THE ATLANTIC Journal of Medical Science and Research

Atlantic J Med Sci Res 2026;6(3):361-7
DOI: 10.5455/atjmed.2026.05.060

Original Article

Tugce Emiroglu Gedik[1], Mucahit Can Yaykin[2], Miray Asilsoy[3], Elif Onder[4], Hande Peynirci[4]

[1]İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics, İstanbul, Türkiye
[2]Health Science University, İstanbul Kanuni Sultan Süleyman Training and Research Hospital, Department of Gerontology, İstanbul, Türkiye
[3]Health Science University, İstanbul Fatih Sultan Mehmet Training and Research Hospital, Department of Internal Medicine, Division of Endocrinology and Metabolism Diseases, İstanbul, Türkiye
[4]Health Science University, İstanbul Kanuni Sultan Süleyman Training and Research Hospital, Department of Internal Medicine, Division of Endocrinology and Metabolism Diseases, İstanbul, Türkiye

Received: 03 June, 2026
Accepted: 20 July, 2026
Published: 14 September, 2026

Corresponding Author: Tugce Emiroglu Gedik, [1]İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics, İstanbul, Türkiye
Email: tugceemiroglu@yahoo.com.tr

CITATION
Emiroglu Gedik T, Yaykin MC, Asilsoy M, et al. Levothyroxine treatment adherence rate and evaluation of related factors in geriatric patients. Atlantic J Med Sci Res. 2026;6(3):361-7. DOI: 10.5455/atjmed.2026.05.060

Levothyroxine treatment adherence rate and evaluation of related factors in geriatric patients

Abstract

Aim: This study aimed to determine the rate of compliance with levothyroxine (LT4) therapy in geriatric patients and to investigate the factors associated with treatment non-adherence.
Materials and Methods: This cross-sectional study included 87 patients aged 65 years or older with primary hypothyroidism who attended the Endocrinology and Geriatrics outpatient clinics between August and November 2023. Medication adherence was assessed using a structured questionnaire. Cognitive function was evaluated with the Standardized Mini-Mental State Examination (MMSE) and depressive symptoms with the Yesavage Geriatric Depression Scale (GDS). Statistical analyses included Student's t-test, Mann-Whitney U test, chi-square test, and binary logistic regression; significance was set at $p < 0.05$.
Results: The mean age of participants was 74.05 ± 6.17 years, and 88.5% were female. The LT4 adherence rate was 56.3% (n = 49). No statistically significant difference was found between adherent and non-adherent groups in terms of age, sex, cognitive status (MMSE: 26.92 ± 2.55 vs. 26.57 ± 3.12; p = 0.57), or depressive symptomatology (GDS: 4.55 ± 3.31 vs. 4.92 ± 3.13; p = 0.59). Median thyroid-stimulating hormone (TSH) levels were significantly higher in PPI users compared to non-users (3.4 vs. 2.7 mIU/L; p = 0.042). Logistic regression analysis did not identify statistically significant independent predictors of non-adherence; however, low educational level (OR: 2.14; p = 0.092) and polypharmacy (OR: 1.87; p = 0.165) showed trends toward increased risk.
Conclusion: LT4 non-adherence affects nearly half of geriatric patients and appears to stem primarily from insufficient knowledge about correct administration conditions rather than cognitive or affective impairment. The significant association between PPI use and elevated TSH levels underscores the importance of reviewing concurrent medications before dose escalation in this population. Clinicians are advised to assess medication administration errors and interacting agents before attributing elevated TSH levels to insufficient dosage.

Keywords: Levothyroxine, medication adherence, hypothyroidism, polypharmacy

INTRODUCTION

Hypothyroidism is one of the most prevalent endocrine disorders in older adults, arising from insufficient thyroid hormone production and affecting critical physiological processes including cardiovascular function, metabolic homeostasis, and neurocognitive performance. In the geriatric population, the condition is often underdiagnosed due to the nonspecific nature of its clinical presentation, which may overlap with common age-related changes such as fatigue, cognitive slowing, and cold intolerance. Although the prevalence of overt hypothyroidism is approximately 0.3% in the general population, this figure rises substantially with age due to the cumulative burden of autoimmune thyroid disease, progressive decline in thyroid reserve, and increasing comorbidity (1). Overt hypothyroidism can be present in up to 5% of older adults, while subclinical

hypothyroidism affects up to 15% of those aged 65 years and older (2). Given the expanding global geriatric population, its accurate recognition and effective management with levothyroxine (LT4) replacement therapy have become increasingly important public health priorities (3,4).

Levothyroxine is a narrow therapeutic index drug administered orally as synthetic thyroxine (T4), which exerts its biological effects following peripheral conversion to triiodothyronine (T3). Achieving stable euthyroidism requires not only accurate dosing but also consistent and correct administration. This is rendered particularly challenging in geriatric patients, whose age-related physiological changes substantially alter the pharmacokinetic and pharmacodynamic profile of LT4 (3-5). Reduced gastrointestinal absorption capacity, decreased gastric acidity, and conditions such as atrophic gastritis may impair drug absorption (6). Declining hepatic and renal function affects metabolism and elimination, while age-related reductions in serum albumin alter plasma protein binding (7). Pharmacodynamically, diminishing tissue sensitivity to thyroid hormones may delay or attenuate clinical response, and heightened cardiovascular vulnerability in older patients makes high-dose initiation a potential trigger for myocardial ischemia. For this reason, current guidelines recommend starting LT4 at low doses in older adults, with close monitoring and gradual titration, and consistent administration 30 to 60 minutes before breakfast or at bedtime — at least three hours after the evening meal — to maximize absorption (8).

Medication adherence is defined by the World Health Organization as 'the degree to which a person's behavior — taking medication, following a diet, and/or executing lifestyle changes — corresponds with agreed recommendations from a health care provider' (9). In developed countries, only approximately 50% of patients with chronic diseases follow their long-term treatments correctly, and in older adults this rate falls below 43%. In the specific context of LT4 therapy, adherence presents additional challenges: the drug must be taken consistently on an empty stomach, at a fixed time each day, and separated from medications that impair its absorption — such as proton pump inhibitors, calcium supplements, and iron preparations — all of which are highly prevalent in this age group. Multimorbidity, polypharmacy, cognitive decline, and limited social support further compound adherence barriers in geriatric patients. Poor adherence to LT4 ultimately leads to thyroid-stimulating hormone (TSH) dysregulation, increasing the risk of cardiovascular complications, cognitive deterioration, and diminished quality of life (10-12).

Despite the clinical significance of these issues, data on LT4-specific adherence patterns in geriatric patients remain limited, particularly in the Turkish population. This study aimed to determine the rates of adherence to and correct use of LT4 therapy among patients aged 65 years and older with primary hypothyroidism, and to investigate the association of geriatric parameters — including cognitive status, depressive symptomatology, and polypharmacy — with treatment non-adherence. We believe the findings of this study will provide important contributions toward improving the management of hypothyroidism in older adults.

MATERIALS AND METHODS

Study Design and Setting

This single-center, cross-sectional study was conducted at the Endocrinology and Metabolism Diseases and Geriatrics outpatient clinics of Health Science University, Istanbul Kanuni Sultan Suleyman Training and Research Hospital between August 1, 2023 and November 1, 2023, following approval by the Health Science University, İstanbul Kanuni Sultan Süleyman Training and Research Hospital Ethics Committee (Decision protocol no: 2023.07.102 Decision date: 27/07/2023) and in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants.

Sample Size

Sample size was calculated based on LT4 non-adherence rates reported in the literature for geriatric populations (ranging from 22% to 50%), with an expected rate of 40%. Using a significance level of $\alpha = 0.05$ and a statistical power of 80% for two-tailed tests, the minimum required sample size was determined to be 80 patients. 105 patients were screened for the study. 13 patients were excluded due to central hypothyroidism, 3 patients refused to participate, and 2 patients had severe hearing loss. Accounting for potential dropouts, a total of 87 patients were enrolled.

Eligibility Criteria

Inclusion criteria: (1) age 65 years or older, (2) confirmed diagnosis of primary hypothyroidism, (3) ongoing oral LT4 therapy for at least six months at a stable dose, (4) regular outpatient follow-up, (5) sufficient cognitive capacity for verbal communication, and (6) willingness to participate in the study. In this context, a "stable dose" was defined as no dose adjustment during the four weeks immediately preceding enrollment; patients who had undergone a dose change earlier within the preceding six-month period but had since maintained a stable dose at the time of assessment remained eligible, which accounts for the dose-change history reported in Table 2.

Exclusion criteria: Patients were excluded if they had: (1) secondary or central hypothyroidism, (2) a history of thyroid cancer, (3) combination thyroid hormone therapy (T3/T4), (4) clinically diagnosed dementia, (5) a history of cerebrovascular disease with sequelae, (6) malabsorption syndrome (including celiac disease or inflammatory bowel disease), (7) active psychiatric disorder, (8) intellectual disability, or (9) severe hearing impairment precluding questionnaire administration.

Data Collection

Data were collected through face-to-face structured interviews. The questionnaire covered sociodemographic characteristics (age, sex, educational level), comorbid conditions, current medications, LT4 dose, duration of hypothyroidism diagnosis,

and LT4 administration habits — including whether the drug was taken on an empty stomach, with water, without concurrent use of absorption-interfering medications, under appropriate storage conditions, and without dose omission. Patients who fulfilled all criteria were classified as "adherent"; those who failed to meet at least one criterion were classified as "non-adherent." Comorbidities, complete medication lists, and thyroid function tests (TSH and free T4) were recorded for all participants. Polypharmacy was defined as the concurrent use of five or more medications daily. A TSH reference range of 0.4 – 4.0 mIU/L was applied. It should be noted that this classification approach—in which failure to meet any single criterion resulted in categorization as non-adherent—may overestimate the prevalence of clinically meaningful non-adherence, as it does not distinguish occasional, minor administration errors from persistent, substantial non-adherence; this limitation is discussed further below.

Cognitive and Mood Assessment

Cognitive function was assessed using the Standardized Mini-Mental State Examination (MMSE), a widely used screening tool evaluating orientation, memory, attention, calculation, and language, with a maximum score of 30. The Turkish validity and reliability of the MMSE was established by Güngen et al. (2002); a score of 24 or above was considered indicative of normal cognitive function (13). Depressive symptomatology was evaluated using the 15-item Yesavage Geriatric Depression Scale (GDS-15), a validated self-report screening tool developed specifically for older adults. The Turkish validity and reliability of the GDS-15 was demonstrated by Durmaz et al. (2018); scores of 0–4 were considered normal, while a score of 5 or above was indicative of possible depressive disorder (14).

Statistical Analysis

Statistical analyses were conducted utilizing SPSS version 31.0 (IBM Corp., Armonk, NY, USA). Continuous variables exhibiting a normal distribution were represented as mean ± standard deviation (mean ± SD), whereas those not following a normal distribution were described using median and minimum–maximum values. The Kolmogorov-Smirnov test was employed to evaluate normality. For group comparisons of continuous variables, the independent samples t-test was applied to normally distributed data, while the Mann-Whitney U test was used for data not normally distributed. Categorical variables were analyzed using the chi-square test. To identify variables potentially associated with LT4 non-adherence, binary logistic regression analysis was performed, and the model's goodness-of-fit was evaluated using the Hosmer-Lemeshow test. A p-value of less than 0.05 was deemed statistically significant across all analyses. Variables entered into the multivariable logistic regression model (educational level, polypharmacy, concurrent medication use, and recent dosage change) were selected a priori based on their clinical relevance and support in the previous literature as plausible correlates of LT4 non-adherence, rather than on statistical significance in univariate analyses alone.

RESULTS

Demographic and Clinical Characteristics

A total of 87 patients were included in the study. The mean age was 74.05 ± 6.17 years, and the majority of patients were female (88.5%, n = 77). Polypharmacy was present in 40.2% of patients, with a median daily medication use of 4 (range: 1–15). The mean duration of hypothyroidism diagnosis was 13.31 ± 7.49 years. Detailed demographic and clinical characteristics are presented in Table 1.

Table 1. Demographic and clinical characteristics of the patients

Variability	Results (n = 87)
Age (year), Mean ± SD	74.05 ± 6.17
Sex, n (%)	
Women	77 (88.5%)
Men	10 (11.5%)
Education level, n (%)	
No education	20 (22.9%)
Primary school	49 (56.3%)
Middle school and above	18 (20.6%)
Number of chronic diseases, Mean ± SD	2.97 ± 1.16
Number of medications, Median (min-maks)	4 (1 – 15)
Polypharmacy (≥ 5), n (%)	35 (40.2%)
Hypothyroidism diagnosis period (year), Mean ± SD	13.31 ± 7.49
Daily LT4 dose (mcg), Mean ± SD	77.79 ± 28.81
TSH (mIU/L), Median (min-maks)	3.09 (0.06 – 26.00)
Free T4 (ng/dL), Mean ± SD	1.33 ± 0.29

LT4: levothyroxine sodium, TSH: thyroid stimulating hormone, T4: tetraiodothyronine

Levothyroxine Use Characteristics and Adherence Rates

The adherence rate to LT4 therapy was 56.3% (n = 49), while 43.7% (n = 38) were classified as non-adherent. Thyroid dysfunction was detected in 29.9% of patients (n = 26). Detailed LT4 use characteristics and adherence findings are presented in Table 2.

Table 2. LT4 medication habits and adherence data

Parameter	n (%)
Storing under proper storage conditions	87 (100.0%)
Concurrent use of other medications	36 (41.4%)
Concurrent PPI use (Among those taking the same medication)	31 (86.1%)
LT4 dose skipping history	11 (12.6%)
Dosage change in the last 6 months	22 (25.3%)
Taken on an empty stomach, n (%)	[AUTHOR: insert n (%)]
Taken only with water, n (%)	[AUTHOR: insert n (%)]
Non-adherence of LT4	38 (43.7%)
Thyroid dysfunction — total	26 (29.9%)
Hypothyroidism	16 (18.4%)
Hyperthyroidism	10 (11.5%)

PPI: proton pump inhibitor, LT4: tetraiodothyronine

Comparison of Adherent and Non-Adherent Groups

No statistically significant difference was found between the adherent and non-adherent groups in terms of age (73.90 ± 5.5 vs 74.16 ± 7.0 years; p = 0.88), sex, number of chronic diseases, number of medications, LT4 dose, TSH, or free T4 levels. Regarding geriatric parameters, MMSE scores (adherent: 26.92 ± 2.55; non-adherent: 26.57 ± 3.12; p = 0.57) and GDS scores (adherent: 4.55 ± 3.31; non-adherent: 4.92 ± 3.13; p = 0.59) did not differ significantly between the two groups. Although the rate of dose change within the last six months was higher in the non-adherent group (28.9%) compared to the adherent group (22.4%), this difference did not reach statistical significance (p = 0.62). A detailed comparison of the two groups is presented in Table 3.

Table 3. Comparison of adherent and non-adherent groups in terms of demographic, clinical and geriatric parameters

Variable	Adherent (n = 49)	Non-adherent (n = 38)	p
Age (Year), Mean ± SD	73.90 ± 5.5	74.16 ± 7.0	0.88
Sex (Woman), n (%)	44 (89.8%)	33 (86.8%)	0.65
Number of chronic diseases, Mean ± SD	2.82 ± 1.09	3.16 ± 1.24	0.17
Number of medications, Median (min-maks)	4 (1 – 9)	4 (2 – 15)	0.72
Polypharmacy, n (%)	18 (36.7%)	17 (44.7%)	0.45
Dose of LT4 (mcg), Mean ± SD	78.67 ± 26.5	76.64 ± 31.8	0.74
TSH (mIU/L), Median	2.9 (0.07 – 7.7)	3.1 (0.07 – 26.0)	0.45
Free T4 (ng/dL), Mean± SD	1.31 ± 0.32	1.32 ± 0.25	0.49
Score of MMSE, Mean ± SD [VERIFY column order]	26.92 ± 2.55	26.57 ± 3.12	0.57
Score of GDS, Mean ± SD	4.55 ± 3.31	4.92 ± 3.13	0.59
Dosage change in the last 6 months, n (%)	11 (22.4%)	11 (28.9%)	0.62
Thyroid dysfunction, n (%)	16 (32.6%)	10 (26.3%)	0.63

LT4: levothyroxine sodium, TSH: thyroid stimulating hormone, MMSE: Standardized Mini Mental Test, GDS: Geriatric Depression Scale

Use of Proton Pump Inhibitor and TSH Levels

Among the 36 patients using concurrent medications, 31 (86.1%) were using a proton pump inhibitor (PPI). When TSH levels were compared between PPI users (n = 31) and non-users (n = 56), median TSH was significantly higher in the PPI group (3.4 [range: 0.07 – 26.0] mIU/L) compared to non-users (2.7 [range: 0.06 – 7.8] mIU/L) (p = 0.042, Mann-Whitney U test). To further evaluate this association, a multivariable linear regression analysis was performed using log-transformed TSH as the dependent variable, adjusting for age, LT4 dose, and polypharmacy. After adjustment, PPI use was no longer significantly associated with TSH levels (β = -0.10, 95% CI: -0.57 – 0.38, p = 0.684), corresponding to a 9% lower geometric-mean TSH in PPI users relative to non-users (ratio = 0.91, 95% CI: 0.57 – 1.46). None of the covariates reached statistical significance (age: p = 0.081; LT4 dose: p = 0.147; polypharmacy: p = 0.164), and variance inflation factors (all < 1.1) indicated no meaningful multicollinearity.

Logistic Regression Analysis

Binary logistic regression analysis performed to identify independent predictors of LT4 non-adherence did not yield a statistically significant model (Hosmer-Lemeshow p = 0.71, Nagelkerke R^2 = 0.08). Nevertheless, low educational level and presence of polypharmacy showed the strongest trends toward increased risk of non-adherence. Detailed results are presented in Table 4.

Table 4. Results of binary logistic regression analysis on LT4 non-adherence

Variable	OR (95% confidence ınterval)	p
Low education level	2.14 (0.85 – 5.32)	0.092
Polypharmacy (≥ 5)	1.87 (0.72 – 4.81)	0.165
Concurrent medication use	1.52 (0.61 – 3.75)	0.324
Dosage changes in the last 6 months	1.35 (0.48 – 3.78)	0.620

DISCUSSION

In this cross-sectional study, the adherence rate to LT4 among geriatric patients with primary hypothyroidism was determined to be 56.3%, with 43.7% categorized as non-adherent. Non-adherence to long-term treatment in chronic diseases has been recognized as a significant public health issue, and hypothyroidism is no exception; non-adherence rates in this condition are estimated to vary widely, ranging from 22% to 82% across different populations (15). A study conducted in the United States indicated that 68.4% of hypothyroid patients achieved a medication possession ratio of 80% or higher during the first year of treatment (16). Bocale et al. reported an adherence rate of 59.4% in a study involving thyroidectomized patients, while a Turkish study found that 34.92% of patients exhibited low or moderate adherence—both findings are broadly consistent with our results (17,18). In a Lebanese cohort, the lowest adherence rates were observed, with only 14.5% of

participants demonstrating high adherence, 30.6% moderate adherence, and 54.9% low adherence (19). The higher non-adherence rate observed in our study may be attributed to the exclusively geriatric nature of our cohort, in whom age-related barriers — including polypharmacy, cognitive changes, and complex comorbidity burdens — are more pronounced. It is also worth noting that the definition and measurement of adherence vary considerably across studies. While the present study, like several others cited above, applied a binary adherent/non-adherent classification, other studies stratify adherence into low, moderate, and high categories using validated adherence scales; such methodological heterogeneity likely contributes to the wide variability in reported adherence rates across the literature and should be considered when comparing findings across studies.

One of the most distinctive findings of our study is the relationship between PPI use and TSH levels. The significantly higher median TSH levels observed in PPI users compared to non-users clinically confirms the well-established negative effect of gastric acid suppression on LT4 absorption. PPIs diminish the absorption of LT4 by elevating gastric pH, which impairs the dissolution of LT4 tablets. Consequently, TSH levels increase significantly following the initiation of PPI therapy, often necessitating an adjustment in the LT4 dosage. Centanni et al. documented that treatment with omeprazole was linked to elevated serum TSH levels in patients receiving LT4 therapy; this effect was mitigated by a 37% increase in the LT4 dose (20). Similarly, lansoprazole was observed to influence TSH levels in individuals with primary hypothyroidism, with 19% of these patients requiring an adjustment in their LT4 dosage following the commencement of lansoprazole treatment (21). The high prevalence of PPI use in our geriatric cohort (86.1%) is not surprising, as older adults frequently require gastroprotective therapy due to the concurrent use of non-steroidal anti-inflammatory drugs, anticoagulants, and other gastrotoxic agents. However, data specifically examining the clinical impact of PPI–LT4 interaction in geriatric populations remain limited, lending additional value to our findings. From a clinical perspective, these results strongly support the need to review potential drug interactions — and to consider separating the administration times of LT4 and PPIs — before considering dose escalation when unexplained TSH elevation is encountered in older patients with hypothyroidism. However, it should be noted that this unadjusted association did not remain statistically significant after adjustment for age, LT4 dose, and polypharmacy in a multivariable regression analysis (β = -0.10, 95% CI: -0.57 – 0.38, p = 0.684), suggesting that the observed relationship may be confounded by these clinical variables rather than reflecting an independent pharmacological interaction. Given the relatively small size of the PPI subgroup (n = 31) in our cohort, this adjusted analysis was likely underpowered to detect a true effect of modest magnitude. Larger, adequately powered studies incorporating multivariable-adjusted models — and ideally accounting for the specific PPI agent, dose, and duration of concomitant use — are therefore needed to clarify whether PPI use independently contributes to TSH elevation in geriatric hypothyroid patients, or whether the crude association observed here reflects the influence of age, LT4 dosing, or overall medication burden.

In our study, neither cognitive status nor depressive symptomatology was significantly associated with LT4 non-adherence. This finding may seem counterintuitive, given that cognitive impairment and depression are widely recognized as barriers to medication adherence in older adults. However, it is important to note that patients with clinically diagnosed dementia were excluded (the MMSE was used solely as a cognitive screening tool in the remaining participants, not as a diagnostic criterion for dementia) from our study, and the mean MMSE scores of both groups fell well within the normal range (26.57 – 26.92), suggesting that our cohort represented a relatively cognitively preserved population. Similarly, mean GDS scores in both groups were below the threshold for possible depressive disorder, indicating a low overall burden of depressive symptoms. This raises the possibility that non-adherence in our cohort was less attributable to forgetfulness, cognitive insufficiency, or depressive withdrawal from self-care, and more plausibly related to insufficient knowledge about correct administration conditions — such as fasting requirements and avoidance of interacting medications. Supporting this interpretation, İğde et al. reported that 19.2% of hypothyroid patients had low treatment motivation and 7.3% had insufficient knowledge regarding their therapy —suggesting that knowledge deficits, rather than cognitive or affective impairment, may be a more prevalent driver of non-adherence in this population (22). Indeed, the literature indicates that patients with mild cognitive impairment are generally able to maintain routine medication-taking habits, yet adherence to complex administration rules tends to decline even in the absence of overt cognitive decline (23). Collectively, these findings strongly suggest that in cognitively preserved older adults, LT4 non-adherence is more likely a knowledge gap than a capacity gap — making structured patient education and clear counseling on administration rules essential components of clinical management. As health literacy and disease-specific knowledge were not directly measured in our study, this interpretation remains hypothesis-generating and warrants confirmation in studies incorporating validated knowledge or health-literacy assessments.

Binary logistic regression analysis did not identify any statistically significant independent predictors of LT4 non-adherence. Nevertheless, low educational level and polypharmacy showed the strongest trends toward increased non-adherence risk. The trend toward increased risk associated with low educational level points to the determinant role of health literacy in treatment adherence and studies showing that education level directly affects medication adherence in chronic diseases support this interpretation (24,25). In a cross-sectional study of 111 primary hypothyroid patients conducted in Iraq, Ali et al. demonstrated a significant positive correlation between higher educational level and improved knowledge, attitude, and practice scores regarding hypothyroidism and LT4 therapy (p = 0.043), with

university or secondary-educated patients showing substantially better disease knowledge than those with primary education (26). Supporting this, Valladales-Restrepo et al., in a real-world observational study of 398 hypothyroid patients in Colombia, found that higher educational attainment was independently associated with greater treatment persistence at one-year follow-up (27). Although these associations did not reach statistical significance in our study, they may reflect true effects that a larger sample would be powered to detect. Additionally, the absence of a significant association between polypharmacy and non-adherence suggests that medication count alone may not be the critical determinant; rather, specific drug interactions — such as concurrent PPI, calcium, or iron use — appear clinically more relevant. Notably, the higher rate of dose changes within the last six months in the non-adherent group suggests that non-adherence may manifest in clinical practice as dose instability, potentially leading to repeated dose titrations without addressing the underlying adherence problem. These results reinforce the value of individualized patient assessment, and suggest that patients with low educational attainment and polypharmacy may benefit from more intensive counseling and structured follow-up to optimize LT4 adherence in geriatric care.

This study has several strengths. It is one of the few studies to specifically examine LT4 adherence in a geriatric population, incorporating validated geriatric assessment tools — namely the MMSE and GDS-15 — alongside clinical and demographic variables. The face-to-face structured interview methodology minimized missing data and allowed for thorough data collection. Furthermore, the identification of a statistically significant association between PPI use and elevated TSH levels represents a clinically meaningful and original contribution of this study.

Several limitations should also be acknowledged. The cross-sectional design precludes the establishment of causal relationships between the identified variables and LT4 non-adherence. The single-center nature of the study and the relatively modest sample size may limit the generalizability of the findings to broader geriatric populations. Additionally, medication adherence was assessed solely through self-report via a structured questionnaire, which may underestimate non-adherence compared to objective measures such as pill counts, electronic monitoring, or drug level assessments — as patients may tend to overreport adherence in a clinical setting. Finally, the absence of data on health literacy and social support represents a further limitation, given the potential relevance of these factors to adherence behavior in older adults. Moreover, the binary adherence classification used in this study, whereby any single deviation from the defined criteria resulted in classification as non-adherent, may not adequately differentiate between minor and clinically significant non-adherence; future studies employing graded, validated adherence scales are warranted to refine this distinction. In addition, the association observed between PPI use and TSH levels was assessed without adjustment for potential confounders such as LT4 dose, polypharmacy, age, or concurrent medication use; an adjusted multivariable analysis was not performed given the limited size of the PPI subgroup, and this finding should therefore be interpreted as hypothesis-generating rather than confirmatory.

CONCLUSION

In conclusion, LT4 non-adherence affects nearly half of geriatric patients with primary hypothyroidism and, in the absence of a significant association with cognitive or affective impairment, may be related in part to insufficient knowledge about correct administration conditions—an interpretation that should be regarded as hypothesis-generating, since health literacy was not directly measured in this study. The significant association between PPI use and elevated TSH levels further highlights the importance of reviewing concurrent medications before dose escalation. These findings underscore that optimizing LT4 therapy in older adults requires a multidimensional approach — integrating targeted patient education, pharmacological awareness, and regular adherence assessment into routine geriatric care.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that there is no financial support.

Ethical Approval
Ethical approval by the Health Science University, İstanbul Kanuni Sultan Süleyman Training and Research Hospital Ethics Committee (Decision protocol no: 2023.07.102 Decision date: 27/07/2023) and in accordance with the principles of the Declaration of Helsinki.

Informed Consent
Written informed consent was obtained from the patient for publication of this research.

REFERENCES

1. Hollowell JG, Staehling NW, Flanders WD, et al. Serum TSH, T4, and thyroid antibodies in the United States population (1988-1994): National Health and Nutrition Examination Survey (NHANES III). J Clin Endocrinol Metab. 2002;87:489-99.
2. Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The colorado thyroid disease prevalence study. Arch Intern Med. 2000;160:526-34.
3. Garber JR, Cobin RH, Gharib H, et al. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. Endocr Pract. 2012;18:988-1028.
4. Jonklaas J, Bianco AC, Bauer AJ, et al; American Thyroid Association Task Force on Thyroid Hormone Replacement. Guidelines for the treatment of hypothyroidism: prepared by the American Thyroid Association Task Force on Thyroid Hormone Replacement. Thyroid. 2014;24:1670-751.

5. Skelin M, Lucijanic T, Amidzic Klaric D, et al. Factors affecting gastrointestinal absorption of levothyroxine: a review. Clin Ther. 2017;39:378-403.

6. Colucci P, Yue CS, Ducharme M, Benvenga S. A review of the pharmacokinetics of levothyroxine for the treatment of hypothyroidism. Eur Endocrinol. 2013;9:40-7.

7. Kim MI, Bertot BE. Hypothyroidism in older adults. Updated December 10, 2025. In: Feingold KR, Adler RA, Ahmed SF, et al., eds. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. access date 03.06.2026.

8. Effraimidis G, Watt T, Feldt-Rasmussen U. Levothyroxine therapy in elderly patients with hypothyroidism. Front Endocrinol (Lausanne). 2021;12:641560.

9. World Health Organization. Adherence to Long-Term Therapies: Evidence for Action. Geneva, Switzerland: World Health Organization; 2003.

10. Biondi B. Cardiovascular effects of mild hypothyroidism. Thyroid. 2007;17:625-30.

11. Sforza N, Rosenfarb J, Rujelman R, et al. Hypothyroidism in hospitalized elderly patients: a sign of worse prognosis. J Endocrinol Invest. 2017;40:1303-10.

12. Osterweil D, Syndulko K, Cohen SN, et al. Cognitive function in non-demented older adults with hypothyroidism. J Am Geriatr Soc. 1992;40:325-35.

13. Güngen C, Ertan T, Eker E, et al. Reliability and validity of the standardized Mini Mental State Examination in the diagnosis of mild dementia in Turkish population. Turk Psikiyatri Derg. 2002;13:273-81.

14. Durmaz B, Soysal P, Ellidokuz H, Isik AT. Validity and reliability of geriatric depression scale-15 (short form) in Turkish older adults. North Clin Istanb. 2018;5:216-20.

15. Okosieme OE. Thyroid hormone replacement: current status and challenges. Expert Opin Pharmacother. 2011;12:2315-28.

16. Briesacher BA, Andrade SE, Fouayzi H, Chan KA. Comparison of drug adherence rates among patients with seven different medical conditions. Pharmacotherapy. 2008;28:437-43.

17. Bocale R, Desideri G, Barini A, et al. Long-term adherence to levothyroxine replacement therapy in thyroidectomized patients. J Clin Med. 2022;11:4296.

18. Dirikoç A, Genç B, Özdemir D, et al. Adherence to levothyroxine treatment and factors related with adherence in patients with hypothyroidism. Ankara Med J. 2021;21:261-273.

19. El Helou S, Hallit S, Awada S, et al. Adherence to levothyroxine among patients with hypothyroidism in Lebanon. East Mediterr Health J. 2019;25:149-59.

20. Centanni M, Gargano L, Canettieri G, et al. Thyroxine in goiter, Helicobacter pylori infection, and chronic gastritis. N Engl J Med. 2006;354:1787-95.

21. Sachmechi I, Reich DM, Aninyei M, et al. Effect of proton pump inhibitors on serum thyroid-stimulating hormone level in euthyroid patients treated with levothyroxine for hypothyroidism. Endocr Pract. 2007;13:345-9.

22. İğde ME, Balcıoğlu H. Evaluation of medication compliance in patients diagnosed with hypothyroidism who applied to family medicine outpatient clinic. Eskisehir Med J. 2024;5:110-6.

23. Jekel K, Damian M, Wattmo C, et al. Mild cognitive impairment and deficits in instrumental activities of daily living: a systematic review. Alzheimers Res Ther. 2015;7:17.

24. Yılmaz F, Yavuz Çolak M. Evaluation of beliefs about medicines and medication adherence among elderly people with chronic diseases. Turkiye Klinikleri J Health Sci. 2018;3:113-21.

25. Demirbaş N, Kutlu R. Treatment adherence and self-efficacy levels of adults using multiple drugs. Ankara Med J. 2020;20:269-80.

26. Ali ZH, Abdulridha MK, Alzajaji QB. Screening factors affecting proper levothyroxine therapy among patients with primary hypothyroidism: a cross-sectional study. J Med Life. 2024;17:177-87.

27. Valladales-Restrepo LF, Londoño-Cano DA, Muñoz-Velez CM, et al. Patterns and persistence of use, effectiveness, safety, clinical inertia, and adherence related to levothyroxine treatment with real-world evidence: an observational, longitudinal and retrospective study. Endocrine. 2026;91:84.