Depression and Anxiety among Diabetic Patients and Associated Factors

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ABSTRACT:

Introduction:
Anxiety and depression considered as the risk factors for diabetes, as well as they are two of its complications. This study was conducted to explain the prevalence of depression and anxiety among T2DM and its associated factors.
Methods:
A cross-sectional study was conducted at the Al-Wafaa (Diabetes Center in Mosul). Patient Health Questionnaire (PHQ - 9) and Generalized Anxiety Disorders (GAD - 7) were used to evaluate all patients for anxiety and depression.
Results:
In this study 380 patients participated their mean age was 55.47 ± 8.35 ranging between 35 – 82 years and the mean BMI was 29.69 ± 5.04. More than half of these patients (54.7%) were men and (98.7%) of them were married. The mean HbA1c level was 8.68 ± 1.47 and the mean duration of diabetes was 10.18 years. The reported prevalence of depression and anxiety were 79.5% and 79.2% respectively.
Conclusion:
Anxiety and depression are common problems among diabetic patients, more than two third of the study population had varying degrees of anxiety and depression. Anxiety and depression in diabetic patients were significantly related to HbA1c, gender, educational level, employment, and monthly income.

Key words: Depression, Anxiety, Diabetes type 2, GAD-7, PHQ-9

القلق والاكتئاب لدي مرضى السكر والعوامل المرتبطة بهما

الملخص:

المقدمة: القلق والاكتئاب من عوامل الخطر لمرض السكري، كما أنهما أحد مضاعفاته. أجريت هذه الدراسة لبيان مدى انتشار الاكتئاب والقلق بين مرضى السكر من النوع الثاني والعوامل المرتبطة بهما
طرائق العمل: أجريت دراسة مقطعية في مركز الوفاء (مركز السكري في الموصل). تم استخدام استبيان صحة المريض (PHQ - 9) واضطرابات القلق المعمم (GAD - 7) لتقييم جميع المرضى من حيث القلق والاكتئاب.
النتائج: بالنسبة للمرضى البالغ عددهم 380 مريضًا، كان متوسط العمر 55.47 ± 8.35 بأعمار تتراوح بين 35 - 82 عامًا وكان متوسط مؤشر كتلة الجسم 29.69 ± 5.04. أكثر من نصف هؤلاء المرضى كانوا رجالًا بنسبة 54.7٪ وكان جميعهم تقريبًا متزوجين (98.7٪). كان متوسط مستوى سكر الدم التراكمي 8.68 ± 1.47 ومدة مرض السكري 10.18 سنة. كان معدل انتشار الاكتئاب والقلق 79.5% و79.2% على التوالي.

الاستنتاج: القلق والاكتئاب من المشاكل الشائعة بين مرضى السكري، وكان أكثر من ثلثي مجتمع الدراسة بدرجات متفاوتة من القلق والاكتئاب. كان القلق والاكتئاب لدى مرضى السكري مرتبطين بشكل كبير بـ مستوى سكر الدم التراكمي والجنس والمستوى التعليمي والتوظيف والدخل الشهري.

الكلمات المفتاحية: الاكتآب، القلق، مرض السكر النوع الثاني

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic condition characterized by an abnormal elevation of blood glucose levels due to disturbed metabolism of carbohydrates, protein, and lipids caused by absolute or relative insulin deficiency. The worldwide burden of diabetes is rising. In 2019 diabetes is anticipated to affect 9.3% (463 million individuals) of the worldwide population, growing to 10.2% (578 million individuals) in 2030 and 9% (700 million individuals) by way of 2045 (1).

American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders (DSM - 5) define depression as a mood disorder with numerous symptoms that affect the functionality of patients. While anxiety can be described as “an uncomfortable feeling of vague fear or apprehension accompanied by characteristic physical sensations" (2).

Anxiety and depression are the risk factors for diabetes, as well as it is one of its complications that are not usually diagnosed, which leads to incompliance, and low quality of life, which predispose to complications and increased risk of death, as well as elevated cost of health care. The development of diabetes in a patient with depression worse the condition and increased the risk of complications. Some factors that lead to diabetes are also associated with depression, for example environmental, socioeconomic state, poor sleep, lifestyle, and diet (3). In diabetic patients, the risk of depression doubles when compared to healthy people, and the incidence of anxiety is up to 40% in diabetics (4).

Environmental factors act to disrupt the homeostasis of the body's stress system (5). The body overcome and adapted the acute stress responses. But over time with chronic activation, the response becomes exaggerated and harmful. It results in activation of the hypothalamus-pituitary-adrenal axis (HPA axis), central nervous system (CNS), and stimulation of inflammatory cytokines production (6). The HPA axis responds by increasing production of cortisol from the adrenal cortex. CNS activation results in increased production of nor adrenalin and adrenalin from the adrenal medulla (7). These stress hormones oppose the anabolic effect of insulin and initiate insulin resistance and DM (8). Pro-inflammatory cytokines production like TNF - α, Il - 6, and interferon - γ are also stimulated by stress. these cytokines act on the hypothalamus and pituitary gland to produce a further amount of cortisol (9). TNFα acts directly on insulin receptors by inhibiting phosphorylation of the insulin receptor subunit and increasing insulin resistance (10). This study was conducted to explain the prevalence of depression and anxiety among T2DM and their associated factors.

MATERIALS AND METHODS:

Study design and setting: This study is cross-sectional study used convenient sampling methods in the Al-Wafaa Center (Diabetes Center in Mosul). The study was conducted from December 2021 to April 2022. This study was approved by the Ethical Committee in the Nineveh Directorate of Health, and also by the Ethical Committee of the Clinical Pharmacy Department at the College of Pharmacy, University of Mosul. All patients signed a consent form and agreed to participate in the study. The HbA1c level, FBS or RBS were obtained from the patient's record. The anxiety and depression were assessed using a validated questionnaire.

Participants: All participats of both gender, were diagnosed with type 2 diabetes regardless of duration or treatment of diabetes. Patients on sleeping pills, patients with psychiatric disorders, pregnant women, and night shift workers were all excluded from the study.

Research instruments: The Arabic version of validated questionnaires was used for data collection in this study. It consists of three parts demographic information, anxiety, and depression as follows:

1 - Sociodemographic information: include information about age, sex, height, weight, BMI, marital state, education level, monthly income, smoking and alcohol intake, diabetes information like medication used, and disease duration. As well as, information regarding current comorbid disease.

2-Patient Health Questionnaire (PHQ-9) is a validated questionnaire shorter than other scales and in addition to clinicians-administration and self-administration. It is also can be administered by telephone for depression screening, determination of severity (11), and monitoring treatment outcome (12). It consists of 9 questions, the score of each one ranged from 0 - 3 (0 - not at all / 1 - several days per week / 2 - more than half of the days / 3 - nearly every days). The total score ranged from 0 - 27 (13), and are divided as follow (0 - 4) no depression, (5 - 9) mild depression, (10 - 14) moderate depression, (15 - 20) moderately severe depression, (≥ 20) severe depression. Arabic version of PHQ-9 was used in this study (14)

3-Generalized Anxiety Disorders (GAD - 7) is a self-administration questionnaire that required 1-2 min. for administration and used as a screening tool for anxiety. It is composed of 7 questions the score of each one ranging from 0 - 3 (0 - not at all / 1 - several days per week / 2 - more than half of the days / 3 - nearly every day). The total score ranged from 0 – 21 (15)**,** and is divided as follow (0 - 4) no anxiety, (5 - 9) mild anxiety, (10 - 14) moderate anxiety, and (≥ 15) severe anxiety. Arabic version of GAD - 7 was used in this study (16).

Statistical analysis: All collected data were analyzed using SPSS version 19. Mean ± SD was used as a continuous variable while percentages and frequencies were used as a categorical variable. The relation between two continuous variables was tested using Spearman's correlation. Mann - Whitney U, and Kruskal Wallis H were used for continuous and categorical variables. A p-value < 0.05 was considered significant.

RESULTS:

The mean age for participants was 55.47 ± 8.35 ranging between 35 – 82 years and the mean BMI was 29.69 ± 5.04. More than half of these patients (54.7%) were men and (98.7%) of the study population were married. The mean HbA1c level was 8.68 ± 1.47 and the mean duration of diabetes was 10.18 years. About 60% of patients were on oral hypoglycemic agents and the rest used Insulin for diabetes. Among the included study population, 35.8% had one comorbid disease and 4.7% had two or more comorbid diseases.

Depression patterns among the study population

The PHQ - 9 was used to assess the patients with T2DM for depression symptoms and to determine the level of depression. Consequently, the study found that only 20.5% had no depression and the remaining patients 79.5% had varying degrees of depression (Table 1). The mean score for depression was 8.84 ± 4.72 and the median was 9. The Kolmogorov-Simonov test showed ($P < 0.05$) which indicated a non-normal distribution of the PHQ - 9 score.

Through the examination of factors associated with depression scores, a significant correlation was found between depression and FBS, RBS, and HbA1c levels ($P < 0.05$). No significant correlation was found with age, BMI, duration of diabetes, and duration of co-morbid disease (Table 2).

Non-parametric statistical tests (Mann - Whitney test for dichotomous data and Kruskal - Wallis test for polychromous data) were used to examine the differences in PHQ - 9 scores among socio-demographic groups of the T2D patients. Significant differences between participants according to gender, educational level, employment, and monthly income. No significant correlation was found between participants according to smoking and marital state. The differences in PHQ - 9 scores between patients on certain medications used for diabetes were examined and no significant differences were found. (Table 3).

Anxiety patterns among the study population.

The GAD – 7 was used to assess the patients with T2DM for anxiety symptoms and to determine the level of anxiety. Consequently, we found that only 20.8% had no anxiety and the remaining patients 79.2% had varying degrees of anxiety (Table 4). The mean score for anxiety was 9.55 ± 5.12 and the median was 10. The Kolmogorov-Smirnov test showed ($P < 0.05$) which indicated a non-normal distribution of the GAD - 7 score.

Non-parametric statistical tests (spearman's correlation) were used to examine the correlation between the GAD - 7 scores and the socio-demographic characteristics of the T2D patients. No significant correlation was found between anxiety and age, BMI, or duration of diabetes. But significant correlation was found between participants according to FBS, HbA1c, and duration of co-morbid disease ($P < 0.05$) (Table 2).

Non-parametric statistical tests (Mann - Whitney test for dichotomous data and Kruskal - Wallis test for polychromous data) were used to examine the differences in GAD - 7 scores among socio-demographic groups of T2D

patients. Significant differences were found between participants according to gender, educational level, employment, and monthly income, while no significant differences were found according to smoking and marital state. The differences between GAD - 7 scores according to the type of medications used for diabetes were examined and showed no significant differences (Table 3).

DISCUSSION:

This study explains the prevalence of depression and anxiety among T2DM. This problem is usually undiagnosed despite its importance as it is associated with psychological changes, loss of interest in usual activity, decrease in physical activity and life style changes which lead to decrease compliance with medications used for diabetes. Also, depression has a negative effect on glycemic control through its effect on insulin sensitivity. Asghar et al found improvement in insulin sensitivity in women after successful management of major depression (17). This study demonstrated that the prevalence of depression among the study population was 76.5%. This is much higher than the prevalence reported in Malaysia 12.3% (18), Malawi 18% (19), Ghana 31.3% (20), Eastern and Northern Sudan 35.6% (21)(22), Western Saudi Arabia 33.8% (23), Pakistan 49.2% (24), Jordan 39.6% (25), Ethiopia 44.7% (26), and Kerman Southern Iran 59% (27) . But is lower than the prevalence in Rwanda 83.8% (28) , Tanzania 87% (29). The difference in prevalence between these studies may be due to different methods, screening tools and cut off point used, different socio-demographic characteristics of the study population and environmental factors.

No significant correlation with age was reported that is similar to the results reported in Central and Eastern Sudan (30)(21), Nigeria (31), Ethiopia (26), and Tanzania (29). However significant association found with age in other study conducted in Southern Iran, significant association with age >54 years was reported in study (32) , also there is an association with age between 31-59 years (33). Another study in Ghana found that no significant correlation was found with BMI (20). In contrast, significant association was reported in studies conducted in Southern Iran (27), Guinea (34), Ethiopia (26). No significant correlation was found between depression and duration of diabetes this finding is similar to finding obtained from other studies (35),(36),(32). Although, another study report significant association with increase duration (37).

Significant correlation was found between depression and blood glucose level (FBS, RBS) and glycemic control. Significant correlation with FBS and HbA1c reported in Southern Iran (27), also significant correlation with FBS reported in Mexican population (37) and no significant correlation in other studies, such as in Nigeria (31), and Ethiopia (26). Some studies reported significant correlation with HbA1c (20), (34),(38),(39). While other studies reported no correlation with glycemic control (21), (39). The hippocampal volume is directly proportional to HbA1c level (40). The same neurodegenerative processes in depression was observed in patients with uncontrolled Glycemic level (41).

Significant difference between female and male was reported which is the same finding were reported by other studies in Ghana (20), Rwanda (28), Guinea (34). In contrast to some other studies which reported a non-significant correlation between male and female as in Malawi (19), Central, Eastern and Northern Sudan (30), 21,(22). Generally female had a higher risk for depression in when compared to male (42). This may be due to changes occur during menstrual cycle, pregnancy and postpartum which made female more susceptible to depression (43).

With regard to smoking no significant difference was found between patients and the same result was observed in another study (36). Although another study reported seven times increase risk of depression in smoking patients in Tanzania (29). No significant association was found with marital state although a higher prevalence in married patients was reported in one study (44) and higher prevalence in patients who are single was reported in another study (45).

Significant difference was found between patients among their educational levels. The same result is reported by other studies (36), (35),(46). Significant difference was found between patients according to employment. Other studies reported a higher prevalence among unemployed patients Eastern Sudan (21), Rwanda (28), and Guinea (34). Significant difference were found between depression and monthly income this finding was supported by other studies (44), (45).

No significant difference found between depression score according to medication used for diabetes which agree with another study (32) While a study in Tanzania found that patients on insulin were two times more likely to develop depression when compared with patients on other medications (29). This relation is confirmed in Korea (47), china (48), and a new available meta-analysis in 2018 (49).

With regard to anxiety disorder among diabetic patient, we also reported a high prevalence of anxiety (79.8%) among diabetic patients which comparable to prevalence of depression (79.5%). This prevalence also higher than prevalence reported in Western Saudi Arabia 38.3% (23), Pakistan 50.7% (24), Jordan 37.7% (25), Kerman Southern Iran 62% (27). No significant correlation between patients according to age was reported, a similar result also reported in other studies conducted in Bahrain (50)(51). But significant correlation was reported in another study (44). No significant correlation was found between anxiety score and BMI this finding also reported in other studies (27),(44). In contrast, significant association was reported in study conducted in Indian (52). No significant correlation was found with duration of diabetes which is also similar outcome attained from other studies (51),(52). In contrast to this result, other studies reported significant association with increase duration (49,(50).

Significant association was found between anxiety and fasting blood glucose level (FBS) same result reported in Southern Iran (27). No significant association was found with post prandial glucose level (RBS). Although significant association with RBS was observed in Indian (52). Significant association were found with glycemic control another study reported significant association with HbA1c

(25). Some studies reported no association with glycemic control (26, 43).

Significant difference between female and male was reported which is compatible with another study (25). In contrast some other studies reported no significant association with gender (44),(51). No significant difference found with regard to smoking which is compatible with another study (51), although another study reported a significant association with smoking (53). No significant association was found with marital state which is compatible with finding observed in another study (51). although a significant association was reported in other studies (44),(53).

Significant difference was observed with educational level which is compatible with finding reported by another study (46). Nevertheless opposite finding was reported in another study (25). Significant difference was found with regard to employment which is compatible with some another study that also reported the association with employment (50). Significant difference were found with monthly income this finding was supported by other study (51). No significant difference found between anxiety and medication used for diabetes and such result is also obtain in other study (51). While other study found that patient on insulin were more likely to develop anxiety compare with patients on other medications (44).

CONCLUSION:

Anxiety and depression are common problems among diabetic patients, more than two third of the study population had varying degrees of anxiety and depression. Anxiety and depression in diabetic patients were significantly related to HbA1c, gender, educational level, employment, and monthly income.

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Table 1: percent and frequency of depression among participant.

Variables	Frequency	Percent
No depression (0 - 4)	78	20.5
Mild depression (5 - 9)	133	35
Moderate depression (10 - 14)	120	31.6
Moderately severe depression (15 - 20)	48	12.6
severe depression (≥ 20)	1	0.3

Table 2: The correlation between demographic characteristics, depression, and anxiety.

Variables	N	Depression		Anxiety	
		Rho*	P value	Rho*	P value
Age	380	-0.028	0.589	-0.064	0.213
BMI	380	0.033	0.525	0.066	0.2
Diabetes duration	380	0.033	0.528	0.003	0.957
Duration of co-morbid disease	136	-0.008	0.928	0.172	**0.045**
FBS	318	0.149	**0.008**	0.16	**0.004**
HbA1c	380	0.275	**<0.05**	0.188	**<0.05**
RBS	64	0.396	**0.001**	0.009	0.964
Number of cigarette	71	0.035	0.771	0.046	0.701

* Spearman's correlation.

Table 3: The differences between demographic characteristics, depression, and anxiety.

Variables	Depression				Anxiety			
	Mean	**Median**	**S.D**	**P-value**	**Mean**	**Median**	**S.D**	**P-value**
Gender*								
Male	8.05	8	4.83	**<0.05**	8.68	8	4.92	**<0.05**
Female	9.8	10	4.41		10.59	12	5.19	
Smoking*								
Yes	8.61	8	5.05	0.533	9.27	9	4.95	0.495
No	8.89	9	4.64		9.61	10	5.17	
Marital state*								
Single	11.4	14	5.17	0.205	9.2	9	3.89	0.892
Married	8.81	9	4.71		9.55	10	5.14	
Educational level**								
Primary	9.56	10	4.76	**0.002**	10.33	11	4.99	**<0.05**
Secondary	7.92	8	4.68		8.95	8	5.29	
University	7.65	8	4.04		7.37	6	4.64	
Employment*								
Not employed	9.24	9	4.75	**0.005**	10.15	11	5.12	**<0.05**
Employed	7.72	8	4.48		7.89	8	4.79	
Monthly income**								
Less than 500000IQD	9.98	10	4.79	**<0.05**	10.79	12	4.95	**<0.05**
500000-1000000IQD	8.2	8	4.59		9.02	9	5.15	
More than1000000IQD	7.35	7	4.04		6.1	5	3.53	
Insulin*								
Yes	9.13	9	4.78	0.364	9.61	9.5	5.41	0.785
No	8.62	8	4.67		9.5	10	4.91	
Glibinclamide*								
Yes	8.35	8	4.88	0.161	9.23	9	4.97	0.407
No	9.09	9	4.62		9.71	10	5.20	
Metformin*								
Yes	8.63	8	4.77	0.215	9.46	9	5.17	0.654
No	9.24	9	4.60		9.71	10	5.05	
Glibrid*								
Yes	8.5	8	4.44	0.77	8.14	7	4.91	0.073
No	8.87	9	4.75		9.69	10	5.13	

Sitagliptin+ Metformin*								
Yes	10.12	10.5	4.69	0.055	10.36	10	4.74	0.305
No	8.68	9	4.70		9.45	9.5	5.17	

*Mann-Whitney U test, **Kruskal-Wallis test.

Table 4: Percent and frequency of poor and good sleep quality among participant.

Variables	**Frequency**	**Percent**
No Anxiety (0-4)	79	20.8
Mild Anxiety (5-9)	109	28.7
Moderate Anxiety (10-14)	125	32.9
Severe Anxiety ≥15	67	17.6

Patient Health Questionnaire-9 (PHQ-9)

Over the last 2 weeks, how often have you been bothered by the following problems?	Not at all	Several Days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

Generalized Anxiety Disorder Screener (GAD-7)

Over the last 2 weeks, how often have you been bothered by the following problems?	Not at all	Several Days	More than half the days	Nearly every day
1. Feeling nervous, anxious or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritated	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3