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Anxiety and Depression in Diabetic Patients According to the Hospital Anxiety and Depression Scale (HADS) Scoring

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Abstract

Objective: This study primarily aimed to evaluate the distribution of depression and anxiety in patients with type 1 and type 2 diabetes mellitus (DM) using the Hospital Anxiety and Depression Scale (HADS) and to compare the obtained results with specific demographic, metabolic, and anthropometric parameters.

Methods: A total of 193 participants were included—52 had type 1 DM (females, 35; males, 17), 86 had type 2 DM (females, 47; males, 39), and 55 were controls (females, 34; males, 21). Depression, anxiety, and anxiety+depression in these patients were evaluated according to the HADS. Data on fasting blood glucose, hemoglobin A1C (HbA1c), triglyceride, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), aspartate aminotransferase (AST), alanine aminotransferase (ALT), albumin, urea, and creatinine levels were evaluated for each patient.

Results: Depression and anxiety scores were significantly higher in patients with type 2 DM than in patients with type 1 DM. In addition, depression, anxiety, and anxiety +depression were higher in females in both types 1 and 2 DM. Moreover, there was a positive correlation between depression and anxiety scores and HbA1c.

Conclusion: Thus, performing psychiatric treatment in addition to diabetic treatment might increase patients' quality of life and social adaptation.

Keywords: Anxiety; Depression; Diabetes mellitus

Introduction

Diabetes mellitus (DM) is a complex disease; it leads to severe physical, psychological, and organic disorders and is frequently accompanied by anxiety and depression [1]. The prevalence of depression and anxiety in diabetic patients are 8.5%–32.5% and 30%, respectively, which are 2-fold higher than those in the general population [2,3].

As mentioned above, although DM leads to organic disorder, it has psychiatric and psychosocial aspects. Patients with DM experience different problems associated with physical, emotional, social, and sexual aspects. In addition, compared with the general population, diabetic patients are subject to 1.5-fold higher risk of depression-associated mortality [4]. Moreover, mental disorders accompanied by diabetes negatively impact chronic micro- and macro-complications. Hence, blood sugar regulation is impaired, thereby decreasing patients' quality of life and the increasing mortality rates [5].

In fact, the prevalence's of anxiety and depression were found to be higher in diabetic patients with poor blood glucose control than in those with good blood glucose control [6]. Diabetes affects sensory functions and leads to electroencephalographic (EEG) and neuropathologic changes in the central nervous system; changes in the sensory functions may be caused by recurrent hypoglycemic attacks [7].

Stress and anxiety are important factors even in patients with irregular blood sugar levels undergoing medical treatment. Epinephrine secretion, which reduces the effect of insulin, increases when an organism encounters anxiety. When one is angry, happy, or excessively emotional, free fatty acid, cortisol, and blood sugar levels are elevated and adrenaline,

noradrenaline, growth hormone, and cortisol levels in the body increase due to stress, leading to hyperglycemia [8]. Moreover, neurohormonal changes, such as hypercortisolism seen in depression, reportedly lead to insulin resistance and diabetes as well as lifestyle changes owing to depression, which may be predisposing to diabetes [9]. Therefore, irregularities in the blood sugar levels can directly affect the brain and its functions.

Insulin-dependent type 1 DM, wherein the blood sugar levels cannot be maintained, causes anxiety and depression by affecting the autonomic and central nervous systems as well as autoimmune mechanisms. In contrast, in older patients with type 2 DM, decreases in both mental and physical energies owing to diabetes, macrovascular complications associated with diabetes during diagnosis, and other comorbidities usually increase the prevalence of mental disorders. Thus, the association between depression and anxiety is high [5]. The Hospital Anxiety and Depression Scale (HADS), which was developed by Zigmond and Snait [10] is currently one of the most widely used scales to evaluate depression and anxiety in DM. The HADS not only helps in diagnosis but also determines the risk group by rapidly scanning anxiety and depression in patients with the disease [10].

Therefore, here, we aimed to evaluate the distribution of depression and anxiety in terms of sex, type and duration of DM, and some demographic and metabolic parameters in patients with type 1 and 2 DM.

Materials and Methods

A total of 193 patients were included in this study; 52 and 86 patients who applied to the Firat University Endocrinology Department had type 1 and 2 DM, respectively. In addition, 55 healthy individuals (age, >18 years) who were admitted to our hospital for annual checkups between June 2018 and December 2018 were included as the control group. The sample size was calculated using PASS software (version 14.0; NCSS, Silver Spring, MD). The power was set at 0.8, and the significance level was set at 0.05. The study was approved by the Firat University Ethics Committee (meeting no., 14; decision no, 2; date, 09. 0.6. 2018). The study was conducted in accordance with the principles of declaration of Helsinki, and written informed consent was obtained from all participants prior to study initiation.

Patients who were aged <21 years; pregnant; used antidepressant or antipsychotic drugs; physical illness, use of tobacco products and alcohol (former and current), and morbidly obese, any eating disorder as well as those with malignancies and/or advanced renal or hepatic disease, hyperthyroidism and hypothyroidism, malignancy, liver, kidney, acute or chronic inflammatory disease or were excluded from the study. The control group comprised healthy individuals who were not medically ill at the checkup. Fasting blood glucose, hemoglobin A1C (HbA1c), triglyceride, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), aspartate aminotransferase (AST), alanine aminotransferase (ALT), albumin, urea, and creatinine levels were obtained from the medical records of all patients and controls. In addition, height, weight, body mass index (BMI), neck, waist, and hip circumference measurements were made and information about the patients' exercise habits and drug use patterns were obtained. The participants' anxiety and depression levels were determined via face-to-face interviews conducted using questions included in the HADS. The scale comprises a total of 14 questions, and the maximum score was 21 for both anxiety and depression. When both conditions were evaluated, the maximum score was 42. The patients were grouped as normal, borderline, and depression or anxiety based on their HADS scores. All patients with HADS scores between 0 and 7 were considered normal, those with scores between 8 and 10 as borderline, and those with scores ≥ 11 as having anxiety in the anxiety scale and having depression in the depression scale. The data were statistically analyzed using the SPSS software, percentage calculation, and student's t-test; furthermore, one-way analysis of variance was performed for parametric data, Mann–Whitney U-test for nonparametric data, and chi-square test for categorical data. Based on the results of this study, the correlations between HADS and sex, anthropometric measurements, metabolic status, exercise status, complication status, ongoing treatment, and laboratory parameters were determined.

Results

A total of 193 individuals [females, 116 (60.1%); males, 77 (39.9%)] were included in the study; 52 patients (26.9%) had type 1 DM, 86 (44.6%) had type 2 DM, and 55 (28.5%) were controls. Annual prevalence rate of severe hypoglycemia 23 to 52 per patient- year for Type 1 diabetes and 2.9 to 23.3 per patient-year for Type 2 diabetes. When patients with type 2 DM were evaluated in terms of sex, the depression, anxiety, and depression+anxiety scores were significantly higher in females than in males (p 0.05 and 0.01, respectively, **Table 1**)

Table 1: Comparison of depression, anxiety, and anxiety +depression scores in terms of sex in patients with type 1 and type 2 DM.

Parameters	Female (n=47)	Male (n=39)	p
Depression score	12 (3-21)	9 (1-18)	0.022
Anxiety score	12 (3-21)	7 (0-21)	0.025
Anxiety+depression score	21 (9-36)	14 (4-36)	0.006
Data were presented as median (min–max).			

When patients diagnosed with type 2 DM were evaluated in terms of the anti-diabetic treatment in terms of their sex, there was a significant difference in all three scores in patients who received one or more oral anti-diabetics in addition to metformin (**Table 2 and Figure 1**) and there was no statistically significant difference between the scores in terms of other treatments (**Table 2 and Figure 1**). Baseline characteristics of the patients (**Table 3**) and level of some biochemical parameters

with and without type 1 and type 2 DM (**Table 4**) were also shown.

Table 2: Comparison of depression, anxiety, and anxiety +depression scores of patients with type 2 DM with metformin +oral anti-diabetics.

Parameters	Female (n=24)	Male (n=21)	p
Depression score	12 (3-21)	7 (2-15)	0.003
Anxiety score	10 (2-17)	6 (0-21)	0.044
Anxiety+depression score	20,5 (11-36)	11 (7-36)	0.004
Data were presented as median (min–max)			

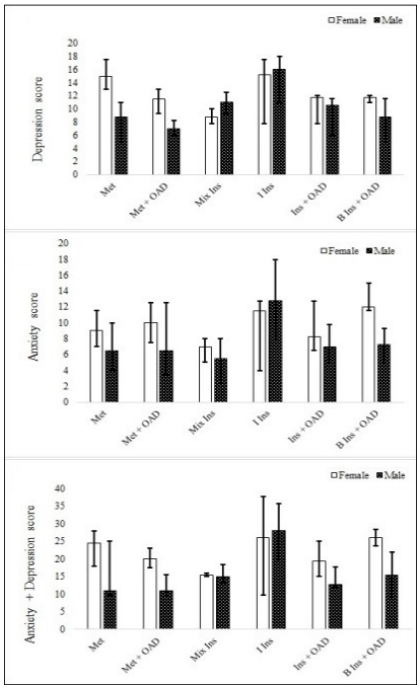

Figure 1: The effect of anti-diabetic agents on the depression, anxiety, and anxiety+depression scores in patients with type 2 diabetes mellitus. B: Basal; I: Intensive; Ins: Insulin; Met: Metformin; OAD: Oral Anti-Diabetics.

Table 3: Baseline characteristics of the patients.

Parameters	Type 1 DM	Type 2 DM	Control	General
Age (year)	30.48 ± 12.5	58.52 ± 11.3	37.24 ± 11.3	44.9 ± 17
Height (m)	1.67 ± 0.1	1.65 ± 0.1	1.66 ± 0.1	1.66 ± 0.9
Weight (kg)	64.62 ± 11.4	82.45 ± 18.7	67.81 ± 12.3	73.46 ± 17.3
BMI (kg/m^2)	23.18 ± 4	30.08 ± 6.2	24.32 ± 3.7	26.5 ± 5.9
Waist circumference (cm)	88.94 ± 46.9	107.32 ± 24.9	81 ± 17.4	94.9 ± 32.9
Hip circumference (cm)	97.43 ± 11.8	116.68 ± 68.4	99.08 ± 14.6	106.5 ± 47.5
Neck circumference (cm)	34.39 ± 2.9	37.11 ± 4.9	35.13 ± 3	35.82 ± 4.1
BMI: Body mass index, DM: Diabetes Mellitus.				

Table 4: Level of some biochemical parameters with and without type 1 and type 2 DM.

Parameters	Type 1 DM	Type 2 DM	Control	General
Fasting glucose (mg/dL)	204.43 ± 106	186.4 ± 95.1	82.91 ± 12.1	161.54 ± 98
HbA1c (%)	8.9 ± 2.9	9.25 ± 2.63	5.3 ± 0.2	8.98 ± 2.7
Triglyceride (mg/dL)	114.36 96.1	181.71 ± 88.4	138.73 ± 80.1	151.7 ± 92.3
Cholesterol (mg/dL)	163.98 ± 45	190.64 ± 48.2	171.4 ± 37	178.5 ± 45.7
LDL - cholesterol (mg/dL)	107.84 ± 39.4	125.06 ± 38.6	101.2 ± 32.1	113.63 ± ± 38.4
HDL - cholesterol (mg/dL)	52.73 ± 14.2	41.61 ± 14.4	42.56 ± 11	44.75 ± 14.2
DM: Diabetes Mellitus, HDL: High-density lipoprotein, LDL: Low-density lipoprotein.				

When diabetic patients were evaluated in terms of sex, the anxiety and anxiety+depression scores were significantly higher in females (p>0.001 for both). However, there were no significant differences between the groups in terms of the depression scores (**Figure 1**). The depression score was higher in patients with type 2 DM than in the control group and in those with type 1 DM (p>0.05 and 0.001, respectively). There was no difference between the groups in terms of anxiety and anxiety +depression scores (**Figure 2**).

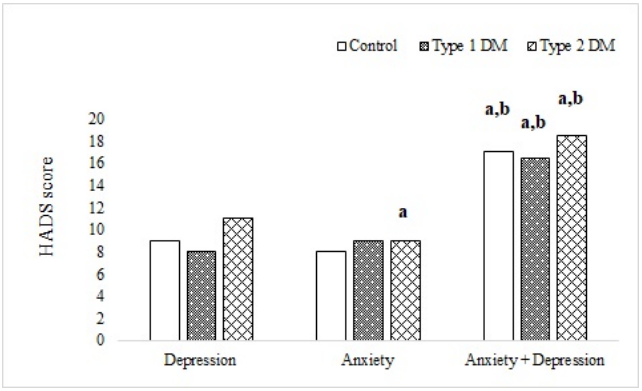

Figure 2: Comparison of depression, anxiety, and anxiety +depression scores in patients with type 1 and type 2 DM. When compared to the depression group: A p<0.05. When compared to the Anxiety group: b p<0.001.

In patients with type 2 DM, the depression scores were significantly higher in patients with neuropathy, nephropathy, coronary artery disease, and diabetic foot than in those without these diseases. However, a statistically significant difference was found only in patients with coronary artery disease in terms of the anxiety score (**Figure 3**).

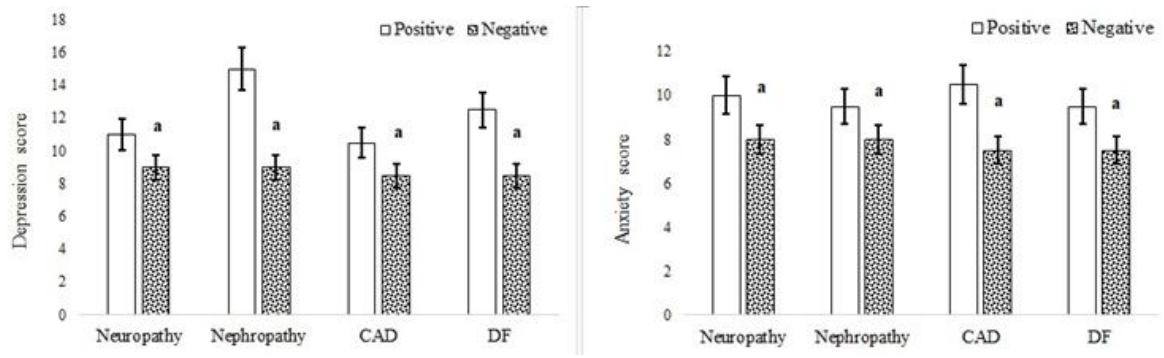

Figure 3: Effect of complications on the depression and anxiety scores in patients with type 2 diabetes mellitus. When positive versus negative; a p<0.05. CAD: Coronary Arterial Disease. DF: Diabetic Foot.

There was a positive correlation between the HbA1c level and depression and anxiety scores in diabetic patients, although not statistically significant (r=0.088, p=0.298; r=0.089, p=0.292 respectively). A statistically significant positive correlation was found in females (r=0.298, p=0.006; r=0.258, p=0.01, respectively); however, in males, there was no statistically significant correlation between the HbA1c level and depression and anxiety scores (r=−0.162, p=0.224; r=−0.065, p=0.628, respectively). However, there was no statistically significant correlation between the HbA1c level and depression and anxiety scores in females and males with type 1 DM (the depression score was r=0.241, p=0.176 for females, r=−0.200, p=0.442 for males; the anxiety score was r=0.330 for females, p= 0.061, r= −0.481, p=0.051 for males). Similarly, there was no statistically significant correlation between the HbA1c level and depression and anxiety scores for females and males with type 2 DM (the depression score was r=0.149, p=0.316 for females, r=−0.089, p=0.589 for males; the anxiety score was r=0.149, p=0.317 for females, r=0.039, p=0.812 for males).

There were significant increases in the depression and anxiety scores as the number and dose of drugs the participants used increased (p<0.05 for all). There was also a positive correlation between the depression score and urea and creatinine levels (p<0.001, r=0.315; p<0.01, r=0.236, respectively). However, there was a negative correlation between the depression score and albumin level (p<0.05, r=−0.173). There was a positive correlation between the depression+anxiety score and urea and creatinine levels (p<0.001, r=0.277; p<0.01, r=0.192, respectively). However, there was a negative correlation between the depression+anxiety score and albumin levels (p<0.05, r=−0.164).

Discussion

In the present study, the prevalences of depression and anxiety were observed to be higher in diabetic patients than in control patients. In addition, the depression, anxiety, and anxiety+depression scores were significantly higher in patients with type 2 DM than in those with type 1 DM. Previous studies have reported that depression and anxiety increase with diabetes [2,11]. Furthermore, depression and anxiety are reportedly more common in patients with type 1 diabetes than in those with type 2 diabetes in all populations. In patients with type 1 DM, life-long insulin-dependence, insulin-related hypoglycemic attacks, family conflicts regarding diabetes management, accompanying chronic diseases and possibility of accompanying autoimmune diseases may emerge, thereby indicating the risk of previous symptoms being associated with diabetes and severe hypoglycemia causing neuropathological changes, thereby laying the ground for depression and anxiety [1]. In this study we reported that annual prevalence rate of severe hypoglycemia 23 to 52 per patient- year for Type 1 diabetes and 2.9 to 23.3 per patient-year for Type 2 diabetes. Annual prevalence rate of severe hypoglycemia in other country was reported 11.5 to 42.8 per patient- year for Type 1 diabetes and 3.2 to 16.37 per patient-year for Type 2 diabetes [12]. Annual prevalence rate of severe hypoglycemia in patients with Type 1 diabetes and Type 2 diabetes throughout world were very close to each other.

Therefore, we suggest that depression and anxiety scores are lower in patients with type 1 DM than in those with type 2 DM because patients with type 1 DM typically live with the disease for a long period of time, thereby coming to terms with their condition. Again, the fact that patients with type 1 DM are younger during disease onset and that there are no accompanying complications might be the reason for the lower rates of depression. Changes in the personality and capabilities of patients with type 1 DM, who have to live with diabetes from an early age, affect their compliance with treatment. Thus, personal differences affect not only the emotional and behavioral consequences of stress but also the hormonal responses of diabetic patients to stress. The social environment also plays a role in helping patients adapt to diabetes. In particular, friends, families, and health-related organizations can be important sources of support to patients [13]. In contrast, because type 2 DM occurs in patients in their middle-age period of life, those who are alive until this age period cannot cope up with their diagnosis; hence, depression and anxiety may be

higher in patients with type 2 DM than in those with type 1 DM. In addition, depression accompanying diabetes affects patients' quality of life, independence, future, and compliance with the disease. Depression hormones affect the course of diabetes. In contrast, dysregulation of blood glucose level in diabetic patients causes an increase in depression. Moreover, an increase in depression is taken as a complication of increased severity of diabetes [14] and anxiety as, disability, loss of competence, and fear of death cause anxiety in diabetic patients.

The prevalences of diabetes, depression, and anxiety were higher in females than in males [15]. The present study emphasizes that poor socioeconomic conditions can cause mental disorders and even depression more frequently in diabetic females. Further, in the present study, depression, anxiety, and anxiety+depression have been observed to increase with age. Studies have shown that the prevalence and severity of depression increase with age, particularly in individuals aged >80 years. However, the prevalence of depression peaks at the least in the middle-age period of an individual's life, particularly between 40 and 45 years of age [16]. In our study, the depression and anxiety+depression scores were significantly higher in individuals aged >65 years than in those aged <65 years. The anxiety scores were also higher in individuals aged >65 years than in those aged <65 years; however, the difference was not statistically significant. Although hypoglycemia and the fear of needles/injections reportedly cause anxiety disorders in patients with type 1 DM, no statistically significant difference was observed in patients with type 1 DM in this study [5]. Some studies reported that patients with type 1 DM experience higher rates of mental disorders than patients with type 2 DM [17]. Again, the fact that patients with type 1 DM are younger and that there are no accompanying complications might be the reason for the lower rates of depression. Changes in the personality and capabilities of patients with type 1 DM, who have to live with diabetes from an early age, affect their compliance with treatment. Thus, personal differences affect not only the emotional and behavioral consequences of stress but also the hormonal responses of diabetic patients to stress. The social environment also plays a role in helping patients adapt to diabetes. In particular, friends, families, and health-related organizations can be important sources of support to patients [13].

The HbA1c level is an important parameter in the treatment follow-up of DM because it reflects glycemic control over the past 2-3 months. The risk of DM complications increases with increasing HbA1c levels. In the present study, the HbA1c levels were positively correlated with depression and anxiety scores. A study reported that the HbA1c level was >7 in 82% of the patients with a depression score >16 and in 40% of the patients with an anxiety+depression score <16 [18]. Another study reported that in patients receiving complex treatment and those with the presence of nephropathy, a high HbA1c level, and a high BMI were associated with a negative course of DM [1]. As in other studies, the HbA1c levels were correlated with the depression (p=0.013) and anxiety+depression (p=0.042) scores in the present study. The HbA1c level was also positively correlated with anxiety; however, the value was not significant. The depression scores were significantly higher in patients with a BMI >30 kg/m^2; however, the anxiety and anxiety+depression scores were high but not statistically significant in those patients. One study compared patients with type 1 and 2 DM and reported that the levels of orientation and cooperation were higher in patients with type 1 DM. The duration of diagnosis, the presence of neuropathy, and HbA1c levels indicate the patient's ability to manage diabetes [1]. Likewise, although not significant, in the present study, the anxiety and anxiety +depression scores decreased as the duration of DM increased in the patients with type 1 DM; moreover, all three scores increased as the HbA1c level increased, but the increase was not significant. In patients with type 2 DM, all the three scores increased as the HbA1c level increased, and only the increase in depression was significant (p=0.045). This can be attributed to the absence of complications in patients with type 1 DM and their acceptance of and adaptation to the disease. In contrast, in patients with type 2 DM, as the DM duration increased, all three scores also increased, although not significant. This may be attributed to the complications accompanying our patients with type 2 DM, the patients' advanced ages, and inconsistencies in their treatment and their inability to accept the disease. In the present study, the presence of neuropathy and high levels of HbA1c increased the risk of comorbidities, which facilitated the accompanying depression and anxiety. A study [19] that evaluated 255 patients with painful diabetic neuropathy reported that 35% and 28% of those patients were diagnosed with anxiety and depression according to the HADS depression and anxiety scoring. Not only patients with neuropathy but also those who passed a certain score on the pain scoring were included in the study; therefore, not only neuropathy but also the pain caused by neuropathy could have affected these scores. In fact, Mc Williams et al. reported that the prevalence of depression was 9.3% in the general population and 20.2% in patients with chronic pain; he also reported that chronic pain may cause depression [20]. In our study, depression (p=0.036) and anxiety (p=0.243) were observed in 57.1% and 42.9% of the patients with neuropathy. The depression score (p=0.031) was significantly higher in patients with neuropathy when the patients' scores were evaluated with HADS, whereas the difference in the anxiety (p=0.231) and anxiety+depression (p=0.077) scores was not statistically significant. In patients without neuropathy, the rates of depression and anxiety were 39.5% and 32%, respectively, which are higher than those reported in patients with painful neuropathy in the aforementioned studies. Therefore, among others, neuropathy may be an important factor affecting depression and anxiety in diabetic patients.

Many studies have reported a correlation between depression and retinopathy, which is one of the chronic microvascular complications of diabetes; those studies have reported that depressive symptoms vary between 35.7% and 50% in patients with diabetic retinopathy [21]. Another study reported that depressive symptoms reportedly increased for 2 years after the loss of vision due to progressive retinopathy and that the depressive symptoms decreased after the transition from fluctuations in visual acuity to stable low vision [22]. The small number of patients with retinopathy in our study prevented us from validating the correlations mentioned in the literature.

Studies with a larger number of patients with retinopathy may provide more enlightening information on this subject.

Depression and anxiety are more common in patients with diabetic foot. Patients with diabetic foot experience difficulties, such as sleep disorders, disruption in mobilization, fatigue, weakness, loneliness, and restrictions in sexual and other areas of life [3]. In such patients, worry owing to the knowledge of the risk of amputation also leads to depression and anxiety. A study reported that depression and other complications were higher in patients with diabetic foot and diabetes for >10 years than in those with diabetes for <10 years [3]. Although the number of patients was limited in our study, our results were comparable with those of other studies. There was an increase in all the three scores in patients with diabetic foot. The increases in the depression ($p=0.009$) and anxiety+depression ($p=0.016$) scores were significant, but the increase in the anxiety ($p=0.102$) score was not. In addition, in our study, the mean duration of diabetes was 17.5 and 9.1 years in patients with and without a diabetic foot. This difference was statistically significant ($p=0.002$) and verified the results of other studies showing that the duration of diabetes is an important risk factor in the development of diabetic foot.

A polypharmacy ≥5 is defined as the cumulative dose of a drug. In a study involving patients with DM, the polypharmacy was found to have a frequency of 78% [23]. In another study, no significant correlations were found between the use of over-the-counter medications and the anxiety and depression scores [24]. In the present study, patients with a polypharmacy >5 exhibited higher depression and anxiety scores. These results suggest that polypharmacy may be a source of stress in this group of patients. Gamma-aminobutyric acidergic (GABAergic) inhibition is an important mechanism that provides the balance between neuronal excitation and inhibition. The GABA neurotransmitter plays a central inhibitory role in regulating anxiety. In the present study, although not statistically significant, the anxiety and depression scores were higher in patients who took GABAergic drugs [25].

Albumin is one of the major proteins synthesized in the liver. Decreased serum albumin levels were observed in medical conditions associated with malnutrition, whereas increased serum albumin levels were reportedly associated with metabolic syndrome, which is an indicator of obesity and excessive nutrition [26]. In addition, it has recently been suggested that serum albumin is associated with insulin resistance. In our study, a negative correlation was found between the albumin levels and the depression and anxiety scores. This result may be attributed to the disease activation or may be associated with the protective effects of albumin. However, a study reported a negative correlation between the albumin level and the depression score [27]. The primary objective of the treatment of diabetes is to regulate blood sugar levels. Niskanen et al. reported that the abovementioned complications should be prevented and effectively treated in diabetic patients with psychosocial problems and depression [28].

Conclusion

In summary, according to HADS, diabetes causes anxiety and depression. Because anxiety and depression decrease the quality of life of diabetic patients, we suggest it is important to screen all diabetic patients for anxiety and depression to eliminate this condition by providing effective treatment. In brief, our results indicate that testing larger numbers of patients in independent clinics will contribute to improving public health to eliminate the unpredictable complications of diabetes and to ensure appropriate treatment goals.

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Disclosure

The authors report no conflicts of interest in this work.

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