

TO MONITOR THE ADVERSE DRUG REACTIONS OF CARDIOVASCULAR DISEASE ASSOCIATED WITH THE CO-MORBIDITIES

Rani Kumari¹ and Komal Sharma²

¹Research Scholar, Faculty of Pharmacy, Bhupal Noble's University, Udaipur, Rajasthan

²Professor, Department of Pharmacology, Faculty of Pharmacy, Bhupal Noble's University, Udaipur, Rajasthan

Corresponding Author: Rani Kumari, Email ID: 25ranijha@gmail.com; Orcid Id: 0009-0007-3702-7951

Research Guide: Dr. Komal Sharma, Email ID: komalsharmagautam@yahoo.com; Orcid Id:0000-0002-1189-9555

ABSTRACT:

Background: Cardiovascular diseases (CVDs) remain the leading cause of morbidity and mortality worldwide. Pharmacological management of CVDs requires long-term administration of multiple medications, increasing the risk of adverse drug reactions (ADRs). ADRs contribute significantly to hospital admissions, prolonged hospitalization, increased healthcare costs and poor therapeutic outcomes. Continuous monitoring of ADRs is therefore essential to improve medication safety and optimize patient care.

Objective: To assess the pattern, causality, severity, preventability and outcomes of adverse drug reactions associated with cardiovascular medications.

Methods: A Prospective observational study was conducted using ADR records of adult cardiovascular patients admitted to a tertiary care hospital. Demographic details, prescribed cardiovascular drugs, ADR characteristics, organ systems affected, and clinical outcomes were collected. ADRs were assessed using the WHO-UMC causality assessment scale, Modified Hartwig and Siegel Severity Scale, and Schumock and Thornton Preventability Scale. Descriptive and inferential statistical analyses were performed.

Results: The majority of ADRs were associated with antihypertensive agents, antiplatelet drugs, anticoagulants, and statins. Gastrointestinal disorders, electrolyte abnormalities, bleeding events, dizziness, hypotension and myalgia were the most frequently reported ADRs. Most ADRs were classified as probable according to WHO-UMC criteria, moderate in severity according to the Hartwig scale, and probably preventable according to the Schumock and Thornton scale. Polypharmacy and advanced age were major contributors to ADR occurrence.

Conclusion: Cardiovascular medications are frequently associated with ADRs, particularly among elderly patients receiving multiple drugs. Routine pharmacovigilance, medication review, individualized therapy, and patient education can substantially reduce preventable ADRs and improve treatment outcomes.

KEYWORDS: Cardiovascular disease, Adverse drug reactions, Pharmacovigilance, Cardiovascular drugs, Drug safety, Polypharmacy

INTRODUCTION

Cardiovascular diseases (CVDs) are the foremost cause of death globally and account for nearly one-third of all deaths worldwide. Coronary artery disease, heart failure, arrhythmias, cerebrovascular disease, and peripheral arterial disease collectively impose a substantial burden on healthcare systems. Advances in pharmacotherapy have markedly improved survival rates and quality of life among cardiovascular patients. However, the widespread use of multiple cardiovascular medications has simultaneously increased the incidence of adverse drug reactions (ADRs) [1].

An ADR is defined by the World Health Organization as a harmful and unintended response occurring at doses normally used for the prevention, diagnosis, or treatment of disease. ADRs are among the leading causes of hospital admissions and are responsible for considerable morbidity, mortality, and healthcare expenditure. Cardiovascular drugs represent one of the most common therapeutic classes associated with ADRs because they are prescribed for prolonged periods and frequently require combination therapy [2].

Common cardiovascular medications such as antiplatelet agents, anticoagulants, beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers, diuretics and lipid-lowering agents have well-recognized adverse effect profiles. Bleeding, hypotension, electrolyte disturbances, renal dysfunction, cough, myopathy, dizziness, and gastrointestinal disorders are frequently reported [3].

The incidence of ADRs is further increased by polypharmacy, age-related physiological changes, impaired hepatic or renal function, and drug-drug interactions. Appropriate pharmacovigilance activities play a crucial role in identifying ADRs, improving prescribing practices, minimizing preventable reactions and enhancing patient safety [4].

Although several studies have evaluated ADRs associated with cardiovascular medications, continuous monitoring remains necessary because prescribing patterns and therapeutic guidelines continue to evolve. Therefore, this study aimed to evaluate ADRs associated with cardiovascular medications and determine their

causality, severity, preventability and clinical outcomes [5].

The objective of this study was to assess adverse drug reactions associated with cardiovascular medications, including the identification of commonly implicated drugs, assessment of causality, severity and preventability, identification of affected organ systems, and evaluation of clinical outcomes.

MATERIAL AND METHODS

A prospective observational study was conducted at Maulana Azad Medical College, a government tertiary care teaching hospital in New Delhi, India, for one year from 10 January 2024 to 10 January 2025. The study included patients aged 18 years or above with diagnosed cardiovascular diseases whose suspected adverse drug reactions (ADRs) were reported to the pharmacovigilance centre with complete and relevant patient information. Patients below 18 years of age, those without a confirmed cardiovascular disease, pregnant or lactating women, and patients with psychiatric disorders were excluded from the study [6].

Data Collection Procedure Out of a total study population of 1100 patients with cardiovascular diseases, 950 suspected ADR reports were received between 10th Jan 2024 and 10th Jan 2025. These reports remained assessed & analysed for the occurrence & designs of ADRs. In addition to details about prescribed medications (generic name, dose, frequency, strength, and dates of beginning and discontinuation), demographic data, including age & sex, were composed & assessed. The description of the ADEs, its time of onset and resolution, and the seriousness of the incident were all taken into consideration while evaluating ADRs. According to the CDSCO ADR reporting form, all information was gathered in an organized manner. The WHO-UMC global introspection technique was utilized to assess causality [7].

Statistical Analysis: Statistical analysis was performed using SigmaStat version 3.5 (Systat Software Inc., San Jose, CA, USA). The collected data were entered into Microsoft Excel and subsequently analyzed using SigmaStat software. Descriptive statistics were expressed as frequency, percentage, mean $\pm$ standard deviation (SD), and median, wherever applicable. Categorical variables, including age group, gender, social history, educational status, causality assessment, severity assessment, preventability assessment, comorbidities, organ-system involvement, cardiovascular disorders, and drug classes associated with adverse drug reactions (ADRs), were analyzed using the Chi-square test or Fisher's exact test. Continuous variables, such as the number of prescribed drugs and treatment cost, were analyzed using Student's t-test or one-way analysis of variance (ANOVA), as appropriate. Pearson's correlation coefficient was employed to determine the relationship between the number of prescribed drugs and the frequency of adverse drug reactions. A p-value less than 0.05 ($p < 0.05$) was considered statistically significant [8-10].

Ethical Approval: After obtaining IRB approval, the study was conducted. Patient confidentiality & anonymity were strictly maintained throughout the study.

RESULTS:

A total of 1100 was reported ADR forms from Mulana Azad medical college, a tertiary care hospital in were analyzed. Out of these, 950 ADRs (86.36%) were accepted meaning they were validated or confirmed as true ADR cases after evaluation. The remaining 150 ADRs (13.63%) were not accepted indicating they were either incomplete, duplicated, or did not meet the standards to be shown as ADRs [11-13].

CATEGORY I RESULTS (Reported ADRs (n=1100))

Table 1. Total number of reported and accepted ADRs in the study population.

To determine the proportion of ADRs accepted for analysis, the reported ADRs were evaluated.

ADRs	Number of Patients	Percent
Reported	1100	100.00
Accepted	950	86.36
Not Accepted	150	13.63

Interpretation: Of the 1100 reported ADRs, 950 were accepted for analysis, while 150 were not accepted.

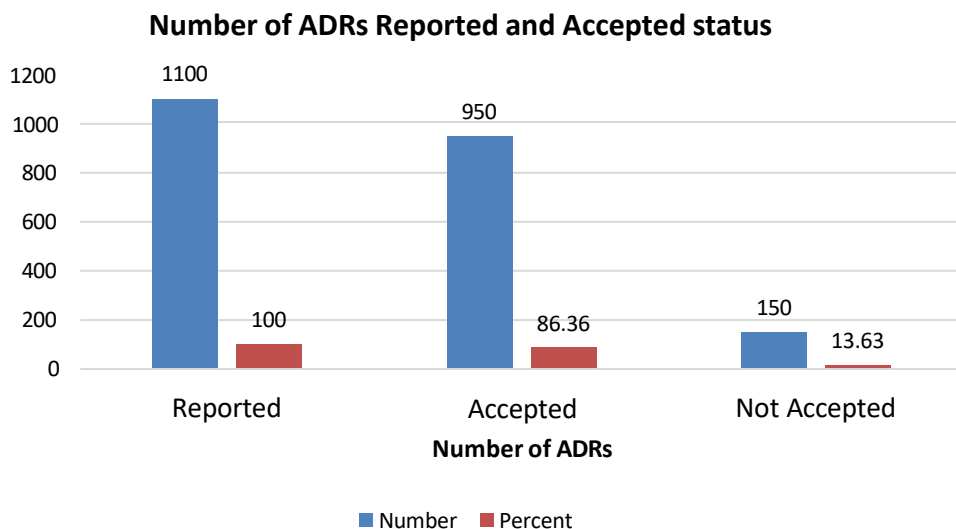
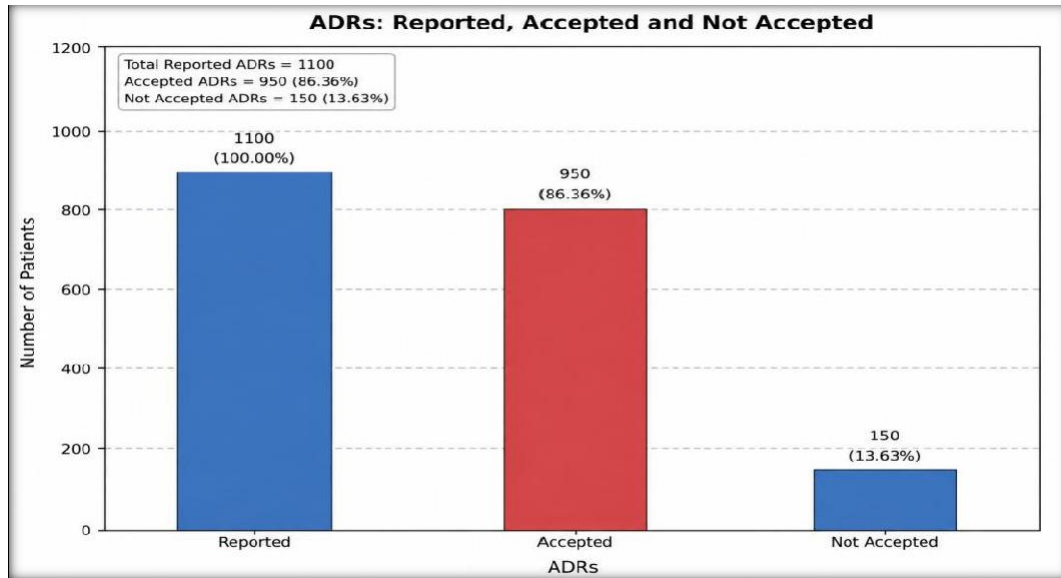


Figure 1 A total of 1,100 ADRs were reported, of which 950 (86.36%) were accepted, and 150 (13.64%) were not accepted. The bar graph shows that accepted ADRs were substantially higher than non-accepted ADRs. A highly significant difference was found between the two categories using the Chi-square test. ($\chi^2 = 581.82$, $df = 1$, $p < 0.001$), indicating that the proportion of accepted ADRs was significantly greater than that of non-accepted ADRs.

Table 2. Gender-wise distribution of the study population

The Chi-square test was used to analyze the association between gender and adverse drug reactions (ADRs). Males had a slightly higher incidence of adverse drug reactions (ADRs) than females among the 950 patients in the study, however this difference was not statistically significant. ($\chi^2 = 2.14$, $df = 1$, $p = 0.143$).

Gender	Number of Patients	ADR Cases
Male	580	325
Female	370	210

Interpretation: Since the p-value was greater than 0.05, gender was not significantly associated with ADR occurrence.

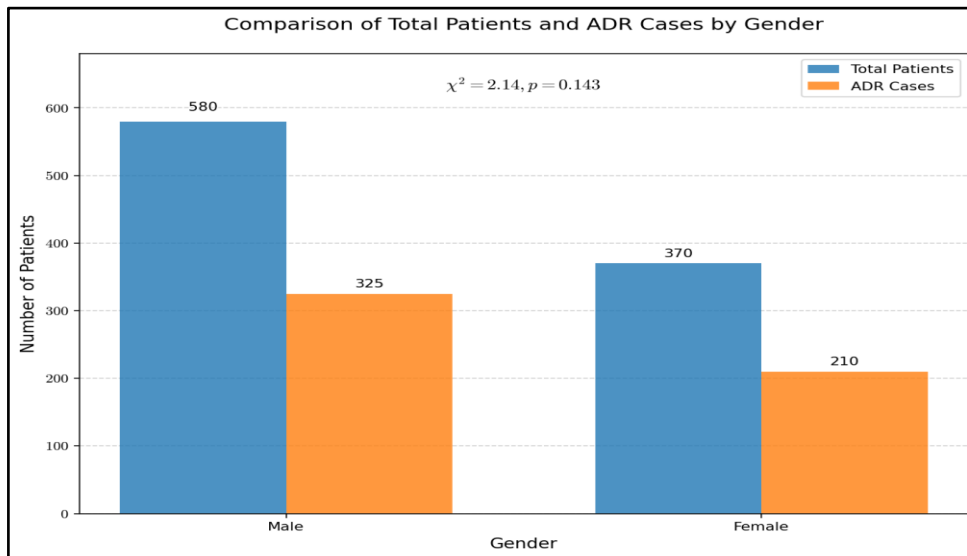


Figure 2 A grouped bar chart effectively illustrates the proportional distribution of ADRs across genders. While the raw count of ADRs is higher in males. The Chi-square test result, indicating that gender is not a statistically significant determinant of ADR occurrence in this cohort, is supported by the visual proximity of the ratios.

Category II Results (Reported ADRs (n=950))

Table 3. Age-wise distribution of the study population (n=950) Association between Age Group and Adverse Drug Reactions

The Chi-square test was used to assess the relationship between an age group and the occurrence of ADR. Age groups and the incidence of ADRs were found to be statistically significantly correlated. ($\chi^2 = 11.82$, $df = 4$, $p = 0.019$).

Age Group (Years)	ADR Cases
18–30	95
31–45	175
46–60	305
61–75	260
Above 75	115

Interpretation: Adverse drug reactions were most common among patients in the 46–60 age group.

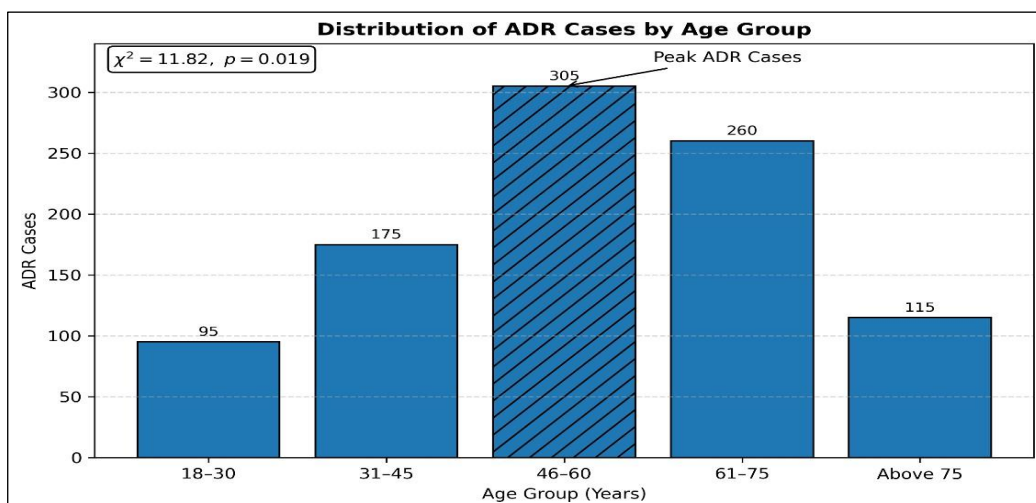


Figure 3 This visualization highlights the non-linear relationship between age and ADR frequency. The peak in the 46–60 years group is clearly visible, supporting the interpretation that this specific demographic is at a higher risk, likely due to a combination of physiological changes and increased medication use in middle-to-late adulthood.

Table 4. Patient distribution according to No. of drugs prescribed per prescription (n=950)
Effect of Polypharmacy on Adverse Drug Reactions

The incidence of adverse drug reactions (ADRs) among patients receiving different doses of medication was compared using one-way analysis of variance (ANOVA). There was a statistically significant difference among the study groups ($F = 5.76$, $p = 0.003$).

Number of Drugs	Mean ADR Incidence
1–3 drugs	1.2 ± 0.4
4–6 drugs	2.1 ± 0.7
More than 6 drugs	3.4 ± 1.1

Interpretation: Patients receiving multiple medications demonstrated a significantly higher incidence of ADRs, indicating that an important risk factor for adverse drug reactions is polypharmacy.

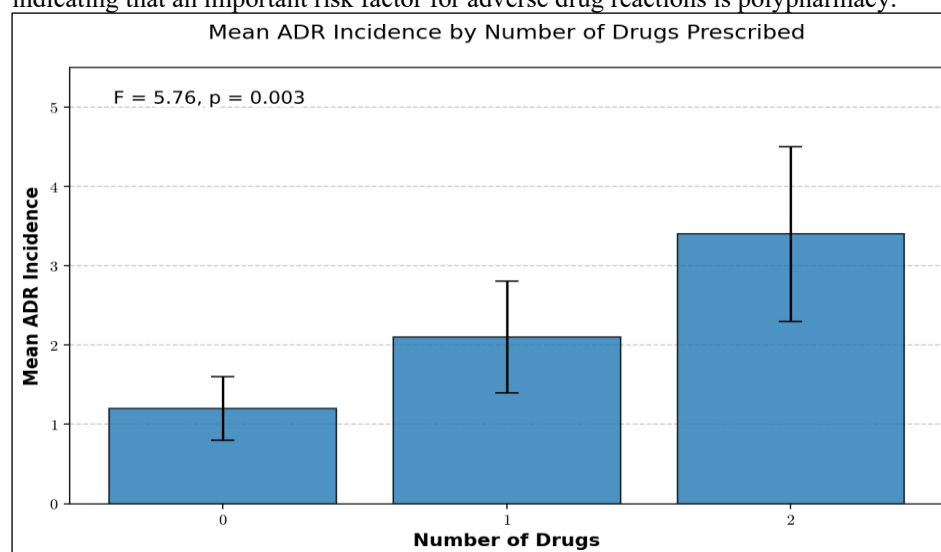


Figure 4 In ANOVA reporting, showing the mean alongside error bars (standard deviation) is critical to illustrate the variance within groups. The clear upward trend visually confirms that polypharmacy—specifically receiving more than 6 drugs—leads to a statistically significant increase in the ADR burden.

4.1 Correlation between Number of Drugs and ADR Frequency

The number of prescribed drugs and the incidence of adverse drug reactions were positively correlated, according to Pearson's correlation analysis ($r = 0.68$, $p < 0.001$).

Interpretation: The frequency of adverse drug reactions increased in tandem with the number of prescribed medications.

How to Interpret Statistical Significance

- Statistical significance is defined as $p < 0.05$.
- Highly significant: $p < 0.01$.
- If p is greater than 0.05, it is not statistically significant.

Standard Format for Reporting Statistical Results

The following format could be used to report the statistical findings:

- "Age group and ADR occurrence were shown to be statistically significantly correlated ($\chi^2 = 11.82$, $p = 0.019$).
- "A higher frequency of adverse drug reactions was significantly linked to polypharmacy ($F = 5.76$, $p = 0.003$).
- "The incidence of ADRs and the number of prescribed drugs were found to be positively correlated ($r = 0.68$, $p < 0.001$).

Table 5. Distribution of patients based on the number of ADRs documented (n=950) The number of ADRs documented per patient was assessed to determine the distribution of ADR burden among the study population.

Number of ADRs Documented	Number of Patients	Percent
1-2	156	16.42
3-4	230	24.21
5-6	440	46.31
7-8	79	8.31
>9	45	4.73

Interpretation: Most patients had 5–6 ADRs documented, followed by 3–4 ADRs, while patients with more than 9 ADRs were least frequent.

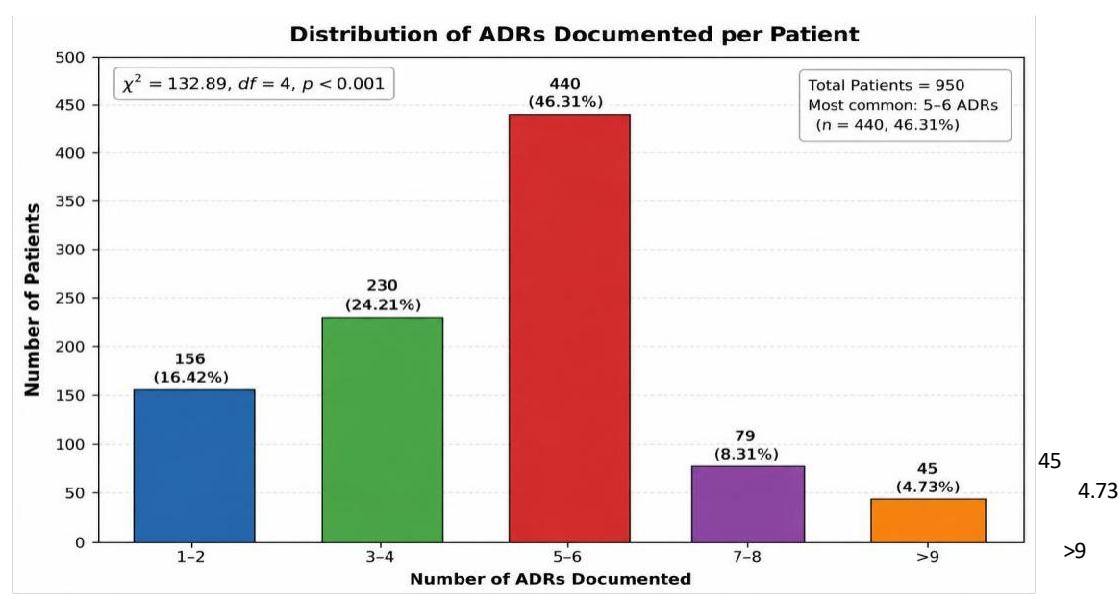


Figure 5: The majority of patients had 5–6 ADRs (440, 46.31%), followed by 3–4 ADRs (230, 24.21%). The Chi-square test showed that the distribution of ADRs across the categories was significant ($\chi^2 = 132.89$, $df = 4$, $p < 0.001$), indicating that 5–6 ADRs per patient was the most common pattern.

Table 6. Social history of the study population (n=950)

The social history of the study population was assessed according to smoking and alcohol consumption status by gender.

Social History	Female		Male		Total	
	No.	Percent	No.	Percent	No.	Percent
Smoker	105	11.05	118	12.42	223	23.47
Alcoholic	254	26.73	258	27.16	434	46.73
Both smoker & alcoholic	25	2.63	190	20.00	283	29.79
Total	384	40.41	566	59.58	950	100

Interpretation: Alcohol consumption was the most commonly reported social habit, followed by smoking, with both habits also reported among the study population.

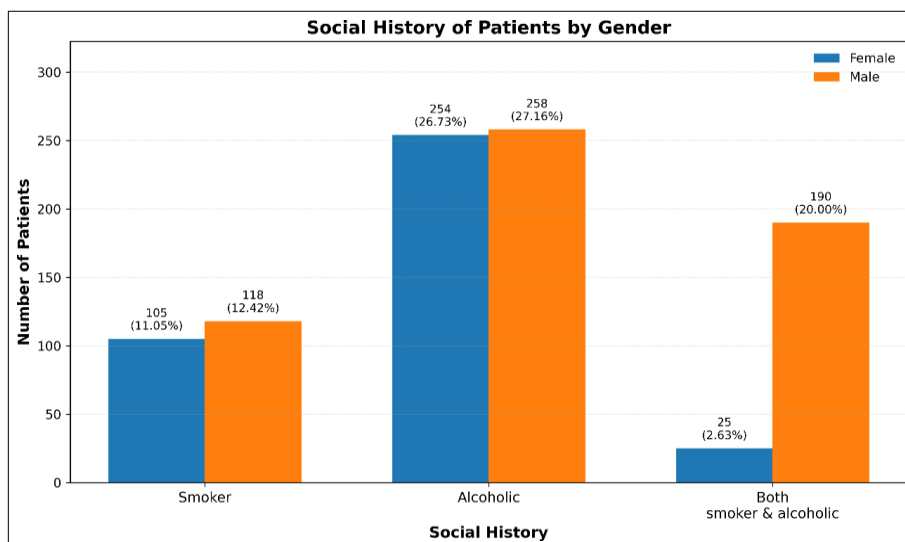


Figure 6: Representing the social history of cardiovascular disease (CVD) patients

Among smokers, **118 males (12.42%)** and **105 females (11.05%)** were reported, indicating slightly higher smoking prevalence in males. Alcohol consumption was observed in **258 males (27.16%)** and **254 females (26.73%)**, showing nearly equal distribution between genders. In the case of both smoking and alcohol use, 190 were males, and 25 were females, indicating that combined habits were much more common among males.

Chi-square analysis showed a significant association between gender and social history ($\chi^2 = 96.08$, $df = 2$, $p < 0.001$). The distribution of smoking and alcohol-related habits differed significantly between male and female patients. **Cramer's V = 0.318**, indicating a **moderate association**.

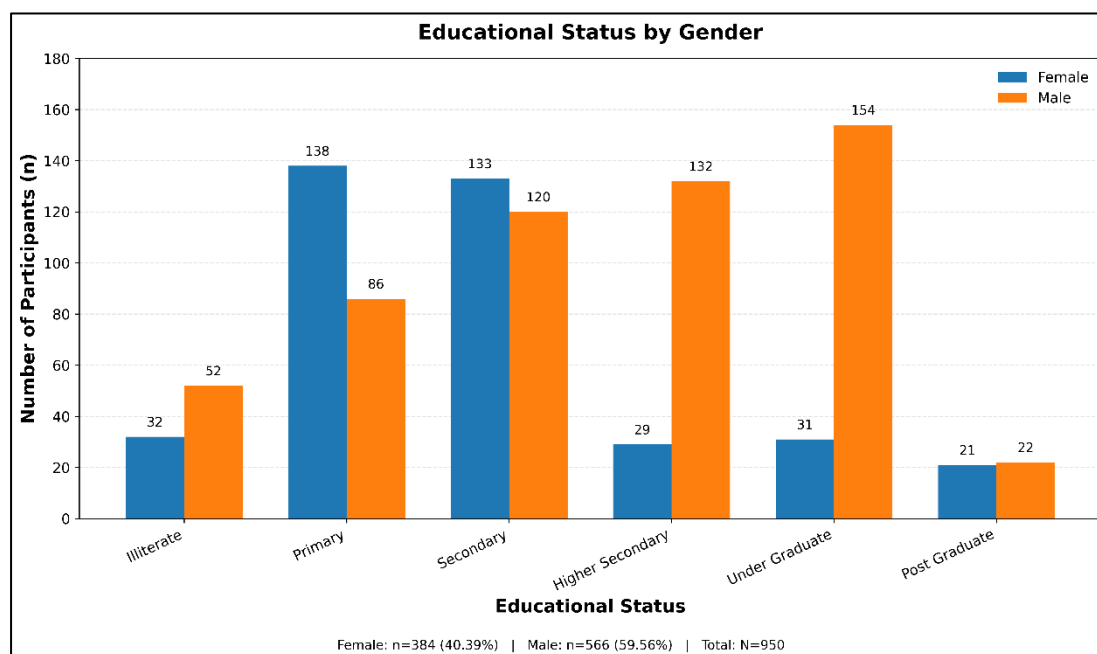
Table 7: Educational Status of the Study Population

The educational status of the study population was assessed by gender to examine the distribution across different education levels.

Educational status	Female		Male		Total	
	No.	Percent	No.	Percent	No.	Percent
Illiterate	32	3.36	52	5.47	84	8.84
Primary	138	14.52	86	9.05	224	23.57
Secondary	133	14.00	120	12.63	253	26.63
Higher Secondary	29	3.05	132	13.89	161	16.94
Under Graduate	31	3.26	154	16.21	185	19.47
Post Graduate	21	2.21	22	2.31	43	4.52
Total	384	40.39	566	59.56	950	100

Interpretation: Secondary education was the most common educational level, followed by primary education, while postgraduate education was least represented.

Figure 7: This graphical representation shows the educational status of cardiovascular patients.



Educational status showed a **statistically significant association with gender** ($\chi^2 = 135.30$, $df = 5$, $p < 0.001$). Primary education was most common among females, whereas undergraduate education was most common among males. This indicates that the educational distribution differed significantly between male and female participants.

Table 8: Cardiovascular drugs associated with adverse drug reaction (n=950) The distribution of adverse drug reactions was assessed according to the individual cardiovascular drugs involved among the study population.

Cardiovascular drugs	Number of patients	Percent
Amlodipine	122	12.84
Telmisartan	105	11.05
Metoprolol	89	9.36
Atorvastatin	85	8.94
Rosuvastatin	65	6.84
Aspirin	56	5.90
Clopidogrel	58	6.10
Ramipril	45	4.73
Perindopril	50	5.26
Torsemide	34	3.57
Digoxin	29	3.05
Nitroglycerin	23	2.42
Ivabradine	20	2.10

Ranolazine	15	1.57
Isosorbide dinitrate	12	1.26
Isosorbide Mononitrate	12	1.26
Sacubitril + Valsartan	17	1.79
Bisoprolol	20	2.10

Nebivolol	10	1.05
Losartan	10	1.05
Nifedipine	13	1.36
Carvediol	1	0.10
Azilsartan	3	0.31
Olmesartan	3	0.31
Medoxomil	3	0.31
Perindopril erbumine	2	0.21
Clinidipine	5	0.52
Diltiazem	4	1.68
Verapamil	4	1.68
Azelnidipine	3	0.31
Furosemide	2	0.21
Indapamide	3	0.31
Hydrochlorothiazide	2	0.21
Telmisartan +Hydrochlorothiazide	1	0.10
Perindopril +Indapamide	1	0.10
Losartan +Amlodipine	1	0.10
Amlodipine + Atenolol	2	0.21
Telmisartan +Metoprolol	1	0.10
Bisoprolol +Hydrochlorothiazide	1	0.10
Ezetimibe	2	0.21
Saroglitazar	1	0.10
Ticagrelor	2	0.21
Prasugrel	3	0.31
Rivaroxaban	2	0.21
Acenocoumarol	2	0.21
Nicorandil	2	0.21
Trimetazidine	2	0.21
Amiodarone	1	0.10

Interpretation: Amlodipine was the most frequently implicated cardiovascular followed by telmisartan and metoprolol, while amiodarone and several combination therapies were the least frequently implicated.

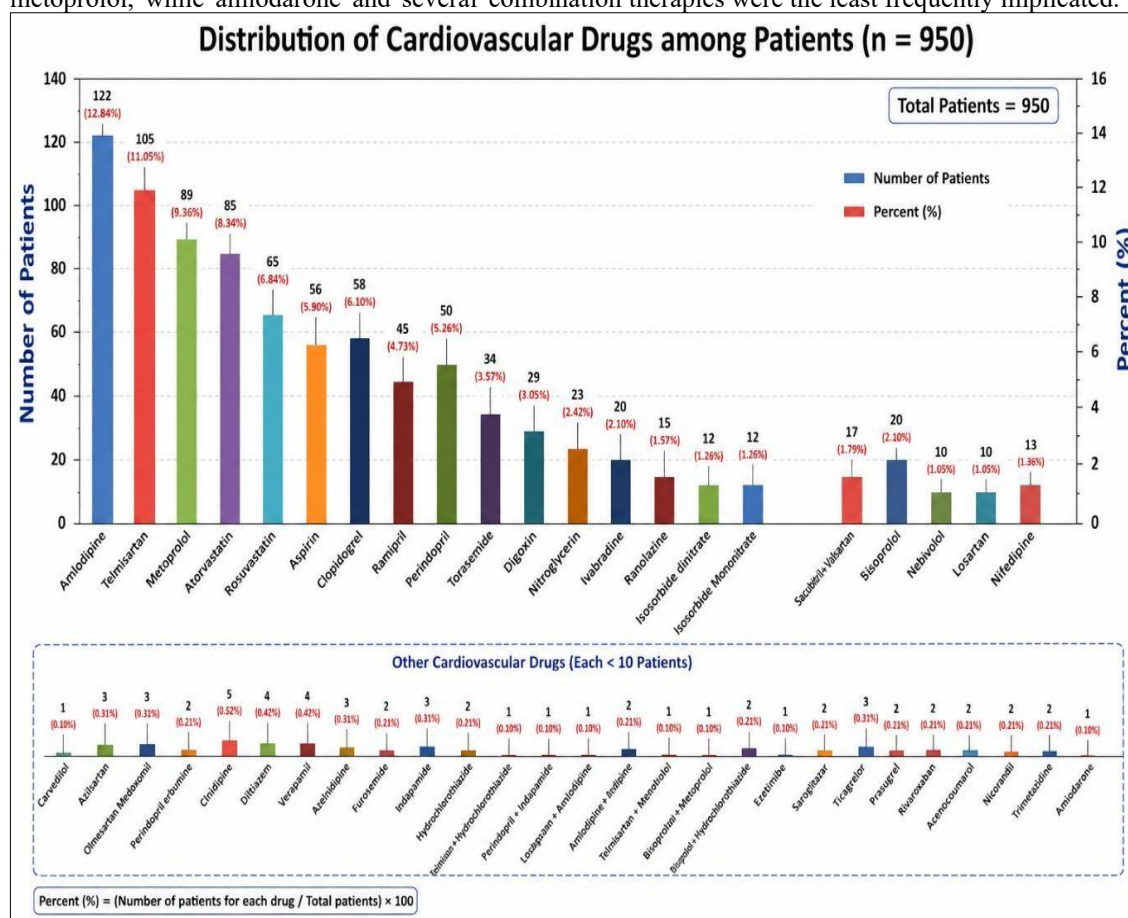


Figure 8: This graph represents cardiovascular drugs and their associated

ADRs.

Amlodipine (12.84%) reported the highest number of ADRs. Followed by Telmisartan (11.05%), Metoprolol (9.36%), and Atorvastatin (8.94%). Other notable contributors include Rosuvastatin (6.84%), Clopidogrel (6.10%), and Aspirin (5.90%). Drugs like Perindopril (5.26%), Ramipril (4.73%), and Torasemide (3.57%) showed a moderate number of ADRs. Digoxin (3.05%) and Nitro-glycerine (2.42%) also contributed to ADRs at moderate levels. Several drugs such as Ivabradine (2.10%), Bisoprolol (2.10%), and Ranolazine (1.57%) had relatively fewer ADRs. Combination therapies and less frequently used drugs (e.g., Telmisartan + Hydrochlorothiazide, Perindopril + Indapamide, Losartan + Amlodipine) showed very low ADR percentages (around 0.10–0.21%). Some drugs like Carvedilol, Amiodarone and Saroglitazar (0.10%) had minimal ADR reports, possibly due to lower usage or better tolerability.

Most ADRs were associated with commonly prescribed medications including calcium channel blockers, antihypertensives, BBs, and statins. Higher ADR percentages in these drugs may reflect their widespread use rather than increased toxicity, while drugs with lower percentages may either be less commonly used or better tolerated.

The Chi-square test showed a highly significant in the distribution of cardiovascular drugs ($p < 0.001$). Amlodipine (12.84%) was the most frequently prescribed drug, followed by Telmisartan (11.05%) and Metoprolol (9.36%), indicating a significant variation in prescribing patterns among patients [14-18].

Table 9: Class-Wise Distribution of ADRs in Cardiovascular Therapy (n=950)

The distribution of adverse drug reactions was assessed according to the cardiovascular drug classes involved among the study population.

Drug Class	Number of Patients	Percent
Antihypertensive Drugs	398	41.89
Lipid-Lowering Agents	212	22.31

Antiplatelet Drugs	148	15.57
Diuretics	62	6.52
Antianginal Drugs	50	5.26
Heart Failure Drugs	35	3.68
Anticoagulants	25	2.63
Antiarrhythmic Drugs	20	2.10

Interpretation: Antihypertensive drugs were the most frequently implicated, followed by lipid-lowering and antiplatelet drugs, while antiarrhythmic drugs were the least frequently implicated.

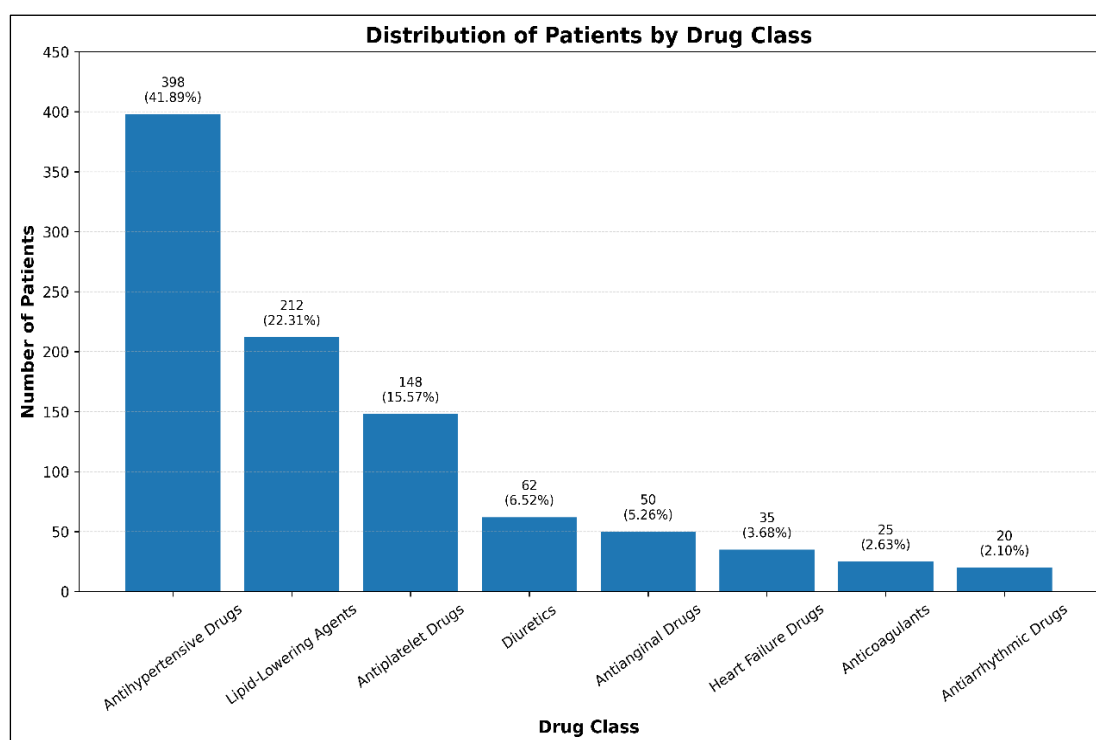


Figure 9: Class wise distributions of ADRs.

A total of ADRs were distributed across different drug classes, with a higher concentration seen in commonly prescribed CVS therapies. **Anti-hypertensive drugs** (41.89%) accounted for the highest proportion of ADRs, indicating that medications used to control blood pressure are the most frequent contributors. This may be due to their widespread and long-term use. **Lipid-lowering agents** (22.31%) were the second major contributors, reflecting the extensive use of drugs like statins in managing cholesterol levels. **Antiplatelet drugs** (15.57%) also showed a significant share of ADRs, likely due to their routine use in preventing CVS events, including heart attacks & strokes. **Diuretics** (6.52%) and **antianginal drugs** (5.26%) contributed a moderate number of ADRs. **Heart failure drugs** (3.68%), **anticoagulants** (2.63%), and **antiarrhythmic drugs** (2.10%) showed comparatively lower percentages of ADRs. The common ADRs were associated with antihypertensive and lipid-lowering drugs, which are commonly prescribed for long-term management of cardiovascular conditions. Lower percentages in other classes may reflect either less frequent use or relatively better tolerability [19-22]. Chi-square analysis showed a statistically significant difference in the distribution

of patients across drug classes ($\chi^2 = 364.91$, $df = 7$, $p < 0.001$).

Table 10: Drug Used in Comorbid conditions and their associated ADRs

(n=950)

The distribution of adverse drug reactions was assessed according to the drug classes involved among the study population.

Drug Class	Number of Patients	Percent
Vitamins & Supplements	250	26.31
NSAIDs / Analgesics	158	16.63
Antidiabetic Drugs	124	13.05
Gastro protective Drugs (GIT Drugs)	110	11.57
Respiratory Drugs	76	8.0
CNS Drugs	61	6.42
Antibiotics	50	5.26
Antidepressant drugs	41	4.31
Anxiolytics / Sedatives	37	3.89
Antiepileptics	28	2.94
Neuropathic Agents	15	1.58

Interpretation: Vitamins and supplements were the most frequently implicated drug class, followed by NSAIDs/analgesics and antidiabetic drugs, while neuropathic agents were least frequently implicated.

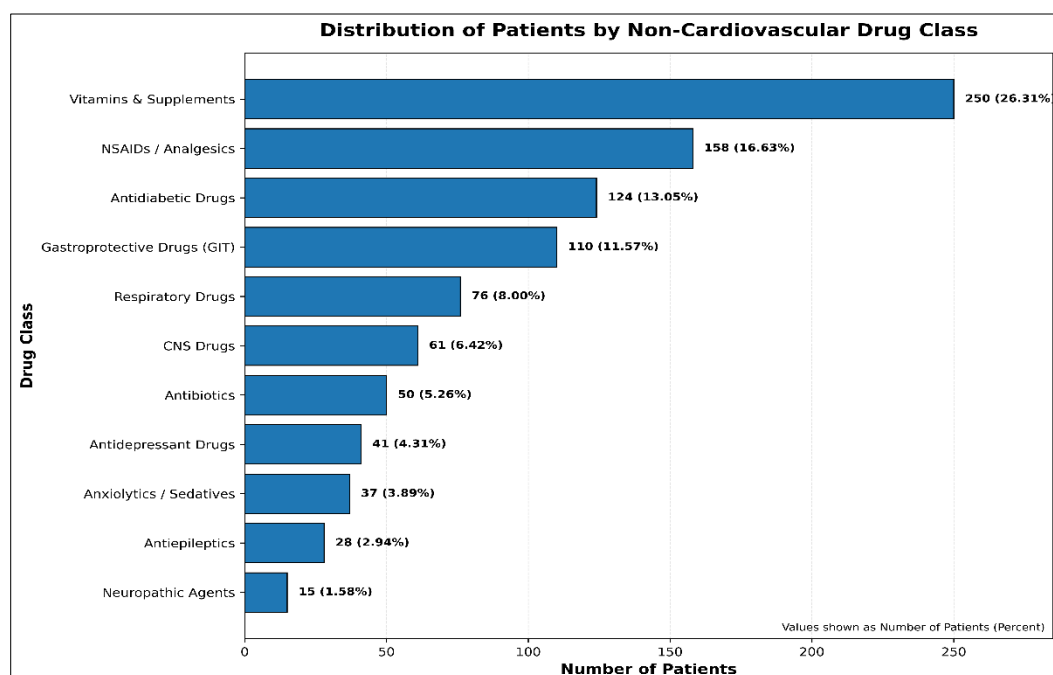


Figure 10: This graph represents the drugs used in comorbid conditions.

ADRs were observed across multiple drug classes, with a higher proportion seen in commonly used supportive and symptomatic treatments.

- Vitamins & supplements (26.31%) accounted for the highest number of ADRs. This may reflect their frequent use as supportive therapy in patients.

- NSAIDs/analgesics (16.63%) were the second leading cause of ADRs, likely due to their widespread use for pain and inflammation.
- Antidiabetic drugs (13.05%) also contributed significantly, which may be due to long-term therapy in diabetic patients.
- Gastroprotective drugs (11.57%) showed notable ADRs, possibly because they are commonly prescribed alongside other medications.
- Respiratory drugs (8.0%) and CNS drugs (6.42%) had a moderate contribution to ADRs.
- Antibiotics (5.26%) antidepressants (4.31%) and anxiolytics/sedatives (3.89%) showed comparatively lower ADR percentages.
- Antiepileptics (2.94%) and neuropathic agents (1.58%) had the least contribution. Chi-square analysis demonstrated a statistically significant difference in the distribution of patients among non-cardiovascular drug classes ($\chi^2 = 566.80$, $df = 10$, $p < 0.001$) [23-25]. =

Table 11: Spectrum of different adverse drug reactions and drug implicated (n=950)

The pattern and distribution of different types of adverse drug reactions were assessed among the study population.

Types of ADRs	Number of Patients	Percent
Gastric irritation	117	12.31
Headache	98	10.31
Dizziness	90	9.47
Nausea	78	8.21
vomiting	70	7.36
Pedal edema	66	6.94
Myalgia	63	6.63
Hypotension	58	6.10
Skin rash	55	5.79
Dry cough	51	5.36
Constipation	37	3.89
Diarrhea	33	3.47
Fatigue	29	3.05
Bradycardia	25	2.63
Hyperglycemia	21	2.21
Hypoglycemia	17	1.79
Insomnia	15	1.57
Pruritus	11	1.15
Palpitations	10	1.05
Others	06	0.63

Interpretation: Gastric irritation was the most frequently reported ADR, followed by headache and dizziness, whereas other ADRs were least frequently reported.

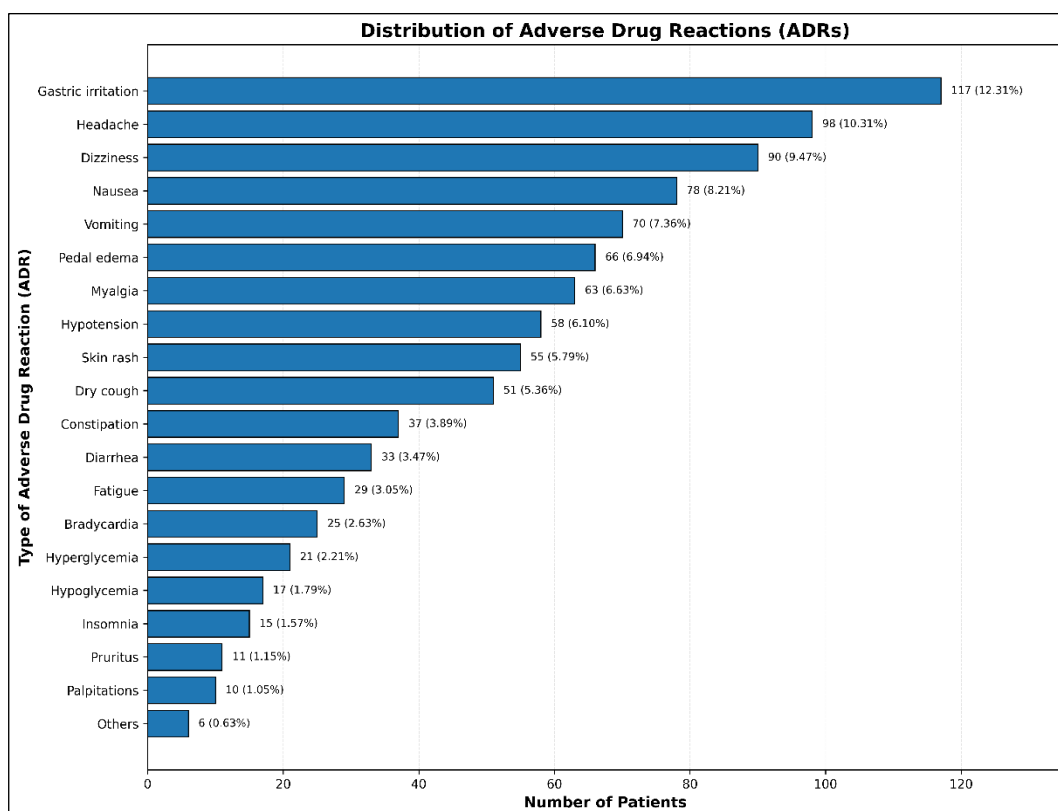


Figure 11: Graphical representation of the spectrum of various ADRs Gastric irritation (12.31%) was the maximum often described ADR indicating that gastrointestinal issues are the most common ADRs followed by headache (10.31%), dizziness (9.47%) and nausea (8.21%). Vomiting (7.36%) and pedal edema (6.94%) were also commonly observed.

Myalgia (6.63%), hypotension (6.10%) and skin rash (5.79%) showed moderate occurrence. Dry cough (5.36%) is notable often associated with certain cardiovascular drugs like ACE inhibitors. Constipation (3.89%), diarrhea (3.47%) and fatigue (3.05%) were reported at lower frequencies. Cardiovascular-related effects such as bradycardia (2.63%) and metabolic effects like hyperglycemia (2.21%) and hypoglycemia (1.79%) were less frequent. Insomnia (1.57%), pruritus (1.15%), palpitations (1.05%) and others (0.63%) had minimal occurrence. Gastrointestinal and central nervous system-related ADRs (like gastric irritation, headache and dizziness) were the most common. In contrast, cardiovascular, metabolic, and dermatological reactions were less frequent. This pattern suggests that most ADRs were mild to moderate in nature and commonly related to drug tolerability rather than severe reactions [26-28].

Chi-square analysis demonstrated a highly significant difference the distribution of ADRs across the various categories ($\chi^2 = 414.80$, $df = 19$, $p < 0.001$).

Table 12: Organ System–Wise Distribution of ADRs (n=950)

The organ systems affected by adverse drug reactions were assessed to determine the pattern of system involvement among the study patients.

Organ System Affected	Number of Patients (n)	Percent
Gastrointestinal System	250	26.31
Central Nervous System	167	17.58
Cardiovascular System	155	16.31
Skin & Appendages	133	14
Musculoskeletal System	95	10
Respiratory System	67	7.05
Metabolic / Endocrine	46	4.84
Hematological	24	2.52

Renal / Urinary	13	1.36
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Interpretation: The gastrointestinal system was the most frequently affected organ system, followed by the central nervous and cardiovascular systems, while the renal/urinary system was least affected.

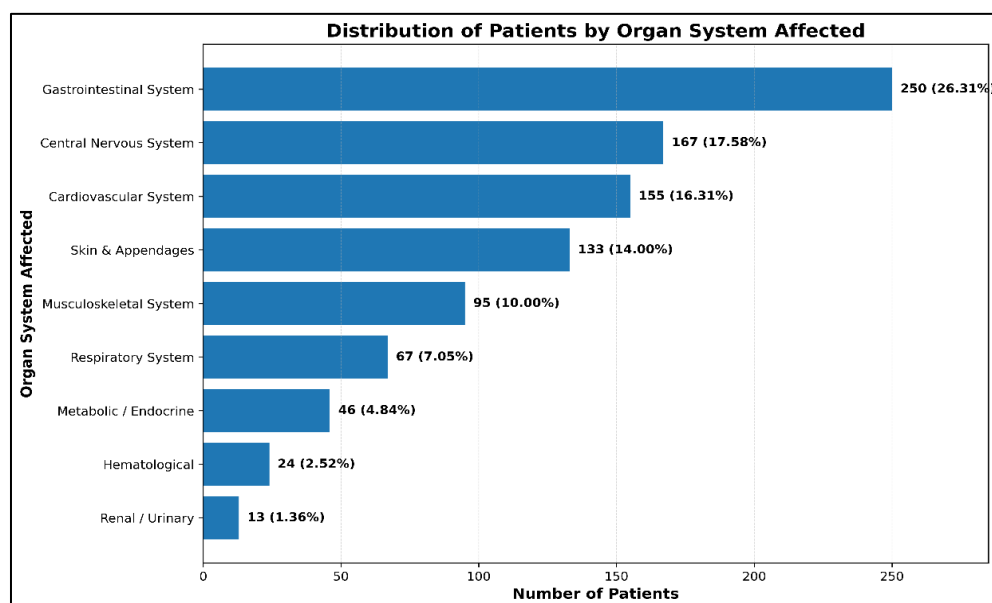


Figure 12: Graphical representation of organ system affected by ADRs

The GI system (26.31%) was the maximum commonly pretentious indicating that ADRs such as gastric irritation, nausea and vomiting were highly prevalent.

The central nervous system (17.58%) was the second most affected with symptoms like headache and dizziness. The cardiovascular system (16.31%) also showed a significant proportion of ADRs including effects like hypotension and bradycardia. Skin & appendages (14%) were commonly involved, presenting as rashes or itching. The musculoskeletal system (10%) showed ADRs such as myalgia.

The respiratory system (7.05%) had fewer ADRs such as cough or breathing-related issues. Metabolic/endocrine system (4.84%) included effects like hyperglycemia or hypoglycemia. Hematological (2.52%) and renal/urinary systems (1.36%) had the lowest number of ADRs, indicating these were less frequently impacted.

The majority of ADRs affected the gastrointestinal, nervous and cardiovascular systems, suggesting that these systems are further liable to drug-related ADRs. In contrast, hematological and renal systems were least affected, indicating relatively fewer complications in these areas [28-30].

Chi-square analysis demonstrated a statistically significant difference the distribution of patients among the affected organ systems ($\chi^2 = 456.63$, $df = 8$, $p < 0.001$).

Table: 13 Distribution of ADRs among different Cardiovascular disorders

The distribution of cardiovascular disorders was assessed among the study population.

Cardiovascular Disorder	Number of Patients	Percent
Hypertension	324	34.10
CAD	77	8.10
Angina/ Ischemic Heart Disease	175	18.42
Stroke / Cerebrovascular disease	132	13.89
Heart Failure	84	8.84
Cholesterol (Dyslipidemia)	60	6.31
Arrhythmias	53	5.57

Peripheral Vascular Disease/Others	45	4.73
Total	950	100

Interpretation: Hypertension was the most frequently observed cardiovascular disorder, followed by angina/ischemic heart disease and stroke/cerebrovascular disease, while peripheral vascular disease/other disorders were least frequent.

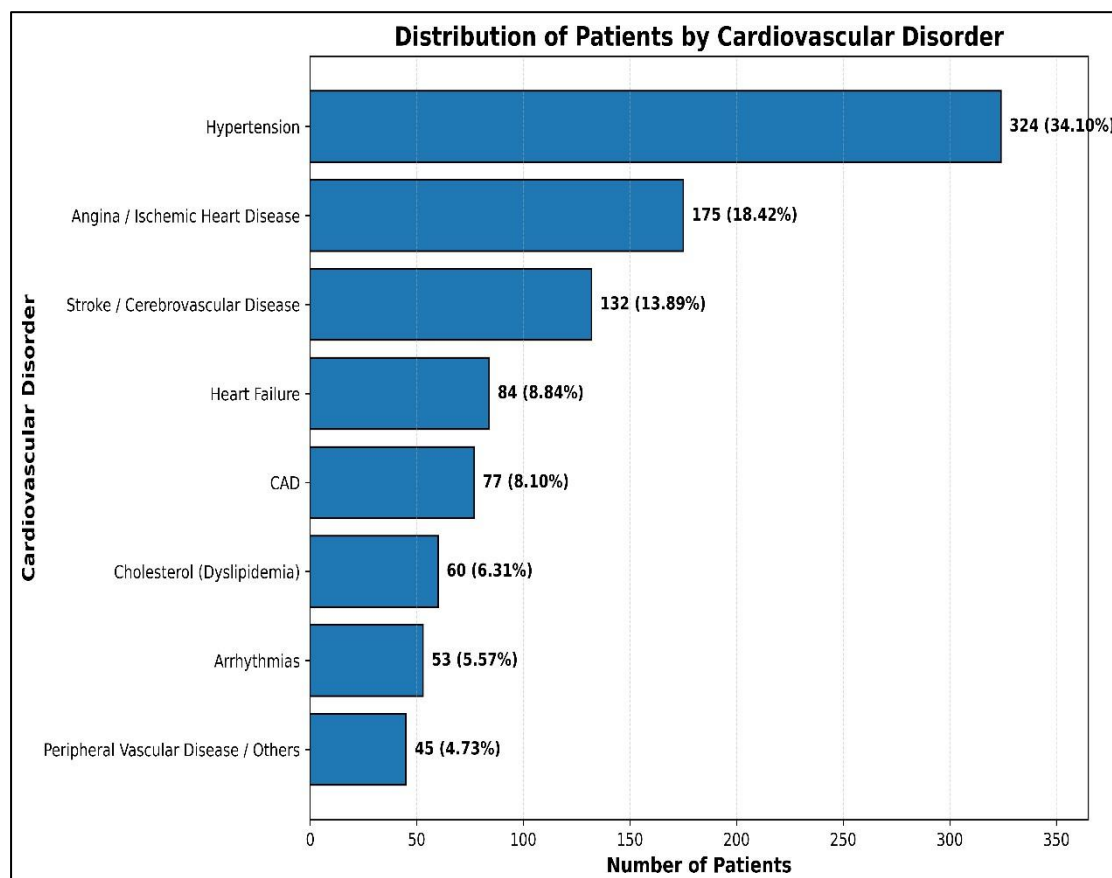


Figure 13: ADRs among different cardiovascular disorders

According to the distribution of cardiovascular disorders, 324 patients (34.10%) had hypertension, which was the most common condition. After that, 175 patients (18.42%) had angina pectoris/ischemic heart disease, and 132 patients (13.89%) had stroke/cerebrovascular disease. 84 patients (8.84%) had heart failure, and 77 patients (8.10%) had coronary artery disease (CAD). There were 60 patients (6.31%) with dyslipidemia, 53 patients (5.57%) with arrhythmias, and 45 patients (4.73%) with peripheral vascular disease/other diseases. In general, the study population's most common cardiovascular condition was hypertension.

ADRs were more common in conditions like hypertension, angina, and stroke mainly because these patients often require long-term, combination drug therapy. Lower ADR percentages in other conditions may be due to fewer medications used or shorter treatment duration.

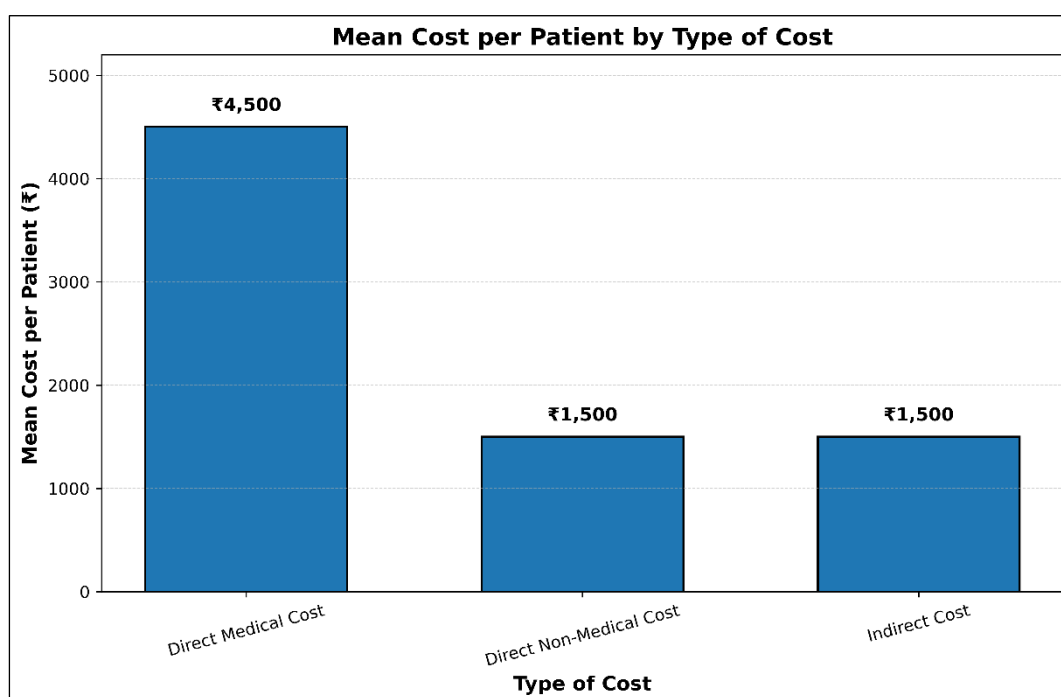
Chi-square analysis: $\chi^2 = 519.00$, $df = 7$, $p < 0.001$, indicating a statistically significant difference in the distribution of cardiovascular disorders.

Table 14: Direct and Indirect Cost of ADRs

The cost analysis was performed using descriptive statistics, with the mean cost per patient calculated for direct medical, direct non-medical, and indirect costs to assess the economic burden associated with patient care.

Type of Cost	Mean Cost per Patient (₹)
Direct Medical Cost	4,500
Direct Non-Medical Cost	1,500
Indirect Cost	1,500

Interpretation: The mean cost per patient was highest for direct medical expenses, while direct non-medical and indirect costs were comparatively lower.

**Figure 14: Graphical representation of cost distribution among CVS patients**

This is the highest component of total cost and includes expenses directly related to treatment such as doctor consultation, diagnostic tests, medications, and hospital charges. These are additional expenses not related to treatment itself, such as transportation to the hospital, food, and accommodation for patients or caregivers. This represents the loss of income or productivity, including wages lost due to illness, hospitalization, or time taken off work by both patients and their caregivers.

The total average cost per patient is approximately ₹7,500, with direct medical costs contributing the largest share, indicating that treatment expenses are the major financial burden. Non-medical & indirect costs also add significantly for overall economic impact of cardiovascular diseases.

Chi-square analysis demonstrated a highly statistically significant difference in the distribution of patients among cardiovascular disorders ($\chi^2 = 519.00$, $df = 7$, $p < 0.001$).

Table 15: Associated co-morbidities among cardiovascular patients (n=950) Distribution of patients according to the type of comorbidities associated with cardiovascular diseases in the study population.

Comorbidity	Number of patients	Percent
Hypertension	328	34.52
Diabetes Mellitus	125	13.15

Chronic Kidney Disease (CKD)	82	8.63
Hyperlipidemia	117	12.31
Stroke / Cerebrovascular Disease	51	5.36
Obesity	66	6.94
Peripheral Vascular Disease	43	4.52
Thyroid Disorders	30	3.15
Chronic Liver Disease	15	1.57

Interpretation: The majority of patients had hypertension, followed by diabetes mellitus and hyperlipidemia, while chronic liver disease was the least common comorbidity.

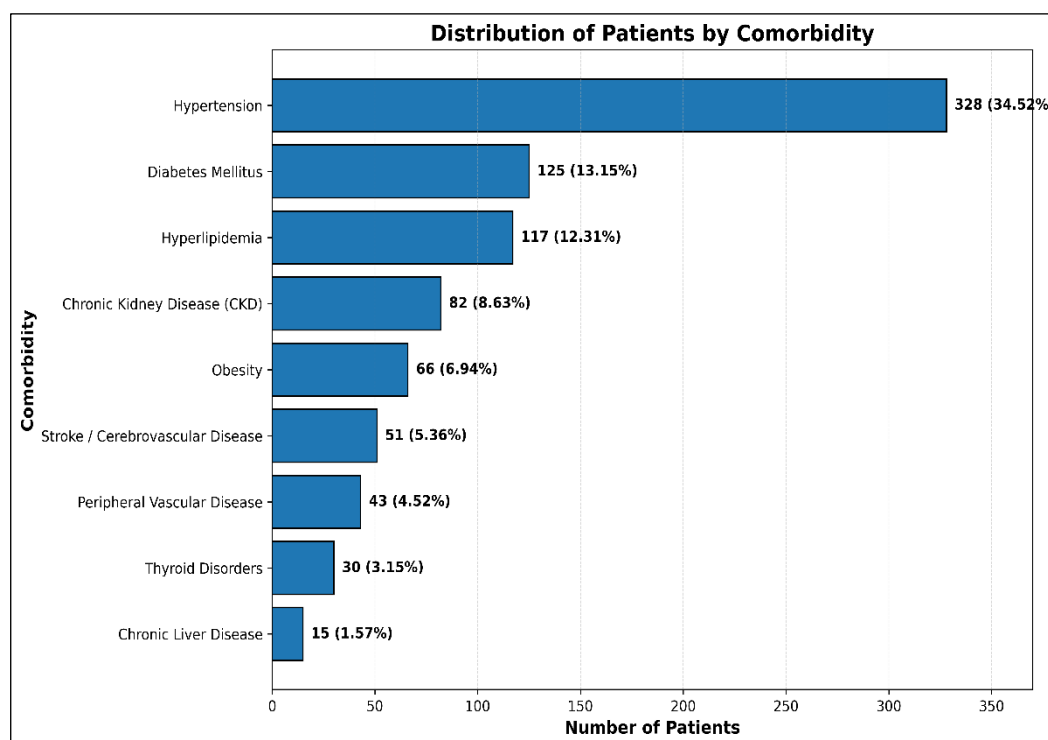


Figure 15: Representation of comorbidities among cardiovascular patients.

Hypertension (34.52%) was the most prevalent comorbidity, indicating that a large proportion of cardiovascular patients also suffer from high blood pressure.

Also common were diabetes mellitus (13.15%) and hyperlipidemia (12.31%), highlighting a strong association between metabolic disorders and cardiovascular diseases. Obesity (6.94%) and chronic kidney disease (CKD) (8.63%) were moderately prevalent, suggesting their role as risk factors.

Stroke/cerebrovascular disease (5.36%) also showed a notable presence among patients. Peripheral vascular disease (4.52%) and thyroid disorders (3.15%) were less frequently observed. Chronic liver disease (1.57%) had the lowest prevalence.

Hypertension, diabetes and hyperlipidemia are the most common comorbidities in cardiovascular patients indicating that these conditions often coexist and may increase the risk and severity of cardiovascular diseases. Proper management of these comorbidities is essential for better patient outcomes.

Chi-square analysis demonstrated a highly statistically significant difference in the distribution of patients among the comorbidity categories ($\chi^2 = 755.58$, $df = 8$, $p < 0.001$), with hypertension (34.52%) being the most frequently reported comorbidity.

Table 16: Causality outcome of suspected adverse drug reactions by WHO-UMC causality scale (n=950)

Distribution of patients according to WHO-UMC causality assessment categories for suspected adverse drug reactions (ADRs).

Outcome	Number of Patients	Percent	Interpretation
Probable	340	35.79	Reasonable time relationship; unlikely due to other causes
Possible	365	38.42	Could be due to drug or other factors; most common category
Certain	65	6.84	Strong evidence with clear temporal relationship and confirmed by rechallenge.
Unlikely	90	9.47	Weak relationship; other causes more likely
Conditional/Unclassified	55	5.78	More data required for proper assessment
Unassessable /Unclassifiable	35	3.68	Insufficient or contradictory data

Interpretation: The table presents ADR causality outcomes, with Possible and Probable being the most common categories, while Certain ADRs accounted for a smaller proportion of the assessed ADRs.

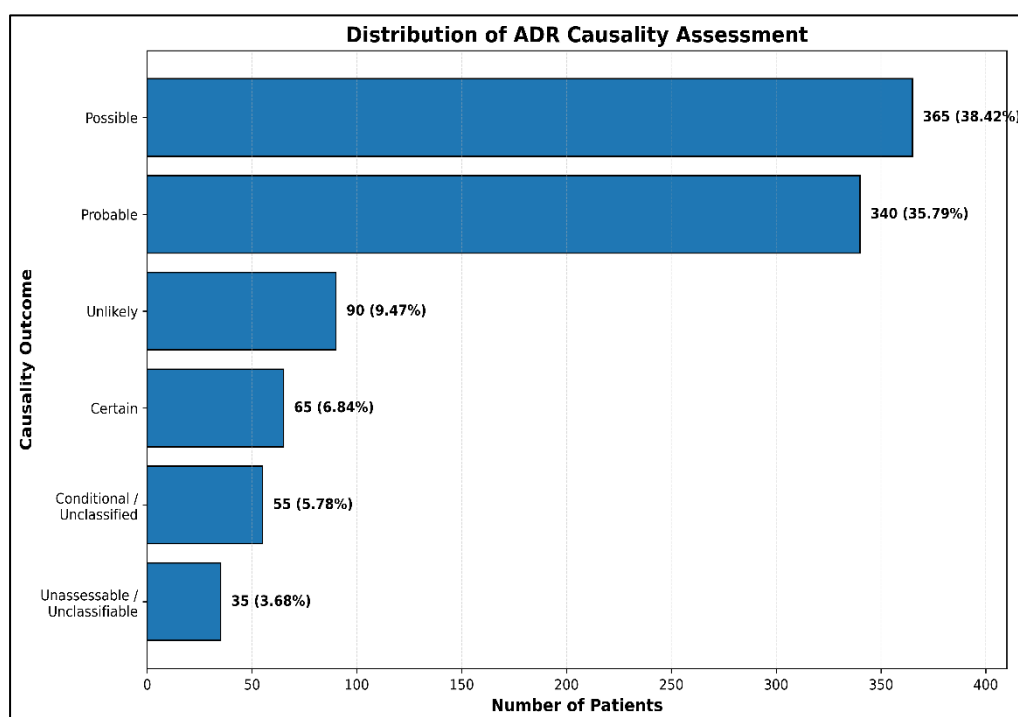


Figure 16 Graph showing the outcomes of suspected adverse drug reactions (ADRs) by WHO-UMC causality scale

Possible (38.42%) was the highest category, meaning the ADRs could be related to the drug but other factors (like disease or other drugs) may also be involved.

Probable (35.79%) was the second most common, suggesting a strong likelihood that the drug caused the ADR, based on clinical evidence and response to drug withdrawal. Unlikely (9.47%) indicates that the ADR is

probably not related to the drug. Certain (6.84%) represents confirmed ADRs with clear evidence, such as a definite relationship and possibly reappearance on re-exposure.

Conditional/Unclassified (5.78%) includes cases where more data is needed for proper classification. Unassessable/Unclassifiable (3.68%) refers to ADRs that cannot be evaluated due to insufficient or unclear information.

Most ADRs fall under possible and probable categories, indicating that while many reactions are suspected to be drug-related, only a smaller proportion are definitively confirmed. This shows the importance of cautious intensive care & thorough evaluation of ADRs.

Chi-square analysis demonstrated a highly statistically significant difference in the distribution of ADR causality outcomes ($\chi^2 = 726.21$, $df = 5$, $p < 0.001$).

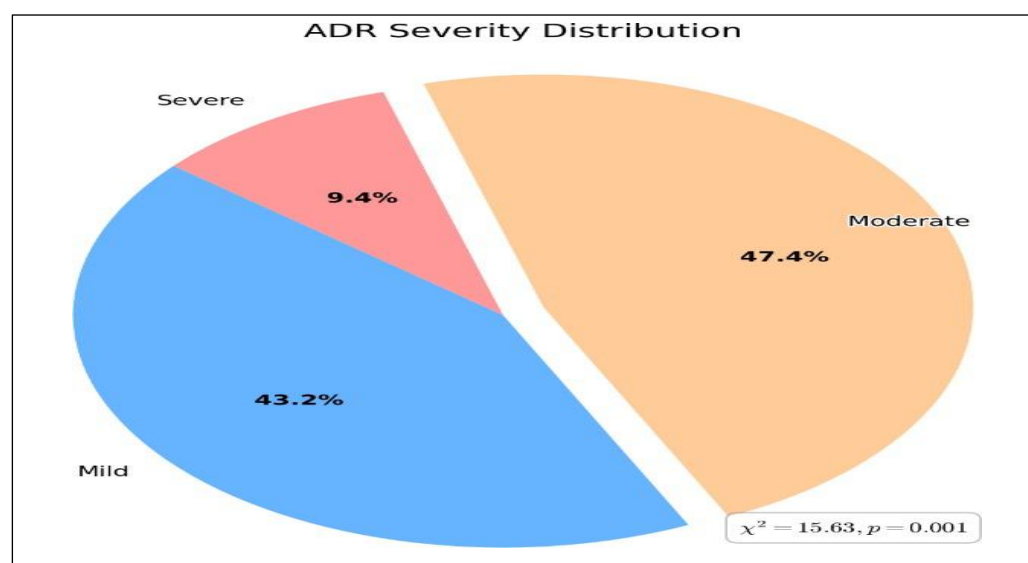
Table 17: Severity-wise distribution of adverse drug reactions by Hartwig & Siegel Severity Scale.

The severity of ADRs was assessed using the Hartwig severity assessment scale. The majority of ADRs were categorized as moderate, followed by mild and severe reactions.

Severity Category	Frequency (%)
Mild	410 (43.2%)
Moderate	450 (47.4%)
Severe	90 (9.4%)

Interpretation: Moderate ADRs constituted the largest proportion of reported reactions.

Fig 17. A pie chart is the most intuitive method for displaying categorical proportions of a whole. It emphasizes that nearly half of the ADRs were moderate in nature, while the relatively small "Severe" slice provides a visual



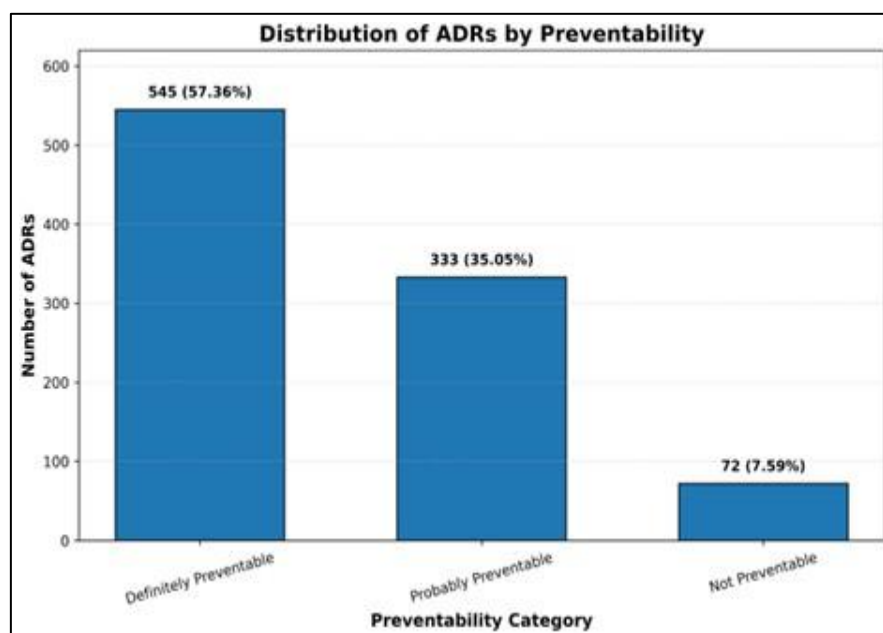
reassuring of patient safety profiles within the study.

Chi-square analysis demonstrated a statistically significant difference among severity categories ($\chi^2 = 15.63$, $df = 2$, $p = 0.001$).

Table 18: Preventability valuation of reported ADRs by Schumock & Thornton Scale

The table shows the distribution of ADRs according to their preventability status.

Preventability	No. of ADRs	Percent
Definitely Preventable	545	57.36
Probably Preventable	333	35.05
Not Preventable	72	7.59
Total	950	100



Interpretation: The majority of ADRs were definitely preventable, followed by probably preventable ADRs, while a smaller proportion were not preventable.

Figure 18: Preventability-wise Distribution of ADRs (Schumock & Thornton Scale)

Most ADRs are definitely preventable, indicating they could be avoided with proper prescribing and monitoring. A moderate number are probably preventable, suggesting better clinical care could reduce them. Very few are not preventable, meaning they occur despite correct treatment.

Chi-square analysis demonstrated a highly statistically significant difference in the distribution of ADRs among the preventability categories ($\chi^2 = 354.52$, $df = 2$, $p < 0.001$).

DECLARATIONS

Informed Consent: Informed consent was obtained from the study participants, wherever applicable.

Consent for Publication: Not applicable.

Conflict of Interest: The authors declare no conflict of interest.

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Data Availability: The data generated and analyzed during the study are available from the corresponding author upon reasonable request.

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REFERENCES

1. World Health Organization. The importance of pharmacovigilance: safety monitoring of medicinal products. Geneva: World Health Organization; 2002.
2. World Health Organization. International drug monitoring: the role of national centres. Geneva: World Health Organization; 1972. WHO Technical Report Series No. 498.
3. Edwards IR, Aronson JK. Adverse drug reactions: definitions, diagnosis, and management. *Lancet*. 2000;356(9237):1255-9.
4. Pirmohamed M, James S, Meakin S, Green C, Scott AK, Walley TJ, et al. Adverse drug reactions as cause

- of admission to hospital: prospective analysis of 18,820 patients. *BMJ*. 2004;329(7456):15-9.
5. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. *JAMA*. 1998;279(15):1200-5.
 6. Davies EC, Green CF, Taylor S, Williamson PR, Mottram DR, Pirmohamed M. Adverse drug reactions in hospital in-patients: a prospective analysis of 3695 patient-episodes. *PLoS One*. 2009;4(2):e4439.
 7. Kongkaew C, Noyce PR, Ashcroft DM. Hospital admissions associated with adverse drug reactions: a systematic review of prospective observational studies. *Ann Pharmacother*. 2008;42(7):1017-25.
 8. Alhawassi TM, Krass I, Bajorek BV, Pont LG. A systematic review of the prevalence and risk factors for adverse drug reactions in the elderly in the acute care setting. *Clin Interv Aging*. 2014;9:2079-86.
 9. Onder G, Pedone C, Landi F, Cesari M, Della Vedova C, Bernabei R, et al. Adverse drug reactions as cause of hospital admissions: results from the Italian Group of Pharmacoepidemiology in the Elderly. *J Am Geriatr Soc*. 2002;50(12):1962-8.
 10. Routledge PA, O'Mahony MS, Woodhouse KW. Adverse drug reactions in elderly patients. *Br J Clin Pharmacol*. 2004;57(2):121-6.
 11. Maher RL, Hanlon J, Hajjar ER. Clinical consequences of polypharmacy in elderly. *Expert Opin Drug Saf*. 2014;13(1):57-65.
 12. Wastesson JW, Morin L, Tan ECK, Johnell K. An update on the clinical consequences of polypharmacy in older adults: a narrative review. *Expert Opin Drug Saf*. 2018;17(12):1185-96.
 13. Viktil KK, Blix HS, Moger TA, Reikvam A. Polypharmacy as commonly defined is an indicator of limited value in the assessment of drug-related problems. *Br J Clin Pharmacol*. 2007;63(2):187-95.
 14. Formica D, Sultana J, Cutroneo PM, Lucchesi S, Angelica R, Crisafulli S, et al. The economic burden of preventable adverse drug reactions: a systematic review of observational studies. *Expert Opin Drug Saf*. 2018;17(7):681-95.
 15. Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. *Am J Hosp Pharm*. 1992;49(9):2229-32.
 16. Schumock GT, Thornton JP. Focusing on the preventability of adverse drug reactions. *Hosp Pharm*. 1992;27(6):538.
 17. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther*. 1981;30(2):239-45.
 18. Meyboom RHB, Hekster YA, Egberts ACG, Gribnau FWJ, Edwards IR. Causal or casual? The role of causality assessment in pharmacovigilance. *Drug Saf*. 1997;17(6):374-89.
 19. World Health Organization. WHO-UMC system for standardised case causality assessment. Uppsala: Uppsala Monitoring Centre; 2018.
 20. Coleman JJ, Pontefract SK. Adverse drug reactions. *Clin Med (Lond)*. 2016;16(5):481-5.
 21. Angamo MT, Chalmers L, Curtain CM, Bereznicki LRE. Adverse-drug-reaction-related hospitalisations in developed and developing countries: a review of prevalence and contributing factors. *Drug Saf*. 2016;39(9):847-57.
 22. Beijer HJM, de Blaey CJ. Hospitalisations caused by adverse drug reactions: a meta-analysis of observational studies. *Pharm World Sci*. 2002;24(2):46-54.
 23. Howard RL, Avery AJ, Slavenburg S, Royal S, Pipe G, Lucassen P, et al. Which drugs cause preventable admissions to hospital? A systematic review. *Br J Clin Pharmacol*. 2007;63(2):136-47.
 24. Davies EC, Green CF, Mottram DR, Pirmohamed M. Adverse drug reactions in hospitals: a narrative review. *Curr Drug Saf*. 2007;2(1):79-87.
 25. Budnitz DS, Lovegrove MC, Shehab N, Richards CL. Emergency hospitalizations for adverse drug events in older Americans. *N Engl J Med*. 2011;365(21):2002-12.
 26. Davies EA, O'Mahony MS. Adverse drug reactions in special populations—the elderly. *Br J Clin Pharmacol*. 2015;80(4):796-807.
 27. Sultana J, Cutroneo P, Trifirò G. Clinical and economic burden of adverse drug reactions. *J Pharmacol Pharmacother*. 2013;4(Suppl 1):S73-7.
 28. Patel TK, Patel PB. Incidence of adverse drug reactions in Indian hospitals: a systematic review of prospective studies. *Curr Drug Saf*. 2016;11(2):128-36.
 29. Kalaiselvan V, Thota P, Singh GN. Pharmacovigilance Programme of India: recent developments and future perspectives. *Indian J Pharmacol*. 2016;48(6):624-8.
 30. Kalaiselvan V, Prasad T, Bisht A, Singh S, Singh GN. Adverse drug reactions reporting culture in Pharmacovigilance Programme of India. *Indian J Med Res*. 2014;140(4):563-4.