Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/fax4rc41

PATTERN OF SERIOUS ADVERSE DRUG EVENTS (SAES) REPORTED TO AN ADR MONITORING CENTRE IN A TERTIARY CARE HOSPITAL IN SOUTHERN INDIA

Dr. Laona Lal[1], Dr. Parvathy V. Nair[2], Dr. Moncy Michael[3*], Dr. Reshma S.[4]

[1]Assistant Professor, Department of Pharmacology, Pushpagiri Institute of Medical Sciences and Research Centre, Thiruvalla, Kerala, India.
[2]Associate Professor, Department of Pharmacology, Government Medical College, Thiruvananthapuram, Kerala, India.
[3*]Assistant Professor, Department of Pharmacology, Government T.D. Medical College Alappuzha, Kerala, India.
[4]Pharmacovigilance associate, Department of Pharmacology, Government T.D. Medical College, Alappuzha, Kerala, India.

***Corresponding Author:** Dr. Moncy Michael
*Assistant Professor, Department of Pharmacology, Government T.D. Medical College Alappuzha, Kerala, India.

ABSTRACT

Background

Adverse drug reactions (ADRs) are a leading cause of morbidity and mortality in health care and have a significant economic impact on health care resources. Serious ADRs (SADRs) are particularly concerning as they may be life-threatening, require hospitalization, or cause permanent disability and necessitates keen monitoring to improve drug safety. This study aimed to analyze the pattern, severity, and outcomes of SADRs reported to the ADR Monitoring Centre of a tertiary care teaching hospital.

Methods

This cross-sectional, record-based descriptive study was conducted from January 2023 to January 2024 at the ADR Monitoring Centre of the Department of Pharmacology, Government T D Medical College, Alappuzha. Data on SADRs reported during this period were collected, including patient demographics, clinical presentations, suspected drugs, route of administration, severity, causality, and outcomes. The seriousness was categorized by FDA criteria and causality assessed by WHO-UMC scale. Descriptive statistics were used for analysis**.**

Results

Of 306 ADRs reported, 159 (51.9%) were classified as serious. The mean age of patients was 52.7 ± 17.91 years, with a female-to-male ratio of 1.03:1. The oral route (55.97%) was most common for drug administration. The most frequently affected organ system was the red and white cell, reticuloendothelial system (28.9%), followed by skin and appendages (22.6%). Anticancer drugs (30.8%) were the leading cause of SADRs, followed by antibiotics (26.4%) and antitubercular drugs (17.6%). Among antibiotics, amoxicillin-clavulanic acid combination accounted for 33.3% of cases. Most SADRs (69.8%) occurred within 7 days of drug therapy. Majority of patients (62.89%) were recovering at the time of reporting. WHO-UMC causality assessment showed 72.3% of cases as possible and 27.6% as "probable." Over half (56.6%) of SADRs caused or prolonged hospitalization, while 6.28% were life-threatening.

Conclusion
The study highlights a high occurrence of SADRs, predominantly associated with anticancer and antimicrobial drugs, and mainly affecting hematological and dermatological systems. Early detection and prompt intervention can significantly improve patient outcomes. These findings emphasize the need for enhanced pharmacovigilance, targeted risk minimization strategies, and regular monitoring of high-risk drug groups in clinical practice.

Keywords: Adverse Drug Reactions, Serious Adverse Drug Reactions, Pharmacovigilance, Drug Safety, Causality, Anticancer Drugs, Antibiotics.

INTRODUCTION

Adverse drug reactions (ADRs) are a major public health problem and contribute significantly to morbidity, mortality and healthcare costs worldwide. The World Health Organization (WHO) defines Adverse drug reaction (ADR) as "one which is noxious and unintended, and which occurs in doses normally used in human for prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological functions."[1] According to WHO, serious adverse drug reactions (serious ADRs) is any unintended medical event that is fatal, life-threatening, necessitates or prolongs hospitalization, or causes permanent or significant disability.[2]

Global estimates suggest that ADRs account for 5-10% of hospital admissions and occur in approximately 10-20% of hospitalized patients, with SADRs responsible for a substantial proportion of these cases.[3] In the 1970s in the US, it was estimated that up to 140 000 deaths per year resulted from ADRs, and 1 in 7 of all hospital days was spent caring for patients experiencing drug toxicity.[4]

Spontaneous reporting through ADR Monitoring centres, play key role in detection, assessment and prevention of ADRs.[1] The drugs frequently linked to SADRs, the affected demographic groups, organ systems involved, are revealed by analyzing individual case report forms. This allows regulators and health care providers to implement targeted risk minimisation strategies and to update guidance on clinical practice accordingly.[5]

AIMS AND OBJECTIVES

Primary Objectives

To describe the pattern of serious adverse reactions, drugs implicated, causality of ADRs reported in the ADR monitoring centre in the department of pharmacology for a period of 1 year.

Secondary Objectives

To describe the major organ systems affected by serious ADRs and outcomes of serious adverse drug reactions reported in the ADR monitoring centre in the department of pharmacology for a period of 1 year.

MATERIALS AND METHODS

The present study was a cross sectional record based descriptive study carried out in the Department of Pharmacology, Government T D Medical College, Alappuzha, from January 2023 to January 2024. The institution was approved as an ADR monitoring centre under the PvPI in 2012 with access to vigiflow.

Inclusion Criteria

Report forms containing serious ADR which were reported in ADR monitoring centre Pharmacology department, Government T D Medical College, Alappuzha. Cases reported from January 2023 to January 2024

Exclusion Criteria

Case reports of HIV patients

Study Procedure

The study was conducted after getting approval from IEC (146/2023 dated 28/11/2023, GTDMCA, IEC) .The ADRs are reported in Suspected ADR (sADR) reporting forms. The data which was received as a part of the Pharmacovigilance Programme of India (PvPI) from the various inpatient departments of the hospital, during the period under study (January 2023 to January 2024 (1 year)), were scrutinized for ADRS. The data was entered in a structured proforma. Patients age, gender, onset, description of reaction, duration, suspected medication, dose, route, severity of reaction, outcomes, relevant laboratory tests & medical history were noted. Seriousness of the reaction will be categorized according to FDA criteria. Causality will be assessed by WHO-UMC scale.

Statistical Analysis

Data was tabulated using Microsoft Excel and presented with the help of descriptive statistics using SPSS software V.27. Data was expressed as mean, standard deviation, frequency and percentage as appropriate. Causality assessment was done by WHO-UMC system & was classified as certain, probable, possible, unlikely, unclassified & unclassifiable.

RESULTS

1. Distribution and reporting of ADRs

A total of 306 ADRS were found and out of which 159 were serious ADRS with occurrence rate of 51.9%.

2. Demographic Details

The age of the participants ranged from 2 years to 87 years with mean age 52.7 ±17.91 years. There were 78 men and 81women with a female: male ratio of 1.03:1.

3. Routes of Administration

Of the 159 serious ADRs, the oral route was the most common route involved accounting for 89(55.97%) cases, followed by the intravenousroute (40.25%). Other routes include subcutaneous (2.51%) and intramuscular routes (1.25%).

4. Clinical presentation of serious adverse drug reactions

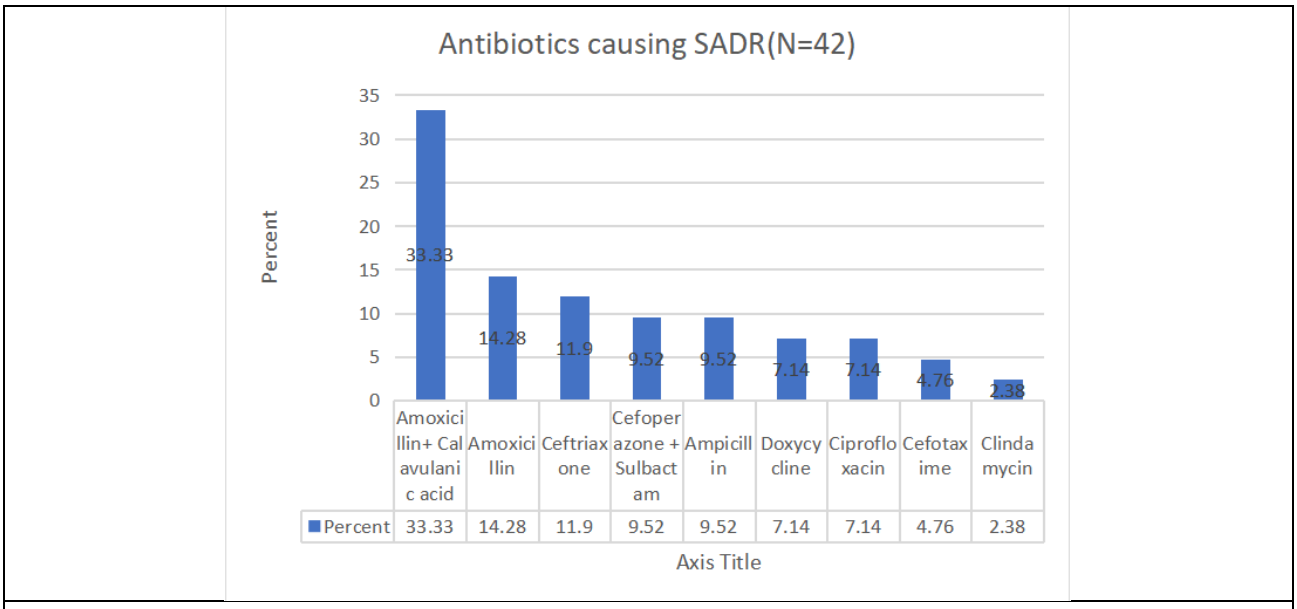
The most common affected body system (as per system organ class [SOC]) was Red and white cell, reticuloendothelial system (46, 28.9%) followed by skin and appendages disorders (37, 22.6%).

5. Causal Drug groups

The most common drug group causing serious ADRs were Anticancer drugs (49, 30.8%) followed by Antibiotics (42,26.4%). In addition, Antitubercular drugs ranked the third common causal group that resulted in serious ADRs in 28 (17.6%) cases.

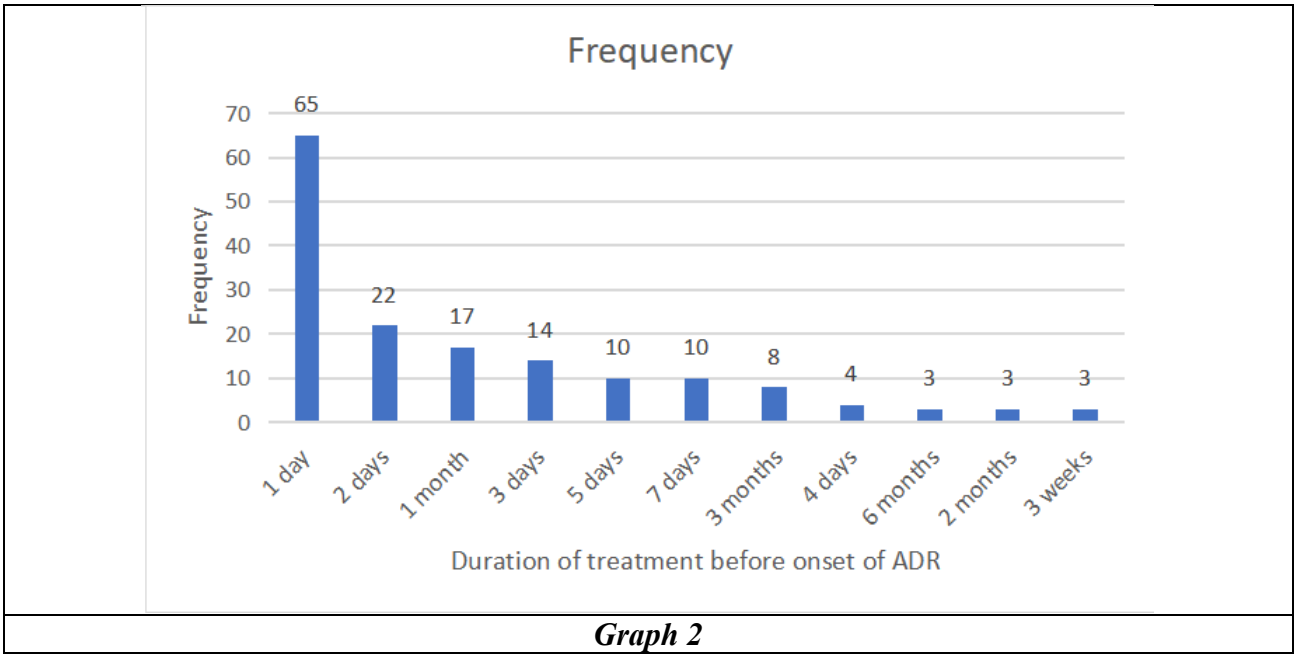
Body system affected	Clinical presentation of the affected system (number of ADRs)	No of ADRs (N=159) %
Skin and Appendages	Generalised pruritis (15), Generalised rashes (8), Angioedema (3), Urticaria (3), Hemorrhagic crusting and erythema (2), ITP (1), SJS (1), Exfoliative dermatitis (1), Mucositis (1), FDE (2)	37(22.6%)
Body as a whole general	Severe sweating and weakness (6), Anaphylaxis (15), Shivering (5), Oedema (1), Hypersensitivity (1), DRESS (1)	28 (17.61%)
Liver and biliary system	Abnormal LFT (13)	13 (8.17%)
Red and white cell, reticuloendothelial system	Neutropenia (36) Pancytopenia (4), Anemia (6)	46(28.93%)
Vision	Optic neuropathy (2)	2 (1.25%)
Hematology	Gingival bleeding (1)	1 (0.62%)
Gastrointestinal	Vomiting (2), Abdominal Pain (2)	4 (2.51%)
Neurology	Tremors (4), EPS (5), Headache (1), Tardive dyskinesia (2)	12 (7.54%)
Kidney	Abnormal RFT (2)	2 (1.25%)
Application site	Blisters (1)	1 (0.62%)
Metabolic and nutritional	Hyperkalemia (1), Hypoglycemia (11), Hypokalemia (1)	13 (8.17%)

Antibiotics constitute 26.4% of the total SADRs out of which Amoxicillin-Clavulanic acid combination was the culprit drug in about 33.3% cases followed by Amoxicillin (14.28%).



Graph 1

6. **Duration of treatment**



Graph 2

Majority of the serious ADRs (111, 69.8%) occurred within 7 days of drug therapy. Out of these 111ADRs, 65 (40.8%) occurred within a day. While 48 (30.2%) serious ADRs such as blood discrepancies occurred during and after 1 week of drug therapy.

7. Outcome of the reaction

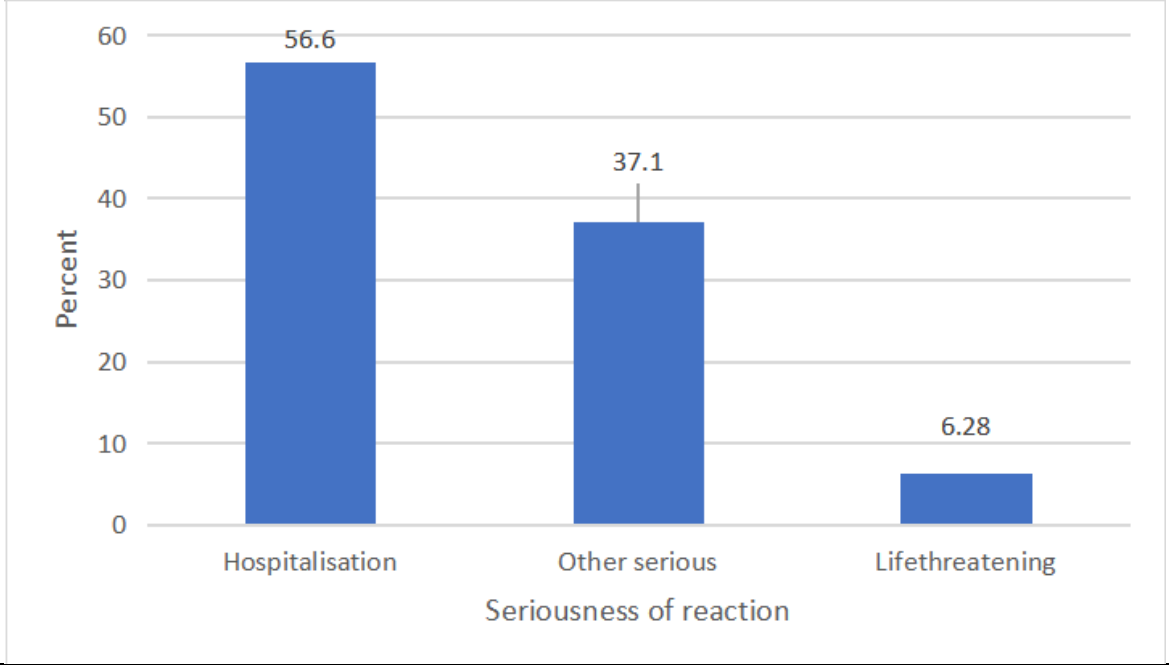
Majority of the serious ADRs were recovering at the time of reporting (100, 62.89%), while the rest 59 (37.1%) recovered from the reaction.139 patients (87.4%) stopped the drug while in 7.5% of patients the drug was changed.

8. Causality assessment

According to the WHO-UMC scale, majority of the serious ADRs were categorized as possible (115, 72.3%) followed by probable (44, 27.6%).

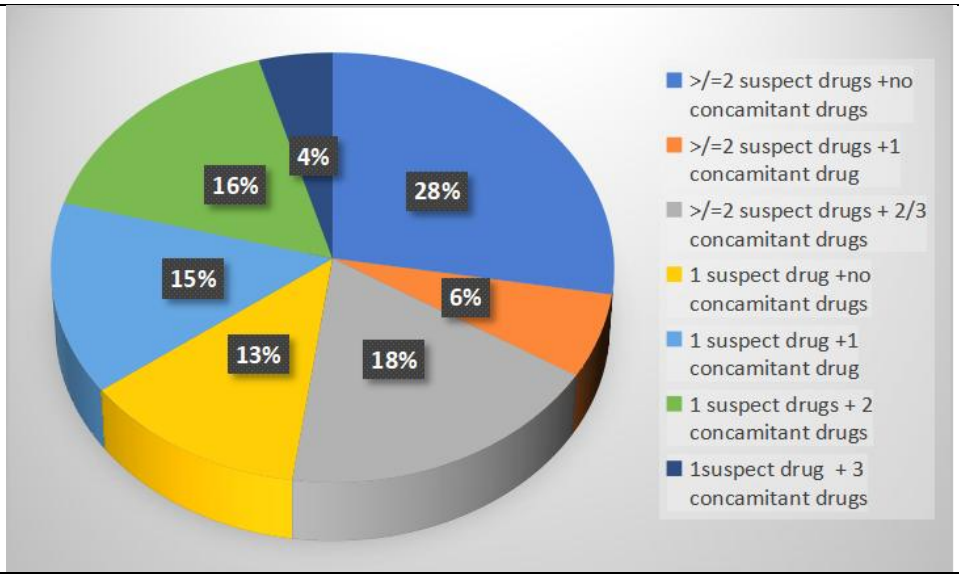
9. Seriousness of reaction

Majority of the serious ADRs (90, 56.6%) were either the cause for hospitalization or prolongation of initial hospitalisation. In addition, other serious ADRs (58) in the form of blood count discrepancies constituted 37.10 %of serious ADRs. 6.28 % of ADRs constituted life threatening serious ADRs.



Graph 3

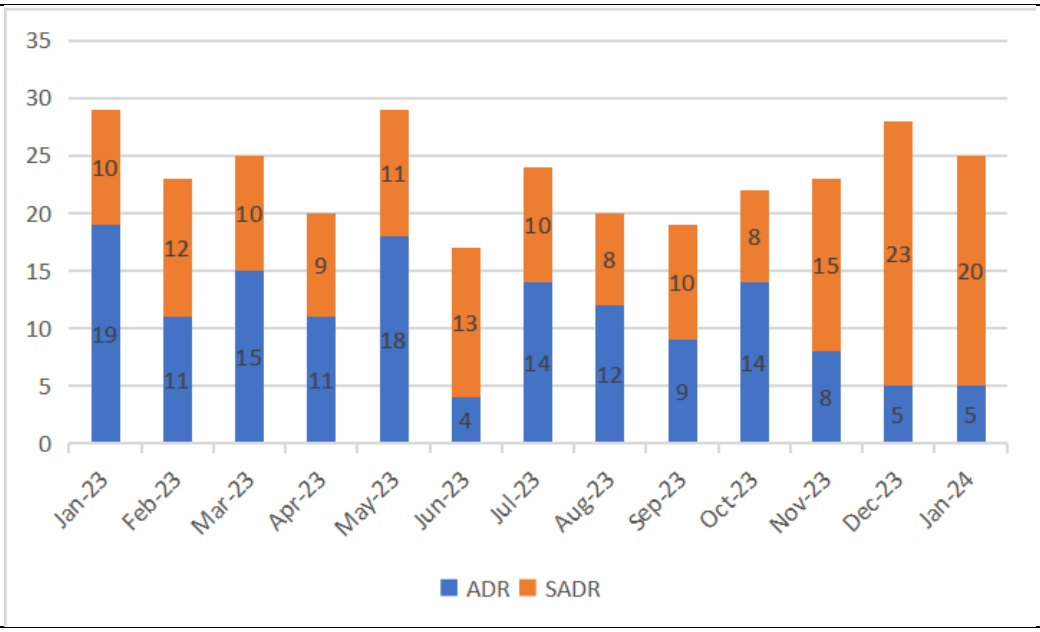
10. Number of drugs taken



Graph 4: Number of drugs taken

Out of 159 serious ADRs,28% of the cases have more than 2 suspect drugs and 24% of the cases had more than 2 suspect drugs with either 1 or 2/3 concomitant drugs.

11. Distribution of ADRs over 1 year Period under study



Graph 5: Distribution of ADRs over 1 year Period

Out of 306 ADRs encountered in the one year period (Jan 2023 to Jan 2024), 159 (51.9%) were SADRs. There is unequal distribution of SADRs while comparing with total ADRs during this period. For instance in June 2023, 76.46% of total ADRs were SADRs while in January 2023 only 34.48% of total ADRs constitute SADRs.

DISCUSSION

The present study was performed to describe the incidence of serious ADRs, main pharmacological classes and individual drugs involved in causing serious ADRs the type and causality of SADRs encountered during our study duration.

This study's demographic data reveals that females were having slightly higher preponderance of ADRs over males. In a similar study done by Singh et al. in central India,[6] of the 239 serious ADRs, 113 (47.28 %) occurred in males, while 125 (52.30 %) were females. In contrast, study conducted by Sharma et al.[7] revealed that males (64 %) as having more ADRs compared to females (36%). This demographic difference can be attributed to the difference in population demographics and health care practices in different regions. A vast study of ADRs based on gender by Sarah Watson et al.,[8] assessed from Vigibase software, over half a century 60.1 % of ADRs were related to female and 39.9 % of males globally. The preponderance of females over males experiencing ADRs has many reasons, such as females being prescribed more medicines compared to males, hormonal changes at different stages, variations in pharmacokinetic and pharmacodynamic effects on drugs, taking higher doses concerning their body weight and social and behavioral factors.[3,9]

The study showed that occurrence rate of serious ADRs is 51.9% (159 out 306 ADRs). Majority of the serious ADRs (90, 56.6%) were either the cause for hospitalization or prolongation of initial hospitalization and 6.28% were life threatening. A meta-analysis of prospective studies in US hospitals estimated the overall incidence of serious ADRs is 6.7% among hospitalized patients, with fatal ADRs accounting for 0.32%.[3] In South India, a study reported that 3.7% of hospitalized patients experienced an ADR, with 0.7% of admissions due to ADRs and 1.8% involving a fatal ADR.[10] Serious ADRs lead to hospitalisation or prolonged hospitalisation, significantly increasing the global economic burden.[11] In our current research the life threatening ADRs encountered were 15 cases of Anaphylaxis and 1 case of DRESS and there was no mortality due to ADRs. A study on serious ADRs done in Central India came across 2 cases (0.53 %) of deaths out of 375 cases due to serious ADRs.[12]

The most common organ systems affected as per SOC classification was red and white cell, reticuloendothelial system (46,28.9%) followed by skin and appendages disorders (37,22.6%). These findings were in accordance with similar studies conducted by Prajapathi et al.[12] and Arulmani R et al.[13] where skin and appendages were the most common organ systems affected due to ADRs. Since our study have included blood count discrepancies (Neutropenia, Pancytopenia and Anemia) in other serious ADRs category we had majority of SADRs falling in this system class. In our study most frequent skin related SADRs were generalized pruritus, rashes, exfoliative dermatitis and angioedema. Most earlier studies had frequently reported that maculopapular rashes, pruritus, urticaria, fixed drug eruptions, bullous eruptions, erythematous rashes, SJS and TEN were the most common ADRs pertaining to skin and appendages.[14,15,16]

In our study, the most common drug group causing serious ADRs were anticancer drugs followed by Antibiotics. In addition, Antitubercular drugs ranked the third common causal group that resulted into various serious ADRs. This finding aligns with some similar studies done globally. A study of serious ADRs from India found that anti-tubercular 34.4 % was the highest, followed by anti-retroviral 20.3% drugs induced serious ADRs.[8] Among the antibiotics, Amoxicillin -Clavulanic acid combination was most frequently encountered antibiotic causing serious ADRs followed by Amoxicillin and Ceftriaxone. These antibiotics were commonly prescribed for upper respiratory tract infections. In a study done by Munir Pirmohamed et al. common drugs causing hospital admissions in UK included low dose Aspirin, Diuretics, Warfarin and Non-steroidal anti-inflammatory drugs (NSAIDS). Polypharmacy is a major factor for the development of ADRs.[17] In the current study, about 24 % of the SADRs have more than 2 culprit drugs in addition to the concomitant drugs. In the study done by Singh et al.[6] showed that more than 18 % of patients encountered more than three drugs. Similarly, majority of the patients were prescribed five or more drugs in a study done in Central India.[12] However, this can be defensible to some extent as majority of these patients were receiving multiple cancer drugs for cancer remission or anti-tubercular drug regimen under National Tuberculosis Elimination programme.

Our findings showed that majority of SADRs occurred within 7 days of drug therapy and about 40 % of these occurred within 1 day of initiating therapy. Those reactions were usually generalized pruritus, drug induced rashes, angioedema and anaphylaxis. Chemotherapy induced neutropenia and pancytopenia usually occurred within 3-7 days after starting the regimen. There was also unequal distribution of SADRs while comparing with total ADRs during the period under study (1 year). For instance in June 2023, 76.46% of total ADRs were SADRs while in January 2023 only 34.48% of total ADRs constitute SADRs. This can be attributed to the infection disease outbreaks in particular seasons resulting in more exposure to drugs and certain adverse drug events display seasonal patterns potentially linked to weather conditions or seasonal factors.[18]

Majority of the serious ADRs were recovering at the time of reporting 62.89%, while 37.1% recovered from the reaction.139 patients (87.4%) stopped the drug while in 7.5% of patients the drug was changed. The causality of majority of serious ADRs to causal drugs was possible in nature according to WHO UMC Scale. Various other factors like disease itself and multiple drug therapy are some attributing factors. This finding is in concordance with similar studies done by Prajapathi et al[12] while in studies done by Selva P et al.[19] and Singh et al[6] most of the ADRS were probable in nature.

CONCLUSION

The results highlight the significant impact of SADRs on patient safety and healthcare resources, with more than half of reported ADRs being categorized as serious. The predominance of anticancer drugs, antibiotics, and antitubercular drugs as causative agents signifies the need for enhanced vigilance during treatment with these therapeutic classes. The early onset of most SADRs within the first week of therapy, particularly within 24 hours, emphasizes the critical importance of close monitoring during the initial phase of treatment. The frequent involvement of hematopoietic and dermatological systems highlights the need for regular monitoring in patients on high-risk medications. These findings

emphasize the need for robust pharmacovigilance programs and healthcare provider training to ensure early SADR detection and optimal patient outcomes.

REFERENCES

[1] Edwards IR, Aronson JK. Adverse drug reactions: Definitions, diagnosis, and management. Lancet 2000;356:1255-9.
[2] World Health Organization. Safety of Medicines-A Guide to Detecting and Reporting Adverse Drug Reactions-Why Health Professionals Need to Take Actions. Geneva: World Health Organization 2002.
[3] Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: A meta-analysis of prospective studies. JAMA 1998;279:1200-5
[4] Atkin PA, Shenfield GM. Medication-related adverse reactions and the elderly: a literature review. Adverse Drug React Toxicol Rev 1995Autumn;14(3):175-91.
[5] Pal SN, Duncombe C, Falzon D, et al. WHO strategy for collecting safety data in public health programmes: complementing spontaneous reporting systems. Drug Saf. 2013;36(2):75-81.
[6] Singh P, Verma S, Vaishnav Y, et al. Probing the in-depth analysis of Serious Adverse Drug Reactions in a tertiary care hospital of Central India. Explor Res Clin Soc Pharm 2025;17:100579.
[7] Sharma M, Baghel R, Thakur S, et al. Surveillance of adverse drug reactions at an adverse drug reaction monitoring Centre in Central India: a 7-year surveillance study. BMJ Open 2021;11(10):1-8.
[8] Watson S, Caster O, Rochon PA, etal. Reported adverse drug reactions in women and men: aggregated evidence from globally collected individual case reports during half a century. E Clinical Medicine 2019;17:100188.
[9] Zucker I, Prendergast BJ. Sex differences in pharmacokinetics predict adverse drug reactions in women. Biol Sex Differ 2020;11(1):1-14.
[10] Ramesh M, Pandit J, Parthasarathi G. Adverse drug reactions in a south Indian hospital--their severity and cost involved. Pharmacoepidemiol Drug Saf 2003;12(8):687-92.
[11] Durand M, Castelli C, Roux-Marson C, et al. Evaluating the costs of adverse drug events in hospitalised patients: a systematic review. Health Econ Rev 2024;14(1):1-14.
[12] Prajapati K, Desai M, Shah S, et al. An analysis of serious adverse drug reactions at a tertiary care teaching hospital. Perspect Clin Res 2016;7(4):181-6.
[13] Arulmani R, Rajendran SD, Suresh B. Adverse drug reaction monitoring in a secondary care hospital in South India. Br J Clin Pharmacol 2008;65:210-6.
[14] Ogar CK, Abiola A, Yuah D, et al. A retrospective review of serious adverse drug reaction reports in the Nigerian VigiFlow database from September 2004 to December 2016. Pharmaceut Med 2019;33(2):145–57.
[15] Mouton JP, Fortuin-de Smidt MC, Jobanputra N, et al. Serious adverse drug reactions at two children's hospitals in South Africa. BMC Pediatr 2020;20(1):3.
[16] Pirmohamed M, James S, Meakin S, et al. Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients. BMJ 2004;329(7456):15-9.
[17] Koh Y, Kutty FB, Li SC. Drug-related problems in hospitalized patients on polypharmacy: The influence of age and gender. Ther Clin Risk Manag 2005;1:39-48.
[18] Marrero O, Hung EY, Hauben M. Seasonal and geographic variation in adverse event reporting. Drugs Real World Outcomes 2016;3(3):297-306.
[19] Selva P, Durairajan S. Exploration and evaluation of adverse drug reactions documented in a tertiary-Care Hospital in Chennai: an in-depth retrospective observational study. Cureus 2024;16(5):e60977.