



RESEARCH ARTICLE

Pharmacovigilance study in geriatric patients of a tertiary care hospital

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ARTICLE INFO ABSTRACT



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Introduction: The aim was to assess, categorize and analyze the adverse drug reactions among geriatric patients in a tertiary care hospital.

Methods: All adverse drug reactions of geriatric patients reported at the Adverse Drug Reaction Monitoring Center, Sri Venkateswara Medical College, Tirupati, under the Pharmacovigilance programme of India, during September 2016 and January 2018 were identified and evaluated. A retrospective analysis was carried out for ADR pattern, drug groups, organ systems implicated in suspect ADR, demographic profile, causality (as per the WHO-UMC scale), severity (Hartwig and Seigel scale), and preventability (Schumock and Thornton criteria) of a said drug.

Results: A total of 120 ADRs were received among geriatric patients. Most of the ADRs occurred in male geriatrics (55.83 %) and (34.2 %) occurred in the age group of 60- 64 years. Antibiotics comprised the major group of drugs causing ADRs (18.3 %). ADRs related to gastrointestinal systems were most common with 31.7 % followed by skin disorders (15 %) and central nervous system disorders (13.3 %). As per the causality assessment scale, the majority of adverse drug reactions were found to be possible (51.7 %).

Conclusions: There were 60.8 % of reactions being mild and 39.2 % were moderate reactions as per severity scale. The majority of the adverse drug reactions were non-serious (33 %) and in the serious category, 27.5 % of ADRs required intervention to prevent permanent damage.

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Introduction

Pharmacovigilance (PV) is the science and activities relating to the detection, assessment, understanding, and prevention of the adverse effects of drugs or any other possible drug-related issues. Adverse drug reactions (ADR) are drug responses that are the noxious, unintended, or unwanted effect of a drug that occurs at normal doses used in humans for prophylaxis, diagnosis,

therapy, or modification of physiological functions (Campbell *et al.*, 2014; Suke *et al.*, 2015). ADRs are common occurrences in a hospital setup, attributed due to the severity and complexity of the disease process, the use of multiple medications, drug interactions, and the possibility of negligence. They are associated with higher rates of morbidity and mortality.



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In the United States of America, ADRs contribute 3.4 to 7 % of hospital admissions. In certain countries, ADRs leading to hospital admissions is 10 % or even more. A study carried out in a territory referral center in South India showed that hospital admissions due to ADRs were 0.7 % of total admissions and deaths due to ADRs accounted for 1.8 % of total admissions (Kalaiselvan *et al.*, 2016). The rate of fatal ADRs in US hospitals was found to be extremely high, close to the 5% estimate based on data from multiple studies around the world, placing these reactions between the fourth and sixth leading causes of death. (Said *et al.*, 2020; Lazarou *et al.*, 1998). The prevalence of ADR is higher among geriatric (5 %) as compared to adults. Pharmacovigilance certainly contributes to ADR monitoring and reporting which helps in the detection and prevention of the reoccurrence of ADRs. Adverse drug reaction reporting directly contributes to increased vigilance and may even influence the recommendations of drug use through regulatory authorities or pharmaceutical manufacturers (Gor *et al.*, 2008). Taking this view in mind we would like to characterize the pattern of adverse drug reactions (ADRs) in geriatric patients reported through a spontaneous reporting system at adverse drug reaction monitoring centre (AMC).

Many research studies from around the world show an increasing ADR rate in elderly patients. Geriatric patients appear to be at risk of ADRs, as this age group is likely to receive multiple medications for their associated medical conditions and thus take multiple prescriptions and over-the-counter drugs (OTC). They exhibit increased pharmacodynamic sensitivity to several commonly used medications. The toxicity of some drug combinations may sometimes be synergistic and be greater than the sum of the risks of toxicity when used alone. Since most ADRs in the elderly are predictable and therefore potentially avoidable, good communication is pivotal in developing an effective therapeutic relationship with the patient and fellow health care professionals. According to the literature, elderly patients are exposed to more drugs and have a higher chance of type A and few type B adverse reactions, much of which can be avoided (Seymour *et al.*, 1998).

Pharmacovigilance or hospital-based monitoring of ADRs, done by a group of doctors, nurses, or other health care professionals detects the incidence of ADRs and provides detailed and accurate information. Currently, data on ADRs in Indian elderly patients is limited. Hence, the present study was conducted to evaluate the pattern of ADRs in elderly inpatients, using the intensive method of ADR monitoring.

Materials and Methods

A retrospective analysis was carried out at Sri Venkateswara Medical College (SVMC)/ Sri

Venkateswara Ramnarain Ruia Government General Hospital (SVRRGGH), Tirupati, Andhra Pradesh, India, recognized Adverse Reaction Monitoring Center (AMC) under the Pharmacovigilance Programme of India (PVPI). The suspected ADRs were reported by health care professionals spontaneously and relevant details of each ADR were collected in spontaneous ADR reporting form. Each ADR report was sent to the National Coordinating Center (NCC) via "Vigiflow". Details of each report were also simultaneously entered in the Microsoft Excel sheet. All ADRs of geriatric patients (≥ 60 years) reported during September 2016 and January 2018 were identified from this database.

The reported ADRs in geriatric patients were evaluated, classified, and assessed after approval from Institutional Ethics Committee SVRRGGH- SVMC, Tirupati, by maintaining strict confidentiality about reporters and patient details.

Doctors, nurses and other health care professionals were encouraged to report ADRs and hands on training was also given to fill ADR forms. The form contains the patient details, treatment is given, reaction details, concomitant drug details, history, and information of de-challenge and re-challenge. The ADR forms received/ collected at AMC were carefully assessed for quality based on the following essential elements: 1 (The patient initials), 5 (start date of reaction), 7 (describe reaction or problem), 8 (suspected medications), 15 (outcomes), 16 (name and professional address of the reporter) and 18 (date of the report) as per the Pharmacovigilance programme of India (PvPI).

Further serious ADRs and causality assessment were also evaluated. Causality was assessed as per the World Health Organization -The Uppsala Monitoring Centre (WHO-UMC) causality assessment scale, which classifies into certain, probable, possible, unlikely, conditional, and unassessable ADR (Parida 2013). The severity of the reaction was assessed using a modified Hartwig and Siegel ADR severity assessment scale, which classifies ADR into mild, moderate, and severe (Harwig *et al.*, 1992). While preventability was evaluated using a modified Schumock and Thornton scale (Schumock *et al.*, 1992).

Study Design

A retrospective analytical study was carried out for all adverse drug reactions in geriatric patients which were reported to AMC during September 2016 and January 2018.

Statistical Analysis

The data were analyzed descriptively using Microsoft Excel 2007, and the results were interpreted as numbers and percentages.

Results and Discussion

A total of 936 ADRs were reported between September 2016 and January 2018 at Adverse Drug Reaction Monitoring Center. Out of which total of 120 (24.78 %) ADRs was from geriatric patients. The data has been presented in **Table 1** and **Figure 1**.

Table 1: Gender-wise distribution of ADRs.

Gender	Number of ADRs [n (%)]
Male	67 (55.8)
Female	53 (44.2)

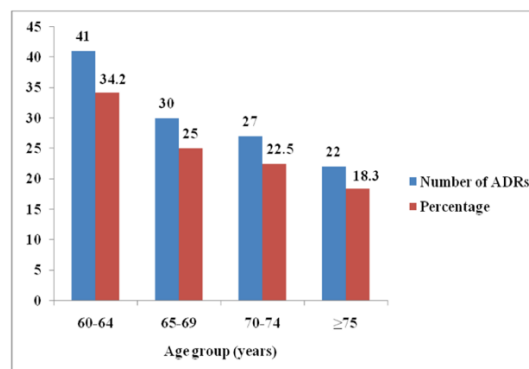


Figure 1. Age-wise distribution of ADRs.

Table 2. Categories of suspected drugs causing ADRs.

Sr. no.	Drug category	Name of drugs	Number of ADRs [n (%)]
1.	Antibiotics	Ceftriaxone, Amoxycillin and clavulanic acid, magnex forte, piperacillin/tazobactam, cefixime, doxycycline, ciprofloxacin, ofloxacin	22(18.3)
2.	Antihypertensives	Amlodipine, enalapril, furosemide, atenolol, spironolactone	16(13.3)
3.	Non-steroidal anti-inflammatory (NSAIDs)	Tramadol, diclofenac, fentanyl, ibuprofen, paracetamol	11(9.2)
4.	Antiplatelet	Aspirin, clopidogrel, enoxaparin	5(4.2)
5.	Antipsychotics	Haloperidol, Librium, amitriptyline, olanzapine, lithium sodium carbonate	7(5.8)
6.	Hormones	Insulin	2(1.7)
7.	Steroids	Dexamethasone, methylprednisolone, cort-S, Budecort	6(5.0)
8.	Vitamins and minerals	Iron folic acid, optineuron, methyl cobalamine	4(3.3)
9.	Antitubercular drugs	(Isoniazid, rifampicin, ethambutol, pyrazinamide)	10(8.3)
10.	Anti hyperlipidemic	Atorvastatin	2(1.7)
11.	Anti ulcer	Pantoprazole, rabeprazole, omeprazole, ranitidine	7(5.8)
12.	Antiretroviral drugs	Tenofovir/lamivudine/efavirenz, Zidovudine/lamivudine/nevirapine	8(6.7)
13.	Others	Septran DS, tamoxifen, ondansetron, theophylline, etc.	20(16.7)

Table 3. Body system involved with ADRs.

Body system	ADRs	Number of ADRs [n (%)]	Cumulative number [n (%)]
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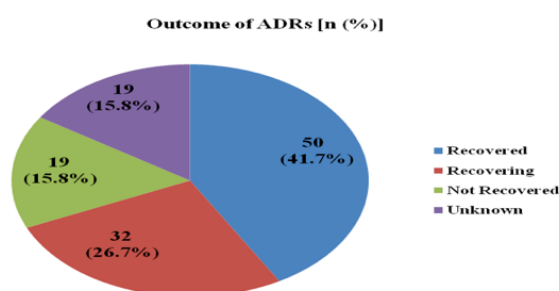
Gastrointestinal disorder	Constipation	12(10)	
	Loose Stools/Diahorrea	11(9.2)	
	Vomiting/Nausea	8(6.7)	
	Gastritis	5(4.2)	38(31.7)
	Glossitis	1(0.8)	
	Oral Candidiasis	1(0.8)	
Skin disorders	Urticarial rash	3(2.5)	
	Itching	6(5.0)	
	Hyperpigmented patches	1(0.8)	
	Erythema multiforme	2(1.7)	
	Disseminated fixed drug eruptions	1(0.8)	18(15.0)
	Exfoliative dermatitis	1(0.8)	
	Erythematous papules	2(1.7)	
	Dress syndrome	1(0.8)	
	Dark purple bruise	1(0.8)	
Central nervous system disorders	Drowsiness	3(2.5)	
	Dizziness	3(2.5)	
	Seizures	1(0.8)	
	Unconsciousness	2(1.7)	16(13.3)
	Irritability/ psychosis	3(2.5)	
	Extrapyramidal symptoms	2(1.7)	
General system disorders	Headache	2(1.7)	
	Pedal / general Oedema	8(6.7)	
	Facial puffiness	2(1.7)	13(10.3)
	Chills/rigors	2(1.7)	
Metabolism disorders	Fever	1(0.8)	
	Hypokalemia	5(4.2)	
	Hyperglycemia	1(0.8)	
	Hypoglycemia	3(2.5)	11(9.2)
	Lipodystrophy	1(0.8)	
Respiratory disorders	Gynaecomastia	1(0.8)	
	Dry Cough	2(1.7)	
	Orthopnea	1(0.8)	5(4.2)
Hepatobiliary disorders	Breathlessness	2(1.7)	
	Hepatitis/abnormal Liver function/hyperbilirubinemia/increase in liver Enzymes	4(3.3)	4(3.3)
Musculoskeletal system	Back pain	1(0.8)	
	Muscle cramps	2(1.7)	3(2.5)
Cardiac disorders	Palpitations	2(1.7)	2(1.7)
Renal and urinary disorders	Nephrotoxicity	2(1.7)	2(1.7)
Others	Tinnitus, anemia, thrombocytopenia, etc.	8(6.7)	8(6.7)

Table 4: Causality assessment and seriousness of ADRs

Category	Types	Number of ADRs [n (%)]	Serious	
			Fatal	0
Causality WHO- UMC Causality Assessment scale	Certain	0	Life-threatening	0
	Probable	58(48.3)	Required /Prolonged hospitalization	28(23.3)
	Possible	62(51.7)	Required intervention	33(27.5)
			Others	26(21.66)
Seriousness	Non- serious	33(27.5)		

Table 5: Severity and preventability assessment of ADRs

Category		Number of ADRs [n (%)]
Severity	Mild	73(60.8)
	Moderate	47(39.2)
Preventability	Probably preventable	60(50)
	Preventable	10(8.3)
	Unpreventable	50(41.7)

**Figure 2: Outcomes of ADRs**

Discussion

A retrospective analytical study was conducted during September 2016 and January 2018 to evaluate the prescribing pattern and ADRs in geriatric patients. Among the ADRs received in geriatric patients, we found male dominance (55.8 %) over females (44.2 %) as given in **Table 1**. Among the ADRs received in geriatric patients, 41 (34.2 %) patients were in between the age group of 60 and 64 years followed by 30 (25 %) patients were in the age group of 65 to 69 years, and showed in **Figure 1**. This was correlated with a similar study conducted in Bengaluru ([Nagaraju et al., 2015](#)). They have studied 50 elderly patients that determined most of the patients were in between the age group of 60 and 65 years. According to another study Veena et al, which showed contrast results to the present study in the dominance of male patients with 55.83 % over female patients (44.17 %) ([Veena et al., 2012](#)).

On analyzing the ADR forms received, polypharmacy is high in the elderly population which is a significant risk factor in the development of ADRs. The findings of this research were compared to those of a study conducted in Tamil Nadu by Mahesh et al., in which 56.53 percent of patients have prescribed 6-10 drugs, while 24 percent of geriatric patients were prescribed 9-12 drugs.

Suspected drugs to cause ADRs were tabulated category-wise in **Table 2**. Antibiotics (18.3 %) were the most reported drugs followed by anti-hypertensive drugs (13.3 %), analgesics (9.2 %), and Antitubercular drugs (8.3 %). The increased usage of antibiotics for various common infections promotes the risk of developing ADRs in elders.

Among the elder people, the usage of NSAIDs was high as these medications are available over the counter (OTC) for relieving the common pain disorders. Another research found that the most common drugs causing ADRs in geriatrics were cardiovascular drugs and antibiotics ([Sharma et al., 2007](#)).

The incidence of ADRs in the respective system was presented in **Table 3**. The greater part of the reported ADRs was of the gastrointestinal system (GIT) (31.7 %) which is due to administration of antibiotics and NSAIDs causing effects like diarrhea, constipation, gastritis, etc. The most affected systems next to GIT were skin (15.0 %), and the central nervous system (13.3 %). The causality assessment of ADRs was performed using the WHO causality assessment scale. It illustrated that in the greater part of cases, a causality relationship as belonging in the class of possible (51.7 %) and probable (48.3 %). On seriousness assessment of ADRs most of the ADRs reported were serious (72.5 %) followed by non-serious (27.5 %) and given in **Table 4**. Among all the patients affected with ADRs, most of the patients 50 (41.7 %) recovered from the symptoms, and 32 (26.7 %) were recovering and represented in **Figure 2**.

On severity assessment of ADRs using modified Hartwig-Sietzel scale. Mild and moderately severe cases in the present study were 60.8 % and 39.2 %. The majority of ADRs were mild in geriatric patients contrary to Pauldurai et al. study ([Pauldurai et al., 2015](#)). This is because the most commonly affected body system was the gastrointestinal system that includes mild reactions such as nausea, vomiting, and diarrhea for which stoppage of drugs and hospitalization is generally not required. 23.3 % cases were serious cases that required stopping of the suspect medication and required hospitalization/prolonged hospitalization and 27.5 % cases required intervention to prevent permanent damage. Antibiotics, diuretics, anticoagulants, hypoglycaemic agents, anticancer drugs, and NSAIDs are responsible for 60 % of ADRs that result in hospitalization and 70 % of ADRs that occur in hospitals ([Brahma et al., 2013](#)). The variability observed in the severity of the reported cases across various studies could be due to differences in the clinical settings and the difference in specialty healthcare services provided by different hospitals. It was observed that 50 % of the reported ADRs were probably preventable and the remaining 41.7 % were not preventable and given in **Table 5**. Preventability according to Schaumock and Toronto scale was mostly probably preventable in geriatric patients.

This was a retrospective analytical study, wherein all ADRs were reported spontaneously. We could analyze the reactions and suspected medications as notified in the reporting form. Details of all the concomitant medications used by geriatric patients for other ailments were lacking

in few ADR forms. Laboratory data was also lacking in few ADR reports. Inability to find incidence rate, underreporting, lack of follow-up data till recovery, lack of information about substituted drugs or treatment of ADRs, lack of information on recently introduced drugs, are the major limitations. A study designed prospectively may overcome such limitations.

Conclusions

The prevalence of ADRs is significant among hospitalized aged patients. In geriatric patients, polypharmacy is the risk factor for the cause of ADRs. Antibiotics are the major inappropriate prescribed class of drugs in patients and are the most common cause of ADRs in the geriatric population. Therefore, the implementation of antibiotic guidelines and strict adherence patterns is necessary to promote rational drug use. Spontaneous reporting of adverse drug reactions to pharmacovigilance centres and the active contribution of health care professionals in identifying the ADRs and bringing alerts could improve the circumstances in health care settings.

Conflict of interest

No conflicts of interest

Acknowledgments

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