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# Editorial

Dear Colleagues,

It is a pleasure to present the December Issue of the Turkish Journal of Family Practice, which reflects the breadth, depth, and evolving priorities of family medicine and primary care. This issue brings together original research articles addressing critical topics such as geriatric depression and nutrition in home healthcare, atrial fibrillation and thromboembolic risk in older adults, defensive medicine practices in driving licence reporting, rational drug use in pulmonology outpatient settings, and the relationship between thyroid hormones and metabolic parameters in euthyroid women. In addition, we are pleased to include a valuable case report in this issue. Finally, we published a Letter to the Editor on home healthcare services to enhance adult immunization coverage, an important innovative preventive care model. On behalf of the Editorial Board, I would like to thank our authors, reviewers, and readers for their contributions throughout the year. We hope this issue will inform your practice, stimulate academic discussion, and inspire further research. We wish you a healthy, peaceful, and productive New Year, and look forward to sharing new scientific contributions with you in the year ahead.

Sincerely,

Sincerely,
Prof. Dr. Yasemin ÇAYIR
Editor-in-Chief
Turkish Journal of Family Practice

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Research Article

# Investigation of the relationship between depression levels and nutritional status in elderly patients receiving home health care services

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This study was previously submitted as a Family Medicine Specialization thesis by Gizem Çetinyol.

## ABSTRACT

**Objective:** The research explores the factors influencing the nutrition levels of people aged 65 years and older enrolled in home health services, focusing on depression levels, functional dependency, existing comorbid conditions and sociodemographic characteristics.

**Methods:** The study is a single-centered, cross-sectional, descriptive, and prospective analysis conducted with patients registered at the Home Health Services at SBÜ Izmir Bozyaka Training and Research Hospital . The sample size was estimated assuming that the prevalence of malnutrition among the elderly was 40%, with a error margin of 0.05% and a 95% confidence interval, and reaching a target of 368 individuals. Sociodemographic data were collected via surveys. Nutrition levels was measured utilizing the Mini Nutritional Assessment Scale- Long Form, functional dependence with the Barthel Index, comorbidities via the Charlson Comorbidity Index, and depression levels using the Yesavage Geriatric Depression Scale. Statistical analysis of the data was performed using IBM SPSS 26 program.

**Results:** Among the respondents, 60.6% (n=223) were female and the mean age was 81.35±7.95 years (range: 65-99). In education terms, 84.8% had completed elementary school or less (n=312), and 79.4% received care from family members (n=292). The average body mass index was 25.4±4.2 kg/m² (min: 16.5 kg/m²; max: 49 kg/m²). Nutritional assessments showed that 29.6% were insufficiently nourished, 44% were at risk of malnutrition. In daily activities, 16.8% were fully dependent, while 47.3% were severely dependent. According to the comorbidity index, 89.1% were at very high risk for mortality. Additionally, 62.5% were confirmed as depressed, with 10.3% likely depressed. A significant association was found between nutrition status and some factors such as caregiver status, gender, dental hygiene and BMI.

**Conclusion:** The study highlights a considerable prevalence of depression and its adverse effect on nutritional health. Depression levels were found to have a strong negative correlation with nutritional status, indicating that high levels of depression may negatively affect the nutritional well-being of older adults and emphasizing the need to address both nutrition and mental health in this demographic group.

**Keywords:** home care services, malnutrition, depressive disorder, aged

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## Introduction

Nowadays, the increasing elderly population has raised an important health problem, especially in developing countries. Improving the livability of elderly individuals is a necessity that affects not only their individual health status but also social welfare.[1] One of the main ways to heal livability is the prevention and management of health problems frequently encountered in the elderly. As an exemple, malnutrition is an important condition that negatively affects both physical and psychological health status of elderly individuals.[2,3]

Home health care services is a service model that enables individuals to receive medical care without leaving their own living spaces and has an crucial role to play in improving the livability of elderly individuals.[4,5] However, it is known that the prevalence of malnutrition and depression is high among individuals benefiting from these services, and that many of them are at risk of malnutrition and depression.[6] Factors such as increasing loneliness in the aging process, loss of relatives, retirement and decreasing social roles increase the risk of depression.[7] Especially in elderly individuals who have difficulty in daily living activities and who are enrolled in home health services, depression may negatively affect the nutritional status of the person and may pave the way for the development of malnutrition. In the literature, it is seen that these two conditions are frequently seen together and negatively affect each other.[3] Although malnutrition decreases the physical endurance and cognitive capacity of the individual, depression increases the risk of malnutrition by negatively affecting the appetite and eating habits of the individual.[3,7]

The main objective of this study was to identify the relationship between depression levels and nutrition levels of people aged 65 years and over enrolled in Home Health Services Unit of SBU İzmir Bozyaka Training and Research Hospital.

## Material and Method

This research is a descriptive, cross-sectional, single-centre survey study. The population of the study included individuals aged 65 years and over who were registered to SBU İzmir Bozyaka Training and Research Hospital Home Health Care Services. Taking the frequency of malnutrition in elderly individuals as 40%, it was aimed to reach at least 368 people as a result of the model sample calculation (according to the Cochran formula) with an error margin of 0.05% and 95% confidence level. The study was completed with 368 people aged 65 years and over, who were registered in the Home Health Care Services of SBU İzmir Bozyaka Training and Research Hospital , who could be fed orally, who were able to answer the questionnaire questions and who agreed to participate in the study. The ethical approval was obtained from the SBU İzmir Bozyaka Training and Research Hospital Clinical Research Ethics Committee on September 14, 2023 (Decision number: 2023/157). “Informed consent form” was obtained from the participants.

A questionnaire was administered to the people registered to the SBU İzmir Bozyaka Training and Research Hospital Home Health Care Services between 01.10.2023- 31.12.2023 by contacting them face-to-face, by telephone, by visiting them at their homes, by informing them about this study during their application to our outpatient clinic, and by making use of patient files. The people were selected according to the ‘simple random sampling’ method, one of the ‘probability-based sampling’ methods.

The sociodemographic information section of the questionnaire applied in the study was prepared by the researcher by reviewing the literature and consists of 7 questions including the descriptive participants' characteristics (gender, age, education level, caregiver, marital status, dental health, dental cleaning frequency). In addition, Mini

Nutritional Assessment Scale (MNA, kappa=0.68, sensitivity=92% and specifity=86% ), Modified Barthel Activities of Daily Living Index (Barthel ADL, Cronbach's alpha=0.93), Modified Charlson Comorbidity Index (CCI) and Yesavage Geriatric Depression Scale (GDS, Cronbach's alpha=0.92) were included in the study questionnaire.[8-10]

For the statistical analysis of this study, IBM SPSS 26.0 software was used. Descriptive statistics were presented as frequency (n), percentage (%), mean ($\bar{X}$), standard deviation (SD), minimum, and maximum values. To test the relationship between categorical variables, the Chi-square test, Fisher's Exact test, and Fisher Freeman Halton Exact test were applied. The normal distribution of continuous data was assessed by examining skewness and kurtosis coefficients.[11] Since the skewness and kurtosis values were within the acceptable ranges, Independent Samples T-test and One-Way Analysis of Variance (ANOVA) were conducted, and Tukey HSD and Tamhane tests were used as post-hoc analyses where appropriate.[12] Pearson correlation analysis was performed to determine the relationships among the scale scores, and the results were considered statistically significant at a level of $p<0.05$. In addition, ordinal logistic regression analysis was performed to identify the factors influencing depression levels, and the results were evaluated using odds ratios (OR).

## Results

The average age of survey participants was 81.4+8 (min. 65-max. 99), and 60.6% were female. 84.8% of the participants had completed primary school, 46.7% were married, and 79.4% had family caregivers. 41% of the participants were in the middle-aged group, while 37.8% were in the elderly group. Detailed information is provided in Table 1.

**Table 1.** Sociodemographic characteristics of the participants

| **Sociodemographic characteristics** | **N** | **%** |
|---|---|---|
| Gender | | |
| Male | 145 | 39.4 |
| Female | 223 | 60.6 |
| Level of Education | | |
| Primary school graduate or less | 312 | 84.8 |
| High school dropout, graduate or university dropout | 51 | 13.9 |
| University graduates or above | 5 | 1.3 |
| Marital Status | | |
| Married | 172 | 46.7 |
| Single | 28 | 7.6 |
| Widow | 168 | 45.7 |
| Caregivers | | |
| Family | 292 | 79.4 |
| Distant Relative | 38 | 10.3 |
| Neighbour | 9 | 2.4 |
| Paid Carer | 13 | 3.5 |
| Lives alone | 16 | 4.4 |
| Does he/she use implants/ dentures? | | |
| None | 89 | 24.2 |
| Using only dentures | 240 | 65.2 |
| Using only implants | 5 | 1.4 |
| Using implants and dentures | 34 | 9.2 |
| Are the teeth kept clean? | | |
| Yes/clean | 189 | 51.4 |
| Occasional / medium cleanliness | 103 | 28.0 |
| No / not clean | 76 | 20.6 |
| Old Age Groups (WHO) | | |
| Early Old Age (65-74 years) | 78 | 21.2 |
| Middle Old Age (75-84 years) | 151 | 41.0 |
| Advanced Old Age (85 years +) | 139 | 37.8 |
| Body Mass Index (WHO) | | |
| Underweight | 5 | 1.3 |
| Normal | 181 | 49.2 |
| Overweight | 138 | 37.5 |
| Obese+ | 44 | 12.0 |
| TOTAL | 368 | 100.0 |

According to the MNA Scale, only 26.4% were in a normal nutritional state. 16.8% of participants were completely dependent on others for daily living activities, 47.3% were highly dependent, and 26.6% were moderately dependent. According to the CCI, 89.1% of participants were found to be at very high risk. In the GDS results, only 27.2% were not depressed.

Significant relationships were found between GDS, Barthel, CCI, and MNA scores ($p<0.001$; $p<0.001$; $p=0.021$). While 60% of those without depression and the majority of individuals with higher levels of independence were in normal nutritional status, 63.2% of those at risk of depression, 59.8% of the highly dependent, and 44.8% of the very high-risk group were at risk of malnutrition. Moreover, 45.2% of those with definite depression and 83.9% of the completely dependent were malnourished. Detailed information is provided in Table 2.

Significant associations were found between MNA, Barthel, and CCI scores and GDS ($p<0.001$; $p<0.001$; $p=0.029$). Most individuals who were malnourished, at risk of malnutrition, completely or highly dependent, and those in the high and very high CCI risk groups were classified as having definite depression. In contrast, the majority of those with normal nutritional status, higher levels of independence, and all individuals in the moderate CCI risk group had no depression. Detailed information is provided in Table 3.

There was no significant difference between the age groups classified according to the WHO and the scores of the MNA, Barthel, and GDS scales. A significant difference was found in CCI between the groups ($p<0.001$). In particular, the CCI scores of the 65-74 age group were lower than those of the 75-84 and 85 and older age groups, indicating that the early elderly group had fewer comorbidities.

By gender, there was no significant difference between genders in Barthel, CCI, and GDS scale scores, but there was a statistically significant difference between women and men in MNA scores ($p=0.006$), with an average of 20.10 for women and 18.43 for men, indicating that women's nutritional status is better than men's.

When analyzed according to marital status, the single group was found to have less comorbidity than the widowed group. No significant differences were found between marital statuses in terms of other scales (MNA, Barthel, GDS).

According to caregiver status, MNA and Barthel scores showed significant differences, with those living alone having better nutritional status and independence; no differences were observed in CCI and GDS scores.

MNA scores were found to be higher in the group using implants and dentures than in the group using neither. Similarly, GDS scores showed that the group using implants and prostheses had lower scores than the group using neither. CCI scores indicate that the group using only dentures has higher comorbidity compared to the group using neither ($p=0.047$). Barthel scores didn’t show a significant difference based on the use of implants and/or dentures ($p=0.308$).

MNA scores showed that the group that always kept their teeth clean had higher scores than the other groups ($p<0.001$). Similarly, MNA scores were significantly higher in the group that did not keep their teeth clean than in the group that did keep their teeth clean ($p=0.013$). There was no significant difference in Barthel and CCI scores.

According to BMI, MNA, Barthel, and GDS scores showed significant differences. The underweight group had lower MNA and Barthel scores, while their GDS scores were higher compared to overweight and obese groups. No significant association was found between BMI and CCI. Detailed information can be found in Table 4.

Participants' MNA (Mean=19.44, SD=5.57), Barthel (Mean=52.19, SD=27.88), CCI (Mean=7.17,

**Table 2.** Chi-square table between MNA and other scales

| | MNA total score | Malnutrition N (%) | At risk of malnutrition N (%) | Normal nutritional levels N (%) | Total | X2 | df | p |
|---|---|---|---|---|---|---|---|---|
| GDS Total Score | No Depression | 1 (1.0) | 39 (39.0) | 60 (60.0) | 100 | 116.6 | 4 | p<0.001 |
| | Possible Depression | 4 (10.5) | 24 (63.2) | 10 (26.3) | 38 | | | |
| | Definite Depression | 104 (45.2) | 99 (43.0) | 27 (11.7) | 230 | | | |
| Barthel Total Score | Completely Dependent | 52 (83.9) | 10 (16.1) | 0 (0.0) | 62 | 189.1 | 8 | p<0.001 |
| | Highly Dependent | 50 (28.7) | 104 (59.8) | 20 (11.5) | 174 | | | |
| | Moderately Dependent | 6 (6.1) | 38 (38.8) | 54 (55.1) | 98 | | | |
| | Mildly Dependent | 1 (6.3) | 5 (31.3) | 10 (62.5) | 16 | | | |
| | Fully Independent | 0 (0.0) | 5 (27.8) | 13 (72.2) | 18 | | | |
| CCI Total Score | Low Risk | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 | 9.6 | 4 | 0.021 |
| | Medium Risk | 0 (0.0) | 0 (0.0) | 2 (100.0) | 2 | | | |
| | High Risk | 7 (18.4) | 15 (39.5) | 16 (42.1) | 38 | | | |
| | Very High Risk | 102 (31.1) | 147 (44.8) | 79 (24.1) | 328 | | | |

**Table 3.** Chi-square table between GDS and other scales

| | GDS total score | No depression N (%) | Possible depression N (%) | Definite depression N (%) | Total | X2 | df | p |
|---|---|---|---|---|---|---|---|---|
| MNA Total Score | Malnutrition | 1 (0.9) | 4 (3.7) | 104 (95.4) | 109 | 116.6 | 4 | p<0.001 |
| | At risk of malnutrition | 39 (24.1) | 24 (14.8) | 99 (61.1) | 162 | | | |
| | Normal nutritional levels | 60 (61.9) | 10 (10.3) | 27 (27.8) | 97 | | | |
| Barthel Total Score | Completely Dependent | 1 (1.6) | 1 (1.6) | 60 (96.8) | 62 | 124.2 | 8 | p<0.001 |
| | Highly Dependent | 22 (12.6) | 23 (13.2) | 129 (74.1) | 174 | | | |
| | Moderately Dependent | 54 (55.1) | 12 (12.2) | 32 (32.7) | 98 | | | |
| | Mildly Dependent | 12 (75.0) | 1 (6.3) | 3 (18.8) | 16 | | | |
| | Fully Independent | 11 (61.1) | 1 (5.6) | 6 (33.3) | 18 | | | |
| CCI Total Score | Low Risk | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 | 9.5 | 4 | 0.029 |
| | Medium Risk | 2 (100.0) | 0 (0.0) | 0 (0.0) | 2 | | | |
| | High Risk | 13 (34.2) | 7 (18.4) | 18 (47.4) | 38 | | | |
| | Very High Risk | 85 (25.9) | 31 (9.5) | 212 (64.6) | 328 | | | |

SD=2.41), and GDS (Mean=16.35, SD=7.43) scores were measured using Pearson Correlation.

The results showed a positive and strong correlation between MNA and Barthel (0.69), a negative and weak-moderate correlation between MNA and Modified CCI (-0.36), and a negative and strong correlation between MNA and GDS (-0.67).

The relationship between the Barthel scale and the CCI scale was negative (-0.31) with a weak correlation, while the relationship between the Barthel scale and the GDS was negative (-0.63) with a strong correlation.

The correlation between the CCI scale and GDS is positive (0.33) and weak to moderate (Table 5).

Ordinal logistic regression analysis was conducted to identify factors associated with depression categories among older adults. The model showed a good fit to the data ($\chi^2$=206.22, df=22, p<0.001), and

**Table 4.** Parametric tests of the scales appl ied to the participants

| | | MNA | | Barthel | | CCI | | Yesavage GDS | |
|---|---|---|---|---|---|---|---|---|---|
| | N | $\overline{X}$ | SD | $\overline{X}$ | SD | $\overline{X}$ | SD | $\overline{X}$ | SD |
| Old Age Groups * | | | | | | | | | |
| Early Old Age (65-74 years) | 78 | 18,87 | 5,78 | 51,87 | 29,82 | 6,31 | 2,67 | 17,35 | 7,86 |
| Middle Old Age (75-84 years) | 151 | 20,04 | 5,68 | 54,74 | 27,60 | 7,23 | 2,39 | 15,69 | 7,50 |
| Advanced Old Age (85 years +) | 139 | 19,11 | 5,32 | 49,60 | 26,99 | 7,60 | 2,16 | 16,50 | 7,09 |
| Tests / p | | 1,525/0,219 | | 1,234/0,292 | | 7,446/ <0,001 | | 1,327/ 0,266 | |
| Difference between groups[a] | | | | | | 1<2; 1<3 | | | |
| Gender** | | | | | | | | | |
| Male | 145 | 18,43 | 6,02 | 53,10 | 27,85 | 7,26 | 2,66 | 17,03 | 7,81 |
| Female | 223 | 20,10 | 5,17 | 51,60 | 27,94 | 7,11 | 2,25 | 15,90 | 7,16 |
| Tests/p | | -2,751/**0,006** | | 0,506/0,613 | | 0,582/0,561 | | 1,422/0,156 | |
| Education Level* | | | | | | | | | |
| Primary school graduate or below | 312 | 19,39 | 5,52 | 50,68 | 27,05 | 7,28 | 2,40 | 16,57 | 7,43 |
| High school dropout, graduate or university dropout | 51 | 19,70 | 5,78 | 59,80 | 30,05 | 6,45 | 2,51 | 15,14 | 7,45 |
| University graduates or above | 5 | 19,80 | 7,82 | 69,00 | 42,78 | 7,60 | 1,52 | 14,80 | 7,89 |
| Tests/p | | 0,074/0,928 | | 3,313/**0,038** | | 2,703/0,068 | | 0,921/0,399 | |
| Difference between groups[a] | | | | *** No significant difference was found in Tukey. | | | | | |
| Marital Status* | | | | | | | | | |
| Married | 172 | 19,34 | 5,90 | 53,81 | 28,49 | 6,98 | 2,39 | 16,54 | 7,82 |
| Single | 28 | 19,77 | 5,28 | 57,32 | 28,04 | 6,32 | 2,28 | 17,75 | 8,13 |
| Widow | 168 | 19,49 | 5,30 | 49,68 | 27,13 | 7,51 | 2,42 | 15,92 | 6,90 |
| Tests/p | | 0,085/0,918 | | 1,450/0,236 | | 4,032/**0,019** | | 0,835/0,435 | |
| Difference between groups[a] | | | | | | 2<3 | | | |
| Caregivers* | | | | | | | | | |
| Family | 292 | 19,35 | 5,66 | 50,96 | 27,55 | 7,274 | 2,52 | 16,46 | 7,53 |
| Distant Relative | 38 | 18,33 | 4,82 | 48,16 | 25,35 | 7,368 | 1,99 | 17,50 | 6,50 |
| Neigbour | 9 | 20,17 | 6,83 | 57,22 | 26,47 | 5,778 | 1,79 | 19,89 | 8,19 |
| Paid Carer | 13 | 18,58 | 4,96 | 46,62 | 31,26 | 6,462 | 1,56 | 13,85 | 6,94 |
| Lives alone | 16 | 24,06 | 2,96 | 85,94 | 14,86 | 6,188 | 1,68 | 11,50 | 5,62 |
| Tests/p | | 3,348/**0,010** | | 6,813/<**0,001** | | 1,910/0,108 | | 2,884/**0,023** | |
| Difference between groups | | 1<5; 2<5; 4<5[b] | | 1<5; 2<5; 4<5[b] | | | | *** No significant difference was found in Tukey.[a] | |

Note: 1: * One-way Variance Test (ANOVA)
** Independent Samples T- Test
a) Post-hoc: Tukey, b) Post-hoc: Tamhane

**Table 4.** Continued

| | | MNA | | Barthel | | CCI | | Yesavage GDS | |
|---|---|---|---|---|---|---|---|---|---|
| | N | $\overline{X}$ | SD | $\overline{X}$ | SD | $\overline{X}$ | SD | $\overline{X}$ | SD |
| Implant/ denture status * | | | | | | | | | |
| None | 89 | 19,11 | 5,58 | 50,29 | 27,81 | 6,640 | 2,55 | 17,40 | 7,36 |
| Using only dentures | 240 | 19,14 | 5,70 | 51,73 | 27,98 | 7,425 | 2,43 | 16,49 | 7,48 |
| Using only implants | 5 | 22,40 | 4,51 | 68,00 | 26,60 | 7,200 | 1,10 | 13,40 | 6,99 |
| Using dentures and implants | 34 | 21,97 | 3,93 | 58,09 | 27,16 | 6,765 | 1,76 | 13,00 | 6,54 |
| Tests/p | | 3,192/**0,024** | | 1,205/0,308 | | 2,677/**0,047** | | 3,248/**0,022** | |
| Difference between groups | | 1<4; 2<4[b] | | | | 1<2[a] | | 4<1; 4<2[a] | |
| Are the teeth kept clean?* | | | | | | | | | |
| Yes/clean | 189 | 20,53 | 5,35 | 54,08 | 29,06 | 7,23 | 2,35 | 15,26 | 7,42 |
| Occasional / medium cleanliness | 103 | 18,85 | 5,54 | 50,10 | 24,56 | 7,48 | 2,33 | 17,20 | 7,52 |
| No/ Not clean | 76 | 17,52 | 5,59 | 50,33 | 29,09 | 6,62 | 2,62 | 17,88 | 7,00 |
| Tests/p | | 9,110/<**0,001** | | 0,893/0,410 | | 2,894/0,057 | | 4,409/**0,013** | |
| Difference between groups[a] | | 2<1; 3<1 | | | | | | 1<3 | |
| Body Mass Index* | | | | | | | | | |
| Underweight | 5 | 6,30 | 2,361 | 22,00 | 16,05 | 25,80 | 4,92 | 25,80 | 4,92 |
| Normal | 181 | 16,96 | 5,321 | 46,19 | 27,55 | 17,69 | 7,39 | 17,69 | 7,39 |
| Overweight | 138 | 22,38 | 4,08 | 60,33 | 26,41 | 14,61 | 7,31 | 14,61 | 7,31 |
| Obese+ | 44 | 21,86 | 3,69 | 54,80 | 27,06 | 15,18 | 6,41 | 15,18 | 6,41 |
| Tests/p | | 51,889/<**0,001** | | 9,404/<**0,001** | | 2,700/**0,046** | | 7,975/<**0,001** | |
| Difference between groups | | 1<2; 1<3; 2<3; 1<4; 2<4[b] | | 1<3; 2<3[a] | | *** No significant difference was found in Tukey.[a] | | 3<1; 4<1; 3<2[a] | |

Note: 1: * One-way Variance Test (ANOVA)
** Independent Samples T- Test
a) Post-hoc: Tukey, b) Post-hoc: Tamhane

the parallel lines assumption was met (p=0.346). The Nagelkerke $R^2$ was 0.52, indicating that approximately 52% of the variance in depression categories was explained by the model.

An increase in BMI was significantly associated with a higher likelihood of being in a higher depression category (OR=1.10, 95% CI=1.02–1.20, p=0.018). Conversely, higher MNA scores were associated with a reduced risk of depression (OR=0.71, 95% CI=0.64–0.79, p<0.001). Similarly, higher Barthel scores, reflecting greater independence in daily living activities, were associated with a lower risk of depression (OR=0.97, 95% CI=0.96–0.99, p<0.001). Caregiver type also emerged as a significant predictor: participants with professional caregivers had a substantially lower risk of depression compared to other groups (OR=0.06, 95% CI=0.01–0.38, p=0.003). The Charlson comorbidity index was not found to have a significant effect on depression (p=0.715) (Table 6).

**Table 5.** Correlation Test Between MNA, Barthel, CCI and GDS Scales

| | MNA | Barthel | CCI | Yesavage GDS |
|---|---|---|---|---|
| MNA | 1 | 0.693** | -0.360** | -0.671** |
| Sig. (2-tailed) | | <0.001 | <0.001 | <0.001 |
| N | 368 | 368 | 368 | 368 |
| Barthel | 0.693** | 1 | -0.313** | -0.631** |
| Sig. (2-tailed) | <0.001 | | <0.001 | <0.001 |
| N | 368 | 368 | 368 | 368 |
| CCI | -0.360** | -0.313** | 1 | 0.334** |
| Sig. (2-tailed) | <0.001 | <0.001 | | <0.001 |
| N | 368 | 368 | 368 | 368 |
| Yesavage GDS | -0.671** | -0.631** | 0.334** | 1 |
| Sig. (2-tailed) | <0.001 | <0.001 | <0.001 | |
| N | 368 | 368 | 368 | 368 |

**. Correlation is significant at the 0.01 level (2-tailed).

**Table 6.** Ordinal logistic regression results (factors associated with depression categories)

| Variable | B (SE) | OR [95% CI] | p value |
|---|---|---|---|
| BMI | 0.099 (0.042) | 1.10 [1.02–1.20] | 0.018 |
| MNA Score | -0.338 (0.053) | 0.71 [0.64–0.79] | <0.001 |
| Barthel Score | -0.028 (0.007) | 0.97 [0.96–0.99] | <0.001 |
| Caregivers (Paid Carer) | -2.773 (0.922) | 0.06 [0.01–0.38] | 0.003 |

Note: (OR: Odds ratio, CI: Confidence Interval). Only statistically significant variables were included in the table. Exp(B) values were calculated by transforming the B coefficients as $e^B$.

## Discussion

In this study, the effects of depression levels on nutritional status were examined among patients aged 65 years and older who were enrolled in home healthcare services. The findings indicate that as the level of depression increases, patients' nutritional status deteriorates. It is thought that loss of appetite, lack of energy, and reduced quality of self-care associated with depression contribute to these results, thereby negatively affecting nutritional status.[13] Similar studies in the literature have also concluded that there is a negative association between depression levels and nutritional status.[14-17] However, most of these studies primarily included physically independent geriatric patients, while research focusing on patients receiving home healthcare remains limited. From this perspective, the present study provides an important contribution to the understanding of this population.

In our study, no significant differences were found between age groups in terms of depression levels, activities of daily living (ADL), or nutritional status. However, some studies have shown that the rates of malnutrition and depression increase with age.[15,18,19] A significant difference was observed between groups in terms of the CCI, with the early elderly group having fewer comorbidities.

It was also observed that individuals cared for by a caregiver were at a higher risk of "malnutrition" or "risk of malnutrition" compared to those living alone. Supporting evidence for this finding exists in the literature.[20] This may be explained by the fact that the individuals living alone in our study had higher mean Barthel ADL scores, indicating greater functional independence (Table 4). Similar

findings have been reported in previous studies.[21] Other studies, however, did not find a significant association between nutritional status and living arrangements.[15] Furthermore, participants with professional caregivers were found to have a 94% lower risk of depression compared with those living alone (95% CI=0.01–0.38, p=0.003).

A statistically significant difference was observed between men and women in terms of MNA scores, with women having better nutritional status. This finding is supported by other studies[18,22], although some research reports no association between gender and nutritional status.[16,23] In our study, no significant relationship was found between gender and depression levels, a result also supported by several studies.[15] Nonetheless, some reports in the literature suggest that women are more prone to depression than men.[19]

No significant associations were found between educational level and nutritional status or depression in our study, a finding consistent with some previous studies.[15] While education level did not show a significant relationship with the dependent variables, certain studies have reported that improved educational attainment is associated with better nutritional outcomes.[16]

A significant association was found between CCI scores and marital status (p=0.019), with unmarried participants having fewer comorbidities compared with widowed individuals. While no significant associations were found between marital status and other scales, some studies have reported that single or widowed individuals experience higher levels of depression than married individuals.[15,24] Other studies have shown no relationship between nutritional status and marital status.[15] Although marital status did not significantly affect ADL in our study, research indicates that individuals with a living spouse tend to have higher Barthel ADL scores compared to divorced or widowed participants.[25]

MNA scores were higher in participants using implants and prostheses compared with those who used neither. However, the opposite has been reported in the literature.[14] Depression levels were also lower among participants using implants and prostheses than among those not using them.

Participants who consistently maintained oral hygiene had higher MNA scores than those in other groups, a finding supported by previous studies.[26] Similarly, studies have demonstrated an association between depression and oral hygiene.[27]

According to our findings, as depression levels increased, nutritional status decreased, and the tendency toward malnutrition rose, a result supported by previous research.[14-16] Furthermore, increasing dependency in ADL and higher CCI scores were associated with a decline in nutritional status (Table 2).

When compared with the literature, it can be suggested that individuals receiving home healthcare services are at higher risk of depression. This may be explained by the higher rates of functional dependency observed in this group (Table 3). Additionally, our study revealed that for every 1-point increase in the MNA score, the risk of depression decreased by approximately 29% (95% CI=0.64–0.79, p<0.001), a finding consistent with previous studies.[15-17] Similarly, each 1-point increase in the Barthel score was associated with a 3% reduction in the likelihood of depression being categorized in higher levels. However, increased CCI scores were not found to have a significant effect on depression levels (p=0.715) (Table 6).

According to the Barthel ADL Scale results, greater independence in daily living activities positively influenced participants' nutritional status.[16,20,22,28] Individuals with higher Barthel ADL scores were more successful in self-care, better able to

meet their nutritional needs, and demonstrated improved nutritional status (Table 2).

The mean total CCI score among participants was 7.2 ± 2.4 (min. 2–max. 17), whereas a similar study reported a score of 2.4 ± 1.9.[29] This difference may be attributed to the higher prevalence of conditions with high comorbidity scores, such as metastatic solid tumors and severe liver disease, in our study population. Karakaş et al. also utilized the CCI scale in their study but did not find a statistically significant difference between comorbidity and mean MNA scores.[16] A high comorbidity burden may contribute to greater functional limitations in daily activities, which in turn negatively affect nutritional status (Table 5).

In some studies, individuals with a BMI below 18 kg/m² have been shown to have higher mortality rates and to be at greater risk of malnutrition. Therefore, in this study, a statistically significant correlation was expected between BMI and MNA, Barthel ADL, CCI, and GDS scores.[30] However, our findings revealed that an increase in BMI was significantly associated with a higher likelihood of being in a more severe depression category. Ordinal logistic regression analysis demonstrated that each one-unit increase in BMI increased the probability of being classified in a higher depression category by 10% (95% CI=1.02–1.20; p=0.018) (Table 6). This finding is consistent with the "U-shaped relationship" frequently emphasized in the literature, whereby both very low and high BMI levels can be risk factors for depression.[14-16,30] Nonetheless, multivariate analyses indicated that BMI may have an independent effect on depression.

### Limitations

The limitations of our study include the single-center structure of the study, the unbalanced distribution of the independent variables, the limited sample size, the fact that the sample was limited to a specific geographical area, the fact that the study was conducted in a certain period of time, and the fact that the depression levels of the participants were determined with a scale. In addition, since the data were collected by self-report method, the tendency of the participants to give socially acceptable answers may have affected the data accuracy. Some potential influential variables may not have been controlled for in the study, which may make it difficult to clearly understand the effects on the dependent variable.

### Conclusion

In this study, malnutrition was detected in approximately one third of the participants (29.6%) and 44% were considered to be at risk of malnutrition. In addition, depression was detected in more than half of the participants (62.5%) and 10.3% were considered to be at risk of depression. This study shows that it is important for primary care family medicine, which is the first point of contact of individuals, and professionals providing home health services to recognize and intervene in the early stages of depression symptoms in order to prevent malnutrition in individuals. Early recognition of possible or existing depression and timely treatment of depression will positively affect the nutritional status of the individual. In this respect, it is important to screen for depression in people who apply to family health centers or home health services and to recognize and treat it early in order to positively affect nutritional status.

## Ethical approval

This study has been approved by the Clinical Research Ethics Committee of SBU İzmir Bozyaka Training and Research Hospital (approval date 14.09.2023, number 2023/157). Written informed consent was obtained from the participants.

## Author contribution

The authors declare contribution to the paper as follows: Study conception and design: GÇ, ÖT; data collection: GÇ, ÖT; analysis and interpretation of results: GÇ, ÖT; draft manuscript preparation: GÇ, ÖT. All authors reviewed the results and approved the final version of the article.

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## Conflict of interest

The authors declare that there is no conflict of interest.

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Research Article

# Investigation of atrial fibrillation frequency in relation to possible thromboembolic events in geriatric patients attending family medicine outpatient clinics

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## ABSTRACT

**Objective:** Atrial fibrillation (AF) is the most common type of arrhythmia and is responsible for a large proportion of hospitalizations. In this study, we aimed to investigate the presence of atrial fibrillation(AF) without developing thromboembolic complications in patients who applied to family medicine.

**Methods:** The study included patients over 65 who applied to A University Training and Research Hospital and a State Hospital Family Medicine polyclinic. Those who had previously been diagnosed with AF were excluded from the study. Electrocardiography (ECG) was performed on patients over 65 who applied to our polyclinics to examine the frequency of AF. To assess the risk of thromboembolism, the $CHA_2DS_2$-VASc score was utilized. This score is a widely accepted and validated risk stratification system designed to predict stroke in patients with non-valvular AF.

**Results:** In a study involving 146 participants with a mean age of 73.86±7.38 years (61.6% female, 38.4% male), AF incidence was 11%. Isolated hypertension was the most common diagnosis, affecting 58% of patients with chronic diseases linked to AF. While AF was more prevalent in men (14.3%), the difference was insignificant (p=0.310). Most patients with AF (87.5%) had a $CHA_2DS_2$-VASc score of 2 or higher. The mean systolic blood pressure was 132.59±22.03 mmHg in non-AF patients compared to 124.00±21.62 mmHg in AF patients. A history of cardiac surgery and arrhythmias was associated with a higher incidence of AF (p=0.010).

**Conclusion:** The prevalence of AF in individuals over 65 years of age was found to be 11%, and the presence of comorbid disease was found to constitute the most important risk group. $CHA_2DS_2$-VASc score was two or above in 87.5% of patients and formed the high-risk group for stroke. In the study, patients with AF diagnosed before the development of thromboembolic complications were referred to the cardiology clinic for thromboembolic prophylaxis. This allowed the organization of cost-effective treatments based on bleeding risk scores and clinical indications. In primary health care services, every patient presentation should be evaluated effectively, and patients with symptoms and findings from a physical examination should be examined for AF.

**Keywords:** atrial fibrillation, thromboembolism, chronic disease, elderly

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## Introduction

Atrial fibrillation (AF) is the most common type of arrhythmia and is responsible for a large proportion of hospitalizations.[1] The incidence of AF in the general population is 1-2%, increasing with age. AF is more common in men. AF can result in heart failure, ischemic stroke, and mortality. Ischemic stroke is one of the most critical complications of AF, causing mortality and morbidity.[2] Although the causes of AF include acute alcohol intake, surgical interventions, electric shock, pericarditis, myocarditis, pulmonary embolism, and hyperthyroidism, the most important causes are cardiovascular diseases such as valvular heart disease, heart failure, coronary artery disease, and hypertension accompanied by left ventricular hypertrophy.[3] In some recent studies, it has been mentioned that inflammation and obesity may also be associated with AF.While cardiovascular diseases are the primary causes of AF, various modifiable and non-modifiable factors associated with individual, family, and lifestyle characteristics also contribute to its development. Consequently, early identification and screening of at-risk individuals in primary care settings are crucial for public health.[4] Anticoagulant therapy recommendations according to ESC(European Society of Cardiology) AF treatment guidelines are shown in Table 1.

Our study aims to assess the frequency of AF through ECG(Electocardiography) screening in patients over 65 years of age who visit the family medicine outpatient clinic. We seek to highlight how this screening contributes to clinical practice. We hypothesize that the prevalence of AF in this patient group may be higher than anticipated, and that early diagnosis could be crucial in reducing morbidity and mortality.

The $CHA_2DS_2VASc$ score calculates the risk of thromboembolism in patients with non-valvular AF. In this scoring, congestive heart failure, hypertension, advanced age, diabetes mellitus, female gender, stroke, and vascular disease accompanying AF are used in the calculation of stroke risk.[2,5,6] The primary target of AF treatment is to reduce cardiovascular mortality and morbidity. To this end, the treatment goals are to prevent thromboembolic events, improve quality of life through symptom control, and reduce hospitalizations. Anticoagulant therapy is the primary treatment method for preventing thromboembolic complications in all types of AF. Studies have shown that vitamin K antagonists (VKA) reduce the risk of stroke by 64% compared to placebo. Still, the INR (International Normalized Ratio) level should be closely monitored using VKAs.[7]

**Table 1.** Anticoagulant therapy recommendations according to ESC AF treatment guidelines

| AF Risk Factor | | Points |
|---|---|---|
| C | Congestive Heart Failure<br>Left Ventricular Dysfunction | 1 |
| H | Hypertension | 1 |
| A2 | Age ≥75 | 2 |
| D | Diabetes Mellitus | 1 |
| S2 | Stroke/Systemic Embolism | 2 |
| V | Vascular Disease/Previous MI/PAH/Atherosclerosis | 1 |
| A | Age 65-74 | 1 |
| Sc | Gender Category (Female) | 1 |
| Recommendation | | $CHA_2DS_2$-VASc Score |
| No Antithrombotic Therapy | | 0 |
| Oral Anticoagulant Therapy | | 1* |
| Oral Anticoagulant Therapy | | ≥2 |

MI: Myocardial Infarction PAH: Pulmonary Arterial Hypertension.
*: Anticoagulant therapy is not recommended if 1 point is obtained from the Female gender category.

Published follow-up studies have shown that a substantial proportion of patients with AF do not receive anticoagulant therapy.[8] However, a large proportion of patients have thromboembolic complications or stroke. Mortality rates of patients with AF-induced thromboembolic events are

higher than those without AF. Although 20% of AF cases with ischemic stroke resulted in mortality and 60% in morbidity, the rate of receiving anticoagulant therapy remained below 50%.[9] Early diagnosis of patients with AF in primary care and early initiation of anticoagulant treatment are essential to prevent possible complications.

## Materials and Methods

This is a cross-sectional analytical study. The study population consisted of patients over 65 who applied to the Ordu University Training and Research Hospital Family Medicine Clinic and the Aybastı State Hospital Family Medicine Polyclinic. The sample size was not calculated, and patients who used our polyclinics between Nov 1, 2021, and May 31, 2022, were included in the study. Those who had previously been diagnosed with AF were excluded from the study. It aimed to examine the frequency of AF by performing electrocardiography (ECG) in patients over 65 who applied to our polyclinics. ECG recordings were obtained using a standard 12-lead electrocardiography device. The dependent variable of our study was the presence of AF. Irregular atrial activation and rhythm with fibrillation waves on ECG were evaluated in favor of AF. The independent variables of our study were age, gender, blood pressure, and laboratory parameters. Blood pressure was measured from both arms in the sitting position after the patients had rested for 5 minutes. Measurements were made using a manual sphygmomanometer, and the average of the two measurements was recorded as the blood pressure value. No formal sample size calculation was conducted for this study. The sample included all eligible patients within the specified timeframe. However, since participants were recruited exclusively from two family medicine outpatient clinics, the findings may not adequately represent the broader population of older adults.

Laboratory assessments were conducted on all participants to evaluate their renal, thyroid, hematologic, and inflammatory status. The following parameters were measured: urea (mg/dL), creatinine (mg/dL), glomerular filtration rate (GFR, mL/min), thyroid-stimulating hormone (TSH, mIU/L), free thyroxine (T4, ng/dL), leukocyte count (µL), hemoglobin (g/dL), mean corpuscular volume (MCV, fL), platelet count (µL), and C-reactive protein (CRP, mg/L). The results of these tests were compared between patients with atrial fibrillation and those without, to identify potential associations.

In this study, AF was identified as the dependent variable. The sample consisted of all individuals over the age of 65 who visited the outpatient clinic during the study period, ensuring that the study population accurately represented this demographic. To assess the risk of thromboembolism, the $CHA_2DS_2VASc$ score was utilized. This score is a widely accepted and validated risk stratification system designed to predict stroke in patients with non-valvular AF. Its validity and reliability have been confirmed in numerous studies.[5] The $CHA_2DS_2VASc$ score is based on several clinical risk factors: congestive heart failure (1 point), hypertension (1 point), age 75 years or older (2 points), diabetes mellitus (1 point), prior stroke/transient ischemic attack/thromboembolism (2 points), vascular disease (1 point), age 65–74 years (1 point), and female sex (1 point). The total score can range from 0 to 9, with higher scores indicating a greater risk of stroke.

Statistical analyses were conducted using SPSS version 25. The normality of the variables was assessed using the Shapiro-Wilk test. Descriptive statistics are presented as means with standard deviations. Parameters that were not normally distributed were compared between groups using the Mann-Whitney U test. Differences between groups regarding chronic diseases were evaluated using the chi-square test.

The study was approved by the Clinical Research Ethics Committee of a Clinical Research and Ethic Comittee of Ordu University.

## Results

The mean age of 146 participants was 73.86±7.38 years; 90 (61.64%) were female, and 56 (38.36%) were male. The incidence of AF on the ECG of the patients was found to be 10,96%. Isolated hypertension was the most common diagnosis of 104 (71.22%) patients with chronic diseases that may be associated with AF, with 32.19%. The presence of comorbidities (additional risk factors accompanying diabetes and hypertension) was 12.33%, and the presence of diabetes and hypertension was 8.90% among other common diseases. Laboratory results were analyzed to identify potential differences between patients with atrial fibrillation (AF-positive) and those without (AF-negative). No statistically significant differences were found in the levels of urea, creatinine, glomerular filtration rate (GFR), thyroid-stimulating hormone (TSH), thyroxine (T4), leukocyte count, hemoglobin, mean corpuscular volume (MCV), or C-reactive protein (CRP) between the two groups ($p > 0.05$ for all comparisons). Platelet levels were found to be statistically significantly higher among patients in the non-AF group compared to those with AF($p=0.035$). These findings suggest that, within our cohort, routine laboratory parameters were not significantly linked to the presence of atrial fibrillation (Table 2).

The mean age of patients with AF on ECG was 74.44±7.5 (years) compared to 74.44±6.53 in the group without AF ($p=0.743$). It was seen that male patients were diagnosed with AF at a higher rate than females (14.29%), but there was no statistically significant difference ($p=0.310$). The rate of accompanying hypertension in the group with AF was calculated as 68.75%. The mean $CHA_2DS_2$-VAS score of patients with AF was 2.94±1.24, and the median was 3 (max5-min1). 87.5% of patients with AF had a $CHA_2DS_2VASc$ score of 2 or above. The mean systolic blood pressure (SBD) was 132.59±22.03 mmHg in the group without AF and 124.00±21.62 mmHg in the group with AF. Diastolic blood pressure (DBP) was 78.84±14.38 mmHg in the group with AF and 75.75±14.95 mmHg without AF. There was no statistically significant difference between the participants' mean systolic and diastolic blood pressure regarding AF presence. The incidence of AF was higher in patients with a history of cardiac surgery and arrhythmia compared to other chronic diseases. It constituted a statistically significant difference between chronic diseases and AF($p=0.010$). There was no statistically significant relationship between other chronic diseases and the presence of AF (Table 3).

## Discussion

Our study examined the presence of AF in patients over 65 who applied to our polyclinics. The incidence of AF increases with age, and the risk of stroke increases with it. Follow-up and treatment of comorbid conditions that increase the risk of AF development play an important role in AF prevention. Thromboembolism prophylaxis is the most essential part of treatment in AF patients. Primordial protection and primary prevention are of great importance in providing primary healthcare. In primordial and primary prevention, it is a priority to increase scanning methods to reach risk groups and prevent disease before it occurs.

The study was conducted during the COVID-19 pandemic, and therefore, hospital admissions were low, resulting in a low number of patients included in the study. Thus, no generalization can be made in the light of the available data. The mean age of 146 participants was 73.86±7.38 years; 90 (61.64%) were female, and 56 (38.36%) were male. In the cohort study of F. Russel Quinn et al. in 22 family medicine centers in 2016, the mean

**Table 2.** Clinical characteristics of the patients who participated in the study

| Clinical Characteristics | | Average | Standard Deviation | n (%) |
|---|---|---|---|---|
| Age (years) | | 73.86 | 7.38 | |
| Gender | Female | | | 90 (61.64) |
| | Male | | | 56 (38.36) |
| Chronic Diseases | None | | | 42 (28.78) |
| | Diabetes | | | 12 (8.23) |
| | Hypertension | | | 47 (32.19) |
| | Chronic Artery Disease | | | 11 (7.53) |
| | History of Cardiac Surgery | | | 1 (0.68) |
| | History of Arrhythmia | | | 1 (0.68) |
| | Congestive Heart Failure | | | 0 (0.0) |
| | Valvular Heart Disease | | | 1 (0.68) |
| | Comorbid Disease | | | 18 (12.33) |
| | Presence of Diabetes and Hypertension | | | 13 (8.90) |
| ECG | No AF | | | 130 (89.04) |
| | Has AF | | | 16 (11.96) |
| Systolic Blood Pressure (mmHg) | | 131.84 | 22.02 | |
| Diastolic Blood Pressure (mmHg) | | 78.57 | 14.37 | |
| Laboratory Parameters | Urea (mg/dL) | 34.03 | 16.96 | |
| | Creatinin (mg/dL) | 0.89 | 0.32 | |
| | GFR (mL/min) | 75.32 | 19.73 | |
| | TSH (mlU/L) | 2.40 | 2.61 | |
| | T4 (ng/dL) | 1.18 | 0.22 | |
| | Leukocyte (µL) | 6827.86 | 2385.54 | |
| | Hemoglobin (g/dL) | 12.84 | 1.87 | |
| | MCV (fL) | 87.90 | 5.45 | |
| | Platelet (µL) | 251.91 | 75.12 | |
| | CRP (mg/L) | 2.47 | 5.15 | |

GFR: Glomerular Filtration Rate TSH: Thyroid Stimulating Hormone MCV: Mean Corpuscular Volume T4: Thyroxine CRP: C-Reactive Protein ECG: Electrocardiography AF: Atrial Fibrillation

age was 73.7±6.9 years; 46.6% of the participants were male, and 54.4% were female.[10] In the study, the mean age of patients with AF was higher, with a significance rate of $p<0.01$. A study conducted by Karaçağlar et al. in 2010 determined that 71.6% of patients with AF were 65 years and older.[11] In our study, the mean age of patients with AF (74.44±6.53) was higher than those without AF (73.79±7.50), although not statistically significant. AF increases with age, which is supported by the data we found. In the study of Karaçağlar, 58.5% of the patients with AF were female. In the Turkish Adult Risk Factor study conducted in Turkey, it was observed that the incidence of AF was 1/7 less in men than in women. The Turkish Adult Risk Factor study is Turkey's most comprehensive AF prevalence and incidence study. This study found that the prevalence of AF in Turkey was lower than in Europe.[12] In the REALISE-AF study conducted in 866 centers in 26 countries, 73.9% of the patients were over 60, and 56% were male.[13] While the increase in AF with age was similar

**Table 3.** AF cases observed on electrocardiography by clinical characteristics of patients

| | | ECG | | | | | | p |
|---|---|---|---|---|---|---|---|---|
| | | No AF, N=130 | | | Has AF, N=16 | | | |
| | | Average | SD | n (%) | Average | SD | n (%) | |
| Age(years) | | 73.79 | 7.50 | | 74.44 | 6.53 | | 0.743* |
| Gender | Female | | | 82 (91.11) | | | 8 (8.89) | 0.310** |
| | Male | | | 48 (85.71) | | | 8 (14.29) | |
| Chronic Diseases | None | | | 37 (88.10) | | | 5 (11.90) | 0.010** |
| | Diabetes | | | 12 (100.00) | | | 0 (0.00) | |
| | Hypertension | | | 44 (93,62) | | | 3(6.38) | |
| | Coronary Artery Disease | | | 9 (81.82) | | | 2 (18.18) | |
| | Comorbidity | | | 16(76.19) | | | 5(23.81) | |
| | Diabetes+Hypertension | | | 12 (92.31) | | | 1 (7.69) | |
| Systolic Blood Pressure (mmHg) | | 132.59 | 22.03 | | 124.00 | 21.62 | | 0.294* |
| Diastolic Blood Pressure (mmHg) | | 78.84 | 14.38 | | 75.75 | 14.95 | | 0.564* |
| $CHA_2DS_2VASc$ | | - | - | | 2.94 | 1.24 | | |

*Mann-Whitney U Test **Chi-square test
ECG: Electrocardiography, AF: Atrial Fibrillation

in studies conducted in Turkey and worldwide, the difference in incidence in the female gender in Turkey and worldwide was attributed to differences in inflammation or blood pressure. These studies provide us with limited data, and more comprehensive studies are needed.

In our study, the incidence of AF on the ECG of the patients was found to be 10.96%. The prevalence of AF was found to be 9.1% in the study by Karaçağlar et al., while in the Rotterdam study, the prevalence of AF was found to be 5.5% at the age of 55 and above, reaching 17.8% at the age of 85 and above.[11] In an AF prevalence study conducted in a family medicine clinic in Canada, the incidence of AF was found to be 8.2% at the age of 60 and above, and it reached 18.22% at the age of 80 and above.[14] The incidence of AF was similar to studies conducted with similar age groups.

Isolated hypertension was the most common diagnosis of 104 patients with chronic diseases that may be associated with AF, with 32,19%. The presence of comorbid diseases (risk factors accompanying diabetes and hypertension) was 12.33%, and the presence of diabetes and hypertension was 8.90%, among other common diseases. In the group with AF, the incidence of hypertension was found to be 68.75%. In the Turkish Adult Risk Factor study, it was observed that hypertension accompanied AF in 65.7% of patients, followed by coronary artery disease in 44.8% and congestive heart failure in 13.4%.[12] In the REALISE-AF study, it was observed that the association of hypertension was 72.2%, the presence of dyslipidemia was 46.3%, congestive heart failure was 45.8%, obesity was 32.7%, and coronary artery disease was 32.3%.[13] In the AF study conducted by the European Society of Cardiology in 2005, it was found that 60% of the patients had a comorbid disease, with hypertension being the most common comorbid disease. In the study, the association of hypertension was found to be 47.5% and the presence of dyslipidemia was found to be 35.5%.[8] In the ROCKET-AF study,

the association of hypertension was found to be relatively high at 90.5%.[15] In studies conducted in Turkey and around the world, hypertension is the most common chronic disease accompanying AF. In another study, data indicated that prolonged exposure to high blood pressure may cause cardiac enlargement and structural and electrical deterioration, which may result in AF.[16] Our study was found to be compatible with the literature.

The mean SBP was 132.59±22.03 mmHg in the group without AF and 124.00±21.62 mmHg in the group with AF. The mean DBP was calculated as 78.84±14.38 mmHg in the group with AF and 75.75±14.95 mmHg in the group without AF. There was no statistically significant difference between the participants' mean systolic and diastolic blood pressure regarding AF presence. In the study of F. Russel Quinn, the mean SBP was 133.2±17.8, the mean DBP was 77.9±11.87 in patients with AF, and no significant difference was observed with those without AF.[10] In the REALISE-AF study, the mean SBP was 132.8±19.4, and the mean DBP was 79.8±11.4. Mean blood pressure was similar in studies conducted with similar age groups.

The mean $CHA_2DS_2VASc$ score of patients with AF was 2.94±1.24, and the median was 3 (max5-min1). The score was two or higher in 87.50% of the patients.[13] In the study of Karaçağlar, it was seen that 87.2% of the patients had a score of 2 or higher.[11] In the study of F. Russel Quinn, it was seen that 91.6% of the patients had a score of 2 or higher.[10] To reduce the risk of thromboembolism in patients with a $CHA_2DS_2VASc$ score of 2 and above, it is highly recommended to administer anticoagulant therapy. The patients included in our study were not receiving antithrombotic or anticoagulant therapy. Patients who were found to have AF in the ECG were referred to the Cardiology clinic for anticoagulant therapy.

In a large-scale primary care cohort study conducted by Khurshid et al. in 2023, the prevalence of atrial fibrillation (AF) was reported as 6.4% in individuals aged 65 to 69, rising to 28.5% among those aged 85 years and older. These findings clearly emphasize that age is one of the strongest determinants of AF development.[17] Globally, analyses based on GBD 2019 data revealed that between 1990 and 2019, the incidence of AF increased by approximately 1.1-fold, while mortality rose by 1.4-fold. This underscores that AF is not only a regional issue but also a growing global public health concern.[18] The GLORIA-AF registry highlighted the presence of distinct comorbidity phenotypes among AF patients, which vary in terms of anticoagulation strategies and long-term prognosis. This variation underscores the necessity for a personalized and patient-centered approach to AF management.[19] Similarly, Machado et al. demonstrated that integrated care models—including medical treatment, psychosocial support, and patient education—can reduce complications such as stroke and heart failure, while also improving the quality of life for patients with AF.[20] International guidelines from the ACC/AHA and ESC emphasize the importance of lifestyle modifications (such as dietary changes, increased physical activity, and alcohol reduction) and opportunistic screening in high-risk groups within primary care as essential strategies for AF prevention and early detection. This perspective is reinforced by a 2024 Medscape report, which highlighted the critical role of primary care physicians not only in diagnosing AF but also in managing it through blood pressure and diabetes control, as well as lifestyle interventions. Importantly, AF has been described as “not merely an arrhythmia, but a complex disease” that requires a multidisciplinary approach.[21] In 2024, Linz et al. reported that the lifetime risk of developing AF in individuals over 45 years old is as high as one in three to one in five. Both the European Society of Cardiology (ESC) and the U.S. Preventive Services Task Force (USPSTF) recommend opportunistic screening for individuals aged 65 years and older. This screening has been shown to detect

approximately 1.4% of previously undiagnosed AF cases.[22] These findings suggest that even simple ECG applications in primary care settings can lead to significant public health benefits. In our study, the prevalence of AF detected via ECG was 10.96%. Consistent with the findings of Linz et al. opportunistic screening proves to be a valuable method for identifying asymptomatic cases. Therefore, implementing low-cost and easily applicable screening strategies in primary care is crucial for the early detection of AF, prevention of complications, and reduction of the disease burden at the population level.

The most significant limitation was the small number of patients included in our study, as well as the inclusion of only those who applied to the family medicine outpatient clinic, which limited the generalizability of our findings to the broader population. Surveying the COVID-19 pandemic significantly reduced hospital admissions, resulting in even fewer patients. In addition, the single-center and short-term design of the study further restricts the strength and external validity of the conclusions

## Conclusion

AF is the most common arrhythmia in Turkey and worldwide, and its incidence increases with age. In most patients, AF is detected during thromboembolic complications. Periodic screening of patients in the risk group may play an essential role in preventing thromboembolic complications before they occur. The ESC Guideline on AF screening, published in 2022, and the US Preventive Services Task Force report do not provide a definitive recommendation due to insufficient randomized controlled trials on unnecessary screening. The guidelines also warn about the cost of unnecessary tests and quaternary protection.[23,24] The frequency of AF is expected to increase with life expectancy. As life expectancy increases, there is an increase in comorbid diseases, which results in an exponential increase in risk factors.

Thromboembolic complications cause severe mortality and morbidity, leading to significant material and non-material problems. In our study, AF patients diagnosed before thromboembolic complications developed were referred to the cardiology clinic for thromboembolic prophylaxis. This allowed the organization of cost-effective treatments based on bleeding risk scores and clinical indications. In primary health care services, every patient presentation should be evaluated effectively, and patients with symptoms and findings from a physical examination should be examined for AF.

## Ethical approval

This study has been approved by the Ordu University's Clinical Research Ethics Committee (approval date 07.10.2021, number 2021/222). Written informed consent was obtained from the participants.

## Author contribution

The authors declare contribution to the paper as follows: Study conception and design: TD, GD; data collection: TD, MK; analysis and interpretation of results: TD, MM, GD; draft manuscript preparation: TD, DG, ÖE. All authors reviewed the results and approved the final version of the article.

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## Conflict of interest

The authors declare that there is no conflict of interest.

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Research Article

# Evaluation of family physicians' attitudes to defensive medicine practices and its effect on providing driving licence reports

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This study has been previously presented as an oral presentation in TAHEV 14. Istanbul Aile Hekimliği Kongresi 10th of June in 2023.

## ABSTRACT

**Objective:** To examine the attitude of family physicians practicing at primary care units in İstanbul regarding defensive medicine practices and their effect on providing driving license health report provisions and the frequency of dispatches.

**Methods:** 396 family physicians practicing in primary care units in Istanbul were included in this observational and descriptive study between March and April 2023. Volunteering physicians were invited to participate in an online questionnaire including sociodemographic characteristics, knowledge and experience questions about defensive medical practice (DMP), the number of examinations and driving license provisions they have issued in the last year, and the rate of referrals to secondary or tertiary health centers. Defensive Medicine Practices Attitude Scale (DMPAS) was also performed online through which negative and positive DMP attitudes were assessed. Participants were classified as having very high (55-44 points), high (43-33 points), moderate (32-22 points), and mild (21-11 points) defensive attitude. Participants' attitudes towards providing driving license health reports were scored with a 5-point Likert-type scale. DMPAS scores were compared in terms of all data.

**Results:** Among 396 participants, more than half were female (54.3%; n=215). Mean age was 39.3±8.9 years [Min 24,0-Max 60.0]. According to DMPAS, 94.5% of the participants exhibited a moderate or higher defensive attitude. Participants who were male ($p < 0.05$), married ($p < 0.05$), and specialist physicians ($p < 0.05$) scored significantly higher in DMPAS compared to their counterparts. As the physicians' age, years of experience, and the number of registered patients increased, DMPAS decreased ($r = -0.668$, $p < 0.001$; $r = -0.638$, $p < 0.00$; $r = -0.154$, $p = 0.002$, respectively).

The study shows that physicians who frequently refer patients to secondary or tertiary hospitals for driving reports and who have a high demand for driving reports among those aged 17 and over in their care population exhibited significantly higher defensiveness scores ($p < 0.05$). In other words, physicians who had more defensive attitudes preferred to consult the provision to the secondary or tertiary hospitals rather than approving the application.

**Conclusion:** Defensive medicine practices in family physicians are relatively high, increasing the dispatch rate in driving license reports. The increasing rate of referrals from primary care units due to defensive medicine practice results in a patient burden on secondary or tertiary healthcare institutions.

**Keywords:** defensive medicine, attitude, defensive practice, driving license health report, primary care, family medicine

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## Introduction

Medical error is defined as inappropriate conduct that causes harm to the patient, including negligence and recklessness.[1] Medical errors, whether personal or system-related, lead to defensive medical practices (DMP). DMP can be defined as healthcare providers straying from sound medical practices to reduce their risk of malpractice liability or other self-protective reasons.[2]

According to Turkish Family Medicine Law, a family physician is defined as a full-time physician obliged to provide preventive and rehabilitative health services, primary diagnosis, and treatment to everyone comprehensively and continuously in a particular place, regardless of the patient's age, gender, and disease, who provides mobile health services to the extent necessary.[3]

Studies have shown that the cost of health services is higher in countries that fail to fulfill the family medicine obligations in primary health care services.[4] Yet, health practice of family physicians should be cost-effective as they provide appropriate, personal, and patient oriented care services to their patients. These expectations are often unmet as physicians' workload and fear of being sued give rise to DMP, which is defined as ordering unnecessary tests and procedures and avoiding treatments for high-risk patients or referrals.[5,6]

### Defensive Medicine Practices

Defensive medicine practices manifest themselves in two dimensions, namely positive and negative responses. It is important to recognize that DMP, whether positive (when extra procedures are performed without proven necessity) or negative (when high-risk patients and methods are avoided), is not just a medicolegal concept but also carries a moral dimension.[1,7,8]

A scoping review investigating the influencing factors of defensive decision-making in primary care reported four main categories. These are (social) media pressure, patients' acting like a consumer and expecting a particular service from the physician as their healthcare provider, thirdly healthcare system-based working conditions that exert pressure on physicians by requiring compliance with external regulations and provisions, and lastly physicians' feelings, experiences and expectations shaping their tolerance for the uncertainty that foster their tendency for defensive medical thinking and practice.[9] Besides these, a lack of clear knowledge of the concepts underlying the word negligence and the legal penalties that will arise in response to these may also lead to defensive medical practices.[1,2]

Although defensive medicine practices are debated in all countries, studies conducted among physicians have shown that they are applied at high rates. Some studies notably conclude that defensive medicine is practiced at a rate of 98% in Japan, between 79-93% in the USA, 80% in Italy, 60% in Israel, and at a rate of 78% in Turkey.[10,11]

One of the obstacles to cost-effectiveness is defensive medicine practices. Physicians and other healthcare professionals use defensive medicine practices to protect themselves from malpractice lawsuits, rather than focusing on ensuring the recovery and wellbeing of their patients.

### Defensive Medicine Practices on Preparing Health Reports

Family physicians are charged with the task of preparing most of the reports. This duty is stated in the family medicine law as follows: "Any kind of report, referral document, prescription, and other documents required to be prepared by primary healthcare institutions and government physicians are prepared by family physicians in

places where family medicine practice has been implemented."[3]

Health report preparation is a challenging expert task that requires a detailed examination and investigation in the field where the report is requested without deviating from the framework of rules and laws. Institutions request these reports to use them as evidence on a specific issue when necessary, to be kept for years. Therefore, it should not be erroneously assumed that the report preparation process is a simple document preparation. The legal aspect of health reports, including driver and driver candidate health reports, overlaps with defensive medical practices developed to avoid the possibility of litigation.

The present study has several aims: To assess the prevalence of defensive medicine attitudes among family physicians and how varying levels of these attitudes affect the number of driver health reports they prepare and refer, and to determine whether these attitudes contribute to a shift in patient load toward secondary and higher-level health services. Additionally, we aim to identify the diversity in family physicians' driver report preparation behaviors and the frequency of problems they may encounter during this process.

## Materials And Methods

This observational, descriptive, analytical study was conducted among family physicians working in family medicine units affiliated with the Istanbul Provincial Health Directorate between March 6 and April 6, 2023. It was approved by the Clinical Research Ethics Committee of the University of Health Sciences, Istanbul Training and Research Hospital, Turkey (date: 14.10.2022, number: 307). The work was started following the principles of the Declaration of Helsinki. The study targeted family physicians who had been employed in the same unit for over a year and was administered online. The study aimed to recruit at least 384 participants, based on an effect size of 0.5, with 80% power and a 5% margin of error, from a population of 4,981 active family medicine units. Ultimately, 396 family physicians who met the inclusion criteria participated in the study and were asked to complete the survey with their informed consent.

The survey consisted of a 41-item online questionnaire including questions about participants' sociodemographic characteristics, knowledge and experiences related to defensive medicine, the number of examinations and driver reports they prepared in the past year, and their attitudes towards defensive medicine as measured by the Defensive Medicine Practices Attitudes Scale (DMPAS).

DMPAS was validated into Turkish by Başer et al. in 2014[12] and began to be widely used in studies due to its high internal consistency. The 15-item scale consists of 3 subscales: six questions measuring attitudes toward positive defensive medicine practices, five questions measuring attitudes toward negative defensive medicine practices, and four questions assessing physicians' knowledge and experiences related to defensive medicine.[12] While the first two sections are administered on a 5-point Likert scale, the third section uses a "Yes/No" option, with questions divided evenly between the two choices.[12] The total scores ranging from 11 to 55 are classified into very high (55-44 points), high (43-33 points), moderate (32-22 points), and low (21-11 points) defensive attitudes. Participants' attitudes toward driver health reports were assessed using a 5-point Likert scale (ranging from 1= never, 2= rarely, 3= sometimes, 4= often, and 5 = always), and DMPAS scores were compared across all the data.

SPSS 28.0 software was used for the statistical evaluation of the data. Descriptive statistics included mean, standard deviation, median, minimum, maximum, frequency, and ratio values. The distribution of variables was assessed using

the Kolmogorov-Smirnov Test. Kruskal-Wallis and Mann-Whitney U Test were employed to analyze quantitative independent data. The relation between continuous variables was evaluated using Spearman's Correlation Analysis.

This research was conducted in accordance with the principles of good clinical practice based on the current guidelines of the Helsinki Declaration, relevant regulations, and ethical principles.

## Results

A total of 396 participants were included in the study. Their sociodemographic characteristics and relevant numerical data related to family medicine units are presented in Table 1. The total number of registered patients in the family medicine units ranged from a maximum of 4085 to a minimum of 328, with units having less than three thousand patients making up 17% of the participants (n=68). The mean number of patients examined by participants was 9672 in the past year, and the mean number of individuals issued driver health reports by participants in the past year was 182. It was observed that 45% of these reports were issued on referral.

Most participants (71.7%, n=284) stated that they had previously heard of the concept of defensive medicine. Yet, a majority of those who had heard about it mentioned that they did not have sufficient knowledge (68.2%, n=270). Approximately one-fourth of participants (24.5%, n=97) reported receiving a punitive warning that could potentially reflect negatively on their salary during their contract period. Nearly all participants (96.7%, n=383) believed a medical malpractice case would impact their medical performance, and only 4.8% (n=19) had been sued for alleged malpractice. Participants' DMPAS scores had a mean of 36.8 ± 8.0, with 19.4% (n=77) indicating a very high, 49.5% (n=196) indicating a high, 25.5% (n=101) indicating a moderate, and 5.6% (n=22) indicating a mildly defensive attitude (Table 2).

Within Positive DMP, participants most frequently relied on maintaining more detailed records to safeguard themselves from legal issues ($M$ = 3.7±1). On the other hand, refusal to request unnecessary tests for protection against legal issues was the least employed practice ($M$ = 3.2±1.2). Within Negative DMP, feelings of unease, driven by the widespread media attention on medical malpractice issues was rated the highest by participants ($M$ = 4.3±0.8). On the other hand, the practice participants least resorted to was avoiding patients with complex medical problems to protect themselves from legal risks ($M$ = 2.5±1.4) (Table 3).

Regarding participants' driver health reports, it was revealed that the question regarding careful examination of patients' data from e-Nabız, which is an application developed for citizens and health professionals, to enable them to access to health data collected from health institutions in Turkey, received the highest score ($M$ = 4.63±0.8), while the question inquiring participants' experience with physical violence from referred patients received the lowest score (M = 1.22±0.6) (Table 4).

When preparing driver and driver candidate health reports, participants most frequently preferred medical school education (75.8%) and experiences gained from colleagues (59.3%) as sources of information. In contrast, the least preferred sources were the Ministry of Health in-service training (12.1%) and national and international guidelines (8.1%). Comparative analyses revealed that DMPAS scores were significantly higher among males than females, married individuals compared to singles, and resident physicians enrolled in Family Physician and Contracted Family Physician Specialist (CFPS) assistant training compared to general practitioners ($p<0.05$) (Table 5).

**Table 1.** Sociodemographic characteristics of participants and numerical data related to family medicine unit

| | | Min - Max | Median | Mean±SD | n (%) |
|---|---|---|---|---|---|
| Age | | 24.0 - 60.0 | 37.0 | 39.3±8.9 | |
| Gender | Male | | | | 181 (%45.7) |
| | Female | | | | 215 (%54.3) |
| Marital Status | Single | | | | 115 (%29.0) |
| | Married | | | | 269 (%67.9) |
| | Divorced | | | | 12 (%3.0) |
| Family Medicine Status | General Practitioner Family Physician | | | | 239 (%60.4) |
| | Family Medicine Specialist | | | | 58 (%14.6) |
| | Contracted Family Physician Specialist (CFPS) assistant | | | | 99 (%25) |
| Professional Experience (Years) | | 1.0 – 34.0 | 11.0 | 12.9 ± 8.3 | |
| Family Medicine Experience (Years) | | 1.0 – 17.0 | 7.0 | 7.7 ± 4.4 | |
| Total Number of Patients Registered in the Family Medicine Unit | | 328 – 4085 | 3716 | 3475 ± 633 | |
| Total Number of Patients ≥17 Years Old Registered in the Family Medicine Unit | | 210 – 3562 | 2465 | 2357 ± 546.5 | |
| Total Number of Patients Applying for Examination* | | 186 - 24000 | 9869 | 9672 ± 3032 | |
| Total Number of Drivers and Driver Candidates Not Referred for Driver Health Report* | | 0.0 – 318 | 84.5 | 102.7 ± 73.3 | |
| Total Number of Drivers and Driver Candidates Referred for Driver Health Report* | | 0.0 – 480 | 69 | 79.1 ± 66.7 | |
| Number of Examinations per Fully Registered Patient* | | 0.57 – 6.67 | 2.75 | 2.78 ± 0.72 | |
| Number of Driver Reports per Registered Population ≥17 Years Old* | | 0.00 – 0.28 | 0,07 | 0.08 ± 0.04 | |
| Referral Rate in Total Driver Reports Issued* | | 0.00 – 1.00 | 0.50 | 0.45 ± 0.27 | |

* Within the Last Year

Participants' familiarity with and knowledge about defensive medicine, experience with receiving punitive warnings or malpractice lawsuits, or their belief that malpractice cases impact medical performance, did not significantly affect their DMPAS score ($p>0.05$). There was a significant negative correlation ($p<0.05$) between participants' age, years of professional and family medicine experience, their total registered patients and number of patients aged over 17 in the family medicine unit, and their DMPAS scores.

Participants' DMPAS scores were negatively correlated ($p<0.05$) with their age, years of professional and family medicine experience, their total registered patients, and the number

**Table 2.** The defensive medicine practices attitude scale (DMPAS) data

| | Min - Max | Median | Mean.±SD |
|---|---|---|---|
| DMPAS Score | 12.0 -55.0 | 38.0 | 36.8±8.0 |
| Negative DMPAS Score | 5.0 – 25.0 | 16.0 | 16.1±4.1 |
| Positive DMPAS Score | 7.0 – 30.0 | 22.0 | 20.8±4.5 |
| **DMPAS Score Distribution** | **n** | | **Percentage** |
| Very high (44-55) | 77 | | 19.4% |
| High (33-43) | 196 | | 49.5% |
| Moderate (22-32) | 101 | | 25.5% |
| Mildly (11-21) | 22 | | 5.6% |

**Table 3.** Distribution of DMPAS responses

| | Strongly Disagree | Disagree | Neutral | Agree | Strongly Agree | Mean ± SD |
|---|---|---|---|---|---|---|
| | n(%) | n(%) | n(%) | n(%) | n(%) | |
| **Positive DMPAS Responses** | | | | | | |
| 1- I request additional tests from my patients beyond what I think is necessary to protect myself from legal issues. | 38 (9.6%) | 66 (16.7%) | 135 (34.1%) | 90 (22.7%) | 67 (16.9%) | 3.2±1.2 |
| 2- I prescribe most medications within my indications for my patients to protect myself from legal issues. | 18 (4.5%) | 64 (16.2%) | 111 (28.0%) | 139 (35.1%) | 64 (16.2%) | 3.4±1.1 |
| 3- I request more consultations related to potential complications in my patients to protect myself from legal issues. | 13 (3.3%) | 58 (14.6%) | 134 (33.8%) | 114 (28.8%) | 77 (19.4%) | 3.5±1.1 |
| 4- I explain medical procedures in more detail to my patients to protect myself from legal issues. | 15 (3.8%) | 48 (12.1%) | 131 (33.1%) | 119 (30.1%) | 83 (21.0%) | 3.5±1.1 |
| 5- I allocate more time to my patients to protect myself from legal issues. | 15 (3.8%) | 56 (14.1%) | 137 (34.6%) | 114 (28.8%) | 74 (18.7%) | 3.4±1.1 |
| 6- I keep more detailed records to protect myself from legal issues. | 9 (2.3%) | 40 (10.1%) | 104 (26.3%) | 154 (38.9%) | 89 (22.5%) | 3.7±1 |
| **Negative DMPAS Responses** | | | | | | |
| 7- I avoid patients with a high likelihood of legal action to protect myself from legal issues. | 93 (23.5%) | 96 (24.2%) | 89 (22.5%) | 664 (16.7%) | 52 (13.1%) | 2.7±1.3 |
| 8- I avoid patients with complex medical problems to protect myself from legal issues. | 135 (34.1%) | 98 (24.7%) | 56 (14.1%) | 59 (14.9%) | 48 (12.1%) | 2.5±1.4 |
| 9- I avoid treatment protocols with high complication rates to protect myself from legal issues. | 20 (5.1%) | 71 (17.9%) | 148 (37.4%) | 108 (27.3%) | 49 (12.4%) | 3.2±1 |
| 10- I prefer non-invasive treatment protocols over invasive ones to protect myself from legal issues. | 18 (4.5%) | 60 (15.2%) | 133 (33.6%) | 124 (31.3%) | 61 (15.4%) | 3.4±1.1 |
| 11- As medical malpractice issues receive more attention in the media, I feel uneasy in my medical practice. | 4 (1.0%) | 11 (2.8%) | 45 (11.4%) | 143 (36.1%) | 193 (48.7%) | 4,.3±0.8 |

**Table 4.** Response distributions of questions related to driver health reports

| | Never | Rarely | Sometimes | Often | Always | Mean ± SD |
|---|---|---|---|---|---|---|
| | n(%) | n(%) | n(%) | n(%) | n(%) | |
| 1- Do you carefully review the "Personal Health Information Form" of the patients who apply for a DHR request? | 7 (1.8%) | 16 (4.0%) | 21 (5.3%) | 95 (24.0%) | 257 (64.9%) | 4.46±0.90 |
| 2- Do you carefully review your patient's e-nabız data when preparing a DHR? | 1 (0.3%) | 20 (5.1%) | 21 (5.3%) | 39 (9.8%) | 315 (79.5%) | 4,63±0.80 |
| 3- Do you detail your physical examination when preparing a DHR for your patients? | 1 (0.3%) | 28 (7.1%) | 93 (23.5%) | 114 (28.8%) | 160 (40.4%) | 4.02±1.0 |
| 4- Do you sometimes have patients who request a report without undergoing a physical examination when they come with a DHR request? | 26 (6.6%) | 96 (24.2%) | 144 (36.4%) | 115 (29.0%) | 15 (3.8%) | 2.99±10 |
| 5- Do you request tests from your patients when preparing a DHR? | 21 (5.3%) | 111 (28.0%) | 169 (42.7%) | 47 (11.9%) | 48 (12.1%) | 2.97±10 |
| 6- Do you sometimes have patients who request a report without undergoing tests when they come with a DHR request? | 29 (7.3%) | 87 (22.0%) | 153 (38.6%) | 102 (25.8%) | 25 (6.3%) | 3.02±1 |
| 7- Do any of your patients who request a DHR express that their requests are for a simple documentation process? | 1 (0.3%) | 21 (5.3%) | 81 (20.5%) | 210 (53.0%) | 83 (21.0%) | 3.89±0.8 |
| 8- Does the possibility of a legal process being initiated against you due to the driver health report you issued concern you? | 16 (4.0%) | 29 (7.3%) | 82 (20.7%) | 137 (34.6%) | 132 (33.3%) | 3.86±1.1 |
| 9- Do you have difficulty explaining the reason for referral to patients you refer when issuing DHR? | 28 (7.1%) | 52 (13.1%) | 95 (24.0%) | 175 (44.2%) | 46 (11.6%) | 3.4±1.1 |
| 10- Have you ever experienced verbal abuse when referring patients you have issued DHR for? | 47 (11.9) | 141 (35.6) | 126 (31.8) | 76 (19.2) | 6 (1.5) | 2,63±1 |
| 11- Have you ever experienced physical violence when referring patients you have issued DHR for? | 332 (83.8%) | 44 (11.1%) | 15 (3.8%) | 5 (1.3%) | 0 (0%) | 1.22±0.6 |
| 12- When you prepare a referral report, is your reason for referral ever questioned by a doctor? | 112 (28.3%) | 131 (33.1%) | 108 (27.3%) | 35 (8.8%) | 10 (2.5%) | 2.24±1 |

DHR: Driver Health Report

of patients aged over 17 in the family medicine unit. This suggests that as physicians age, gain more experience, and register more patients, their defensive attitudes tend to decrease (Table 6).

Moreover, DMPAS scores were negatively correlated ($p<0.05$) with the total number of patients examined and the number of driver health reports issued without referral by participating physicians in the last year. Furthermore, DMPAS scores were positively correlated ($p<0.05$) with the number of referral driver health reports issued and the referral rate in drive reports. In other words, as physicians' defensive attitudes decreased, they conducted more examinations and issued more driver health reports without referrals. Conversely, when their defensive attitudes increased, these numbers declined, whereas the number of referral driver health reports increased. In short, it has been observed

**Table 5.** Relation between sociodemographic characteristics and DMPAS score

| | | DMPAS Score | | | P* |
|---|---|---|---|---|---|
| | | Min-Max | Median | Mean.±SD | |
| Gender | Woman | 12 – 51 | 36 | 34.5 ± 8.0 | <**0.001**[m] |
| | Man | 20 – 55 | 40 | 39.6 ± 6.9 | |
| Marital Status | Married | 22 - 50 | 41 | 40.6 ± 6.5 | |
| | Single | 12 - 55 | 37 | 35.1 ± 8.0 | <**0.001**[K] |
| | Divorced | 31 - 51 | 39 | 39,.7 ± 5.9 | |
| Family Medicine Status | General Practitioner | 17 - 50 | 36 | 34.9 ± 8.1 | |
| | Specialist | 12 - 55 | 40 | 38.7 ± 8.5 | <**0.001**[K] |
| | CFPS assistant | 23 - 51 | 41 | 40.4 ± 5.5 | |

* The statistically significant difference was defined as p < 0.05
[m] Mann-Whitney u test test / K Kruskal-Wallistest
CFPS Contracted Family Physician Specialist

**Table 6.** Relation of data with DMPAS scores

| | DMPAS Score | | Negative DMPAS Score | | Positive DMPAS Score | |
|---|---|---|---|---|---|---|
| | r | P* | r | P* | r | P* |
| Age | -0.668 | <**0.001** | -0.649 | <**0.001** | -0.163 | <**0.001** |
| Years of Professional Experience | -0.638 | <**0.001** | -0.609 | <**0.001** | -0.599 | <**0.001** |
| Years of Family Medicine Experience | -0.572 | <**0.001** | -0.552 | <**0.001** | -0.525 | <**0.001** |
| **Number of Patients Registered in the Family Medicine Unit** | | | | | | |
| Total Number of Patients | -0,154 | **0,002** | -0.163 | **0.001** | -0.115 | **0.022** |
| Number of Patients Aged 17 and Over | -0.320 | <**0.001** | -0.310 | <**0.001** | -0.278 | <**0.001** |
| **Numerical Data for the Family Medicine Unit in the Last 1 Year** | | | | | | |
| Total Number of Patients Applying for Examination | -0.253 | <**0.001** | -0.287 | <**0.001** | -0.195 | <**.001** |
| Total Number of Driver Health Reports Issued Without Referral | -0.475 | <**0.001** | -0.440 | <**0.001** | -0.479 | <**0.001** |
| Total Number of Driver Health Reports Issued for Referred Drivers | 0.477 | <**0.001** | 0.377 | <**0.001** | 0.533 | <**0.001** |
| Number of Examinations for Registered Patients | -0.235 | <**0.001** | -0.255 | <**0.001** | -0.199 | <**0.001** |
| Number of Driver Reports Issued per Population Aged 17 and Over | 0.007 | 0.887 | -0.002 | 0.968 | -0.009 | 0.864 |
| Number of Driver Reports Issued Without Referral per Population Aged 17 and Over | -0.418 | <**0.001** | -0.374 | <**0.001** | -0.448 | <**0.001** |
| Number of Driver Reports Issued for Referred Drivers per Population Aged 17 and Over | 0.551 | <**0.001** | 0.457 | <**0.001** | 0.589 | <**0.001** |
| Total Referral Rate in the Issued Driver Reports | 0.572 | <**0.001** | 0.477 | <**0.001** | 0.629 | <**0.001** |

* The statistically significant difference was defined as p < 0.05
r Spearman correlation test

that defensive physicians refer their patients more frequently when issuing driver reports. No significant correlation was found between DMPAS scores and the total number of driver reports per population aged 17 and over (p>0.05).

## Discussion

Our study's DMPAS scores indicated that 94.5 % of participants exhibited a moderate or higher defensive attitude. This aligns with findings from a study in Japan where 98% of gastroenterologists practiced defensive medicine, and a study in Pennsylvania, USA, where 93% of participants did the same.[13,14] Similarly, a study conducted in the Karşıyaka district of İzmir, Turkey, among family physicians determined that 93.8% exhibited moderate or higher defensive medicine practices.[15]

In Turkey, the percentage of physicians who had never heard of DMPs was 59.1% and 61%, according to studies by Başer et al. in 2014 and Özata et al. in 2019, respectively.[15,16] This figure decreased to 45% in Karasu's 2024 survey.[17] In our research, we found that this rate had fallen further to 22.3%. Over the years, awareness of the DMP issue has probably increased because physicians have faced more frequent medicolegal penalties.

Based on participants' responses to the DMPAS, the most common defensive medical practice that participants engaged in moderately or more frequently was the influence of the media (96.2%). This was followed by recommendations for detailed record keeping (87.7%), and providing detailed explanations (84.2%). Similarly, a study conducted in the UK among family physicians revealed that 90.3% spent more time on paperwork and 86.6% provided more information about treatment plans to patients.[8] In another study with family physicians in Italy, 82.8% reported adding unnecessary notes to patient records as a defensive measure, while 43.5% expressed concern over the media's accusatory attitude.[18]

In line with previous studies, men were found to be more defensive than women, and married individuals were more defensive compared to singles.[10,19,20] Additionally, consistent with the literature, it was observed that as participants' age, professional experience, and duration of work as a family physician increased, their DMPAS scores significantly decreased.[10,14,21,22] This suggests that as physicians accumulate experience, their improved adherence to medical standards and communication skills help them adopt fewer defensive attitudes.

We conclude that specialist physicians and CFMS assistants resort to defensive medical practices significantly more than general practitioners. This may be attributed to the fact that specialist physicians are, on average, 3.6 years younger than general practitioners. We also suspect that negative legal experiences encountered during their specialization training might have contributed to this tendency.

We found that as the number of registered patients and examinations increased among the participating physicians, their defensive attitudes decreased. This could imply that defensive physicians opt for units with smaller populations to reduce legal risks, and that patients may prefer physicians who demonstrate less defensiveness.

As DMPAS scores increase, the referral rate for driver health reports and the number of referred reports increase, while the number of without-referral driver health reports issued decreases. Although many studies have shown that DMP's raise healthcare costs, our study did not explore this issue.[23-25] It is clear that more referrals to higher-level healthcare institutions for driver's licenses will lead to higher healthcare costs. As of now, there is no other study that combines driver reports and defensive medicine practices to our

knowledge. Assessing the applicants' suitability for driving is a challenging task that requires medical knowledge, professional experience, and a comprehensive understanding of regulations. The tendency to protect oneself from legal complications aligns with the cautious approach present in issuing driver health reports. Our study quantitatively demonstrates the link between defensive medical practices and driver health report practices. Additionally, 96% of participants expressed varying levels of concern about legal risks when preparing driver health reports, further confirming this connection.

### Limitations

As our study was conducted among family physicians working in primary healthcare centers in Istanbul, the findings may not be generalizable to the entire country, different medical specialties, or various positions within medicine, including general practitioners, research assistants, specialists, subspecialists, and academic in public and private hospitals. A limitation of this study is that the physicians involved confirmed the accuracy of their annual examination and report counts, as they provided their own statements.

### Conclusion

The current study reveals that attitudes toward defensive medicine are widespread among primary care doctors. This tendency results in more referrals instead of preparing health reports. Although many physicians have heard of defensive medicine as a concept, they often lack a deeper understanding regarding what it entails. Defensive physicians tend to refer more patients when issuing driver health reports. Additionally, applicants often lack sufficient knowledge about the process of obtaining these reports, and physicians frequently face verbal abuse when issuing driver health reports.

The increase in referral driver reports due to defensive medicine practices leads to transferring the patient load to higher-level healthcare institutions. Reducing these practices that adversely affect the healthcare system and patients calls for providing legal protection for physicians and developing policies that offer state support, which will allow physicians to feel more secure in their practices.

## Ethical approval

This study has been approved by the Clinical Research Ethics Committee of the University of Health Sciences Turkey, Istanbul Training and Research Hospital (approval date 14.10.2022, number 307). Written informed consent was obtained from the participants.

## Author contribution

The authors declare contribution to the paper as follows: Study conception and design: SK, ZAS; data collection: SK; analysis and interpretation of results: SK, İGK., ZAS; draft manuscript preparation: SK, İGK, ZAS. All authors reviewed the results and approved the final version of the article.

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## Conflict of interest

The authors declare that there is no conflict of interest.

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Research Article

# Rational drug use and associated factors in pulmonology outpatients: a cross-sectional study

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## ABSTRACT

**Objective:** Rational drug use (RDU) refers to administering medications that are appropriate to patients' clinical needs, in doses that meet their individual needs for a sufficient duration, and at the lowest possible cost. Despite the clinical importance of RDU, irrational drug use remains prevalent, particularly in pulmonology patients. In this context, the objective of this study is to evaluate RDU knowledge and identify associated sociodemographic and clinical factors in pulmonology outpatients.

**Methods:** The sample of this cross-sectional, single-center study consisted of 317 outpatients aged 18 years or older who presented to a secondary chest diseases hospital between February and May 2023. The patients were assessed using a structured questionnaire containing items on their sociodemographic and general health characteristics and the validated 21-item Rational Drug Use Scale (RDUS). The collected data were analyzed using parametric and chi-square tests, as well as correlation and logistic regression analyses.

**Results:** The mean age of the study sample, 59.6% of which were females, was 50.0 ± 13.0 years. Of the 317 patients, 78.9% had chronic diseases, and 38.8% were taking ≥5 medications (polypharmacy). The mean RDUS score of the sample was 29.78±4.77, indicating insufficient knowledge. The mean RDUS score of the patients aged ≤45 years was significantly higher than that of those aged >45 years (p=0.007). The mean RDUS score of the patients living in urban areas was significantly higher than that of those living in rural areas (p=0.031). A strong correlation was found between patients' education level and RDUS score. Accordingly, the mean RDUS score of patients with higher education was significantly higher than that of patients with other education levels (p=0.001). Multivariate analysis revealed higher education levels ([Odds Ratio (OR)=3.45, p=0.005], living in urban areas [OR=2.46, p=0.031], and young age [<45 years] [OR=0.958 per year, p=0.001]) as independent predictors of having sufficient RDU knowledge.

**Conclusion:** In conclusion, we found that outpatient pulmonology patients' RDU knowledge was independently associated with age, education level, and place of residence. In light of these findings, targeted educational interventions to improve medication adherence, reduce adverse events, and optimize treatment outcomes should be primarily focused on patients who are elderly, have low educational levels, reside in rural areas, and have respiratory diseases.

**Keywords:** rational drug use, pulmonology, health literacy, polypharmacy, patient education

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## Introduction

Rational drug use (RDU) refers to using the right drug, in the right dose, for the right duration, and at the lowest cost.[1] RDU aims to reduce adverse drug reactions, drug interactions, and unnecessary healthcare costs and increase drug efficacy.[2] Unnecessary and inappropriate drug use is a widespread problem both globally and nationally. In particular, over-the-counter use of antibiotics, unconscious use of analgesics, and polypharmacy constitute major public health problems.[3,4]

Many factors affect RDU, including health literacy, socioeconomic status, the presence of chronic diseases, access to healthcare services, and the ability to communicate effectively with healthcare providers.[5] Patients are expected to use the medications prescribed specifically for them by physicians in the recommended doses and durations. However, patients often discontinue treatment early as soon as they feel better, which can negatively affect the efficacy of the drug and lead to serious consequences such as drug resistance, disease recurrence, and increased risk of complications.[6] The structure of the healthcare system, primary and secondary healthcare practices, and physicians' prescribing habits also directly affect drug use patterns.[7]

It is, therefore, crucial to identify and implement strategies to promote RDU. Outpatient clinics, especially those where chronic conditions such as respiratory diseases are treated, are critical venues for understanding and improving medication use, as they involve frequent, long-term prescribing. Therefore, identifying gaps in outpatients' RDU knowledge and drug use patterns may help tailor effective interventions. In this context, this study was carried out to evaluate RDU knowledge and identify associated sociodemographic and clinical factors in pulmonology outpatients.

## Materials and Methods

### Study design and setting

This study was designed as a cross-sectional, single-center study. The study protocol was approved by the Giresun University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (Approval Date 25.12.2023, Approval Number: 25.12.2023/12) and the Provincial Health Directorate. The study was conducted between February 1st, 2023, and May 1st, 2023, at Dr. Ali Menekşe Pulmonology Hospital, a secondary chest diseases hospital, consisting only of internal medicine and pulmonology outpatient clinics, serving approximately 150 patients daily, including both scheduled and walk-in visits, per the ethical considerations outlined in the World Medical Association Declaration of Helsinki. A secondary chest diseases hospital provides a relevant setting for evaluating RDU, as chronic respiratory conditions often require long-term pharmacotherapy, including antibiotics, inhalers, and corticosteroids. Written informed consent was obtained from the participating patients prior to the conduct of the study.

### Population and sample

The study population consisted of patients aged 18–80 years who visited the pulmonology outpatient clinics during the study period, voluntarily agreed to participate in the study, were fluent in Turkish, had no cognitive impairments, and had no psychiatric conditions affecting their ability to respond. The study sample was created using convenience sampling, that is, only patients who met the study's inclusion criteria and volunteered to participate in the study were included in the sample. Patients that are under 18 years, those who did not consent to participate in the study, those who could not communicate in written or verbal Turkish, and those who were diagnosed with psychiatric disorders that may affect cognitive

skills, such as schizophrenia, bipolar disorder, and psychosis, were excluded from the study. Power analysis revealed that the sample must comprise a minimum of 207 patients in order to achieve 95% reliability, 90% power, and an effect level of 0.25. In the end, the study sample consisted of 317 patients.

### Data collection

The study data were collected through face-to-face interviews with patients using a structured questionnaire consisting of items assessing their sociodemographic and general health characteristics, as well as the validated 21-item Rational Drug Use Scale (RDUS), developed by the researchers based on relevant literature. A team of researchers conducted the interviews collaboratively. The questionnaire's first and second parts comprised items assessing patients' sociodemographic characteristics (age, gender, marital status, education level, and employment status) and general health characteristics (chronic diseases, medication use, number of medications used, and smoking status), respectively. RDUS consists of 21 (10 true and 11 false) statements that evaluate rational drug use. Participants were asked to assign one of the following answer choices to each statement: correct (2 pts), incorrect (0 pts), and not sure (1 pt). Accordingly, the highest and lowest scores that can be obtained from RDUS are 42 and 0 pts, respectively. Higher RDUS scores indicate higher RDU knowledge. RDUS' Turkish validity and reliability studies, i.e., psychometric assessments featuring Cronbach's alpha, structural validity, and item analysis, were conducted by Demirtaş et al., who reported RDUS' Cronbach's alpha as 0.78.[8] Accordingly, we deemed the patients who scored 35 pts and above in RDUS to have sufficient RDU knowledge.

The study's dependent variables were patients' RDUS scores and whether they had sufficient RDU knowledge (RDUS score ≥35 pts), and the independent variables were sociodemographic characteristics, including age, gender, education level, place of residence, and marital status, and general health characteristics, including smoking status, medication use, and chronic diseases.

### Statistical analysis

SPSS 24.0 (Statistical Product and Service Solutions for Windows, Version 24.0, IBM Corp., Armonk, NY, U.S., 2016) software package was used to conduct the statistical analyses of the collected data. The results of the statistical analyses were expressed using descriptive statistics, i.e., means, medians, standard deviations, and standard errors in the case of continuous variables, and numbers (n) and percentage (%) values in the case of categorical variables. Kolmogorov-Smirnov test, histograms, skewness, and kurtosis values were used to assess the conformity of numerical variables to normal distribution. The independent samples t-test was used to compare variables between two groups, while the analysis of variance (ANOVA) test was used to compare variables between more than two groups. Patients were classified according to the pre-determined RDUS cut-off score and compared in terms of independent variables using the chi-squared test. Pearson's correlation analysis was used to assess the relationship between age and RDUS score. Backward stepwise logistic regression analysis was applied to variables found to be significantly related to RDU knowledge in one-way analyses. Probability (p) statistics of $< 0.05$ were deemed to indicate statistical significance.

## Results

The mean age of the study sample, 59.6% of which were females, was 50.0 ± 13.0 years. The mean RDUS scores of the subgroups created based on patients' sociodemographic and health characteristics are given in Table 1. Of the 317 patients, 78.9% had at least one chronic disease. While 20.8% were not taking any medications, 38.8% were using five or more medications, indicating a high rate

**Table 1.** Mean scores on the Rational Drug Use Scale according to sociodemographic variables

| Variables | | n (%) | Mean ± SD | Statistics |
|---|---|---|---|---|
| Gender | Female | 189 (59.6) | 30.03 ± 4.82 | t=-1.147 df=315 p=0.252 |
| | Male | 128 (40.4) | 29.41 ± 4.69 | |
| Age groups | ≤45 years | 103 (32.5) | 30.98 ± 4.80 | F=4.986 **p=0.007** |
| | 46-55 years | 65 (20.5) | 29.29 ± 5.00 | |
| | ≥65 years | 149 (47.0) | 29.16 ± 4.51 | |
| Marital status | Married | 199 (62.8) | 29.71 ± 4.76 | F=3.033 **p=0.050** |
| | Single | 64 (20.2) | 30.87 ± 4.81 | |
| | Widowed | 54 (17.0) | 28.74 ± 4.55 | |
| Cigarette smoking | Smoker | 211 (66.6) | 29.75 ± 4.72 | t=-0.160 df=315 p=0.873 |
| | Non-smoker | 106 (33.4) | 29.84 ± 4.89 | |
| Residence status | Province | 144 (45.4) | 30.76 ± 4.86 | F=7.032 **p=0.001** |
| | District | 84 (26.5) | 29.52 ± 4.49 | |
| | Village | 89 (28.1) | 28.43 ± 4.55 | |
| Education level | Literate | 90 (28.4) | 28.09 ± 4.22 | F=9.045 **p=0.001** |
| | Primary School | 92 (29.0) | 29.24 ± 4.93 | |
| | Middle School | 29 (9.1) | 29.83 ± 3.87 | |
| | High School | 79 (24.9) | 31.15 ± 4.24 | |
| | University | 27 (8.5) | 33.19 ± 5.60 | |
| Employment status | Working | 143 (45.1) | 30.55 ± 4.68 | F=3.741 **p=0.025** |
| | Not working | 82 (25.9) | 29.45 ± 5.01 | |
| | Retired | 92 (29.0) | 28.88 ± 4.54 | |
| Number of medications | No medication | 66 (20.8) | 30.38 ± 4.74 | F=0.904 p=0.406 |
| | 1-4 medications | 128 (40.4) | 29.83 ± 5.06 | |
| | ≥5 medications | 123 (38.8) | 29.41 ± 4.46 | |
| Medication use status | Non-user | 66 (20.8) | 30.38 ± 4.74 | t=-1.149 df=315 p=0.251 |
| | User | 251 (79.2) | 29.62 ± 4.77 | |
| Number of diseases | 0 | 68 (21.5) | 30.35 ± 4.90 | F=0.845 p=0.498 |
| | 1 | 95 (30.0) | 30.15 ± 4.86 | |
| | 2 | 115 (36.3) | 29.40 ± 4.60 | |
| | 3 | 36 (11.4) | 29.06 ± 4.90 | |
| | 4 | 3 (0.9) | 28.33 ± 3.06 | |
| Chronic disease status | Yes | 250 (78.9) | 29.59 ± 4.75 | t=-1.381 df=315 p=0.168 |
| | No | 67 (21.1) | 30.49 ± 4.80 | |
| Chest disease | Yes | 142 (44.8) | 28.86 ± 4.63 | t=-3.138 df=315 **p=0.002** |
| | No | 175 (55.2) | 30.53 ± 4.76 | |
| Coronary artery disease | Yes | 102 (32.2) | 29.50 ± 4.38 | t=-0.718 df=315 p=0.473 |
| | No | 215 (67.8) | 29.91 ± 4.95 | |
| Endocrine diseases | Yes | 81 (25.6) | 29.88 ± 4.50 | t=0.213 df=315 p=0.832 |
| | No | 236 (74.4) | 29.75 ± 4.83 | |
| Psychiatric illness | Yes | 19 (6.0) | 30.16 ± 4.31 | t=0.357 df=315 p=0.722 |
| | No | 298 (94.0) | 29.76 ± 4.80 | |
| Malignancy | Yes | 14 (4.4) | 29.00 ± 4.96 | t=-0.625 df=315 p=0.532 |
| | No | 303 (95.6) | 29.82 ± 4.76 | |
| Total | | 317 (100.0) | 29.78 ± 4.77 | |

Bold p-values indicate statistical significance (p≤0.05).
SD: Standard deviation; df: Degrees of freedom.

**Table 2.** Distribution of rational drug use knowledge according to sociodemographic and health variables

| Variables | | No knowledge of rational drug use (<35 points) | Knowledge of rational drug use (≥35 points) | Statistics |
|---|---|---|---|---|
| Gender | Female | 147 (77.8) | 42 (22.2) | $\chi^2$=1.201 df=1 p=0.273 |
| | Male | 106 (82.8) | 22 (17.2) | |
| Age groups | ≤45 years | 72 (69.9) | 31 (30.1) | $\chi^2$=11.464 df=2 **p=0.003** |
| | 46-55 years | 51 (78.5) | 14 (21.5) | |
| | ≥65 years | 130 (87.2) | 19 (12.8) | |
| Marital status | Married | 160 (80.4) | 39 (19.6) | $\chi^2$=11.847 df=2 **p=0.003** |
| | Single | 43 (67.2) | 21 (32.8) | |
| | Widowed | 50 (92.6) | 4 (7.4) | |
| Smoking | Active smoker | 171 (81.0) | 40 (19.0) | $\chi^2$=0.594 df=1 p=0.441 |
| | Never | 82 (77.4) | 24 (22.6) | |
| Residence status | Province | 103 (71.5) | 41 (28.5) | $\chi^2$=13.344 df=2 **p=0.001** |
| | District | 69 (82.1) | 15 (17.9) | |
| | Village | 81 (91.0) | 8 (9.0) | |
| Education level | Literate | 82 (91.1) | 8 (8.9) | $\chi^2$=29.434 df=4 **p=0.001** |
| | Primary School | 77 (83.7) | 15 (16.3) | |
| | Middle School | 25 (86.2) | 4 (13.8) | |
| | High School | 56 (70.9) | 23 (29.1) | |
| | University | 13 (48.1) | 14 (51.9) | |
| Employment status | Working | 107 (74.8) | 36 (25.2) | $\chi^2$=4.485 df=2 p=0.106 |
| | Not working | 67 (81.7) | 15 (18.3) | |
| | Retired | 79 (85.9) | 13 (14.1) | |
| Groups by number of medicines | No medication | 49 (74.2) | 17 (25.8) | $\chi^2$=3.212 df=2 p=0.201 |
| | 1-4 medications | 100 (78.1) | 28 (21.9) | |
| | ≥5 medications | 104 (84.6) | 19 (15.4) | |
| Medication use status | No | 49 (74.2) | 17 (25.8) | $\chi^2$=1.604 df=1 p=0.205 |
| | Yes | 204 (81.3) | 47 (18.7) | |
| Number of diseases | 0 | 50 (73.5) | 18 (26.5) | $\chi^2$=5.741 df=4 p=0.291 |
| | 1 | 72 (75.8) | 23 (24.2) | |
| | 2 | 98 (85.2) | 17 (14.8) | |
| | 3 | 30 (83.3) | 6 (16.7) | |
| | 4 | 3 (100.0) | 0 (0.0) | |
| Chronic disease status | Yes | 204 (81.6) | 46 (18.4) | $\chi^2$=2.350 df=1 p=0.125 |
| | No | 49 (73.1) | 18 (26.9) | |
| Chest disease | Yes | 123 (86.6) | 19 (13.4) | $\chi^2$=7.401 df=1 **p=0.007** |
| | No | 130 (74.3) | 45 (25.7) | |
| Coronary artery disease | Yes | 86 (84.3) | 16 (15.7) | $\chi^2$=1.893 df=1 p=0.169 |
| | No | 167 (77.7) | 48 (22.3) | |
| Endocrine diseases | Yes | 68 (84.0) | 13 (16.0) | $\chi^2$=1.157 df=1 p=0.282 |
| | No | 185 (78.4) | 51 (21.6) | |
| Psychiatric illness | Yes | 16 (84.2) | 3 (15.8) | $\chi^2$=0.243 df=1 p=0.622 |
| | No | 237 (79.5) | 61 (20.5) | |
| Malignancy | Yes | 12 (85.7) | 2 (14.3) | $\chi^2$=0.317 df=1 p=0.574 |
| | No | 241 (79.5) | 62 (20.5) | |
| Total | | 253 (79.8) | 64 (20.2) | |

Bold p-values indicate statistical significance (p≤0.05).
df: Degrees of freedom; $\chi^2$: Chi-square.

of polypharmacy. The mean RDUS of patients aged 45 and under was significantly higher than that of patients aged 46-55 and those aged 65 and over (p=0.007) (Table 1). In parallel, the mean RDUS score of employed patients was found to be significantly higher than that of retired patients (p=0.025) (Table 1).

Distribution of patients' sociodemographic and general health characteristics by the RDU knowledge groups is shown in Table 2. Accordingly, factors such as young age, higher level of education, and living in urban areas were significantly associated with higher RDU knowledge. On the other hand, there was no significant relationship between RDUS scores and the presence of chronic diseases or medication use. On the other hand, the mean RDUS score of patients with chest diseases was significantly lower than that of patients without chest diseases (p=0.007) (Table 2).

The question that the patients answered correctly at the highest rate on RDUS was Question 11 (95.6%), followed by Question 12 (94.3%), Question 3 (90.9%), Question 14 (88.6%), and Question 8 (87.7%). On the other hand, the question that the patients answered correctly at the lowest rate on RDUS was Question 19 (20.5%), followed by Questions 15 and 16 (30.3%), Question 9 (31.5%), and Question 5 (37.2%) (Table 3).

**Table 3.** Distribution of responses to the rational drug use scale

| Items | Correct answer | Wrong answer | I don't know |
|---|---|---|---|
| 1. Only physicians can recommend medicines | 206 (65.0) | 0 (0.0) | 111 (35.0) |
| 2. Recommend medication to a relative with similar complaints; it's okay to be present | 181 (57.1) | 121 (38.2) | 15 (4.7) |
| 3. Whether we need medication when we get sick, the doctor determines that it is not | 288 (90.9) | 27 (8.5) | 2 (0.6) |
| 4. Medicines can have negative effects as well as positive ones | 216 (68.1) | 0 (0.0) | 101 (31.9) |
| 5. All medicines produce the same side effects | 118 (37.2) | 57 (18.0) | 142 (44.8) |
| 6. It is not harmful to take the medicine more often than the doctor prescribes | 189 (59.6) | 59 (18.6) | 69 (21.8) |
| 7. Using medicines should be taken on an empty or full stomach can be found in the instructions | 191 (60.3) | 43 (13.6) | 83 (26.2) |
| 8. Failure to take the medication for the duration of treatment prescribed by the doctor may impede recovery | 278 (87.7) | 4 (1.3) | 35 (11.0) |
| 9. Herbal products can be used instead of medicines | 100 (31.5) | 160 (50.5) | 57 (18.0) |
| 10. Consuming herbal products as much as desired has no health effects; there's no harm | 136 (42.9) | 95 (30.0) | 86 (27.1) |
| 11. Any adverse effects while taking medication; we should consult our doctor | 303 (95.6) | 0 (0.0) | 14 (4.4) |
| 12. Our physician is still using while organizing our treatment; we must | 299 (94.3) | 6 (1.9) | 12 (3.8) |
| 13. When we feel well during treatment, the medicine we can stop using it | 146 (46.1) | 141 (44.5) | 30 (9.5) |
| 14. We can ask our pharmacist where we should store our medicines at home | 281 (88.6) | 7 (2.2) | 29 (9.1) |
| 15. The duration of treatment for each medicine is the same | 96 (30.3) | 44 (13.9) | 177 (55.8) |
| 16. Herbal products are completely harmless | 96 (30.3) | 37 (11.7) | 184 (58.0) |
| 17. Medicines can be used in the same amount in all age groups | 145 (45.7) | 59 (18.6) | 113 (35.6) |
| 18. Not too many medicines but enough medicines using it helps us heal | 211 (66.6) | 33 (10.4) | 73 (23.0) |
| 19. More expensive medicines are more effective | 65 (20.5) | 78 (24.6) | 174 (54.9) |
| 20. Any medicine can be used safely during pregnancy | 132 (41.6) | 35 (11.0) | 150 (47.3) |
| 21. Some medicines are addictive | 141 (44.5) | 29 (9.1) | 147 (46.4) |

Data presented as n (%).

**Table 4.** Logistic regression analysis of primary variables associated with rational drug use knowledge

| Variable | B | S.E. | Wald | df | p | OR | 95% Confidence Interval |
|---|---|---|---|---|---|---|---|
| Residing in rural areas vs urban areas | 0.898 | 0.416 | 4.664 | 1 | 0.031 | 2.46 | 1.09 - 5.55 |
| Higher education vs other (lower) education | 1.237 | 0.444 | 7.762 | 1 | 0.005 | 3.45 | 1.44 - 8.23 |
| Age | -0.043 | 0.011 | 14.767 | 1 | 0.001 | 0.96 | 0.94 – 0.98 |

The primary variables included in the logistic regression analysis model to analyze their relationship with RDU knowledge were age, being single, living in urban areas, i.e., cities or counties, being a university graduate, and not having chest diseases. Patients living in urban areas had higher odds of having sufficient RDU knowledge than those living in rural areas ((Odds Ratio (OR) = 2.46, p = 0.031)). Similarly, patients who had graduated from a university exhibited better RDU knowledge compared to those with other education levels (OR = 3.45, p = 0.005). Frequency of RDU decreased by 4.2% with increasing age (OR=0.958, p=0.001) (Table 4).

## Discussion

RDU is essential for maximizing therapeutic benefits, minimizing adverse effects, and ensuring the responsible use of healthcare resources. Despite its importance, inappropriate drug use, including non-adherence, polypharmacy, and misuse of common medications such as antibiotics and analgesics, remains a persistent challenge in clinical practice. In this context, we evaluated RDU knowledge among pulmonology outpatients presented to a secondary chest diseases hospital and identified key sociodemographic and clinical factors associated with sufficient RDU knowledge.

The mean RDUS score of our sample is lower than the mean RDUS scores reported in two other studies in the literature assessing RDU (29.78 ± 4.77 vs. 37.42 and 38.82).[9,10] Analysis of RDU scores with respect to gender revealed that the mean RDU score of female patients was higher than that of male patients, although not significantly. We found a significant relationship between marital status and RDUS scores, with single individuals having the highest scores and widowed individuals having the lowest scores. This finding may be attributed to the fact that individuals living alone reportedly have more time to spare and attach greater importance to health information.[11]

The subgroups of younger, employed, and more highly educated patients had higher mean RDUS scores than the others. Analysis of RDUS scores by age groups revealed that the mean RDUS score of patients aged 45 years and under was higher than that of older age groups. As a matter of fact, one other study also reported higher RDU levels in young patients than in elderly patients.[12] Our results indicate that younger age, higher education level, and living in urban areas are significantly associated with greater RDU knowledge. Our finding of patients living in rural areas having lower RDU knowledge is consistent with the findings of a recent study conducted in Turkey, highlighting significant disparities in medication use behaviors between urban and rural settings.[13] Along these lines, Yilmaz Kara et al. reported distinct variations in RDU behaviors among adult populations, further supporting the findings of our study.[14] These findings may be explained by the fact that younger individuals are likely to have higher health literacy and easier access to information through digital resources, compared to older individuals who live in rural areas and may not have sufficient access to various media tools.[12] Our finding that mean RDUS scores significantly increased with increasing education levels, with illiterate patients having the lowest mean RDUS score, emphasizes

the effect of health literacy on RDU.[15] Similarly, another study reported a significant difference between the RDUS scores of patients with different education levels, particularly those aged over 65 years.[12] We also found that employment status was significantly associated with RDUS scores, with employed patients having higher scores than retired patients. A study on health awareness and medication use habits reported similar findings.[11] These findings may be attributed to the fact that employed individuals are more exposed to health information and participate in regular health screenings more frequently than unemployed individuals.

45.5% of our sample have been living in urban areas, and we found living in urban areas to be one of the strong predictors of sufficient RDU knowledge. In parallel, another study found that living in urban areas was significantly associated with ease of access to healthcare services.[12] Similarly, other studies have reported that patients living in urban areas have higher RDUS scores than those living in rural areas, as they have easier access to healthcare services, higher opportunities to communicate with healthcare providers, and greater access to educational opportunities.[16] We believe that our hospital's proximity to the city center was a factor in facilitating patients' access to healthcare services.

78.9% of the patients in our sample had at least one chronic disease, indicating a high prevalence of chronic diseases. In contrast, a study conducted in a family medicine outpatient clinic in the city of Samsun, neighboring Giresun, where our hospital is located, reported that the rate of patients with at least one chronic disease constituted only 18% of their sample.[17] The high rate of patients with at least one chronic disease in our sample is expected, considering that our study was carried out in a secondary chest diseases hospital. Considering that chronic diseases can directly affect the frequency of medication use, the fact that 20.8% of the patients in our sample did not use any medication, when considered together with the fact that 78.9% of our patients were diagnosed with at least one chronic disease, suggests the medication adherence of patients diagnosed with chronic diseases. Similarly, in a study conducted with 387 patients, 39.5% of whom had a chronic disease, it was reported that 29.5% of the patients had been using medications regularly.[9] These findings may help develop strategies to reduce the overall incidence of complications associated with chronic diseases. On the other hand, our analyses of the relationships between RDUS scores and health status characteristics, i.e., presence of chronic diseases, coronary artery disease, endocrine diseases, psychiatric diseases, and malignancies, revealed no significant relationship, except for the presence of chest diseases. The RDUS scores of patients with chest diseases were significantly lower than those of other patients. As a matter of fact, a study reported that patients with chronic respiratory diseases may have low awareness of drug use and difficulties in using inhaler drugs and may, therefore, have a higher rate of irrational drug use and resort to alternative means.[18]

38.8% of the patients in our sample met the criteria for polypharmacy, which refers to the use of five or more medications. It has been reported in the literature that polypharmacy is common among patients with chronic diseases and increases the risk of drug interactions and side effects.[11,19] A study conducted with 1081 patients admitted to an internal medicine outpatient clinic found that 13.4% of the patients were using five or more medications.[20] The high rate of polypharmacy in our study may be attributed to the fact that 57.4% of our patients were illiterate or only had elementary school education, and 78.9% had at least one chronic disease. On the other hand, we did not find any significant relationship between the number of medications used and RDUS scores. Then again, patients who have not been using any medication had higher RDUS scores

compared to those who have been using five or more medications, suggesting that polypharmacy may be either related to lower health literacy or not related to health literacy at all. In line with the literature data, among patients under 65 years of age, the mean RDUS score of patients using 1 to 3 medications was higher than that of others.[21]

The study's single-center design, relatively small sample size, and the fact that it was conducted in a secondary healthcare facility consisting of only two departments limit the generalizability of its findings to other populations. Larger-scale, multicenter studies with broader patient profiles involving tertiary healthcare facilities are needed to increase the scope, validity, and reliability of this study's findings. In addition, face-to-face completion of the data collection tools may have led to response bias.

## Conclusions

We found that factors such as young age, higher education, and living in urban areas were significantly associated with higher RDU awareness. However, we did not find any significant relationship between RDUS scores and the presence of chronic diseases and medication use status, suggesting that educational interventions, as well as awareness-raising programs aimed at increasing RDU, should primarily target elderly patients, patients with low education levels, and patients living in rural areas. Increased RDU awareness is likely to facilitate the management of chronic diseases, whereas increased health literacy is likely to prevent unnecessary or incorrect use of drugs and reduce the number of visits to healthcare facilities due to unwarranted side effects. Measures aimed at increasing patients' RDU knowledge and awareness should be organized across all levels of healthcare, particularly primary healthcare services, which are more likely to play a crucial role in promoting RDU and directly impact local variations in medication use.

## Ethical approval

This study has been approved by the Giresun University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (approval date 25.12.2023, number 12). Written informed consent was obtained from the participating patients prior to the conduct of the study.

## Author contribution

The authors declare contribution to the paper as follows: Study conception and design: NGK; data collection: MK; analysis and interpretation of results: AO; draft manuscript preparation: NGK, MK. All authors reviewed the results and approved the final version of the article.

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## Conflict of interest

The authors declare that there is no conflict of interest.

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Research Article

# Relationship of thyroid hormones and metabolic parameters in euthyroid women

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## ABSTRACT

**Objective:** Thyroid hormones play a role in metabolic regulation, yet their associations with obesity and insulin resistance in euthyroid individuals remain unclear. This study aimed to evaluate the relationship between thyroid-stimulating hormone (TSH), fT3, fT4, and the fT3/fT4 ratio with metabolic parameters in euthyroid women.

**Methods:** In this retrospective cross-sectional study, 236 euthyroid women aged 18–65 were recruited from a tertiary hospital in Istanbul between May and September 2023. Participants were categorized as individuals with normal weight, overweight, or obesity. Thyroid hormones and metabolic parameters (waist circumference, triglycerides, HDL-C, insulin resistance) were analyzed. Statistical analyses included correlation tests and ANCOVA for age adjustment.

**Results:** No significant differences in thyroid hormone levels were found across BMI groups after adjusting for age. TSH was positively correlated with BMI and triglyceride levels. fT3 and the fT3/fT4 ratio were positively associated with insulin resistance and negatively associated with HDL-C.

**Conclusion:** fT3 and the fT3/fT4 ratio may reflect metabolic alterations in euthyroid individuals. These findings highlight the potential relevance of thyroid hormone evaluation in assessing metabolic risk, especially among individuals with obesity or insulin resistance. Further multicenter studies are warranted.

**Keywords:** thyroid hormones, insulin resistance, obesity, metabolic syndrome

## Introduction

Thyroid hormones regulate metabolic rate and oxygen consumption. They also influence protein synthesis and catabolism. They facilitate intestinal glucose absorption and hepatic gluconeogenesis. They also promote lipolysis and increase circulating free fatty acids. Thyroid hormones also influence lipid metabolism, contributing to lower cholesterol levels in the blood. Proper thyroid function is crucial for metabolic balance and healthy body composition. They influence metabolic processes relevant to growth, energy expenditure, and nutrient regulation.[1]

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The impact of these hormones on metabolic parameters is primarily characterized by their role in regulating energy homeostasis, lipid metabolism, and gluconeogenesis, which influence overall body metabolism.[2] Key metabolic parameters influenced by thyroid hormones include insulin resistance, abdominal obesity, waist circumference, and dyslipidemia.[3] Early detection and prevention of insulin resistance have been effective in reducing the risk of cardiometabolic diseases. However, there is conflicting evidence regarding the relationship between normal-range thyroid hormone levels and insulin resistance.[4]

Obesity is defined as a chronic metabolic condition characterized by excessive fat accumulation in the body, often accompanied by insulin resistance. This condition affects multiple systems, particularly the cardiovascular and endocrine systems, and poses significant health risks.[5] In recent years, the relationship between thyroid hormones and obesity has been widely discussed. The effect of normal-range thyroid hormone levels on body weight and metabolic risk parameters remains unclear.[6]

The objective of this study is to conduct a retrospective investigation to determine whether thyroid hormones (Thyroid-stimulating hormone (TSH), fT3, fT4) and the fT3/fT4 ratio are associated with obesity, insulin resistance, and other metabolic parameters (waist circumference, triglyceride, High-density lipoprotein- cholesterol (HDL-C)) in euthyroid women. This study focused exclusively on women to control for the potential confounding effects of sex on thyroid hormone regulation and metabolic responses. Previous researches has demonstrated that hormonal variations between men and women significantly influence fat distribution, insulin sensitivity, and overall metabolic homeostasis.[7,8] Therefore, limiting the sample to euthyroid women allowed for a more homogeneous population and improved the internal validity of our findings.

We hypothesize that thyroid hormone parameters within the normal range are significantly associated with insulin resistance and metabolic alterations in euthyroid women. Clarifying these associations in euthyroid women could contribute to early identification of metabolic risks in primary care settings.

## Material and Methods

This retrospective, cross-sectional study was conducted at the family medicine and obesity outpatient clinics of a tertiary hospital in Istanbul between May and September 2023.

### Population

A priori power analysis was performed using G*Power version 3.1.9.7 to estimate the minimum required sample size. Based on a level of 0.05, statistical power of 0.95, and a medium effect size (f=0.25), the analysis indicated that at least 159 participants were needed. The final sample of 236 women exceeded this requirement, ensuring adequate statistical power for the analyses.

Female patients aged 18–65 who visited the outpatient clinics during the study period were screened for eligibility. Data were collected by reviewing patient files and electronic health records. Participants were included consecutively based on their fulfillment of inclusion criteria and absence of any exclusion criteria. No random sampling method was applied. Out of 281 initially eligible women, 45 were excluded due to incomplete data, yielding a final sample size of 236 participants. Exclusion criteria included: Male sex, Age <18 year, Pregnancy or lactation,

History of thyroid disease/diabetes/cardiovascular disease/cancer/renal failure, Use of medications affecting thyroid function (e.g., amiodarone, steroids, lithium), Thyroid hormone levels outside the reference range.

### Study variables

Participants were classified into three BMI categories: normal weight (18.5–24.9 kg/m²), overweight (25.0–29.9 kg/m²), and obesity (≥30 kg/m²). Serum levels of TSH, fT3, fT4, and the calculated fT3/fT4 ratio were compared across BMI categories. Metabolic parameters included waist circumference, triglycerides, HDL-C, and insulin resistance, assessed via the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) index. HOMA-IR was calculated using the formula: (fasting glucose × fasting insulin) / 405.

### Ethical approval

The Declaration of Helsinki was followed in the planning and execution of this study. The study was approved by the İstanbul Medeniyet University Göztepe Training and Research Hospital Clinical Research Ethics Committee on 27.09.2023 (decision no: 2023/0637).

### Data analyses

All statistical analyses were conducted using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics included frequency (%), mean ± standard deviation, and median (min–max) values. Normality was assessed via the Shapiro-Wilk and Kolmogorov-Smirnov tests. Normality was assessed via the Shapiro-Wilk and Kolmogorov-Smirnov tests. Parametric tests: Student's t-test, One-way ANOVA, Bonferroni post-hoc. Non-parametric tests: Mann-Whitney U, Kruskal-Wallis, Dunn post-hoc. Covariate adjustment was done using ANCOVA for age. Correlations were evaluated using Pearson or Spearman coefficients depending on data distribution. Categorical variables were compared using the Chi-square test. Statistical significance was defined as $p<0.05$.

To visually summarize the correlations between thyroid hormone levels and metabolic parameters, a heatmap was generated based on the correlation coefficients obtained in this study. This visual was created using ChatGPT (OpenAI) for graphical assistance.

## Results

The present study was conducted with 236 women under follow-up and treatment in the Obesity and Family Medicine outpatient clinics between May 2023 and September 2023.

### Descriptive characteristics

Table 1 presents the descriptive characteristics of the study participants. The study included 236 women aged 18–64 years (mean: 32.9±7.8). The mean BMI was 32.9±7.8 kg/m² (range: 18.5–55.8). The data revealed that 67.4% (n=159) had obesity, 16.9% (n=40) were overweight, and 15.7% (n=37) had a normal weight. The average waist circumference was 101.1±17.1 cm, with values ranging from 62 to 154 cm. Of the study participants, 27.5% (n=65) had various chronic diseases, and 41.1% (n=97) had insulin resistance.

### Group comparisons

As shown in Table 2, age significantly differed across BMI groups, with normal-weight participants being younger than overweight and individuals with obesity (p=0.001).

Waist circumference increased with BMI, and all pairwise comparisons were statistically significant (p=0.001). HDL-C levels were significantly lower in the group of obesity compared to normal-weight participants (p=0.001).

**Table 1.** Descriptives of the participants

| Variables | Groups | n (%) |
|---|---|---|
| Gender | Female | 236 (100.0) |
| Age (years) | Mean ± SD | 43.1±13.4 |
| | Median (Min-Max) | 46 (18-64) |
| BMI (kg/m$^2$) | Mean ± SD | 32.9±7.8 |
| | Median (Min-Max) | 32.5 (18.5-55.8) |
| | Have Obesity | 159 (67.4) |
| | Overweight | 40 (16.9) |
| | Normal | 37 (15.7) |
| Waist circumference (cm) | Mean ± SD | 101.1±17.1 |
| | Median (Min-Max) | 102 (62-154) |
| Insulin resistance | No | 139 (58.9) |
| | Yes | 97 (41.1) |
| Other chronic diseases | No | 171 (72.5) |
| | Yes | 65 (27.5) |

SD: Standard Deviation; BMI: Body Mass Index.

**Table 2.** Comparison analyses by groups

| Variables | | Groups | | | p |
|---|---|---|---|---|---|
| | | Obesity (n=159) | Overweight (n=40) | Normal (n=37) | |
| Age (years) | Mean ± SD | 46.7±11.5 | 44.1±11.8 | 26.2±9.4 | [a]0.001** |
| | Median (Min-Max) | 49 (19-64) | 46 (18-61) | 23 (18-61) | |
| Waist circumference (cm) | Mean ± SD | 109.2±12.2 | 95.2±4.8 | 72.6±7.9 | [b]0.001** |
| | Median (Min-Max) | 108 (85-154) | 95.5 (86-108) | 72 (62-97) | |
| HDL-C (mg/dL) | Mean ± SD | 54.6±14.7 | 59.3±17.1 | 62.9±9.4 | [b]0.001** |
| | Median (Min-Max) | 52 (29-131) | 56.5 (33-99) | 62 (43-84) | |
| Triglyceride (mg/dL) | Mean ± SD | 134.4±61.5 | 108.2±49.7 | 83.5±40.5 | [a]0.001** |
| | Median (Min-Max) | 122 (42-354) | 100.5(40-243) | 66 (40-182) | |
| Insulin (mU/L) | Mean ± SD | 12.7±8.2 | 9.9±4.4 | 8.6±5.7 | [a]0.002** |
| | Median (Min-Max) | 9.9 (1.8-45) | 8.8 (3.1-21.9) | 7.2 (1.9-28.3) | |
| TSH (mIU/L) | Mean ± SD | 2.1±0.9 | 1.9±0.8 | 1.8±0.8 | [a]0.213 |
| | Median (Min-Max) | 1.9 (0.6-4.3) | 1.8 (0.7-3.8) | 1.7 (0.6-4.1) | |
| fT3 (ng/L) | Mean ± SD | 3.0±0.3 | 2.9±0.3 | 3.1±0.4 | [b]0.214 |
| | Median (Min-Max) | 3 (2.1-4) | 2.9 (2.3-3.9) | 3.1 (2.5-3.9) | |
| fT4 (ng/dL) | Mean ± SD | 1.2±0.1 | 1.2±0.2 | 1.2±0.2 | [b]0.899 |
| | Median (Min-Max) | 1.2 (0.9-1.6) | 1.2 (1-1.6) | 1.2 (0.9-1.5) | |
| fT3/fT4 | Mean ± SD | 2.6±0.4 | 2.6±0.3 | 2.7±0.4 | [b]0.379 |
| | Median (Min-Max) | 2.5 (1.7-4) | 2.6 (1.8-3.1) | 2.7 (2-3.7) | |
| HOMA-IR | Mean ± SD | 3.0±2.2 | 2.4±1.3 | 1.9±1.2 | [a]0.001** |
| | Median (Min-Max) | 2.3 (0.4-11.7) | 2 (0.7-6.8) | 1.7 (0.4-6.1) | |
| Insulin resistance | No | 86 (61.9) | 25 (18.0) | 28 (20.1) | [c]0.049* |
| | Yes | 73 (75.3) | 15 (15.5) | 9 (9.3) | |
| Other chronic diseases | No | 112 (65.5) | 31 (18.1) | 28 (16.4) | [c]0.599 |
| | Yes | 47 (72.3) | 9 (13.8) | 9 (13.8) | |

[a]Kruskal Wallis Test; [b]One-way ANOVA Test; [c]Pearson Chi-Square Test.
*p<0.05; **p<0.01.
SD: Standard Deviation; HDL-C: High Density Lipoprotein-Cholesterol; TSH: Thyroid Stimulating Hormone; HOMA-IR: Homeostatic Model Assessment for Insulin Resistance.

Triglyceride and insulin levels were also significantly higher in the obesity group compared to both overweight and normal-weight individuals (all p<0.05). Overweight participants had higher triglyceride and insulin levels than the normal-weight group (p=0.027 and p=0.025, respectively).

No significant differences were found among groups for TSH, fT3, fT4, or the fT3/fT4 ratio (p>0.05). HOMA-IR levels were highest in the obesity group (p=0.001), and insulin resistance was more prevalent in this group compared to normal-weight participants (p=0.049).

There were no significant differences in the prevalence of other chronic diseases between groups (p>0.05).

As seen in Table 3, when ANCOVA analysis was performed to eliminate the age difference between the groups, it was seen that the fT3 and fT3/fT4 ratio measurements of the cases according to the groups did not show any statistically significant difference (p>0.05).

A comparison of thyroid function parameters between individuals with and without insulin resistance revealed that fT3 levels (3.1±0.4 vs. 2.9±0.3 ng/L, p=0.001) and the fT3/fT4 ratio (2.7±0.4 vs. 2.5±0.3, p=0.001) were significantly higher in the insulin-resistant group. This finding suggests a link between elevated fT3 and metabolic imbalance. In contrast, TSH (p=0.446) and fT4 (p=0.323) demonstrated no significant differences between the groups. The statistical analyses encompassed the Student's t-test for normally distributed variables (fT3, fT3/fT4) and the Mann-Whitney U test for non-normally distributed variables (TSH, fT4). The findings suggest that increased fT3 and fT3/fT4 ratio may be associated with insulin resistance, while TSH and fT4 remain unaffected.

**Table 3.** Evaluation of fT3 and fT3/fT4 ratio measurements according to groups when the age effect is eliminated

| | | fT3 (ng/L) | fT3/sT4 |
|---|---|---|---|
| Obesity | Mean ± SD | 3.1±0.1 | 2.6±0.4 |
| Overweight | Mean ± SD | 3.1±0.1 | 2.6±0.3 |
| Normal | Mean ± SD | 3.1±0.1 | 2.7±0.5 |
| | p | [a]0.870 | [a]0.82 |

[a]ANCOVA Test

## Correlation analyses

The relationships between thyroid hormones and metabolic parameters are presented in Table 4. TSH levels showed weak but statistically significant positive correlations with triglyceride levels (r =0.167, p =0.010) and BMI (r =0.130, p =0.047). No significant associations were observed between TSH and HOMA-IR, age, or waist circumference (p>0.05).

fT3 levels were positively correlated with HOMA-IR (r =0.268, p =0.001) and BMI (r =0.145, p =0.026), and negatively correlated with HDL-C (r =–0.230, p =0.001) and age (r =–0.256, p=0.001). No significant relationships were found between fT3 and waist circumference or triglyceride levels (p>0.05).

fT4 showed no statistically significant correlations with any of the metabolic parameters, including waist circumference, HOMA-IR, BMI, triglycerides, or HDL-C (p>0.05).

The fT3/fT4 ratio was negatively associated with age (r=–0.162, p=0.001) and HDL-C (r=0.201, p=0.002), and positively associated with HOMA-IR (r=0.285, p=0.001). No significant associations were found between the fT3/fT4 ratio and BMI, waist circumference, or triglyceride levels (p>0.05). These correlations are visually presented in Figure 1, where the heatmap summarizes the relationships between thyroid parameters and metabolic indicators.

**Table 4.** Correlation of thyroid hormones (TSH, fT3, fT4) and fT3/fT4 ratio with metabolic parameters

| | | TSH (mIU/L) | fT3 (ng/L) | fT4 (ng/dL) | fT3/fT4 |
|---|---|---|---|---|---|
| Age (years) | ‡r | -0.019 | -0.256 | -0.060 | -0.162 |
| | p | 0.777 | 0.001** | 0.355 | 0.012* |
| Waist circumference (cm) | r | 0.086‡ | 0.049† | -0.034† | 0.060† |
| | p | 0.188 | 0.450 | 0.598 | 0.363 |
| HOMA-IR | ‡r | 0.109 | 0.268 | -0.092 | 0.285 |
| | p | 0.096 | 0.001** | 0.159 | 0.001** |
| Triglyceride (mg/dL) | ‡r | 0.167 | 0.042 | -0.109 | 0.110 |
| | p | 0.010* | 0.516 | 0.094 | 0.093 |
| HDL-C (mg/dL) | r | -0.153‡ | -0.230† | 0.022 † | -0.201† |
| | p | 0.019* | 0.001** | 0.737 | 0.002** |
| BMI (kg/m²) | ‡r | 0.130 | 0.145 | 0.075 | 0.060 |
| | p | 0.047* | 0.026* | 0.260 | 0.350 |

†Pearson Correlation Coefficiency; ‡Spearman Correlation Coefficiency.
*p<0.05; **p<0.01.
TSH: Thyroid Stimulating Hormone; HOMA-IR: Homeostatic Model Assessment for Insulin Resistance; HDL-C: High Density Lipoprotein-Cholesterol; BMI: Body Mass Index.

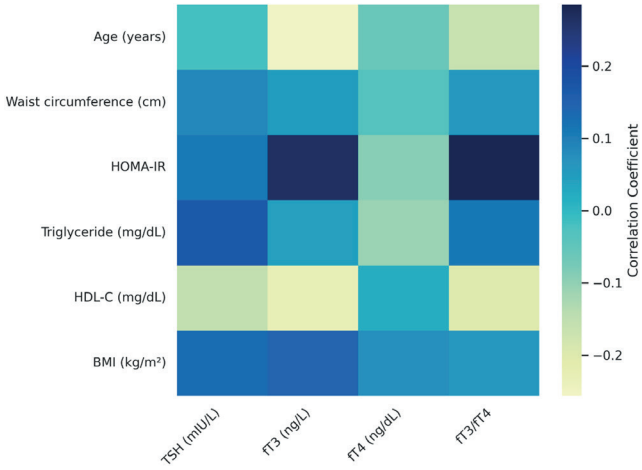


**Figure 1.** Heat map of correlation analyses

## Discussion

Thyroid hormones play a significant role in regulating metabolic processes, and their potential influence on metabolic syndrome (MetS) and lipid metabolism has been widely investigated. In our study, we aimed to explore the relationship between thyroid hormone levels (TSH, fT3, fT4, and the fT3/fT4 ratio) and metabolic syndrome parameters such as waist circumference, lipid profile, and other markers. Below, we discuss the key findings in the context of existing literature.

TSH, fT3, fT4, and the fT3/fT4 ratio did not show a statistically significant relationship with waist circumference in our investigation. This finding contrasts with some earlier researches that found favorable correlations between waist circumference and abdominal obesity and TSH, fT3, and fT3/fT4 ratios. These discrepancies may be attributed to differences in study populations (e.g., general vs. clinical samples), sample sizes, age distributions, or sex ratios. Menopausal status, which influences both thyroid hormone levels and fat distribution, may also contribute to divergent findings. Furthermore, variations in assay methods, geographic and dietary iodine exposure, and inclusion/exclusion of subclinical thyroid disorders may influence outcomes. Therefore, our findings should be interpreted with caution, and future multicenter studies with stratified analyses are warranted.

Elevated upper-normal TSH levels were linked to a 1.9-fold increased risk of metabolic syndrome in postmenopausal women, according to Park et al.[9]

Additionally, TSH levels and waist circumference were found to positively correlate by De Pergola et al., confirming the hypothesis that elevated TSH levels could lead to greater visceral fat formation.[10]

However, Roos et al. did not find a relationship between TSH and MetS risk in euthyroid individuals after adjustments for age and sex.[11] Similarly, Mehran et al. reported that no significant correlation existed between TSH levels and metabolic syndrome risk in euthyroid individuals.[12] These contradictory findings highlight the complexity of thyroid hormone regulation and its potential interaction with other metabolic factors.

Roos et al. also observed a negative correlation between fT4 and insulin resistance, along with other MetS components, after age and sex adjustments.[11] In contrast, Mehran et al. found a negative relationship between higher fT4 levels and triglycerides, hypertension, and waist circumference in euthyroid individuals.[12] Our study found no significant relationship between fT4 and triglycerides or HDL cholesterol levels. Kim et al. also did not observe a relationship between fT4 and MetS parameters in euthyroid individuals.[13]

Interestingly, Tarcin et al. reported a positive correlation between fT4 levels and MetS, which contradicts most studies suggesting a negative relationship between fT4 and these parameters. This suggests that fT4 may interact differently with MetS components depending on individual metabolic states.[14] Jin et al. confirmed that even within the normal range, thyroid hormones can have significant associations with MetS components, particularly emphasizing the role of fT4 in reducing T3 conversion and contributing to adverse metabolic profiles.[15]

These inconsistencies across studies may stem from methodological differences, including variations in study design (e.g., cross-sectional vs. longitudinal), population characteristics (e.g., age, BMI, menopausal status), sample sizes, and the presence or absence of confounding factor adjustments. Differences in laboratory assays and reference ranges may also influence the observed associations between fT4 and metabolic parameters.

De Pergola and Wolffenbuttel indicated that increased fT3 could be a compensatory mechanism in response to visceral fat accumulation, rather than a direct cause of obesity. Their findings point toward fT3 enhancing thermogenesis and metabolic activity to counteract excessive nutrient loads, suggesting that elevated fT3 levels are not necessarily a cause of obesity but rather a response to it.[14,16]

Our study did not find a significant correlation between TSH, fT3, fT4, or the fT3/fT4 ratio with waist circumference. However, some studies, such as the Lifelines Cohort Study conducted in the Netherlands, reported a positive relationship between elevated fT3 and waist circumference.[17] Kitahara et al. found that in euthyroid adults, BMI and waist circumference were positively correlated with TSH and fT3, but not with fT4, suggesting that thyroid function could influence abdominal obesity.[18]

Ambrosi et al. and Lai et al. also reported positive correlations between TSH and waist circumference, supporting the idea that elevated TSH levels could be linked to visceral fat accumulation.[19,20] De Pergola et al. found a negative correlation between fT4 and waist circumference, whereas Mehran et al. observed a positive relationship between lower fT4 levels and waist circumference.[10,12] Yang et al. found that in postmenopausal women, fT3 was positively correlated with visceral fat, while fT4 was negatively correlated, further supporting the idea of differential roles for thyroid hormones in metabolic syndrome components.[21]

These contrasting findings emphasize the complexity of the relationship between thyroid hormones and abdominal obesity. De Pergola and Knudsen suggested that the fT3/fT4 ratio may reflect increased peripheral conversion of fT4 to fT3, contributing to enhanced visceral fat accumulation through increased sympathetic activity and energy expenditure.[10,22]

In our study, the lack of significant correlations between TSH, fT3, fT4, and the fT3/fT4 ratio with waist circumference may be due to the retrospective nature of the study, where measurements were taken by different individuals. This heterogeneity could have introduced variability in the data, potentially affecting the results. Additionally, factors such as smoking, menopause, and dietary influences—known to impact thyroid hormone levels—were not accounted for, which could have influenced the observed correlations.

TSH and HDL cholesterol levels were shown to be significantly correlated negatively in our study. Similarly, after controlling for age and sex, Roos et al. found a favorable connection between TSH and triglycerides.[11] While lower fT4 levels and higher fT3/fT4 ratios were associated with elevated triglycerides and decreased HDL cholesterol levels, Xu et al. showed that greater TSH levels were favorably connected with triglyceride levels, regardless of obesity status.[6] Higher fT3, higher fT3/fT4 ratios, higher triglyceride levels, and lower HDL cholesterol were all positively correlated, according to Jin et al.[15]

Waterhouse et al. reported that after adjusting for BMI, the relationship between TSH and triglycerides was no longer significant, suggesting that factors such as age, sex, obesity, and diet could affect the observed correlations between thyroid hormones and lipid metabolism.[23] Mehran et al. also found no significant correlation between TSH and lipid profile after adjusting for confounding factors, reinforcing the complexity of these relationships.[12]

Jin et al. indicated that thyroid hormone impacts lipid metabolism within the normal thyroid function range, suggesting that even small variations in thyroid hormone levels could affect lipid profiles.[15] Xu et al. proposed that lipid values might be sensitive to small changes in the Hypothalamus-Pituitary-Thyroid (HPT) axis, which could help explain the observed correlations.[6] Walczak and Sieminska highlighted that lipid accumulation outside of adipose tissue in individuals with obesity could lead to lipotoxicity, which might impair thyroid function and exacerbate lipid metabolism disturbances.[24] Jin et al. further proposed that leptin elevation in individuals with obesity could affect the HPT axis, contributing to lipid metabolism dysregulation, although further research is required to validate these mechanisms.[15]

In line with earlier research, we found a negative relationship between HDL cholesterol levels and TSH, fT3, and the fT3/fT4 ratio. However, our focus on women only and the elimination of confounding factors like smoking, menopause, and diet may have contributed to the lack of significant correlations between fT4 and triglycerides or HDL cholesterol, as well as between fT3, fT3/fT4 ratios, and triglycerides.

While there was no significant link between age and TSH or fT4, we did find a significant negative correlation between age and fT3 and the fT3/fT4 ratio. Age and fT3 and TSH were found to be negatively correlated by Spira and De Pergola, respectively.[10,25] According to Wolffenbuttel, TSH and fT4 levels stay largely constant with aging, but fT3 levels decline.[16]

These findings suggest that age-related changes in thyroid hormone levels could be influenced by reduced TSH bioactivity, decreased hypothalamic sensitivity to thyroid hormones, alterations in serum leptin levels, and increased systemic inflammation, which may impact hypothalamic regulation. Reduced peripheral 5-deiodinase

activity, leading to decreased conversion of fT4 to fT3, could also contribute to lower fT3 levels with aging. [7]

### Limitations

This study has several limitations that should be considered when interpreting the results. First, the cross-sectional design limits the ability to draw causal inferences between thyroid hormone levels and metabolic parameters. While associations were observed, the direction of these relationships remains unclear. Second, the study was conducted in a single-center tertiary hospital in Istanbul, which may limit the generalizability of the findings to broader populations with diverse cultural and socioeconomic backgrounds.

Another limitation is the use of self-reported data, which could introduce recall or reporting bias, particularly in the collection of demographic and clinical characteristics. Furthermore, the study sample was restricted to women aged 18–65, meaning that the results may not be applicable to men or individuals outside this age range. Future studies with larger, multicenter samples, longer follow-up periods, and more comprehensive data collection methods are needed to further clarify the relationships between thyroid hormones and metabolic parameters.

## Conclusion

This study demonstrated significant associations between thyroid hormone levels within the reference range and several metabolic markers in euthyroid women. Specifically, fT3 levels were negatively associated with HDL-C and positively associated with BMI and insulin resistance. Additionally, the fT3/fT4 ratio was found to correlate positively with insulin resistance and negatively with HDL-C. TSH was weakly but significantly associated with both triglyceride levels and BMI.

These findings suggest that even in the absence of overt thyroid dysfunction, variations in thyroid hormones may reflect or contribute to adverse metabolic profiles. Monitoring the fT3/fT4 ratio and fT3 levels may offer additional insights for assessing metabolic risk in individuals with obesity or insulin resistance.

Given the cross-sectional nature of this study, causal relationships cannot be established. Further prospective studies are warranted to clarify whether subtle shifts in thyroid hormone dynamics within the euthyroid range have prognostic value in metabolic health.

## Ethical approval

This study has been approved by the İstanbul Medeniyet University Göztepe Training and Research Hospital Clinical Research Ethics Committee (approval date 27.09.2023, number 2023/0637). Informed consent was obtained from all patients before their participation.

## Author contribution

The authors declare contribution to the paper as follows: Study conception and design: FAE, KG; data collection: FNYS; analysis and interpretation of results: FAE, HHM; draft manuscript preparation: FNYS. All authors reviewed the results and approved the final version of the article.

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## Conflict of interest

The authors declare that there is no conflict of interest.

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Case Report

# Bullous pemphigoid associated with dipeptidyl peptidase-4 inhibitor in primary care: Case report

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## ABSTRACT

Bullous pemphigoid is the most common bullous chronic autoimmune skin disease. Recent studies suggest dipeptidyl peptidase-4 inhibitors used in the treatment of type-2 diabetes as possible predisposing agents of bullous pemphigoid. It is thought to be important for primary care physicians, who are the most common referral point of patients and where drug use is examined in detail, to keep in mind that drugs such as dipeptidyl-peptidase-4 inhibitors may cause bullous pemphigoid and to refer to dermatology for early treatment.

In this context, a 70-year-old female patient with a diagnosis of type 2 diabetes mellitus presented to our outpatient clinic with pruritic, erythematous bullous lesions diffusely distributed over the body, occurring one week after initiation of a vildagliptin-containing medication. There was no mucosal involvement. The patient initially received treatment with the presumptive diagnoses of allergy and scabies; however, as no improvement was observed, a detailed medical history was obtained. Based on the clinical findings, drug-induced bullous pemphigoid was suspected, and the vildagliptin-containing medication was discontinued. The patient was subsequently referred to the dermatology department. Histopathological examination and direct immunofluorescence findings were consistent with bullous pemphigoid. Following drug withdrawal and a short course of oral corticosteroid therapy, a marked improvement of the lesions was achieved.

With this case, we aimed to draw attention to the approach of bullous pemphigoid disease developing as a result of vildagliptin use in a patient with type-2 diabetes who presented to primary care and to increase awareness on this issue.

**Keywords:** bullous pemphigoid, dipeptidyl peptidase-4 inhibitors, primary care

## Introduction

Bullous pemphigoid (BP), characterized by severe pruritus, tense bullae and edematous erythema, is the most common autoimmune bullous disease and mainly affects the elderly.[1,2] Drug-associated BP, which accounts for up to 10% of pemphigus cases, is a term that indicates clinical, histologic, or immunopathologic features of the idiopathic form of bullous pemphigoid associated with systemic or topical administration of certain drugs.[3]

In recent years, the incidence has increased in association with different medications, including diuretics, beta-blockers and antibiotics (Table 1), and has recently been associated with the use of dipeptidyl peptidase-4 (DPP4) inhibitors, which are

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**Table 1.** Medications implicated in drug-associated bullous pemphigoid

| Likely associationa | Probable associationb | Uncertain associationc |
|---|---|---|
| Alogliptin | Actinomycin-D | Aldesleukin (IL-2) |
| Anagliptin | Adalimumab | Amantadine |
| Aspirin | Amoxicillin | Amlodipine |
| Biostim® | Ampicillin | Anthralin (dithranol) |
| D-Penicillamine | Arsenic | Azapropazone |
| Enalapril | Atezolizumab | Captopril |
| Erlotinib | Bumetanide | Coal tar |
| Etanercept | Celecoxib | Complementary medicines |
| Everolimus | Cephalexin | Dabrafenib |
| Furosemide | Chloroquine | Doxepin |
| Ibuprofen | Ciprofloxacin | Enoxaparin |
| Levofloxacin | Diclofenac | Escitalopram |
| Linagliptin | Dorzolamide | Fluorouracil |
| Nivolumab | Durvalumab | Flupenthixol |
| Pembrolizumab | Efalizumab | Galantamine hydrobromide |
| Phenacetin | Fluoxetine | Herpes zoster vaccine |
| Psoralens with UVA | Gabapentin | Influenza vaccine |
| Rifampicin | Griseofulvin | Iodide |
| Serratiopeptidase | Hepatitis B vaccine | Levetiracetam |
| Sirolimus | Hexavalent combined | Mesalazine |
| Sitagliptin | vaccine | Nadolol |
| Teneligliptin | Hydrochlorothiazide | Nifedipine |
| Tetanus toxoid | Infliximab | Novoscabin (benzyl |
| Tiobutarit | Ipilimumab | benzoate) |
| Vildagliptin | Lisinopril | Omeprazole |
| | Losartan | Placental extracts |
| | Mefenamic acid | Photodynamic therapy |
| | Metamizole | Risperidone |
| | Metronidazole | Rotavirus vaccine |
| | Penicillin | Sulfonamide |
| | Rosuvastatin | Swine flu vaccine |
| | Spironolactone | Timolol |
| | Sulfasalazine | Valsartan |
| | Terbinafine | |
| | Ustekinumab | |

recommended in combination or as monotherapy for the treatment of type-2 diabetes.[4] In DPP4 inhibitor-associated BP, lesions usually begin several months to years after the start of use of a DPP-4 inhibitor. Available data describe a relatively higher risk with vildagliptin. This is followed by linagliptin, sitagliptin and saxagliptin.[5]

Drug-associated BP also tends to occur without severe urticaria or erythema at the base of the lesions, unlike inflammatory bullous pemphigoid.

Stopping the DPP-4 inhibitor results in complete resolution of symptoms in about one third of patients. Patients who are still symptomatic should be referred to a dermatologist for treatment with corticosteroids or tetracyclines.[6]

When the drug is not withdrawn after diagnosis, the response is mild or reappears after a short time.[5,7]

To prevent recurrence, the addition of systemic corticosteroids is recommended. In moderate to severe cases, an initial oral corticosteroid dose of 1 mg/kg/day is advised, while lower doses of 0.2–0.5 mg/kg/day are administered in mild cases.[2,8] The dose is gradually reduced in the absence of new lesions and when the disease stabilizes. After one month of treatment, improvement is usually marked. It may persist for up to several months after drug discontinuation and is characterized by rare relapses.[9]

With this case report, we aimed to draw attention to drug-associated bullous pemphigoid disease through a case of bullous pemphigoid secondary to vildagliptin use and to draw attention to the importance of recognition by primary care physicians and appropriate referral for early treatment.

## Case Presentation

### Patient information

A 70-year-old female patient with a history of hypertension and type 2 diabetes mellitus (DM) presented with erythematous, pruritic, tense bullae that initially appeared on the arms and legs and progressively spread over the entire body. No mucosal involvement was detected (Figure 1).

### Medical history

The patient reported that the skin lesions appeared after she restarted her oral antidiabetic therapy containing vildagliptin, which she had been using irregularly for approximately two years. The eruptions began one week after reinitiating the medication.

She had previously visited the emergency department twice for these complaints — initially diagnosed and treated for allergy, and later for scabies — but no clinical improvement was observed. The patient subsequently presented to

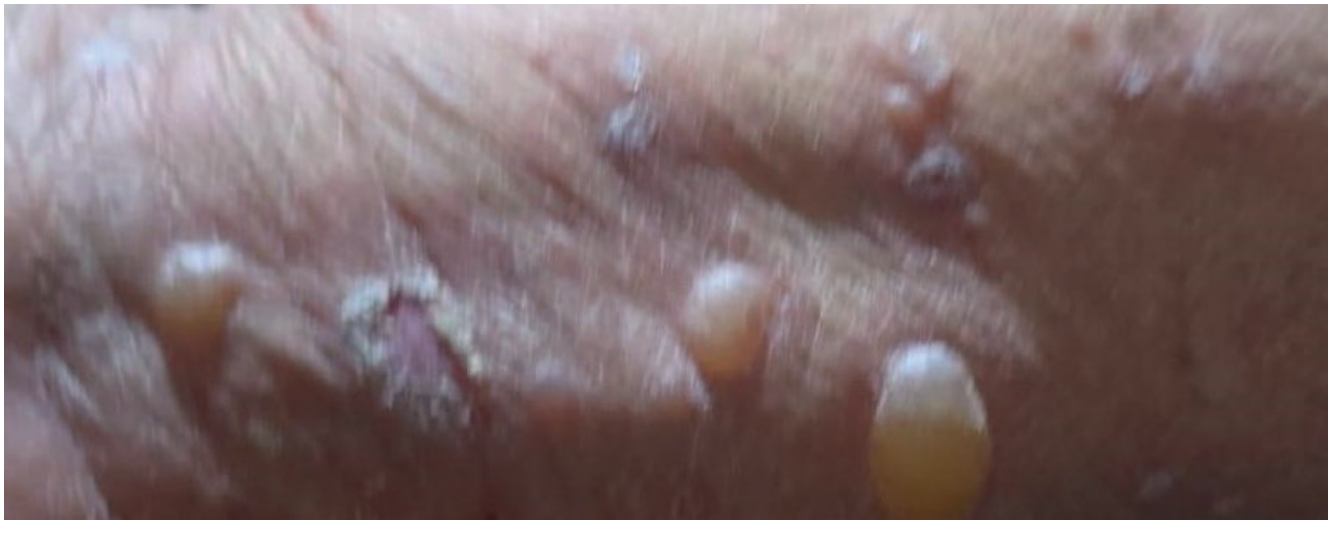

**Figure 1.** Active erythematous vesicles with areas of crusting on the patient's forearm and wrist region prior to treatment

our family medicine outpatient clinic, where a detailed history was obtained and her medications were reviewed.

### Current medications

Silazapril + Hydrochlorothiazide, Pitavastatin, Vildagliptin, Propranolol.

#### *Preliminary diagnosis and management*

Considering the possibility of bullous pemphigoid induced by vildagliptin, the medication was discontinued, and the patient was referred to the dermatology outpatient clinic. Following consultation with the internal medicine department, insulin therapy was initiated in place of the discontinued oral antidiabetic agent.

#### *Dermatological evaluation and diagnosis*

The dermatology specialist also suspected drug-induced bullous pemphigoid and referred the patient to a tertiary center for biopsy.

#### *Biopsy findings*

- Histopathology: Subepidermal bullae formation, infiltration of polymorphonuclear leukocytes within the bullae, perivascular mononuclear inflammatory cell infiltration in the dermis, and orthokeratosis in the epidermis.
- Direct Immunofluorescence (DIF): Linear positivity for C3 and IgG along the basement membrane zone; negative for IgA, IgM, and fibrinogen.
- Diagnosis: Findings consistent with *bullous pemphigoid*.

### Treatment and clinical course

Following the discontinuation of the vildagliptin-containing medication, a marked regression of the lesions was observed. The dermatology department initiated a 14-day oral corticosteroid regimen: First 5 days: 16 mg twice Daily, Subsequent 9 days: 16 mg once Daily. Significant clinical improvement of the lesions was achieved after treatment (Figure 2).

## Discussion

Bullous pemphigoid is an acquired autoimmune disease characterized by subepidermal blistering and mainly affects the elderly. The pathogenesis of the condition has not yet been fully elucidated, but it is widely accepted that there may be a strong correlation with various drugs.[10]

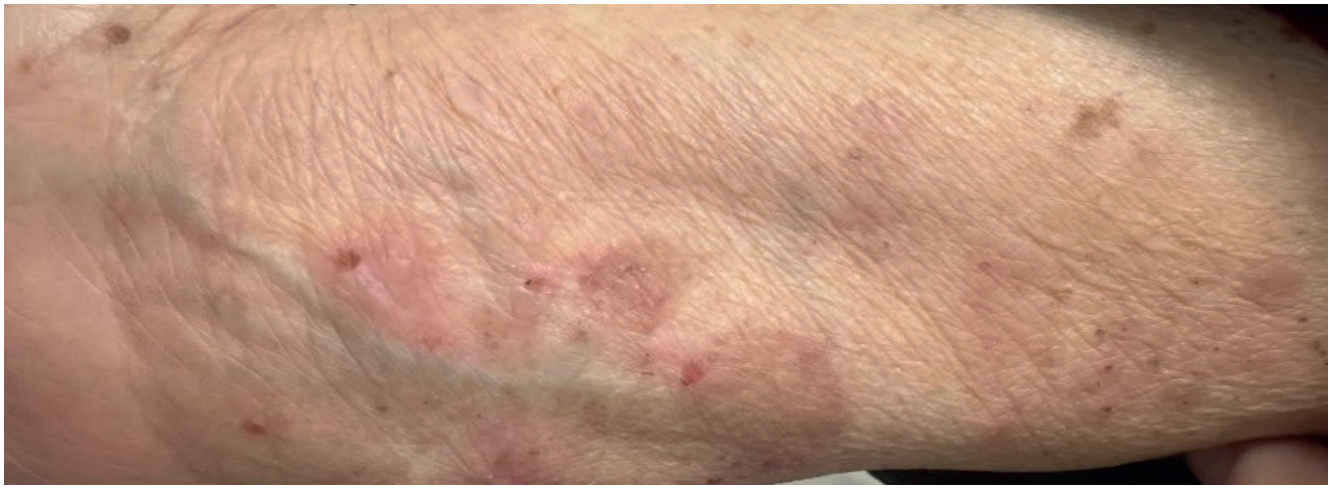

**Figure 2.** Regressed lesions on the patient's forearm and wrist region after treatment

To date, more than 60 drugs have been reported to induce BP, including some antibiotics, anti-hypertensive drugs, anti-TNF-α drugs and vaccines.[11] Among all classes of drugs, robust evidence suggests that DPP-4 inhibitor prior use carries the highest risk for BP. In a meta-analysis by Kridin and Cohen, it was reported that the risk of developing BP increased 3.2-fold following DPP-4 inhibitor administration, and this risk was found to have the highest association with vildagliptin among DPP-4 inhibitors.[12],[13]

Currently, there is a rapidly increasing volume of publications on DPP-4 inhibitor-associated BP, which means that it is now an important topic in this field.[11]

In addition, the present cases demonstrated the difficulty in the diagnosis of BP associated with DPP-4 inhibitors. This is due to the fact that drug-induced BP presents a diverse clinical picture in terms of agents and cutaneous inflammations, especially latency duration. Because of these features, clinicians should be fully aware of the potential risk. The current cases demonstrate the importance of early diagnosis and prompt withdrawal of agents to prevent exacerbation of skin symptoms. Since complete remission takes at least 2 weeks to achieve, appropriate withdrawal of agents is required for remission of BP in suspected cases.[14]

### Conclusion

Drug-induced BP is difficult to diagnose, unlike its idiopathic counterpart. This is because in both cases the clinical picture and histopathologic findings have only subtle differences. Patients presenting with BP and receiving multiple therapies should always be suspected to have a drug-induced variant of the condition. This possibility should be considered as most patients respond rapidly to treatment and do not relapse after discontinuation of the suspected drug.

Primary care physicians have great importance in identifying drug-induced BP cases early and organizing the treatment of patients by providing a multidisciplinary approach with the relevant units.

Therefore, we suggest that the diagnosis of drug-induced BP should be kept in mind among elderly diabetics presenting to primary care with initial signs and symptoms of BP.

## Ethical approval

Informed consent form was obtained from the patient for this case.

## Author contribution

The authors declare contribution to the paper as follows: Study conception and design: KK; data collection: KK; analysis and interpretation of results: KK; draft manuscript preparation: KK. All authors reviewed the results and approved the final version of the article.

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## Conflict of interest

The authors declare that there is no conflict of interest.

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Letter to the Editor

# Leveraging home healthcare to enhance adult immunization coverage

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Dear Editor,

Home healthcare services provide essential medical care through mobile health teams to individuals who are bedridden or unable to access healthcare facilities due to chronic conditions. Despite their importance, adult immunization has not been systematically prioritized within this care framework.

Adult immunization rates in Türkiye are known to be low, and globally, adult vaccination coverage remains suboptimal compared to recommended targets.[1,2] Patients receiving home healthcare represent a particularly high-risk group, as they often encounter significant barriers to accessing vaccines.[3] Home visits thus constitute a critical and underutilized opportunity to evaluate vaccination status and address gaps in coverage. The COVID-19 pandemic demonstrated the feasibility of home-based vaccination through successful administration of COVID-19 vaccines in this population.

Family physicians, who are entrusted with the mission of preventive health care, have sought to integrate immunization into home visits to reduce disease burden and enhance cost-effectiveness within the health system. At the Family Medicine Clinic of Istanbul Prof. Dr. Cemil Taşcıoğlu City Hospital, we pioneered home-based vaccination by systematically reviewing patient vaccination status using the ATS (National Vaccine Tracking System) and the national e-Nabız platform. Pneumococcal and influenza vaccines were subsequently administered to eligible high-risk individuals.

To expand this initiative across Istanbul, the Istanbul Provincial Directorate of Health convened a meeting on July 31, 2024, under the leadership of Prof. Dr. Güzin Zeren Öztürk and Prof. Dr. Seçil Arıca, focusing on safe immunization practices in home healthcare. This meeting provided practical guidance for healthcare teams and promoted multidisciplinary collaboration through regular training and knowledge-sharing. Consequently, approximately 2,000 high-risk patients receiving home healthcare services in Istanbul were vaccinated in their homes with pneumococcal and influenza vaccines, following informed consent.

The main challenges encountered included vaccine hesitancy among patients and caregivers, as well as logistical constraints. These barriers, however, were largely mitigated through targeted

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communication and effective coordination within care teams.

Looking ahead, sustaining and scaling adult immunization in home healthcare services will require strengthening regulatory frameworks, expanding education and training programs, and enhancing monitoring systems at both local and national levels. Such efforts are essential to fully realize the preventive potential of home healthcare as a platform for improving adult vaccination coverage.

Sincerely,

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## Conflict of interest

The authors declare that there is no conflict of interest.

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