# Adverse drug reaction monitoring in geriatric patients of rural teaching hospital

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## ABSTRACT

*This Study was performed to monitor adverse drug reaction in geriatric patients in Medicine ward of Rajah Muthiah Medical College and Hospital. Demographic analyses of prospective study revealed that out of 520 patients, 342 (65.76%) were males and 178 (34.23%) were females. Study reveals that 56.53% of geriatric patients were prescribed 6-8 drugs for their treatment. The patientshad developed ADRwithin the age range of 65 to 69 years (39.17%) followed by 60 to 64 years (29.89%) , 24 patients (24.74%) of age 70 to 74years and 6 patients above 75years. The majority of ADR was hypoglycemia followed by sedation, rash, hard stool and swelling at injection site. It is evident that Antimicrobial agents were mainly suspected followed by cardiovascular drugs, Endocrine acting drugs.The causality assessment of ADRs was performed using WHO –UMC scale illustrate that in greater part of the cases, a causality relationship belongs to the class of 'probable' 68 (70.10%) and 'possible' 27 (27.83%) while 2(2.06%) cases was found to be 'certain'. After estimating the severity by Hart wig's scale, out of 97 ADRs, 11(19.29%) were severe, 39 (68.42%) were moderately severe, while 7(12.28%) were mild in nature. The implementation of antibiotic guidelines in hospital setting and severe adherence to encourage the rational use. Clinical pharmacist responsible for identifying the ADR and educating the healthcare professionals regarding the need of reporting the occurrence could improve ADR.*

**Keywords:** Adverse Drug Reaction, Geriatric Patients, the Causality Assessment WHO –UMC scale, Hart wig's scale, Rational use.
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## INTRODUCTION

WHO (2002) defines that 'Any response to a drug which is noxious and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function'.About one-third of the elderly patients are hospitalized due to adverse drug reactions (ADRs),[1-2] which have also reported to be amongst the most important reasons of morbidity and mortality. The majority of type adverse drug reactions (80%) contribute to morbidity and mortality.[3-5]**.**The majority of studies haverevealed that incidence of ADRs is higher in the olderthan adults [6, 7].

Although, the review of literature has revealed the need of Indian studies to recognize ADRs especiallyalong with Indian ambulatory older patients, one study performed with older inpatients has revealed that one-third of hospitalized older incident 419 ADRs. It has been deviated that older age is not a predictor for adverse drug

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reactions but simply a marker for co-morbidity, altered pharmacokinetics,[8] altered pharmacodynamics and polypharmacythe factors that are the majority constantly correlated with adverse drug reactions, polypharmacy is reflected on to be the most significant. In the older patients, the collection of disorders necessitates the use of numerous drugs. In adding, their modified pharmacokinetics and pharmacodynamics result in an increased sensitivity to many drugs[9]. Studies from out of the country as well as India have expressed that polypharmacy is common and correlated with raised potential for adverse drug reactions, inappropriate prescription and drug interactions [10-12].This study was aimed to identify ADRs and assess their causality and severity in hospitalized geriatric patients of a rural tertiary care hospital.

## MATERIALS AND METHODS

This prospective observational study was carried out in the Medicine ward of Rajah Muthiah Medical College and Hospital, Annamalai University during one year from January 2013 to January 2014.The research protocol was approved by Institutional Human Ethical Committee. The study included 520 hospitalized patients of geriatric age group (≥ 60years) of both sex. Demographic data, medical and medication history were collected from the patient's case sheet after getting consent from the patients. Then collected information was analyzed according to their age, gender and therapeutic category.

The study was conducted in both genders of geriatric patients. All the adverse drug reactions were established through an interview by the researcher were documented in the case record form with all needed information. Then recognize and documenting of the adverse drug reactions. The variance analysis of the reports, the judgment of the treating physician was also attained. The investigator was not the component of a treating group of the geriatric patient and was not engaged in any therapeutic decisions associated to the patients involved in thestudy. All suspected ADR were investigated thoroughly and causality relationship between the reaction and suspected drug was founded and confirmed by a physician.

All collected data were analyzed to discover (i) Incidence of patients rising ADE for the duration of therapy (ii) Age and gender sharing of information of ADEs (iii) System wise sharing of information of ADEs (iv) Causality assessment were used by WHO-UMC scale and Naranjo's probability score (v) Hart wig severity scale ofADEs usage.All collected data were scrutinized with the SPSS version 20 for data management and analyzes in the study. The socio-demographic data were calculated and expressed as percentages. The summarized results were arranged and put into a table form with the use of Microsoft word 2010.

## RESULTS AND DISSCUSSION

A total of 520 geriatric cases were collected from the Rajah Muthiah Medical College and Hospital. In our total study population 342(65.76%) cases were males and 178(34.23%) were females. Tabulated data of study population is given in Table-1.

Out of 520 geriatric patients,the majority of the elderly patients (38.84%) belongs to age group 60-64 years among that 123 were males and 79 were females followed by age group 65-69 years(29.23%) among them 99 were males and 53 were female and above75 years (12.11%) patients among them 45 were males 18 were females. 93% of geriatric patients belong to rural area and only 6.34% geriatric patients belong to urban area (Town). Most of the geriatric patients (95%) were illiterate, remaining 5% of geriatric patients were literate. A study done by MdRafiq Islam [13]in rural area of Bangladesh (n=300) showed that 61% were illiterate.93.84% of geriatric patients were married and 5.19% were widower. Only 0.38% of geriatric patients were never married.Geriatric patient's personal habits were observed that reveals 65.57% (n=341) of the patients used Tobacco products.59.03 % (n=307) of patients used alcohol and habit of smoking. 4.2% of patients had habit of smoking only. 1.53% patients used only alcohol.This study indicates that most prevalent diseases were cardiovascular diseases (28.26%) followed by Respiratory diseases (19.80%), Hepatic diseases (18.65%), Endocrine diseases (14.03%), Nervous diseases (7.85%), Gastrointestinal diseases (6.92%) and other diseases (4.42%).

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**Table 1: Characteristics of hospitalized geriatric patients**

| Characters | Number of Patients | Percentage (%) |
|---|---|---|
| **Gender** | | |
| Male | 342 | 65.76 |
| Female | 178 | 34.23 |
| **Age Groups** | | |
| 60 - 64 | 202 | 38.84 |
| 65 – 69 | 152 | 29.23 |
| 70 – 74 | 103 | 19.80 |
| ≥ 75 | 63 | 12.11 |
| **Demographic Status** | | |
| Urban | 33 | 6.34 |
| Rural | 487 | 93.65 |
| **Literacy Status** | | |
| Illiterate | 494 | 95 |
| literate | 26 | 5 |
| **Marital Status** | | |
| Never married | 2 | 0.38 |
| Separated | 3 | 0.57 |
| Widow | 27 | 5.19 |
| Married | 488 | 93.84 |
| **Therapeutic Category** | | |
| Cardiovascular System | 147 | 28.26 |
| Respiratory System | 103 | 19.80 |
| Hepatic System | 97 | 18.65 |
| Endocrine system | 73 | 14.03 |
| Nervous System | 41 | 7.85 |
| Gastrointestinal System | 36 | 6.92 |
| Others | 23 | 4.42 |
| **Number of drugs Prescribed** | | |
| ≤ 5 | 61 | 11.73 |
| 6 - 8 | 294 | 56.53 |
| 9 – 12 | 124 | 23.84 |
| > 12 | 41 | 7.88 |

The majority of patients in our study had co morbid conditions. The prevalent co morbidities in our study are very similar to the ones reported in another Indian study.[14]Loss of functional reserve with aging makes geriatric patients vulnerable to the development of multiple diseases affecting different body systems. The presence of co morbidities means that multiple and complex drug therapy is required and thus the chances of ADRs and drug interactions are greater. The study reveals that 56.53% of geriatric patients were prescribed   6-8 drugs for their treatment of diseases followed by 9-12 drugs (23.84%), ≤ 5 drugs(11.73%) and >12 drugs (7.88%).Poly pharmacy unfortunately is very common in India[15] and some other countries[16-18].It results in increased cost of treatment, which may lead to non-adherence by patients as they have more medicines than they can cope with. It also increases the risk of significant adverse drug interaction.

**Table-2: Gender wise distribution of ADR**

| Gender | Number of ADR | Percentage (%) |
|---|---|---|
| Male | 71 | 73.19 |
| Female | 26 | 26.80 |

**Table-3: Age wise distribution of ADR**

| Age Groups | Number of ADR | Percentage (%) |
|---|---|---|
| 60 - 64 | 29 | 29.89 |
| 65 – 69 | 38 | 39.17 |
| 70 – 74 | 24 | 24.74 |
| ≥ 75 | 6 | 6.18 |

National Pharmacovigilance Programme of India has been in place since January 2005. Among various people, the Geriatric population is the most vulnerable to the development of ADRs for the obvious reasons. In the present study explain that 97 out of 520 geriatric patients (18.65%) developed ADRs. On one hand, it is higher than the reported incidence of ADRs of 3-6% in general population [19]and, it ishigher than that found in geriatric patients from UK

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(14.7) [20]and on the other hand it is lesser than USA and Europe (20%).Several factors – genetic, ethnic, dietary, environmental, or simply less reporting of ADRsby patients may account for this relatively lower rate of ADRs among Indian geriatric patients. Out of total 520patients, 97 patients (18.65%) developed ADRs. 71 (73.19%) were male and 26 (26.80%) were Female. More incidences of ADR are in male than female. Several studies have found that ADRs are more common in females than in males. (Table- 2).

Most of the patients belong within the age range of 65 to 69 years (39.17%) n=38 followed by that of 60 to 64 years (29.89%) n=29. Only 24 patients (24.74%) the age of 70 to 74years and 6 patients above 75years age had developed ADR. (Table-3)

**Table-4: Adverse drug reactions observed from geriatric patients**

| Drugs | Adverse Drug Reaction | Number of Patients |
|---|---|---|
| Insulin | Hypoglycemia | 5 |
|  | Sweating Increased | 3 |
| Digoxin | Palpitation | 2 |
| Amitriptyline | Blurred Vision | 1 |
|  | Dryness Of Mouth | 3 |
| Chlorpheniramine Maleate | Sedation | 4 |
| Enalapril | Cough | 3 |
|  | Hypotension | 2 |
| Atenolol | Bradycardia | 2 |
| Gentamycin | Tinnitus | 1 |
| Furosemide | HyponatraemiaHypokalaemia | 2 |
|  |  | 3 |
| Alprazolam | Sedation | 3 |
| Diclofenac Sodium | Rash | 4 |
|  | Abdominal Pain | 3 |
| Ceftriaxone | Diarrhoea | 2 |
|  | Vomiting | 2 |
|  | Rash | 3 |
|  | Swelling at injection site | 4 |
| Amlodipine | Oedema Peripheral | 3 |
|  | Constipation | 1 |
|  | Headache | 2 |
| Ferrous Supplement | Constipation | 3 |
| Aspirin, | Gastritis | 3 |
| Isosorbide Mononitrate | Headache | 3 |
| Metformin | Giddiness | 3 |
| Heparin | Haematuria | 1 |
| Atorvastatin | Muscle Spasm | 2 |
| Clopidogrel | Giddiness | 3 |
|  | Cough | 2 |
| Diazepam | Dizziness | 3 |
| Spironolactone | GI Upset | 1 |
| Promethazine | Swelling at injection site | 2 |
| Metronidazole | Dizziness | 2 |
| Ampicillin | Diarrhea | 2 |
| Ondansetron | Constipation | 2 |
| Cremaffin Syrup | Hard stool | 4 |
| Pantoprazole | Gastritis | 1 |
| Ofloxacin | Vomiting | 2 |

The majority of ADR was Hypoglycemia and followed by Sedation, Rash, hard stool and swelling at injection site. All other ADRs were noted in the Table-4.

28 drugs were suspected the cause of the reported ADRs. Suspected drugs are revealed in a grouping wise way in table-5.33. It is evident that Antimicrobial agents were the mainly frequently suspected drugs go behind by cardiovascular drugs, Endocrine system acting drugs.Another study from India[21]found that cardiovascular drugs and antimicrobials were the commonest drugs leading to ADR in elderly. A study from the UK[22]showed that most frequently implicated drug groups causing ADRs in elderly were loop diuretics, opioids, steroids, anticoagulants, and antimicrobials. Thus, cardiovascular drugs and antimicrobials were figured as two of the commonest drug groups causing ADRs in elderly.

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**Table-5: Drug categories and drugs causing ADR**

| S.No | Drug Categories | Name of Drugs |
|---|---|---|
| 1. | Antibiotics | Ofloxacin, Ceftriaxone, Metronidazole Ampicillin , Gentamycin |
| 2. | NSAIDS | Diclofenac Sodium, Aspirin |
| 3. | Antidiabetics | Metformin, Insulin,Glimepiride |
| 4. | Antihypertensive | Amlodipine, Enalapril |
| 5. | Selective B1 Receptor Antagonist | Atenolol |
| 6. | Angina drug | Isosorbide mononitrate |
| 7. | Diuretics | Furosemide, Spironolactone |
| 8. | Anti-Histamine | Chlorpheniramine  Maleate |
| 9. | Antiarrhythmic | Digoxin |
| 10. | Anti-Depressant | Amitriptyline |
| 11. | Vitamins& Minerals | Ferrous sulphate |
| 12. | Anticoagulant | Heparin |
| 13. | Cholesterol-Lowering Agent | Atorvastatin |
| 14. | Stool Softener Agent | Cremaffin Syrup |
| 15. | Anti-Emetic | Ondansetron |
| 16. | Anti-Anxiety | Diazepam |
| 17. | Anti-Platelet | Clopidogrel |
| 18. | Anti-Psychotic | Promethazine |
| 19. | Proton Pump Inhibitor | Pantoprazole |

**Table-6: Body System with ADR**

| S.No | Body system | ADR | Number of ADR | Percentage(%) |
|---|---|---|---|---|
| 1 | Cardiovascular system | Hypotension<br>Palpitation<br>Bradycardia | 2<br>2<br>2 | 6 | 6.18 |
| 2 | Gastrointestinal system | Dryness Of Mouth<br>Gastritis<br>Diarrhea<br>Vomiting<br>Abdominal Pain<br>Constipation<br>GI Upset<br>Hard stoo | 3<br>4<br>4<br>4<br>3<br>6<br>1<br>4 | 29 | 29.89 |
| 3 | Endocrine system | Hypoglycaemia | 5 | 5 | 5.15 |
| 4 | Dermatological system | Rash | 7 | 7 | 7.21 |
| 5 | ENT | Tinnitus | 1 | 1 | 1.03 |
| 6 | Respiratory system | Cough | 5 | 5 | 5.15 |
| 7 | Hematology | Hyponatraemia | 2 | 2 | 2.06 |
| 8 | Musculoskeletal system | Swelling At Injection Site<br>Oedema Peripheral<br>Muscle Spasm | 6<br>3<br>2 | 11 | 11.34 |
| 9 | Diuretic system | Hypokalaemia<br>Haematuria | 3<br>1 | 4 | 4.12 |
| 10 | Central nervous system | Sweating Increased<br>Headache<br>Sedation<br>Dizziness<br>Giddiness | 3<br>5<br>7<br>5<br>6 | 26 | 26.80 |
| 11 | Ophthalmology | Blurred Vision | 1 | 1 | 1.03 |

The incidence of an individual event in the respective systems is revealed in table-6. The greater part of reported adverse drug events had influenced in  gastrointestinal system (29) followed by Central nervous system (26), musculoskeletal system (11), Dermatological system (7), Cardiovascular system (6), Endocrine system and Respiratory system  (5) , Diuretic system (4), Hematologic system (2).  The least affected systems were ENT, and Ophthalmology (1 each). These findings are similar to those in another Indian study[21].

**Causality Assessment of ADR**
The Causality analysis of ADRs is done by using either WHO-UMC criteria or Naranjo's scale. However, there are very few studies wherein causality analysis of ADRs in geriatric patients has been carried out by both methods used concurrently. In this study, the researcher carried out causality assessment using both the methods with the view to find whether there is any difference in assessment outcome by both methods. Researcher has found that there was no

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significant difference (p>0.05) in the assessment result by both methods and thus both methods evaluate the causality assessment equally. (Table-7)

**Table-7: Causality Assessment of ADR**

| Causality Category | WHO – UMC scale Number of ADR (%) | Naranjo Scale Number of ADR (%) |
|---|---|---|
| Certain/ Definite | 2(2.06) | 0 |
| Probable | 68(70.10) | 68 (70.10) |
| Possible | 27 (27.83) | 29(29.89) |
| Unlikely | 0 | 0 |
| conditional /Unclassifiable | 0 | NA |
| Total | 97 (100) | 97 (100) |

The causality assessment of the ADRs was performed using both the WHO – UMC criteria and Naranjo's scale. The analysis using WHO –UMC scale illustrate that in greater part of the cases, a causality relationship was belonging in the class of 'probable' 68 (70.10%) and 'possible' 27 (27.83%) while in 2(2.06%) cases it was found to be 'certain'. No case fell in the category of unlikely/doubtful and conditional/unclassifiable (Table-7). Causality was also assessed using Naranjo's algorithm. This is an objective questionnaire-based method of evaluation. The common association was of probable 68 (70.10%) and possible 29 (29.89%) categories by this method. No statistically significant difference was found in causality analyzes by both the methods (p>0.05).

**Severity of ADR (Hart wig Scale)**
The results of causality assessment are to rate the rigorousness of a specified ADR. For this reason, the most regularly and greatest scale is Hart wig's scale. Though the constraint of the scale is that, in a certain case of ADR the level of severity can be owed only at the ending result. This diminishes the use of scale to an academic use only. We have still utilized the scale to learn the outline of the severity level of ADRs in older patients. We examined that almost two-thirds of the geriatric patients (68.42%) who occurrence ADR were at level 3 or 4 meaning that they have need of admission to the hospital for treating of ADR, or duration of hospital stay by at least a day in case of previously hospitalized patients and need of either an antidote or interventional treatment. One fifth of the patients (19.29%) necessitated direct admission to ICU or undergoes permanent injury or fatality that is level 5 or 6 or 7 of Hart wig's scale. If these results are explained, we can believe a related scenario in other older patients who are on drug remedy. We need to exercise prudence and bring under control in prescribing in older patients, identify the incidence of ADRs at the initial stage or at least be ready to get ready for meeting the circumstances efficiently.

**Table-8: Severity of ADR (Hart wig Scale)**

| Severity | Levels | Number of ADR | Total (%) |
|---|---|---|---|
| Mild | 1 | 5(5.15) | 20 (20.61) |
| | 2 | 15(15.46) | |
| Moderate | 3 | 57(58.76) | 74 (76.28) |
| | 4 | 17 (17.52) | |
| Severe | 5 | 3(3.09) | 3 (3.09) |
| | 6 | 0 | |
| | 7 | 0 | |

After the estimating the severity assessment by Hart wig scale, out of 97 adverse drug reactions, 11(19.29%) were severe, 39 (68.42%) were moderate, while 7(12.28%) were mild in nature. (Table-8).This estimation indicates that most of the ADR were moderate level, it may be overcome through effective health care team.

## CONCLUSION

Adverse Drug Reactions are one of the drug-related problems in the hospital background and are a confront for making sure drug safety. Antibiotics embrace the major number of the drug family and inpatient prescriptions and thus are the majority unreasonably prescribed drug class. So, the implementation of antibiotic guidelines for the hospital setting and severe adherence should makes sure to encourage the rational use. The development and use of clinical decision support systems can promote rational antibiotic use. The health system should encourage the spontaneous reporting of Adverse Drug Reactions to antibiotics and other drugs, suitable documenting and periodic reporting to regional Pharmacovigilance centres to make sure drug safety. The energetic contribution of a well-

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trained clinical pharmacist for identify the Adverse Drug Reactions and bring the alertness classes for the healthcare professionals as regards the need of reporting the occurrence could improve the circumstances in underneath-reported hospitals.

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