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Fatigue and depression in elderly patients with poorly controlled diabetes

Irfan Esen, MD[a], Selin Akturk Esen, MD[b,*], Hakan Demirci, MD[c]

Abstract

In this study, it was aimed to evaluate the severity of depression and fatigue in patients with type 2 diabetes mellitus (T2DM), aged ≥ 60 years, with poor diabetes control. Between December 2018 and June 2019, 310 patients aged ≥ 60 years, with hemoglobin A1C ≥ 10%, followed-up with the diagnosis of T2DM for at least 3 years in the internal medicine outpatient clinics of Bursa Yüksek İhtisas Training and research hospital were included in the study. The geriatric depression scale (GDS) and fatigue severity scale (FSS) questionnaires were administered. Patients were analyzed according to their sociodemographic and clinical characteristics, according to their GDS and FSS scores. The GDS and FSS scores were higher in the female patients than in the male patients, those with diabetes aged ≥ 21 years than those aged < 21 years, those using premixed insulin than those using basal bolus insulin and oral antidiabetic drug for + basal insulin, and those living alone than in those living with their families. The FSS score was higher in patients with vitamin D levels < 20 ng/mL. The factors affecting the GDS score were the FGS and FSS scores in the multivariate analysis. The factors affecting the FSS score were the GDS, diabetes age, hemoglobin level, and vitamin D level in the multivariate analysis. Poorly controlled diabetes affects elderly patients more in terms of their mental and physical health. Therefore, these patients should be considered in terms of psychosocial aspects to increase treatment compliance and effects.

Abbreviations: FSG = fasting serum glucose, FSS = fatigue severity scale, GDS = geriatric depression scale, HBA1C = hemoglobin A1C, HDL = high-density lipoprotein, LDL = low-density lipoprotein, OAD = oral antidiabetic drug, T2DM = type 2 diabetes mellitus, TG = triglyceride.

Keywords: depression, elderly, fatigue, HbA1c, type 2 diabetes mellitus

1. Introduction

Type 2 diabetes mellitus (T2DM) is a major global health concern.[1] It is 1 of the most important causes of disease burden, especially in elderly patients.[1] It is a chronic process that requires constant support and training for patient management to prevent acute complications and reduce the risk of long-term complications. In developed countries, the prevalence of diabetes is higher in adults aged 65 and over.[2] In Canada, the prevalence of diabetes in adults aged 65 and over is 14% to 23%.[3] The aging of the population, increasing inactivity, and the increase in obesity are among the factors that cause the increase in diabetes.[4] T2DM has a detrimental effect on the loss of organ function during the natural aging process in the elderly.[5] In particular, diabetic effects such as glucose toxicity, insulin resistance, and increased fat accumulation may increase the development of sarcopenia and frailty in this patient group.[6] In studies conducted, it has been determined that 40% of the diabetic elderly have more than 1 comorbidity, and 40% to 50% have 3 or more comorbidities.[7,8] When all these negative factors are considered together, in the long term, T2DM can impair mental health and quality of life.

Depressive symptoms and fatigue are 3 times more common in elderly patients with diabetes.[9] Depression can lead to mental health deterioration, decreased quality of life, decreased working ability, and a further increase in complaints due to existing diseases.[10] Although the exact cause of depression is unknown, changes in neurochemicals in the brain, genetics, medical conditions, disability, social isolation, and psychosocial stressors have been implicated in depression, and many of these factors are more common in older adults.[11,12] In patients 65 years of age and older, depression has been associated with emotional distress, increased health care costs, morbidity, higher risk of suicide, and death from other causes.[13] Fatigue is a physical and mental exhaustion condition that is seen in physical and mental illnesses, including weakness and lack of energy,[14] and unless it is controlled, it can negatively affect the daily activities of people. Fatigue is more common in patients with depression.[15] In addition, fluctuations in glucose levels seen in patients with T2DM, drug side effects due to

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Ethics approval and consent obtained from Ankara City Hospital Ethics Committee.

[a] Yüksek İhtisas Üniversitesi, Faculty of Medicine Department of Internal Medicine, Turkey, [b] Ankara Şehir Hastanesi, Department of Medical Oncology, Turkey, [c] Bursa Yüksek İhtisas Training and Research Hospital, Department of Family Medicine, Turkey.

** Correspondence: Selin Akturk Esen, Ankara Şehir Hastanesi, Department of Medical Oncology, Turkey (e-mail: drselin16@hotmail.com).*

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polypharmacy, fear of coping with the disease on its own, and development of various complications in the short and long term can trigger fatigue, which may make the management of diabetes more difficult.

2. Aims

This study aimed to measure the severity of depression and fatigue in T2DM patients, aged ≥ 60 years, with poor diabetes control and evaluate this situation comprehensively.

3. Methods

Between December 2018 and June 2019, 310 patients aged 60 and over, followed-up with the diagnosis of T2DM in the Internal Medicine outpatient clinics of Bursa Yüksek İhtisas training and research hospital were included. The inclusion criteria were as follows: having a diagnosis of T2DM for at least 3 years; being aged 60 or over; having a hemoglobin A1C (HBA1C) level ≥ 10%; not having any acute or severe diseases, such as stroke, acute renal failure, or cognitive impairments.

The geriatric depression scale (GDS) and fatigue severity scale (FSS) questionnaires were given to the patients, who were asked to fill them out. The GDS, consisting of 30 questions, was developed by Yesavage[16] and adapted to Turkish by Ertan et al[17] While yes answers to some questions are coded as 0 points and no answers as 1 point, in some questions, the coding is in the opposite direction. The total score obtained is the depression score. An increase in this score indicates the presence of depression. The total score range varies between 0 and 30. A GDS score between 0 and 10 is accepted as no depression, 11 to 13 as possible depression, and ≥ 14 indicates definite depression. The FSS includes 9 items related to fatigue and uses a 7-point Likert-type scale. The Turkish version of the FSS has been shown to be valid and reliable in different patient populations.[18] A score of 4 or higher indicates severe fatigue.

In addition, the patients' age, sex, duration of diabetes, diabetes treatment, comorbidities, educational status, marital status, and smoking status were noted. The body mass index (BMI) was calculated using the following equation: body weight (kg)/height^2 (m). The World Health Organization defined anemia as a hemoglobin concentration below 12 g/dL for women and 13 g/dL for men.[19,20] Serum vitamin B_{12}, hemoglobin, fasting serum glucose (FSG), triglyceride (TG), high-density lipoprotein (HDL) cholesterol, vitamin D, and HbA1c levels were measured. A serum vitamin B_{12} level of 200 to 300 pg/mL is considered as a borderline value (additional tests are needed) and < 200 pg/mL is considered as vitamin B_{12} deficiency.[21] A serum ferritin level < 15 ng/mL is considered as an iron deficiency.[22] Vitamin D deficiency was defined as a vitamin D level < 20 ng/mL.[23] The low-density lipoprotein (LDL) level was calculated using the Friedewald formula: LDL (mg/dL) = Total cholesterol (mg/dL) – HDL (mg/dL) – TG (mg/dL)/5.[24] Non-HDL cholesterol was calculated with the "total cholesterol-HDL" formula.

Written informed consent form was obtained from all of the patients. This study was approved by the Ethics Committee of Health Sciences University Bursa Yüksek İhtisas training and research hospital (Decision number 2011-KAEK-25 2019/05-09.

3.1. Statistical analysis

The suitability of the continuous variables to normal distribution was examined using the Kolmogorov–Smirnov and Shapiro-Wilk tests. In the comparisons of 2 groups, the independent samples *t*-test was used in the comparisons of the groups with normal distribution, and the Mann-Whitney *U* test was used in the comparisons of groups that did not have normal distribution. In the comparisons between the 3 groups, ANOVA was used if the data were compatible with normal distribution; however, if the data were not normally distributed, the Kruskal–Wallis test was used. Correlation coefficients and statistical significance were calculated using the Spearman test for relations between non-normally distributed or ordinal variables. The effects of different predictors on the FSS and GDS scores were examined using a multivariate linear regression model. Statistical analyses were performed using the SPSS software (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, version 21.0. Armonk, NY), and statistical significance was set at $P < .05$.

4. Results

In total, 310 patients were included in this study. Of these, 192 (61.9%) were female, and 118 (38.1%) were male. The median age of the patients was 67 years (60–88 years). There were 108 patients (34.8%) between 60 and 64 years old, 164 patients (52.9%) between 65 and 74 years old, 32 patients (10.3%) between 75 and 84 years old, and 6 patients (1.9%) ≥85 years old. The median duration of diabetes was 10 years (range: 3–37 years). There were 160 patients (51.6%) with a diabetes duration ≤ 10 years, 100 patients (32.3%) with a duration of 10 to 20 years, and 50 patients (16.1%) aged ≥ 21 years. Of the patients, 61.3% had accompanying comorbidities, and 38.7% had no known additional disease. The median FSG score was 233.10 mg/dL (86–459). The median HBA1C level was 11.1% (range: 10–16.89%). There were 104 patients (35.5%) with a GDS score of < 10, 42 patients (13.5%) with a GDS score of 11 to 13, and 164 patients (52.9%) with a GDS score of ≥ 14. There were 66 patients (21.3%) with an FSS score of < 4 and 244 patients (78.7%) with an FSS score of ≥ 4. Other sociodemographic and laboratory values of the patients are summarized in Table 1.

In the comparisons between the women and men, both the GDS and FSS scores were found to be significantly higher in the women ($P < .001$ and $P < .001$, respectively). The FSS and GDS scores differed between the diabetes duration groups ($P < .001$ and $P = .001$, respectively). The GDS score was significantly higher in patients with diabetes aged ≥ 21 years than in patients aged ≤ 10 years and when compared to the patients aged 11–20 years ($P < .001$ and $P = .014$, respectively). The FSS score was found to be statistically significantly higher in the patients with diabetes aged ≥ 21 years than in those aged ≤ 10 years ($P < .001$) (Table 2).

When the patients were grouped according to the treatments they received, the FSS ($P < .001$) and GDS scores ($P = .002$) differed. The GDS score was found to be statistically significantly higher in the patients using premixed insulin (2 injection daily) than in those using an oral antidiabetic drug (OAD) + basal insulin (1 injection daily), and it was also significantly higher in the patients using basal bolus insulin (4 injections daily) than in those using an OAD + basal insulin ($P = .005$ and $P < .001$, respectively). Similarly, the FSS score was found to be significantly higher in patients using premixed insulin when compared to patients using an OAD + basal insulin, and it was also significantly higher in patients using basal bolus insulin than in those using an OAD + basal insulin ($P < .001$ and $P < .001$, respectively). Geriatric depression and the FSS scores were significantly higher in patients living alone than in those living with their families (spouse or children) ($P = .014$ and $P = .038$, respectively) (Table 2).

The FSS score was significantly higher in individuals with vitamin D levels < 20 ng/mL than in those with vitamin D levels ≥ 20 ng/mL ($P = .006$), but no difference was found between the 2 groups in terms of the GDS score ($P = .92$). When the patients were examined according to their vitamin B_{12} levels, the GDS scores varied between the groups ($P = .033$). In the subgroup analyses, patients with vitamin B_{12} levels < 200 pg/mL had significantly higher GDS scores than those with a level ≥ 300 pg/mL ($P = .044$). In addition, patients with vitamin B_{12} levels

Table 1

Sociodemographic, clinical and laboratory characteristics of the patients.

Variables		N (%)(?>	Median (Minimum; Maximum)(?>
Sex	Female	192 (%61.9)	
	Male	118 (%38.1)	
Age (yr)			67 (60;88)
Age category (yr)	60–64	108 (%34.8)	
	65–74	164 (%52.9)	
	75–84	32 (%10.3)	
	≥85	6 (%1.9)	
Duration of diabetes (yr)			10 (3;37)
Diabetes duration category (yr)	≤10	160 (%51.6)	
	11–20	100 (%32.3)	
	≥21	50 (%16.1)	
Comorbidity	No	120 (%38.7)	
	CVD	108 (%34.8)	
	Other	82 (%26.5)	
Hypertension	No	210 (%67.7)	
	Yes	100 (%32.3)	
CD	No	298 (%96.1)	
	Yes	12 (%3.9)	
Hyperlipidemia	No	52 (%16.8)	
	Yes	258 (%83.2)	
CKD	No	274 (%88.4)	
	Yes	36 (%11.6)	
FSG			233.1 (86.0;459.0)
HBA1C (%)			11.1 (10.0;16.8)
BMI (kg/m^2)	18.5–24.9	48 (%15.5)	
	25–29.9	92 (%29.7)	
	≥30	170 (%54.8)	
Marital status	Married	218 (%70.3)	
	Divorced/widow	92 (%29.7)	
Education level	< high school	284 (%91.6)	
	high school	16 (%5.2)	
	> high school	10 (%3.2)	
GDS category	≤10	104 (%33.5)	
	11–13	42 (%13.6)	
	≥14	164 (%52.9)	
FSS category	<4	66 (%21.3)	
	≥4	244 (%78.7)	
Ferritin category (ng/mL)	<15	30 (9.7%)	
	≥15	278 (90.3%)	
Vitamin B12 category (pg/mL)	<200	32 (10.3%)	
	200–299	84 (27.1%)	
	≥300	194 (62.6%)	
Vitamin D category (ng/mL)	<20	272 (87.7%)	
	≥20	38 (12.3%)	

BMI = body mass index, CD = cerebrovascular disease, CKD = chronic kidney disease, CVD = cardiovascular disease, FSG = fasting serum glucose, FSS = fatigue severity scale, GDS = geriatric depression scale, HBA1C = hemoglobin A1C.

of 200 to 299 pg/mL had significantly higher GDS scores than those with levels ≥ 300 pg/mL ($P = .045$). There was no significant relationship between the FSS scores and vitamin B_{12} levels ($P = .47$). No relationship was found between the patients' age, BMI, smoking, presence of anemia, ferritin, LDL, non-HDL, and TG levels and the FSS and GDS scores (Table 2).

In the correlation analysis, a positive correlation was found between the GDS and FSS scores, FSG levels, and duration of diabetes ($P < .01$, $P < .01$, $P < .01$, respectively). There was a negative correlation between the GDS score and hemoglobin levels ($P < .01$). While there was a positive correlation between the FSS score and FSG levels and the diabetes duration ($P < .01$, $P < .01$, respectively), there was a negative correlation between the FSS score and the hemoglobin and vitamin D levels ($P < .01$, $P < .01$, respectively). While there was a negative correlation between the diabetes duration and hemoglobin levels ($P < .01$), a positive correlation was found between the diabetes duration and vitamin D levels ($P < .05$). In addition, a negative correlation was found between age and HBA1c with the hemoglobin levels ($P < .05$, $P < .05$ respectively) (Table 3).

When the factors affecting the GDS score were examined, the FSG and FSS scores, diabetes age, and hemoglobin level were determined as statistically significant factors in the univariate analysis ($P < .001$, $P < .001$, $P < .001$, and $P = .002$, respectively). In the multivariate analysis, the FGS and FSS scores were found to be significant ($P = .002$ and $P < .001$, respectively) (Table 4). Considering the factors affecting the FSS score, the GDS score, diabetes age, hemoglobin, vitamin D, and FSG were significant in the univariate analysis ($P < .001$, $P < .001$, $P < .001$, $P = .007$, and $P < .001$, respectively); the GDS score, diabetes age, hemoglobin, and vitamin D were significant in the multivariate analysis ($P < .001$, $P = .025$, $P = .001$, and $P < .001$, respectively) (Table 5).

5. Discussion

In this study, depressive symptoms were found in 66.5% (13.6% probable depression, 52.9% definite depression) of the patients aged over 60 years with poorly controlled T2DM. In addition, the FSI score was ≥ 4 in 78.7% of the patients.

Table 2

Comparison of patient characteristics according to fatigue severity scale and geriatric depression scale.

		FSS		GDS	
		Median (Minimum;Maximum)	***P*-value**	**Median (Minimum;Maximum)**	***P*-value**
Sex	Female	6.11 (1.1;9)	**<.0001****	16 (1;29)	**<.0001****
	Male	4.6 (0.4;7)		10 (0;26)	
Duration of diabetes (yr)	≤10	5.50 (0.4;7.5)	**<.0001****	12 (1;26)	**.001****
	11–20	6 (2;7)		14 (0;29)	
	≥21	6.3 (3.8;9)		18 (1;28)	
Age category (yr)	60–64	5.75 (0.4;9)	.98	15 (1;25)	.90
	65–74	5.6 (2;7.5)		14 (0;29)	
	75–84	6.11 (1.1;7)		14.5 (1;24)	
	>85	5.6 (5.5;6)		14 (10;21)	
Diabetes treatment	OAD	5.45 (0.4;9)	**<.0001****	13.5 (1;29)	**.002****
	OAD + basal insulin	4.3 (2.1;7)		10 (0;22)	
	Premixed insulin	6.3 (2;7)		17 (1;24)	
	Basal bolus insulin	6 (2;7)		15 (3;28)	
BMI category	18.5–24.9	5.25 (1.1;7)	.93	14 (0;26)	.46
	25–29.9	6 (4;7)		14 (1;28)	
	≥30	5.7 (2.1;9)		14 (1;29)	
Social environment	Living with family	5.2 (0.4;9)	**.038***	13 (0;28)	**.014***
	Living alone	5.5 (1.1;7)		16.5 (3;29)	
Smoke	No	5.7 (0.4;9)	.58	14 (0;29)	.30
	Yes	5.6 (2;7)		12 (1;26)	
Vitamin D (ng/mL)	<20 ng/mL	5.9 (1.1;9)	**.006****	14 (0;29)	.92
	≥20 ng/mL	4.6 (0.4;7)		15 (2;25)	
Anemia	Yes	6 (2;7)	.196	15 (0;27)	.39
	No	5.65 (0.4;9)		14 (1;29)	
Ferritin (ng/mL)	<15	6.11 (2;7)	.23	14 (4;29)	.63
	≥15	5.7 (0.4;9)		14 (0;28)	
Vitamin B12 (pg/mL)	<200	5.11 (2.2;7)	.47	15 (1;29)	**.033***
	200–299	6 (2;7.5)		13 (1;24)	
	≥300	5.7 (0.4;9)		11.5 (0;25)	
LDL cholesterol (mg/dL)	<100	5.6 (2;9)	.53	14 (1;27)	.82
	≥100	5.8 (0.4;7.5)		14 (0;29)	
Non-HDL cholesterol (mg/dL)	<130	5.5 (2;7)	.34	15 (1;27)	.92
	≥130	5.9 (0.4;9)		14 (0;29)	
Triglyceride (mg/dL)	<150	6 (0.4;9)	.39	14 (1;29)	.88
	≥150	5.6 (2;7.5)		14 (0;28)	

BMI = body mass index, HDL = high density lipoprotein, LDL = low density lipoprotein, OAD = oral antidiabetic drugs.
***P* < .01, **P* < .05.

Table 3

Correlation analysis of patient characteristics with fatigue severity scale and geriatric depression scale scores.

No		1Decimal?>	2Decimal?>	3Decimal?>	4Decimal?>	5Decimal?>	6Decimal?>	7Decimal?>	8Decimal?>	9Decimal?>
1	GDS	1.000	**.533****	–.061	**.218****	**.199****	.020	**–.164****	.111	.019
2	FSS	**.533****	1.000	.002	**.216****	**.197****	.087	**–.280****	.021	**–.211****
3	HBA1C	–.061	.002	1.000	**.420****	–.009	**–.143***	.035	.004	**–.122***
4	FSG	**.218****	**.216****	**.420****	1.000	.003	–.097	–.074	–.078	–.108
5	Duration of diabetes	**.199****	**.197****	–.009	.003	1.000	.074	**–.367****	.015	**.125***
6	Age	.020	.087	**–.143***	–.097	.074	1.000	**–.119***	.027	–.009
7	Hemoglobin	**–.164****	**–.280****	.035	–.074	**–.367****	**–.119***	1.000	–.092	.068
8	Vitamin B12	.111	.021	.004	–.078	.015	.027	–.092	1.000	**.139***
9	Vitamin D	.019	**–.211****	**–.122***	–.108	.125*	–.009	.068	**.139***	1.000

FSG = fasting serum glucose, FSS = fatigue severity scale, GDS = geriatric depression scale, HBA1C = hemoglobin A1C.
***P* < .01,
**P* < .05 Pearson correlation.

Current depressive symptoms and fatigue rates in these patients can make treatment compliance difficult and create a vicious circle.[25] Depression rates differ in elderly patients with T2DM in studies conducted in different geographies. While the depression rate in T2DM patients was 29.7% in the study conducted by Gorska-Ciebiada et al[26] in Poland, this rate was 26% in a study conducted in China and 15.4% in a study conducted in Japan.[27] In another study conducted in Vietnam, the depression rate in this patient population was 79.4% (69.4% mild depressive symptoms and 10% moderate and severe depressive symptoms).[28] The reason for the different rates of depression may be due to the evaluation of the patients with different geographies or different ethnic origins, and with different assessment scales. In addition, the fact that the patient recruitment criteria of the studies are different may also affect this situation. Previous studies have found a relationship between poor disease control and increased depressive symptoms in T2DM patients.[29] In the current study, examining the elderly with poorly controlled

Table 4

Univariate and multivariate regression analysis for geriatric depression scale.

		Univariate regression analysis					Multivariate regression analysis					
		Unstandardized coefficients		Standardized coefficients				Unstandardized coefficients		Standardized coefficients		
	Model	*B*	Std. Error	Beta	t	*P*-value		*B*	Std. Error	Beta	*t*	*P*-value
1	FSG	.022	.005	.247	4.477	**<.0001****	1	.014	.004	.154	3.124	**.002****
2	FSS	2.330	.219	.517	10.613	**<.0001****	2	2.090	.228	.464	9.158	**<.0001****
3	Duration of diabetes	.170	.048	.199	3.561	**<.0001****						
4	Hemoglobin	–.837	.267	–.176	–3.138	**.002****						

Dependent variable: GDS.
FSG = fasting serum glucose, FSS = fatigue severity scale, GDS = geriatric depression scale.

Table 5

Univariate and multivariate regression analysis for fatigue severity scale.

		Univariate regression analysis					Multivariate regression analysis					
		Unstandardized coefficients		Standardized coefficients				Unstandardized coefficients		Standardized coefficients		
	Model	*B*	Std. Error	Beta	*t*	*P*-value		*B*	Std. Error	Beta	*t*	*P*-value
1	GDS	.115	.011	.517	10.613	**<.0001****	**1**	.100	.011	.450	9.197	**.000****
2	Duration of diabetes	.046	.011	.244	4.421	**<.0001****	**2**	.022	.010	.114	2.249	**.025***
3	Hemoglobin	–.315	.057	–.298	–5.480	**<.0001****	**3**	–.173	.053	–.164	–3.261	**.001****
4	Vitamin D	–.029	.011	–.154	–2.732	**.007****	**4**	–.032	.009	–.170	–3.639	**.000****
5	FSG	.004	.001	.206	3.692	**<.0001****						

Dependent variable: FSS.
FSG = fasting serum glucose, FSS = fatigue severity scale, GDS = geriatric depression scale.

diabetes, instead of only diabetic elderly, may have led to higher rates of depression and fatigue. For this reason, especially in the presence of poorly controlled diabetes in the elderly, it is necessary to examine the psychosocial aspects of the patients as well as controlling diabetes.

In this study, the GDS scores were significantly higher in the women compared to men. There may be several reasons for higher rates of depression in diabetic elderly women when compared to men. The genetic inheritance of major depressive disorder is estimated to be 30% to 40%, and there is evidence that women have a stronger genetic risk than men.[30] Estrogen exerts attenuating effects on sympathoadrenal response and may exert activating or reducing effects on hypothalamicpituitary-adrenocortical axis responses.[31] However, a reduced hypothalamicpituitary-adrenocortical axis response to stress can easily put women at risk for depression. In various studies conducted with T1DM and T2DM patients, it was observed that women had higher depression rates than men.[32] In the current study, FSI scores were significantly higher in women when compared to men. In a study evaluating FSI in patients with T2DM, the FSI scores were higher in the women when compared to the men, as in the current study.[33] Increased fatigue with increasing age has been reported in both men and women.[34] In addition, women are 1.5 times more likely to experience fatigue than men. Depressive women are also more likely to experience somatic symptoms such as low energy, fatigue, and pain.[35] Thus, in the study herein, the high level of fatigue in the female patients may have resulted from the high rates of depression.

In this study, the FSI and GDS scores were significantly lower in the patients living with their spouse or family when compared to those living alone. In a different study conducted on diabetic patients in Turkey, the severity of fatigue was found to be higher in those living alone when compared to those living with their spouse or children.[33] In patients who live alone, the inability to share the responsibility of the disease with their spouse or family and the person's effort to overcome the disease alone may be the reason for this situation.

Herein, a significant relationship was found between depressive symptoms and the duration of diabetes. As the duration of diabetes increased, the depression score increased. In addition, it was observed that the FSI values increased with the increase in the duration of diabetes. In a previous studies, similar to this study, it was shown that depression rates increased as the duration of diabetes increased.[28] Microvascular and macrovascular complication rates that increase with the duration of diabetes may reduce the ability to cope with the disease and trigger depression. Moreover, it was found in this study that the GDS and FSS scores were significantly higher in the patients who received basal bolus insulin therapy or premix insulin therapy when compared to patients using an OAD + basal insulin therapy. The number of daily insulin applications of the patient may increase the their anxiety and trigger depression and fatigue. There may be various reasons for the development of depression and fatigue in patients using insulin. For example, the pain and discomfort experienced by the patient during the injection, the decrease in the quality of life, the fear of experiencing hypoglycemia due to misunderstandings in the treatment may be the cause of this situation.[36]

In this study, the FSI scores were significantly higher in the patients with a vitamin D level < 20 ng/mL than in those with ≥ 20 ng/mL. In older people, the skin's ability to synthesize vitamin D is significantly reduced. Vitamin D is also involved in various processes through its unique receptor (vitamin D receptor) and is also required for bone and skeletal muscle metabolism.[37] Therefore, vitamin D deficiency can be associated with musculoskeletal pain and bone disorders. The reason for fatigue in these patients may be that these functions are not fulfilled by vitamin D. Similar to the current study, in the study of Pennisi et al, patients with fatigue showed lower levels of vitamin D when compared with those without fatigue.[38] In contrast, another study on chronic fatigue syndrome did not reveal any association between perceived fatigue and vitamin D levels.[39] It was also reported that vitamin supplements do not affect fatigue in frail elderly patients.[40] In this study, there was no difference between the vitamin D groups in terms of depression scores. Similar to the current study, a population-based observational study of 527 participants in Japan failed to find an association between 25 (OH) D3 and depressive symptoms.[41] A published review examined the effects of vitamin D supplementation on depressive symptoms. The results of this review of 7 studies showed that vitamin D supplementation had no overall effect on depressive symptoms.[42] A population cohort study of people aged 65 and over in the Netherlands reported that 25 (OH) D levels were 14% lower in those diagnosed with both minor depression and major depression.[43] Using different depression scales in studies on vitamin D and reporting results from geographies with different climates may cause different results. In addition, patients with low vitamin D levels but taking vitamin D supplements were included in the current study. This may be a confounding factor and may have affected the results.

It was previously reported that psychiatric disorders, such as depression, are more common in the presence of anemia.[44] On the contrary, some other studies did not find a relationship between the hemoglobin level and depression.[45] In the correlation analysis performed in herein, a negative correlation was found between the hemoglobin values and FSI and GDS scores. Depression may occur as a result of anemia. Anemia may lead to impaired quality of life, and a deterioration in mood and fatigue.[46] In addition, malfunctions in cerebral oxygen transport due to anemia may trigger this situation. However, the deterioration of a balanced diet due to depression may further exacerbate depression by triggering anemia. In addition, in this study, no relationship was found between the vitamin B_{12} level and FSS score. Depression scores were higher in patients with vitamin B_{12} levels of 200 to 299 pg/mL and < 200 pg/mL compared to those with 300 pg/mL. In previous studies, it was reported that a low vitamin B_{12} level affects mental health negatively.[47] In different observational studies, no relationship was found between the vitamin B_{12} level and poor mental health.[48]

This study had some limitations. The fact that the study was conducted in a single tertiary hospital prevented it from being generalizable. Therefore, the admission of primary and secondary care patients aged 60 and over could not be evaluated. The diabetic complications of the patients were evaluated, but information about the complications of the patients could not be obtained. The number of drugs used daily by the patients and hypo-hyperglycemia attacks were also not evaluated. All of these may be factors that can affect depression and fatigue. In addition, no evaluation was made regarding the mental health of the patients, such as the presence of dementia. None of the patients were using iron or vitamin B_{12} replacements; however, patients using vitamin D were not excluded from the study. This can cause a confounding effect with vitamin D related analysis. However, the strength of the study was that a large number of poorly controlled elderly patients were evaluated.

6. Conclusion

Higher rates of depression and fatigue were found in patients aged ≥ 60 years with an HBA1C value of 10%, especially in the women, patients with a long diabetes duration, patients receiving basal bolus insulin and premix insulin therapy, and patients living alone. In addition, those with low vitamin D levels were associated with fatigue, while those with low vitamin B_{12} levels were found to have a higher rate of depression. In the multivariate regression analysis, the most effective parameters for the FSS score were the GDS score, diabetes age, hemoglobin, and vitamin D levels, while the most effective parameters for the GDS score were the FSG and FSS scores. Although diabetes is an important health problem among elderly patients, poorly controlled diabetes affects these patients more in terms of mental and physical health. Therefore, while evaluating these patients, psychosocial aspects should also be considered in order to increase treatment compliance and treatment effect, eliminate possible adverse effects of depression on treatment, and break the possible vicious circle.

Author contributions

Conceptualization: Irfan Esen, Selin Akturk Esen, Hakan Demirci.
Data curation: Irfan Esen, Selin Akturk Esen.
Formal analysis: Irfan Esen, Selin Akturk Esen.
Funding acquisition: Irfan Esen, Selin Akturk Esen.
Investigation: Irfan Esen, Selin Akturk Esen.
Methodology: Irfan Esen, Selin Akturk Esen, Hakan Demirci.
Project administration: Irfan Esen, Selin Akturk Esen, Hakan Demirci.
Resources: Irfan Esen, Selin Akturk Esen.
Software: Selin Akturk Esen.
Supervision: Irfan Esen, Selin Akturk Esen.
Validation: Selin Akturk Esen.
Visualization: Irfan Esen.
Writing – original draft: Irfan Esen.

References

[1] Collaborators, G.D.a.I.I.a.P. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990 to 2015: a systematic analysis for the global burden of disease study 2015. Lancet. 2016;388:1545–602.
[2] King H, Aubert RE, Herman WH. Global burden of diabetes, 1995–2025: prevalence, numerical estimates, and projections. Diabetes Care. 1998;21:1414–31.
[3] Association, C.D. An economic tsunami: The cost of diabetes in Canada. 2010.
[4] O'Shea M, Teeling M, Bennett K. The prevalence and ingredient cost of chronic comorbidity in the Irish elderly population with medication treated type 2 diabetes: a retrospective cross-sectional study using a national pharmacy claims database. BMC Health Serv Res. 2013;13:23.
[5] Federation, I.D. IDF Diabetes Atlas. 6th ed. 2013. Available at: https://www.idf.org/sites/default/files/EN_6E_Atlas_Full_0.pdf [access date June 12, 2015].
[6] Morley JE, et al. Frailty, sarcopenia and diabetes. J Am Med Dir Assoc. 2014;15:853–9.
[7] Maddigan SL, Feeny DH, Johnson JA. Health-related quality of life deficits associated with diabetes and comorbidities in a Canadian national population health survey. Qual Life Res. 2005;14:1311–20.
[8] Wolff JL, Starfield B, Anderson G. Prevalence, expenditures, and complications of multiple chronic conditions in the elderly. Arch Intern Med. 2002;162:2269–76.
[9] Moreh E, Jacobs JM, Stessman J. Fatigue, function, and mortality in older adults. J Gerontol A Biol Sci Med Sci. 2010;65:887–95.
[10] Judd LL. Psychosocial disability during the long-term course of unipolar major depressive disorder. Arch Gen Psychiatry. 2000;57:375–80.
[11] Blazer DG. Depression in late life: review and commentary. J Gerontol A Biol Sci Med Sci. 2003;58:249–65.
[12] Bruce ML. Psychosocial risk factors for depressive disorders in late life. Biol Psych. 2002;52:175–84.
[13] Charney DS. Depression and bipolar support alliance consensus statement on the unmet needs in diagnosis and treatment of mood disorders in late life. Arch Gen Psychiatry. 2003;60:664–72.
[14] Davis MP, Walsh D. Mechanisms of fatigue. J Support Oncol. 2010;8:164–74.
[15] Kalra S, Sahay R. Diabetes fatigue syndrome. Diabetes Ther. 2018;9:1421–9.
[16] Yesavage JA. Development and validation of a geriatric depression screening scale: a preliminary report. J Psychiatr Res. 1982;17:37–49.
[17] Ertan TE, Şar V. Geriatrik depresyon ölçeğinin Türk yaşlı nüfusunda geçerlilik ve güvenilirliği. Nöropsikiyatri Arşivi. 34:62–71.
[18] Gencay-Can A, Can SS. Validation of the Turkish version of the fatigue severity scale in patients with fibromyalgia. Rheumatol Int 2012;32:27–31.

[19] Eisenstaedt R, Penninx BW, Woodman RC. Anemia in the elderly: current understanding and emerging concepts. Blood Rev. 2006;20:213–26.
[20] WHO. The Global Prevalence of Anaemia in 2011. Geneva, Switzerland: World Health Organization, 2015.
[21] Oberley MJ, Yang DT. Laboratory testing for cobalamin deficiency in megaloblastic anemia. Am J Hematol. 2013;88:522–6.
[22] Fairbanks VF. Laboratory testing for iron status. Hosp Pract (Off Ed). 1991;26(Suppl 3):17–24.
[23] Giustina A. Controversies in Vitamin D: summary statement from an international conference. J Clin Endocrinol Metab. 2019;104:234–40.
[24] Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem. 1972;18:499–502.
[25] Mezuk B. Depression and type 2 diabetes over the lifespan: a meta-analysis. Diabetes Care. 2008;31:2383–90.
[26] Gorska-Ciebiada M. Mild cognitive impairment and depressive symptoms in elderly patients with diabetes: prevalence, risk factors, and comorbidity. J Diabetes Res. 2014;2014:179648.
[27] Bai YL. Correlates of depression in type 2 diabetic elderly patients: a correlational study. Int J Nurs Stud. 2008;45:571–9.
[28] Vu HTT. Depressive symptoms among elderly diabetic patients in Vietnam. Diabetes Metab Syndr Obes. 2018;11:659–65.
[29] De la Roca-Chiapas JM. Association between depression and higher glucose levels in middle-aged Mexican patients with diabetes. Rev Invest Clin. 2013;65:209–13.
[30] Sullivan PF, Neale MC, Kendler KS. Genetic epidemiology of major depression: review and meta-analysis. Am J Psychiatry. 2000;157:1552–62.
[31] Kajantie E, Phillips DI. The effects of sex and hormonal status on the physiological response to acute psychosocial stress. Psychoneuroendocrinology. 2006;31:151–78.
[32] Fisher L. A longitudinal study of affective and anxiety disorders, depressive affect and diabetes distress in adults with Type 2 diabetes. Diabet Med. 2008;25:1096–101.
[33] Aylaz R. Relationship between social support and fatigue in patients with type 2 diabetes mellitus in the east of Turkey. Jpn J Nurs Sci. 2015;12:367–76.
[34] Akerstedt T. Aging and the change in fatigue and sleep – a longitudinal study across 8 years in three age groups. Front Psychol. 2018;9:234.
[35] Silverstein B. The role played by depression associated with somatic symptomatology in accounting for the gender difference in the prevalence of depression. Soc Psychiatry Psychiatr Epidemiol. 2013;48:257–63.
[36] Brod M, Alolga SL, Meneghini L. Barriers to initiating insulin in type 2 diabetes patients: development of a new patient education tool to address myths, misconceptions and clinical realities. Patient. 2014;7:437–50.
[37] Stewart JW. Serum 25-hydroxyvitamin D is related to indicators of overall physical fitness in healthy postmenopausal women. Menopause. 2009;16:1093–101.
[38] Moreira Bde S. The geriatric depression scale and the timed up and go test predict fear of falling in community-dwelling elderly women with type 2 diabetes mellitus: a cross-sectional study. BMC Geriatr. 2016;16:56.
[39] Earl KE. Vitamin D status in chronic fatigue syndrome/myalgic encephalomyelitis: a cohort study from the North-West of England. BMJ Open. 2017;7:e015296.
[40] Latham NK. A randomized, controlled trial of quadriceps resistance exercise and vitamin D in frail older people: the Frailty Interventions Trial in Elderly Subjects (FITNESS). J Am Geriatr Soc. 2003;51:291–9.
[41] Nanri A. Serum 25-hydroxyvitamin d concentrations and season-specific correlates in Japanese adults. J Epidemiol. 2011;21:346–53.
[42] Shaffer JA. Vitamin D supplementation for depressive symptoms: a systematic review and meta-analysis of randomized controlled trials. Psychosom Med. 2014;76:190–6.
[43] Hoogendijk WJ. Depression is associated with decreased 25-hydroxyvitamin D and increased parathyroid hormone levels in older adults. Arch Gen Psychiatry. 2008;65:508–12.
[44] Vulser H. Association between depression and anemia in otherwise healthy adults. Acta Psychiatr Scand. 2016;134:150–60.
[45] Lever-van Milligen BA. Hemoglobin levels in persons with depressive and/or anxiety disorders. J Psychosom Res. 2014;76:317–21.
[46] Cella D. The longitudinal relationship of hemoglobin, fatigue and quality of life in anemic cancer patients: results from five randomized clinical trials. Ann Oncol. 2004;15:979–86.
[47] Seppala J. Association between vitamin b12 levels and melancholic depressive symptoms: a Finnish population-based study. BMC Psych. 2013;13:145.
[48] Beydoun MA. Serum folate, vitamin B-12, and homocysteine and their association with depressive symptoms among U.S. adults. Psychosom Med. 2010;72:862–73.