

# Evaluation of Medication Adherence According to Frailty Status in Older Diabetic Patients

Yaşlı Diyabetik Hastalarda Kırılganlık Durumuna Göre İlaç Uyumunun Değerlendirilmesi

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## ABSTRACT

**OBJECTIVE:** This study aimed to investigate the relationship between frailty and medication adherence in elderly patients with diabetes mellitus.

**MATERIALS and METHODS:** A cross-sectional study was conducted at Konya City Hospital between May and November 2021, including 194 diabetic patients aged 60 years and older. Frailty status was assessed using the FRAIL scale, and medication adherence was evaluated with the 8-item morisky medication adherence scale. The Modified Charlson Comorbidity index was used to quantify comorbidity burden. Statistical analyses included the chi-square test, Mann-Whitney U test, Kruskal-Wallis test, and logistic regression models.

**RESULTS:** The median age of the participants was 67 years (IQR: 64-71), and 69.6% were female. The prevalence of frailty was 50%, and no significant association was found between frailty and medication adherence ( $p=0.318$ ). However, variables independently associated with low adherence included shorter diabetes duration ( $p=0.049$ ), lack of diabetes education ( $p=0.020$ ), and higher HbA1c levels ( $p=0.010$ ). Patients with low adherence monitored their blood glucose significantly less frequently ( $p=0.008$ ) and had a higher risk of hospitalization.

**CONCLUSION:** Frailty was not significantly associated with medication adherence in elderly diabetic patients. Instead, diabetes education, glycemic control, and self-monitoring practices played a more significant role. These findings highlight the importance of structured education programs and individualized interventions to improve adherence. Future studies with larger sample sizes and longitudinal follow-up are needed to better understand the complex interplay between frailty and adherence.

**KEYWORDS:** Diabetes mellitus, frailty, medication adherence, elderly

## ÖZ

**AMAÇ:** Bu çalışma, yaşlı diyabet hastalarında kırılganlık ile ilaç uyumu arasındaki ilişkiyi araştırmayı amaçladı.

**GEREÇ ve YÖNTEM:** Kesitsel nitelikteki bu çalışma, Mart-Kasım 2021 tarihleri arasında Konya Şehir Hastanesi'nde gerçekleştirildi ve 60 yaş ve üzerindeki 194 diyabet hastası dahil edildi. Kırılganlık durumu FRAIL ölçeği ile, ilaç uyumu ise 8 maddelik morisky ilaç uyumu ölçeği ile değerlendirildi. Komorbidite yükü, Modifiye Charlson Komorbidite indeksi kullanılarak ölçüldü. İstatistiksel analizlerde ki-kare testi, Mann-Whitney U testi, Kruskal-Wallis testi ve lojistik regresyon modelleri kullanıldı.

**BULGULAR:** Katılımcıların medyan yaşı 67 idi (ÇEY: 64-71) ve %69,6'sı kadındı. Kırılganlık prevalansı %50 olarak saptandı ve kırılganlık ile ilaç uyumu arasında anlamlı bir ilişki bulunmadı ( $p=0,318$ ). Ancak, düşük uyumun bağımsız belirleyicileri arasında daha kısa diyabet süresi ( $p=0,049$ ), diyabet eğitimi almamış olmak ( $p=0,020$ ) ve yüksek HbA1c düzeyleri ( $p=0,010$ ) yer aldı. Düşük ilaç uyumu gösteren hastaların kan şekeri takibini daha az sıklıkla yaptığı ( $p=0,008$ ) ve hastaneye yatış risklerinin daha yüksek olduğu görüldü.

**SONUÇ:** Yaşlı diyabet hastalarında kırılganlık ile ilaç uyumu arasında anlamlı bir ilişki saptanmadı. Bunun yerine, diyabet eğitimi, glisemik kontrol ve öz izlem uygulamaları ilaç uyumunda daha belirleyici faktörler olarak öne çıktı. Bu bulgular, yapılandırılmış eğitim programlarının ve bireyselleştirilmiş müdahalelerin ilaç uyumunu artırmadaki önemini vurgulamaktadır. Kırılganlık ve uyum arasındaki karmaşık ilişkinin daha iyi anlaşılabilmesi için daha geniş örneklemli ve uzunlamasına takipli çalışmalara ihtiyaç vardır.

**ANAHTAR KELİMELEER:** Diabetes mellitus, kırılganlık, ilaç uyumu, yaşlı

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## INTRODUCTION

Frailty is a common geriatric syndrome characterized by a decline in physiological reserves, leading to increased vulnerability to adverse health outcomes, including falls, hospitalizations, and mortality (1). Among older adults, frailty is frequently associated with multiple chronic diseases such as hypertension, diabetes, and cardiovascular diseases, making disease management more challenging (2). Medication adherence is crucial for achieving optimal treatment outcomes in these patients. However, frailty may negatively impact adherence due to factors such as cognitive impairment, polypharmacy, functional limitations, or insufficient caregiver support (3).

Previous studies have demonstrated that frail older adults exhibit lower adherence to medications across various chronic conditions, including hypertension and osteoporosis (4). Frailty-related factors, such as reduced mobility and medication-related beliefs, have been identified as mediators of poor adherence in community-dwelling elderly individuals with chronic diseases (5). Despite its clinical importance, the relationship between frailty and medication adherence in older adults with diabetes has not been extensively investigated. Given that poor adherence is associated with adverse outcomes such as poor glycemic control, increased hospitalizations, and higher mortality rates, identifying the factors influencing adherence in frail diabetic patients is essential.

In many global classifications, including those by the United Nations, individuals aged 60 years and older are considered elderly, while the World Health Organization often uses 65 years as a threshold in clinical and health-related contexts (6). In this study, we adopted the 60-year cut-off, which is commonly used in geriatric research and public health studies.

This study aims to evaluate the relationship between frailty and medication adherence in older adults with diabetes mellitus (DM) and to identify factors associated with poor adherence. Understanding these associations may help in developing targeted interventions to improve medication adherence and clinical outcomes in frail elderly diabetic patients.

## MATERIALS & METHODS

### Study Design and Participants

This cross-sectional study was conducted between May and November 2021 at Konya City Hospital, involving 194 patients aged 60 years and older diagnosed with type 2 DM. Patients were excluded if they had dementia, communication barriers, active cancer, intellectual disabilities, or refused to participate. The study was conducted in accordance with ethical principles, and ethical approval was obtained from the institutional review board on April 26, 2021, with decision number 30,162. Written informed consent was obtained from all participants prior to data collection. The study was carried out in accordance with ethical principles and was approved by the Hamidiye Scientific Research Ethics Committee of the University of Health Sciences on April 26, 2021 (decision no: 30162). Written informed consent was obtained from all participants prior to data collection.

### Data Collection

Demographic and clinical data, including age, gender, marital status, education level, diabetes duration, comorbidities, medication use, and HbA1c levels, were recorded. Frailty status was assessed using the FRAIL scale (7), with patients categorized as non-frail (score =0), pre-frail (scores 1-2), and frail (scores  $\geq 3$ ). Medication adherence was evaluated using the 8-item morisky medication adherence scale (MMAS-8), and classified as low (score <6), medium (score 6-7), and high adherence (score =8) based on the thresholds proposed by Morisky et al (8,9). The Modified Charlson Comorbidity index (10,11) was used to quantify comorbidity burden.

### Definitions

Frailty was determined using the FRAIL scale, a validated questionnaire assessing fatigue, resistance, ambulation, illnesses, and weight loss (7). The validity and reliability of the Turkish version were confirmed (8). Medication adherence was evaluated using the MMAS-8, and patients were categorized as having low adherence with a score below 6, moderate adherence with a score between 6 and 7, and high adherence with a score of 8, based on the validated Turkish version (8). Polypharmacy was defined as the use of more than four daily medications. Diabetes complications were defined as the presence of any of the following conditions: diabetic nephropathy, retinopathy, neuropathy, diabetic foot, stroke, or coronary artery disease.

**Statistical Analysis**

All statistical analyses were conducted using SPSS version 27.0 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was assessed using the Kolmogorov-Smirnov and Shapiro-Wilk tests. Since most variables did not follow a normal distribution, continuous data were expressed as median (1<sup>st</sup>-3<sup>rd</sup> quartile) and compared using the Kruskal-Wallis or Mann-Whitney U tests, as appropriate. Effect sizes for non-parametric tests were reported using eta squared ( $\eta^2$ ), calculated from Kruskal-Wallis H statistics. Categorical variables were presented as numbers and percentages, and comparisons between groups were performed using Pearson's chi-square test. Effect sizes for chi-square tests were calculated using Cramér's V. For post-hoc pairwise comparisons following Kruskal-Wallis or chi-square tests, Bonferroni correction was applied to adjust for multiple testing. Univariate and multivariate logistic regression analyses were performed to identify variables associated with low medication adherence. Odds ratios with 95% confidence intervals were reported.

In the multivariate model, a backward stepwise elimination method was used. Statistical significance was set at  $p < 0.05$  for all analyses. All 194 participants had complete data for the variables analyzed, and no imputation was required. A formal sample size calculation was not performed prior to the study; the sample consisted of all eligible patients available during the study period.

**RESULTS**

The study included 194 patients, with a median age of 67 years (IQR: 64-71), and 69.6% were female. Among them, 50% were classified as frail, 30.9% as pre-frail, and 19.1% as non-frail. Frail patients were older ( $p=0.048$ ) and more likely to be single/widowed ( $p=0.003$ ) or illiterate ( $p < 0.001$ ). Diabetes duration was significantly longer in frail individuals ( $p=0.009$ ), and they had higher rates of polypharmacy ( $p=0.020$ ) and diabetes-related complications ( $p=0.004$ ). Blood glucose monitoring was significantly lower in the frail group ( $p=0.015$ ), while there were no significant differences in HbA1c levels or MMAS-8 scores across frailty (Table 1).

**Table 1.** Baseline characteristics and frailty status of patients

Parameters	Total (n=194)	Non-frail (n=37)	Pre-frail (n=60)	Frail (n=97)	p value	Effect size	OR (95% CI)
Age, years	67 (64-71)	65 (64-71)	67 (64-70)	69 (65-73)	0.048	0.021	1.078 (1.022-1.137)
Gender							
Woman	135 (69.6)	23 (62.2)	38 (63.3)	74 (76.3)	0.127		
Male	59 (30.4)	14 (37.8)	22 (36.7)	23 (23.7)			
Single/widow	45 (23.2)	3 (8.1)	10 (16.7)	32 (33.0)	0.003*	0.242	1.899 (1.018-3.542)
Lives alone	19 (9.8)	3 (8.1)	9 (15.0)	7 (7.2)	0.261		
Illiterate	45 (23.2)	4 (10.8)	5 (8.3)	36 (37.1)	<0.001†	0.330	5.770 (2.593-12.844)
Duration of DM	10 (6-20)	10 (4-15)	10 (6-16)	15 (10-20)	0.009‡	0.039	1.045 (1.010-1.081)

Table 1. Continued							
Parameters	Total (n=194)	Non-frail (n=37)	Pre-frail (n=60)	Frail (n=97)	p value	Effect size	OR (95% CI)
Diabetes education	121 (62.4)	24 (64.9)	38 (63.3)	59 (60.8)	0.896		
No BG monitoring	38 (19.6)	4 (10.8)	7 (11.7)	27 (27.8)	0.015§	0.208	3.016 (1.398-6.505)
Polypharmacy	115 (59.3)	19 (51.4)	29 (48.3)	67 (69.1)	0.020¶	0.200	2.280 (1.268-4.098)
HbA1c,	7.5 (6.5-9.2)	7.2 (6.6-8.2)	7.8 (6.5-9.5)	7.6 (6.4-9.5)	0.485		
Complications of DM	139 (71.6)	23 (62.2)	36 (60.0)	80 (82.5)	0.004**	0.241	3.031 (1.561-5.885)
History of hypoglycaemia	101 (52.1)	16 (43.2)	31 (51.7)	54 (55.7)	0.435		
mCCI	6 (5-9)	5 (4-8)	5 (4-7)	8 (6-10)	<0.001††	0.168	1.444 (1.268-1.646)
MMAS-8	6 (4-8)	7 (5-8)	6 (3-7)	7 (4-8)	0.318		

Note: Odds ratios (OR) and 95% confidence intervals (CI) were calculated using the frail group as the reference category.  
 DM: Diabetes mellitus; BG: Blood glucose; HbA1c: Hemoglobin A1c; mCCI: Modified Charlson Comorbidity index; MMAS: Morisky medication adherence scale

\* In post-hoc analysis, non-frail and frail groups had statistically significant differences (p=0.003).  
 † Post-hoc analysis revealed statistically significant differences between non-frail and frail groups (p=0.003) and pre-frail and frail groups (p<0.001).  
 ‡ Post-hoc analysis revealed statistically significant differences between non-frail and frail groups (p=0.004).  
 § Post-hoc analysis revealed statistically significant differences between non-frail and frail groups (p=0.017).  
 ¶ Post-hoc analysis revealed statistically significant differences between pre-frail and frail groups (p=0.010).  
 \*\* Post-hoc analysis revealed statistically significant differences between non-frail and frail groups (p=0.013) and between pre-frail and frail groups (p=0.002).  
 †† Post-hoc analysis revealed statistically significant differences between non-frail and frail groups (p<0.001) and between pre-frail and frail groups (p<0.001).

According to MMAS-8 scores, 36.6% of patients had low adherence, 33.5% had moderate adherence, and 29.9% had high adherence. Patients with low adherence had shorter diabetes duration (p=0.016) and were less likely to have received diabetes education (p=0.015). Lack of blood glucose

monitoring (p=0.008) and lower polypharmacy rates (p=0.010) were also associated with low adherence. HbA1c levels were significantly lower in the high-adherence group (p=0.014), while frailty scores did not differ across adherence groups (Table 2).

**Table 2.** Medication adherence levels according to MMAS-8 score

Parameters	Low (n=71)	Moderate (n=65)	High (n=58)	p value	Effect size
Age, years	67 (65-71)	66 (63-70)	69 (65-72)	0.085	
Gender					
Woman	45 (63.4)	50 (76.9)	40 (69.0)	0.228	
Male	26 (36.6)	15 (23.1)	18 (31.0)		
Single/widow	18 (25.4)	9 (13.8)	18 (31.0)	0.068	
Lives alone	8 (11.3)	5 (7.7)	6 (10.3)	0.771	
Illiterate	14 (19.7)	13 (20.0)	18 (31.0)	0.240	
Duration of DM, years	10 (5-15)	13 (8-20)	15 (10-20)	0.016*	0.020
Diabetes education	35 (49.3)	44 (67.7)	42 (72.4)	0.015†	0.209
No BG monitoring	22 (31.0)	10 (15.4)	6 (10.3)	0.008‡	0.224
Polypharmacy	34 (47.9)	38 (58.5)	43 (74.1)	0.010§	0.217
HbA1c,	7.7 (6.8-9.7)	7.7 (6.6-9.5)	7.0 (6.3-8.3)	0.014¶	0.034
Complications of DM	47 (66.2)	45 (69.2)	47 (81.0)	0.154	
History of hypoglycaemia	30 (42.3)	42 (64.6)	29 (50.0)	0.031**	0.189
mCCI	6 (5-9)	6 (4-10)	8 (5-10)	0.054	
Frail score	3 (1-3)	2 (1-4)	3 (1-3)	0.976	

DM: Diabetes mellitus, BG: Blood glucose, HbA1c: Hemoglobin A1c, mCCI: Modified Charlson Comorbidity index  
 \* Post-hoc analysis revealed statistically significant differences between low and high groups (p=0.010).  
 † Post-hoc analysis revealed statistically significant differences between low and high groups (p=0.008).  
 ‡ Post-hoc analysis revealed statistically significant differences between low and high groups (p=0.005).  
 § Post-hoc analysis revealed statistically significant differences between low and high groups (p=0.002).  
 ¶ Post-hoc analysis revealed statistically significant differences between low and high groups (p=0.007).  
 \*\* Post-hoc analysis revealed statistically significant differences between low and medium groups (p=0.009).

In univariate analysis, factors associated with low medication adherence included shorter diabetes duration (p=0.007), lack of diabetes education (p=0.005), absence of blood glucose monitoring (p=0.003), polypharmacy (p=0.015), higher HbA1c levels (p=0.019), and a history

of hypoglycemia (p=0.039). Multivariate analysis showed that shorter diabetes duration (p=0.049), lack of diabetes education (p=0.020), and higher HbA1c levels (p=0.010) were independently associated with low adherence (Table 3).

**Table 3.** Factors associated with low medication adherence (univariate and multivariate analysis)

Variables	Univariate logistic regression		Multivariate logistic regression	
	OR (95% CI)	p	OR (95% CI)	p
Duration of DM, years	0.950 (0.916-0.986)	0.007	0.961 (0.924-1.000)	0.049
Diabetes education	2.391 (1.307-4.374)	0.005	2.171 (1.132-4.163)	0.020
No BG monitoring	3.003 (1.451-6.214)	0.003		
Polypharmacy	2.099 (1.156-3.810)	0.015		
HbA1c,	1.174 (1.027-1.341)	0.019	1.205 (1.045-1.389)	0.010
History of hypoglycaemia	1.866 (1.033-3.371)	0.039		

Note: Multivariate logistic regression was performed using the backward stepwise method.  
 OR: Odds ratios, CI: Confidence intervals, DM: Diabetes mellitus

**DISCUSSION**

This study evaluated the relationship between frailty and medication adherence in older patients with DM. Contrary to some previous findings, our results did not demonstrate a statistically significant association between frailty and medication adherence, as indicated by MMAS-8 scores across frailty groups (p=0.318) and across adherence levels (p=0.976). This suggests that frailty alone may not be a primary determinant of medication adherence in elderly diabetic patients. While some studies suggest that frailty is associated with lower adherence due to physical and cognitive limitations (12,13), others propose that external support systems and individualized treatment plans may mitigate its impact (14,15).

Frailty has been widely reported among diabetic populations, with varying prevalence rates. Cacciatore et al. (12) observed a frailty prevalence of 41.3% in diabetic patients followed over 12 years and highlighted its impact on mortality. Similarly, Xiu et al. (16) reported that among 240 diabetic patients with a mean age of 68.89±6.88 years, 39.16% were robust, 45.8% were pre-frail, and 15.04% were frail. Thein et al. (17) found a frailty prevalence of 18.9% in their diabetic cohort and noted a higher incidence of cognitive impairment in frail individuals.

In our study, the prevalence of frailty was higher, which may be attributed to factors such as the impact of the COVID-19 pandemic leading to fewer hospital visits by non-frail individuals, the older age of our participants, and the study setting being a tertiary care hospital.

Frailty is closely linked to diabetes complications. Studies have shown that frail diabetic patients exhibit higher rates of microvascular and macrovascular complications (13), and in our study, frail patients also had significantly higher rates of diabetes complications. Additionally, our study found that frailty was significantly associated with longer diabetes duration and higher comorbidity burden, aligning with the literature (14,18). These findings suggest that frailty should be systematically considered in the management of elderly diabetic patients, given its potential implications on overall disease progression and prognosis. These results are in line with previous studies that highlighted the impact of frailty and polypharmacy on adherence, particularly in older adults with osteoporosis and other chronic diseases (19).

Although frailty was not significantly associated with adherence in our study, other factors such as shorter diabetes duration, lack of diabetes education, absence of blood glucose monitoring, and higher HbA1c levels were identified as independently associated with low adherence.

These findings align with previous studies that highlight the critical role of structured education and self-management strategies in improving medication adherence (20,21). Similarly, a recent study conducted in Turkey emphasized the role of frailty in diabetic care, reporting comparable rates of frailty and medication adherence patterns (22). Poor adherence has been associated with worsening glycemic control over time (23) and increased hospitalization risk (24). A meta-analysis of adherence studies reported that only 51.2% of diabetic patients adhere to antihyperglycemic therapy, with better adherence being linked to fewer microvascular and macrovascular complications (25). Furthermore, interventions such as improving physician-patient communication, enhancing motivation strategies, and simplifying dosing regimens have been shown to improve adherence (26,27).

Polypharmacy also emerged as a factor associated with adherence, although it did not remain significant in the multivariate model. The relationship between polypharmacy and adherence is complex, as multiple medications may either improve disease management or contribute to treatment burden and non-adherence. Some studies have suggested that an increasing number of prescribed medications does not necessarily lead to lower adherence, particularly if patients receive appropriate education and support (28,29). Other studies indicate that polypharmacy may be a burden, leading to lower adherence and treatment discontinuation (30). Therefore, ensuring adequate patient education and individualized treatment planning is crucial in managing polypharmacy-related adherence challenges.

Education plays a crucial role in improving medication adherence. Multiple studies have shown that diabetes education is associated with better adherence (27). Williams et al. (31) demonstrated that poor medication adherence was linked to higher glucose and HbA1c levels. Our study supports these findings, as patients who received diabetes education exhibited significantly better adherence. Given the strong association between education and adherence, personalized diabetes education tailored to patients' socio-cultural levels should be prioritized in diabetes management strategies.

Frailty is often accompanied by cognitive decline, which can further impact adherence. Studies have shown that frail

diabetic patients exhibit worse cognitive function compared to their non-frail counterparts, and cognitive impairment may contribute to difficulties in medication management (32). Additionally, poor adherence has been frequently reported in frail individuals with hypertension and other chronic diseases (33). This highlights the need for targeted interventions that address both physical and cognitive impairments in frail elderly patients.

This study has several strengths. Unlike many previous studies focusing only on insulin-treated diabetic patients, we included a broader elderly population with type 2 diabetes, regardless of their treatment modality. Additionally, frailty was assessed alongside sociodemographic and clinical characteristics, providing a multidimensional understanding of its impact on medication adherence. By using validated tools such as the FRAIL scale and MMAS-8, the study ensures methodological reliability. The comprehensive approach adopted in this study enhances the generalizability and practical relevance of its findings for geriatric diabetes care.

This study has certain limitations. Its cross-sectional design precludes the establishment of causal relationships, and reliance on self-reported adherence measures may introduce recall bias. Furthermore, social desirability bias may have influenced participants' responses, as they may have sought to present themselves more favorably. The possibility of a Type II error-failing to detect a true association due to limited statistical power-should also be considered, particularly in interpreting the lack of a significant association between frailty and adherence. Although higher HbA1c levels and a history of hypoglycemia were associated with poor adherence, these findings should be interpreted with caution given the study's cross-sectional nature. Additionally, while frailty was assessed using the FRAIL scale, alternative tools incorporating objective physical performance measures may offer further insights. The single-center design and relatively small sample size may limit the generalizability of the findings. However, all 194 participants had complete datasets; thus, no missing data handling was required. The absence of an a priori sample size calculation and power analysis represents another limitation. Future multicenter, longitudinal studies are warranted to

better evaluate the long-term impact of frailty on medication adherence and related clinical outcomes.

## CONCLUSION

In conclusion, while frailty was not significantly associated with medication adherence in our study, other factors such as diabetes education, glycemic control, and self-monitoring practices played a more prominent role. These findings underscore the value of patient-centered interventions, including structured education programs and simplified medication regimens, to enhance adherence in elderly diabetic patients. Further research is needed to explore the nuanced interplay between frailty and adherence behaviors in this population.

Ethics: The study was carried out in accordance with ethical principles and was approved by the Hamidiye Scientific Research Ethics Committee of the University of Health Sciences on April 26, 2021 (decision no: 30162). Written informed consent was obtained from all participants prior to data collection.

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