Drug utilisation among older inpatients in a teaching hospital in Western Nepal

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ABSTRACT

Introduction: The proportion of the elderly population in Nepal, though low, is steadily increasing. Studies on drug utilisation among geriatric patients in Western Nepal, a region with the highest proportion of the elderly in all of Nepal, are lacking. The present study was carried out at the Manipal Teaching Hospital, a 700-bed teaching hospital in Pokhara, Western Nepal.

Methods: The study was carried out from June I, 2005 to May 3I, 2006 using case records of discharged patients aged 60 years and older. This was an observational study that utilised a retrospective case notes review methodology. The microorganisms isolated on culture and their antibiotic sensitivity patterns were studied. Drug consumption was measured by the defined daily dose (DDD) per 100 bed-days. The mean cost of the drugs was calculated. The percentage of drugs prescribed by generic name and the percentages of fixed-dose combinations used were noted. The basic demographic information of older inpatients, drug utilisation patterns, drug consumption using DDD, organisms isolated and their antibiotic sensitivity patterns, and the mean cost of the drugs were studied.

Results: A total of 548 patients were admitted. Hypertension, acute exacerbation of chronic obstructive pulmonary disease and cancer were the most common illnesses among the patients. The mean number of drugs consumed by each patient was 7.73. Escherichia coli and Pseudomonas aeruginosa were the most common microorganisms isolated. Ranitidine, multivitamins, amlodipine, ipratropium and dextrose normal saline were most commonly prescribed. The DDD per 100 bed-days of ranitidine and omeprazole (highest values) was 33.48 and 3.51, respectively. The mean cost of drugs was USD26.6, and antibiotics accounted for around 40 percent of the cost. <u>Conclusion</u>: The use of a high number of drugs, and of parenteral drugs and intravenous fluids, is a common problem. The prescription of generic drugs is low. Guidelines for the use of drugs in the elderly are required and further studies are needed on this issue.

Keywords: drug utilisation, geriatric drugs, prescribing guidelines

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INTRODUCTION

Drug utilisation research has been defined by the World Health Organisation as "the marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences". Pharmacoepidemiology applies epidemiological methods to studies of the clinical use of drugs in populations.⁽¹⁾ Nepal is a small, developing country in South Asia situated between China and India. The 2001 census stated that the population of Nepal was 23 million, and the estimated population at the beginning of 2007 was 27 million. Due to a high fertility rate, the population of Nepal is predominantly young. The proportion of elderly persons aged 65 years and older was stated as 4.2% in the 2001 census. The Western development region in which Pokhara is situated has the highest proportion of the elderly population among the developed regions of Nepal.⁽²⁾

The Manipal Teaching Hospital (MTH) is a tertiary care teaching hospital (700-bed) attached to the Manipal College of Medical Sciences, Pokhara, Nepal. Previous studies among inpatients in the hospital had found a high but varying percentage of patients aged 60 years and older. In one study, the percentage was 51.2%,⁽³⁾ while in another, it was 19%.⁽⁴⁾ Thus, patients aged 60 years and older constitute a significant percentage of inpatients in the hospital. In the elderly, altered pharmacokinetics and pharmacodynamics can alter drug responsiveness. As a result of having multiple diseases, the elderly may be on multiple drugs, leading to potential drug interactions, adverse drug reactions and poor compliance.⁽⁵⁾ Previous studies in different countries have also found inappropriate prescriptions among in the elderly.^(6,7)

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Previous studies in Nepal were carried out in the Tribhuvan University Teaching Hospital in the Kathmandu Valley, and these were done using a random sample of inpatients. The first study was carried out in 1994⁽⁸⁾ and the second in 2002–2003.⁽⁹⁾ Polypharmacy was found to be common, and there was a lot of scope for improvements to the practice of prescribing drugs to the elderly. Studies on prescription and drug use among the elderly in hospitals outside the Kathmandu Valley are lacking. The western development, with a relatively high proportion of the elderly and older patients (aged \geq 60 years), is an important region that should be studied. The objectives of this study were: (1) to obtain basic demographic information and the morbidity profile (morbidities and comorbidities) of inpatients aged 60 years and older admitted to the hospital during the study period; (2) to obtain information on the distribution of patients by department, and the mean number of days of hospitalisation and of drugs prescribed; (3) to analyse the utilisation of the medicines prescribed; (4) to obtain information on commonly isolated microorganisms and their antibiotic sensitivity patterns; (5) to measure the consumption of commonly prescribed drugs in defined daily dose (DDD) per 100 bed-days; and (6) to calculate the costs incurred on drugs.

METHODS

The study was carried out at MTH, Pokhara, Nepal from June 1, 2005 to May 31, 2006. The researchers visited the Medical Records department of the hospital daily and analysed the case records of patients aged 60 years and older who had been discharged on that particular day. This was an observational study done using a retrospective case notes review methodology. Elderly inpatients (aged ≥ 60 years) admitted to various departments of the hospital during the study period, such as the general medicine, general surgery, obstetric and gynaecology, orthopaedics, oncology, otorhinolaryngology and opthalmology departments, were included. Patient details were entered into a specially-designed proforma. Age, gender, the department to which the patient was admitted, the date of admission and date of discharge were noted. The address, diagnosis and the drugs prescribed during the patients' hospital stay along with their dose, frequency, duration and route of administration were recorded. Investigations for hepatic and renal functions, if they were carried out, were noted. The organisms were isolated on culture and their sensitivity patterns were recorded.

The number of drugs prescribed to a particular patient during the period of hospitalisation, and the number of intravenous fluids (IVFs), topical preparations, antibiotics and inhaled medicines provided were noted. When the same medicine was prescribed by different routes, it was taken to be a single medicine. In order to calculate the duration of hospitalisation, the date of admission was included, but the date of discharge was excluded. The mean and standard deviations (SD) of the total number of drugs and days of hospitalisation were calculated. The percentage of drugs prescribed by generic name was also calculated. Information on commonly used drugs, antibiotics, non-steroidal anti-inflammatory drugs, intravenous fluids, cardiovascular drugs and diuretics was obtained. The authors collected information on the utilisation of all drugs in older patients during the study period, but only the details of the commonly used drugs are presented here. The cost of the drugs was calculated using the price list supplied by the hospital pharmacy. The mean and SD cost of the drugs and antibiotics were calculated.

The anatomical therapeutic chemical (ATC) classification divides drugs into different groups according to the organ or system on which they act and their chemical, pharmacological and therapeutic properties.^(10,11) The DDD is the assumed average maintenance dose for a drug used for its main indication in adults.⁽¹⁰⁾ The DDD provides a fixed unit of measurement that is independent of price and formulation, and makes it easier to compare drug utilisation across studies. The major benefit of studying drug utilisation using DDD is that the dosage and the duration of use are both factored in to the calculation. The dosage, frequency and duration of use are variable in elderly patients, and these differences can be overcome by using the DDD as a measure of drug consumption. The consumption of drugs was measured in DDD/100 bed-days. This was calculated using the following formula:

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DDD/100 \text{ bed-days} = \frac{\text{Drug consumption in mg} \times 100}{\text{DDD (mg)} \times \text{no. of days in study period} \times \text{total no. of beds} \times \text{occupancy index}}
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The study was carried out for a period of 365 days, and found that the total number of beds used was 300 and the average occupancy index was 0.3. The occupancy index for every month was calculated by the Medical Records department. The occupancy index is the average monthly occupancy index for the twelve months of our study period. The index was calculated every day and was derived by dividing the number of beds occupied by the total number of beds. The daily occupancy index was averaged out to obtain the monthly index.

RESULTS

548 patients aged \geq 60 years were admitted to MTH

Characteristic	No. (%)		
	n = 548		
Gender			
Male	344 (62.8)		
Female	204 (37.2)		
District			
Pokhara city	170 (31)		
Kaski	121 (22.1)		
Syangja	64 (11.7)		
Tanahu	39 (7.1)		
Parbat	35 (6.4)		
Baglung	34 (6.2)		
Others	85 (15.5)		
Department			
Medicine	316 (57.7)		
Surgery	105 (19.2)		
Oncology	40 (7.3)		
Orthopedics	34 (6.2)		
Others	53 (9.7)		

Table I. Characteristics of geriatric patients admittedduring the study period.

Table II. Specimens sent for culture and sensitivitytestings and the common organisms isolated.

during the study period. Table I shows the gender					
distribution, town and district from which the patients					
hailed, and the department that each patient was admitted					
into. There were more male than females patients, and					
a large percentage were from Pokhara city and Kaski					
district. The majority of patients were admitted to					
the medicine and surgery departments. 145 (26.4%)					
patients were aged 60–65 years, 135 (24.6%) were aged					
65-70 years, and 116 (21.2%) were aged 70-75 years.					
79 (14.1%) patients were aged 75-80 years, while 75					
were aged 79 years and older. The five most common					
diagnoses were hypertension (n = 150, 27.4%), acute					
exacerbation of chronic obstructive pulmonary disease					
(COPD) (n = 112, 20.4%), cancer (n = 97, 17.7%),					
cerebrovascular accidents (n = 54, 9.8%) and type 2					
diabetes mellitus ($n = 44, 8.0\%$).					

A total of 4,236 drugs were prescribed to elderly inpatients during the study period. 1,561 (36.8%) drugs were prescribed by generic name. 751 (17.7%) drugs were administered in fixed-dose combinations (FDCs). 1,582 of the 4,236 (37.3%) drugs were prescribed parenterally. 5–10 drugs were prescribed to 266 (48.5%) patients, 10–15 drugs to 129 (23.5%) patients and 1–5 drugs to 119 (21.7%) patients. The mean number of drugs administered was 7.73 \pm 4.24, while the mean number of days of hospitalisation was 7.04 \pm 5.39 days.

Serum creatinine estimation was carried out in 254 (46.3%) patients, while liver function tests were performed in 51 (9.3%) patients. These were linked to the use of hepatotoxic or nephrotoxic medicines in most cases. In addition, a large proportion of the older patients were likely to have impaired hepatic or renal

Characteristic	No. (%)		
Specimens	60		
Organisms isolated in:	50		
Sputum	26 (43.3) ³		
Normal flora	12		
P. aeruginosa	I (2)†		
H. parainfluenzae	4 (8)		
K. pneumoniae	2 (4)		
Enterobacter spp.	I (2)		
E. coli	I (2)		
Others	5 (10)		
Urine	18 (30)*		
E. coli	5 (10)†		
Insignificant bacteriuria	5 (10)		
No growth	4 (8)		
P. aeruginosa	2 (4)		
Others	2 (4)		
Pus	13 (21.7) ³		
E. coli	3 (6)†		
P. aeruginosa	2 (4)		
S. aureus	2 (4)		
Enterococcus spp.	2 (4)		
Others	4 (8)		
Blood	5 (8.3)*		
P. aeruginosa	I (2)†		
Pseudomonas spp.	I (2)		
No growth	3 (6)		
Stool	4 (6.7)*		

* Percentage of total number of specimens sent for culture and sensitivity testings.

[†] Percentage of total number of organisms isolated.

E.: Escherichia; P.: Pseudomonas; H.: Haemophilus; K.: Klebsiella; spp.: species; S.: Staphylococcus

function. Injections were prescribed in 340 (62.0%) patients, antibiotics in 287 (52.4%) patients and IVFs in 191 (34.8%) patients. Antibiotics were prescribed for bacteriologically-proven infection (BPI) in 30 patients. Table II shows the common specimens isolated and sent for culture and sensitivity testings. Table III shows the antibiotic sensitivity pattern of the commonly-isolated microorganisms. Escherichia (E.) coli was resistant to cefixime, cefotaxime, ampicillin, ciprofloxacin and cotrimoxazole in many cases. However, the small number of isolates made it difficult to draw firm conclusions. Table IV shows the overall commonly used drugs and the drugs in selected therapeutic categories. Table V shows the ATC codes and DDD/100 bed-days of selected drugs. The most DDD/100 bed-days were for ranitidine, followed by ipratropium, omeprazole, coamoxicolav and amlodipine. The mean cost per prescription of drugs was 1702.57 ± 1286.4 Nepalese rupees (USD26.6 ± 20.1) [64 Nepalese rupees = 1 USD]. The mean cost of antibiotics was 681.52 ± 584.3 Nepalese rupees (USD10.6 \pm 9.13). Antibiotics accounted for approximately 40% of the total amount of money spent on drugs.

Organism isolated	No. (%) of antibiotic sensitivity								
-	Netilmicin	Cefazolin	Cefixime	Cefotaxime	Ampicillin	Coamoxiclav	Ciprofloxacin	Cotrimoxazole	Gentamicin
E. coli	4/4 (100)	2/3 (66.7)	1/3 (33.3)	1/3 (33.3)	1/4 (25)	0/1	1/3 (33.3)	1/3 (33.3)	60 (3/5)
P. aeruginosa	ND	ND	ND	1/1 (100)	ND	ND	0/1	1/2 (50)	100 (3/3)
H. parainfluenzae	ND	1/1 (100)	ND	3/3 (100)	3/4 (75)	3/4 (75)	0/1	1/1 (100)	ND`́
Enterococcus spp.	ND	ND	ND	ND	2/3 (66.7)	ND	0/1	0/1	20 (1/5)

Table III. Antibiotic sensitivity patterns of commonly isolated microorganisms.

ND: not done; E.: Escherichia; P.: Pseudomonas; H.: Haemophilus; spp.: species

DISCUSSION

There were more male than female patients in this study, and a majority of the patients were from Pokhara city and the Kaski district (in which Pokhara is located) and were admitted to the departments of medicine and surgery. This trend is similar to that observed in previous studies.(3,12) This data provides useful information about the catchment area of the hospital and the distance that patients have to travel in order to access specialised care. This is especially important in a mountainous country like Nepal. The proportion of older patients (age ≥ 60 years) had been observed to be high in previous studies,^(3,12) and this had motivated the authors to conduct a detailed study on drug utilisation in older patients. In this study, the majority of the elderly were younger than 75 years of age, while in a study in the Caribbean, the majority of the patients were older than 75 years of age.⁽¹³⁾

The most common reasons for admission were cancer (n = 85 cases, 15.5%), complications due to hypertension (especially cerebrovascular accidents) (n = 82, 15.0%), various types of elective and emergency surgeries (n = 56, 10.2%) and acute exacerbation of COPD (n = 38, 6.9%). In a previous study among the elderly at Kathmandu, respiratory and cardiovascular diseases were shown to be the predominant reasons for admission,⁽⁹⁾ while another study conducted at our hospital found that COPD, hypertension and type 2 diabetes mellitus were the most common diseases among medical inpatients.⁽¹²⁾ In the present study, 37 (6.7%) patients were on maintenance therapy for hypertension and 36 (6.6%) for asthma and COPD. The presence of multiple diseases is common among the elderly, as in our study patients. The chronic diseases had a significant influence on the drugs administered in the study. This is a confounding factor when correlating the drugs prescribed with the reason for admission. However, as the chronic illness from which the patient was suffering was also mentioned in the case notes, the drugs used for maintenance treatment could be worked out.

In the present study, a large number of patients were admitted to the department of medicine. In another study, hypertension was the most common diagnosis, followed

by cerebrovascular accidents, psychotic disorders and diabetes.⁽¹³⁾ The average number of drugs prescribed per patient was 7.73. A majority of the patients received 5-15 drugs. In a previous study on fluoroquinolone utilisation, the number of drugs prescribed was 6.5.⁽⁴⁾ At the Tribhuvan University Teaching Hospital in Kathmandu, the average drug exposure was found to be 11.2,⁽⁸⁾ while a more recent study found an average number of 10.73.⁽⁹⁾ Our number was thus less than those previously reported. In a Caribbean study carried out among institutionalised patients residing in government-funded nursing homes, the average number of drugs prescribed was 2.87.⁽¹³⁾ The average number of drugs prescribed is dependent on a variety of factors. Compared to Tribhuvan University Teaching Hospital, MTH has a more active drug and therapeutic committee, and its departments of pharmacy and pharmacology have carried out a number of initiatives to promote the more rational use of medicines.⁽¹⁴⁾ It is difficult to explain the relatively higher number of drugs prescribed with respect to the Caribbean nursing homes.

A high number of drugs prescribed can also lead to a higher risk of the occurrence of adverse effects, drug interactions and medication errors.^(15,16) Drug utilisation tends to be largely related to admitting diagnosis or cause and concomitant chronic illnesses that require maintenance treatment. Hypertension, as mentioned in the study, included mainly uncontrolled hypertension. Hypertension associated with complications, such as heart failure, cor pulmonale and hypertension associated with comorbid conditions, were differentiated. COPD and type 2 diabetes mellitus were also similarly classified.

FDCs were also commonly prescribed. This had also been observed in previous studies carried out in Kathmandu.^(8,9) This study noted the use of a FDC of amoxicillin and clavulanic acid. The use of a FDC of ampicillin and clavulanic acid. The use of a FDC of ampicillin and clavalin was reduced after it was banned by the hospital Drug and Therapeutics Committee (DTC). FDCs have both advantages and disadvantages. A major disadvantage is that FDCs expose patients to the actions of various pharmacologically-active ingredients

Name of drug	No. of prescriptions (%) n = 548		
Overall			
Ranitidine	164 (29.9)		
Multivitamins	159 (29)		
Amlodipine	130 (23.7)		
lpratropium	120 (21.9)		
Dextrose normal saline	116 (21.2)		
Omeprazole	111 (20.2)		
Aspirin	96 (17.5)		
Sabutamol	93 (17)		
Frusemide	85 (15.5)		
Diclofenac	84 (15.3)		
Paracetamol	76 (13.9)		
Antibiotics			
Gentamicin	68 (12.4)		
Coamoxiclav	65 (11.9)		
Ciprofloxacin	57 (10.4)		
Cardiovascular drugs			
Amlodipine	130 (23.7)		
Aspirin	96 (17.5)		
Frusemide	85 (15.5)		
Atenolol	49 (8.9)		

Table IV. Commonly used drugs overall and in specific

therapeutic categories.

Table V. ATC codes and DDD/100 bed-days of selected drugs.

Drug name	ATC code	DDD/100 bed-days
Ranitidine	A02B A02	33.48
Amlodipine	C08C A01	2.94
lpratropium*	R03B B01	1.86, 1.43
Dextrose normal saline	B05 BB02	4.58 liters/ 100 bed-days
Omeprazole	A02B C01	3.51
Aspirin	B01A C06	0.92
Gentamicin	J 01G B03	0.49
Coamoxiclav	J01C R02	3.22
Ciprofloxacin [†]	J01M A02	0.61, 0.37
Paracetamol	N02B E01	0.36
Diclofenac	M01A B05	1.45

* Ipratropium has two DDDs; one for inhaled aerosol and the other for inhaled solutions.

 † Ciprofloxacin has two DDDs; one for oral and the other for parenteral use.

ATC: anatomical therapeutic chemical; DDD: defined daily dose.

present in them and often may not deliver the required amount of individual ingredients. In the elderly with impaired hepatic and renal function, FDCs may lead to unnecessary and prolonged exposure to drugs and can increase the risk of toxicity. The challenge would be to ensure that proper amounts of each individual drug reach the body system. As FDCs are mass produced and the relative proportion of the ingredients is fixed, titration of ingredients in individual cases may not be possible.

In this study, only 36.8% of drugs were prescribed by generic name. We considered a drug to have been prescribed by brand name if it was referred to by brand name even once in the case sheet. The use of generic names was observed to be low in the two studies by the Tribhuvan University Teaching Hospital.^(8,9) Two recent studies among outpatients in MTH showed that the percentage of drugs prescribed by generic name was less than 20%.^(17,18) Encouragement of generic prescribing has been taken up as a matter of priority by the DTC of our hospital. This may have been an important reason why the use of generics was higher in this study compared to studies in other locations. A number of educational interventions have been carried out to improve prescription practices. The medical superintendent of the hospital has issued a notice strongly recommending the use of generic names in the hospital.

The liver and kidney are the major organs responsible for drug metabolism and excretion. Serum creatinine estimation can be considered as an index of renal function, and it was carried out in 46% of patients. As this was a retrospective study, it would be difficult to comment on serum creatinine estimation not been carried out in the rest of the patients. Economic considerations may have played a part in this.

Injections were prescribed in 62% of patients. At Tribhuvan University Teaching Hospital, nearly onethird of the drugs, excluding IVFs, were prescribed parenterally.⁽⁸⁾ IVFs were prescribed to 34.8% of patients. In our hospital, dextrose normal saline (DNS) was the most commonly prescribed IVF. In a recent study, 73% of patients were prescribed antibiotics and 72% received drugs intravenously.⁽⁹⁾ The high use of injections is a matter of concern. The study population was elderly inpatients from various departments of the teaching hospital. In addition to IVFs, ranitidine, coamoxiclav and gentamicin were the other drugs commonly prescribed via the parenteral route. Injections were commonly used in cases of acute exacerbation of COPD, in various complications associated with hypertension, in chemotherapy for different types of cancers, in various surgeries and for different infections. Because of the extra expense, effort and hazards involved, the parenteral route of drug administration should be used only after a proper assessment of its real need has been conducted.(8)

Studying the appropriateness of parenteral drugs and whether they could be replaced by oral drugs can be a useful subject for future study. In MTH, only disposable syringes are used for injections, which can minimise the risk of infections. The use of antibiotics for BPI continues to be low. In a previous study on antibiotic use, antibiotics were used for BPI in around 25% of patients.⁽³⁾ In a study in the intensive care unit of of MTH, 84.5% of antibiotics were prescribed without bacteriological support.⁽¹⁹⁾ The number of specimens sent for culture and sensitivity testings was low. The department of microbiology maintains a database on the sensitivity patterns of commonly isolated microorganisms, and the department of clinical pharmacology publishes the quarterly antibiogram in the Drug Information Bulletin. Empirical use of antibiotics can lead to inappropriate therapy and contribute to antibiotic resistance. E. coli and Pseudomonas aeruginosa were the commonest organisms isolated. The resistance of E. coli to certain commonly used antibiotics is a matter of concern. E. coli resistance to common antibiotics was also seen in previous studies in our institution.^(3,4) The hospital infection control committee is currently in the process of framing the antimicrobial use guidelines for common infectious diseases in the hospital.

Ranitidine, multivitamins, amlodipine, ipratropium and DNS were the most commonly prescribed drugs. At Tribhuvan University Teaching Hospital, 5% dextrose, frusemide and ranitidine were most commonly used.⁽⁸⁾ The same pattern has been found in a recent study.⁽⁹⁾ In the Caribbean, aspirin, ferrous sulfate, folic acid and bendrofluazide were most commonly prescribed drugs.⁽¹³⁾ The use of drugs depends on many factors, including the disease condition, economic status of the patient, pharmaceutical promotion and the availability of drugs, and may not be comparable between various locations.

In South Asia, the social norms favour a more doctor-centred relationship. Traditional medical practice has an unequal power relationship; the doctor occupies a superior position and the patient is in a helpless and often, hapless, role.⁽²⁰⁾ Many patients are illiterate and lack access to sources of medical information. Based on the authors' personal experience, refusal of drug treatment in the elderly is often associated with withdrawal of the individual from the hospital and the adoption of complementary remedies, most commonly at home. In our study, two patients refused treatment and discharged themselves from the hospital. Data on refusal of drug treatment was not available. This may be a confounding variable, and one that was not anticipated by the study. Studies on the refusal of drug treatment and its potential implications should be undertaken in order to understand this issue better.

that observed previously. The major use of ranitidine was for prophylaxis of stress ulcers. We have not come across studies measuring drug utilisation in geriatric inpatients using DDD/100 bed-days in the literature. The mean cost of drugs was USD26.6, and antibiotics accounted for around 40% of the total cost. The studies carried out at Tribhuvan University Teaching Hospital did not measure costs. In a previous study, the cost was around USD14.(10) A study of fluoroquinolone utilisation found the average drug cost to be USD13.⁽⁴⁾ Cost is an important factor influencing access to medicines in developing countries. The high use of intravenous drugs, IVFs and coamoxiclav may have partly accounted for the high cost. An early shift to oral drugs and guidelines for the use of IVFs can be considered to reduce the cost of medicines.

The study had some limitations. It was retrospective and the quality of prescribing was not assessed. The rationality of prescribing was also not looked into. The total number of beds to which elderly patients could be admitted was an estimate and may not have reflected the reality. The present study helped to create a drug utilisation database for older patients. With the aging of the population, drug use in older patients is becoming more important and has to be studied in greater detail. In conclusion, the present study identified certain lacunae in prescribing drugs to older inpatients. Polypharmacy and the high use of parenteral drugs and intravenous fluid were noted. Commonly isolated microorganisms were found to be resistant to certain antibiotics. The mean cost of the drugs was high. Guidelines and further studies on the use of drugs in older patients are required, and measures to reduce the average cost of medicines should be considered.

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