Prescribing Patterns and Predictors of High-Level Polypharmacy in the Elderly Population: A Prospective Surveillance Study From Two Teaching Hospitals in India

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ABSTRACT

Background: Polypharmacy has been reported to increase the risks for inappropriate prescribing, adverse drug reactions, geriatric syndromes, and morbidity and mortality in elderly populations in the United States and Europe. Data on prescribing patterns and polypharmacy in the elderly population in India are limited.

Objectives: The aims of this study were to assess prescribing patterns and to determine the predictors of high-level polypharmacy in the elderly population in 2 tertiary care hospitals in India.

Methods: This prospective surveillance study used medical records from patients aged 60 to 95 years admitted to the medicine wards of the 2 tertiary care hospitals between January 2008 and June 2009. Data on medication prescribing from admission through discharge were reviewed. Diseases were coded using the World Health Organization (WHO) *International Classification of Diseases, 10th Revision*, and medications were coded using the WHO Anatomical, Therapeutic, and Chemical classification. Concordance of prescribing with the indications in the product labeling as listed in the American Hospital Formulary Services Drug Information 2007 was determined. The prevalences of polypharmacy (5–9 medications) and high-level polypharmacy (≥10 medications) were determined. Bivariate analysis and multivariate logistic regression analysis were used to determine the influential predictors of high-level polypharmacy during hospital stays.

Results: Data from 814 patients were included (493 [60.6%] men, 321 [39.4%] women; median age, 66 years [range, 60–95 years]). Systemic antibacterials were the most commonly prescribed therapeutic class of medications (574 [70.5%]), and pantoprazole was the most commonly prescribed medication (498 [61.2%]). The majority (7/10 [70.0%]) of the most commonly prescribed medications were prescribed as indicated. Medications prescribed "off-label" included pantoprazole (432/498 [86.7%]), ceftriaxone (212/259 [81.9%]), and atorvastatin (109/237 [46.0%]). Polypharmacy and high-level polypharmacy were prescribed in 366 (45.0%) and 370 (45.5%) patients, respectively. On multivariate logistic regression analysis, multiple (≥3) diagnoses (odds ratio [OR] = 1.55; 95% CI, 1.16–2.08; $P = 0.003$), angina pectoris (OR = 2.58; 95% CI, 1.50–4.37; $P < 0.001$), and a length of stay ≥10 days (10–<15 days, OR = 3.14; 95% CI, 2.09–4.71; $P < 0.001$; and ≥15 days, OR = 5.74; 95% CI, 2.43–13.51; $P < 0.001$) were found to be predictors of high-level polypharmacy during hospital stays.

Conclusions: The campaign for rational drug use in hospitalized elderly patients in India should promote pantoprazole, ceftriaxone, and atorvastatin prescribing in concordance with their indications. Interventions to reduce the high-level polypharmacy in the elderly during their stays in tertiary care hospitals in India should focus on patients with ≥3 diagnoses, angina pectoris, and/or ≥10 days of hospital stay. (*Am J Geriatr Pharmacother*. 2010;8:271–280)

Key words: aged, drug utilization, geriatrics, India, polypharmacy, risk.

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INTRODUCTION

Worldwide, life expectancy has increased by 2 years in the past decade due to social, economic, and health care improvements.[1] As a result, the elderly population is increasing and is expected to reach 1.4 billion by 2050.[2] In 2007, the elderly population in India (93 million) constituted 12.8% of the worldwide elderly population, and this number is expected to increase to 100 million by 2013.[1,3] Health care utilization is also expected to increase.[4]

Although there is no consensus[5] on the definitions of *polypharmacy* and *high-level polypharmacy* (also known as *excess polypharmacy*), these terms have been defined as the concurrent prescribing of 5 to 9 drugs[6–8] and ≥10 drugs,[5,9] respectively. *Polypharmacy* has also been defined as prescribing more drugs than are clinically indicated, or as unnecessary prescribing.[10] Polypharmacy increases with age (47% at a mean age of 74.5 years and 66.1% at 84 years).[11,12] Safe and effective prescribing in the elderly is difficult because of altered pharmacokinetics and pharmacodynamics and age-related changes in body composition and physiology.[2] Polypharmacy has been reported to increase the risks for inappropriate prescribing, adverse drug reactions, geriatric syndromes, and morbidity and mortality in elderly populations in the United States and Europe.[13]

The health care system in India is diverse, with a wide range of health care facilities in the private, corporate, and government sectors. Outpatient and inpatient services are available in all 3 sectors in varying capacities and scopes. Inpatient services are available at primary, secondary, and tertiary care hospitals. Based on their affiliations with medical schools, these hospitals are categorized as teaching or nonteaching. Physicians at primary care hospitals might provide care to patients with early-stage diseases or minor ailments. Referral from primary care hospitals to secondary and tertiary care centers is routine in the management of complex cases.

The secondary centers employ general surgical and medical teams. General medical teams have ≥1 physician with specialization in general medicine. Tertiary care hospitals are mainly referral centers for complex cases and specialized treatment; however, they also provide basic health care services. Only 3.4% of the total government expenditure in India is spent on health care services. Considering low per-capita per-year health care expenditure (3404 Indian rupees [INR] [US $1 = 46 INR]) and 91.4% out-of-pocket expenditure on health care,[1] polypharmacy is a serious concern to patients in India, especially the elderly, due to socioeconomic challenges such as social isolation, financial insecurity, and the lack of a government-funded health insurance program.[4]

Because geriatrics is not a widely practiced clinical specialty in India, few hospitals in India have geriatric clinics. Previously published studies from India have reported that the rates of polypharmacy and inappropriate medication prescribing (as assessed using updated modified Beers criteria[14]) in the elderly population are high (31.5%–67.8% and 17.9%, respectively).[15,16] However, those studies lacked systematic descriptions of medication prescribing in elderly patients and did not assess the determinants of polypharmacy. Sociodemographic factors, such as age, sex, education level, socioeconomic status, and employment, have been examined as determinants of polypharmacy in Ireland[17] and the United States.[18] Factors related to the health care system (eg, apparent pressure from patients, prescriber-related factors [high patient load, prescribing practice, practice structure], free access to medications)[7,19–21] and disease (eg, multiple comorbidities, chronic illness[22,23]) have also been explored as predictors of polypharmacy. However, based on the findings from a literature search, none of those variables have been tested as predictors of polypharmacy in hospitalized elderly patients in India. This study aimed to determine prescribing patterns, concordance of medication prescribing with approved indications, prescribing patterns in the most commonly treated disease conditions, and predictors of high-level polypharmacy in hospitalized elderly patients in India.

METHODS

This prospective, active-surveillance study was conducted over a period of 18 months (January 2008 to June 2009) in the medicine wards at St. John's Medical College Hospital, Bangalore, India, and Jagadguru Sri Shivarathreeshwara (JSS) Hospital, Mysore, India. Both are 1200-bed, representative tertiary care teaching hospitals. The study protocol and written informed-consent form were approved by the ethics committees at both hospitals.

Data from patients aged 60 to 95 years admitted to the medicine wards at the 2 hospitals between January 2008 and June 2009 were included in the study. Data from patients treated in the outpatient departments, intensive care units, and intensive therapy units of these hospitals were excluded because the focus of the study was on data from elderly patients in typical medicine wards at tertiary care teaching hospitals. Patients admitted to the medicine wards during the study period

were identified daily (Monday–Saturday) by a graduate clinical pharmacist using the wards' census registers. Data from patients admitted on Sundays and those who were discharged within a day before the next morning check of census registers were excluded. It was not possible to include all admitted elderly patients due to the availability of only 1 graduate clinical pharmacist per hospital for this study and due to the unavailability of patients' medical records in electronic format at the study settings. However, to determine the generalizability of the study findings, statistical comparisons were made between the patients included and not included in the study.

Admission notes, outpatient records, discharge summaries from previous hospitalizations, demographics, and medical histories were reviewed on the day of patients' inclusion. When necessary, patients and/or their caregivers were interviewed during hospitalization for clarification of medical history information. Diagnoses were recorded from daily reviews of clinicians' notes. If necessary, clinicians were interviewed for clarification of their notes on the information on diagnosis. Medications prescribed from admission through discharge were recorded from daily reviews of treatment charts and nurses' notes, as well as discharge summaries.

Data from data-collection forms were input into a specially designed Microsoft Access database (Microsoft Corporation, Redmond, Washington). To check the quality of the documentation by the graduate clinical pharmacists and to minimize transcription errors, a senior academic clinical pharmacist/pharmacologist reviewed 10% of the data-collection forms for consistency of information transferred from patients' medical records. All of the forms in the database were also reviewed against the data-collection forms for consistency of information.

Polypharmacy was defined as the concurrent prescribing of 5 to 9 medications, and *high-level polypharmacy* was defined as the concurrent prescribing of ≥10 medications. The highest number of concurrently prescribed medications during the hospital stay was used for grouping patients into categories of concurrent medication prescribing. Assessments of prescribing included over-the-counter and prescription allopathic medications, including those prescribed for as-needed use when actually administered. Diagnoses were coded using the World Health Organization (WHO) *International Statistical Classification of Diseases, 10th Revision* (*ICD-10*).[24] The medications were coded using the WHO Anatomical, Therapeutic, and Chemical classification.[25] Whether medications were prescribed as indicated or "off-label" was assessed using the American Hospital Formulary Services Drug Information (2007).[26]

Statistical Analysis

Comparisons between groups were conducted using the Pearson χ^2 test for categoric variables and the Mann-Whitney *Z* test for continuous variables. Pearson correlation coefficients (*r*) were calculated for the correlations. Using bivariate analysis by Pearson χ^2 test, predictors of high-level polypharmacy during hospital stay at $P < 0.05$ were identified. Age, sex, number of diagnoses, hospital length of stay (LOS), and disease conditions (eg, essential hypertension, diabetes, chronic obstructive pulmonary disease [COPD], angina pectoris) were tested using bivariate analysis. Multivariate logistic regression was used to assess the influence of the predictors of high-level polypharmacy that were identified on bivariate analysis. Statistical analysis was carried out using SPSS version 17.0 (Systat Software, Inc., Chicago, Illinois). $P < 0.05$ was considered statistically significant.

RESULTS

During the study period, 4366 elderly patients (59.1% men, 40.9% women) were admitted to the medicine wards of the 2 study hospitals. Among these, 814 were included in the study (493 [60.6%] men, 321 [39.4%] women). The sex distribution in the study patients was similar to that of patients not included in the study (n = 3552; 58.8% men, 41.2% women; χ^2 = 0.89). The median age of the study patients was 66 years (range, 60–95 years), and the median age of patients not included in the study was 67 years (range, 60–101 years) (Mann-Whitney $Z = -0.876$; P = NS). Median LOS was not significantly different between the patients included in the study and those not included in the study (7 days [range, 1–48 days] vs 7 days [range, 1–43 days, respectively]; Mann-Whitney $Z = -1.676$). Characteristics of the study patients are shown in **Table I**.

Most Commonly Prescribed Medications

The most commonly prescribed medication classes and individual medications in the study population are listed in **Table II**. Antibacterials were frequently prescribed (574/814 [70.5%]) in patients with infectious diseases (*ICD-10* codes A01–A04, A06, A09, A15–A17, A27, A41, A91, A92, and A98) (98.3% [113/115]), respiratory system disorders (*ICD-10* codes J01, J06, J12, J15, J17, J18, J20, J22, J40, J42–J44, and J90) (95.0% [320/337]), and genitourinary system disorders (*ICD-10* codes N04, N08, N10, N13, N17, N18, N20, N23, N39, and N40) (82.2% [111/135]). Sixty-one patients (7.5%) received thiazide diuretics, and 20 (2.5%) received psycholeptics/psychoanaleptics.

Table I. Characteristics of patients in this study of prescribing patterns and high-level polypharmacy in an elderly population in 2 tertiary care hospitals in India (N = 814).

Characteristic	No. (%) of Patients
Sex	
Male	493 (60.6)
Female	321 (39.4)
Age	
Median (range), y	66 (60–95)
Age group	
60–<70 y	488 (60.0)
70–<80 y	255 (31.3)
≥80 y	71 (8.7)
Hospital length of stay	
Median (range), d	7 (1–48)
Range group	
1–<10 d	650 (79.9)
10–<15 d	131 (16.1)
≥15 d	33 (4.1)
No. of diagnoses	
1 or 2	420 (51.6)
3 or 4	338 (41.5)
≥5	56 (6.9)
No. of concurrently prescribed medications	
1–4	78 (9.6)
5–9	366 (45.0)
≥10	370 (45.5)
Most common diseases (*ICD-10* code)	
Essential hypertension (I10)	345 (42.4)
Diabetes mellitus (E11)	291 (35.7)
COPD (J44)	153 (18.8)
Angina pectoris (I20)	75 (9.2)

ICD-10 = International Statistical Classification of Diseases, 10th Revision[24]; COPD = chronic obstructive pulmonary disease.

Table II. Medications most commonly (≥20% of patients) prescribed during hospital stays in this study of prescribing patterns and high-level polypharmacy in an elderly population in 2 tertiary care hospitals in India (N = 814).

Anatomic Class/Therapeutic Class/ Medication (ATC Code)	No. (%) of Patients
Alimentary tract (A)	737 (90.5)
Acid-related disorders (A02)	563 (69.2)
Pantoprazole (A02BC02)	498 (61.2)
Diabetes drugs (A10)	314 (38.6)
Insulin (A10AD, A10AB)	245 (30.1)
Blood and blood-forming agents (B)	431 (52.9)
Antithrombotic (B01)	347 (42.6)
Aspirin (B01AC06)	257 (31.6)
Clopidogrel (B01AC04)	216 (26.5)
Cardiovascular system (C)	563 (69.2)
Diuretics (C03)	230 (28.3)
Furosemide (C03CA01)	185 (22.7)
Calcium channel blockers (C08)	230 (28.3)
Amlodipine (C08CA01)	227 (27.9)
Agents acting on renin–angiotensin system (C09)	205 (25.2)
Lipid-modifying agents (C10)	219 (26.9)
Atorvastatin (C10AA05)	237 (29.1)
Antibiotics for systemic use (J)	592 (72.7)
Antibacterials for systemic use (J01)	574 (70.5)
Ceftriaxone (J01DD04)	259 (31.8)
Nervous system (N)	463 (56.9)
Analgesics (N02)	300 (36.9)
Paracetamol (N02BE01)	250 (30.7)
Respiratory system (R)	386 (47.4)
Drugs for obstructive airway disease (R03)	335 (41.2)
Salbutamol (R03AC02)	250 (30.7)

ATC = Anatomical, Therapeutic, and Chemical classification.[25]

Concordance of Medication Prescribing With Approved Indications

The majority (7/10 [70%]) of the medications most frequently prescribed during hospital stay were prescribed as indicated. The medications most commonly prescribed off-label were pantoprazole (86.7% [432/498]), ceftriaxone (81.9% [212/259]), and atorvastatin (46.0% [109/237]). The 2 most common reasons for prescribing pantoprazole off-label were to prevent gastrointestinal adverse effects of medications and stress ulcers during the hospital stay (91.9% [397/432]). Among the patients who received ceftriaxone (n = 259), 47 (18.1%) received prescriptions as indicated. Ceftriaxone was commonly prescribed in the empiric treatment of respiratory tract infections (43.2% [112]), in patients with viral infections (20.5% [53]),

and for surgical prophylaxis (12.4% [32]). The most common reason for prescribing atorvastatin off-label was for the primary prevention of cardiovascular events without multiple (≥3) risk factors (70.6% [77/109]). Off-label prescribing of pantoprazole, ceftriaxone, and atorvastatin accounted for 2869, 1297, and 790 patient-days, respectively, of treatment during hospital stays.

Prescribing Patterns in the Most Commonly Treated Disease Conditions

Essential hypertension, diabetes mellitus, and COPD were the most commonly treated disease conditions in the 2 medicine wards in this study. In the treatment of essential hypertension (n = 345), amlodipine administered as monotherapy or in combination with β-blockers or angiotensin receptor blockers was most commonly prescribed on admission (171 [49.6%]), during hospital stay (227 [65.8%]), and on discharge (202 [58.6%]). For the treatment of diabetes (n = 291), metformin, gliclazide, and glyburide were the drugs most commonly prescribed on admission (30.2% [88], 22.0% [64], and 17.5% [51], respectively); during hospital stays, metformin, gliclazide, and glimepiride were most commonly prescribed (28.2% [82], 18.2% [53], and 13.4% [39]); and on discharge, the most common treatments were metformin, glimepiride, and gliclazide (33.0% [96], 14.1% [41], and 13.1% [38]). Insulin was prescribed for diabetes in 29.2% (85) of patients on admission, 84.2% (245) during hospital stays, and 69.4% (202) on discharge. For the treatment of COPD (n = 153), salbutamol, theophylline, and tiotropium bromide were the drugs most commonly prescribed on admission (34.0% [52], 21.6% [33], and 9.8% [15]); during hospital stay, these medications were salbutamol, ipratropium bromide, and prednisolone (81.0% [124], 64.7% [99], and 35.9% [55]); on discharge, they were salbutamol, prednisolone, and budesonide (71.9% [110], 26.8% [41], and 24.8% [38]).

Concurrent Medication Use

There was no difference between the sexes in the median (range) number of medications prescribed concurrently during hospital stays (men, 9 [1–22]; women, 9 [1–20]) (Mann-Whitney $Z = -0.409$). The number of concurrently prescribed medications during hospital stays increased significantly with the number of diagnoses (8 [1–22], 10 [2–21], and 11 [1–22] with 1 or 2, 3 or 4, and ≥5 diagnoses, respectively; $r = 0.118$; $P < 0.001$ [1-tailed]) and LOS (8 [1–22], 11 [3–22], and 12 [7–21] with LOS 1–<10, 10–<15, and ≥15 days; $r = 0.35$; $P < 0.001$ [1-tailed]). However, the number of concurrently prescribed medications was not significantly increased with age (9 [1–22], 9 [3–20], and 9 [2–22] with age 60–<70, 70–<80, and ≥80 years; $r = 0.027$; P = NS). Medications prescribed concurrently during hospital stays differed significantly between patients with essential hypertension and those with angina (10 [1–22] vs 11 [6–19]; Mann-Whitney $Z = -3.626$; $P < 0.001$). The difference was not significant versus those with diabetes (9 [1–22]; Mann-Whitney $Z = -0.872$) or versus those with COPD (10 [2–19]; Mann-Whitney $Z = -0.746$).

Predictors of High-Level Polypharmacy

Prevalences of polypharmacy and high-level polypharmacy during hospital stays were 45.0% (366/814) and 45.5% (370/814), respectively. The predictors of high-level polypharmacy during hospital stays are listed in **Table III**.

Bivariate analysis identified multiple (≥3) diagnoses ($P = 0.009$), angina pectoris ($P = 0.003$), and LOS ≥10 days ($P < 0.001$) as predictors of high-level polypharmacy during hospital stays. On multivariate logistic regression, multiple diagnoses (odds ratio [OR] = 1.55; 95% CI, 1.16–2.08; $P = 0.003$), angina pectoris (OR = 2.58; 95% CI, 1.50–4.37; $P < 0.001$), and LOS ≥10 days (10–<15 days, OR = 3.14; 95% CI, 2.09–4.71; $P < 0.001$; ≥15 days, OR = 5.74; 95% CI, 2.43–13.51; $P < 0.001$) were found to be predictors of high-level polypharmacy during hospital stays.

DISCUSSION

Based on findings from PubMed and OvidSP searches using the search terms *drug utilization, elderly, inpatients, polypharmacy,* and *India*, this is the largest prospective study that has assessed prescribing patterns in, and first to report the predictors of high-level polypharmacy in, the hospitalized elderly population in India. In the study, antibiotics prescribing was extensive (72.7%) and not significantly different from that observed in 400 elderly patients in an emergency department (17.7% of elderly patients accounted for the highest percentage [23.5%] of antibiotic prescriptions) prescription audit study from a tertiary care hospital in India.[27] These findings might have been partly due to diagnoses of infections during hospital stays and/or systemic oral antimicrobials prescribed before, and used during, hospitalization. However, ceftriaxone was prescribed off-label in 81.8% of patients who received this drug.[26] Off-label prescribing of ceftriaxone (73.0%) was also found in an Australian concurrent observational assessment (N = 671; median age, 69 years [range, new-

Table III. Predictors of high-level polypharmacy during hospital stays in this study of prescribing patterns and high-level polypharmacy in an elderly population in 2 tertiary care hospitals in India (N = 814).

Characteristic	n/N (%) Prescribed High-Level Polypharmacy During Hospital Stay	Bivariate Analysis			Multivariate Logistic Regression*		
		OR	95% CI	*P*	OR	95% CI	*P*
Sex							
Male	225/493 (45.6)	1 (Ref)	–	–	–	–	–
Female	145/321 (45.2)	0.98	0.74–1.30	0.477	–	–	–
Age group							
60–<70 y	226/488 (46.3)	1 (Ref)	–	–	–	–	–
70–<80 y	116/255 (45.5)	0.97	0.71–1.31	0.446	–	–	–
≥80 y	28/71 (39.4)	0.75	0.45–1.25	0.169	–	–	–
No. of diagnoses							
1 or 2	169/420 (40.2)	1 (Ref)	–	–	–	–	–
≥3	201/394 (51.0)	1.43	1.07–1.91	0.009	1.55	1.16–2.08	0.003
Disease							
Essential hypertension (primary)	172/345 (49.9)	1 (Ref)	–	–	–	–	–
Diabetes mellitus	138/294 (46.9)	0.89	0.65–1.21	0.256	–	–	–
COPD	80/153 (52.3)	1.1	0.75–1.61	0.343	–	–	–
Angina pectoris	51/75 (68.0)	2.14	1.26–3.63	0.003	2.58	1.50–4.37	<0.001
Hospital length of stay							
1–<10 d	310/650 (47.7)	1 (Ref)	–	–	–	–	–
10–<15 d	97/131 (74.0)	3.13	2.06–4.76	<0.001	3.14	2.09–4.71	<0.001
≥15 d	29/33 (87.9)	7.95	2.76–22.87	<0.001	5.74	2.43–13.51	<0.001

OR = odds ratio; COPD = chronic obstructive pulmonary disease.
*R^2 = 0.07 (Hosmer and Lemeshow), 0.09 (Cox and Snell), 0.11 (Nagelkerke); model $\chi^2(1) = 74.11$; $P < 0.001$ ($df = 5$); constant OR = 0.03 ($P < 0.001$).

born to 99 years]).[28] In a retrospective review conducted at an academic practice in the United States,[29] the rate of off-label prescribing of proton pump inhibitors (PPIs) in geriatric patients (age, ≥65 years) was reported as 29.0%. This rate was 45.0% in a medical-record abstraction conducted at a US Veterans Affairs medical center.[30] Although PPIs are effective and well tolerated in the prevention of gastric and duodenal ulcers associated with NSAID use, this indication is not listed in the American Hospital Formulary Services Drug Information (2007).[26] Also, they may not be useful in preventing the gastrointestinal adverse effects of all other medications.[31] The finding of the off-label prescribing of atorvastatin in this study could not be supported due to a lack of published studies.

In 2009 in India, the median costs of typical doses of pantoprazole (40 mg/d), ceftriaxone (2 g/d), and atorvastatin (10 mg/d) were 5 INR (range, 2–7 INR), 148 INR (90–358 INR), and 6 INR (1–12 INR), respectively.[32] In this study, off-label prescribing of pantoprazole, ceftriaxone, and atorvastatin accounted for additional total costs of 14,345, 905, and 191,956 INR, respectively (costs per patient, 41.9, 905, and 44 INR; per-capita per-year expenditures on health, 1.2%, 26.6%, and 1.3%).[1] These findings suggest that interventions to rationalize medication prescribing in hospitalized elderly patients in India should focus on increasing adherence to indications when prescribing pantoprazole, ceftriaxone, and atorvastatin.

The common classes of medications prescribed in the elderly (those that act on the cardiovascular system and the alimentary tract) reported in the literature[33–35] were also recorded in this study. Because the 2 study hospitals offer psychiatric services, patients with psychiatric

diseases are admitted to psychiatry wards and hence only those patients with concomitant psychiatric illness (2.5%) received psycholeptics/psychoanaleptics. Similar to findings from another prospective observational study from the Government Medical College and Hospital, Chandigarh, India (N = 300),[36] amlodipine administered as monotherapy or in combination with β-blockers or angiotensin receptor blockers was the treatment of choice (65.8%) for essential hypertension in the elderly. These drug combinations are recommended for use in essential hypertension by the National Institutes of Health, ESH/ESC Hypertension Guidelines Committee, and WHO in India.[37–39] The high rate of prescribing amlodipine in this study might have been due to its low cost to patients (80 INR/y) compared with angiotensin-converting enzyme inhibitors (1660 INR/y for lisinopril) and β-blockers (318 INR/y for atenolol). This lower cost to patients might increase prescribing rates.[32,36] Although thiazide diuretics are indicated for the treatment of essential hypertension, their prescribing rate was low (2.5%) in this study. A similar finding was reported in a prospective cohort study in patients aged ≥65 years from the United States (marked drop, from 60.0% to 38.0%, in thiazide diuretic use from 1990–1999)[40] and a cross-sectional survey of general practitioners treating adults aged <65 years and elderly patients with hypertension (4.2% of general practitioners prescribed thiazide diuretics).[41]

New practice guidelines[42,43] might have influenced the prescribing of metformin in this study and other studies.[44,45] Glyburide use was discontinued in all patients following hospitalization because of its risk for hypoglycemia, and these patients were switched to comparatively better-tolerated sulfonylureas, such as gliclazide or glimepiride.[46–50] Oral hypoglycemic agents such as metformin, gliclazide, and glimepiride were prescribed less commonly (28.2%, 18.2%, and 13.4%, respectively) compared with insulin (84.2%) during hospital stays in the present study; this finding was similar to that from a previously published prospective, observational study in 102 patients with diabetic nephropathy (mean [SD] age, 55.1 [9.5] years) in a tertiary care hospital in India (8.9%).[51] There was a 40.2% increase in insulin use from admission to discharge, presumably for better glycemic control. A prospective study in 578 elderly patients in a tertiary care referral hospital in northern India reported a high rate of oral hypoglycemic prescribing just before admission (19.6%), and reported hypoglycemia due to the use of oral hypoglycemic agents as the most common cause of hospital admissions for adverse drug reactions (30.8%).[16] Based on these findings, patient education regarding oral hypoglycemic–induced hypoglycemia in the elderly population in primary and secondary health care centers might reduce the risks associated with the use of these agents.

The frequent (21.6%) prescribing of theophylline on admission in the treatment of COPD might have been due to its low out-of-pocket cost (2.5 INR per 400-mg tablet) compared with that of inhaled bronchodilators (82 INR for 1 metered-dose inhaler containing 200 doses of salbutamol at 100 μg per dose) in India. Theophylline use was discontinued in all patients after hospitalization because of the availability of more effective alternatives and the risk for adverse effects due to its narrow therapeutic index.[52] The frequent (64.7%) prescribing of ipratropium reported during hospital stays was likely due to the combined use of salbutamol and ipratropium nebulization for the treatment of acute exacerbations of COPD. The severity of COPD during hospital stays required the use of prednisolone in 35.9% of cases.

In contrast with findings from a cross-sectional analysis in 523 community-dwelling elderly patients[5] and a population-based cohort study in 601 elderly patients[9] in Finland, age and female sex were not observed as predictors of high-level polypharmacy. This finding suggests that elderly Indian women remain healthier, as supported by the lower proportion of hospitalized women observed in this study (39.4% vs 60.6% men) and greater life expectancy of Indian women compared with men (65 vs 63 years).[1]

The link between the number of diseases and high-level polypharmacy is likely due to diagnoses (eg, cardiovascular disease, diabetes mellitus, COPD) that pose several therapeutic challenges secondary to a variety of complications.[5] In addition to antianginals, concurrent administration of antihypertensives, antidiabetics, and lipid-lowering agents for cardiovascular risk reduction might predispose patients with angina to high-level polypharmacy.[53–55] Future studies should weigh the benefits of cardiovascular risk reduction in patients with angina against the adverse effects of high-level polypharmacy. In this study, LOS was a predictor of polypharmacy. Patients with longer LOSs might have been more seriously ill, thus requiring many concurrently prescribed medications.

The high prescribing rates in this study, at least on the basis of indication, suggest that high-level polypharmacy is common and might be justified in some elderly patients. Although polypharmacy might point to the likelihood of exposure to medication-related problems, it might not necessarily reflect inappropriate medication

usage because, in some patients, the concurrent prescribing of additional medications might be appropriate. For example, a combination of 3 antihypertensive drugs (eg, a statin, aspirin, and a folic acid supplement) at low doses might reduce cardiovascular events.[56] However, high-level polypharmacy in the elderly should be evidence based and should avoid potentially inappropriate medications that increase the risk for adverse consequences.[14,57] The key to treating the elderly is not necessarily to set a limit on the number of medications concurrently prescribed, but to find the right medications at the right dosages and to be used for the shortest possible duration on a case-by-case basis.[58] Balance between the risks and benefits of polypharmacy in the elderly population can be achieved by consistent review of medication lists and reevaluation of indications and therapeutic outcomes.[59]

Not all of the patients admitted to the hospital during the study period could be included primarily due to limited human resources. Because the study did not include the patients in other wards, and because the characteristics of patients in other wards might be different from those observed in this study, the results cannot be generalized. This study did not assess the consequences of high-level polypharmacy or the need to reduce it.

CONCLUSIONS

In this study in elderly inpatients from 2 tertiary care hospitals in India, the majority of the medications frequently prescribed during hospital stays were prescribed as indicated. The campaign for rational drug use in the elderly population should promote the prescribing of atorvastatin, ceftriaxone, and pantoprazole in concordance with their indications for use. The prevalences of polypharmacy and high-level polypharmacy (45.0% and 45.5%, respectively) suggest that there is large scope to assess the consequences of these practices in the hospitalized elderly population in India. Interventions to reduce high-level polypharmacy during stays in tertiary care hospitals should focus on patients who have multiple diagnoses, angina pectoris, and/or an LOS ≥10 days. Large-scale studies are needed to confirm the prevalence, predictors, and rationality of high-level polypharmacy in hospitalized elderly patients in India.

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REFERENCES

1. World Health Statistics 2009. Geneva, Switzerland: World Health Organization Press; 2009.
2. Sandhiya S, Adithan C. Drug therapy in elderly. *J Assoc Physicians India*. 2008;56:525–531.
3. Shah N. Oral health care system for elderly in India. *Geriatr Gerontol Int*. 2004;4(Suppl 1):162S–164S.
4. Ingle GK, Nath A. Geriatric health in India: Concerns and solutions. *Indian J Community Med*. 2008;33: 214–218.
5. Jyrkkä J, Enlund H, Korhonen MJ, et al. Patterns of drug use and factors associated with polypharmacy and excessive polypharmacy in elderly persons: Results of the Kuopio 75+ study: A cross-sectional analysis. *Drugs Aging*. 2009;26:493–503.
6. Stewart RB, Cluff LE. A review of medication errors and compliance in ambulant patients. *Clin Pharmacol Ther*. 1972;13:463–468.
7. Bjerrum L, Søgaard J, Hallas J, Kragstrup J. Polypharmacy in general practice: Differences between practitioners. *Br J Gen Pract*. 1999;49:195–198.
8. Finkers F, Maring JG, Boersma F, Taxis K. A study of medication reviews to identify drug-related problems of polypharmacy patients in the Dutch nursing home setting. *J Clin Pharm Ther*. 2007;32:469–476.
9. Jyrkkä J, Enlund H, Korhonen MJ, et al. Polypharmacy status as an indicator of mortality in an elderly population. *Drugs Aging*. 2009;26:1039–1048.
10. Montamat SC, Cusack B. Overcoming problems with polypharmacy and drug misuse in the elderly. *Clin Geriatr Med*. 1992;8:143–158.
11. Viktil KK, Blix HS, Moger TA, Reikvam A. Polypharmacy as commonly defined is an indicator of limited value in the assessment of drug-related problems. *Br J Clin Pharmacol*. 2007;63:187–195.
12. Flaherty JH, Perry HM III, Lynchard GS, Morley JE. Polypharmacy and hospitalization among older home care patients. *J Gerontol A Biol Sci Med Sci*. 2000;55: M554–M559.
13. Hajjar ER, Cafiero AC, Hanlon JT. Polypharmacy in elderly patients. *Am J Geriatr Pharmacother*. 2007;5:345–351.

14. Fick DM, Cooper JW, Wade WE, et al. Updating the Beers criteria for potentially inappropriate medication use in older adults: Results of a US consensus panel of experts [published correction appears in *Arch Intern Med*. 2004;164:298]. *Arch Intern Med*. 2003;163:2716–2724.
15. Mandavi, Tiwari P, Kapur V. Inappropriate drug prescribing identified among Indian elderly hospitalized patients. *Int J Risk Saf Med*. 2007;19:111–116.
16. Malhotra S, Karan RS, Pandhi P, Jain S. Drug related medical emergencies in the elderly: Role of adverse drug reactions and non-compliance. *Postgrad Med J*. 2001;77: 703–707.
17. Odubanjo E, Bennett K, Feely J. Influence of socioeconomic status on the quality of prescribing in the elderly—a population based study. *Br J Clin Pharmacol*. 2004;58: 496–502.
18. Perry BA, Turner LW. A prediction model for polypharmacy: Are older, educated women more susceptible to an adverse drug event? *J Women Aging*. 2001;13:39–51.
19. Hessel A, Gunzelmann T, Geyer M, Brähler E. Utilization of medical services and medication intake of patients over 60 in Germany—health related, social structure related, socio-demographic and subjective factors [in German]. *Z Gerontol Geriatr*. 2000;33:289–299.
20. Little P, Dorward M, Warner G, et al. Importance of patient pressure and perceived pressure and perceived medical need for investigations, referral, and prescribing in primary care: Nested observational study. *BMJ*. 2004;328:444.
21. Perkins AJ, Kroenke K, Unützer J, et al. Common comorbidity scales were similar in their ability to predict health care costs and mortality. *J Clin Epidemiol*. 2004;57: 1040–1048.
22. Linjakumpu T, Hartikainen S, Klaukka T, et al. Use of medications and polypharmacy are increasing among the elderly. *J Clin Epidemiol*. 2002;55:809–817.
23. Al-Windi A. Determinants of medicine use in a Swedish primary health care practice population. *Pharmacoepidemiol Drug Saf*. 2005;14:47–51.
24. *International Statistical Classification of Diseases,* 10th Rev. Geneva, Switzerland: World Health Organization; 2005.
25. WHO Collaborating Center for Drug Statistics Methodology. ATC/DDD Index. http://www.whocc.no/atcddd/. Accessed September 1, 2009.
26. Gerald KM, ed. American Hosital Formulary Services Drug Information. Bethesda, Md: American Society of Health System Pharmacists; 2007.
27. Gupta M, Malhotra S, Chandra KK, et al. Utilization of parenteral anti-infective agents in the medical emergency unit of a tertiary care hospital: An observational study. *Pharmacoepidemiol Drug Saf*. 2004;13:653–657.
28. Robertson MB, Korman TM, Dartnell JG, et al, for the Victorian Drug Usage Evaluation Group. Ceftriaxone and cefotaxime use in Victorian hospitals. *Med J Aust*. 2002;176:524–529.
29. George CJ, Korc B, Ross JS. Appropriate proton pump inhibitor use among older adults: A retrospective chart review. *Am J Geriatr Pharmacother*. 2008;6:249–254.
30. Dries AM, Richardson P, Cavazos J, Abraham NS. Therapeutic intent of proton pump inhibitor prescription among elderly nonsteroidal anti-inflammatory drug users. *Aliment Pharmacol Ther*. 2009;30:652–661.
31. Rostom A, Dube C, Wells G, et al. Prevention of NSAID-induced gastroduodenal ulcers. *Cochrane Database Syst Rev*. 2002;(4):CD002296.
32. Current Index of Medical Specialities. Bangalore, India: CPMedica India Private Limited; 2009.
33. Kaufman DW, Kelly JP, Rosenberg L, et al. Recent patterns of medication use in the ambulatory adult population of the United States: The Slone survey. *JAMA*. 2002;287:337–344.
34. Flores LM, Mengue SS. Drug use by the elderly in Southern Brazil [in Portuguese]. *Rev Saude Publica*. 2005;39:924–929.
35. German PS, Burton LC. Medication and the elderly. Issues of prescription and use. *J Aging Health*. 1989;1:4–34.
36. Jhaj R, Goel NK, Gautam CS, et al. Prescribing patterns and cost of antihypertensive drugs in an internal medicine clinic. *Indian Heart J*. 2001;53:323–327.
37. US Department of Health and Human Services. National Institutes of Health. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. NIH Publication No. 04-5230. http://www.nhlbi.nih.gov/guidelines/hypertension/jnc7full.pdf. Accessed August 13, 2009.
38. Cifkova R, Erdine S, Fagard R, et al, for the ESH/ESC Hypertension Guidelines Committee. Practice guidelines for primary care physicians: 2003 ESH/ESC hypertension guidelines. *J Hypertens*. 2003;21:1779–1786.
39. World Health Organization Country Office for India. Hypertension. Standard Treatment Guidelines. http://www.whoindia.org/LinkFiles/Standard_Treatment_Guidelines_(STGs)_STG_content_hypertension.pdf. Accessed August 13, 2009.
40. Psaty BM, Manolio TA, Smith NL, et al, for the Cardiovascular Health Study. Time trends in high blood pressure control and the use of antihypertensive medications in older adults: The Cardiovascular Health Study. *Arch Intern Med*. 2002;162:2325–2332.
41. Jafar TH, Jessani S, Jafary FH, et al. General practitioners' approach to hypertension in urban Pakistan: Dis-

turbing trends in practice [published correction appears in *Circulation*. 2005;111:e448]. *Circulation*. 2005;111: 1278–1283.
42. Rodbard HW, Blonde L, Braithwaite SS, et al, for the AACE Diabetes Mellitus Clinical Practice Guidelines Task Force. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the management of diabetes mellitus [published correction appears in *Endocr Pract*. 2008;14:802–803]. *Endocr Pract*. 2007;13 (Suppl 1):1–68.
43. Indian Council of Medical Research. Guidelines for Management of Type 2 Diabetes. http://icmr.nic.in/guidelines_diabetes/guide_diabetes.htm. Accessed August 13, 2009.
44. Lub R, Denig P, van den Berg PB, et al. The impact of new insights and revised practice guidelines on prescribing drugs in the treatment of Type 2 diabetes mellitus. *Br J Clin Pharmacol*. 2006;62:660–665.
45. Johnson JA, Pohar SL, Secnik K, et al. Utilization of diabetes medication and cost of testing supplies in Saskatchewan, 2001. *BMC Health Serv Res*. 2006;6:159.
46. Blonde L, Rosenstock J, Mooradian AD, et al. Glyburide/metformin combination product is safe and efficacious in patients with type 2 diabetes failing sulphonylurea therapy. *Diabetes Obes Metab*. 2002;4:368–375.
47. Holstein A, Plaschke A, Egberts EH. Lower incidence of severe hypoglycaemia in patients with type 2 diabetes treated with glimepiride versus glibenclamide. *Diabetes Metab Res Rev*. 2001;17:467–473.
48. Sills MN, Ogu CC, Maxa J. Prolonged hypoglycemic crisis associated with glyburide. *Pharmacotherapy*. 1997;17:1338–1340.
49. Tessier D, Dawson K, Tétrault JP, et al. Glibenclamide vs gliclazide in type 2 diabetes of the elderly. *Diabet Med*. 1994;11:974–980.
50. Hanefeld M, Patwardhan R, Jones NP, for the Rosiglitazone Clinical Trials Study Group. A one-year study comparing the efficacy and safety of rosiglitazone and glibenclamide in the treatment of type 2 diabetes. *Nutr Metab Cardiovasc Dis*. 2007;17:13–23.
51. Devi DP, George J. Diabetic nephropathy: Prescription trends in tertiary care. *Indian J Pharm Sci*. 2008;70: 374–378.
52. Bertino JS Jr, Walker JW. Reassessment of theophylline toxicity. Serum concentrations, clinical course, and treatment. *Arch Intern Med*. 1987;147:757–760.
53. Fraker TD Jr, Fihn SD, Gibbons RJ, et al, for the 2002 Chronic Stable Angina Writing Committee and the American Heart Association. 2007 Chronic angina focused update of the ACC/AHA 2002 guidelines for the management of patients with chronic stable angina: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines Writing Group to develop the focused update of the 2002 guidelines for the management of patients with chronic stable angina [published correction appears in *J Am Coll Cardiol*. 2007;50:e1]. *J Am Coll Cardiol*. 2007;50:2264–2274.
54. Chandra KK, Malhotra S, Gupta M, et al. Changing trends in the hospital management of unstable angina: A drug utilization analysis. *Int J Clin Pharmacol Ther*. 2004;42:575–580.
55. Malhotra S, Grover A, Verma NK, Bhargava VK. A study of drug utilisation and cost of treatment in patients hospitalised with unstable angina. *Eur J Clin Pharmacol*. 2000;56:755–761.
56. Yusuf S, Pais P, Afzal R, et al, for the Indian Polycap Study (TIPS). Effects of a polypill (Polycap) on risk factors in middle-aged individuals without cardiovascular disease (TIPS): A phase II, double-blind, randomised trial. *Lancet*. 2009;373:1341–1351.
57. Bergman-Evans B. Evidence-based guideline. Improving medication management for older adult clients. *J Gerontol Nurs*. 2006;32:6–14.
58. Planton J, Edlund BJ. Strategies for reducing polypharmacy in older adults. *J Gerontol Nurs*. 2010;1–5.
59. Ballentine NH. Polypharmacy in the elderly: Maximizing benefit, minimizing harm. *Crit Care Nurs Q*. 2008;31: 40–45.

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