

# The association of diabetes duration and glycemic control with depression in elderly men with type 2 diabetes mellitus

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**Background:** The prevalence of depression and type 2 diabetes mellitus (T2DM) are increasing in the elderly and are reportedly related to each other. We evaluated the relationship between T2DM-related factors and the degree of depression in elderly patients with T2DM based on gender. **Materials and Methods:** A total of 155 patients with T2DM (56 males and 99 females aged  $\geq 65$  years) from seven hospitals were included in the study. To assess the status of depressive symptoms, the short form of the Geriatric Depression Scale-Korean version (SGDS-K) was used. We evaluated DM-related factors, such as T2DM duration, hemoglobin A1c (HbA1c) levels, and T2DM complications, as well as other possible factors that could affect depression, such as cognitive function, physical function, education level, and other personal factors. **Results:** Mean age of the participants was 71.3 years with a mean HbA1c level of 7.6%. Males in the good glycemic control group (HbA1c  $<7\%$ ) showed lower SGDS-K scores compared to those in the poor glycemic control group, and the mean SGDS-K score was higher in the group with a longer duration of DM (M10 years); however, no difference was observed in females. Males and females with microvascular and macrovascular complications tended to have higher SGDS-K scores than participants with no microvascular or macrovascular complications. A multiple linear regression analysis revealed that DM duration and HbA1c level were independently associated with SGDS-K scores in males. **Conclusion:** Greater depression was associated with poorer glycemic control and a longer duration of DM in elderly males with T2DM.

**Keywords:** Depressive symptoms, diabetes mellitus, elderly, type 2

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## INTRODUCTION

The population aged 65 years or older in Korea is increasing, with a proportion of 13.8% in the overall population.<sup>[1]</sup> Depression and type 2 diabetes mellitus (T2DM) are one of the most common diseases in the elderly, with depression being more prevalent in the elderly with T2DM. It was reported that approximately

30% of people with diabetes have depressive symptom, 10% have major depression, and people with diabetes have twice the risk of depression compared with individuals without diabetes.<sup>[2]</sup>

The relationship between depression and T2DM seems to be bidirectional.<sup>[3]</sup> The diagnosis of diabetes itself and the burden associated with its complications might lead to depressive symptoms. Several factors associated

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with depressive symptoms such as physical inactivity, hypercaloric diet, and obesity might induce insulin resistant.<sup>[4]</sup> Although the mechanism remains unclear, neuroendocrine changes, such as chronic dysregulations of the hypothalamic–pituitary–adrenal (HPA) axis and the sympathetic nervous system (SNS), may provide a unifying explanation.<sup>[5]</sup>

There have been studies linking T2DM and depression. It was reported that depression is associated with a 60% increase in the risk of T2DM, and T2DM is associated with only modest increase risk of depression.<sup>[3]</sup> Another study showed that the risk of developing diabetes was three times higher for patients reporting a high versus low number of depressive symptoms.<sup>[6]</sup> In some studies, diabetic patients with depression are associated with poor glycemic control, lower adherence to diet, exercise, and taking medications, compared to those without depression.<sup>[7,8]</sup> However, other studies reported conflicting results claiming a negative relationship between depression and glycemic control, DM duration, or DM complications.<sup>[9,10]</sup> It is suspected that the relationships between depression and T2DM-related factors may vary based on the background of the subject.

Therefore, we aimed to evaluate the relationships between T2DM-related factors and the degree of depression based on gender in elderly patients with T2DM. We also evaluated and took into consideration other possible factors that can affect depression, such as cognitive function, physical function, education level, and other personal factors.

## MATERIALS AND METHODS

### Study subjects

This cross-sectional study included elderly patients  $\geq 65$  years with T2DM who visited the departments of endocrinology and metabolism of seven general hospitals in Korea between February 2008 and June 2011. Patients with active infection, malignancy, dementia, depression, or gait disturbance were excluded from the study.

Sample size was calculated using the formula:

$$n = (Z_{1-\alpha})^2 \times (P [(1 - P)]/D^2), Z_{1-\alpha} = Z_{0.95} = 1.96$$

Where  $Z$  is the level of confidence (95%) according to a standard normal distribution,  $P$  is the proportion of diabetic patients with severe depression (10% in this study),<sup>[2]</sup> and  $D$  is the margin of error (0.05). In this study, the minimum sample size needed was 138 patients.

A total of 155 enrolled patients had visited one of the seven hospitals and received treatment such as oral

hypoglycemic agents or insulin or lifestyle modification. One patient withdrew from the study; therefore, the data of 154 patients were used for the analysis. Approval for this study was granted by the Institutional Review Board at each participating hospital, and all enrolled participants provided written informed consent.

### Data collection

The participants' clinical characteristics and diabetic complications were assessed on enrollment in the study. All participants were interviewed to identify the duration of T2DM, level of education, number of family members, sleeping habits, smoking history, alcohol consumption, physical activity, and various comorbid conditions, including hypertension, dyslipidemia, coronary heart disease (CHD), myocardial infarction (MI), and cerebrovascular disease (CVD). Diabetic complications were assessed based on the medical record findings for each participant. CHD, MI, and CVD were classified as macrovascular diseases, and diabetic neuropathy/nephropathy/retinopathy was classified as microvascular diseases. Diabetic neuropathy was defined using neurological symptoms, current perception thresholds, vibratory perception thresholds, nerve conduction velocity, or through a cardiovascular autonomic function test. Diabetic nephropathy was defined using the urinary albumin-to-creatinine ratio and serum creatinine assays, and diabetic retinopathy was defined through a fundoscopic examination.

To assess the status of depressive symptoms, we used the short form of the Geriatric Depression Scale-Korean version (SGDS-K), which is a depression measuring tool consisting of 15 questions and used extensively in older populations,<sup>[11,12]</sup> with scores of 0–4 being considered normal, 5–8 (mild depression), 9–11 (moderate depression), and 12–15 (severe depression). We used the Korean version of the Mini-Mental State Examination (K-MMSE),<sup>[13]</sup> which is one of the most widely used tools to measure global cognitive functions.<sup>[14]</sup> MMSE is a 30-point questionnaire that examines functions, including registration, attention and calculation, recall, language, the ability to follow simple commands and orientation. Any score  $\geq 24$  points (out of 30) indicates a normal cognition. Below this, scores can indicate severe (0–9 points), moderate (10–18 points), or mild (19–23 points) cognitive impairment. The Seoul Instrumental Activity of Daily Living (S-IADL) score was also implemented.<sup>[15]</sup>

To assess the physical functional status in participants, grip strength and sit-to-stand tests were conducted. Grip strength of each hand was measured twice using a dynamometer two times, and the mean was used in the analysis. The sit-to-stand tests were timed in sets of five cycles with the arms crossed.

Laboratory tests included glycated hemoglobin A1c (HbA1c), total cholesterol, triglycerides, high-density lipoprotein-cholesterol, and low-density lipoprotein-cholesterol.

### Statistical analysis

Continuous variables are reported as means  $\pm$  standard deviations, and categorical variables are expressed as frequencies and percentages. Mean SGDS-K scores according to HbA1c level, T2DM duration, and T2DM complications were compared using the *t*-test. Correlation analysis and multiple regression analysis were used to establish the relationships between SGDS-K and multiple variables. All analyses were performed with SPSS version 16 software (SPSS, Inc., Chicago, IL, USA). A value of  $P < 0.05$  was considered statistically significant.

## RESULTS

### Baseline characteristics of the participants

A total of 154 participants with T2DM were included in the current analysis. The baseline characteristics of the participants are shown in Table 1. Males made up 35.7% of the study group and females made up 64.3%. Mean T2DM duration was 12.8 years (range: 1 month–40 years), and mean HbA1c was 7.6% (range: 5.7%–14%). About 23.5% of the participants were included in an unschooled category, whereas participants with higher education comprised 27.5% of all participants. T2DM-associated complications were absent for 52.7% of the participants, but 32.8% had microvascular complications such as neuropathy, retinopathy, and nephropathy. Around 4.6% had macrovascular complications and 9.9% had both microvascular and macrovascular complications.

The mean SGDS-K score was 4.8 (range: 0–15). The mean K-MMSE and S-IADL scores were 24.7 and 2.7, respectively. Female participants had lower K-MMSE scores, better S-IADL scores, and poorer SGDS-K scores than males.

### Geriatric Depression Scale-Korean according to type 2 diabetes mellitus-related factors in males and females

When we assessed SGDS-K according to the glycemic control, based on the HbA1c  $<7\%$  and  $>7\%$ , the well-controlled group showed significantly lower SGDS-K scores compared to the less-controlled group ( $1.94 \pm 2.59$  vs.  $4.54 \pm 3.57$ ,  $P = 0.016$ ) in males. On the other hand, mean SGDS-K scores of both the groups did not show any significant differences in females [Figure 1a].

After classifying T2DM duration into two groups ( $<10$  years and  $>10$  years), mean SGDS-K scores were higher in the group with a longer duration of T2DM in both gender groups, but this trend showed significance in the male

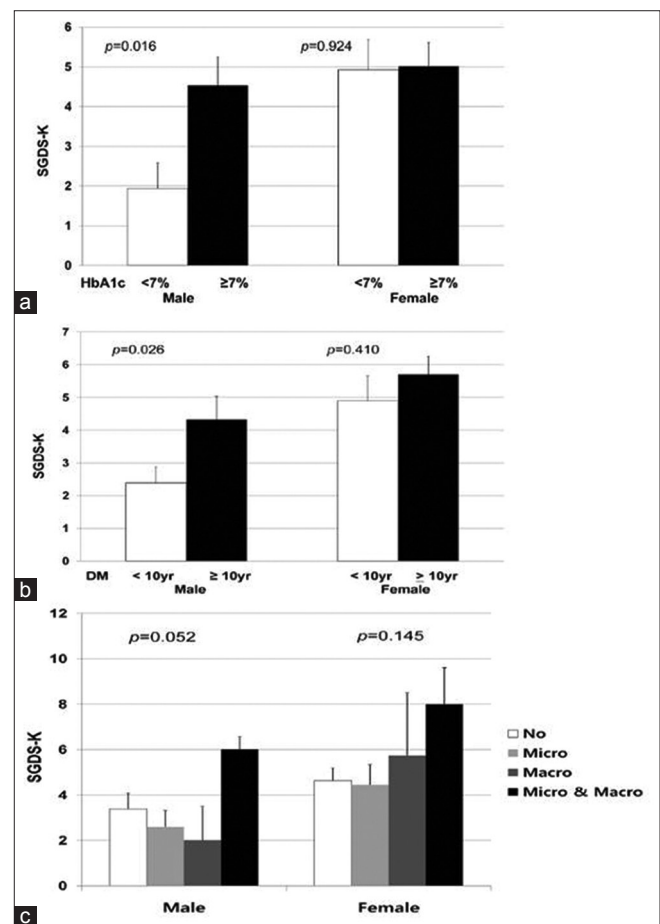
group ( $4.33 \pm 3.84$  in the longer duration group vs.  $2.39 \pm 2.29$  in the shorter duration group,  $P = 0.026$ ) [Figure 1b], but not in the female group ( $5.71 \pm 4.53$  vs.  $4.90 \pm 4.28$ ,  $P = 0.410$ ).

Males and females with both microvascular and macrovascular complications tended to have higher SGDS-K scores compared to participants with no complications or with only microvascular or macrovascular complications ( $P = 0.052$  in males,  $P = 0.145$  in females) [Figure 1c].

### Correlations between Geriatric Depression Scale-Korean and multiple variables

We analyzed the correlations between SGDS-K scores and multiple variables including age, body mass index, HbA1c, T2DM duration, sleeping habits, number of family members, education levels, K-MMSE, S-IADL, and physical function status [Table 2].

In males, HbA1c and T2DM duration showed a positive correlation with SGDS-K ( $r = 0.436$ ,  $P = 0.004$  and  $r = 0.406$ ,



**Figure 1:** Geriatric Depression Scale-Korean scores according to Type 2 diabetes mellitus-related factors in males and females Geriatric Depression Scale-Korean scores according to (a) hemoglobin A1c level, (b) diabetes mellitus duration, and (c) diabetes mellitus complications. micro: microvascular complications; macro: macrovascular complications; micro and macro: both microvascular and macrovascular complications

**Table 1: Baseline characteristics of the study participants**

Character	Total	Male	Female	P
n (%)	154	55 (35.7)	99 (64.3)	
Age (years)	71.3±4.6	72.2±5.4	70.7±4.1	0.034
DM duration (years)	12.8±9.3	11.2±9.2	13.8±9.3	0.679
BMI (kg/m <sup>2</sup> )	25±3.5	25.2±2.8	25.0±3.8	0.055
Sleep duration (h)	6.7±1.6	6.9±1.7	6.7±1.6	0.932
Number in family	2.7±1.8	2.3±1.6	2.5±1.9	0.053
HbA1c (%)	7.6±1.4	7.5±1.4	7.7±1.4	0.624
Total cholesterol (mg/dL)	162.3±36.6	155.7±31.6	166.0±38.9	0.207
Triglyceride (mg/dL)	137.6±98.0	144.0±85.3	134.4±104.2	0.551
HDL cholesterol (mg/dL)	51.7±31.1	45.0±11.2	55.1±37.0	0.273
LDL cholesterol (mg/dL)	89.1±32.5	86.5±28.3	90.5±34.6	0.411
K-MMSE	24.7±4.2	26.0±3.7	24.0±4.3	0.009
S-IADL	2.7±3.9	1.7±2.4	3.3±4.4	0.002
SGDS-K	4.8±4.2	3.5±3.4	5.4±4.4	0.005
Education level, n (%)				
Unschooling	36 (23.5)	4 (7.4)	32 (32.3)	<0.001
Elementary school	53 (34.6)	11 (20.4)	42 (42.4)	
Middle school	21 (13.7)	11 (20.4)	10 (10.1)	
High school	22 (14.4)	11 (20.4)	11 (11.1)	
College	20 (13.1)	17 (31.5)	3 (3)	
Missing	2			
Physical activity, n (%)				
In bed or seated	20 (13.1)	4 (7.7)	12 (13.2)	0.002
Light activities	71 (46.4)	18 (34.6)	47 (51.6)	
Heavy activities	62 (40.5)	30 (57.7)	32 (35.2)	
Missing	1			
Physical function				
Grip strength	23.03±7.06	29.71±6.65	19.52±4.15	<0.001
Sit-to-stand test	16.53±5.63	14.33±4.59	17.74±5.80	0.099
DM treatment modality, n (%)				
Lifestyle modification	3 (2.3)	2 (4.3)	1 (1.2)	0.740
Oral medication only	99 (76.7)	35 (74.5)	64 (78)	
Insulin only	8 (6.2)	4 (8.5)	4 (4.9)	
Oral medication+insulin	19 (14.7)	6 (10.9)	13 (15.9)	
Missing	25			
Diabetic complications, n (%)				
None	69 (52.7)	24 (51.1)	45 (53.6)	0.932
Microvascular	43 (32.8)	17 (36.2)	26 (31)	
Macrovascular	6 (4.6)	2 (4.3)	4 (4.8)	
Microvascular and macrovascular	13 (9.9)	4 (8.5)	9 (10.7)	
Missing	23			

Data are means±SDs or n (%). P values are for the comparisons between males and females by the independent t-test. SD=Standard deviation; HDL=High-density lipoprotein cholesterol; LDL=Low-density lipoprotein, K-MMSE=Korean version of Mini-Mental State Examination; S-IADL=Seoul Instrumental Activity of Daily Living; SGDS-K=Short form of the Geriatric Depression Scale-Korean version; BMI=Body mass index; DM=Diabetes mellitus; HbA1c=Hemoglobin A1c

$P = 0.003$ , respectively), and this correlation remained significant after the correction of age. Although T2DM duration and S-IADL seemed to have a positive correlation with SGDS-K in the female, this was not significant after the correction of age.

### Regression analysis between Geriatric Depression Scale-Korean and multiple variables

We performed a regression analysis using the SGDS-K score as the dependent variable and age, T2DM duration, HbA1c

level, S-IADL score, and the number of family members as independent variables, based on the results shown in Table 2. T2DM duration and HbA1c level were significant predictors of the SGDS-K score ( $R^2 = 0.340$ ,  $P = 0.024$ ) in males but not in females [Table 3].

### DISCUSSION

We analyzed the relationships between T2DM-related factors and the degree of depression using the SGDS-K score based on



**Table 2: Correlations of short form of the Geriatric Depression Scale-Korean version scores and multiple variables**

Variables	SGDS-K		SGDS-K (age corrected)	
	r	P	r	P
Male				
Age	0.123	0.386		
BMI	0.062	0.676	0.078	0.667
HbA1c	0.436	0.004	0.423	0.014
DM duration	0.406	0.003	0.426	0.013
Sleep duration	0.198	0.159	-0.019	0.916
Number of in family	0.124	0.376	0.062	0.730
Education	0.005	0.970	0.093	0.606
K-MMSE	-0.132	0.348	0.032	0.858
S-IADL	0.114	0.421	0.101	0.578
Grip strength	-0.235	0.096	-0.124	0.491
Sit-to-stand test	0.232	0.101	0.174	0.334
Female				
Age	-0.061	0.554		
BMI	0.009	0.932	0.020	0.872
HbA1c	0.110	0.331	0.018	0.887
DM duration	0.210	0.040	0.129	0.297
Sleep duration	-0.043	0.673	0.140	0.257
Number of in family	0.058	0.567	0.026	0.832
Education	0.039	0.706	0.102	0.414
K-MMSE	-0.150	0.138	-0.219	0.075
S-IADL	0.202	0.045	0.036	0.774
Grip strength	-0.086	0.397	-0.100	0.419
Sit-to-stand test	0.063	0.542	0.069	0.578

SGDS-K=Short form of the Geriatric Depression Scale-Korean version; K-MMSE=Korean version of Mini-Mental State Examination; S-IADL=Seoul Instrumental Activity of Daily Living; DM=Diabetes mellitus; HDL=High-density lipoprotein cholesterol; LDL=Low-density lipoprotein; HbA1c=Hemoglobin A1c

**Table 3: Results of a regression analysis for male and female short form of the Geriatric Depression Scale-Korean version scores and multiple variables**

Variables	Male		Female	
	$\beta$	P	$\beta$	P
Age	0.178	0.066	-0.112	0.356
DM duration	0.113	0.035	0.024	0.703
HbA1c	0.862	0.044	-0.02	0.958
S-IADL	0.097	0.631	0.029	0.832
Number of in family	0.209	0.911	0.044	0.872

$R^2=0.340$ ,  $P=0.024$  in males. SGDS-K=Short form of the Geriatric Depression Scale-Korean version; S-IADL=Seoul Instrumental Activity of Daily Living; DM=Diabetes mellitus; HbA1c=Hemoglobin A1c

the gender in elderly participants with T2DM. Higher scales of depressive symptom showed an association with higher HbA1c levels and longer duration of T2DM in male participants but not in females. Males and females with both microvascular and macrovascular complications tended to have higher SGDS-K scores than those without complications or those with only microvascular or macrovascular complications.

Previous studies have reported an association between the degree of depression and T2DM-related factors. Other

studies have reported that diabetic patients with depression show an association with higher HbA1c levels and lower adherence to diet, exercise, and taking medications, compared to those without depression.<sup>[7,8]</sup> On the contrary, in 3305 Japanese patients with T2DM, higher score of depressive symptoms was not associated with higher HbA1c levels.<sup>[16]</sup> Rezvafar *et al.* reported no significant association between the level of depressive symptoms and HbA1c level, but an association was found between depression and T2DM duration.<sup>[17]</sup> Van Tilburg *et al.* found an association between depression scores and HbA1c levels in patients with Type 1 DM, but not in patients with T2DM.<sup>[9]</sup> In an Iranian study, depression was not correlated with a duration of diabetes and glycemic control.<sup>[10]</sup> In the present study, an association between depressive symptoms and either higher HbA1c levels or longer duration of T2DM in males was noted. Blood glucose is known to affect mood, and inversely depression has been suggested to be a possible cause of inadequate metabolic control in T2DM patients.<sup>[18]</sup> Duration of diabetes has been reported to have an influence on the development of depression. The longer the duration of T2DM, the risk for developing diabetic complications and health-care expenditures increases, resulting in a higher risk of psychological illnesses.<sup>[19]</sup>

In the current study, the mean SGDS-K score in females was comparable regardless of the level of HbA1c or duration of DM, whereas SGDS-K according to the level of HbA1c and the duration of T2DM showed significant results only in males. It has been reported that women suffer from depression twice as much as males, and possible contributing factors according to gender are higher stress experiences and reactivity to stress caused by hormonal effects, more negative self-concepts, and distress due to rumination.<sup>[20]</sup>

Taking these into consideration, there is speculation that depression could be less affected by glucose levels in females, based on the findings in this study. Furthermore, in view of the impact of sexual hormones on glucose homeostasis, the molecular pathways involved in insulin resistance might affect gender specificity mechanism in the development of diabetic complications. Some factors, such as Vitamin D levels,<sup>[21]</sup> which may differ between males and females and may be associated with hyperglycemia and insulin resistance, could have affected the results. Further studies are needed to support the gender-specific relationships between depressive symptoms and DM-related factors.

The association between depression and diabetic complications seems to be bidirectional. According to Bruce *et al.*, complications of T2DM negatively affect patient health, which increase the risk of depression.<sup>[22]</sup> Some studies reported that microvascular complications

in patients with T2DM are associated with geriatric decline and functional disabilities,<sup>[23-25]</sup> as well as with duration of diabetes and glycemic control.<sup>[26,27]</sup> Le Floch *et al.*<sup>[28]</sup> reported that the classical microvascular complications of diabetes were associated with impaired Geriatric Scale scores in French patients. In Turkish geriatric patients with T2DM, depression status evaluated using GDS was strongly influenced by T2DM duration and diabetic complications, especially diabetic neuropathy.<sup>[29]</sup> However, in the present study, only patients with both microvascular and macrovascular complications showed a trend of higher SGDS-K scores. Depression is linked to dysregulation of the HPA axis, activation of the SNS, and proinflammatory and procoagulant markers, which may play a role in the progression of microvascular and macrovascular complications in patients with T2DM.<sup>[5]</sup> de Groot *et al.*<sup>[30]</sup> reviewed 27 studies and demonstrated a significant and consistent association of diabetes complications and depressive symptoms in patients with Type 1 and Type 2 DM. The effect size for macrovascular complications was 0.20. In addition, the effect sizes for retinopathy, nephropathy, neuropathy, and sexual dysfunction were 0.17, 0.25, 0.28, and 0.32, respectively.

The present study had some limitations. The study was cross sectional; thus, we were unable to determine whether depressive symptoms preceded or developed subsequent to poor glycemic control. The sample size was relatively small, and the participants were enrolled from several general hospitals, raising concern about the generalizability of our results. Finally, we relied on the SGDS-K without an accompanying diagnostic interview by a professional; however, the SGDS-K is a useful clinical screening tool for evaluating the extent of depression in older populations. The strengths of this study include the fact that it was a multicenter study, and that many factors that could affect the depressive scale, such as cognitive function, ability to be independent, and physical functioning, were also measured. We analyzed the relationships between T2DM-related factors and the degree of depression based on the gender in elderly patients with T2DM.

## CONCLUSIONS

High depressive scale was associated with poorer glycemic control and a longer duration of DM in elderly male patients with T2DM. Future longitudinal studies are needed to reveal the causality between depression and DM-related factors and its gender-specific relationship.

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### Conflicts of interest

There are no conflicts of interest.

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