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Assessment Of Adverse Drug Reaction Patterns and Their Associated Risk Factors in Clinical Pharmacotherapy

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ABSTRACT

Clinical pharmacotherapy and can influence medication safety and effectiveness. The current research investigated ADR patterns and their risk factors in patients receiving pharmacotherapy. An observational study was performed during six months involving 150 patients. ADRs were characterized based on clinical pattern, involved therapeutic class, causality, severity and preventability of the reactions, while patient-related and therapy-related risk factors were statistically analyzed. Out of 150 patients, 36 (24.0%) suffered from ADRs with the total number of 45 ADR occurrences reported. The most common type of adverse drug reaction was gastrointestinal reaction (26.7%), neurological (20.0%) and dermatological reactions (17.8%). The most frequently implicated therapeutic classes were antimicrobial drugs (24.4%), cardiovascular (20.0%) and antidiabetic drugs (15.6%). The majority of ADRs was classified as mild and moderate, and 40.0% of ADRs were definitely or probably preventable. Multiple regression analysis revealed that polypharmacy was an independent risk factor of ADR occurrence, whereas patient's age was another significant factor affecting the risk of ADRs.

Keywords: Adverse drug reactions; Clinical pharmacotherapy; Polypharmacy; Pharmacovigilance; Medication safety

1.INTRODUCTION

An adverse drug reaction (ADR) is one of the key issues related to clinical pharmacotherapy since drugs that should be beneficial to patients can cause some unexpected and adverse effects [1]. An ADR can manifest itself in minor and temporary symptoms or more severe reactions necessitating change in therapy or even hospitalization [2]. The significance of adverse drug reactions has been increasing as a result of the increased use of several drugs for chronic conditions and comorbidities [3].

An ADR can be responsible for morbidity, extended stays in hospitals, need for additional treatment, and higher health care costs [4]. Thus, the role of pharmacovigilance is critical in terms of the detection, analysis, knowledge, and prevention of medication-related problems [5].

1.1 Patterns and Clinical Characteristics of ADRs

ADR patterns depend on the specific medication, the therapeutic group, patient demographics and clinical conditions [6]. The ADRs may be assessed based on the affected organ system,

type of clinical effect, severity, causality and preventability [7]. This type of evaluation enables identification of common medicines causing ADRs and clinically relevant ADRs which require closer observation [8].

Causality evaluation reveals the probability that the medication causes the reaction while the severity evaluation assesses the clinical impact of the reaction [9]. Evaluation of preventability will reveal whether the reaction could be avoided by proper prescribing and dose adjustment.

1.2 Risk Factors Associated with ADRs

There are several individual and therapy-related risk factors that could affect the development of adverse drug reactions. Some of the most important risk factors are age, sex, polypharmacy, co-morbidity, duration of therapy, type of therapeutic drugs used, kidney or liver dysfunction and history of drug or allergic reactions [10]. The risk factor of polypharmacy is especially important, as multiple drugs taken simultaneously can cause side effects and drug interactions.

1.3 Research Rationale, Aim and Objectives

In spite of increased focus on pharmacovigilance, the profiles of ADRs and the risk factors linked to them differ from one patient group to another. It is therefore necessary to perform an evaluation of the profiles of ADRs and their risk factors.

Aim:

To assess adverse drug reaction patterns and identify their associated risk factors in clinical pharmacotherapy.

Objectives:

1. To determine the frequency and pattern of adverse drug reactions (ADRs) among patients receiving clinical pharmacotherapy.
2. To identify the major therapeutic drug classes and organ systems associated with ADRs.
3. To assesses the severity, causality and preventability of identified ADRs.
4. To examine the patient- and treatment-related factors associated with the occurrence of ADRs.
5. To identify the significant risk factors associated with ADR occurrence in clinical pharmacotherapy.

2. REVIEW OF LITERATURE

The literature on ADRs included studies conducted in different patient groups and in various therapeutic settings and revealed that the risk of ADRs depended on patient characteristics, medication factors, genetic differences, and specific medications. The current literature also discussed the importance of pharmacovigilance and identification of high-risk patients in improving medication safety.

Ruangritchankul et al. (2021) [11] performed a literature review of ADRs in association with acetylcholinesterase inhibitors in older patients living with dementia. It was shown that older patients were especially vulnerable to adverse effects due to physiological changes related to aging, multiple comorbidities, and concomitant medication use. Clinically significant ADRs

related to the use of acetylcholinesterase inhibitors were discussed in the review, and the importance of proper medication review and monitoring among older adults was noted. Age, comorbidities, and polypharmacy appeared to be the key elements in the assessment of ADR risk.

Yadesa et al. (2021) [12] conducted a systematic review and meta-analysis of ADR prevalence, characteristics, and predictors in hospitalised older adults. It was stated that ADRs were a significant problem of medication safety in this group of patients. Several patient- and treatment-related characteristics were revealed which were predictors of higher ADR risk. The influence of polypharmacy and other clinical characteristics was particularly discussed in the study, and the identification of high-risk patients could allow the early detection and prevention of ADRs.

Zucker and Prendergast (2020) [13] assessed differences in pharmacokinetics of medications between men and women and their associations with ADRs. It was shown that women had higher chances to have ADRs in association with many medications, and pharmacokinetic differences contributed to such results. The study suggested that the differences in the exposure and elimination of drugs by males and females affected the risk of ADRs. Such evidence supported the need to take sex differences into account while assessing the risk of ADRs.

Swen et al. (2023) [14] explored the role of a 12-gene pharmacogenetic panel for the reduction of ADRs via genotype-guided prescribing in a multicenter, controlled, cluster-randomized crossover implementation study. Pharmacogenetic-guided prescribing reduced the incidence of ADRs among patients receiving drugs with actionable pharmacogenetic recommendations. The results revealed the potential benefit of integrating genetic factors in personalized pharmacotherapy, and individual differences in drug response were found to be a critical aspect of ADR prevention.

Zou et al. (2024) [15] assessed adverse drug events in association with linezolid with the help of pharmacovigilance data from the U.S. FDA Adverse Event Reporting System covering 2004-2023. Several safety signals related to the use of linezolid were revealed in the study. It was also revealed that real-world pharmacovigilance databases allowed identifying and characterizing ADRs related to different medicines, and the nature and frequency of ADRs differed according to medications.

3. MATERIAL AND METHOD

3.1 Study Design and Setting

The study followed a prospective observational design to assess adverse drug reaction (ADR) patterns and their associated risk factors among patients receiving clinical pharmacotherapy. Patients attending or admitted to selected clinical departments were observed over a period of six months. Relevant demographic, clinical and medication-related information was collected systematically during the study period.

3.2 Study Population and Sample Size

The study subjects comprised of patients taking one or more medicines as per prescription within the study period. The final sample comprised of 150 patients. Selection of study

subjects involved consecutive sampling method whereby eligible patients were enrolled to reach the predetermined sample size.

Male or female patients undergoing pharmacological treatment and having adequate information about their medications were included. Patients who did not have complete medical history, adequate information about their medicines, or enough information to assess suspected adverse drug reaction were excluded from the study.

3.3 Data Collection and ADR Assessment

Data collection was done using an organized ADR data collection sheet. The data was gathered from the patient's file, drug administration list, laboratory findings, and clinical examination of the patient. The parameters involved are the age, sex, diagnosis, comorbidities, drugs used, total number of drugs used, duration of drug usage, hepatic/renal dysfunction, and history of drug allergy or ADRs.

The suspected ADRs were categorized based on their clinical presentation, organ systems involved, and probable drug classes. Polypharmacy is considered when there is concurrent administration of five or more medicines. Causality was assessed using the WHO–UMC causality scale, while the severity and preventability of the ADRs were determined based on clinical criteria**.**

3.4 Outcome Measures and Statistical Analysis

The main outcomes were the incidence and pattern of ADRs, drug classes involved, body systems affected, causality, severity, and preventability of the ADRs. The study also sought to determine patient- and treatment-related factors related to ADRs.

Analysis of data involved the use of relevant statistical packages. Frequencies and percentages were used to analyze categorical data, while continuous data was analyzed by mean and standard deviation. Statistical association between categorical data and ADRs was done using Chi-square test/Fisher's exact test. Odds ratio and 95% Confidence Interval was used to determine predictors of ADRs using logistic regression. P-value less than 0.05 was taken as statistically significant.

3.5 Ethical Considerations

Ethical clearance was secured from the relevant Institutional Ethics Committee prior to data collection. Patient confidentiality was kept intact during the research period, and any identifying information was removed from the analysis dataset.

4. RESULT AND DISCUSSION

The results of the current study have been analyzed with respect to the prevalence and patterns of ADRs and with respect to the most important factors that contributed to the development of ADRs. The data collected from 150 respondents have been analyzed with regard to the demographic and clinical parameters, the prevalence of ADRs, involved organ systems, types of therapeutic drugs, the causality, severity and preventability of ADRs. In addition, some statistical analysis has been conducted to determine important risk factors for the development of ADRs.

4.1 Demographic and Clinical Characteristics

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The total number of patients in this research was 150 patients. Out of those 150 patients, 47 (31.3%) were 60 years or older, whereas 42 (28.0%) of the patients were in the age range of 46 to 59 years. The percentage of female patients was 52.0%. Cardiovascular disease and endocrine disorders were some of the commonest health conditions that occurred in this study. Polypharmacy occurred in 62 patients (41.3%).

Table 1. Demographic and Clinical Characteristics of Participants (N = 150)

Characteristics	Category	Frequency (n)	Percentage (%)
Age	18–30 years	24	16.0
	31–45 years	37	24.7
	46–59 years	42	28.0
	≥60 years	47	31.3
Gender	Male	72	48.0
	Female	78	52.0
Major condition	Cardiovascular disorders	42	28.0
	Diabetes/endocrine	33	22.0
	Infectious diseases	27	18.0
	Respiratory disorders	21	14.0
	Others	27	18.0
Number of medicines	<5	88	58.7
	≥5	62	41.3
Comorbidities	Present	85	56.7
	Absent	65	43.3
Duration of therapy	≤1 month	42	28.0
	1–6 months	46	30.7
	>6 months	62	41.3

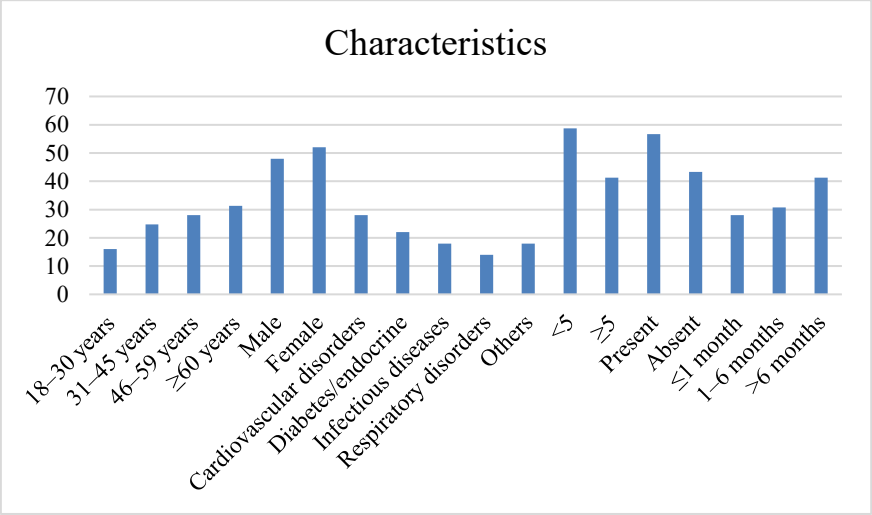


Figure 1: Graphical Representation of Demographic and Clinical Characteristics of Participants (N = 150)

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Age distribution of the population revealed considerable presence of elderly patients, people with co-morbidities, and those using many medications. These factors played a role in ADR detection due to the previous association between such parameters and increased risk of developing medicine-related ADRs.

4.2 Overall Occurrence of ADRs

Out of the 150 patients, 36 patients (24.0%) suffered from at least one ADR while 114 (76.0%) did not have any ADR. There were 45 ADRs that occurred. Out of the 36 patients who suffered from ADRs, 27 patients (75.0%) suffered from one ADR while 9 (25.0).

Table 2. Distribution and Frequency of ADRs

ADR Status	Frequency (n)	Percentage (%)
Patients with ADRs	36	24.0
Patients without ADRs	114	76.0
Single ADR*	27	75.0
Multiple ADRs*	9	25.0
Total ADR events	45	—

*Percentage calculated among the 36 patients experiencing ADRs.

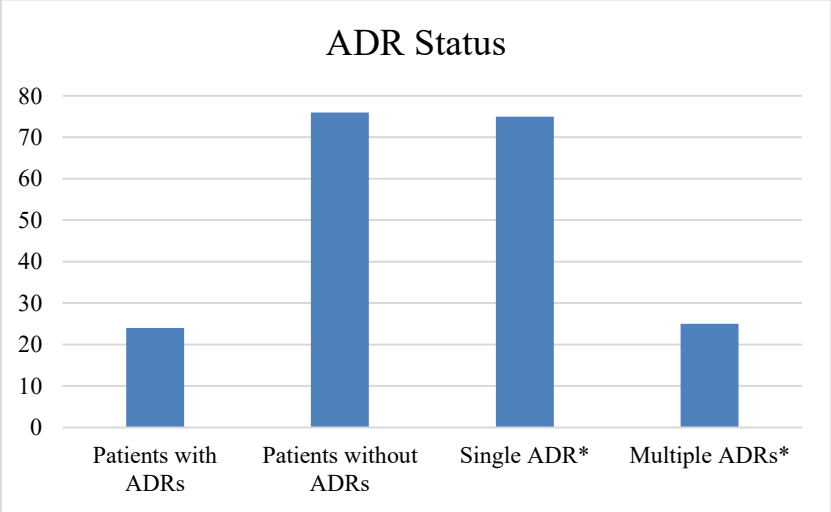


Figure 2: Graphical Representation of Distribution and Frequency of ADRs

The results revealed that close to one-quarter of the respondents encountered an ADR, suggesting that adverse events resulting from drugs were of significance in pharmacotherapy.

4.3 Pattern of Adverse Drug Reactions

The highest percentage of adverse drug reactions was gastrointestinal (26.7%), followed by neurologic (20%) and skin reactions (17.8%).

Table 3. Pattern of ADRs According to Organ System (n = 45 ADRs)

Organ System	Major Manifestations	n	%
Gastrointestinal	Nausea, vomiting, diarrhoea	12	26.7
Neurological	Dizziness, headache, drowsiness	9	20.0
Dermatological	Rash, itching, urticaria	8	17.8
Cardiovascular	Hypotension, palpitations	6	13.3

Metabolic/endocrine	Hypoglycaemia, electrolyte disturbances	4	8.9
Hepatic	Elevated liver enzymes	3	6.7
Renal	Altered renal function	2	4.4
Others	Other manifestations	1	2.2
Total		45	100.0

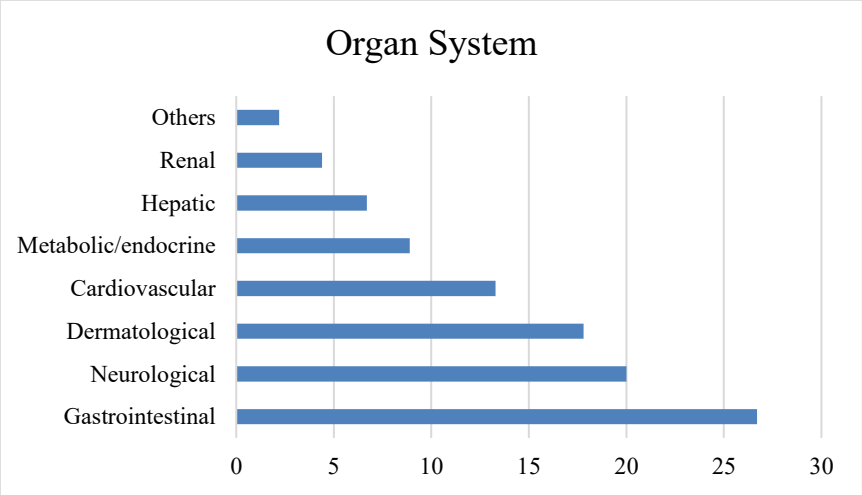


Figure 3: Graphical Representation of Pattern of ADRs According to Organ System (n = 45 ADRs)

The frequency of gastrointestinal and neurologic symptoms implied the need for special consideration of these organ systems during medication monitoring. Dermatological responses were also fairly common, including rash, itching, and hives.

4.4 Therapeutic Drug Classes Associated with ADRs

Antimicrobials made up the highest percentage of ADRs (24.4%), while cardiovascular drugs followed second (20.0%), and antidiabetics third (15.6%)

Table 4. Distribution of ADRs According to Therapeutic Drug Class

Therapeutic Class	ADRs (n)	Percentage (%)
Antimicrobial agents	11	24.4
Cardiovascular medicines	9	20.0
Antidiabetic medicines	7	15.6
Analgesics/NSAIDs	6	13.3
CNS medicines	5	11.1
Gastrointestinal medicines	3	6.7
Respiratory medicines	2	4.4
Others	2	4.4
Total	45	100.0

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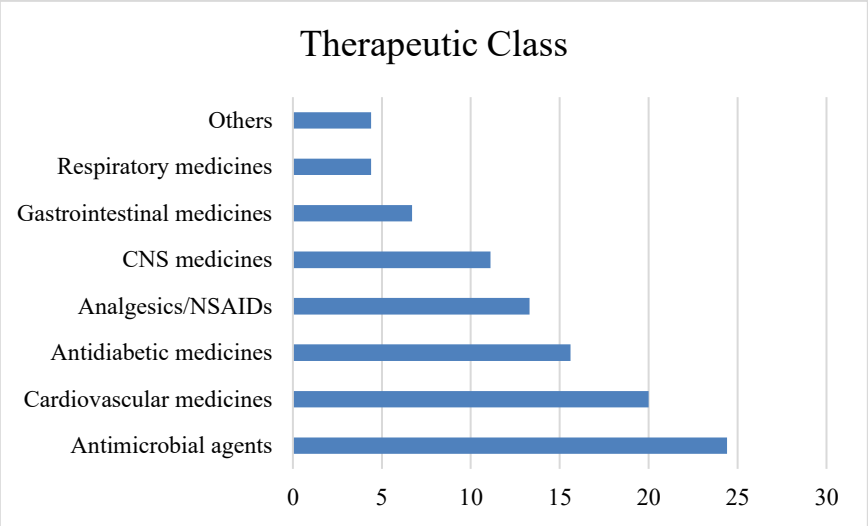


Figure 4: Graphical Representation of Distribution of ADRs According to Therapeutic Drug Class

These results showed that ADRs were influenced by the type of drugs used. Intensified surveillance for drugs that commonly lead to ADRs could aid in early detection and treatment of drug-related issues.

4.5 Causality, Severity and Preventability

Probable and possible were the most common categories of ADRs at 51.1% and 40%, respectively. In terms of severity, the majority were mild (48.9%), moderate (42.2%) and only 8.9% were severe. Approximately 40%

Table 5. Causality, Severity and Preventability of ADRs (n = 45)

Assessment	Category	n	%
Causality	Certain	4	8.9
	Probable	23	51.1
	Possible	18	40.0
Severity	Mild	22	48.9
	Moderate	19	42.2
	Severe	4	8.9
Preventability	Definitely preventable	6	13.3
	Probably preventable	12	26.7
	Not preventable	27	60.0

The preponderance of mild to moderate ADRs indicated that most reactions were clinically manageable. Nevertheless, the occurrence of severe ADRs was still significant from the standpoint of patient safety. In addition, the identification of preventable ADRs revealed areas where medication management could be optimized.

4.6 Association Between Risk Factors and ADR Occurrence

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Associations between certain patient factors and occurrence of adverse drug reactions were explored. Increased age, polypharmacy, and the presence of other conditions correlated significantly with ADR occurrence.

Table 6. Association Between Selected Risk Factors and ADR Occurrence (N = 150)

Risk Factor	ADR Present n (%)	ADR Absent n (%)	p-value
Age <60 years (n=103)	18 (17.5)	85 (82.5)	
Age ≥60 years (n=47)	18 (38.3)	29 (61.7)	0.005
Male (n=72)	15 (20.8)	57 (79.2)	
Female (n=78)	21 (26.9)	57 (73.1)	0.382
<5 medicines (n=88)	12 (13.6)	76 (86.4)	
≥5 medicines (n=62)	24 (38.7)	38 (61.3)	<0.001
No comorbidity (n=65)	10 (15.4)	55 (84.6)	
Comorbidity present (n=85)	26 (30.6)	59 (69.4)	0.031

Higher incidence of adverse drug reactions occurred in patients who were using five or more drugs, and this was an indication that polypharmacy plays a significant role in the development of adverse reactions. Older patients (≥60 years) also developed adverse drug reactions more frequently.

4.7 Multivariable Analysis of ADR Risk Factors

A multivariate logistic regression analysis was done to assess the association between certain variables and ADRs while controlling for other factors**.**

Table 7. Multivariable Logistic Regression Analysis of ADR Risk Factors

Predictor	Adjusted Odds Ratio (AOR)	95% CI	p-value
Age ≥60 years	2.18	1.01–4.70	0.047
Female gender	1.29	0.59–2.81	0.522
Polypharmacy (≥5 medicines)	3.05	1.39–6.69	0.005
Presence of comorbidity	2.01	0.91–4.45	0.084

The significant predictors of ADRs were polypharmacy, where patients taking five or more drugs had about thrice higher chance of developing an ADR compared to the others. Age greater than 65 years was also another important predictor of ADR development. A total of 24.0% of the 150 study participants developed ADRs; gastrointestinal, neurological and dermatological types of reactions were the commonest types of ADRs. Antimicrobial, cardiovascular and antidiabetic drugs were the main drug groups involved, and majority of ADRs were of mild to moderate intensity. The results underscored the need for medication review, surveillance of elderly patients and prudent management of polypharmacy.

5. CONCLUSION AND RECOMMENDATIONS

The study analyzed patterns of adverse drug reactions in 150 patients, of which 24.0% had adverse drug reactions. The most common ADRs were those involving gastrointestinal system, neurological system and skin. Antimicrobial drugs, cardiovascular drugs and

antidiabetic drugs were the commonest drug classes involved in ADRs. The majority of ADRs were mild to moderate in intensity. Polypharmacy was found to be the best predictor of ADRs, while age was significantly associated with risk of ADRs. The results stressed the need for ADR surveillance and safe management of medicines.

Medication review must be done to minimize risks associated with polypharmacy.

1. Older patients and polypharmacy patients should be monitored closely in clinical setting.
2. Commonly implicated drug classes must be monitored to detect ADRs early.
3. Pharmacovigilance and ADR reporting should be promoted in clinical setting.
4. Risk factors of patients must be taken into consideration during planning and monitoring of pharmacotherapy.

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