

Analysis of Drug Classes Associated with Serious Adverse Drug Reactions Leading to Hospital Admission

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Abstract:

Background: Serious adverse drug reactions (ADRs) are a significant cause of morbidity, mortality, and hospital admissions worldwide, imposing substantial clinical and economic burden on healthcare systems.

Aim: To evaluate the pattern of serious ADRs requiring hospitalization, identify commonly implicated drugs, assess causality, and determine clinical outcomes.

Methodology: A hospital-based retrospective observational study was conducted at the Department of Pharmacology, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India, over six months. A total of 80 serious ADR cases reported to the Adverse Drug Reaction Monitoring Centre were analyzed. Causality was assessed using the WHO-UMC scale, and severity and outcomes were evaluated using standard criteria. Data were analyzed using descriptive statistics.

Results: The majority of patients were aged 41–60 years (35%) and male (57.5%). Cutaneous reactions (27.5%) were the most common, followed by gastrointestinal (20%) and hematological (15%) manifestations. Antibiotics (32.5%) were the leading causative drug class. Most ADRs were categorized as probable (47.5%). Recovery was observed in 77.5% of patients, while mortality occurred in 5%.

Conclusion: Serious ADRs predominantly affected middle-aged adults, with antibiotics being the principal contributors. Strengthened pharmacovigilance and rational prescribing are essential to reduce hospitalization and adverse outcomes.

Keywords: Adverse drug reactions, Hospitalization, Pharmacovigilance, Antibiotics, Causality assessment.

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Introduction

Serious adverse drug reactions (ADRs) constitute a major global public health concern and are increasingly recognized as a significant cause of morbidity, mortality, and healthcare utilization [1]. The World Health Organization defines an adverse drug reaction as a noxious and unintended response to a medicinal product occurring at doses normally used in humans for prophylaxis, diagnosis, therapy, or modification of physiological function. A serious ADR is one that results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, leads to persistent or significant disability, or results in a congenital anomaly [2]. Among these outcomes, hospitalization represents a critical indicator of severity, reflecting not only the clinical impact of the reaction but also its economic and systemic burden on healthcare services.

Hospital admissions due to ADRs account for a substantial proportion of emergency visits and inpatient stays worldwide [3]. Studies from both developed and developing countries suggest that a considerable percentage of hospitalizations are either directly caused by ADRs or complicated by drug-related events during treatment. The pattern of serious ADRs requiring hospitalization varies depending on demographic characteristics, disease prevalence, prescribing practices, availability of medicines, and pharmacogenetic differences within populations. Elderly patients, children, and individuals with multiple comorbidities are particularly vulnerable due to polypharmacy, altered pharmacokinetics, and impaired organ function [4]. In addition, the increasing use of high-risk medications such as anticoagulants, antineoplastic agents, antiepileptics, antibiotics, and cardiovascular drugs has contributed to the rising incidence of severe drug-related complications.

Understanding the pattern of serious ADRs necessitates systematic pharmacovigilance and robust reporting mechanisms [5]. The Uppsala Monitoring Centre, functioning as a WHO Collaborating Centre for International Drug Monitoring, plays a pivotal role in collecting, analyzing, and disseminating global ADR data. Through the international database VigiBase, it supports signal detection and risk assessment. At the national level, pharmacovigilance programs aim to identify trends in drug safety, detect rare but severe reactions, and implement regulatory measures to minimize harm. Despite these systems, underreporting remains a persistent challenge, particularly in low- and middle-income countries, limiting the comprehensive assessment of ADR burden [6].

Serious ADRs leading to hospitalization often involve specific organ systems [7]. Cutaneous reactions such as Stevens–Johnson syndrome and toxic epidermal necrolysis, hematological abnormalities including aplastic anemia and severe thrombocytopenia, hepatotoxicity, nephrotoxicity, and anaphylactic reactions are commonly implicated. Drug-induced hypoglycemia, bleeding complications from anticoagulants, and electrolyte disturbances also frequently necessitate emergency care. The pattern may further be influenced by inappropriate prescribing, drug–drug interactions, medication errors, and lack of patient awareness regarding potential side effects. Preventable ADRs, which arise from incorrect dosing, failure to consider contraindications, or inadequate monitoring, represent a significant proportion of hospital admissions, highlighting the need for rational prescribing and patient education [8].

The economic burden associated with serious ADRs is substantial. Hospitalization increases direct medical costs due to diagnostic investigations, therapeutic interventions, prolonged hospital stays, and intensive care requirements [9]. Indirect costs include loss of productivity, long-term disability, and increased caregiver burden. Beyond financial implications, serious ADRs erode patient trust in healthcare systems and may lead to poor adherence to essential medications. Therefore, identifying patterns of serious ADRs requiring hospitalization is essential for developing targeted preventive strategies, optimizing pharmacotherapy, and enhancing patient safety [10].

In recent years, advances in clinical pharmacology, pharmacogenomics, and electronic health records have provided new opportunities for early detection and risk stratification of ADRs. Risk assessment tools, medication reconciliation practices, and active surveillance models have shown promise in reducing preventable drug-related admissions. However, variations in healthcare infrastructure, reporting culture, and regulatory enforcement continue to influence the accuracy and completeness of ADR data across regions.

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A systematic evaluation of the pattern of serious ADRs requiring hospitalization offers valuable insights into high-risk drugs, susceptible populations, and common clinical manifestations. Such analysis facilitates evidence-based interventions, strengthens pharmacovigilance frameworks, and informs policy decisions aimed at improving medication safety. In the context of evolving therapeutic modalities and expanding pharmaceutical markets, continuous monitoring and research are imperative to mitigate the impact of severe drug-related harm. Hence, studying the epidemiological and clinical profile of serious ADRs leading to hospitalization remains a critical priority for clinicians, researchers, and health authorities committed to ensuring safer pharmacotherapy and reducing avoidable healthcare burdens.

Methodology

Study Design: This study was designed as a hospital-based retrospective observational study conducted to evaluate the pattern of serious adverse drug reactions (ADRs) requiring hospitalization. The study aimed to systematically analyze reported serious ADR cases, identify commonly implicated drugs, assess causality, severity, preventability, and evaluate clinical outcomes among hospitalized patients.

Study Area: The study was carried out in the Department of Pharmacology, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India.

Study Duration: The study was conducted over a period of six months from April 2025 to September 2025

Study Participants

Inclusion Criteria

- Patients of all age groups and either gender who experienced serious adverse drug reactions requiring hospitalization.
- ADRs reported to the AMC during the study period.
- Cases classified as serious according to WHO criteria (resulting in hospitalization, prolongation of hospital stay, life-threatening events, disability, or death).
- ADRs categorized as certain, probable, or possible according to WHO causality assessment scale.

Exclusion Criteria

- Non-serious ADRs not requiring hospitalization.
- ADRs with incomplete or insufficient clinical data for assessment.
- Cases categorized as unlikely according to WHO causality assessment.

- Reactions attributed to drug overdose, medication errors, or intentional self-harm.

Sample Size: A total of 80 patients who fulfilled the inclusion criteria were included in the study.

Procedure: Data were collected from Individual Case Safety Reports (ICSRs) submitted to the Adverse Drug Reaction Monitoring Centre. Each case record was thoroughly reviewed for demographic details including age and gender, clinical diagnosis, suspected drug(s), indication for drug use, dosage, route of administration, duration of therapy, time interval between drug intake and onset of reaction, and past history of drug allergy.

Serious ADRs were defined according to the World Health Organization (WHO) definition. Only those reactions that occurred after drug administration and showed clinical improvement following withdrawal (dechallenge) of the suspected drug were considered. Rechallenge was not performed in any case due to ethical considerations.

Causality assessment was carried out using the WHO-UMC causality assessment scale, categorizing reactions as certain, probable, possible, or unlikely. Only certain, probable, and possible cases were included in the final analysis. Severity of ADRs was assessed using the Modified Hartwig and Siegel Scale, and preventability was evaluated using the Modified Schumock and Thornton criteria.

ADRs were further classified based on the affected organ system, pharmacological class of the suspected drug, and clinical outcome (recovery,

prolonged hospitalization, complications, or death). The pattern of ADRs was analyzed to determine the most frequently implicated drug groups and the nature of serious reactions leading to hospitalization.

Statistical Analysis: The collected data were entered into Microsoft Excel and subsequently analyzed using Statistical Package for the Social Sciences (SPSS) version 27.0. Descriptive statistics such as frequency, percentage, mean, and standard deviation were used to summarize demographic characteristics and ADR patterns. Categorical variables were expressed as proportions and percentages. Where applicable, inferential statistical tests such as Chi-square test were applied to determine associations between variables. A p-value of less than 0.05 was considered statistically significant.

Result

Table 1 shows the distribution of study participants according to age group among the total sample of 80 individuals. The highest proportion of participants belonged to the 41–60 years age group, comprising 28 individuals (35%), indicating that middle-aged adults formed the majority of the study population. This was followed by the 19–40 years age group with 24 participants (30%), reflecting a substantial representation of young adults. Participants aged more than 60 years accounted for 18 individuals (22.5%), while the least represented group was those aged 18 years or younger, with 10 participants (12.5%). Overall, the data suggest that the study population was predominantly composed of adults between 19 and 60 years of age.

| Age Group (Years) | Frequency (n) | Percentage (%) |
|-------------------|---------------|----------------|
| ≤18 | 10 | 12.5 |
| 19–40 | 24 | 30 |
| 41–60 | 28 | 35 |
| >60 | 18 | 22.5 |
| Total | 80 | 100 |

Table 2 shows the distribution of study participants according to gender among the total sample of 80 individuals. Out of the total participants, 46 were males, accounting for 57.5% of the study population, while 34 were females, representing 42.5%. This indicates that male participants constituted the

majority in the present study, with a difference of 15% compared to female participants. Overall, the gender distribution demonstrates a relatively higher representation of males than females in the study sample.

| Gender | Frequency (n) | Percentage (%) |
|--------------|---------------|----------------|
| Male | 46 | 57.5 |
| Female | 34 | 42.5 |
| Total | 80 | 100 |

Table 3 shows the distribution of serious adverse drug reactions (ADRs) according to the organ system affected among 80 cases. The majority of

serious ADRs involved the cutaneous system, accounting for 22 cases (27.5%), indicating that skin-related reactions were the most common

presentation. This was followed by gastrointestinal involvement in 16 cases (20%), and hematological reactions in 12 cases (15%). Hepatic complications were observed in 10 cases (12.5%), while renal system involvement was noted in 8 cases (10%). Cardiovascular ADRs constituted 7 cases (8.8%). A

smaller proportion of cases (5; 6.2%) were categorized under other systems. Overall, the findings suggest that cutaneous and gastrointestinal systems were the most frequently affected organ systems in serious ADRs within the study population.

| Organ System Affected | Frequency (n) | Percentage (%) |
|-----------------------|---------------|----------------|
| Cutaneous | 22 | 27.5 |
| Gastrointestinal | 16 | 20 |
| Hematological | 12 | 15 |
| Hepatic | 10 | 12.5 |
| Renal | 8 | 10 |
| Cardiovascular | 7 | 8.8 |
| Others | 5 | 6.2 |
| Total | 80 | 100 |

Table 4 shows that out of 80 serious adverse drug reactions (ADRs), antibiotics were the most frequently implicated drug class, accounting for 26 cases (32.5%), indicating they are the leading contributors to serious ADRs in this dataset. Antiepileptics were the second most common, responsible for 12 cases (15%), followed by NSAIDs with 10 cases (12.5%). Antitubercular drugs and anticancer drugs

contributed 9 (11.3%) and 8 (10%) cases respectively, while antidiabetics accounted for 6 cases (7.5%). The remaining 9 cases (11.2%) were attributed to other drug classes. Overall, the distribution suggests that antibiotics and antiepileptics together make up nearly half of the serious ADRs reported, highlighting the need for careful monitoring of these medications.

| Drug Class | Frequency (n) | Percentage (%) |
|----------------------|---------------|----------------|
| Antibiotics | 26 | 32.5 |
| Antiepileptics | 12 | 15 |
| NSAIDs | 10 | 12.5 |
| Antitubercular Drugs | 9 | 11.3 |
| Anticancer Drugs | 8 | 10 |
| Antidiabetics | 6 | 7.5 |
| Others | 9 | 11.2 |
| Total | 80 | 100 |

Table 5 shows the distribution of serious adverse drug reactions (ADRs) according to causality assessment based on the WHO-UMC scale and their clinical outcomes among 80 patients. Under causality assessment, the majority of ADRs were categorized as probable (38 cases, 47.5%), followed by possible (28 cases, 35%), while 14 cases (17.5%) were classified as certain, indicating a substantial proportion with a strong or reasonable temporal relationship to the suspected drug. Regarding clinical outcomes, most patients recovered completely (62

cases, 77.5%), and 8 patients (10%) were in the process of recovering at the time of assessment. However, 6 patients (7.5%) experienced prolonged hospital stay due to the severity of the reaction, and 4 cases (5%) resulted in death. Overall, the findings suggest that although most serious ADRs had favorable outcomes, a notable proportion led to significant morbidity and mortality, highlighting the need for vigilant pharmacovigilance and timely intervention.

| A. Causality Assessment (WHO-UMC Scale) | | |
|--|----------------------|-----------------------|
| Causality Category | Frequency (n) | Percentage (%) |
| Certain | 14 | 17.5 |
| Probable | 38 | 47.5 |
| Possible | 28 | 35 |
| Total | 80 | 100 |
| B. Clinical Outcome | | |
| Outcome | Frequency (n) | Percentage (%) |
| Recovered | 62 | 77.5 |
| Recovering | 8 | 10 |
| Prolonged Hospital Stay | 6 | 7.5 |
| Death | 4 | 5 |
| Total | 80 | 100 |

Discussion

The present study analyzed the pattern of serious adverse drug reactions (ADRs) requiring hospitalization among 80 patients and demonstrated that adults in the 41–60 years age group (35%) were most commonly affected, followed by those aged 19–40 years (30%). Together, these age groups constituted 65% of the total cases, indicating that the economically productive population is disproportionately impacted. A similar predominance of adults has been reported by Prajapati et al. (2016) [11], who observed that the majority of serious ADRs occurred in adults, accounting for approximately 62% of cases. In contrast, Arulmani et al. (2008) [12] reported relatively higher involvement of pediatric (17.3%) and geriatric (14.4%) populations, which differs from our findings where pediatric patients constituted only 12.5% and elderly patients 22.5%. The relatively lower pediatric proportion in our study may reflect cautious prescribing practices and lower drug exposure in children, whereas the notable representation of elderly patients aligns with known pharmacokinetic and pharmacodynamic changes in this age group.

With regard to gender distribution, our study demonstrated male predominance (57.5%) compared to females (42.5%). This observation is consistent with the findings of Prajapati et al. (2016), who reported 58% male predominance. However, it contrasts with Arulmani et al. (2008), where females constituted 64.5% of ADR cases. The variation in gender distribution across studies may be attributed to differences in healthcare utilization patterns, sociocultural factors, and prescribing trends. Our findings suggest that although males were slightly more affected, serious ADRs remain a significant concern for both genders, emphasizing the need for inclusive pharmacovigilance practices as advocated by Singh and Kanase (2017) [13].

In the present study, cutaneous manifestations were the most frequently affected organ system (27.5%), followed by gastrointestinal (20%) and hematological (15%) systems. The predominance of

dermatological reactions is comparable to the findings of Prajapati et al. (2016), who also reported skin as the most commonly involved organ system (approximately 34%) (Reference 3). Similarly, Arulmani et al. (2008) documented dermatological involvement in 36% of ADR cases (Reference 6). However, studies by Sriram et al. (2011) [14] and Kamalaraj et al. (2012) [15] reported gastrointestinal system involvement as the most common (around 28–30%), which contrasts with our findings. These differences may reflect variability in prescribing patterns, study populations, and reporting practices. Hematological and hepatic ADRs in our study (together 27.5%) highlight the potential severity of systemic drug toxicity, consistent with multicentric data reported by Barvaliya et al. (2011) [16], who emphasized the life-threatening nature of severe cutaneous ADRs such as Stevens–Johnson syndrome and toxic epidermal necrolysis.

Antibiotics were the leading causative drug class in our study (32.5%), followed by antiepileptics (15%) and NSAIDs (12.5%). This pattern aligns closely with Prajapati et al. (2016), who reported antimicrobials as the most common offending agents (about 35%), followed by antiepileptics. Arulmani et al. (2008) also identified antimicrobials as a major contributor to ADRs. Conversely, some studies have demonstrated a predominance of antitubercular therapy (ATT) and antiretroviral therapy (ART) in causing serious ADRs, particularly in settings with high tuberculosis and HIV burden. In our study, antitubercular drugs accounted for 11.3% and anticancer drugs for 10% of cases, indicating their significant yet comparatively lower contribution. The high proportion of antibiotic-related ADRs in our findings underscores the importance of rational prescribing and antimicrobial stewardship, as emphasized under the Pharmacovigilance Programme of India.

Causality assessment in our study revealed that 47.5% of ADRs were categorized as probable, 35% as possible, and 17.5% as certain according to WHO-UMC criteria. This distribution is comparable to findings by Prajapati et al. (2016), where probable

reactions constituted the majority (around 50%). Similar observations were reported by Sriram et al. (2011). The predominance of probable cases reflects strong temporal associations but limited rechallenge due to ethical concerns. Preventability assessment principles proposed by Schumock and Thornton 1992 [17], though earlier, remain foundational in understanding avoidable ADRs. Our findings suggest that while many reactions may not be entirely preventable, early recognition and intervention can mitigate severity.

Regarding outcomes, 77.5% of patients recovered completely and 10% were recovering, which is comparable to recovery rates of 70–80% reported in similar tertiary care studies. However, 7.5% experienced prolonged hospitalization and 5% resulted in mortality, underscoring the potential life-threatening nature of serious ADRs. Severe cutaneous reactions with high SCORTEN scores have been associated with increased mortality, as reported by Barvaliya et al. (2011), reinforcing the clinical significance of early detection and aggressive management.

Overall, the findings of the present study are largely consistent with Indian tertiary care data, particularly regarding adult predominance, cutaneous involvement, and antimicrobial causation. However, differences in gender distribution and organ system predominance compared to certain studies highlight regional and institutional variations. Strengthening pharmacovigilance reporting systems, promoting rational drug use, and ensuring vigilant monitoring (especially during the initial weeks of therapy) are essential to reduce hospitalization and mortality associated with serious ADRs.

Conclusion

The present study highlights that serious adverse drug reactions (ADRs) requiring hospitalization predominantly affected adults aged 41–60 years (35%), with a higher incidence among males (57.5%). Cutaneous reactions (27.5%) were the most frequently involved organ system, followed by gastrointestinal (20%) and hematological (15%) manifestations. Antibiotics (32.5%) emerged as the leading causative drug class, underscoring the need for rational prescribing and close monitoring. Most ADRs were categorized as probable (47.5%) according to the WHO-UMC scale, and encouragingly, the majority of patients recovered completely (77.5%). However, prolonged hospitalization (7.5%) and mortality (5%) indicate significant clinical impact. These findings emphasize the importance of strengthening pharmacovigilance systems, early detection, and preventive strategies to minimize serious drug-related harm and reduce healthcare burden.

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