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Adverse drug reactions and its associated factors among geriatric hospitalized patients at selected comprehensive specialized hospitals of the Amhara Region, Ethiopia: a multicenter prospective cohort study

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Abstract

Background Adverse drug reactions are more prevalent in geriatric patients and are frequently associated with a range of polypharmacy-related issues as well as some physiological aging-related alterations. These affect the pharmacokinetic and pharmacodynamic properties of drugs. This study aimed to assess the magnitude of ADRs and their contributing factors among geriatric patients admitted at Comprehensive Specialized Hospitals of the Amhara Region.

Methods A multicenter prospective cohort study was carried out from May 2023 to August 2023 on geriatric patients admitted to four randomly selected comprehensive hospitals in the Amhara region. We used logistic regression to find the factors influencing the occurrence of ADRs. A P value of less than 0.05 was deemed statistically significant.

Results During the study's follow-up period, 373 patients in total were included. An incidence rate of 31.10% (95% CI: 26.38–35.82) was obtained from the identification of 121 ADRs in total. The organ most frequently affected by ADRs was the gastrointestinal tract (28.92%), followed by the cardiovascular system (19.01%), and the drug class most often implicated in ADRs was antibiotics (21.49%), then anticoagulants (12.40%). ADRs were substantially linked to being overweight ($P < 0.001$), having been hospitalized in the previous six months ($P = 0.000$), and hyperpolypharmacy ($p = 0.047$). 93.39% of all ADRs received the interventions. 85.12% of the adverse drug reactions were successfully resolved.

Conclusions This study found that over one-third of older people and individuals admitted to the hospital experienced ADRs. Overweight, hyperpolypharmacy, and patients who had previously been admitted during the

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preceding six months were significantly linked with the occurrence of ADRs. Improving the drug safety of elderly patients, particularly those who are admitted, should be a greater priority for healthcare professionals.

Keywords Adverse drug reactions, Geriatrics, Comprehensive specialized hospitals, Ethiopia

Background

Adverse drug reactions (ADRs) are one of the leading causes of morbidity and mortality in healthcare [1, 2]. The number of adverse medication occurrences is increasing due to the prescribing of medication for multiple diseases by geriatric populations, which is becoming a serious healthcare issue [3, 4]. Research from throughout the world has shown that 15–50% of older persons develop ADRs, and severe reactions can result in hospitalization or extended hospital stays [5]. Researchers have implicated adverse drug reactions as the fourth to sixth leading cause of death in the United States [6]. These unfavorable occurrences raise healthcare expenses and resource consumption in addition to endangering patient safety. According to the World Health Organization (WHO), adverse drug reactions (ADRs) are a response to a drug that is noxious and unintended and that occurs at doses commonly employed in man for the prevention, diagnosis, or treatment of disease, or changes of physiological function of the patients [7, 8].

Several important factors influence the occurrence of adverse medication reactions in hospitalized older adults. Age-related changes in pharmacokinetics and pharmacodynamics further complicate pharmacological management and increase sensitivity to ADRs [9]. Polypharmacy, which is common in this age group, also raises the risk of drug interactions and side effects [10]. Comorbidities, which are prevalent in the geriatric population, not only increase medication complication schedules but also increase the risk of ADRs [11]. Inadequate medication monitoring may lead to unidentified ADRs, which worsens health consequences [12]. ADRs are also caused by several other factors, some of which are modifiable (e.g., smoking or alcohol use), while others are not, such as age, the existence of other diseases, or genetic factors, which are particularly prevalent in geriatric persons (≥65 years) [1, 13, 14]. Because some drugs have been associated with increased adverse drug reactions in older adults, lists of potentially inappropriate medications (PIMs) for this demographic (such the international Beers Criteria and the PRISCUS list) have been published [15, 16]. Because they often exhibit nebulous symptoms such as falls, exhaustion, cognitive impairment, or constipation—all of which have various etiologies—they may find it challenging to recognize adverse drug responses [14].

Adverse drug reactions are quite common in hospitalized geriatric patients [17], and they can lead to a greater risk of infection, higher medical expenses, or higher mortality rates, which can result in serious health problems and prolonged hospital stays [18, 19]. Analyzing the frequency and contributing factors of adverse ADRs in hospitalized older patients tackles a crucial problem in geriatric care. In addition to offering crucial information on the particular risk factors linked to ADRs in this group, this study emphasizes how Ethiopia's healthcare system needs to enhance pharmacovigilance and implement customized drug management plans. The results demonstrate the link between comorbidities, polypharmacy, and demographic factors, thereby assisting doctors and policymakers in making informed decisions about treating older patients and ensuring their safety.

Researchers are investigating clinical pharmacy interventions as an essential tactic to reduce ADRs, given their substantial influence on patient outcomes. By implementing pharmaceutical care, we aim to enhance medication safety and improve therapeutic outcomes [20]. Previous studies have demonstrated that pharmacist interventions can significantly decrease the incidence of ADRs and improve patient adherence [21, 22]. To the best of our knowledge, no previous studies have investigated adverse medication occurrences in geriatric patients. This study aimed to identify the incidence of ADRs in hospitalized geriatric patients and their causality, severity, preventability, and contributory factors. Additionally, we have interventions to address ADRs.

Methods and materials

Study design, and period

The study design was a multicenter prospective cohort study of geriatric patients admitted to the medical wards of four selected hospitals in the Amhara regional state. The study period was from May 2023 to August 2023. The study participant was followed until they were discharged from the hospital to provide appropriate therapies for ADR alleviation and to monitor them during that time.

Study setting

This research was carried out in public health institutions located in the Amhara regional state of Ethiopia. The Amhara Region is situated in the northwestern and central parts of Ethiopia, positioned between latitudes 9° and 23° 45'N and longitudes 36° and 40° 30'E. Elevation varies from 700 m in the eastern regions to over 4620 m in the northwestern area. The total area is 170,000 km², organized into 11 administrative zones and 105 Woredas. This region contains eight comprehensive specialized hospitals. Felege Hiwot, University of Gonder, Debere

Tabor, and Dessie Comprehensive Specialized Hospitals were randomly selected as data sources for the study.

Inclusion and exclusion criteria

Patients admitted to the selected hospitals during the study period who were 65 years of age or older, geriatric patients who stay in the hospital for a minimum of 24 h or longer, providing enough time to monitor and identify ADRs, patients in the hospital have had at least one prescription filled out. This makes sure that the study's emphasis is on patients who are at risk of ADRs as a result of medication and who give their written, informed consent to take part in the research were included in the study. Unless a caregiver or legal representative is available to assist, patients with severe cognitive impairment or dementia are unable to provide informed permission or participate consistently in follow-up, and patients who do not take medicine throughout their hospital stay and who are admitted for reasons unrelated to medication (such as surgery or trauma) were not included.

Sample size determination and sampling technique

The sample size was calculated based on a single proportional formula $n = \frac{(Z\alpha/2)^2 P(1-P)}{d^2}$; Z = 1.96, the proportion of ADE occurrence (P) = 0.5 and marginal error (d) = 5%, then the sample size is equal to 384. Including a 10% contingency for patients who declined to participate in the study and non-respondents led to a final sample size of 422. We allocated a portion of the total sample size to each comprehensive hospital based on the patients admitted within the previous three months. Proportional allocation of samples to the total population of each hospital was applied using the formula as follows: n = nf×N/ni

Where n = required sample size for each hospital, nf = patients admitted in the previous three months at each hospital, N = sample size calculated from a single proportional formula and ni = total number of geriatric patients from four selected hospitals who were admitted in the previous three months. The source population and the samples were $N = 809$ and $n = 422$, respectively.

Study participants at FHCSH = 230*422/809 = *120 (*17 were excluded during follow-up).

Study participants at UGCSH = 201*422/809 = *105* (12 were excluded during follow-up).

Study participants at DTCSH = 167*422/809 = *87* (9 were excluded during follow-up).

Study participants at DCSH = 211*422/809 = *110* (11 were excluded during follow-up).

Finally, 373 patients were used for analysis after 49 patients were eliminated because they were unable to complete their follow-up (Fig. 1). We applied a consecutive sampling technique among all patients who met the inclusion criteria.

Study variable

The incidence of adverse drug reactions is the dependent variable for this study. The study examined factors such as age, gender, education level, marital status, occupation, body mass index (BMI), GFR (Modification of Diet in Renal Disease [23], drug source, social drug use (such as alcohol, khat, and smoking), drug class, number of prescribed drugs, type of medical condition, number of comorbidities, and length of hospitalization to determine the incidence of adverse drug reactions.

Data collection instrument, procedures, and quality assurance

The data abstraction tool was developed by reviewing the literature for important variables [24–29]. An interdisciplinary team validates and examines the assessment tools to ensure the accuracy and dependability of the results. The assessment tools were assessed by one epidemiologist and two MSc. in clinical pharmacy. We first created the data collection sheet in English, translated it into the local language of Amharic, and then translated it back into English to maintain consistency. We used 10% of randomly chosen sample patients in a pretest to evaluate the tool's quality before actual data gathering. Before it was put to use for data collection, a few adjustments were performed.

Not only does the questionnaire cover sociodemographic information such as age, gender, residence, marital status, educational attainment, occupation, alcohol use, and cigarette smoking, but it also covers clinical and related factors such as past medical history and current diagnosis, comorbidities, complications, hospitalization history within the last six months, and ADRs history. Along with the Schumock and Thornton scale, Hartwig's Severity Assessment Scale Naranjo Causation Scale, and the intervention tool were used.

Prior to starting work, data collectors were trained on the goals of the study, the data collection checklist, and how to recognize and record adverse drug reactions to ensure data accuracy. Under the supervision of four senior clinical pharmacists (MSc. in clinical pharmacy), four clinical pharmacists with bachelor's degrees in pharmacy were to collect the data. Data was gathered through patient interviews, in-person observations, and a review of their lab, prescription, and medical records. Every day, the completed data collection forms were reviewed and monitored. Doctors and nurses were informed of any changes to medication management.

Outcome measures and ADRs detection

The main finding of this study is the prevalence of ADRs. The secondary outcome focuses on ADRs' severity, preventability, and outcome, as well as their causal link to medications. Medical and pharmaceutical records,

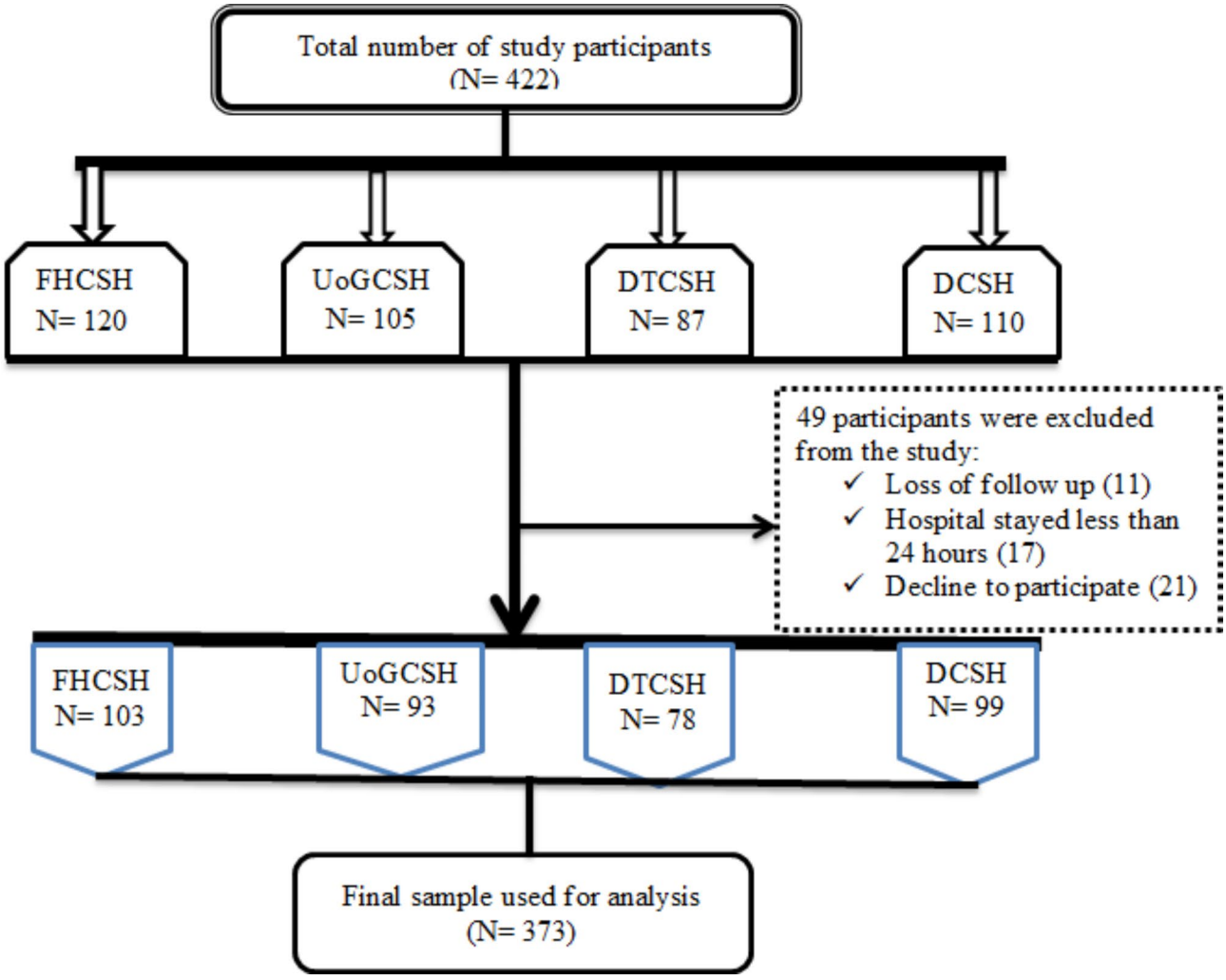

Fig. 1 Flow chart of enrolments and exclusion among geriatric patients from May 2023 to August 2023

laboratory inspections, patient interviews, and direct observation were used to identify ADRs. Standard instruments have been used to evaluate the study's ADRs' severity, causative connection, and preventability.

To assess the causality of ADRs, the modified Naranjo Causation Scale was employed. The alternatives for ten of the questions on this tool are "yes," "no," and "don't know." Four different point values (-1, 0, +1, or +2) are assigned to each response. Response was considered after each participant's points were added up to a total score that might be anywhere between −4 and +13. A score of nine or more was considered "definite," five to eight was considered "possible," one to four was considered "possible," and zero or less was considered "doubtful" [25]. Using Hartwig's Severity Assessment Scale, which comprises seven questions, the severity of the present ADRs was evaluated and categorized as mild (levels 1 and 2), moderate (levels 3 and 4), and severe (levels 5 and above) [26]. The precise criteria developed by Schumock and Tornton were applied to determine the preventability of the ADRs.

Schumock and Tornton's criteria were employed to determine the preventability of the ADRs. The tool comprises three sections: non-preventable (part III), possibly preventable (part II), and preventable (part I). There are five questions categorized as preventable, four as possibly preventable, and one as non-preventable. Each response was divided into yes and no categories. When answering one or more of the par I questions are true, and then adverse medication occurrences were definitely preventable. The assessors will move on to part II if every response is negative. When answering one or more of the part II questions is yes, then the adverse medication event is likely avoidable. Part III moved forward if all of the responses were negative which is not preventable [24]. Reports indicate the organ most commonly affected by adverse drug reactions and the drugs most frequently associated with these reactions. The incidence of adverse drug reation per 100 admissions was calculated by

Table 1 Socio-demographic characteristics of study participants (*N* = 373)

Variables	Categories	*N* (%)	Mean ± SD
Age	65–74	284 (76.14)	69.83 ± 6.76
	≥ 75	89 (23.86)	
Sex	Male	167 (44.77)	
	Female	206 (55.23)	
Marital status	Single	47 (12.60)	
	Married	201 (53.89)	
	Divorced	56 (15.01)	
	Widowed	69 (18.50)	
Religion	Orthodox	299 (80.16)	
	Muslim	62 (16.62)	
	Protestant	9 (2.41)	
	Others	3 (0.81)	
Occupational	Farmer	249(66.76)	
	Merchant	70 (18.77)	
	Government employee	12 (3.22)	
	Retire	42 (11.26)	
Residence	Rural	254 (68.10)	
	Urban	119 (31.90)	
Source of Drug	Free	198 (53.08)	
	Payment	175 (46.92)	
Alcohol use	Yes	169(45.31)	
	No	204(54.69)	
Smoking	Smoker	19 (5.09)	
	Nonsmoker	354(94.91)	
Physical exercise	Yes	206 (55.23)	
	No	167 (44.77)	

dividing the total number of ADRs identified by the total number of admissions and then multiplying by 100.

Pharmacists play a part in the management of patients in geriatrics to maximize pharmacotherapy. They are responsible for making sure that the medications they give patients are appropriate and safe for usage. After examining various literatures [30–32], we created an intervention tool and tailored it to our research objectives and study subjects.

Data processing and analysis procedures

Every day, the data's completeness was verified. All patient data that had been gathered was entered into Epi Data version 7.1 and exported to STATA version 14.1 for cleaning and analysis respectively. Categorical data were represented by frequency and percentages, while continuous variables were represented by the mean (standard deviation) or median (interquartile range, IQR), depending on the kind of distribution. After an evaluation of the Hosmer-Leme show goodness-of-fit test, a logistic regression model was used. Using bivariate logistic regression analysis, potential variables for multivariate logistic regression analysis were identified. Thus, covariates having a p-value < 0.25 were added to a multivariate logistic regression in order to identify statistically significant predictors of ADR frequency. A P-value of less than 0.050 was then used to assess statistical significance.

Table 2 Clinical characteristics of study participants (*N* = 373)

Variables	Categories	*N* (%)	Mean(St. deviation)
GFR (ml/min/1.73 m2)	≥ 60	197 (52.82)	Median (IQR) 61.47 (47.29–78.59)
	30–59	145 (38.87)	
	< 30	197 (52.82)	
BMI (K.g/m2)	< 18.5	20 (5.36)	22.48 ± 2.98
	18.5–14.9	282 (75.60)	
	≥ 25	71 (19.03)	
Liver function	Normal	281 (75.34)	
	Abnormal	92 (24.66)	
Length of Hospitalization	< 6	111 (29.76)	8.09 ± 4.17
	6–10	185 (49.60)	
	> 10	77 (20.64)	
History of hospitalization in the last 6 months	Yes	226 (60.59)	
	No	147 (39.41)	
CCI score			2.71 ± 1.14
Complications	Yes	157 (42.09)	
	No	216 (57.91)	
Traditional medicine use history	Yes	8 (2.14)	
	No	365 (97.86)	
Had a history of adverse drug reaction	Yes	20 (5.36)	
	No	353 (94.64)	
Preexisting Comorbidity	Yes	206 (55.23)	
	No	167 (44.77)	
Number of medications	< 5	131 (35.12)	5.69 ± 2.46
	5–9	206 (55.23)	
	≥ 10	36 (9.65)	

NB: BMI: Body Mass Index, CCI: Charlson Comorbidity Index, GFR: Glomerular Filtration Rate, IQR: Interquartile Range, SD: Standard Deviation

Results

Socio-demographic characteristics of study participants

A total of 373 people were involved in the study during the study period. The patients' mean (±SD) age was 69.83±6.76 years, and the majority of them were female (55.23%). 80% of the participants were orthodox, and around half of the patients (53.89%) were married. Furthermore, over 50% of the patients received free medication and engaged in physical exercise (Table 1).

Clinical characteristics of study participants

In the six months before the study period, 60% of the participants had previously been admitted to the hospital. Three-quarters of the study participants had normal BMIs (75.6%) and liver function (75.34%). More than half of the patients did not have any complications. The patient's mean (SD) duration of hospital stay was 8.09±4.17 days, and their median (IQR) GFR was 61.47 (47.29–78.59) ml/min/1.73 m2 (Table 2).

Medical characteristics of the study participants

The study found that the most common diagnosis for the patients was pneumonia (46.92%), which was followed by heart failure (24.42%), stroke (24.93%), and hypertension (20.64%) (Table 3).

Medication pattern of the study participants

A total of 2125 medications were prescribed to the study participants. Most patients received antibiotics (66.22%), diuretics (42.63%), anticoagulants (34.32%), and analgesics (29.56%) (Table 4).

Incidence and causality of ADRs

Throughout the study period, 116 patients had 121 ADRs found in them. The overall incidence of ADR was determined to be 31.10% (95% CI: 26. 38–35.82) per 100 admissions. By using the Naranjo causality assessment tool for ADRs, 13.11% of ADRs were definite, 54.45% of ADRs were probable, 45.37% of ADRs were possible, and 7% were doubtful ADRs (Fig. 2).

Severity and preventability of ADRs

According to the adjusted Hartwig ADRs severity evaluation scale, 35.53% of ADRs were classified as mild, 56.2% as moderate, and 8.27% as severe (Table 5). The modified Shumock and Thornton method was employed to assess the preventability of reported adverse drug reactions. The application of this scale revealed that 33.89% of adverse drug reactions (ADRs) were definitively prevented, 28.10% were probably prevented, and 38.01% were not prevented (Fig. 3).

ADRs are categorized based on organ system

Adverse reactions related to drugs were classified based on the affected organ system. The organ systems most frequently impacted included the digestive system (28.92%), cardiovascular system (19.01%), endocrine and metabolic system (16.53%), and hematological system (12.41%). The most frequently reported adverse drug reactions were stomach ulcers (9.09%), hypotension (8.26%), and edema (7.44%) (Table 6).

Potential insulting classes of medications associated with ADRs

Antibiotics represented the highest proportion of medications associated with adverse drug reactions, accounting for 21.49%. This was followed by anticoagulants at 12.40%, angiotensin-converting enzyme inhibitors (ACIs) at 9.92%, calcium channel blockers (CCBs) at 8.26%, and diuretics also at 8.26% (Fig. 4).

Adverse drug reaction interventions and its outcome

Our research indicates that interventions were implemented to address the high prevalence of adverse drug experiences. The interventions administered included regimen modification (42.15%), unchanged offending drugs (6.61%), and an average duration of 4.77 (±5.11) days to reverse adverse drug reactions. Furthermore, 80% of the adverse drug reactions had resolved (Table 7).

Table 3 Medical characteristics of study participants (*N* = 373)

Variables	Frequency	Percentage
Pneumonia	175	46.92
Heart Failure	106	28.42
Stroke	93	24.93
Hypertension	77	20.64
Peptic ulcer disease	73	19.57
Ischemic heart disease	55	14.75
Valvular heart disease	42	11.26
Tuberculosis/Fibrosis	39	10.46
Diabetic mellitus	36	9.65
Asthma /Chronic obstructive pulmonary disease	31	8.31
Anemia	29	7.77
Cor pulmonale	28	7.51
Acute kidney injury /Chronic kidney disease	28	7.51
Chronic liver disease	20	5.36
Deep vein thrombosis	17	4.56
Malaria	5	1.34
Epilepsy	5	1.34
Others	25	6.70

Others* Meningitis (4), Thyroid disorder (4), Pulmonary embolism (4), Arrhythmia (3), Arthritis (3), Shocke (3), Benign Prostate Hyperplasia (2), Interstitial Lung Disease (2)

Table 4 Medication characteristics of study participants (*N* = 373)

Class of Medication	Frequency	Percentage
Antibiotics	247	66.22
Diuretics	159	42.63
Anticoagulants	128	34.32
Analgesics	111	29.76
Ant-dyslipidemia /Statins	102	27.35
PPI	96	25.74
Antiplatelet	90	24.13
CCBs	77	20.64
Steroids	75	20.11
H2Blocker	58	15.55
ACEIs	50	13.40
Beta-blockers	46	12.33
Insulin	40	10.72
Digoxin	27	7.24
Antiemetic	22	5.90
Iron/Vitamins	20	5.36
Bronchodilators	20	5.36
Anti TB medications	12	3.22
Others	33	8.85

Others* Antimalarial (6), Anticonvulsant (5), Antithyroid (5), Vasodilator (4), Antidepressant (3), Anthelmintic (3), Antiviral (3), Antifungal (2), Phosphodiesterase (2)

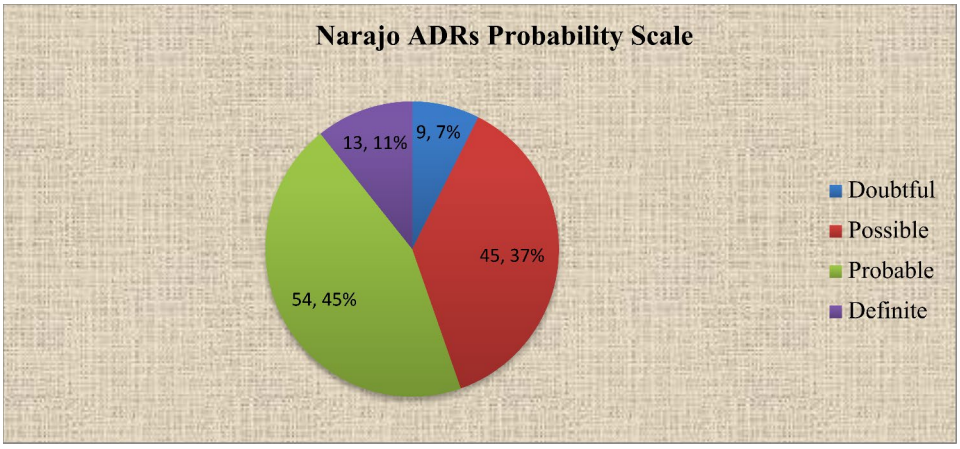

Fig. 2 Narajo ADRs probability scale of study participants ($n=121$)

Table 5 Severity of ADRs based on the modified Hartwig ADRs Severity Assessment Scale of study participants (121)

Level	Description	*N* (%)
1	An ADR occurred but required no change in treatment with the suspected drug	27 (22.31)
2	The ADR required that treatment with the suspected drug be held, discontinued, or otherwise changed. No antidote or other treatment requirement was required. No increase in hospital stays.	16 (13.22)
3	The ADR required that treatment with the suspected drug be held, discontinued, or otherwise changed AND/OR an antidote or another treatment was required. No increase in hospital stays.	54(44.63)
4	Any Level 3 ADR which increases the length of stay by at least 1 day	14(11.57)
5	Any level 4 ADR which requires intensive medical care.	7(5.79)
6	The ADR caused permanent harm to the patient	3(2.48)
7	The ADR which led to the death of the patient	0
	Total	100

Note: level 1 & 2 are mild, level 3 &4 are moderate, and level 5 and above are severe

Factors that associated to the occurrences of ADRs

Univariate and multivariate logistic regression analyses were conducted to identify the factors contributing to the occurrences of ADRs. Following a univariate analysis, multivariate logistic regression was performed on variables with p-values below 0.25. The multivariate analysis identified significant associations between adverse drug reactions (ADRs) and several independent factors: prior hospital admissions within the last six months, hyperpolypharmacy, and overweight status.

When controlling for other variables, individuals experiencing hyperpolypharmacy (defined as taking more than ten medications) exhibited a greater likelihood of ADRs compared to those on fewer than five prescriptions (<5 drugs) [AOR=2.812, 95% CI: 1.029–8.515; $p=0.047$]. Overweight patients exhibited a 3.76-fold increased likelihood of experiencing ADRs in comparison to normal-weight patients (AOR=3.761; 95% CI, 1.722–8.211; $P<0.001$). Patients with prior admissions within the last six months exhibited a 5.585 times higher likelihood of experiencing ADRs compared to those without previous admissions (AOR=5.585; CI: 2.713–11.499; $P=0.000$) (Table 8).

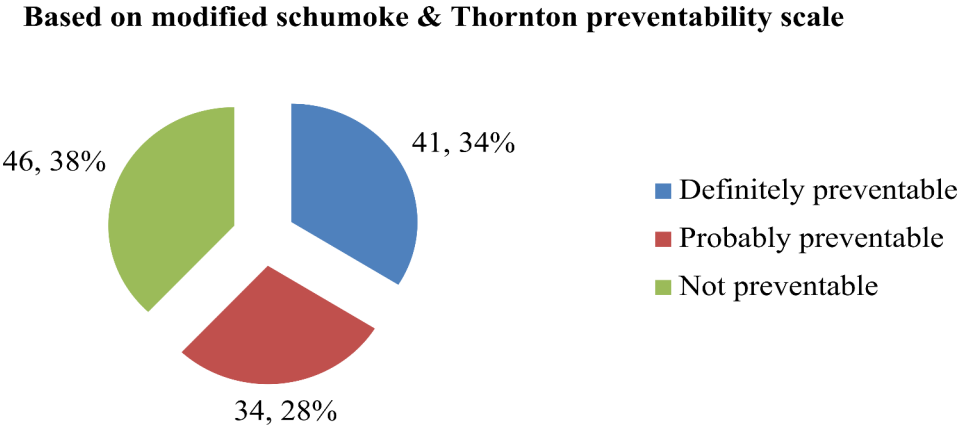

Fig. 3 Preventability of adverse drug reactions based on modified Schumock and Thornton preventability criteria among geriatrics patients (121)

Table 6 Patterns of adverse drug reactions of study participants

System	*N* (%)	ADRs	*N* (%)	Drug involved	Naranjo ADE Probability Scale
Gastrointestinal	35(28.92)	Gastrointestinal ulcer	11(9.09)	Aspirin (5)	Probable
				Clopidogrel (2), Warfarin(4)	Possible
		Diarrhea	8(6.61)	Clarithromycin(5)	Probable
				Rifampicin (3)	Possible
		Hepatotoxicity	7(5.78)	Pyrazinamide (2)	Definite
				Propylthiouracil (1), Atorvastatin (4)	Possible
		Constipation	6(4.96))	Morphine (5)	Probable
				Verapamil (1)	Definite
		Vomiting	3(2.48)	Ceftriaxone (1), Cimetidine(2)	Probable
Cardiovascular	23(19.01)	Hypotension	10(8.26)	Enalapril (5), Metoprolol succinate (3)	Probable
				Mannitol (2)	Possible
		Edema	9(7.44)	Amlodipine (6), Nifedipine(3)	Possible
		Tachycardia	3(2.48)	Salbutamol (3)	Doubtful
		Bradycardia	1(0.83)	Metoprolol (1)	Possible
Endocrine and metabolic	20(16.53)	Hypoglycemia	8(6.61)	Insulin (6)	Definite
				Ceftriaxone + Vancomycin (2)	Doubtful
		Hyperkalemia	6(4.96)	Spironolactone(2)	Probable
				Enalapril (4)	Probable
		Hyponatremia	4(3.31)	Furosemide (3)	Possible
				RHZE (1)	Doubtful
		Hypocalcaemia	2(1.65)	Furosemide (2)	Possible
Hematologic	15(12.41)	Anemia	7(5.79)	Sulfamethoxazole + Trimethoprim (4)	Probable
				Levodopa (1), Levofloxacin (2)	Possible
		Thrombocytopenia	4(3.31)	Heparin (4)	Definite
		Bleeding	4(3.31)	Warfarin (1), Warfarin + UFH (3)	Probable
Neuromuscular and skeletal dermatologic	12(9.91)	Skin rash	7(5.78)	Sulfamethoxazole + Trimethoprim (3)	Possible
				Phenytoin (2)	Doubtful
				Nevirapine (1), Digoxin(1)	Probable
		Hypersensitivity	3(2.48)	Amoxicillin /clavulanate(3)	Probable
		Myalgia	2(1.65)	Atorvastatin (2)	Possible
Others	16(13.22)	AKI	10(8.26)	Vancomycin(5), Tenofovir(1), Enoxaparin(3)	Probable
				Gentamicin (1)	Possible
		Dizziness	3(2.48)	Furosemide (1)	Doubtful
				Quinine (2)	Possible
		Dry cough	3(2.48)	Enalapril (3)	Possible

Note: AKI: Acute Kidney Injury, UFH: Unfractionated Heparin, RHZE: Rifampin; Isoniazid; Pyrazinamide; Ethambutol

Discussion

Growing geriatrics is linked to taking more medications, and taking more prescriptions raises the possibility of ADRs, drug interactions, and poor adherence, all of which can have an impact on patient treatment outcomes [33]. In this study, a total of 121 adverse drug events were reported in 116 patients, with an incidence rate of 31.10% (95% CI: 26.38 −35.82) per 100 hospitalizations. This implies that geriatric patients who are hospitalized are genuinely overburdened with ADRs. The incidence noted in this study corresponds with findings reported in various international contexts. In multicenter research conducted in the United States, the incidence of ADRs among hospitalized older patients was approximately 30% [34]. A supplementary study indicated an incidence of 29.6% for ADRs, reinforcing the notion that geriatric patients exhibit increased susceptibility to such events [19]. In variations on other studies, this one reports on it that is higher than most other studies' findings [17, 29, 35, 36]. However, this is less than research that found 47.2 ADRs per 100 hospital admissions in the Netherlands [37], Brazil 46.2% [38], and Europe 48.5% [39]. Potential factors contributing to this disparity encompass differences in patient demographics, medication management practices, and healthcare procedures. The rising prevalence of polypharmacy and inadequate monitoring

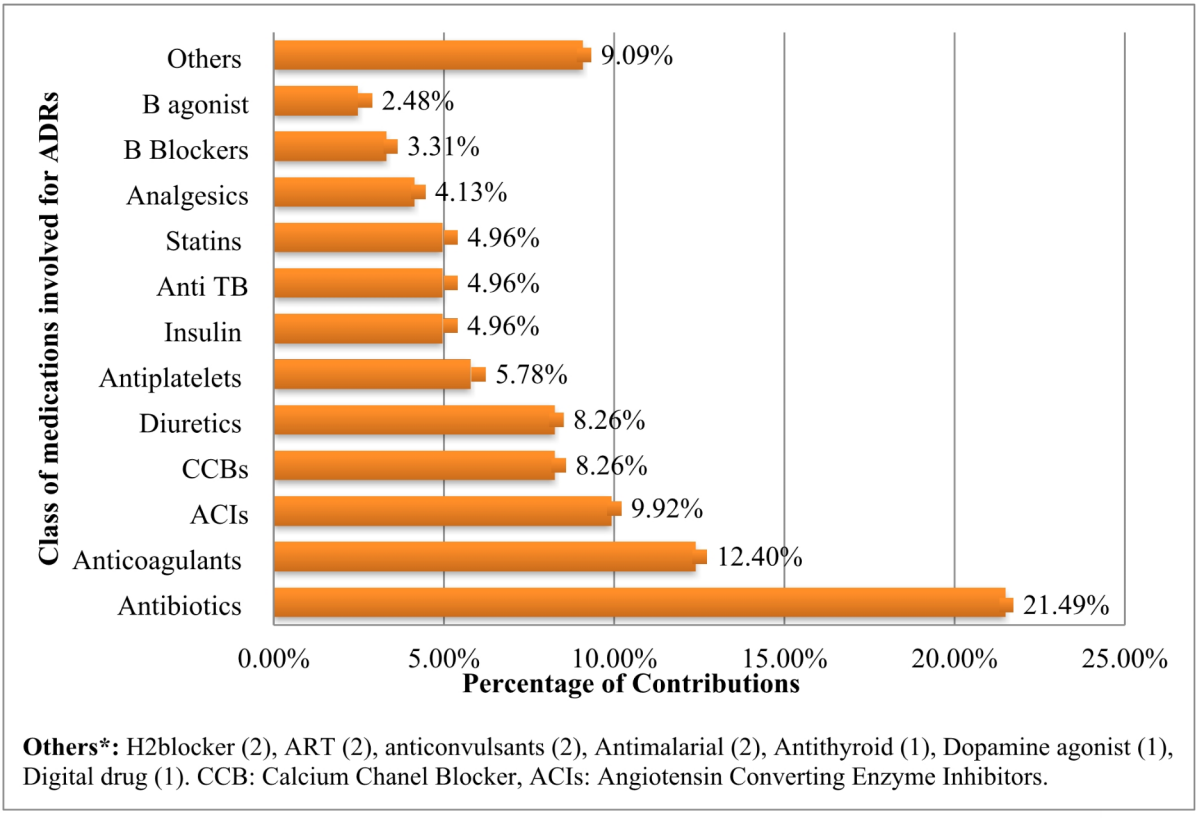

Fig. 4 Pattern of drug classes that were involved in ADRs among study participants ($n=121$)

Table 7 Interventions on adverse drug reactions in geriatrics patients (121)

Variables	Means of intervention	Frequency	Percentage
Interventions provided	Regimen modification	51	42.15
	Discontinued	17	14.05
	New medication given	15	12.40
	Switch to alternative drugs	11	9.09
	Need for monitoring	10	8.26
	Hold	9	7.44
	None	8	6.61
Outcomes (ADRs reversed/cured)	Yes	103	85.12
	No	18	14.88
Time taken to reverse/cure ADRs (days)	Mean(± SD) 4.77 (± 5.11) days		

of prescription regimens, both significant factors in the occurrence of ADRs, may explain the elevated rates observed in various studies.

The Naranjo algorithm was employed to assess the causal relationship between the medication and the incidence of adverse drug reactions. Of the total adverse ADRs, 13.11% were classified as definite, 54.45% as probable, 45.37% as possible, and 7% as doubtful. Our findings align closely with another study employing the Naranjo technique, which identified that 15% of adverse drug reactions (ADRs) were classified as definite, while approximately 50% were deemed probable [40], and in Japanese 9.1% were definite [41]. As opposed to research done in Jimma, which found that 26.72% of ADRs were definite, 60.34% were probable, and 12.93% were possible [29]. More than three-fourths of ADRs were probable in a Spanish study that found definite (23.69%) or probable (76.31%) [42] and in Korea (15.3%) cases of definite and (84.7%) of probable [43]. The definition of adverse drug reactions, the detection strategy, the study's temporal steering, healthcare practices, regional variations, and

Table 8 Factors associated with ADR occurrence of study participants ($n = 373$)

Variables	Categories	ADR					*P*-Value
		Yes (116)	No (257)	COR (95% CI)	*P*-Value	AOR (95% CI)	
Sex	Male	42	125	1		1	
	Female	74	132	1.668(1.063–2.619)	0.026	1.538(0.901–2.626)	0.115
Age	65–74	79	205	1		1	
	≥ 75	37	52	1.846(1.125–3.029)	0.015	1.665(0.921–3.011)	0.092
Length of Hospitalization	< 6	27	84	1		1	
	6–10	60	125	1.493(0.877–2.542)	0.139	0.779(0.409–1.482)	0.446
	> 10	29	48	1.879 (0.998–3.539)	0.051	0.748(0.335–1.668)	0.478
Number of medications	< 5	21	110	1		1	
	5–9	76	130	3.062(1.774–5.285)	0.000	1.686(0.809–3.516)	0.160
	≥ 10	19	17	5.854(2.621–13.077)	0.000	2.812(1.029–8.515)	**0.047***
CCI				1.455(1.195–1.770)	0.000	1.141(0.701–1.856)	0.597
Source of drug	Free	47	151	1		1	
	Payment	69	106	2.091(1.339–3.267)	0.001	(0.487–1.445)	0.527
Liver Function	Normal	82	199	1		1	
	Abnormal	34	58	1.423 (0.867–2.335)	0.163	1.048(0.574–1.914)	0.878
Cigarette smoking	Yes	9	10	2.077(0.821–5.258)	0.123	1.112(0.353–3.505)	0.856
	No	107	247	1		1	
Place of Resident	Urban	44	75	1		1	
	Rural	72	182	0. 0.674(0.425–1.069)	0.094	1.391(0.691 - 2.804)	0.355
BMI	< 18.5	1	19	0.140 (0.0184–1.065)	0.058	0.088(0.011–0.735)	0.025
	18.5–24.9	77	205	1		1	
	≥ 25	38	33	3.066(1.796–5.234)	0.000	3.761(1.722–8.211)	**0.001***
GFR(ml/min/1.73 m2)	≥ 60	52	145	1		1	
	30–59	46	99	1.296 (0.808–2.077)	0.282	0.861(0.488–1.520)	0.607
	< 30	18	13	3.861 (1.769–8.427)	0.001	2.642 (0.958–7.287)	0.060
Previous Admission in the last 6 months	Yes	100	126	6.498 (3.632–11.625)	0.000	5.585(2.713–11.499)	**0.000***
	No	16	131	1		1	
Pre-existence comorbidity	Yes	71	135	1.426 (0.912–2.228)	0.119	0.887(0.485–1.624)	0.698
	No	45	122	1			
Complication	Yes	37	120	0.535(0.337–0.848)	0.008	1.113 (0.603–2.055)	0.733
	No	79	137	1		1	

Note: BMI: Body Mass Index, CCI: Charlson Comorbidity Index, GFR: Glomerular Filtration Rate, COR: crude odd ratio; CI: confidence interval; AOR: adjusted odd ratio.
* p-value

the age ranges of geriatric patients are all responsible for the variation in ADE incidence among previous research.

The current study assessed the severity of ADRs using a modified Hartwig Severity Assessment Scale. 35.53% of ADRs were mild, 56.2% were moderate, and 8.27% were severe, according to our data. According to a study done in Sodo, Ethiopia, 1.6% of ADRs were severe, 43.7% were moderate, and 54.7% were mild [44], in Australia 6% were severe [45] and moderate 63.26%, severe 8.16%, and mild 28.57% were observed in India [46]. However, this finding differs from a London study that indicated that 4% were categorized as life-threatening, 57% as serious, and 28% as substantial [17], and in India, 20.23% were severe ADRs [47].

Based on modified versions of the Schumock and Thornton preventable tool, our results indicated that 33.89% of ADRs were definitely prevented, 28.10% of ADRs were probably prevented, and 38.01% were not prevented. It aligns with studies carried out by a Canadian systematic review of 38% [48] and in the Netherlands found that 70.3% were assessed as preventable [37]. The disparate findings from the Jimma study indicate that it was not preventable (10.9%), definitely preventable (19.0%), and probably preventable (73.1%) [49], in Uganda found 54% preventable events (definite 2% and probable 52%) [50]. Instead of employing preventive likelihood scales to classify ADRs as preventable, the authors may have made prescription errors, which could account for the discrepancy.

The organ primarily responsible for the generation of ADRs was reviewed. In order to determine which organ was most impacted by ADRs, the study included thorough patient observation, medication orders, and laboratory results. In line with previous studies [29, 35,

51], ADRs most commonly impacted the gastrointestinal (28.92%), cardiovascular (19.01%), endocrine and metabolic (16.53%), and hematologic (12.41%) systems. Conversely, an investigation conducted in the United Kingdom indicates that the cardiovascular system is the main organ impacted by adverse drug experiences [17]. These differences could be due to differences in patient profiles, prescription practices, or the kind of drugs that are often utilized in each region. Therefore, when these individuals are given potentially harmful medications, healthcare professionals should monitor them closely.

In actuality, the pharmacological classes' most common offending agents responsible for the prevalence of ADRs in our analysis were antibiotics (21.49%); followed by anticoagulants (12.40%), ACIs (9.92%), CCBs (8.26%), and diuretics (8.26%). Which is consistent with the majority of earlier research [29, 35, 47, 52, 53]. This is due to the likelihood of utilizing antibiotics while a patient is in the hospital is rising. Another study showed that cardiovascular medications were the primary class of prescription implicated for ADRs [45, 54]. Since the results of several studies indicate that offenders are similar, appropriate monitoring of patients on those classes of drugs is necessary.

According to multivariate analysis, patients who had been admitted within the preceding six months, being overweight, and hyperpolypharmacy were the factors associated with the occurrence of ADRs in this study. Numerous research have shown an association between the risk factor and the length of hospital stays [29, 44, 55, 56]; However, because of the factor's confounding effect and correlation with other factors, this link is eliminated in our findings in a multivariate analysis.

Being overweight raised the likelihood of acquiring ADRs by 3.76 times. ADR risk may be raised by obesity, a condition marked by an inappropriate or excessive accumulation of fat in adipose tissue [28, 57]. Obesity increases the risk of adverse ADRs due to variability in medication distribution.

Consistent with our findings, earlier research has demonstrated that individuals with a ploy pharmacy were more likely than those with nonpolypharmacy to experience adverse drug reactions [44, 55, 58–60]. This is an important result since, unlike some other risk factors, the usage of many drugs may be modifiable. ADRs have also been linked to patients who were admitted during the previous six months, according to research. It is consistent with studies conducted for a previous study [49, 61]. This could be explained by immunologic reactions that tend to worsen with repeated exposure because of immunologic memory, as well as cross-reactions to several drugs.

With respect to the ADRs improvement intervention, 85.12% of ADRs were successfully reversed or cured, demonstrating the potential of timely interventions, including modifying dosages and regimens, to reduce ADRs in the elderly population. However, the fact that 14.88% of cases did not address ADRs indicates that managing ADEs in older patients is still challenging, especially when such patients have additional comorbidities. This finding was less than those of earlier studies [27, 62]. Regimen modification was the most often used strategy (42.15%), followed by drug discontinuation (14.05%), monitoring (8.26%), and medication holding (7.44%). This is corroborated by the earlier researchers [63, 64]. According to research, the best options can lower the frequency of ADRs and enhance treatment outcomes for geriatric patients [65]. Holding medicine can help ADRs be resolved without making the issue worse, even if careful observation is still necessary to identify and treat ADRs early. Reversing or curing an ADE took an average of 4.77 days (±5.11). This length of time is consistent with earlier research [34, 66], which indicates that, depending on the severity of the event and the kind of intervention used, the resolution of ADRs in geriatric individuals may take several days to more than a week.

Limitations and strengths

The study's weaknesses include the lack of sufficient scientific evidence, which compromises the results about causation. This is because laboratory tests verify the causality of ADRs using particular drug doses. An overestimation or underestimation of ADRs could therefore affect the causality score and the validity of the study's findings. Further researchers shall address this issue. The study participants also exhibited nonresponse bias. There are various strengths to this study, including being multicenter, identifying ADRs through prospective follow-up of hospitalized geriatric patients by using standard tools, and having interventions provided. Furthermore, this study will establish the standard for forthcoming investigation in this area since it is the first of its type on geriatrics in Ethiopia. It moreover acts as a guide for enhanced medication safety practices, with an emphasis on reducing the occurrence of ADRs in older adults patients, take advantage of polypharmacy, and enhancing patient outcomes in environments with constrained healthcare resources. The feature study will focus on comparative research between various geographic areas or healthcare environments, as well as long-term cohort studies to track the effects of ADRs over time and evaluate their combined effects on patient outcomes such as quality of life, hospital readmission, morbidity, and mortality.

Conclusions

This study found that over one-third of hospitalized geriatric patients experienced adverse drug reactions. Overweight, hyperpolypharmacy, and patients who

had previously been admitted within the preceding six months were significantly associated with the risk of adverse drug reactions. Our investigation confirms earlier results that older people are particularly susceptible to ADRs. To avoid this, it is therefore imperative to determine the underlying causes and take prompt treatment. Adverse drug events can result from medication errors that occur throughout the prescription filling, administration, and monitoring phases of medication use. In particular, those in this age group, pose a significant risk of death, serious damage, or disability if they are not averted. However, four-fifths of the issues were resolved by pharmacist interventions, even in cases where ADR rates were high. Pharmacies should strictly adhere to patient safety by offering the necessary interventions at any step of the medication process.

Abbreviations

ADRs	Adverse Drug Reactions
AOR	Adjusted odds ratio
BMI	Body Mass Index
CCI	Charlson's comorbidity index
CI	Confidence Interval
COR	Crude odds ratio
DCSH	Dessie Comprhensive Specialized Hospital
DTCSH	Debre Tabor Comprhensive Specialized Hospital
FHCSH	Felege Hiwot Comprhensive Specialized Hospital
GFR	Glomerular Filtration Rate
SD	Standard deviation
UGCSH	University of Gondar Comprhensive Specialized Hospital

Supplementary Information

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Supplementary Material 1

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SB, TA, SA, TS; acquisition of data and analysisTA, TM, FN, SA, TS; interpretation of data: all authors; drafting the article: SB, TM, FN; revising the article: and final approval of the article: all authors.

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Data availability

Upon reasonable request, any data related to this study can be obtained from the corresponding author.

Declarations

Ethics approval and consent to participate

The ethical review committee of Debre Tabor University's College of Health Science, Department of Pharmacy has approved ethical authorization with reference number 058/2023. A support letter was sent to each of the four comprehensive hospitals. The directors of those healthcare organizations were then asked to sign a letter approving the usage of patient records as a source of data. Participants were informed about the purpose and design of the study before data collection. Furthermore, they provided their official consent to participate in the research. Written informed consent was obtained from all the study participants. Patients' medical registration numbers (MRNs) were swapped out for new codes during the data collecting and entry process. Besides, to protect its confidentiality, the gathered data was similarly kept in a locked cabinet and on a computer with a strong password. The study followed Helsinki legislation in terms of doing it in a properly anonymous and confidential manner.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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