

EVALUATION OF A DRUG UTILIZATION PATTERN AND USE OF POTENTIALLY INAPPROPRIATE MEDICATIONS AMONG GERIATRIC PATIENTS ADMITTED TO A MEDICAL INTENSIVE CARE UNIT OF A TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT

Objectives: The aim of the study was to evaluate a drug utilization pattern and use of potentially inappropriate medications (PIMs) among geriatric patients admitted to a medical intensive care unit (MICU) of a tertiary care teaching hospital.

Methods: A prospective and observational study was conducted among geriatric patients admitted to a MICU of a tertiary care teaching hospital. The data relevant to study variables were collected in a pre-designed case record form. Evaluation of a drug utilization pattern was carried out using WHO core drug prescribing indicators, and the use of PIMs among patients was evaluated using the Beers criteria 2019.

Results: The average duration of stay in MICU per patient was 6.98 ± 1.82 days. Hypertension and diabetes mellitus were the two most common comorbidities found in the geriatric patients. Average 10.29 ± 3.46 drugs were prescribed per patient. Average 0.77 ± 0.08 antibiotics were prescribed per patient. Nearly half of the drugs were prescribed in the form of parenteral formulations. About 14.6% of the prescribed drugs were found to be potentially inappropriate according to Beer's criteria 2019.

Conclusion: The majority of the drug classes were prescribed to geriatric patients for the appropriate indications. Prescribing PIMs to geriatric patients was common. The Beers criteria have not yet found their way into mainstream clinical practice.

Keywords: Beers criteria, Drug utilization pattern, Geriatric patients, Medical ICU, Potentially Inappropriate medications.

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INTRODUCTION

Geriatric medicine is a subspecialty of gerontology concerned with people over the age of 65 [1]. Elderly individuals face unique health challenges. Pharmacological changes observed in elderly individuals include alterations in the first-pass metabolism, bioavailability, metabolism, and excretion of the drugs [2]. The elderly have the highest drug intake, and the majority of them take at least three prescribed drugs at the same time [3]. Although the elderly account for the majority of total drug usage, only 5% of randomized and control trials have been planned specifically for them [4]. As a result, evidence from younger subjects is used to direct prescriptions for the elderly.

Comorbidities necessitate the use of multiple drugs in elderly individuals, which increases irrational prescribing, inappropriate drug usage, non-compliance, economic burden, adverse drug reactions (ADRs), and drug-drug interactions (DDIs) [5]. According to a study done on hospitalization due to ADRs, the elderly are several times more likely to be hospitalized than others, and approximately half of these ADRs are avoidable ones [6]. They are also more prone to medication errors as a result of pathophysiological changes associated with aging. Thus, it is important to evaluate the pattern of drug utilization in the elderly population regularly to better understand these processes and make drug usage more rational, effective, and safe. It is also necessary to improve prescribing patterns for geriatric patients by developing prescription recommendations.

The World Health Organization (WHO) defined drug utilization in 1977 as the study of drug marketing, drug distribution, prescriptions, and usage in society, with a particular focus on the related medical, social, and economic consequences. Drug utilization research can provide insight into various elements of drug use and prescribing, including pattern, quality, determinants, and outcomes. Because patients are extremely

ill and typically suffer from chronic critical illnesses, the medical intensive care unit (MICU) is an important platform for conducting drug utilization studies. To evaluate drug utilization patterns, there are various prescribing indicators created by International Network for the Rational Use of Drugs and WHO [7].

The term potentially inappropriate medications (PIMs) refer to therapeutic medications whose risks may outweigh its benefits, particularly when more effective pharmacological alternatives are available. Approximately one-third of the elderly population was prescribed at least one PIM, according to a prospective study conducted in India [8]. Such practices can increase the risk of developing ADRs by many times. Thus, to ensure patient safety, improve quality of life, and reduce drug-related mortalities and morbidities, medications included in PIMs must be contraindicated for the elderly. The Beers criteria developed by the American Geriatrics Society (AGS) can be used as an assessment tool for the use of PIM in the elderly [9]. The Beers criteria list drugs that should be avoided in the elderly, irrespective of the patient's diagnosis. This study aimed to evaluate drug utilization patterns using WHO core prescribing indicators and use of PIM using the Beers criteria 2019, in geriatric patients admitted to a MICU of a tertiary care teaching hospital.

METHODS

This was a prospective and observational study, conducted at the MICU of a tertiary care teaching hospital in Gujarat, India, from November 2021 to March 2022. Patients of either gender, aged 65 years and above, and admitted to MICU of study site during the study period were included in the study, while patients admitted in wards were excluded. The study was started only after the Institutional Review Board approved the study protocol (AMCMET Institutional Review Board).

MICU of the study site was visited and eligible participants were approached. The participants were explained the rationale of the study in their local language and only those who were willing to enroll in the study were included in the study. Written informed consent was obtained from the participants before enrolling them in the study.

The case record sheets of the participants were evaluated and all the data relevant to the study variables were collected. The patients' basic demographic details, indication for admission to MICU, system(s) involved, comorbidities, the total number of drugs prescribed, and duration of stay in MICU, were obtained. In detail information of the drugs prescribed, an indication of drugs, dosage schedule of drugs (dose, route, frequency, and dosage form), duration of drug treatment, drugs prescribed by generic names, fixed-dose combinations (FDCs) prescribed, and the occurrence of any ADR were collected and entered into pre-designed case record form. Confidentiality of the collected data of the patients was maintained.

Drug utilization pattern evaluation was carried out using WHO core drug prescribing indicators:

1. An average number of drugs per prescription
2. Percentage of the drugs prescribed by generic names
3. Percentage of the encounters with antibiotics prescribed
4. Percentage of the encounters with an injection prescribed
5. Percentage of the drugs prescribed from an essential drug list [10].

We used national list of essential medicines (NLEM) 2015 of India to evaluate the percentage of the drugs prescribed from an essential drug list. The use of PIMs among geriatric patients was evaluated using the Beers criteria 2019. To evaluate potential DDIs between drugs Medscape Drug Interaction Checker was used.

Statistical Package for the Social Sciences software, version 20.0 (IBM Corporation, Armonk, NY, USA) was used to carry out appropriate statistical analysis. Categorical data were presented using numbers and percentages. Quantitative data were presented with mean±SD. χ^2 test was used to analyze categorical variables between groups. One-way analysis of variance (One-way ANOVA) followed by Tukey's *post hoc* test was used to compare mean±SD between groups.

RESULTS

A total of 134 geriatric patients' prescription data were evaluated during the study period. The study included 74 (55.2%) males and 60 (44.8%) females, giving a 1:0.81 male to female ratio. The mean age of patients was 72.36±5.89 years, and their ages ranged from 65 to 90 years. The majority of patients (n=54, 40.3%) were from the age group of 65–69 years, followed by the age group of 70–74 years (n=35, 26.1%) (Fig. 1). The common indications for admission to MICU in

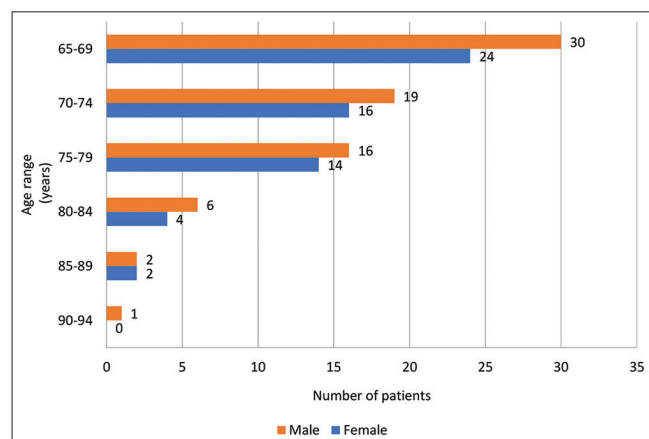


Fig. 1: Age- and gender-wise distribution of the geriatric patients (n=134)

these patients were cardiovascular system (CVS) disorders (32.8%), respiratory system disorders (20.9%), nervous system disorders (15.7%), and gastrointestinal system disorders (12.7%) (Table 1). Acute coronary syndrome and acute pulmonary edema accounted for the majority of admission to the MICU. Comorbidities were found in around 104 patients. Hypertension and diabetes mellitus were the two most common comorbidities found in the patients (Table 2). The average duration of stay in MICU per patient was 6.98±1.82 days (Range: 3–17 days).

A total of 1379 drugs were recorded from the prescriptions of 134 geriatric patients. Average 10.29±3.46 drugs were prescribed per patient (Range: 4–27 drugs). Among the total drugs prescribed, about 58.2% of drugs were prescribed by their generic names, and 41.8% of drugs by their brand names. In 69 patients (51.5%) antibiotic drugs were prescribed. Average 0.77±0.08 antibiotics were prescribed per patient (Table 3). A total of 10 different types of antibiotics were used in the patients. Ceftriaxone, amoxicillin with clavulanic acid, and ciprofloxacin were some commonly prescribed antibiotics. Around 57.9% of the drugs were prescribed in the form of injections. Nearly 61.5% of the drugs were prescribed from the NLEM 2015 of India (Table 3).

Nearly half of the drugs (n=798, 57.9%) were prescribed in the form of parenteral formulations, while oral formulations accounted for 39.2% of the total drugs prescribed. Pantoprazole, ceftriaxone, and enoxaparin were some commonly prescribed drugs parenterally, while enalapril, amlodipine, and metoprolol were some commonly prescribed oral drugs (Table 4). FDCs were prescribed to 37 (27.6%) patients. Aspirin + Clopidogrel, and Amoxicillin + Clavulanic acid were two commonly prescribed FDCs. Only 4.4% of all prescribed drugs were FDCs. Drugs acting on the CVS and blood were the most frequently prescribed drugs and accounted for nearly one-third (34.4%) of the total prescribed drugs. This included anti-hypertensives, anti-coagulants, drugs for dyslipidemia, inotropic agents, and antiplatelet drugs. Drugs acting on the gastrointestinal tract were the second common class of the prescribed drugs and comprised 17.3% of the total prescribed drugs. This included proton-pump inhibitors, antacids, antiemetics, and laxatives. Drugs acting on the renal system constituted about 13.8% of the total prescribed drugs.

About 35.1% and 48.5% of patients were subjected to polypharmacy (5–9 drugs) and extreme polypharmacy (≥10 drugs), respectively.

Table 1: Diagnostic indications for admission to medical intensive care unit (n=134)

Indications	Number of patients (%)
Cardiovascular system disorders	44 (32.8)
Respiratory system disorders	28 (20.9)
Nervous system disorders	21 (15.7)
Gastrointestinal system disorders	17 (12.7)
Renal system disorders	12 (9)
Endocrine system disorders	9 (6.7)
Other systems disorders	3 (2.2)

Table 2: Common comorbid conditions among geriatric patients (n=104)

Comorbid conditions	Number of patients (%)
Hypertension	43 (41.3)
Diabetes mellitus	37 (35.6)
COPD*	20 (19.2)
Dyslipidemia	19 (18.3)
CKD*	18 (17.3)
Bronchial asthma	16 (15.4)
Hypothyroidism	11 (10.6)

*COPD-Chronic obstructive pulmonary disease, CKD-Chronic kidney disease

Table 3: Drug utilization pattern in geriatric patients using WHO core drug prescribing indicators

WHO core drug prescribing indicators	Total number of drugs	Average drugs per prescription/percentage of drugs/percentage of encounters	WHO's Standard derived
Drugs prescribed	1379	10.29	1.6–1.8
Drugs prescribed by generic name	802	58.2	100
Drug encounters with antibiotics	104	51.5	20–26.8
Drug encounters with injections	798	57.9	13.4–24.1
Drugs prescribed from NLEM*	848	61.5	100

*NLEM: National list of essential medicines

Table 4: Commonly prescribed parenteral and oral drugs to geriatric patients

Parenteral drugs (n = 798)		
Drug name	Pharmacological class	Prescriptions n (%)
Pantoprazole	Proton-pump inhibitors	90 (11.3)
Ceftriaxone	Cephalosporin antibiotics	53 (6.6)
Enoxaparin	Anticoagulants	50 (6.3)
Heparin	Anticoagulants	46 (5.8)
Furosemide	Loop diuretics	44 (5.5)
Insulin	Insulin and analogs	37 (4.6)
Ondansetron	Antiemetics	31 (3.9)
Oral drugs (n = 541)		
Drug name	Pharmacological class	Prescriptions n (%)
Enalapril	ACE* inhibitors	51 (9.4)
Amlodipine	Calcium channel blockers	50 (9.3)
Metoprolol	β adrenergic blockers	43 (8)
Atorvastatin	Statins	35 (6.5)
Aspirin + Clopidogrel	NSAIDs + Antiplatelets	28 (5.2)
Spironolactone	Potassium-sparing diuretics	24 (4.4)
Ibuprofen	NSAIDs*	24 (4.4)

*ACE-Angiotensin converting enzyme, NSAIDs: Non-steroidal anti-inflammatory drugs

Polypharmacy and extreme polypharmacy were common among the age group of ≥ 85 years. The average drugs prescribed within the age group of 65–74 years, 75–84 years, and ≥ 85 years were 9.42 ± 4.32 , 10.08 ± 3.78 , and 11.36 ± 2.28 , respectively. One-way ANOVA followed by Tukey's *post hoc* test was used for inter-group comparison. Results were expressed in Mean \pm SD. $p \leq 0.05$ was considered statistically significant. The test revealed that the difference in the mean of the three different groups was statistically significant.

Use of PIMs

Out of 1379 prescribed drugs, about 201 drugs (14.6%) were found to be potentially inappropriate according to Beer's criteria 2019. PIMs were prescribed in around 62 (46.3%) patients. PIMs were most commonly prescribed in patients aged 85–94 years, with an average 4.8 PIMs per prescription. While an average of 4.1 and 2.2 PIMs were prescribed per patient in the age group of 75–84 years and 65–74 years, respectively. Enoxaparin and furosemide were the two most commonly prescribed PIMs (Table 5). About 80%, 70%, and 33.7% of the patients were prescribed PIMs in the age group of 85–94 years, 75–84 years, and 65–74 years, respectively. There was a significant difference in prescribing PIMs to different age groups. The difference was statistically significant (p -value-0.0002) ($p \leq 0.05$ was considered statistically significant).

According to the Medscape drug interaction checker, 77 patients (57.5%) had more than one DDI. Among all potential DDIs, 12 interactions were found to be serious and 202 drugs required close monitoring. The average DDI per prescription was 1.6. The most common potential DDIs were found between the classes of angiotensin-converting enzyme inhibitors and non-steroidal anti-inflammatory drugs (NSAIDs).

DISCUSSION

The mean age of the patients was 72.36 ± 5.89 years in our study, while the mean age of the patients was 70.38 ± 0.58 years in a study done by Balaji *et al.* [11]. Male preponderance (55.2%) in sex distribution of geriatric patients was seen in our study. The average duration of stay in MICU per patient was 6.98 ± 1.82 days in our study, which is comparatively higher than observed in a study done by Jhaveri *et al.* where it was 5.07 days [12].

CVS disorders and RS disorders were the major indications for admission to MICU in our study, while CVS disorders and CNS disorders accounted for the majority of admission in a study done by Kaur *et al.* [13]. The most common comorbid condition among geriatric patients in our study was hypertension, which is understandable because 40.5% of the geriatric population has hypertension in India [14]. It is postulated that various factors such as stress, diet, physical inactivity, and aging-related pathological changes in the CVS may reduce blood vessel compliance in the geriatric population, which increases their blood pressure. It has also been suggested that reduced baroreceptor sensitivity may increase the resistance and thus increase blood pressure [15]. Diabetes mellitus was the second most common comorbid condition among geriatric patients. Our study shows that non-communicable diseases are the primary cause of health hazards in geriatric patients, particularly in developing countries, and this is in line with the current pattern of disease distribution.

Average 10.29 ± 3.46 drugs were prescribed per patient in our study, while the average drugs prescribed in a study done by Balaji *et al.* were 9.37 ± 3.34 [11]. Average number of drugs prescribed increased with increase in age in our study and it was maximum among the age group of ≥ 85 years. This might be because of multiple co-morbidities among these patients. Polypharmacy was evident in our study. Polypharmacy is the primary cause of health-care risk in the geriatric population [16]. It occurs when patients are taking more than 4 drugs [16]. Despite being polypharmacy, this cannot be considered irrational because acute life-threatening conditions necessitate the use of multiple drugs in geriatric patients admitted to a MICU, and empirical therapy is necessary until a definitive diagnosis is made. Furthermore, the multiple comorbidities in geriatric patients necessitate the use of many drugs.

As per the standard laid down by the WHO, the ideal prescribing is 100% usage of generic drugs [15]. In the present study, we found that about 58.2% of all the drugs were prescribed by their generic names. While, only 0.30% of all the drugs were prescribed by their generic names in a study done by Ambwani *et al.* [4]. Reduced use of generic drugs may be due to non-understanding of the WHO's prescribing rules, and lack of confidence in generic drugs' quality.

According to the WHO's ideal standard prescription, the number of antibiotics should be between 20% and 26.8% [17]. In the present study, this number was 51.5%, which is high compared to the standard derived to be ideal. This finding implies the necessity for the regulation of antibiotic prescription. Ceftriaxone was the most frequently prescribed antimicrobial agent. This was in accordance with a study done by John *et al.* which revealed that cephalosporins were the most commonly prescribed antimicrobials in MICU setup [18]. Ceftriaxone is a frequently prescribed antimicrobial agent in MICU due to its high efficacy in a wide

Table 5: Commonly prescribed potentially inappropriate medications to geriatric patients according to the Beers criteria 2019

Name of the drug	n (%)	Rationale	Recommendations
Enoxaparin	50 (24.9)	Increase risk of bleeding	Reduce dose if Cr Cl < 30 ml/min*
Furosemide	44 (21.9)	May cause SIADH or hyponatremia	Use with caution
Aspirin	28 (14)	Increased risk of GI bleed or Peptic ulcer in high-risk groups	Avoid chronic use (avoided with exception), Use with caution in ≥ 70 years
Spirolactone	24 (12)	May cause SIADH or hyponatremia	Avoid if Cr Cl < 30 ml/min*
Ciprofloxacin	19 (9.5)	Increased risk of CNS adverse effects (e.g., confusion and seizures) and tendon rupture	Dose Reduction if Cr Cl < 30 ml/min*

*Cr Cl: Creatinine clearance

range of severe infections, such as multi-resistant typhoid fever, bacterial meningitis, abdominal sepsis, complicated urinary tract infections, and septicemias, and its longer duration of action.

Parenteral preparations were the most frequently prescribed (57.9%) among all formulations, which is similar with a study done by Balaji *et al.*, where about 51.12% of all the drugs were prescribed in the form of parenteral preparations [11]. This finding was higher than the standard for parenteral formulations (13.4–24.1%) as per the WHO [17]. Pantoprazole was found to be the most commonly prescribed parenteral drug. This is consistent with the findings of a study done in Nepal, which also revealed that pantoprazole is most frequently prescribed for patients admitted in MICU compared with other drugs. However, one must consider the cost of proton pump inhibitors therapy, which is costlier than H2-blockers. Enalapril was found to be the most commonly prescribed oral drug. This might be because of the large number of hypertensive cases in our study. Drugs acting on the CVS and blood were the most frequently prescribed drugs in our study, which is similar to the previous studies [13,19]. Anti-hypertensives were the most frequently prescribed drug class to geriatric patients in our study, which is comparable with a study done by Ambwani *et al.* [4].

FDCs accounted for only 4.4% of all the prescribed drugs. In FDCs, the dose of any one particular drug component cannot be independently adjusted if required. In addition, it is difficult to identify one particular drug component that is causing beneficial or harmful effects. As a result, their risk/benefit ratio should be evaluated before prescription [20]. In India, the number of FDCs available in the market is around 60% of all available formulations, while the usage of FDCs was relatively low in our study, showing the rational use of medicines.

Moreover, we found that about 61.5% of the total prescribed drugs were from the NLEM in our study. Essential drug list comprises the most cost-effective drugs for a particular indication. It is developed in compliance with the standard treatment guidelines by keeping in mind the health-care needs of the majority of the population. Selecting drugs from the essential drug list results in better care, rational use of drugs, and more efficient use of health-care resources [21].

As per the AGS updated Beers criteria 2019, 14.6% of the prescribed drugs were found to be potentially inappropriate in geriatric patients in our study. While, about 27.5% and 25% of the prescribed drugs were found to be potentially inappropriate in a study done in USA, and Ireland, respectively [4]. Among the three categories in Beers criteria, Category 1, which includes medications to be avoided in geriatric patients, forms a major category of inappropriate drug usage. In our study, 10 different drugs were prescribed to geriatric patients from the Category 1. Enoxaparin, diuretics like spironolactone, NSAIDs like aspirin, and fluoroquinolone antibiotics like ciprofloxacin were some commonly prescribed PIMs from this category. NSAIDs were common PIMs, followed by antihistaminic in a similar study done by Fadare *et al.* [22] In our study, drugs from Category 2 of Beers criteria, which include medications to be avoided in geriatric patients with other comorbid conditions, were not prescribed. Category 3 includes medications to be used with caution. Furosemide was from this category. Although the incidence of prescribing PIMs was less in our study compared to other similar studies, we still need to make more

of an effort to spread awareness regarding Beers criteria updated list and rational prescription for prescribing to geriatric patients to all the practicing physicians. This will help in reducing the incidence of potential DDIs and ADRs in the geriatric patients.

CONCLUSION

The majority of the drug classes were prescribed to geriatric patients for the appropriate indications. Multiple comorbidities in geriatric patients lead to polypharmacy in our study. Thus, drug utilization pattern was not in accordance with the WHO's ideal standard. Our study clearly shows that prescribing PIMs to geriatric patients is quite common. Despite being often referenced in several studies, the Beers criteria have not yet found their way into mainstream clinical practice. It is very important that prescribers be aware of the Beers criteria and that they rigorously adhere to them while treating geriatric patients.

LIMITATIONS OF THE STUDY

The sample size of our study was not adequate to generalize the findings to the entire elderly population. We included only those geriatric patients in our study who were admitted to the MICU. More such studies in other specialties are required to determine the prevalence of prescribing PIMs to geriatric patients so as to make practitioners aware of this public health issue. Despite having some limitations, we believe our study provides medical professionals with much new information in prescribing practice to facilitate the rational use of medications in elderly populations.

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AUTHORS' CONTRIBUTIONS

All the authors have contributed equally to the data collection, its interpretation, and preparation of the manuscript.

CONFLICTS OF INTEREST

The authors have no conflicts of interest.

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