Adverse Drug Reactions: A Retrospective Analysis from the ADR Monitoring Centre at a Tertiary Care Hospital

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Received: 2024-02-12, Revised: 2024-03-13, Accepted: 2024-03-147, Published: 2024-03-31

Abstract

Background: Adverse Drug Reactions (ADRs) present significant challenges in healthcare, necessitating vigilant monitoring and analysis to enhance medication safety protocols. This retrospective study aimed to analyse ADRs reported at an Adverse Drug Reactions Monitoring Centre (AMC) to understand prevalence, patterns, and characteristics of ADRs.

Methods: Retrospective data from January to December 2023 were collected from the AMC at Vaishampayan Memorial Medical College, Solapur. A total of 282 ADR reports were analysed for frequency, severity, implicated medications, patient demographics, and associated clinical factors. Causality assessment was performed using the WHO- Uppsala Monitoring Centre scale.

Results: The majority of ADRs were associated with the oral route of drug administration (79.43%), and most were categorized as minor severity (68.44%) and probable causality (91.84%). Common ADR symptoms included vomiting (9.55%) and rash (9.22%). Antimicrobial agents were the most suspected drugs causing ADRs (17.38%). The study revealed discrepancies in ADR reporting patterns and highlighted the importance of pharmacovigilance in capturing and addressing ADR occurrences.

Conclusion: Our study provides valuable insights into the prevalence, patterns, and characteristics of ADRs, emphasizing the need for continued surveillance and reporting to promote patient safety and improve healthcare outcomes. Strategies to improve ADR reporting and enhance medication safety protocols are warranted to optimize patient care.

J Pharm Care 2024; 12(1): 3-8.

Keywords: Adverse Drug Reactions; Pharmacovigilance; Medication Safety

Introduction

Adverse Drug Reactions (ADRs) are defined by World Health Organization (WHO) as 'any noxious change suspected to be due to a drug, occurs at doses normally used in humans, requiring treatment or dose reduction, or necessitating caution in the future use of the same drug' (1). ADRs present a significant challenge in modern healthcare, representing a complex interplay between medication use, patient factors, and clinical outcomes. These unintended and harmful responses to medications encompass a spectrum of manifestations ranging from mild discomfort to severe morbidity and mortality. Monitoring and analysing ADRs are crucial components of pharmacovigilance, aiming to identify, understand, and mitigate risks associated with medication use. Thus, ADR reporting is necessary to identify and monitor adverse reactions to medications, facilitate early detection of safety issues, improve drug safety profiles, support evidence-based decision-making, enhance pharmacovigilance systems, and ultimately safeguard patient well-being.

In India, the rate of ADR reporting is less than 1%, whereas worldwide, it is 5%, owing to the need for greater awareness about pharmacovigilance (PV) and ADR monitoring among healthcare providers and patients (2). To promote vigilance of adverse drug reactions in India, the Central Drugs Standard Control Organization (CDSCO) initiated a nationwide pharmacovigilance programme in 2010, coordinated by the Indian Pharmacopoeia Commission (IPC) in Ghaziabad, with the process executed through ADR Monitoring Centres

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(AMCs), currently 150 operational AMCs throughout the country.

By retrospectively examining ADR data, valuable insights are gained regarding the frequency, severity, implicated medications, patient demographics, and associated clinical factors. Thus, the aim and objective of this study is to comprehensively analyse ADRs to improve medication safety protocols, optimize drug utilization practices, and inform healthcare providers about potential risks related to specific medications or patient populations.

Methods

A total of 282 suspected ADR reports were received from various clinical departments at the ADR Monitoring Centre at Vaishampayan Memorial Medical College, Solapur, on the prescribed "Suspected Adverse Drug Reaction Reporting Form" version 1.3 provided by the IPC in the last year, spanning from January 2023 to December 2023. Causality assessment was performed using the WHO Uppsala Monitoring Centre (UMC) Causality Assessment Criteria (3). Subsequently, the reports were uploaded into the Vigiflow software which serves as a national pharmacovigilance database, enabling regulatory authorities to monitor the safety of medicines and vaccines within their respective countries, while also facilitating global information sharing through a web-based system that manages adverse event reports and sent to the National Coordination Centre, Indian Pharmacopoeia Commission Ghaziabad, which further forwarded them to the Uppsala Monitoring Centre, Sweden, for maintaining the ADR database, conducting further analysis, and signal detection. These reports were then retrospectively analysed for the type and pattern of ADRs reported, demographic profile of patients, organ system involvement, causative drugs, severity, outcome, management, and causality assessment after obtaining approval from Institutional Ethics Committee (IEC).

Analysis of causality and severity of ADRs:

- **WHO-UMC Causality Categories (3):**
  - Certain: Events or laboratory test abnormalities with a plausible time relationship to drug intake, not explainable by disease or other drugs, with a response to withdrawal that is plausible, and may include definitive pharmacological or phenomenological evidence, and rechallenge satisfactory if necessary.
  - Probable/Likely: Events or laboratory test abnormalities with a reasonable time relationship to drug intake, unlikely to be attributed to disease or other drugs, with a clinically reasonable response to withdrawal, and rechallenge is not necessary.
  - Possible: Events or laboratory test abnormalities with a reasonable time relationship to drug intake, which could also be explained by disease or other drugs, and may lack clear information on drug withdrawal.
  - Unlikely: Events or laboratory test abnormalities with a time to drug intake that makes a relationship improbable (though not impossible), where disease or other drugs provide plausible explanations.
  - Conditional/Unclassified: Events or laboratory test abnormalities where more data are needed for proper assessment, or additional data are under examination.
  - Unassessable/Unclassifiable: Reports suggesting adverse reactions that cannot be judged due to insufficient or contradictory information, and data cannot be supplemented or verified.
- **Karch and Lasagna severity grading (4):**
  - Minor: No therapy, antidote or prolongation of hospitalization is required.
  - Moderate: Requires change in drug therapy, specific treatment or prolongs hospital stay.
  - Severe: Potentially life-threatening, causes permanent damage or requires intensive medical treatment.
  - Lethal: Directly or indirectly contributes to death of the patient.

Data was collected and entered into Microsoft Excel 2019. Descriptive statistics such as frequencies and percentage will be calculated for categorical variables.

Results

During the study period of January 2023 to December 2023, a total of 282 adverse drug reactions were reported from the outpatient and inpatient departments of Shri Chhatrapati Shivaji Maharaj Sarvopchar Rugnalay, Solapur.

Demographic characteristics, including age and gender, are presented in Table 1. According to age-wise distribution, only 7.8% of the reported adverse drug reactions were reported in the paediatric age group (1-18 years), with the mean age of patients being 42.7 years. Gender distribution showed male predominance (63.1%).

Table 1. Demographic Characteristics.

Parameters	Number of ADRs (%) (n=282)
Age-wise distribution:	22 (7.8%)
1-18 years	127 (45.04%)
19-40 years	95 (33.69%)
41-60 years	38 (13.47%)
>60 years	
Gender-wise distribution:	178 (63.12%)
Male	104 (36.88%)
Female	

Table 2 outlines various characteristics of adverse drug reactions (ADRs). The majority of ADRs were reported with oral route of drug administration (79.4%), followed by parenteral administration (18.4%). According to the Karch and Lasagna severity grading, 68.4% were categorized as Minor, and 29.43% were classified as moderate. Causality assessment according to the WHO-UMC scale revealed that the majority were categorized as probable (91.8%), followed by possible (8.2%). Furthermore, the majority of cases were in the recovering phase (85.1%), and in most instance, the drug was withdrawn (74.1%).

Table 2. Characteristics of ADR

Parameters	Number of ADRs (%) (n=282)
Route of drug administration	24 (79.43%)
Oral	52 (18.44%)
Parenteral	6 (2.13%)
Topical	
Severity	193 (68.44%)
Minor	83 (29.43%)
Moderate	6 (2.13%)
Severe	0 (0%)
Lethal	
Causality assessment as per WHO-UMC Scale	
Certain	0
Probable	259 (91.84%)
Possible	23 (8.16%)
Unlikely	0
Conditional	0
Unassessable	0
Outcome	
Recovered	26 (9.22%)
Recovering	240 (85.11%)
Not Recovered	2 (0.71%)
Fatal	0 (0%)
Unknown	14 (4.96%)
Action taken	
Drug withdrawn	209 (74.11%)
Dose reduced	1 (0.35%)
Stopped and then restarted	31 (11%)
Drug continued	39 (13.83%)
Unknown	2 (0.71%)

The system wise distribution of adverse drug reactions (ADRs) was highest in both the gastrointestinal (GIT) and generalized, each accounting for 27.6%, followed by CNS at 22.3%. Meanwhile, the minimum was observed in cardiovascular (CVS) related reactions at 0.71%. Nausea emerged as the most commonly reported ADR symptom (9.5%), followed by rash (9.2%). In terms of specific drugs, antimicrobial agents were the most suspected, accounting for 17.3%, followed by vaccines and cardiovascular (CVS) related drugs, accounting for 16.6% and 16.3% respectively.

Table 3 presents the frequency of adverse drug reaction (ADR) symptoms, classified by the involvement of organ systems, along with the corresponding drugs associated with each ADR symptom.

Overall, the data underscores the complex relationship between patient characteristics, drug administration practices, and the occurrence of ADRs, emphasizing the need for comprehensive monitoring, assessment, and management strategies in healthcare settings.

Table 3. Frequency of ADR symptoms based on system involved and the corresponding drugs associated.

System involved n (%)	Symptoms (n=282)	Suspected drugs
SKIN 43 (15.25%)	Rash (26),	Albumin (1), Anti-snake venom (10), Albendazole (2), Amoxiclav (1), Carbamazepine (1), Ciprofloxacin (5), Fluconazole (4), Gliclazide (1), Leflunomide (1)
	Skin hyperpigmentation (2),	Norfloxacin (2)
	Urticaria (15)	Anti-snake venom (14), Cefixime (1)
Gastrointestinal 78 (27.66%)	Abdominal pain (7)	Paracetamol (4), Pantoprazole (2), Simvastatin (1)
	Constipation (18)	Amitriptyline (1), Calcium (13), Folic acid (1), Multivitamin (3)
	Diarrhoea (16)	Amoxiclav (10), Azithromycin (4), Misoprostol (1), Pantoprazole (1)
	Epigastric discomfort (8)	Paracetamol (8)
	Nausea (27)	Vitamin D_3 (3), Aspirin (1), Metformin (21), Paracetamol (1), Syndopa (1)
	Vomiting (2)	Ibuprofen (2)
Cardiovascular 2 (0.7%)	Postural hypotension (1)	Telmisartan (1)
	Tachycardia, sweating (1)	Remdesivir (1)
Central nervous system 63 (22.3%)	Drowsiness (4),	Cetirizine (3), Diazepam (1)
	Febrile convulsion (5),	DPT Vaccine (3), Penta vaccine (2)
	Dizziness (11),	Atenolol (9), Losartan (1), Propranolol (1)
	Headache (19),	Vitamin D_3 (2), Dienogest (1), Fluconazole (4), Nitroglycerine (1), Pantoprazole (8), Tamsulosin (3)
	Tingling & numbness (1),	Iron sucrose (1)
	Sedation (21),	Cough syrup (1), Cetirizine (13), Chlorpheniramine (1), Chlorpromazine (1), Divalproex (1), Phenytoin (1), Levocetirizine (1), Olanzapine (1), Pregabalin (1)
	Tremor (2)	Salbutamol (1), Propranolol (1)
Respiratory system 12 (4.26%)	Dry cough (12)	Enalapril (10), Captopril (2)
Ocular: 6 (2.1%)	Dry eye (1),	Moxifloxacin eye drop (1)
	Itching/ ocular discomfort (5)	Moxifloxacin eye drops (4), Ciprofloxacin eye drops (1)
Generalized 78 (27.6%)	Agitation (4),	Escitalopram (4)
	Ankle oedema (13),	Amlodipine (13)
	Bad taste (3),	Polyvitamine (3)
	Chills (17),	Anti-snake venom (17)
	Fatigue (2),	Atorvastatin (2)
	Fever (1),	DPT Vaccine (1)
	Flushing (1),	Folic Acid (1)
	Hair fall (2),	Sumatriptan (2)
	Hot flushes (1),	Prednisolone (1)
	Metallic taste (10),	Ferrous fumarate (1) Metronidazole (9)
	Muscle ache (3),	Atorvastatin (3)
	Oedema (2),	Dexamethasone (1), Amlodipine (1)
	Restlessness (2),	Escitalopram (2)
	Weight gain (17)	Glimepiride (6), Olanzapine (10), Prednisolone (1)

Discussion

In the realm of pharmacotherapy for various illnesses, drugs typically exhibit both favourable and adverse effects. Therefore, implementing a comprehensive strategy involving prevention, treatment, and rehabilitation is essential to effectively manage these adverse outcomes. However, a significant disparity exists between the occurrence and reporting of adverse drug reactions (ADRs) in India and globally. Despite being significant contributors to morbidity and mortality in hospital settings, many cases of ADRs remain unreported, representing only the tip of the iceberg. This study aims to retrospectively analyse ADRs reported at an Adverse Drug Reactions Monitoring Centre (AMC), focusing on identifying patterns, types of ADRs, causative drugs, and demographic profiles of affected patients.

During the study period from January 2023 to December 2023, a total of 282 adverse drug reactions (ADRs) were reported from the outpatient and inpatient departments of Shri Chhatrapati Shivaji Maharaj Sarvopchar Rugnalay, Solapur. Considering demographic characteristics, including age and gender, it's notable that adverse drug reactions (ADRs) among the paediatric population are quite common, which may have severe consequences. However, spontaneous ADR reporting in this age group is not as frequent. In our study, only 7.8% of ADRs were reported in the paediatric age group. Similar findings were observed in a study conducted by Nandal et al., (5), where 7.5% of ADRs were reported in patients aged 1-18 years. The mean age of patients was 42.75 years, similar to the study conducted by Gupta et al., (6), where the mean age was 43.1 years. The present study showed male predominance at 63.1%, similar to previous studies conducted by Gupta et al., (6), where male predominance was reported at 61.7%.

The majority of adverse drug reactions (ADRs) were reported with the oral route of drug administration (79.43%), followed by parenteral (18.44%) and topical (2.13%), which differed from the findings of a study conducted by Singh et al., (7), where the majority of ADRs were associated with the parenteral route (56.89%), followed by oral (41.81%) and topical (1.29%). According to the Karch and Lasagna severity grading, 68.44% were categorized as Minor, 29.43% moderate, and 2.13% severe. This contrasts with the findings of a study conducted by Sre et al., (8), who assessed severity using the Hartwig Severity Assessment Scale, where 48.85% were mild, 36.9% were moderate, and 14.25% were severe. Causality assessment using the WHO-UMC scale showed that the majority of ADRs were categorized as probable (91.84%), with possible accounting for the remaining 8.16%. In comparison, Raju et al., (9) reported 65.7% probable and 34.2% possible ADRs in their study.

In contrast to the study conducted by Sen et al., (10), which reported the majority of cutaneous ADRs (45%), followed by generalized ADR and GIT involvement (15% each), our study revealed that the maximum number of ADRs were reported in both GIT and generalized ADR, accounting for 27.66%, followed by CNS at 22.34%. The most commonly reported ADR symptom in our study was nausea (9.55%), followed by rash at 9.22%. Conversely, in the study by Jose et al., (11), rash was the most common symptom reported, followed by vomiting, accounting for 10.5% and 6.6%, respectively. Antimicrobial agents were identified as the most suspected drugs causing ADRs in our study, accounting for 17.38%, similar to Sre et al.,'s findings, where antibiotics were the most suspected drugs causing ADRs, accounting for 35.3% (8).

The limitations of our study include its retrospective design, reliance on data from a single institution, potential introduction of bias, limited generalizability, underestimation of adverse drug reaction (ADR) incidence due to spontaneous reporting, and lack of assessment regarding comorbidities or concurrent medications.

In conclusion, our study provides valuable insights into the prevalence, patterns, and characteristics of adverse drug reactions (ADRs) in our clinical setting. The findings underscore the importance of vigilance in recognizing and managing ADRs, particularly in vulnerable populations such as children. Furthermore, the discrepancies in ADR reporting patterns highlight the need for improved pharmacovigilance systems to capture and address these occurrences effectively. By identifying common ADRs, causative drugs, and affected patient demographics, our study contributes to enhancing medication safety protocols and optimizing patient care. Moving forward, continued surveillance and reporting of ADRs are essential for promoting patient safety and improving healthcare outcomes.

References

1. Mayathevar B, Thiyagarajan D, Soundararajan T, Vallish BN, Rizwan SA. A prospective study on adverse drug reactions reported in a tertiary referral hospital. International Journal of Basic & Clinical Pharmacology. 2017;6(1):25.
2. Shukla S, Sharma P, Gupta P, et al. Current Scenario and Future Prospects of Adverse Drug Reactions

(ADRs) Monitoring and Reporting Mechanisms in the Rural Areas of India. Curr Drug Saf. 2024;19(2):172-90.

3. Shukla AK, Jhaj R, Misra S, Ahmed SN, Nanda M, Chaudhary D. Agreement between WHO-UMC causality scale and the Naranjo algorithm for causality assessment of adverse drug reactions. J Family Med Prim Care. 2021;10(9):3303.
4. Srinivasan R, Ramya G. Adverse drug reaction-causality assessment. Int J Res Pharm Chem. 2011;1(3):606-12.
5. Nandal DH, Mahajan SN, Narwane SP, Kunkulol RR, Baheti T. Study of ADR (Adverse Drug Reactions) Reporting in Pravara Rural Hospital, Loni. Pravara Medical Review. 2019;11(1):4-7.
6. Gupta A, Kaur A, Shukla P, Chhabra H. Adverse Drug Reactions pattern in a tertiary level teaching hospital: A Retrospective Study. Indian Journal of Pharmacy Practice. 2017;10(1).
7. Singh P, Agrawal M, Hishikar R, Joshi U, Maheshwari B, Halwai A. Adverse drug reactions at adverse drug reaction monitoring center in Raipur: Analysis of spontaneous reports during 1 year. Indian J Pharmacol. 2017;49(6):432-437.
8. Kalyani SS, Srihitha P. An epidemiological study on adverse drug reactions in Indian population: Meta-Analysis. International Journal of Pharmaceutical and Clinical Research. 2017;9(10):654-59.
9. Raju SK, Kamble S. A prospective, observational study of the spontaneous reporting patterns of adverse drug reactions in a tertiary care teaching hospital. Journal of Pharmacology and Pharmacotherapeutics. 2022;13(3):272-7.
10. Sen M, Singh A, Misra M. Retrospective analysis of adverse drug reactions reported at ADR monitoring centre under PvPI in a tertiary care hospital. Int J Basic Clin Pharmacol. 2018;7(7):303-8.
11. Jose J, Rao PG. Pattern of adverse drug reactions notified by spontaneous reporting in an Indian tertiary care teaching hospital. Pharmacol Res. 2006;54(3):226-33.

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Mukadam MF, Gawali PU. Adverse Drug Reactions: A Retrospective Analysis from the ADR Monitoring Centre at a Tertiary Care Hospital.J Pharm Care 2024;12(1): 3-8.