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Research Article

PROFILE OF ADVERSE DRUG REACTIONS IN A TERTIARY CARE HOSPITAL: A CROSS-SECTIONAL STUDY

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ABSTRACT

Objective: The objective of this study was to analyze incidence, presentation, severity of adverse drug reaction, and identification of offending drug in a tertiary care hospital setting.

Methods: This was a cross-sectional study conducted in the department of pharmacology of a tertiary care medical institute for assessing the clinical spectrum and pattern of adverse drug reactions (ADRs). Total 50 patients with ADRs were included in this study on the basis of a predefined inclusion and exclusion criteria. Demographic details and history were noted in all cases. The Naranjo scale was used to determine the causality and categorize it into definite, probable, possible, or doubtful causation. Severity of the ADR was assessed using the modified Hartwig scale. The Statistical Package for the Social Sciences 23.0 version was used for statistical analysis. For statistical purposes, $p<0.05$ was considered as significant.

Results: In this study, out of 50 patients, there were 36 (72%) males and 14 females (28%). There was a male preponderance with M: F ratio being 1:0.388. The most common ADR symptoms were itching (76%) and skin rashes (26%). Antimicrobials were the leading cause of ADRs (14%), followed by antiretroviral agents (10%) and non-steroidal anti-inflammatory drugs (6%). The Naranjo scale classified 14% of ADRs as definite, 44% as probable, and 42% as possible. Severity assessment revealed 54% mild, 40% moderate, and 6% severe ADRs. The most affected age group among males was 41–50 years (20%), while among females, it was 31–40 years (10%).

Conclusion: Prompt recognition and management of ADRs are crucial for minimizing their adverse effects on patient health and for guiding safer prescribing practices in clinical settings.

Keywords: Adverse drug reaction, Naranjo scale, Modified Hartwig scale, Pharmacovigilance.

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INTRODUCTION

Adverse drug reactions (ADRs) are defined by the World Health Organization as any noxious, unintended, and undesired effect of a drug that occurs at doses used for prophylaxis, diagnosis, or therapy [1]. ADRs are a significant concern in public health due to their impact on patient safety and health-care systems. They contribute to patient morbidity and mortality, leading to increased health-care burden. Understanding and managing ADRs is essential to enhance patient care and improve therapeutic outcomes [2]. ADRs can profoundly alter patient management, significantly influencing clinical decisions and outcomes. When a patient experiences an ADR, health-care providers often need to modify the treatment regimen, which may involve discontinuing the offending drug, reducing its dose, or substituting it with an alternative therapy. This can complicate the management of the primary condition for which the drug was prescribed, potentially leading to suboptimal treatment outcomes. ADRs can also necessitate additional diagnostic tests, prolonged hospital stays, and increased frequency of follow-up visits, all of which contribute to higher health-care costs [3].

The burden of ADRs is particularly pronounced in India, where the incidence of ADRs has been reported to be around 6–7%. This figure may be an underestimate due to underreporting and lack of comprehensive pharmacovigilance systems. The incidence of ADRs can lead to increased morbidity and mortality, highlighting the need for improved monitoring and reporting mechanisms in health-care settings [4]. Documenting the incidence and types of ADRs is crucial for several reasons. First, it helps identify the most common and severe reactions associated with specific drugs, thereby guiding safer prescribing practices. Second, it aids in understanding the risk factors and mechanisms underlying these reactions, which can inform preventive strategies. By systematically collecting and analyzing ADR data, health-care institutions can identify trends, implement targeted interventions, and ultimately improve patient safety [5].

Common drugs involved in ADRs include anticancer drugs, antiretroviral drugs, antibacterials, and anti-tuberculosis drugs. Other drugs commonly causing ADRs are antiepileptics and non-steroidal anti-inflammatory drugs (NSAIDs). Additional categories contributing to ADRs included antidiabetic, antihyperlipidemic, antihypertensive, antiulcer, antipsychotic, vaccines, and immunosuppressant drugs [6].

Minor ADRs include symptoms such as nausea, vomiting, mild skin rashes, or headaches. These reactions, while uncomfortable, typically do not pose significant health risks and can often be managed with simple interventions or by discontinuing the offending drug. On the other hand, severe ADRs can have serious and life-threatening consequences. These include anaphylaxis, Stevens–Johnson syndrome, toxic epidermal necrolysis, and drug-induced liver injury. Cardiovascular ADRs, such as arrhythmias or myocardial infarction, and hematological reactions, such as agranulocytosis or thrombocytopenia, are also critical concerns. Identifying and managing these severe ADRs requires prompt recognition and intervention to mitigate risks and prevent adverse outcomes [7].

Despite the significant impact of ADRs on patient health and health-care systems, there are notable knowledge gaps in understanding

their incidence, risk factors, and mechanisms. In India, the lack of comprehensive data and robust pharmacovigilance practices hinders efforts to address these gaps [8]. This study aims to fill these knowledge gaps by systematically investigating the incidence, types, and identification of offending drug in a tertiary care hospital setting.

METHODS

This was a cross-sectional study conducted in the department of pharmacology of a tertiary care medical institute for assessing the clinical spectrum and pattern of ADRs. Fifty consecutive patients reporting any kind of adverse drug reaction were included in this study on the basis of a predefined inclusion criteria. Confidentiality of the participants was strictly maintained. The sample size was determined based on pilot studies examining the profile of patients reporting any kind of ADR. To achieve a power (1-Beta error) of 80% and a confidence interval (1-Alpha error) of 95%, a minimum sample size of 45 patients was required. Consequently, we included 50 cases in this study.

In all the participants, a detailed history including demographic details such as age, gender, and socioeconomic status was noted. A comprehensive history was documented, including drug history, personal history, family history, present and past medical history, and any history of previous drug allergies. Any adverse event was classified as an ADR following consultation with the treating physician. A thorough clinical evaluation and detailed analysis of the data were conducted to assess the pattern, extent, severity, and duration of the reactions. This evaluation also aimed to identify any predisposing or underlying diseases/pathological factors and to determine if any other organs or systems were involved as part of the drug reaction. The reported ADRs were analyzed to determine their clinical types and the causative drugs. The Naranjo scale [9] (A standardized tool used to assess the likelihood that an ADR is related to a specific drug) was used to determine the causality and categorize it into definite, probable, possible, or doubtful causation. Severity of the ADR was assessed using the modified Hartwig scale (Table 1) [10].

The data analysis was done using mean and standard deviation for quantitative variables and the association between two different discrete variables was assessed by Chi-square test. The Statistical Package for the Social Sciences 23.0 version was used for statistical analysis. Microsoft excel was used to generate graphs and tables wherever necessary. All responses were reported in terms of percentages. For statistical purposes, $p<0.05$ was considered as significant.

Inclusion criteria

The following criteria were included in the study:

1. Patients with any severity of adverse drug reaction
2. Age above 18 years
3. Those who gave written and informed consent to be part of study.

Exclusion criteria

The following criteria were excluded from the study:

1. Age <18 years
2. Those who refused consent to be part of study
3. Women who are pregnant or breastfeeding
4. Cases of deliberate overdosing by patients or prescribing errors.

RESULTS

In this study of 50 patients with adverse reactions, there were 36 (72%) males and 14 females (28%). There was a male preponderance with M: F ratio being 1:0.388 (Fig. 1).

The analysis of the gender-wise age distribution of the studied cases showed that among males, the most commonly affected age group was 41–50 years (20.00%), followed by the 51–60 years group (18.00%). The age group above 60 years accounted for 14.00%, while the 31–40 years group represented 10.00%. The 21–30 years group made up 8.00%, and the least affected age group was 18–20 years (2.00%). For females, the most commonly affected age group was 31–40 years (10.00%). The 51–60 and 21–30 years groups each comprised 6.00%, while the 41–50 years group constituted 4.00%. The least affected age groups among females were above 60 years (2%) and 18–20 years (no patients). The mean age of male and female patients was found to be 43.12±14.78 and 37.64±12.02 years, respectively (Table 1). The mean age of male and female patients was found to be comparable with no statistically significant difference (p=0.222) (Table 2).

The analysis of the signs and symptoms of ADRs among the cases showed that the most common complaint was itching (pruritus), which reported in 76.00% of the cases. Skin rashes were the second most frequent symptom, occurring in 26.00% of the cases. Other notable symptoms included nausea and vomiting and dizziness/giddiness,

Table 1: Modified Hartwig scale for assessment of severity of ADR

Severity level	Criteria
Mild	Level 1: ADR requires no change in treatment with the suspected drug. Level 2: ADR requires that treatment with the suspected drug is held, discontinued, or otherwise changed.
Moderate	Level 3: ADR requires that treatment with the suspected drug is held, discontinued, or otherwise changed, and/or an antidote or other treatment is required. Level 4: Any level 3 ADR that increases the length of hospital stay by at least 1 day.
Severe	Level 5: Any level 4 ADR that requires intensive medical care. Level 6: ADR causes permanent harm to the patient. Level 7: ADR either directly or indirectly leads to the death of the patient.

ADR: Adverse drug reaction

Table 2: Gender-wise age distribution of the studied cases

Age in years	Males (%)		Females (%)	
18–20	1	2.00	0	0.00
21–30	4	8.00	3	6.00
31–40	5	10.00	5	10.00
41–50	10	20.00	2	4.00
51–60	9	18.00	3	6.00
Above 60	7	14.00	1	2.00
Total	36	72.00	14	28.00
Mean age	43.12±14.78		37.64±12.02	

p=0.222 95% CI = −14.4005–3.4405

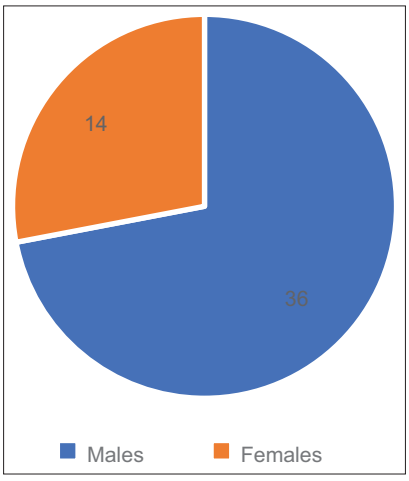

Fig. 1: Gender distribution in the studied cases

each affecting 10.00% of the cases. Abdominal pain or discomfort was reported by 8.00% of the patients, while headache, diarrhea, breathlessness, jaundice, dry mouth, and leg edema were each reported by 6.00% of the cases. Weight gain, muscle pain (myalgia), fatigue, and palpitations were each noted in 4.00% of the patients. Less common symptoms included constipation, sleep disturbances, arrhythmia, and tremors, each observed in 2.00% of the cases. In many patients, more than 1 sign and symptom was present (Table 3).

The analysis of the class of drugs causing ADRs among the 50 cases revealed that antimicrobials were the most common drugs causing ADRs, reported in seven cases (14.00%). This was followed by antiretroviral agents, responsible for ADRs in five cases (10.00%). NSAIDs, antihypertensives and diuretics, and oral hypoglycemic agents each accounted for 3 cases (6.00%). Antiepileptics and corticosteroids were each reported in 4 cases (8.00%). Bronchodilators caused ADRs in 2 cases (4.00%), whereas opioid analgesics were responsible for ADRs in 2 cases (4.00%). Hypolipidemic agents, antiemetics, anticancer agents, antihistaminics, anticholinergics, anxiolytics, antidepressants, hematinics, and Vitamin A analogs each caused ADRs in 2 cases (4.00%) as well. Antipsychotics were noted in 1 case (2.00%) (Fig. 2).

Antimicrobials were the most common cause of ADRs (14%), with amoxicillin (6%), ciprofloxacin (4%), and ceftriaxone (4%) being the primary culprits. Antiretroviral agents accounted for 10% of ADRs, notably efavirenz (6%) and zidovudine (4%). NSAIDs caused 6% of ADRs, primarily ibuprofen (4%). Other notable classes included antihypertensives and diuretics (6%), oral hypoglycemic agents (8%), and antiepileptics (8%), with significant drugs being amlodipine (4%), metformin (4%), glibenclamide (4%), carbamazepine (4%), and phenytoin (4%). Corticosteroids and antihistaminics did not cause any ADRs in this study (Table 4).

The causality assessment of ADRs using the Naranjo scale revealed that 7 cases (14%) were classified as definite, indicating a high likelihood that the ADRs were related to the specific drugs. The majority of cases, 22 (44%), were categorized as probable, and 21 cases (42%) were deemed possible, indicating a potential but less certain link to the drugs. There were no instances where the ADRs were unlikely to be drug-related (Table 5).

The severity assessment of ADRs using the modified Hartwig scale for the 50 cases revealed that the majority of ADRs were mild, with 27 cases (54%). Moderate ADRs were observed in 20 cases (40%), while severe ADRs were noted in 3 cases (6%) (Table 6).

Table 3: Signs and symptoms of adverse drug reaction in studied cases

Signs and symptoms of adverse drug reaction	No of cases	Percentage
Skin rashes	13	26.00
Itching (pruritus)	38	76.00
Nausea and vomiting	5	10.00
Headache	3	6.00
Abdominal pain or discomfort	4	8.00
diarrhea	3	6.00
Constipation	1	2.00
Sleep disturbances	1	2.00
Weight gain	2	4.00
Arrhythmia	1	2.00
Breathlessness	3	6.00
Dizziness/giddiness	5	10.00
Leg edema	3	6.00
Muscle pain (Myalgia)	2	4.00
Tremors	1	2.00
Jaundice	3	6.00
Fatigue	2	4.00
Dry mouth	3	6.00
Palpitations	2	4.00
Others	12	24.00

*In many patients more that 1 sign/symptom was documented

DISCUSSION

ADRs are common occurrence. Many times, mild ADRs go unreported. However, the presence of severe ADRs in a subset of patients necessitates prompt recognition and intervention to mitigate adverse outcomes. Enhanced awareness and systematic reporting of ADRs are crucial steps toward reducing their incidence and ensuring safer pharmacotherapy. In our study, there was a male preponderance with M: F ratio being 1:0.388. Shamna *et al*. conducted a prospective study to detect and analyze ADRs of antibiotics in inpatients of a tertiary care hospital [11]. For this purpose, the authors undertook a study comprising a 6-month period using active and passive spontaneous reporting methods. The study found that 49 ADRs were reported, with a higher incidence in males (53.06%) and the geriatric age groups. However, the authors such as Murali *et al*. [12] and Drici and Clément [13] reported ADRs to be more common amongst females.

In our study, the mean age of male and female patients was found to be 43.12±14.78 and 37.64±12.02 years, respectively. Martin *et al*. conducted an analysis of 48 cohort studies to investigate age- and sex-specific incidence rates of suspected ADRs to newly marketed drugs recorded by general practitioners [14]. For this purpose, the authors collected data from 48 national cohort studies using prescription-event monitoring and questionnaires sent to prescribers. The study found that during the 48 cohort studies, 513,608 patients were investigated. The incidence of suspected ADRs was 12.9/10,000 patient-months for males and 20.6/10,000 patient-months for females. Suspected ADRs to newly marketed drugs were more common in adults aged 30–59 years. Similar age groups were also reported by Yadesa *et al*. [15] and Onder *et al*. [16]

The analysis revealed that the most common ADR was itching (76.00%) followed by skin rashes (26.00%). Other notable symptoms included nausea and vomiting, and dizziness (each 10.00%), abdominal pain (8.00%), headache, diarrhea, breathlessness, jaundice, dry mouth, and leg edema (each 6.00%). Weight gain, muscle pain, fatigue, and palpitations were noted in 4.00% of patients. Less common symptoms (2.00%) were constipation, sleep disturbances, arrhythmia, and tremors. Many patients experienced more than one sign and symptom. Gaur *et al*. conducted a study to analyze ADRs in a teaching hospital [17]. For this purpose, the authors undertook a retrospective study in which

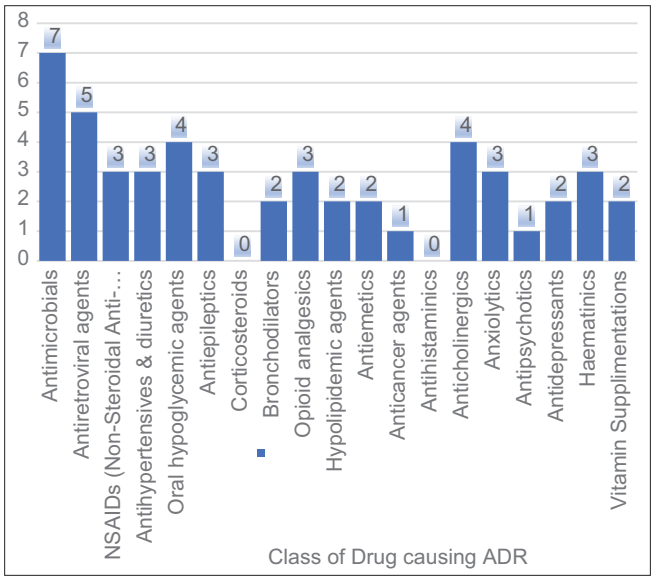

Fig. 2: Class of drugs causing adverse drug reactions in studied cases

Table 4: Drugs causing adverse drug reaction in studied cases

Class of drug	Number of cases	Percentage (%)	Generic Name of drug	Number of cases (percentage)
Antimicrobials	7	14.00	Amoxicillin	3 (6.00)
			Ciprofloxacin	2 (4.00)
			Ceftriaxone	2 (4.00)
Antiretroviral agents	5	10.00	Zidovudine	2 (4.00)
			Efavirenz	3 (6.00)
NSAIDs	3	6.00	Ibuprofen	2 (4.00)
			Naproxen	1 (2.00)
Antihypertensives and diuretics	3	6.00	Amlodipine	2 (4.00)
			Hydrochlorothiazide	1 (2.00)
Oral hypoglycemic agents	4	8.00	Metformin	2 (4.00)
			Glibenclamide	2 (2.00)
Antiepileptics	3	8.00	Carbamazepine	2 (4.00)
			Phenytoin	2 (4.00)
Corticosteroids	0	0.00	-	-
Bronchodilators	2	4.00	Salbutamol	1 (2.00)
			Ipratropium	1 (2.00)
Opioid analgesics	2	4.00	Morphine	1 (2.00)
			Codeine	1 (2.00)
Hypolipidemic agents	2	4.00	Atorvastatin	1 (2.00)
			Simvastatin	1 (2.00)
Antiemetics	2	4.00	Ondansetron	1 (2.00)
			Metoclopramide	1 (2.00)
Anticancer agents	2	4.00	Methotrexate	1 (2.00)
			Cyclophosphamide	1 (2.00)
Antihistaminics	0	0.00	---	----
Anticholinergics	2	4.00	Atropine	1 (2.00)
			Scopolamine	1 (2.00)
Anxiolytics	4	8.00	Diazepam	2 (4.00)
			Alprazolam	2 (4.00)
Antipsychotics	1	2.00	Haloperidol	1 (2.00)
Antidepressants	3	6.00	Fluoxetine	2 (4.00)
			Sertraline	1 (2.00)
Hematinics	2	4.00	Iron supplementation	1 (2.00)
			Folic acid	1 (2.00)
Vitamin A analogues	2	4.00	Isotretinoin	2 (4.00)

NSAIDs: Non-Steroidal Anti-Inflammatory Drugs

Table 5: Causality as per Naranjo scale

Naranjo scale	Number of cases	Percentage
Definite (≥9)	7	14
Probable (5–8)	22	44
Possible (1–4)	21	42
Doubtful (0)	0	0
Total	50	100

Table 6: Severity of ADR as per modified Hartwig scale

Modified Hartwig scale	Number of cases	Percentage
Mild	27	54
Moderate	20	40
Severe	3	6
Total	50	100

ADR: Adverse drug reaction

466 ADRs were recorded in 251 patients. The most common ADRs in the table involved gastrointestinal disorders (31.16%), with symptoms such as nausea, vomiting, diarrhea, and gastritis being frequent. Skin and appendages disorders were also prevalent (22.42%), including rashes, urticaria, and angioedema. Central and peripheral nervous system disorders accounted for 27.35%, with dizziness, sedation, and headaches being major reactions. Hormonal system disorders (8.07%) such as acne and hyperprolactinemia, and psychiatric disorders (3.81%) like altered behavior, were less common but notable. Similar adverse drug reaction profile was also reported by the authors such as Gonzalez *et al*. [18] and Gupta and Udupa [19].

The analysis of ADRs identified antimicrobials (14.00%) as the most common class causing ADRs. Antiretroviral agents accounted for 10.00%, followed by NSAIDs and antihypertensives/diuretics, each causing 6.00% of ADRs. Oral hypoglycemic agents and antiepileptics each caused 4.00% of ADRs. Bronchodilators, opioid analgesics, hypolipidemic agents, antiemetics, anticancer agents, anticholinergics, anxiolytics, and antidepressants each contributed 2.00–4.00% of ADRs. Corticosteroids and antihistaminics did not cause any ADRs in this study. Malathi *et al*., in their study of ADRs, found that anticancer drugs had the highest number of ADRs, followed by antiretroviral drugs, antibacterials, anti-tuberculosis drugs, antiepileptics, NSAIDs, anti-snake venom, and intravenous fluids. Other drug categories contributing to ADRs included antidiabetics, antihyperlipidemic, antihypertensives, antiulcer medications, antipsychotics, vaccines, and immunosuppressants [20]. Other than anticancer and immunosuppressant drugs the rest of drug profile in this study was found to be similar to our study.

CONCLUSION

This study underscores the importance of identifying and documenting ADRs to enhance patient safety, optimize therapeutic outcomes, and reduce healthcare costs. Prompt recognition and management of ADRs are crucial for minimizing their adverse effects on patient health and for guiding safer prescribing practices in clinical settings.

AUTHORS' CONTRIBUTIONS

The authors would like thanks to SN- Concept, design, clinical protocol, manuscript preparation, editing, statistical analysis, and interpretation; VR- Manuscript review, literature survey and preparation of figures, coordination, and manuscript revision.

CONFLICTS OF INTEREST

None.

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