Research Paper

Drug utilization pattern and pharmacoeconomic analysis in geriatric medical in-patients of a tertiary care hospital of India

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ABSTRACT

Objective: To evaluate drug utilization pattern in terms of defined daily dose along with pharmacoeconomic analysis in geriatric patients admitted in medical ward of a tertiary care hospital. **Materials and Methods:** Retrospective medical record analysis was performed for indoor cases of the geriatric patients (age ≥65 years) admitted in medicine ward from January 2010 to December 2010 were analyzed for demographics, indications for admission, various systems involved, duration of hospital stay, various drugs prescribed, and adverse drug reaction. The drugs were categorized by anatomical therapeutic classification and defined daily dose was calculated. The World Health Organization prescribing indicators were assessed. Cost of the drugs was calculated to assess the economic burden. **Results:** Cardiovascular diseases were the common cause for admission. Antiplatelet drugs-B01AC (93%), H_2 blockers-A02BA (77.22%), antiemetics-A03FA (67.6%), vasodilators-C01D (55%), and hypolipidemic drugs-C10AA (52%) were commonly utilized groups. Average number of drugs per patient was 9.37 (95% CI: 9.09-9.64). Average number of antimicrobials prescribed per patient was 0.91 (95% CI: 0.82-0.99). Cefotaxime was the commonly prescribed antimicrobial drug. Average cost of treatment was ₹540.5 (95% CI: ₹458.0-623.0). Patients shared 45% of the economic burden for prescribed medicines. The average economic burden for drugs was significantly higher in expired than survived patients (₹749.49 vs. 457.59). **Conclusion:** Polypharmacy and irrational use of medicines are common problems in geriatric prescription. Prescription guidelines should be formatted for them.

Key words: Drug utilization research, geriatric population, pharmacoeconomic, polypharmacy, prescription audit, rational use of medicine, retrospective study

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INTRODUCTION

The elderly population is increasing rapidly worldwide. Their growth rate (1.9%) is higher than general population (1.2%).[1] At present, India is the third country after China and USA with large elderly population in the world. Elderly population has special problems related to health, social support, and economic security. Their healthcare need differs from younger people. Though elderly are reported to be responsible for half the total drug usage, less than 5% of randomized control trials have been designed for them.[2] Therefore, data available from younger

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subjects are used to guide prescribing in elderly. Physiological and pharmacological variations in elderly population include decreased total body mass, blood flow to various organs, immunity, and nervous functions; down- or upregulation of various receptors; and disturbance in first pass metabolism, bioavailability, metabolism, and excretion.[3,4] Presence of comorbidities in elderly people require use of multiple medications which increase the irrational prescription, use of inappropriate medications, noncompliance, economic burden, adverse drug reactions (ADRs), and drug interactions.[5] The overall incidence of ADR is two to three times higher and most of them are potentially avoidable in elderly patients.[6] These hurdles in pharmacotherapy can be overcome by periodic evaluation of drug utilization and optimizing prescribing pattern by forming prescription guidelines for geriatric patients. Drug utilization research is an important tool to analyze the use of drugs with special emphasis on medical, social, and economic consequences in a society.[7] The assumed average maintenance dose per day for a drug used for its main indication in adults is called defined daily dose (DDD).[8] It is an internationally accepted tool for comparing drug utilization. The present study evaluated drug utilization pattern in terms of DDD along with pharmacoeconomic analysis in geriatric medical in-patients.

MATERIALS AND METHODS

This retrospective study was conducted after permission of Institutional Review Board, Government Medical College, Bhavnagar, Gujarat, India. Indoor cases of geriatric patients (age ≥65 years) admitted in medicine ward between January 2010 and December 2010 were collected from medical record section of Sir Takhtsinhji General Hospital, Bhavnagar. Data were collected for demographics, diagnosis, hospital stay duration, treatment, outcome, and documented ADR.

Data were analyzed for age and gender distribution; common indications for admission and systems involved, hospital stay duration, and total number of drugs prescribed per patient.

Drug utilization pattern was evaluated by proportion of patients receiving particular drugs, its pharmacological groups, anatomical therapeutic classification (ATC) code, and DDD/100 bed-days using following equation.[8]

$$\text{DDD/100 bed days} = \frac{\text{Total dose in mg during study period} \times 100}{\text{DDD of drug} \times \text{study duration (days)} \times \text{bed strength} \times \text{Avg. bed occupancy rate}}$$

The bed strength and average bed occupancy rate were 30 and 0.3, respectively for geriatric patients in medical ward.

Other prescribing indicators like total number of antimicrobial drugs per patient, proportion of fixed dose combinations (FDCs), use of drugs by generic and brand, oral and parenteral formulations, National and WHO Essential Medicine Lists,[9,10] and costliest drugs were evaluated. ADRs were assessed for causative drugs by Naranjo's algorithm, severity by Modified Hartwig and Siegel Scale, and preventability by Modified Schumock and Thornton criteria.[11-13]

Cost of generic and brand drugs were calculated from hospital formulary and Indian Drug Review (2010), respectively. Cost of laboratory investigations, ward charges, and nursing care were not included.

Statistical analysis

Data were expressed as proportions and mean (95% confidence interval (CI)). Mostly descriptive statistics was used. Comparisons of categorical and continuous variables between survived and expired patients were done using Chi-square and unpaired *t*-test, respectively. Hospital stay and economic burden were compared between common geriatric diseases by one-way analysis of variance (ANOVA) followed by Tukey-Kramer multiple comparison test. All the statistical comparisons were done with GraphPad Instat 3.0 (Trial Version). $P < 0.05$ was considered statistically significant.

RESULTS

Total 12,227 patients including 706 (5.77%) geriatric patients were admitted in medicine ward. Total 30 patients who were admitted only for observation were excluded. Total 357 (52.12%) patients were female among the 676 included. Mean age of geriatric patients was 72.69 years (95% CI: 72.12-73.27). Average hospital stay was 5.07 days (95% CI: 4.80-5.34). There was no significant difference among male and female (4.80 days (95% CI: 4.43-5.18) vs 5.31 days (95% CI: 4.92-5.69); $P = 0.067$) for hospital stay. The five most common conditions for admission were ischemic heart disease (IHD, 39.49%), hypertension (37.27%), cerebrovascular (CV) stroke (27.81%), diabetes mellitus (18.49%), and congestive heart failure (CHF, 14.79%). Multiple systems were involved in 57.25% patients. Cardiovascular system (80.02%) was the most commonly involved system followed by central nervous system (22.18%), hematological (19.23%), endocrine (18.63%), respiratory (18.04%), renal (15.53%), gastrointestinal tract (7.84%), and genitourinary system (2.95%).

Total 6,314 drugs were prescribed in all the cases with 45.1% parenteral, 47.2% oral, and 7.7% other formulations. Total 207 different types of drugs were prescribed by generic (48.79%) and brand (51.21%) names. Parenteral formulations and fixed dose combinations (FDCs) were prescribed in 25.60 and 17.87% of patients, respectively. Total 101 (48.79%) and

92 (44.44%) drugs were prescribed from National and WHO Essential Drug lists, respectively. Average number of drugs prescribed per patient was 9.37 (95% CI: 9.09-9.64).

Total drug utilization during study period in terms of DDD/100 bed-days was 19,731.81. The most commonly prescribed drugs were from the cardiovascular system (31.12%), alimentary tract and metabolism (25.72%), and blood and blood forming organs (15.66%).

Utilization pattern of commonly prescribed drugs are shown in Table 1. Ranitidine (58.14%), metoclopromide (54.29%), furosemide (41.12%), and cefotaxime (23.37%) were the commonly prescribed parenteral drugs. Etofylline + theophylline (deriphylline; 14.05%) and multivitamins (7.1%) were the commonly prescribed FDCs. Deriphylline (14.05%), carvedilol (5.77%), budesonide (5.03%), and liquid cremaffin (4.73%) were the commonly used drugs not included in National List of Essential Medicine-2011 of India. Atorvastatin (50.59%), clopidogrel (31.5%), famotidine (19.08%), deriphylline (14.05%), and alprazolam (7.99%) were the commonly prescribed drugs not available in WHO Essential Medicine List. At least one antimicrobial drug was prescribed in 352 (52.07%) cases. Average number of antimicrobials

Table 1: Commonly utilized drugs, their ATC classification, and DDD/100 bed days in geriatric population

Systems	Groups	ATC code	Drugs	Cases (%)	DDD
Alimentary tract and metabolism	Proton pump inhibitor	A02BC01	Omeprazole	149 (22)	26.6
	H2 receptor blocker	A02BA02	Ranitidine	393 (58.1)	23.4
		A02BA03	Famotidine	129 (19.1)	18.2
	Belladonna alkaloids and tertiary amines	A03A01	Atropine	122 (18)	8.6
	Propulsive	A03FA03	Domperidone	48 (7.1)	3.8
		A03FA01	Metoclopromide	367 (54.3)	40.6
	Serotonin 5HT3 antagonist	A04AA01	Ondansetron	42 (6.2)	4.0
	Biguanides	A10BA02	Metformin	35 (5.2)	3.2
	Insulin and analogues	A10AC01	Plain insulin	89 (13.2)	6.0
Blood and blood forming organs	Antithrombotic platelet aggregation inhibitor	B01AC04	Clopidogrel	213 (31.5)	40.5
		B01AC06	Aspirin	416 (61.5)	-
		B01AB01	Heparin	91 (13.5)	17778.1
	Antithrombotic enzymes	B01AD01	Streptokinase	22 (3.3)	361.6
	Antianemic preparations	B03AA07	Ferrous sulfate	31 (4.6)	10.2
		B03BB01	Folic acid	118 (17.5)	371.7
	Solutions producing osmotic dieresis	B05BC01	Mannitol	67 (9.9)	-
Cardiovascular system	Digitalis glycoside	C01AA05	Digoxin	45 (6.7)	6.0
	Adrenergic and dopaminergic agent	C01CA04	Dopamine	76 (11.2)	2.1
		C01CA07	Dobutamine	89 (13.2)	1.7
		C01CA24	Adrenaline	112 (16.6)	23.9
		C01DA08	Isosorbide dinitrate	321 (47.5)	48.1
	High ceiling diuretics	C03CA01	Furosemide	278 (41.1)	65.8
	β blocking agents selective	C07AB02	Metoprolol	115 (17)	4.7
	Selective CCB vascular effects-dihydropyridines	C08CA01	Amlodipine	118 (17.5)	29.0
	ACE inhibitor plain	C09AA02	Enalapril	239 (35.4)	97.7
	Statins	C10AA05	Atorvastatin	342 (50.6)	55.6
Genitourinary and sex hormones	Imidazole derivatives	G01AF01	Metronidazole	104 (15.4)	29.2
Systemic hormonal preparation, exclusive insulin and sex hormone	Glucocorticoid	H02AB02	Dexamethasone	47 (7)	63.6
Anti-infective for systemic use	Third generation cephalosporins	J01DD01	Cefotaxime	158 (23.4)	12.1
		J01DD04	Ceftriaxone	71 (10.5)	12.7
	Fluoroquinolone	J01MA02	Ciprofloxacin	93 (13.8)	13.7
Nervous system	Analgesics-anilides	N02BE01	Paracetamol	58 (8.6)	11.5
	Hydantoin derivatives	N03AB02	Phenytoin	103 (15.2)	9.2
	Anxiolytic-benzodiazepine derivatives	N05BA01	Diazepam	51 (8)	6.6
		N05BA12	Alprazolam	54 (8)	13.3
Respiratory system	Selective β_2 adrenoreceptor agonists	R03AC02	Salbutamol	59 (8.7)	2.0

ATC=Anatomical therapeutic classification, DDD=defined daily dose, CCB=calcium channel blocker, ACE=angiotensin converting enzyme

prescribed per patient was 0.91 (95% CI: 0.82-0.99). Total 39 different types of antimicrobials were used. The five most commonly used antimicrobials were cefotaxime, metronidazole, ciprofloxacin, ceftriaxone, and levofloxacin. Their contribution in total cost of drugs was 20.79%. Flouroquinolones + metronidazole (17.61%) and third generation cephalosporin + metronidazole (16.48%) were the commonly prescribed empirical regimens. Culture and sensitivity testing was done in 88 patients.

Average cost of treatment per patient was ₹540.50 (95% CI: ₹458.04-622.97). Hospital and patient shared 55.28 and 44.72% of the total treatment cost, respectively. Average cost of drugs prescribed from National and WHO essential drug lists per patient were ₹444.73 (95% CI: ₹371.95-517.52) and ₹348.41 (95% CI: ₹245.75-401.07), respectively. There was no significant difference in cost of treatment for male and female patients (₹453.95 (95% CI: ₹368.78-539.13) vs ₹617.83 (95% CI: ₹481.87-753.81); $P = 0.0518$). The cost of treatment was significantly higher in expired than survived patients ($P < 0.05$) [Table 2].

Mortality rate was 28.4% with septicemia (21.9%) being the commonest cause. Subgroup analysis between survived and expired patients is shown in Table 2. Table 3 shows the comparison of cost burden between common geriatric diseases. Human-albumin, streptokinase, protein powder, enoxaparin sodium, and noradrenaline were the most five costliest drugs prescribed among 6.7% patients with 11.43% contribution to the total cost of drugs. ADRs were documented in eight (1.18%) patients. Description of ADR, causative drugs, causality, severity, and preventability assessment are mentioned in Table 4.

DISCUSSION

In our study, incidence of geriatric admission was around 6% with preponderance of female patients. The mean age and hospital stay are in accordance with previous reports.[14-16] Observed pattern of diseases and associated comorbid conditions in our geriatric patients are similar to other studies.[14-16]

Total number of drugs prescribed per patient is found higher in our study.[14-16] Five or more drugs were prescribed in 95% cases. It may be related with multiple comorbidities in our geriatric population. Use of polypharmacy increases the risk of drug interactions, ADRs, and economic burden. Total 18% patients received one or more FDCs. FDC enhances drug

Table 2: Various parameters between survived and expired patients

Parameters	Survived (*n*=484)	Expired (*n*=192)	*P* value
Male-female ratio	0.87:1	0.96:1	*0.62
Mean age in years	72.5 (71.8-73.2)	73.2 (72.1-74.4)	0.32
Duration of hospital stay in days	5.59 (5.29-5.88)	3.76 (3.23-4.29)	<0.0001
Patients having multiple system involvement	235 (48.6%)	152 (79.2%)	*<0.0001
Ten most common drugs prescribed	Aspirin (71.9%) Atorvastatin (57%) Isosorbide dinitrate (55%) Ranitidine (50%) Metoclopromide (45.9%) Enalapril (37%) Furosemide (42.4%) Clopidogrel (34.9%) Omeprazole (27.1%) Famotidine (23.3%)	Ranitidine (78.7%) Metoclopromide (75.5%) Aspirin (45.3%) Atorvastatin (40.6%) Furosemide (38%) Cefotaxime (36.5%) Dobutamine (33.9%) Dopamine (32.8%) Isosorbide dinitrate (30.2%) Metronidazole (28.1%)	-
Five most common antimicrobials	Cefotaxime (18.2%) Metronidazole (10.3%) Ceftriaxone (6.4%) Ciprofloxacin (5.4%) Cefadroxyl (3.1%)	Cefotaxime (36.5%) Ciprofloxacin (34.4%) Metronidazole (28.1%) Ceftriaxone (20.3%) Levofloxacin (7.3%)	-
Total number of drugs per patient	9.2 (8.9-9.5)	9.7 (9.2-10.3)	0.08
Total number of parenteral drugs per patient	4.1 (3.9-4.3)	5.2 (4.8-5.7)	<0.0001
Total number of antimicrobials per patient	0.8 (0.65-0.84)	1.3 (1.2-1.5)	<0.0001
Total cost of treatment per patient (₹)	457.6 (380.7-534.5)	749.5 (535.8-963.2)	0.0017
Total cost burden on hospital (₹)	247.4 (192.0-302.7)	426.58 (278.9-574.3)	0.006
Total cost burden on patient (₹)	214.0 (163.7-265.0)	325.0 (177.4-472.5)	0.08
Total cost of antimicrobials per patient (₹)	132.5 (101.3-163.7)	242.8 (158.3-327.3)	0.003

Categorical data is expressed as absolute number (percentage) and continuous data as mean (95% confidence interval (CI)). **P* value for Chi-square test, whereas rest *P* values are for unpaired *t*-test.

Table 3: Comparison of cost burden between common geriatric diseases

Indication for the admission	Duration of hospital stay (days)	Cost burden on hospital (₹)	Cost burden on patient (₹)	Total cost of treatment (₹)
Ischemic heart disease (*n*=285)	5.09 (4.76-5.43)	210.48 (170.79-250.17)	218.69 (144.62-292.78)*	426.91 (337.48-544.91)
Hypertension (*n*=248)	5.39 (4.95-5.84)	322.35 (216.52-428.17)	233.62 (149.11-318.14)	550.72 (413.22-688.23)
Cerebrovascular stroke (*n*=186)	4.91 (4.41-5.41)	367.47 (210.22-524.73)	138.15 (101.74-174.57)^^	501.50 (335.36-667.66)
Diabetes mellitus (*n*=123)	5.96 (5.25-6.67)	251.66 (161.08-342.25)	413.52 (215.93-611.11)*#^^	665.16 (444.99-885.34)*
Congestive heart failure (*n*=101)	5.18 (4.54-5.83)	149.62 (98.72-200.53)	149.37 (116.11-182.64)#	296.04 (230.03-362.05)*
P value (ANOVA)	0.08	0.04	0.004	0.04
F (df)	2.073 (4, 938)	2.491 (4, 938)	3.776 (4, 938)	2.479 (4, 938)

Data expressed in mean (95% CI). *#*P*<0.05 and ^^*P*<0.01 between two pairs by Tukey-Kramer Multiple Comparisons test. ANOVA=Analysis of variance, DF=Degrees of freedom

Table 4: Adverse drug reactions with causative drugs, causality, severity, and preventability assessment

Description of ADR	Causative drugs	Causality assessment (Naranjo algorithm)	Severity assessment (Modified Hartwig and Siegel Scale)	Preventability assessment (Modified Schumock and Thornton)
Dry cough (*n*=3)	Enalapril	Score 6 (probable)	Level 3	Definitely preventable
Bleeding from oral cavity (*n*=1)	Heparin, aspirin, clopidogrel	Score 7 (probable)	Level 2	Definitely preventable
Hemoptysis (*n*=1)	Aspirin, heparin	Score 6 (probable)	Level 3	Definitely preventable
Hemoptysis (*n*=1)	LMWH	Score 7 (probable)	Level 2	Definitely preventable
Loose stool (*n*=1)	Aspirin	Score 6 (probable)	Level 2	Definitely preventable

ADR=Adverse drug reaction, LMWH=Low molecular weight heparin

adherence, and reduces the packaging and shipping cost in developing countries. However, sizes of the benefits are not clear.[17] It can hamper the dose titration needed in any stage of pharmacotherapy of geriatric patients. Less than 50% of the total prescribed drugs were from the national and WHO essential drug lists. It suggests poor adherence to these lists in our set up. Being tertiary care teaching hospital, use of generic name and drugs from the essential drug list should be practiced and promoted.

Aspirin, ranitidine, metoclopramide, atorvastatin, and isosorbide dinitrate were commonly utilized drugs in our study. Ranitidine, aspirin, and diclofenac are reported as commonly utilized drugs by Shah *et al*., 2012.[15] Whereas; ranitidine, multivitamins, amlodipine, ipratropium, and dinitrosalicylic acid are commonly observed drugs by Shankar *et al*., 2010.[16] Aspirin was prescribed in low dose for treatment and prevention of IHD. Its use is justifiable with the total number patients with cardiovascular disease. However, it should be prescribed with caution in patients aged 80 years or more due to lack of evidences for benefit versus risk.[18] Use of parenteral ranitidine for prophylaxis of gastric irritation due to concomitant drugs without history of peptic ulcer seems irrational.[19] Metoclopramide was prescribed for vomiting. Its use should be restricted to gastroparesis as risks of extrapyramidal adverse effects are high in elderly people.[18] Instead of metoclopramide, ondansetron should be prescribed. Use of atorvastatin and isosorbide dinitrate is justifiable with cardiovascular conditions. Deriphyllin was the most commonly prescribed drug not included in national and WHO essential drug list. It is commonly prescribed antiasthmatic drug.[20] Though, it has narrow safety index, it is commonly used in emergency to terminate asthmatic attack in majority Indian tertiary care hospitals. Antimicrobials were prescribed mainly as empirical regimen. Cefotaxime was the commonly used antimicrobial as against ciprofloxacin reported by Shah *et al*.[15] Use of culture specific antimicrobials should also be promoted to reduce chances of drug resistance.

Cost of treatment per patient was ₹540.5 (10 USD; 1 USD = 54 INR) with 45% cost shared by patient. Cost of treatment per patient is comparatively lower in our study than reported by Shankar *et al*., (10 vs. 26.6 USD).[16] It may be due to use of higher number of antimicrobials and its 40% contribution in overall cost in Shankar *et al*.[16] In our study, antimicrobials have contributed 20% in cost of total treatment. Moreover, prescription with generic name was higher in our study (48.79 vs 36.8%).[16] Prescribing drugs with generic name, avoiding irrational use of drugs, and polypharmacy can help in reducing the cost of treatment and economic burden. Presence of multiple comorbidities and use of more parenteral and antimicrobial drugs are responsible for greater economic burden in expired than

survived patients. Overall, economic burden for the drugs shared by hospital is not significantly affected by common geriatric diseases and comorbid conditions. However, diabetes mellitus has increased the total cost shared by patients in our set up. This could be due to lack of insulin in hospital supply formulary. It should be included in hospital supply formulary.

ADRs were documented in 1.18% patients. Reported incidence of ADRs in elderly varies from 1.52 to 61.8%.[5,6,21,22] Low incidence may be due to retrospective nature of present study, lack of awareness of reporting, and documenting the ADRs among physicians. All the ADRs in our study were due to drugs used to treat cardiovascular problems in elderly as commonly observed in western study.[21] One Indian study has reported antidiabetic and antibacterial drugs as commonly implicated drugs causing ADRs in elderly.[6] Because of less number of ADR we could not estimate association of ADR with demographics, comorbid conditions, and mortality.

This study has some limitations. Findings of this study can only be generalized to tertiary care teaching hospital in a developing country. Only in-patients were included in the study. Line of treatment varies from physician to physician for the given condition and study provides no data for the same. However, it identified certain lacunae in prescribing pattern, need for the guidelines, and further studies for drug usage in geriatric patients.

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