

Original Article

Care Dependency and Diabetes Self-Care Activities in Elderly Individuals with Diabetes

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Citation: Emine E, Sevgi K, Ezgi Ü, Melike B. Care dependency and diabetes self-care activities in elderly individuals with diabetes. Elderly Health Journal. 2020; 6(2): 131-139. **Introduction:** Changing lifestyle, physical inactivity, and obesity lead to increased diabetes prevalence in the elderly. Diabetes management involves self-care activities, such as medical nutrition therapy, physical activity, use of pharmacologic agent, self-monitoring of blood glucose, foot care, and smoking cessation. Physiological, biological, mental changes that show up with aging and the physiological profile of the elderly individuals can increase care dependency. This study aimed to evaluate the level of care dependency in elderly individuals with diabetes and their diabetes self-care activities and to determine the adaptable factors related to care.

Methods: This descriptive study sampled 136 elderly individuals aged over 65 who presented to the outpatient diabetes center of a hospital in Turkey during 2019. The data were collected using an "Introductory Information Form", the "Diabetes Self-Care Activities Questionnaire", and the "Nursing Care Dependency Scale". The data were analyzed on SPSS software package using descriptive statistics, the Spearman correlation test, student T-test, and one way ANOVA.

Results: The mean age of the participants was 71.9 ± 5.652 . Regarding the self-care activities of the participants, the lowest mean score was in the exercise domain (2.15 ± 2.01) , and the highest mean score was in the foot care domain (6.03 ± 2.02) . The mean care dependency score of the participants was 84.6 ± 1.26 , which meant slight dependency. As for the mean care dependency score of the participants, the lowest mean score belonged to memory (4.91 ± 0.43) and mobility (4.91 ± 0.28) domains. The mean care dependency score of the participants who did not receive diabetes training (84.86 ± 0.59) was higher than those who did (84.22 ± 1.90) (p < 0.05). The increase in the care dependency scores of the participants also increased their general diet, special diet and foot care scores.

Conclusion: Assessment of diabetes self-care activities together with care dependence in elderly people can be used to plan personalized diabetes management.

Keywords: Aged, Self Care, Diabetes Mellitus, Nursing Care

Introduction

Diabetes is a public health problem that has increased threefold in the last 20 years all over the world and is growing in the 21st century (1). With the progressing age, the incidence of diabetes increases, as well. According to the International Diabetes Federation (2019), one in five diabetic patients (136 million people) are in the group aged 65 or over. These data point to significant increases in number of individuals with diabetes in the aging populations in the future and the inevitable public health problems

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and economic issues that will accompany (1). Diabetes is a chronic disease that affects individuals of all ages and their relatives, is irreversible, has a heavy economic burden due to chronic damages, reduces selfcare activities and quality of life, and shortens the life expectancy (2-6). If diabetes is not treated and managed well and timely in elderly, it causes acute and chronic complications, thereby increasing mortality and morbidity (6, 7).

The goal of diabetes management is to achieve glycemic control and to prevent complications. The effective management of diabetes is possible by maintaining diabetes self-care activities (8, 4). Due to the physiological, biological, and mental changes showing up with advancing age, care dependency increases (9-12). When a person with care dependency cannot practice self-care, new problems may arise and these emerging problems may also increase care dependency (13).

Care dependency is defined as the need for support in at least one care area to address a lack of self-care (14). Care areas that one may need supporting include nutrition, continence, body posture, mobility, day-night pattern, dressing and undressing, body temperature, body cleansing, avoiding dangers, communication, establishing relationships with others, following rules, daily activities, recreational activities, and memory and learning ability (15). Elderly people diagnosed with diabetes have emerging needs, such as medical aid and compliance with treatment, and these needs require new self-care activities (15). Indeed, medical nutrition therapy, physical activity, foot care, self-monitoring of blood glucose, smoking cessation and the use of oral antidiabetic drugs and insulin are diabetes self-care activities that should be maintained by individuals with diabetes (16, 7) Both physiological changes and new requirements related to diabetes management increase individuals' care dependency (17, 18).

It is the responsibility of the nurse to assess the selfcare of individuals, to ensure that their self-care needs are met, and to help them regain independence if possible (19). Fulfilling this responsibility requires knowledge and awareness of care dependency. The dependence of elderly people on care has been studied in various populations. Some studies have evaluated the care dependency among elderly individuals who had chronic obstructive pulmonary disease (COPD), heart failure, multimorbidity, were receiving treatment at nursing homes or as inpatients (20-26, 13). In all of the studies that could be accessed, it was determined that the studied population had restrictions / obstacles to performing daily living activities. However, there was no study examining the care dependency status of individuals with diabetes who continued their outpatient treatment and were seen to carry out their daily living activities.

The main task of diabetes care providers is to recommend effective self-care regimens and encourage patients to perform the necessary self-care behaviors (27, 16) According to Orem, individuals have the capacity to learn and develop, and self-care is something that can be learned. Also, self-care agency can be improved. Nurses create conditions that maximize older people's potential for independence and help them make autonomous decisions (28). With the nursing care provided, the dependency level of individuals can be changed. Nurses can positively change the self-care activities of the individuals with their own interventions to reduce dependence on care. Knowing the relationship between the level of care dependency and self-care activities in elderly individuals with diabetes will raise awareness on this issue. Determining the levels of care dependency and related factors will guide nurses. For this reason, the present study aimed to evaluate the level of care dependency of elderly people with diabetes and their diabetes self-care activities and to determine the adaptable factors related to care dependency.

Methods

Study design

This study used a descriptive design and was carried out in the outpatient diabetes center of an education and research hospital. The study sample consisted of elderly people with diabetes who presented to the Diabetes Center Polyclinic of a Training and Research Hospital in Üsküdar district of Istanbul for four months (June-September 2019). The data were collected using an "Interview Form", which aimed to collect information about patients' clinical and laboratory findings and sociodemographic characteristics, the "Diabetes Self-Care Activities Questionnaire", and the "Nursing care dependency scale"(4, 29).

Variables of the research

The dependent variables of the study included care dependency levels and diabetes self-care activities of the patients, and the independent variables consisted of descriptive characteristics of the patients (age, educational status, chronic disease status, the status of receiving diabetes training, treatment type, body mass index, and duration of diabetes).

Setting and participants

We used the purposive sampling method in the study. The sample of the study consisted of 136 patients who applied to the Training and Research Hospital Diabetes Center outpatient clinic and met the study criteria. These criteria included patients who were older than 65, had type 2 diabetes, did not have a communication problem, could understand and answer questions, and did not have a psychiatric or cerebral disorder as defined by the Diagnostic and Statistical Manual of Mental Disorders of the American Psychiatric Association (30). Individuals aged under 65 with communication problems were not included in the sample.

Data collection procedures and instruments

The forms used in data collection were filled out by the researchers by interviewing the elderly people face-to-face. The researchers administered the Interview Form, the Diabetes Self-Care Activities Questionnaire, and the Nursing Care Dependency scale to patients who presented to the clinic, met the inclusion criteria, agreed to participate in the study, and submitted written and verbal consent after they were informed. Each interview took approximately 10-15 minutes. Data about HgA1c, height, weight, and waist circumference measurements to be used in the study were obtained from the outpatient files with the permission of the patients.

The interview form

This form was designed in light of the literature (31, 32, 14). The interview form consisted of three parts. The first part included questions about clinical and laboratory findings (height, weight, waist circumference, Body Mass Index (BMI)), the questions in the second part were about socio-demographic characteristics (age, gender, the status of education, marital status, income status, health insurance, employment, and job), and the third part questioned the disease history (family history of diabetes, duration of diabetes, type of treatment, and the status of other chronic diseases).

The Turkish Diabetes Self-Care Activities Summary Questionnaire (T-SDSCA)

To determine the self-care activities of the individuals with diabetes in this study, the Summary of Diabetes Self-Care Activities Questionnaire – SDSCA was employed (4). It is the revised form of the "Diabetes Self-Care Activities Questionnaire" (DSCA), which was developed by Toobert and Glasgow (1994) (33).

The responses on the questionnaire are marked on a scale to show a day between 0 and 7. Only item 11, which questions smoking, is responded as "0 - I do not smoke or 1- I smoke (and the number of cigarettes consumed a day). Each sub-dimension of the scale is scored separately and can be used independently. Accordingly;

The first four items on the scale are used to determine the status of nutritional practices. The mean of the items 1 and 2 shows the overall diet score, and the mean of the items 3 and 4 shows the recommended special diet score (the score of the 4^{th} item is inversed). The mean score of all items makes up the "diet score".

The mean of the items 5 and 6 indicates the "exercise score".

The mean of the items 7 and 8 shows the "blood sugar test score".

The mean of the items 9 and 10 corresponds to the "foot care" score.

Item 11 shows the smoking status (0 = non-smoker, 1 = smoker) and the number of cigarettes consumed a day. The scores of the sections other than the item 11 questioning smoking are expected to be high. A high score related to a given section indicates that the self-care activity in that section is performed more often.

The researchers who developed and redesigned the scale stated that the data to be obtained with the new version (day/week) would not be directly compared with findings (scored over 100 points) obtained by

the previous studies but that comparison would be possible after the conversion of the data obtained (33). The validity and reliability study of this questionnaire in our country was carried out by Coşansu in 2009 (4). Cronbach's alpha coefficients of the questionnaire, which is called The Turkish Diabetes Self-Care Activities Summary Questionnaire (T-SDSCA), were found as .59 for diet, .70 for exercise, .94 for blood sugar test, and .77 for foot care.

The Nursing- Care Dependency Scale (NCD)

This scale, which was developed by Dijkstra in the Netherlands in 1994, was based on Virginia Henderson's human needs and developed to evaluate patients' care dependency status (34). The reliability and validity study of the scale for the Turkish context was carried out by Yönt et al. in 2010 (29). The scale has a 5-point Likert-type scoring system and consists of 17 items that question daily life activities. The items are rated between 1 = completely care dependent and 5 = almost independent. The minimum and maximum scores that can be obtained from the scale range between 17 and 85. A high score indicates that the patient is independent in meeting self-care needs, while a low score shows that the patient is dependent on others in meeting their care needs. Cronbach's alpha value of the scale is 0.91. In our study, Cronbach's alpha value was determined as 0.92.

Ethical considerations

The study was approved by the Ethical Research Committee of Uskudar University Medical Sciences Institute (Issue: 61351342/2019-68). In addition, the written permission of the Training and Research Hospital Diabetes Center Policlinic were obtained. We paid special care to the principle of volunteering in participation in the study and explained the purpose of the study, our expectations, and legal rights to the patients making up the study group. Afterward, written and verbal informed consent of the patients was obtained.

Data analysis

The data were analyzed on SPSS version 22.0 software package using parametric and nonparametric statistical analyses. Descriptive data were presented using numbers, percentages, and mean scores. The relationship between scale scores and independent variables was evaluated with ANOVA and T-test in the data meeting the parametric assumptions, while Kruskal Wallis Variance analysis and the Mann-Whitney U test were employed to analyze data that did not meet the parametric assumptions. The relationship between care dependency and self-care activities was evaluated multivariate regression analysis. with The significance level and confidence interval of the obtained findings were accepted as p < 0.05 and 95%, respectively.

Results

According to the findings, 55.9% of the elderly were primary school graduates, 86.8% were married, 94.9% were unemployed, 79.4% had a moderate economic status, 98.5% had social security, and 72.1% lived with their spouse and children. The mean age was 71.9 ± 5.65 years, and the mean number of children was 2.5 ± 0.63 .

Of the elderly with diabetes, 78.6% (107 people) were overweight or obese, and the mean BMI was 29.7 \pm 4.85. As for chronic complications, 60.3% (82 people) of the elderly had hypertension, and 39.7% (34 people) had cardiovascular diseases. The mean HgA1c was 7.84 \pm 1.65.

Findings indicated that 41.2% of the elderly had diabetes for 15 years or more, 50.7% were treated with oral antidiabetics, 10.3% were using insulin, and the mean duration of insulin use was 2.72 ± 5.2 years. Also, 60.3% of the elderly had diabetes in their family, 55.1% of them had a first degree relative with diabetes, and 8.8% had a second degree relative with diabetes. Besides, the spouse of 16.9% of the elderly had diabetes.

The lowest mean score was in the "exercise" domain (2.15 ± 2.01) , and the highest mean score was in the "foot care" domain (6.03 ± 2.02) (Table 1). The mean care dependency score of the elderly was 84.6 ± 1.26 .

We found that none of the participants had marked the "completely care dependent" option in all 17 sub-items of the NCD Scale. Only five participants marked the "to a great extent care dependent" option. Five people marked the "partially care dependent" option and "day/night pattern and memory, daily activities" items. Thirtythree people marked the "to a very extent dependent" option, and the most marked item was "mobility". The mean score of this item was 4.91 \pm 0.28. The second most marked item in this option was "body posture" (7 people), and the mean score was 4.94 ± 0.22 . The third most marked items were "avoidance of danger" and "recreational activities", with a mean score of 4.98 ± 0.12 . The analysis of the mean item scores indicated that the lowest mean score belonged to "memory and mobility" items (Table 2).

A statistically significant difference was found between the mean care dependency scores of the elderly in terms of receiving diabetes training in the past year (p < 0.05). The mean care dependency score of the patients who had not received any diabetes training (84.86 \pm 0.59) was significantly higher than those who had received training (84.22 \pm 1.90) (p < 0.05). There was a statistically significant difference between the mean care dependency scores of the elderly in terms of the number of diabetes training sessions (p < 0.05). Further analysis indicated that the mean care dependency score of those who had received diabetes training three times (84.17 \pm 2.37) was significantly lower (p < 0.05). There was no significant difference between the mean care dependency scores in terms of diabetes treatment type, BMI status, and the duration of diabetes (p > 0.05). An insignificant negative relationship was found between age and care dependency (r = -0.07, p = 0.415). Also, an insignificant negative relationship was found between HgA1c levels and care dependency scores (r = -0.01, p = 0.906) (Table 3)

The relationship between care dependency and self-care activities was evaluated with regression analysis. The independent variables included in the model explained 98% of care dependency (R2 = 0.975). The regression model established was significant due to the values of F and P (F = 721.6and p < 0.001) in the ANOVA table. According to the coefficients table, when other variables were kept constant, a one-unit increase in the overall diet score created 1.743 units increase in the care dependency score. The coefficient was significant (p = 0.001). When other variables were kept constant, a one-unit increase in special diet score created 2.037 units increase in the care dependency score. The coefficient was significant (p = 0.001). When other variables were kept constant, a one-unit increase in foot care score created 3,318 units increase in the care dependency score, which yielded a significant coefficient (p < 0.001). Exercise, blood sugar, and the number of cigarettes consumed daily had no significant effect on care dependency (Table 4).

Discussion

The mean care dependency score of the participants was 84.6 ± 1.26 , which meant slight dependency. Regarding the self-care activities of the participants, the lowest mean score was in the "exercise" domain and the highest mean score was in the "foot care" domain. As for the mean care dependency score of the participants, the lowest mean score belonged to memory and mobility domains. The mean score of care dependency of individuals who did not receive diabetes training was higher than those who did. The increase in the care dependency scores of the participants also increased their general diet, special diet, and foot care scores.

 Table 1. Distribution of the average self-care activities of the elderly (n= 136)

Self care activities (range= 0-7)	Mear	n ± SD	
Diet	3.8 ±	= 1.43	
Exercise	2.1	5 ± 2.01	
Blood sugar test	3.37 ± 2.84		
Foot care	6.03	± 2.02	
Smoking status (n = 136)	Ν	%	
Yes	10	7.4	
No	126	92.6	

Table 2. Distribution of responses to nursing care dependency scale items

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	Ability to sort out daily	0	0	2	0	1	0.7	1	0.7	134	98.5	4.97 ± 0.19	
activities		_	_	_	_	_	_	_					
Participating in social 0 0 0 0 0 2 1.5 134 98.5 4.98 ± 0.12		0	0	0	0	0	0	2	1.5	134	98.5	4.98 ± 0.12	
activities				-		-							
Using / remembering 0 0 2 1.5 2 1.5 1 0.7 131 96.3 4.91 ± 0.43		0	0	2	1.5	2	1.5	1	0.7	131	96.3	4.91 ± 0.43	
knowledge / skills	8												
learned earlier Learning new 0 0 0 0 1 0.7 135 99.3 4.99 ± 0.08		0	0	0	0	Δ	Δ	1	07	125	00.2	4.00 + 0.09	
		0	0	0	U	0	U	1	0.7	135	99.5	4.99 ± 0.08	
knowledge / skills and recalling previously													
learned knowledge /													
skills	6												

In previous studies, the care dependency scores were lower. For example, the score was found 62.8, 55.3 and 62.9 in hospitalized elderly patients; 74.2 and 69.5 in elderly individuals who did not receive care and received care, respectively; 59.74 in elderly individuals with mobility disorders; 55.3 in patients admitted to a geriatric unit; 71.51 in patients hospitalized in internal medicine and surgical clinics; 59.8 in patients undergoing laparoscopic abdominal surgery; 62.55 in patients with chronic renal failure; and 48.80 in patients diagnosed with COPD (22, 23, 32, 33-42). In these studies, the difference between care dependency scores can be explained by the different characteristics of samples. In all studies, the level of care dependency increased with advancing age (22, 23, 32, 38-42). However, studies also showed that age alone was not a determining factor in the level of care dependency. Indeed, the level of care dependency was higher in cases, such as a decrease in daily life activities, mobility disorder, and functional limitation (39) impaired cognitive functions (38, 26); decreased selfcare agency and the length of hospital stay (40, 23); and multi-morbidity (41, 42, 26). However, the sample of the present study consisted of patients who did not have problems in performing daily life activities and mobility, did not have functional limitations and cognitive problems, and came to the policlinic for prescription and follow-up on their own.

Descriptive characteristics	Answers	n	Care dependency Mean score	SD
Having diabetes	Yes	49	84.2	1.9
education in the past year	No	87	84.8	0.59
				a t = 2.91 p = 0.04*
Number of diabetes	None	87	84.8	0.59
education	Once	14	84.2	1.89
	Twice	12	84.3	1.78
	Three times	23	84.1	2.037**
				^b $\mathbf{F} = 2.81 \text{ p} = 0.042*$
Diabetes treatment	Diet	7 85.0 69 84.7	0.00	
	Pills	69	84.7	1.35
	Pills and insulin	46	84.6	1.3
	Insulin	14	84.6 1.3 84.7 1.07	1.07
				^{<i>b</i>} $\mathbf{F} = 0.34 \mathbf{p} = 0.800$
Duration of	Less than 1 y.	5	85.00	0.00
diabetes	1-5 years	30	84.9	0.25
	6-9 years	21	84.1	2.11
	10-14 years	24	84.6	1.43
	15 years and over	56	84.5	1.12
	5			^{<i>b</i>} F = 1.201 p = 0.3
BMI	Normal	29	84.8	0.40
	Overweight	47	84.3	1.91
	Obese	60	84.7	0.78
				^{<i>b</i>} $\mathbf{F} = 1.650 \text{ p} = 0.196$

Table 3. Distribution of mean scores of care dependency according to descriptive characteristics of the elderly (n =
136)

Table 4. Regression analysis for care dependency in the elderly and levels of self-care activities

Variable	Coefficients	Standard error	t	р	
Overall diet score	1.74	0.51	3.45	0.001*	
Special diet score	2.04	0.59	3.40	0.001*	
Exercise	0.87	0.61	1.42	0.156	
Blood sugar test	0.27	0.43	0.62	0.533	
Foot care	3.32	0.57	5.76	0.000*	
Number of cigarettes smoked per day	-0.11	0.43	-0.24	0.806	

*p < 0.05

Regarding the items of the nursing care dependency scale, all of the individuals with diabetes who participated in the study were found independent in "meeting their needs for eating and drinking", "continence", and "maintaining body temperature in different environmental conditions". Also, 33% of this group stated that they were "care-dependent to a limited extent" in meeting other needs, especially in "ability to move and achieving the appropriate mobility to do a job", "avoidance of dangers", and "participation in social activities". While two of the participants in the study stated that they were partially dependent in terms of "going to sleep and maintaining sleep", partial and to a great extent dependency was observed in "mobility" (one person), "sequencing daily activities" (three individuals), and "using/remembering the previously knowledge/skills learned" (four individuals). When the mean item scores were examined, the lowest mean score determined to belong to the "memory and mobility" item. These results could not be compared with the results of previous studies

due to the difference in sample characteristics. However, the dependency of older adults with diabetes in memory and mobility to a great extent can be explained by their advanced age as problems with memory and mobility increase with age (28).

Differences were found between the age, diabetes education status and the average scores of care dependency. An insignificant negative relationship was found between age and care dependency (r = -0.07, p =0.415). The age of individuals with diabetes making up the sample of this study ranged between 65 and 91, and the mean age was 71.9 years. The negative relationship between age and care dependency supports previous studies (22, 23, 32, 39-42). However, a weak relationship can be explained by the characteristics of the sample. The sample of the study consisted of patients who could do their self-care.

The analysis of the mean care dependency scores of the elderly according to their status of receiving diabetes training in the past year showed that the mean care dependency scores of those who had not received any diabetes training were significantly higher than those who had. Similarly, as the number of diabetes training times increased, the level of care dependency increased, as well. This result supports the study result of Buss et al. Their study showed that training interventions had no effect on care dependency (38). Training that is related to the management of the disease increases the level of care dependency, and this can be explained by increased awareness of individuals about their needs and meeting them. The content of diabetes training consists of information and practices required for diabetes self-care. The individual with diabetes is taught about medical nutrition therapy, physical activity, implementing self-medication, monitoring the results, and protection against risks (16). A person, who does not know the emerging needs of the disease and how to meet the needs, cannot evaluate the status of dependency in these matters. The dependency levels of individuals who had received diabetes training were higher compared to others, and this can be related to their awareness of emerging needs.

Diabetes treatment requires the self-care of the individual along with parameters, such as medical nutrition, exercise, medication therapy, monitoring blood glucose, going to routine health checks, and avoiding risks. Self-care is related to the self-care agency of the individual. Self-care agency is the ability to take up or implement health activities to maintain life, health, and well-being (15, 43). The level of HbA1c in individuals with diabetes is related to individuals' meeting their needs. HbA1c level is expected to be low in individuals with diabetes who are not dependent on others for care and who have high self-care agency (43). Although it was insignificant, a negative relationship was an expected result.

There was no significant difference between mean care dependency scores in terms of diabetes treatment type, BMI status, and duration of diabetes. This finding can be explained with the characteristics of the study sample. The sample group consisted of individuals who could do self-care for diabetes and were not dependent on care.

According to the regression model established between care dependency and diabetes self-care activities, when other variables were kept constant, a one-unit increase in overall diet score created a 1.74 unit increase in care dependency score. The coefficient was significant. When other variables were kept constant, a one-unit increase in the special diet score created a 2.03 unit increase in the care dependency score, which yielded a significant coefficient. The overall diet score shows how long the individual has followed a healthy diet plan in the past seven days and in the past month. The special diet score, on the other hand, is related to the food groups and the amount consumed in the past week. Care dependency is defined as the need for support in at least one care area to compensate for a lack of a self-care area (14). According to this definition, the higher the self-care agency of individuals is, the better the nutritional compliance score can be considered. Söderhamn et al. found a significant relationship between the low selfcare agency of elderly patients and the risk of malnutrition (44).

When other variables were kept constant, a one-unit increase in foot care score created a 3.31 unit increase in care dependency score. The coefficient was significant. This result is consistent with previous a study (45). This study by Erkoç and his friends, which evaluates the foot care behaviors of older adults, shows that elderly people wash their feet every day, use warm water while washing their feet, dry their feet and toes after each wash, cut their toenails superficially and flatly, and use appropriate socks and shoes. showed.

Conclusions

Elderly individuals with diabetes have a care dependency problem, especially in terms of memory, memory and mobility dimensions, and cannot perform exercise and self-care activities. As the foot care, general diet and special diet self-care activities scores increased, the care dependency score increased, as well. According to these findings, it is important to give importance and priority to exercise and memory dimensions when planning the care of elderly people with diabetes. The findings can be used to improve diabetes care for elderly patients. Assessment of diabetes self-care activities and dependency levels in older adults and knowledge of modifiable factors related to care dependency can be used in planning personalized diabetes management. In addition, it is recommended to repeat this study in the elderly with diabetes who have different physiological profiles (in hospital, at home).

Study limitations

The results of this study, which was conducted in a local center, cannot be generalized to the whole universe.

Conflict of interest

The authors of this paper have no conflicts of interest.

Authors' contributions

All authors contributed extensively to the work presented in this manuscript. Sevgi Kızılcı supervised the study and drafted the manuscript; Sevgi Kızılcı and Emine Ekici revised the manuscript critically for important intellectual content. We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

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