

SPONTANEOUS REPORTING OF ADVERSE DRUG REACTIONS IN GERIATRIC PATIENTS IN INDIA

Background: In India, spontaneous reporting of adverse drug reactions (ADRs) by health-care professionals was initiated in 2010. The drug safety issues for geriatric population are critical due to age-related physiological, pharmacodynamic, and pharmacokinetic changes.

Aims & Objective: To assess the spontaneous reports of ADRs observed in geriatric patients (over 65 years of age) in India from 1 July 2011 to 31 June 2013.

Materials and Methods: The spontaneous reports of 4357 elderly patients (≥ 65 years) were retrieved at National Pharmacovigilance Centre from the database containing all ADR reports from 90 ADR Monitoring Centres (AMCs) in India under Pharmacovigilance Programme of India (PvPI) for 2 years. These reports were analyzed for various characteristics of patients, drugs, and ADRs using a search and analysis tool.

Results: Of the 4357 geriatric individual case safety reports, more ADRs were reported in the male (57.77%) than in the female (41.38%) patients. Of the total geriatric patients, ADRs reported from 1120 (25.71%) patients were found to be serious, of which 8 (0.71%) were fatal. Cisplatin, carboplatin, cyclophosphamide, acetylsalicylic acid, and insulin were the common drugs prescribed to the elderly patients, and the most common ADRs reported were vomiting, diarrhea, and constipation. In geriatric population, ADRs mostly affected gastrointestinal system and skin and appendages system.

Conclusion: This study from spontaneous reporting indicates the common ADRs in the geriatric patients in India, which will help health-care professionals to better understand the drug safety issues in elderly.

Key Words: Adverse Drug Reaction; Geriatric; India; Spontaneous Reporting

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INTRODUCTION

India is a vast country with diversity, both physically and culturally. As per census 2001, the geriatric population accounted for 7.4% of the total population, which increased to 8.2% by 2011 and is likely to be 10.7% by the year 2021.^[1,2] Drugs play a crucial role in geriatric health care as they treat chronic diseases, alleviate pain, and improve quality of life.^[3] About one-third of the elderly patients are hospitalized due to adverse drug reactions (ADRs),^[4,5] which have also reported to be among the leading causes of morbidity and mortality.^[6-8] Majority of type A adverse drug reactions (80%) contribute to morbidity and mortality.^[9,10] Majority of studies have shown that prevalence of ADRs is higher in the elderly than in the adults.^[11] Factors such as higher socioeconomic status, increased use of medications by the elderly, increased potential for drug-drug interactions, increased number of concurrent diseases patients suffered from, compliance to therapy by patients, and inappropriate prescribing were found to be significantly associated with the occurrence of ADRs in geriatric patients.^[12,13] An association between old age and increased rate of ADRs is established arising out of confounding association between age and polypharmacy contributed by age-related physiological, pharmacodynamic, and pharmacokinetic changes, which

affect drug handling, drug response, and sensitivity in these patients.^[9,14,15] Moreover, preventable ADRs were found to be more common in geriatric patients.^[16]

In various studies, the most common classes of drugs causing ADRs in geriatric population are found to be antidiabetics, nonsteroidal anti-inflammatory drugs, anticancer drugs, cardiovascular drugs, oral anticoagulants, and antiplatelets drugs,^[17-19] and the most common ADRs being edema, nausea or gastrointestinal disturbances, drowsiness or fatigue, headache, and nightmares.^[19,20]

At present, the prevalence of ADRs in geriatric population is very limited in India.^[21,22] This study aimed to identify ADRs in geriatric patients reported under Pharmacovigilance Programme of India (PvPI) and to establish evidence-based data to ensure the safe use of medicines in this population.

MATERIALS AND METHODS

A prospective observational study was carried out at National Coordination Centre-PvPI (NCC-PvPI), Indian Pharmacopoeia Commission, Ghaziabad, from July 2011 to June 2013 for the individual case safety reports (ICSRs) of the patients above 65 years of age, reported from 90

ADR Monitoring Centres (AMCs) under PvPI across India. In this study, data of 4357 elderly patients who reported ADRs to their nearest AMC were included. Data of each patient were collected using structured format. For details of each patient, an ADR form was completed with regard to patient age, sex, diagnosis, prescribed medications, daily doses, treatment durations, indications for each drug, ADR occurred, laboratory investigation reports, and history.

The details of each patient were then entered into a web-based WHO Global ICSR database "VigiBase" and sent to NCC-PvPI via Uppsala Monitoring Centre's ICSR management system "VigiFlow". At NCC, these reports were reviewed, evaluated, and further committed to the WHO Collaborating Centre for International Drug Monitoring, the Uppsala Monitoring Centre (WHO-UMC), Sweden. These 4357 committed reports were then analyzed for various characteristics of patients, drugs, and ADRs using search and analysis VigiBase tool "VigiLyze."

RESULTS

Of the total 50,490 ICSRs found under PvPI in the 2-year study of ADRs, 4,357 (8.63%) were reported by the geriatric patients from the 90 AMCs across India, of which 3,387 (77.74%) patients belong to the age group 65–74 years and the remaining 970 (22.26%) were 75 years or older. These 4,357 ICSRs had a total of 5,115 ADRs and 13,957 prescribed drugs.

Of the total 4357 ICSRs from geriatric patients, 2517 (57.77%) were reported from male patients and 1803 (41.38%) from female patients. Remaining 0.85% ICSRs were unknown. Sex distribution of ICSRs from geriatric patients is shown in Figure 1.

Of the total geriatric patients, 1120 (25.71%) were found to be having serious ADRs as compared to 2484 (57.01%) patients with nonserious ADRs (Figure 2). Remaining 17.28% were unknown. Of the total 1120 serious ICSRs, 8 (0.71%) were found to be fatal, 582 (51.96%) with prolonged hospitalization, 61 (5.45%) with life-threatening conditions, 48 (4.29%) with disability, 398 (35.54%) with other serious conditions, and 23 (2.05%) with unknown serious ADRs.

Gastrointestinal system disorders were found to be associated with 1246 ADRs, followed by skin and appendages disorders with 770 ADRs and central and peripheral nervous system disorders with 533 ADRs. The

system organ class of the reported ADRs is shown in Figure 3.

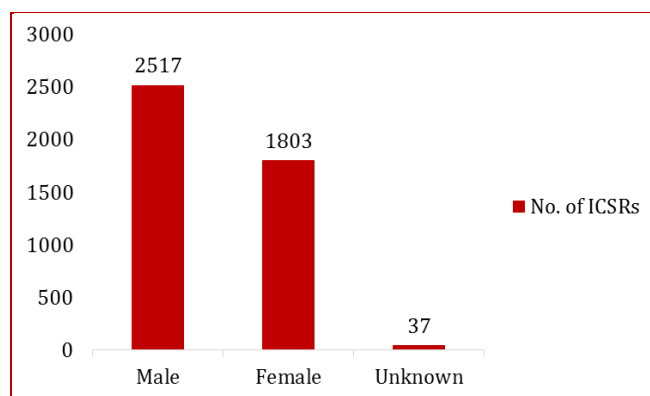


Figure-1: Gender distribution of ICSRs

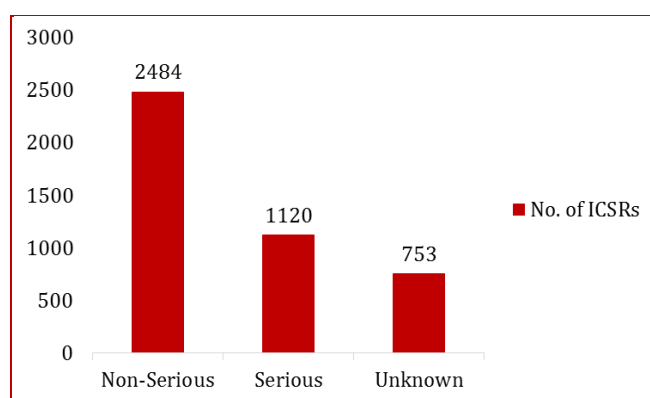


Figure-2: Serious vs Non-Serious

Total 4643 ADRs were found to be caused by the suspected drugs, of which vomiting (287), diarrhea (230), and constipation (189) were among the most common ADRs observed in this study. Among the 5997 suspected drugs prescribed to the patients, cisplatin was found to have caused maximum ADRs (334), followed by carboplatin (225) and cyclophosphamide (172). Table 1 shows the profile of top 10 drugs prescribed to the geriatric patients causing ADRs.

DISCUSSION

In our 2-year study from 2011 to 2013, ADRs reported under PvPI by the geriatric population were found to be 8.63%. Indian data contributed 1.73% of the geriatric ICSRs in the UMC Global database. The ADR reporting in this study was lower as compared to a similar 2-year study in Italy conducted by Cutroneo et al.,^[23] in which 21.7% ADRs from 1307 reports were found to be from geriatric patients.

In this study, more ADRs were reported in male patients than in female patients. In contrast, Conforti et al.^[24] reported higher ADRs in women than in men.

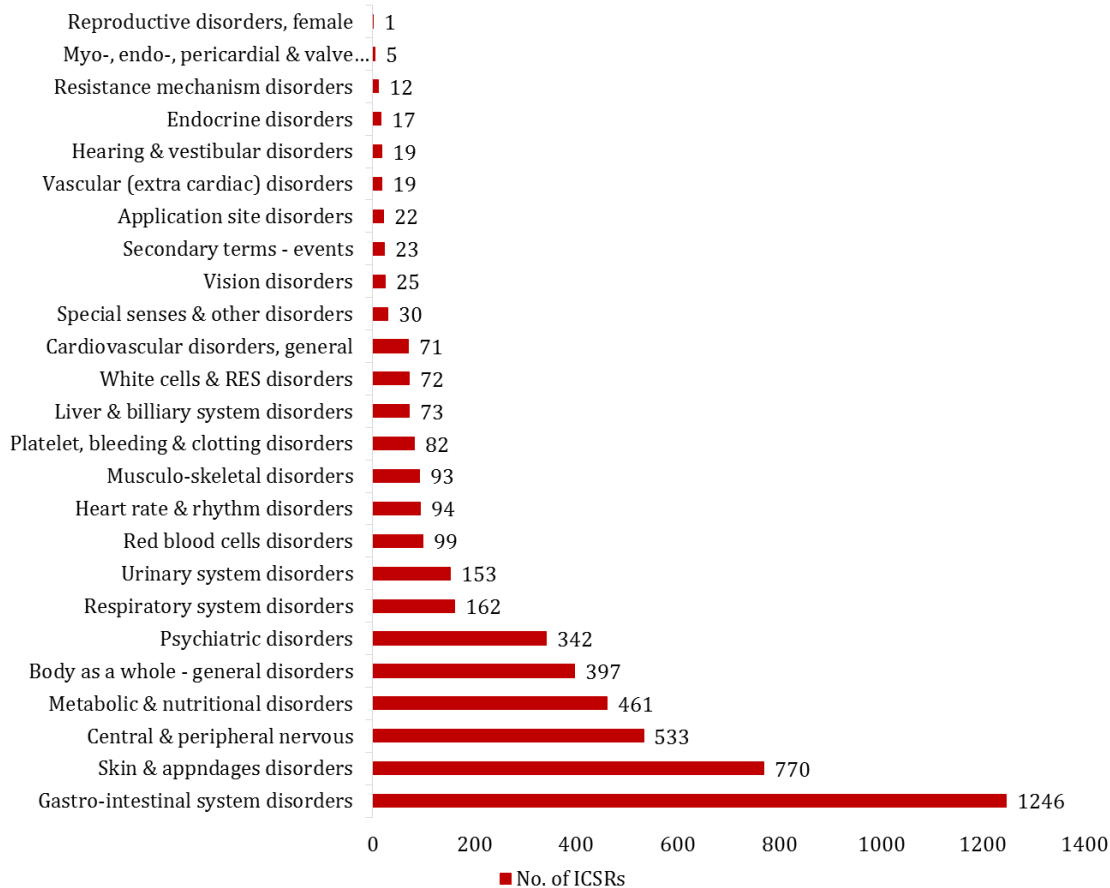


Figure-3: System organ class in reported ICSRs

Table-1: Top 10 drugs prescribed to the geriatric patients causing ADRs

No.	Top 10 Suspected Drugs	No. of ADRs	Most Common ADRs
1.	Cisplatin	334	Vomiting (68), Alopecia (39), Anorexia (29), Constipation (24), Diarrhoea (24), Fever (19), Anaemia (11)
2.	Carboplatin	225	Alopecia (41), Constipation (21), Vomiting (21), Anaemia (19), Anorexia (13), Leg pain (12), Myalgia (11), Diarrhoea (10)
3.	Cyclophosphamide	172	Alopecia (41), Nausea (17), Vomiting (13), Constipation (12), Leucopenia (10)
4.	Acetylsalicylic acid	134	Gastritis (8), Abdominal pain (13), GI haemorrhage (9)
5.	Insulin	128	Hypoglycaemia (93), Sweating increased (20),
6.	Amlodipine	113	Oedema peripheral (34), Oedema dependent (10), Hyponatraemia (8), Oedema(8), Constipation(6), Headache(6)
7.	Ceftriaxone	95	Diarrhoea (18), Vomiting (9), Rigors (7), Rash (6)
8.	Furosemide	81	Hyponatraemia (39), Hypokalaemia (18)
9.	Docetaxel	74	Anorexia (11), Diarrhoea (11), Alopecia (9), Constipation (7), Vomiting (7)
10.	Diclofenac	70	Gastritis (15), Rash (7), Abdominal pain (6)

Serious ADRs accounted for 25.71% of the total ADRs reported under PvPI, of which 0.71% were fatal. In this 2-year study, serious ADRs were found to be about four times and fatal ADRs about two times of the estimated serious and fatal ADRs in patients admitted to US hospitals, from a 30-year study conducted by Lazarou et al.^[7]

In this study, anticancer drugs were found to be among the top 10 drugs inducing ADRs in geriatric patients; cisplatin was the topmost causing maximum number of ADRs (334), which was about 7.1% of the total ADRs induced by the suspected drugs. The most common ADRs

induced by cisplatin include vomiting, alopecia, anorexia, constipation, and diarrhea. The second drug was carboplatin (with 225 ADRs) followed by cyclophosphamide (with 172 ADRs) most commonly causing alopecia, constipation, and vomiting. Prasad et al.^[25] studied the similar pattern of ADRs due to cancer chemotherapy in a 6-month study in eastern India and found that 87% patients receiving chemotherapy developed ADRs mainly due to cisplatin and cyclophosphamide, thereby commonly causing nausea and vomiting.

The most commonly observed ADR in this study was

vomiting, with about 6.2% of the total ADRs due to suspected drugs, followed by diarrhea (4.96%), constipation (4.07%), and hypoglycemia (3.70%). In most of the cases, gastrointestinal system was affected. Gurwitz et al.^[26] in a year study also reported gastrointestinal adverse events among the most common types of ADRs in the elderly. Another 18-year study of suspected ADRs reported to the Committee on Safety of Medicines in relation to patient age by Castleden and Pickles^[27] also showed gastrointestinal system to be the most common system affected by ADRs.

Elderly people are more prone to ADRs, possibly due to the changes in pharmacokinetics, pharmacodynamics, and homeostasis with the advancing age,^[28] which can alter drug absorption, distribution, metabolism, and excretion, thereby altering drug's effects.^[29]

CONCLUSION

Our study revealed the most commonly prescribed drugs and their adverse reactions in the geriatric population in India. This will help health-care professionals to better understand the patient safety while prescribing drugs to the elderly patients.

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