patient with diabetes has been suggested as one of the possible causes of an inadequate metabolic control, especially for those patients who cannot achieve an adequate glycemic control despite intensive medical recommendations.

Several studies observed higher rates of depression in patients with diabetes and tried to demonstrate the association between the presence of depressive symptoms and an increased prevalence of clinical complications of the DM. Anderson et al. conducted a meta-analysis of 42 studies investigating the association between depression and diabetes [12]. The authors found that the presence of diabetes doubles the odds of having depression. This risk remained even after controlling for both types of diabetes or different diagnostic methods for depression across studies. O'Connor et al. followed a retrospective cohort of patients with diabetes to investigate the prevalence of depression [13]. The authors observed an increase prevalence of depression in patients with diabetes compared to a non-diabetic sex- and age-matched control group.

Furthermore, several authors found an association between depression and a poor metabolic control of T2DM. In a meta-analytic review of the literature, Lustman et al. investigated the association between depression and diabetes glycemic control [14]. The authors observed that depression was significantly associated with hyperglycemia in patients with type 1 and type 2 diabetes ($p < 0.0001$). In the same line, de Groot et al., conducted a meta-analysis examining the association between depression and diabetes outcomes [15]. Twenty-seven studies were included and the authors found a significant association between depression and clinical complications of diabetes ($p < 0.00001$).

The purpose of this study is to investigate the association between depression and the clinical control of diabetic type 2 patients with respect to HbA1c levels in a sample of Saudi patients. This is important for our population and the finding can be used as a basic of treating depression and furthermore controlling diabetes.

Subjects and methods

Patients with Type 2 diabetes presenting for routine care at PSMMC Alwazarat primary care health clinic (Chronic Disease Clinic "CDC") were asked to participate in this study. All patients gave verbal consent. Data was collected using a verified questionnaire. Only non-complicated type 2 diabetes mellitus patients without psychiatric disease or psychological factors that could affect patients' depressive status and who might have hyperlipidemia and hypertension were included in this study.

The following patients were excluded from this study:

- Current or prior history of psychiatric diagnosis.
- History of thyroid disease, malignancy, liver insufficiency, renal failure, coronary artery disease, cerebro-vascular disease, dementia, pregnancy, recent infection or illness that could have affected glucose control.

Power of the study is 80. Confidence level is 95%. Prevalence of depression in diabetic patients is 30%. Statistical significance was declared for $P < 0.05$. The final sample contained 240 patients with type 2 diabetes. Demographic characteristics of the patients are presented in Table 1. Glycemic control was assessed by HbA1c, a generally accepted index of the average blood glucose level over the last 12 to 16 weeks.

HbA1c was measured by use of ion-exchange high-performance liquid chromatography, a methodology that measures only the A1c fraction of glycohemoglobin.

HbA1c <7 considered controlled and HbA1c ≥7 considered uncontrolled according to the ADA guideline in 2011 [16].

Demographic information, drug and medical history as well as results of the routine measurement of HbA1c performed during the clinical visit, were obtained from the medical record after the visiting of the patients.

Depression was screened by Zung Self-Rating Depression Scale (SDS) by a well-trained research interviewer, this tool was generally accepted and used for its ability to cover affective, psychological and somatic symptoms associated with depression and for its sensitivity for correctly identifying when depression is present [17]. Scores above 50 have been assigned as depression. All values were presented as a mean ± standard deviation (SD) and differences were compared using Chi-square Test and T-test.

The study was approved by both Ethics and Research Scientific Committee at the Research Deputy of Prince Sultan military medical city in Riyadh.

RESULTS

Two hundred and forty patients from 278 participants provided verbal consent and completed the study survey. Patients' socio-demographic characteristics by Zung SDS are presented in Table 1. Only 84 patients (35%) met the Zung Self-Rating Scale criteria for a diagnosis of depressive symptoms (SDS score ≥ 50). The glucose control index, diabetes duration, therapy, hyperlipidemia and the hypertension are presented in Table 2. HbA1c was "< 7%" (controlled diabetes) in 56 patients out of 240 (23.4%), 12 of the 56 were with depressive symptoms (21.43%) compared to 184 patients out of 240 (76.7%) with HbA1c "≥ 7%" (uncontrolled diabetes), 72 of the 184 were with depressive symptoms (39.13%).

Of the total 84 patients with depressive symptoms there was 42 patients with minimal to mild depression

(50%), 29 patients with moderate to marked depression (34.5%) and 13 patients with severe to extreme depression (15.5%) (Table 1, Figure 1).

Of the total 84 patients with depressive symptoms we found 12 patients with controlled diabetes (14.3%) compared to 72 patients with uncontrolled diabetes (85.7%) (Table 2, Figure 2).

The relationship between the depression screening result and other variables are presented in Table 3.

In this Type 2 diabetic group depressive Symptoms were significantly associated with marital status (P=0.048), longer duration of diabetes mellitus (P=0.043), using insulin injection (P=0.036), uncontrolled hypertension (P=0.0079), hyperlipidemia (P=0.004), and lower education level (P= 0.0001) but it was not significantly associated with the age of patient, Depression was more prevalent among women with diabetes than men (P = 0.0001).

To explore the relation between Zung SDS Criteria and glucose control, we compared patients with high HbA1c "≥7%" (Uncontrolled diabetes) and low HbA1c "<7%" (Controlled diabetes) in Table 4. The high HbA1c group (Total n=184) had a mean HbA1c of 8.7%±1.2% compared with 6.04%±0.62% for the low group (Total n=56). Of 84 patients with Depressive Symptoms, 12 (14.3%) had low HbA1c and 72 (85.7%) had high HbA1c. There was no significant relation between Depressive symptoms and glucose control index.

Table 1. Socio-demographic characteristics by Depressive symptoms Grouping by Zung Self-Rating Scale (SDS)

Patients	SDS Index			
	Below 50[1] n=156 (%)	**50 – 59** [2] n=42 (%)	**60 – 69**[3] n=29 (%)	**70 and Over**[4] n=13 (%)
Age (Years)				
25 - 35	22 (14.1)	8 (19.1)	1 (3.5)	0 (0)
35- 45	41 (26.3)	3 (7.1)	17 (58.6)	0 (0)
45 - 55	38 (24.4)	11 (26.2)	1 (3.5)	1 (7.7)
55 - 65	51 (32.7)	15 (35.7)	9 (31.03)	10 (76.9)
65 - 75	4 (2.6)	5 (11.9)	1 (3.5)	2 (15.4)
Sex				
Male	99 (63.5)	10 (23.8)	7 (24.1)	4 (30.8)
Female	57 (36.5)	32 (76.2)	22 (75.9)	9 (69.2)
Marital Status				
Single	15 (9.6)	7 (16.7)	2 (6.9)	0 (0)
Married	123 (78.9)	28 (66.7)	17 (58.6)	9 (69.2)
Divorced	5 (3.2)	2 (4.8)	5 (17.2)	0 (0)
Widow	13 (8.3)	5 (11.9)	5 (17.2)	4 (30.8)
Education				
Read & Write	17 (10.9)	15 (35.7)	5 (17.2)	6 (46.2)
Elementary School	21 (13.5)	9 (21.4)	6 (20.7)	4 (30.8)
Middle School	15 (9.6)	6 (14.3)	7 (24.1)	2 (15.4)
High School	59 (37.8)	8 (19.1)	5 (17.2)	1 (7.7)
Graduate or higher	44 (28.2)	4 (9.5)	6 (20.7)	0 (0)
Occupation				
Non-Employee	61 (39.1)	25 (59.5)	8 (27.6)	3 (23.1)
Employee	55 (35.3)	9 (21.4)	15 (51.7)	2 (15.4)
Retired	40 (25.6)	8 (19.1)	6 (20.7)	8 (61.5)
Income (SR)				
< 5000	87 (55.8)	31 (73.8)	12 (41.4)	5 (38.5)
5000 – 10000	32 (20.5)	4 (9.5)	2 (6.9)	4 (30.8)
10000 – 15000	8 (5.1)	1 (2.4)	4 (13.8)	4 (30.8)
15000 – 20000	15 (9.6)	4 (9.5)	8 (27.6)	0 (0)
20000 - 25000	1 (0.6)	2 (4.8)	2 (6.9)	0 (0)
> 25000	13 (8.3)	0 (0)	1 (3.5)	0 (0)

[1] Within normal range no psychopathology.
[1] Presence of minimal to mild depression.
[1] Presence of moderate to marked depression.
[1] Presence of severe to extreme depression.

Table 2. Glucose control and medical history characteristics by Zung Self-Rating Scale (SDS)

Patients	SDS Index			
	Below 50 n=156 (%)	**50 – 59** n=42 (%)	**60 – 69** n=29 (%)	**70 and Over** n=13 (%)
Glucose control index				
HbA1c < 7 (controlled)	48 (30.8)	5 (11.9)	5 (17.2)	2 (15.4)
HbA1c ≥ 7 (uncontrolled)	108 (69.2)	37 (88.1)	24 (82.8)	11 (84.6)
Diabetes Duration				
< 5 years	28 (18)	6 (14.3)	0 (0)	0 (0)
5 – 10 years	30 (19.2)	4 (9.5)	7 (24.1)	0 (0)
10 -15 years	35 (22.4)	10 (23.8)	10 (34.5)	2 (15.4)
> 15 years	63 (40.4)	22 (52.4)	12 (41.4)	11 (84.6)
Therapy [1]				
Diet	146 (93.6)	38 (90.5)	28 (96.6)	13 (44.8)
Exercise	123 (78.8)	30 (71.4)	20 (69)	10 (34.5)
OHA	156 (100)	42 (100)	29 (100)	13 (44.8)
Insulin Therapy	51 (32.7)	14 (33.3)	17 (58.6)	8 (27.6)
Hyperlipidemic	131 (84)	39 (16.7)	29 (100)	13 (23.1)
Hypertensive	133 (85.3)	39 (16.7)	29 (100)	13 (23.1)

[1] Therapy overlapping in the entire patient.

Table 3. The Association between Sociodemographic characteristics and depressive symptoms

Patients	Depressive Symptoms N=84(%)	No Depressive Symptoms N=156(%)	Statistic	P Value
Age (Years)			Unpaired T-test; t = 1.56	P=0.12
25 - 35	9 (10.7)	22 (14.1)		
35- 45	20 (23.8)	41 (26.3)		
45 - 55	15 (17.9)	38 (24.4)		
55 - 65	35 (41.7)	51 (32.7)		
65 - 75	5 (5.9)	4 (2.6)		
Sex			X^2 =32.3	P=0.000000013
Male	21 (25)	99 (63.5)		
Female	63 (75)	57 (36.5)		
Marital Status			X^2 =7.87	P=0.048
Single	9 (10.7)	15 (9.6)		
Married	54 (64.3)	123 (78.9)		
Divorced	7 (8.3)	5 (3.2)		
Widow	14 (16.7)	13 (8.3)		
Education			X^2 =32.45	P=0.0000015
Read & Write	26 (30.9)	17 (10.9)		
Elementary School	19 (22.6)	21 (13.5)		
Middle School	15 (17.9)	15 (9.6)		
High School	14 (16.7)	59 (37.8)		
Graduate or higher	10 (11.9)	44 (28.2)		
Occupation			X^2 =0.5	P=0.78
Non-Employee	36 (42.9)	61 (39.1)		
Employee	26 (30.9)	55 (35.3)		
Retired	22 (26.2)	40 (25.6)		
Income (SR)			X^2 =15.75	P=0.008
< 5000	48 (57.1)	87 (55.8)		
5000 – 10000	10 (11.9)	32 (20.5)		
10000 – 15000	9 (10.7)	8 (5.1)		

Patients	Depressive Symptoms N=84(%)	No Depressive Symptoms N=156(%)	Statistic	P Value
15000 – 20000	12 (14.3)	15 (9.6)		
20000 - 25000	4 (4.8)	1 (0.6)		
> 25000	1 (1.2)	13 (8.3)		

Table 4. Glucose control and Medical history characteristics by Depressive Symptoms grouping

Patient status	Depressive Symptoms N=84(%)	No Depressive Symptoms N=156(%)	Statistic	P Value
Glucose control Index			X^2 =3.07	P=0.08
HbA1c < 7 "Controlled"	12 (14.3)	48 (30.8)		
HbA1c ≥ 7 "Uncontrolled"	72 (85.7)	108 (69.2)		
Insulin therapy	39 (46.4)	51 (32.7)	X^2 =4.4	P=0.04
Diabetes duration			X^2 =8.14	P=0.04
< 5 years	6 (7.1)	28 (18)		
5 – 10 years	11 (13.1)	30 (19.2)		
10 -15 years	22 (26.2)	35 (22.4)		
> 15 years	45 (53.6)	63 (40.4)		
Hyperlipidemic	81 (96.4)	131 (84)	X^2 =8.22	P=0.004
Hypertensive	81 (96.4)	133 (85.3)	X^2 =7.06	P=0.008

Fig 1. The distribution of the Zung score in the total sample

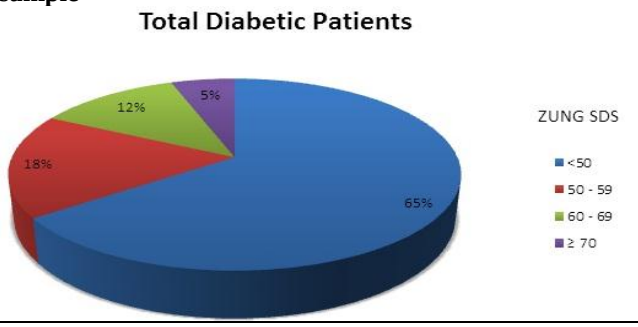
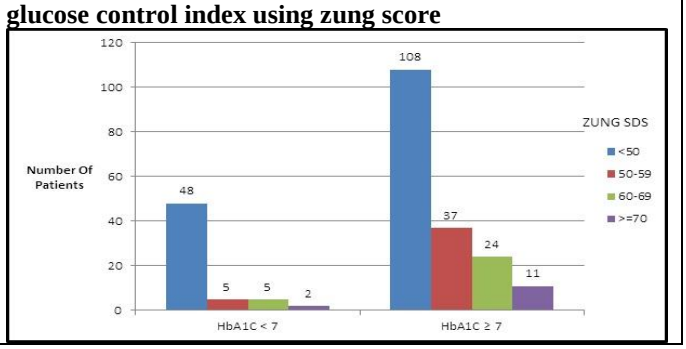


Fig 2. Shows the relation between the depression and glucose control index using zung score



DISCUSSION

The results of the present study show that depressive symptoms as measured by the Zung Self-Rating Depression Scale is significantly associated with duration of type 2 diabetes and the values of insulin injection, but there is no significant association between depressive symptoms and HbA1c. These results contradict the findings of some earlier studies and raise questions about the link between depressive mood and glycemic control in diabetes.

Although prior evidence for a link between depressive symptoms and metabolic control has been provided primarily by cross-sectional studies, several prospective studies have examined the effects of treatment-related improvement of depressive symptoms on diabetes control, but results were mixed. Some of these studies were complicated by the fact that patients were treated with pharmacologic agents that may have had direct effects on metabolic control [6,18].

A study of patients with type 2 diabetes reported a difference in effects of cognitive behavior therapy between treatment and control at 6-month follow-up that was due as much to deterioration in the control group as to improvements with treatment [19]. Thus, the evidence of a link between depression and glycemic control has been modest at best, and our current findings raise further doubts about this hypothesized relationship.

Although it was not the focus of the present study to test any possible mechanisms by which depression and glycemic control could be related, we observed that patients with longer duration of diabetes, especially those on insulin therapy had higher Zung score.

Diabetes mellitus could affect the mood through at least two mechanisms; either through biochemical changes due to hyperglycemia or through psychosocial problem of chronicity of disease [20].

It is well known that depression is more common in women than men. Our sample included a larger proportion of women (68.6%) consistent with the gender distribution for lifetime prevalence of major depression, which is almost twice as high in women as in men [21].

In conclusion, our findings indicate that there is no link between depressive mood and glycemic control,

and raises questions about the importance of depressive symptoms were negatively associated, for the management of glucose metabolism in treatment of diabetes. Of note, the presence of psychiatric comorbidity in diabetic patients should always be investigated and a carefully monitoring of the metabolic control might be important of those individuals who exhibit clinical depression. Nevertheless, it would be advantageous to have other cross-sectional studies to better understand the nature of those associations.

This study was limited by the use of self-reported questionnaire data, because patients may have overestimated the actual symptoms to provide a socially desirable response. Non-response to the patient questionnaire and missing HbA1c values are unlikely to have biased our results: non-responders and responders were similar in variables of interest at diagnosis. Finally, the study could be cross-sectional and any causal interpretation should be made with caution.

Based on our results and discussion, depression in people with diabetes has a negative impact on the quality of life as well as on the prognosis of diabetes. Therefore, a timely identification of patients with depression is justified since there are several intervention options ranging from non-pharmacological, educational and psychotherapeutic approaches to pharmacological treatments. There are also different procedures from the monitoring of well-being and the presence of diabetes-related distress if more formal screening for more severe mental disorders like clinical or major depression is not available.

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