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RESEARCH

POLYPHARMACY PREVALENCE AMONG GERIATRIC PATIENTS IN PRIMARY HEALTHCARE SETTINGS ACROSS TURKEY: A CROSS-SECTIONAL ANALYSIS THROUGH THE NATIONWIDE PRESCRIPTION INFORMATION SYSTEM

ABSTRACT

Introduction: Polypharmacy has become a common health problem as populations age. We aimed to determine the prevalence of chronic and cumulative polypharmacy in the geriatric population using primary healthcare services in Turkey.

Materials and Methods: The electronic prescriptions ordered by family physicians across Turkey for geriatric patients (≥ 65 years) in the Prescription Information System during 2018 were studied. Chronic polypharmacy criteria were proportion of patients who were given prescriptions containing ≥ 5 drugs four or more times during a year. Cumulative polypharmacy was defined as proportion of patients who were prescribed ≥ 5 drugs with different ATC4 codes in a month or in each quarter of the year.

Results: Turkey's total population is 82 million; 7,186,204 are aged 65 and over, constituting 8.8% of the total. Of this geriatric population, 6,104,798 (85.0%) had at least one prescription in 2018. Each geriatric patient had 6.4 prescriptions, with each prescription containing an average of 2.9 drugs with different fourth-level Anatomical Therapeutic Chemical codes. Each drug was prescribed in 2.7 boxes on average. Of these prescribed patients, 14.3% received prescriptions containing ≥ 5 drugs four or more times during 2018. The percentage of patients who received at least one prescription per month containing ≥ 5 drugs ranged between 16.4% and 20.7%. The most commonly prescribed drugs were acetylsalicylic acid, diclofenac, paracetamol, and pantoprazole.

Conclusion: Polypharmacy is a critical health problem among geriatric population in Turkey as in other industrialized countries. Educating physicians as well as the public is essential to overcome polypharmacy.

Keywords: Geriatrics; Polypharmacy; Epidemiology; Prescriptions.

INTRODUCTION

As multimorbidity is becoming a major issue with increasing ageing populations, multidrug use (i.e., polypharmacy) is a common health problem in the geriatric population, leading to increased drug side effects, drug–drug interactions, decreased patient adherence to treatment, and increased morbidity (1,2). Although there is no consensus on the definition of polypharmacy, it is commonly referred to as the concurrent use of multiple, unnecessary, or ineffective drugs by a patient (3). Various indicators of polypharmacy have been used in the literature (4). The number of concomitant medications taken in a day, the average number of medications prescribed in a year, and the 20-day average of the number of medications prescribed at two-week intervals have been suggested as indicators of simultaneous multidrug use (5). The proportion of patients prescribed with five or more drugs in each quarter of the year has been considered a marker of cumulative multidrug use, and the proportion of patients taking five or more drugs that are prescribed at least three or four times a year has been defined as chronic multidrug use (6,7). The simultaneous use of five or more drugs has been reported to increase side effects and drug–drug interactions and thus is considered the most common indicator of polypharmacy (8). Based on these definitions, the prevalence of polypharmacy ranges between 45% and 82% in the geriatric populations (9,10).

Similar to other developing countries, the proportion of elderly people is increasing in the Turkish population. Individuals over 65 years constitute 8.8% of the population of 82 million of Turkey in 2018 (11). However, the prevalence of polypharmacy in the elderly has not been comprehensively studied at the population level.

The primary aim of this study was to determine the prevalence of chronic and cumulative polypharmacy in patients aged 65 and over who use primary healthcare services across Turkey.

MATERIALS AND METHODS

Study design and population

This was a retrospective study in which electronic prescription data were analyzed. Prescriptions from family physicians across Turkey for patients aged 65 and over and entered into the Prescription Information System (PIS) during 2018 were studied. The PIS is a nationwide database where family physicians enter their prescription data. The PIS was developed and is still operated by the Turkish Medicines and Medical Devices Agency (TMMDA) to monitor and encourage rational drug prescription across the country (12).

The study sample was composed of all electronic prescription data entered in the PIS between January 1, 2018 and December 31, 2018 by family physicians for patients aged 65 and over. The Anatomical Therapeutic Chemical (ATC) classification system of the World Health Organization Collaborating Center for Drug Statistics Methodology was used for the drug nomenclature (13).

The electronic prescription data from the PIS were obtained as the number of patients and prescriptions and did not include individual data of any patient or physician. The study was approved by the Baskent University Medical and Health Sciences Ethics Committee (Project no: KA19/241; Date: 09.07.2019) and supported by Baskent University Research Fund. The PIS data was used with the permission and contribution of the TMMDA's Department of Rational Drug Use (E.116688, 11.07.2019).

Outcome variables: polypharmacy indicators

The average number of prescriptions per patient, the average number of drug items, and the average number of boxes per prescription were calculated. Due to their limited systemic effects, topical dermatological agents were excluded from the analysis.

Chronic polypharmacy was defined as the



proportion of patients prescribed four or more prescriptions over one year, each of which contained 3, 4, or ≥ 5 drugs per prescription with different ATC 4 codes. Since this criterion aimed to determine chronic systemic multidrug use, topical dermatological agents (ATC code D) with limited systemic effects and systemic antibiotics (ATC codes J01) generally used in the treatment of acute infections were excluded.

Cumulative polypharmacy was defined as the proportion of patients who were prescribed ≥ 5 drugs with different ATC 4 codes in a month or in each quarter of the year. This criterion aimed to evaluate the multiple use of systemic drugs within a certain period. Therefore, while topical dermatological agents (ATC code D) were excluded from the analysis, systemic antibiotics (ATC codes J01) with the potential to interact with the concomitant drugs were included.

The 10 most commonly prescribed drugs (excluding topical dermatological agents [ATC code D] and systemic antibiotics [ATC codes J01]) were listed according to their ATC 4 and ATC 5 codes. The 10 most common diagnoses entered into the PIS database and the distribution of patients and prescriptions for these diagnoses were also evaluated. The International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) was used for the definition and coding of diagnoses.

Statistical analysis

The average number of prescriptions per patient was calculated by dividing the total number of prescriptions issued to number of geriatric patients in primary healthcare settings across Turkey in 2018. In other words, dividing the total number of prescriptions (denoted as y) by the number of patients (denoted as x) yields the average number of prescriptions per patient (p). This is expressed mathematically as $p=y/x$. The average number of drug items and the number of boxes were calculated as per prescription in

a similar way. Other data were summarized as descriptive statistics (mean, standard deviation, frequency, and percentage) and were presented in tables and figures. Since the data were obtained not as individual patient data, but as an aggregate data of the number of patients, prescriptions, drug items, and boxes, etc.; significance tests could not be performed.

RESULTS

Turkey's population aged 65 and over in 2018 was 7,186,204. Of this population, 6,104,798 (85.0%) had at least one prescription in primary healthcare settings in 2018. The percentage of prescribed patients rose with increasing age, reaching 91.4% for patients aged 85 and over (Figure 1). While the prescription rate was higher in female patients than in male patients aged 65–69 years (84.0% vs. 77.9%), this difference disappeared in older age groups (Figure 1).

Over 39 million prescriptions were issued to population over 65 in 2018, which corresponds to an average of 6.4 prescriptions per patient. Each prescription contained an average of 2.9 individual drug items, and each drug was prescribed in an average 2.7 boxes (Table 1). There was a systemic antibiotic in 7.7% of all prescriptions.

Chronic polypharmacy

The percentage of patients prescribed with four or more prescriptions over one year, each containing 3, 4, or ≥ 5 drugs per prescription were 15.9%, 9.9%, and 14.3%, respectively, with no gender difference (Table 2). The percentage of patients chronically prescribed multiple drugs rose with increasing patient age (Figure 2).

Cumulative polypharmacy

The percentage of patients who received at least one prescription containing ≥ 5 drugs in a month ranged between 16.4% and 20.7%, being slightly higher during the winter months (Table 3, Figure 3A). The percentage of patients who

Figure 1. Percentage of Turkey's population aged 65 and over having at least one prescription in primary healthcare settings in 2018.

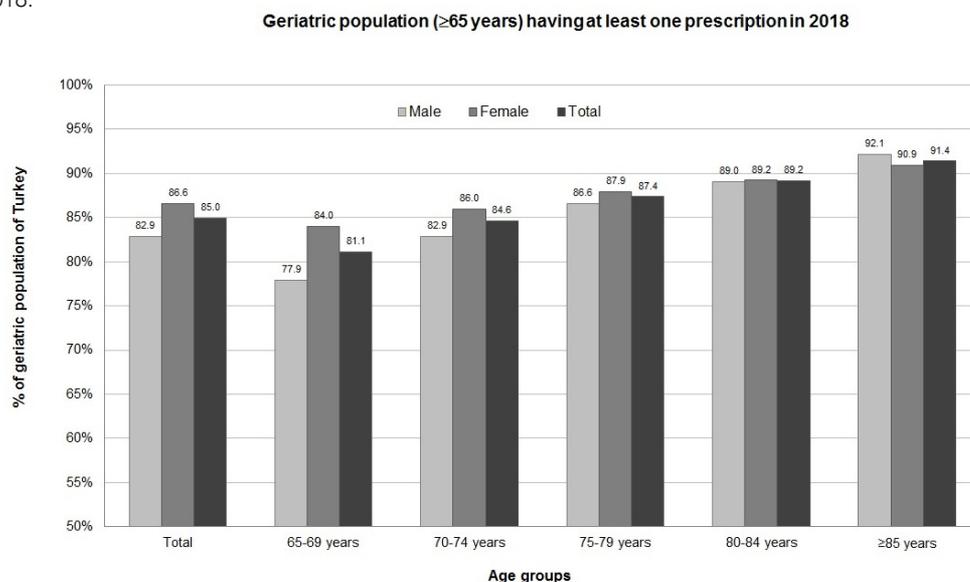


Table 1. Basic characteristics of prescriptions for geriatric patients in primary healthcare settings across Turkey in 2018.

	Male	Female	Total ^a
Total population of Turkey aged 65 years and over in 2018	3,170,132	4,016,072	7,186,204
Prescribed patients	2,626,705	3,476,943	6,104,798
Prescriptions	16,676,117	22,438,776	39,117,912
Prescriptions containing antibiotics	1,324,083	1,694,810	3,019,303
Individual drug items in all prescriptions	46,672,701	66,673,332	113,353,487
Drug boxes in all prescriptions	124,830,141	175,775,687	300,622,579
Prescription per patient	6.3	6.5	6.4
Individual drug items per prescription	2.8	3.0	2.9
Drug boxes per prescription	7.5	7.8	7.7
Drug boxes per item	2.7	2.6	2.7

^aTotal number of patients includes individuals whose gender information has not been entered.



Figure 2. . Percentage of geriatric patients in primary healthcare settings who were given 4 or more prescriptions containing ≥ 5 drugs in 2018.

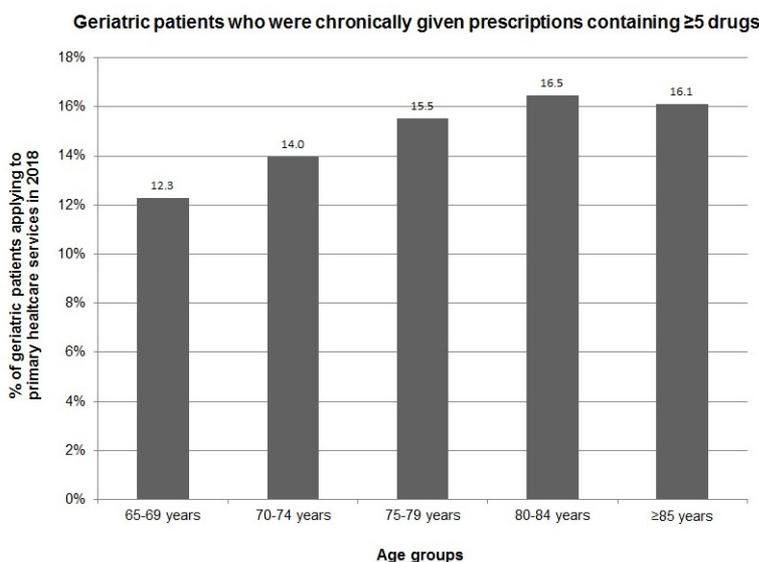


Table 2. The patients who were chronically prescribed multiple drugs (4 or more prescriptions over one year, each containing 3, 4, or ≥ 5 drugs per prescription).

Chronic polypharmacy (≥ 4 prescriptions per year)	Male	Female	Total
3-drug prescriptions	185,791 (15.8%)	195,652 (15.9%)	448,956 (15.9%)
4-drug prescriptions	116,187 (9.9%)	122,149 (10.0%)	280,028 (9.9%)
≥ 5 -drug prescriptions	167,710 (14.2%)	176,738 (14.4%)	402,969 (14.3%)
Total	1,178,818	1,227,142	2,827,643 ^a

^aTotal number of patients includes individuals whose gender information has not been entered

received at least one prescription containing ≥ 5 different drugs in a quarter was 28.3%, 26.4%, 24.8%, and 25.7% in the first, second, third, and fourth quarters of 2018, respectively (Table 3, Figure 3B).

Common drugs and diagnoses

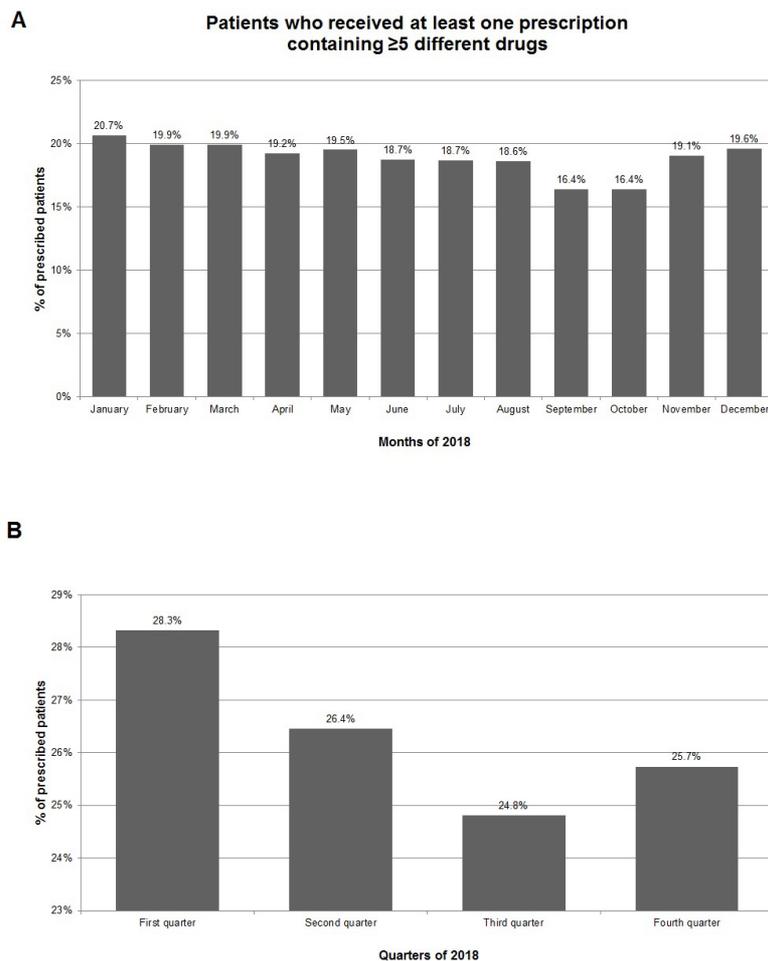
Proton pump inhibitors and acetic acid derivatives constituted the most commonly prescribed group of drugs, followed by platelet aggregation inhibitors and anti-inflammatory drugs, such as anilides and propionic acid

derivatives at the ATC 4 level (Table 4). At the ATC 5 level, acetylsalicylic acid, diclofenac, paracetamol, and pantoprazole were the most commonly prescribed drugs (Table 4). The most common diagnoses in the analyzed prescriptions were essential hypertension, myalgia, gastroesophageal reflux, and benign prostate hyperplasia.

DISCUSSION

Polypharmacy is a growing medical concern among the elderly population, causing critical

Figure 3. Percentage of prescribed patients who received at least one prescription containing ≥ 5 drugs in a month (A) or in each quarter (B) of the year.



problems such as increased healthcare costs, a high risk of adverse drug reactions, drug-drug interactions, medication non-adherence, reduced functional capacity, and cognitive impairment (1,2). In this prescription-based nationwide study, we determined the prevalence of chronic and cumulative polypharmacy in the geriatric population of 6,104,798 individuals using primary healthcare services in Turkey.

Similar to previous studies, the present study showed that 85% of Turkey's population aged 65 years and over received at least one prescription drug during 2018. A survey conducted by in-home interviews in the United States of 2,206 community-dwelling adults aged 62 years and over reported that 87% were using at least one prescription medication (14). Prescriptions containing systemic antibiotics constituted 7.7% of all prescriptions



Table 3. The patients who were cumulatively prescribed ≥ 5 drugs.

Timeframe	Number of prescribed patients	Patients who received at least one prescription containing ≥ 5 different drugs	
		n	%
First quarter (January-March)	4,760,283	1,348,384	28.3%
January	2,761,601	570,826	20.7%
February	2,562,455	510,417	19.9%
March	2,733,532	544,401	19.9%
Second quarter (April-June)	4,806,627	1,271,332	26.4%
April	2,632,597	506,631	19.2%
May	2,785,906	543,469	19.5%
June	2,522,276	472,896	18.7%
Third quarter (July-September)	4,448,414	1,103,600	24.8%
July	2,637,344	492,563	18.7%
August	2,448,043	456,207	18.6%
September	2,022,176	331,619	16.4%
Fourth quarter (October-December)	4,533,457	1,166,790	25.7%
October	2,210,510	362,790	16.4%
November	2,640,460	503,152	19.1%
December	2,583,139	506,687	19.6%

in our study. Depending on the study setup and population, antibiotic prescription rates in primary care have shown large variability of between 20% and 41% in the literature (15,16). The lower antibiotic prescription rate in our study is thought to be the result of regulatory restrictions imposed on antibiotic prescription in primary care in Turkey in recent years. Additionally, elderly patients are usually treated by systemic antibiotics in secondary

and tertiary hospitals rather than in primary care.

Chronic polypharmacy is an indicator of healthcare quality in the Organisation for Economic Co-operation and Development (OECD) resources (17). The OECD indicator for chronic polypharmacy among the elderly is the proportion of people 75 years and over who are taking ≥ 5 drugs chronically, which is defined as medication prescribed for more than 90 days or

Table 4. Considering the number of patients, 10 most commonly prescribed drugs at ATC4 and ATC5 level.

ATC4 Code	Name	Male		Female		Total ^a	
		n	%	n	%	n	%
A02BC	Proton pump inhibitors	1,082,459	41.2%	1,702,555	49.0%	2,785,272	45.6%
M01AB	Acetic acid derivatives and related substances	886,245	33.7%	1,411,783	40.6%	2,298,298	37.6%
B01AC	Platelet aggregation inhibitors excluding heparin	983,573	37.4%	1,094,577	31.5%	2,078,277	34.0%
N02BE	Anilides	716,621	27.3%	1,147,141	33.0%	1,863,947	30.5%
M01AE	Propionic acid derivatives	727,977	27.7%	1,093,753	31.5%	1,821,973	29.8%
M02AA	Anti-inflammatory preparations, non-steroids for topical use	623,395	23.7%	1,032,524	29.7%	1,656,108	27.1%
R05X	Other cold preparations	725,510	27.6%	879,684	25.3%	1,605,406	26.3%
C07AB	Beta blocking agents, selective	610,965	23.3%	793,974	22.8%	1,405,014	23.0%
C09DA	Angiotensin II antagonists and diuretics	410,754	15.6%	974,356	28.0%	1,385,158	22.7%
C08CA	Dihydropyridine derivatives	370,858	14.1%	632,566	18.2%	1,003,496	16.4%
ATC5 Code	Name						
B01AC06	Acetylsalicylic acid	828,083	31.5%	964,593	27.7%	1,792,788	29.4%
M01AB05	Diclofenac	682,593	26.0%	1,081,009	31.1%	1,763,794	28.9%
R05X	Other cold preparations	725,510	27.6%	879,684	25.3%	1,605,406	26.3%
N02BE01	Paracetamol	494,815	18.8%	812,304	23.4%	1,307,235	21.4%
A02BC02	Pantoprazole	456,711	17.4%	708,201	20.4%	1,165,008	19.1%
C07AB02	Metoprolol	446,289	17.0%	513,983	14.8%	960,332	15.7%
A10BA02	Metformin	371,780	14.2%	589,156	16.9%	960,987	15.7%
A11DB	Vitamin B1 in combination with vitamin B6 and/or vitamin B12	362,409	13.8%	574,483	16.5%	937,007	15.3%
A02BC03	Lansoprazole	363,242	13.8%	567,072	16.3%	930,402	15.2%
M01AE17	Dexketoprofen	361,156	13.7%	561,044	16.1%	922,306	15.1%
	Total number of patients	2,626,705		3,476,943		6,104,798	

^aTotal number of patients includes individuals whose gender information has not been entered.



four or more prescriptions in a year. According to 2016 data, this proportion varies between 44% and 87% among European countries (17). Although previous local and small-size studies for Turkey reported that higher rate of chronic polypharmacy (18), in the present study, only 14.3% of patients aged ≥ 65 years received prescriptions containing ≥ 5 drugs four or more times during one year. Thus, it is noteworthy that the chronic polypharmacy rate in Turkey is remarkably lower than European countries. This low rate is thought to be due to the difference between our study and the OECD indicator in terms of patient age and the definition of chronic polypharmacy. While our study population consisted only of elderly patients who used primary healthcare services, chronic polypharmacy data in other European countries include all people in prescribing databases that cover patients with chronic diseases who apply to the second- and third-level healthcare services and potentially use many medications chronically.

In our study, the prevalence of cumulative polypharmacy (the percentage of patients who received five or more drugs in a prescription in a month) ranged between 16.4% and 20.7% during 2018. In the literature, the prevalence of polypharmacy between 27% and 67%, depending on the design and population of the studies. In a National Health Survey from Spain, the prevalence of polypharmacy (≥ 5 medications) and hyperpolypharmacy (≥ 10) in 7,023 participants aged 65 and over was 27.3% and 0.9%, respectively (19). In primary care setting studies from Turkey, the prevalence of polypharmacy ranged between 33% and 42%, and the number of medicines used per day was 4.3-4.7-in adults aged ≥ 65 years (20,21). The accessibility to health services, female gender, depression, and chronic diseases were reported to be significant risk factors for polypharmacy (20). In a registry-based cross-sectional study from Sweden, in a cohort of 15,945 patients aged 75 years and over, the proportion of patients who used five or more medications at the same time was reported to be 33.4% (22). In an Italian registry-based

study (the REPOSI register), the prevalence of polypharmacy (five or more different medications in a prescription) was 51.9% at hospital admission and 67.0% at discharge among 1,332 inpatients aged ≥ 65 years across 38 internal medicine wards in Italy (23). The comparability of polypharmacy rates between studies is limited because of the differences between the populations and the parameters of polypharmacy in studies.

Proton pump inhibitors, anti-inflammatory drugs, and antiplatelets were the most often prescribed medications. The most commonly prescribed specific molecules were acetylsalicylic acid, diclofenac, paracetamol, and pantoprazole. In a survey of adults aged 62 years and over from the United States, lipid-lowering medications were reported to be the most commonly prescribed agents followed by antiplatelets, anti-inflammatory drugs, and proton pump inhibitors (14). In another survey of 164,513 multimorbid patients aged over 65 years from Spain, proton pump inhibitors, lipid-lowering medications, and antiplatelets were the most commonly prescribed drugs in primary care settings (24). Although the most prescribed drugs in our study were similar to other countries, considering the most common diagnosis, hypertension, it is remarkable that lipid-lowering and antihypertensive drugs were not prescribed frequently, due to the fact that these drugs are usually prescribed in secondary and tertiary care services rather than primary care in Turkey.

The main limitation of the present study was that it analyzed the drug use of the elderly population through prescriptions. Although the major way to access drugs in Turkey is through prescriptions, people may freely obtain over-the-counter medications or dietary supplements. This study did not evaluate patients' access to these substances or medication adherence. Considering the increasing use of over-the-counter medications and herbal or dietary supplements among older adults and critical drug-herb and drug-supplement interactions

(14,25), non-prescription medication should also be taken into account in future polypharmacy studies. Furthermore, this study focused primarily on the number of medications in prescriptions, but not on unnecessary or inappropriate drug prescription, which is a critical component of potentially inappropriate medication use along with polypharmacy.

In conclusion, 85.0% of Turkey's geriatric population had at least one prescription in 2018. Each patient had an average of 6.4 prescriptions, and each prescription contained

2.9 medications on average. The percentage of patients who were chronically prescribed with five or more medications was 14.3%, and those who were cumulatively on polypharmacy ranged between 16.4% and 20.7% during the year. The most commonly prescribed drugs were proton pump inhibitors, anti-inflammatory drugs, and antiplatelets. Polypharmacy is a critical health problem among the geriatric population in Turkey as in industrialized countries. Educating physicians as well as the public is essential to overcome polypharmacy.

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