

Drug Utilization Study of Anti- Platelet Agents in Cardiac Disorders: A Cross Sectional Study

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ABSTRACT

Background: Cardiovascular diseases are a severe condition in which multiple antiplatelet and other drugs are used among the cardiac patients with co-morbidities which leads to polypharmacy and other drug related problems. The primary objective of the study was to evaluate the drug utilisation of antiplatelet among the patients having cardiac disorders. The study also focuses on monitoring the medication adherence as well as to evaluate the adverse drug reactions.

Method: After obtaining approval from the IEC, patients diagnosed with various cardiovascular diseases were included in the study. The data were collected from the patient case profile and prescriptions and noted in a self-designed data collection form. The statistical analysis was performed using Microsoft Excel Software 2007.

Result: Out of 172 patients with various cardiovascular diseases, majority were males 113 (65.69%) and females 59 (34.30%). The common co-morbidities related to CVDs are hypertension, diabetes mellitus, LRTI, AKI, hypothyroidism and CKD. The most frequently prescribed antiplatelet was aspirin (55.44%) and dual antiplatelet was aspirin+clopidogrel (6.27%). The medication adherence was seen to be less in majority of the patients. A total number of 42 adverse reactions were found in the following study. Polypharmacy was observed.

Conclusion: This study provides adequate information into overall pattern of antiplatelet drugs used among the various cardiac disorders. Patients must be provided with adequate information and knowledge in order to improve the medication adherence. Treatment must be tailored to the patient after careful consideration of harm versus benefit and a clear plan should be conveyed to patients and their health team.

Keywords: *Cardiovascular Disease, Antiplatelet Drugs, Aspirin, Clopidogrel, Adverse Drug Reactions.*

INTRODUCTION

Cardiovascular disease is one of the major causes of mortality in India. According to the studies, it is estimated that nearly one fourth of all the death in India occurs due to CVD. The cardiovascular system consists of the heart and blood vessel. There is a wide array of problems that may arise within the cardiovascular system, for example, endocarditis, rheumatic heart disease, abnormalities in the conduction system.

Antiplatelet medications remain a cornerstone of therapy for atherosclerotic cardiovascular and cerebrovascular diseases. Since the observation that thrombi occluding coronary arteries were platelet-rich in content, antiplatelet agents have been extensively researched and developed as potential therapies in the prevention and management of arterial thrombosis. Platelet activation and aggregation is considered to be central to arterial thrombus production. Antiplatelet therapy has been successful in reducing mortality and morbidity in acute myocardial infarction. Recent advances in understanding the molecular basis of the role of platelets in cardiovascular thrombosis have enabled the development of new agents with the potential to further reduce mortality and morbidity. There are four main groups: Aspirin, Thienopyridines (ticlopidine, ticagrelor and clopidogrel), Dipyridamole (cilostazol), and Platelet α Ib β 3 (glycoprotein IIb/ IIIa) receptors antagonists (abciximab, tirofiban, eptifibatide).

DUE plays an important role in modernized clinical settings, health care management programs, hospitals and communities by taking into account therapeutic drug class and disease condition to evaluate patient- specific care systems. Drug utilization evaluation, according to the World Health Organization, is an ongoing systematic, criterion-based program of medicine evaluation that aids in applicability. DUE improve medication use by: 1. Promoting optimal medication therapy. 2. Preventing medication-related problems. 3. Rational use of drug and management of cardiovascular risk factors. The term polypharmacy was used over half centuries ago to refer to issues related to multiple- drug consumption and excessive use of drugs. According to Mamnoon, *et al*; the use of 5 or more medications is an acceptable definition of polypharmacy.

An adverse drug reaction (ADR) can be defined as ‘An appreciably harmful or unpleasant reaction resulting from an intervention related to the use of a medicinal product; adverse effects usually predict hazard from future administration and warrant prevention, or specific treatment, or alteration of the dosage regimen, or withdrawal of the product’. According to Iyer, *et al.*, over 30% of all adverse drug reactions occur due to drug interactions, which are considered potentially preventable with early detection, highlighting the importance of early identification.

Aims And Objectives

AIM: Drug utilization study of anti- platelet agents in cardiac disorders: A cross- sectional study.

Primary Objectives:

To analyze anti- platelet drug utilization evaluation in patients with cardiac disorders in a tertiary careteaching hospital.

Secondary Objectives:

To assess the medication adherence.

To assess the adverse drug reactions.

MATERIALS AND METHODS

Inclusion criteria

- Patients of either gender aged above 18.
- Outpatients and Inpatients.
- Cardiovascular disease patients.

Exclusion criteria

- Pregnant and Lactating women.
- Case files with insufficient data.
- Self- medications

Sources of data and materials

- Patient case sheet.
- Laboratory data.
- Patient medication treatment chart.
- Standard databases like CIMS, Drugs.com, Micromedex
- MMAS- 8, Drug interaction and ADR forms.
- Drug interaction and ADR forms.

Method of collecting data and study procedure

- The data required for the study has collected by reviewing the prescription list and patient case sheet.
- Thedata collected have noted in a self- designed patient data collection form and open ended questionnaire.
- The patients who are in accordance with the inclusion criteria have enrolled into the study.
- Patients admitted in the ward as well as patients visiting the OPD have reviewed with the aid of patient consent form.
- Antiplatelet drugs which are prescribed for the treatment of various cardiac disorders by the physicianhave noted in the self- prepared data collection form.
- All the patients admitted in the ward will be reviewed on daily basis.
- Patients with known complaint will be interviewed with open ended questions regarding their medical history and recruited if they meet the study criteria. Patient’s demographic details such as age, gender, education level, lifestyle, economic status, will be collected.

- The method also includes checks on the medication chart to find any medication related problems like medication adherence and adverse drug reactions along with their laboratory data using MMAS- 8, ADR form respectively. Interpretation of data to generate the result.
- Tabulation of various data based on respective parameters. Evaluation of results to find the final inference.

Statistical analysis

The data was collected and entered in Microsoft Excel Software 2019 and interpreted by descriptive statistics that was presented to analyze and express the report as counts and percentages in the form of tables, charts and graphs.

Ethical considerations

Confidentiality was maintained throughout the study. Written informed consent was obtained from all the participants. There is no physical harm to the participants, as there is no intervention.

Ethical clearance

Yes, the ethical clearance letter no. SIMS&RC/IEC/14/2022-23 dated 22/09/2022 has been obtained from the institution.

RESULTS

Patients Department Wise Categorisation

Out of 172 cases, the patients are divided into 2 categories according to the department. Patients are mainly categorized into two mainly as inpatients and outpatients.

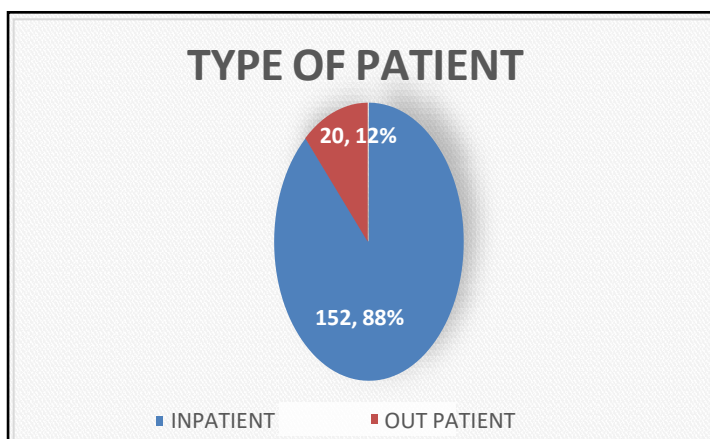


Fig No: 1. Patients department wise categorization.

Patient’s Age Wise Categorisation

Out of 172 cases, the patients are divided into 7 categories according to their age. Patients who are aged between 55- 65 have high percentage for receiving the treatment of various cardiovascular diseases. A total of 154 patients were above 50 years of age, while 18 were below 50 years of age.

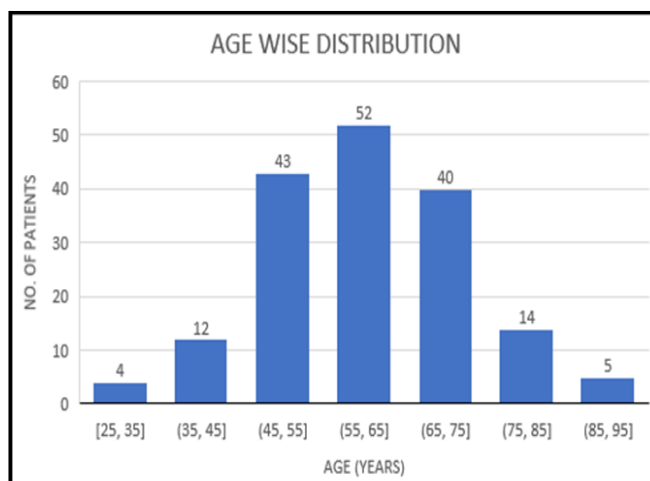


Fig No: 2. Patients age wise categorization.

Gender Wise Distribution

In the current study, the dominant gender was males (113) followed by females (59).

Table No: 1. Gender wise distribution.

PATIENT'S GENDER	NO. OF PATIENTS	PERCENTAGE
MALE	113	65.69%
FEMALE	59	34.30%

PATIENT'S DIAGNOSIS

Out of 172 cases, the patients diagnosed with different CVDs were listed below in table and depicted in chart.

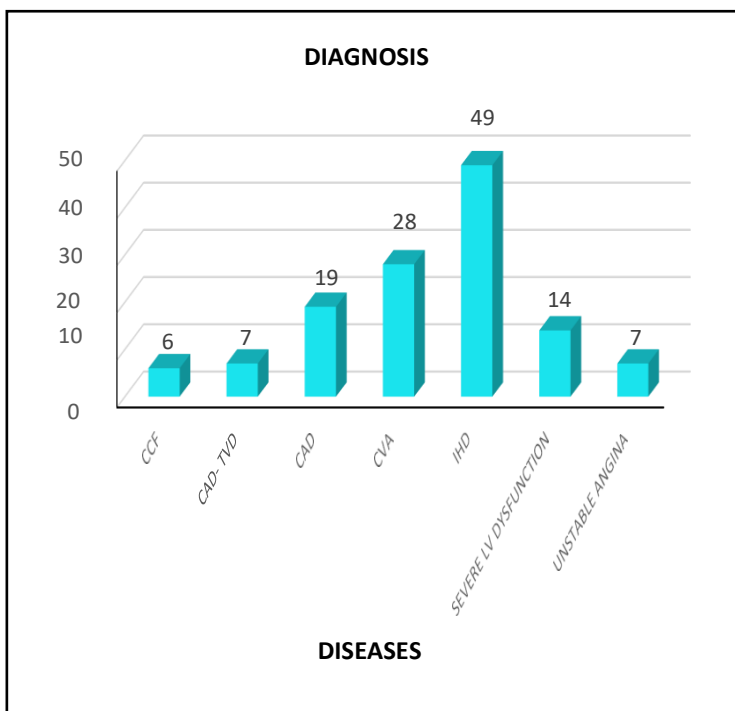


Fig No: 3. Patient's diagnosis.

Patients With Co-Morbidities

Out of 172 cases, 150 cardiovascular disease patients were assessed with co-morbidities whilst 22 were free from any co-morbidities.

Table No: 2. Patients co-morbidity.

CATEGORY	NO. OF PATIENTS	PERCENTAGE
PATIENTS WITH CO-MORBIDITY	150	87.20%
PATIENTS WITHOUT CO-MORBIDITY	22	12.70%

Types Of Co-Morbid Conditions

Various co-morbidities diagnosed for the 172 patients having CVDs were listed out below.

Table No: 3. Patients co-morbid conditions.

CO-MORBIDITY	NO. OF PATIENTS	PERCENT
CKD	6	2.89%

AKI	11	5.31%
HYPOTHYROIDISM	8	3.86%
LRTI	12	5.79%
HTN	96	46.37%
DM	74	35.74%

SPREAD OF DRUGS

In the 172 cases collected for the current study, the most commonly prescribed antiplatelet drugs for the treatment of various cardiovascular disease is tabulated below. A total of 303 antiplatelet drugs were prescribed, out of which T. Ecosprin (aspirin) is the most prescribed antiplatelet drug, followed by T. Clopilet (clopidogrel), T. Brilinta (ticagrelor), T. Pletoz (cilostazol) and T. Clopilet A (clopidogrel and aspirin) respectively.

Table No: 4. Spread of antiplatelet drugs.

SPREAD OF DRUGS	NO. OF DRUGS	%
T. ECOSPRIN	168	55.44%
T. CLOPILET	87	28.71%
T. BRILINTA	19	6.27%
T. PLETOZ	10	3.30%
T. CLOPILET A	19	6.27%
TOTAL	303	100%

Types Of Antiplatelet Therapy

Out of total 1302 drugs prescribed; 303 antiplatelet drugs were prescribed over the study period. Amongst all the patients who received APDs, 92.45% prescribed were MAPT followed by DAPT prescribed to 7.16%.

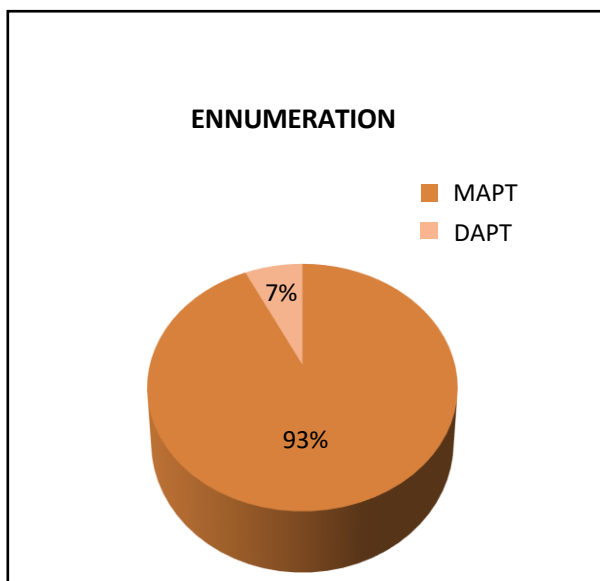


Fig No: 4. Types antiplatelet therapy.

Prescribing Pattern Of Drugs Other Than Antiplatelet Agents

Many other drugs were prescribed with antiplatelet agents and they were also further classified into the basic classes that were anti-hypertensive, Anti-diabetic, Anti-hyperlipidemic etc. Highest number of drugs prescribed were from anti-hyperlipidemic 17.96%, followed by Anti-hypertensives 15.89% , Antacids 14.80%, etc.

Table No: 5. Class of drugs other than antiplatelet.

CLASS OF DRUGS	NUMBER OF DRUGS	PERCENT
ANTIHYPERTENSIVES	131	15.89%
ANTIHYPERLIPIDEMIC	148	17.96%
ANTIANGINAL	41	4.97%
ANTICOAGULANTS	39	4.73%
ANTIDIABETIC	105	12.74%
DIURETICS	73	8.85%
ANTACIDS	122	14.80%
ANTIEMETIC	42	5.09%
ANTIBIOTICS	49	5.94%
ANTICONVULSANTS	23	2.79%
BRONCHODILATORS	44	5%
ANTITHYROID	7	1%
TOTAL	824	100%

Degree Of Adherence

Out of 172 patients, 119 patients who have scored less than 6 (69.18%) shows the lowest adherence to the medications followed by 44 patients who have scored between 6 to 8 (25.58%) tends to show moderate adherence.

Table No:6. Degree of adherence.

MMAS-8 SCORE	NO. OF PATIENTS	MEDICATION ADHERENCE	PERCENT
< 6	119	LOW	69.18%
6 to 8	44	MODERATE	25.58%
8	9	HIGH	5.23%

Adverse Drug Reactions

Out of 172 cases, a total number of 23 adverse drug reactions were found to occur by single drug use of Aspirin 39.13% (N=9) , followed by Clopidogrel 13.04% (N=3) etc. There were adverse drug reactions caused by the combination of drugs like Aspirin- Heparin sodium 15.78% (N=3) followed by Aspirin- Clopidogrel 10.52% (N=2) and Atorvastatin- Clopidogrel 10.52% (N=2). The following results have been tabulated below.

Table No: 7. ADRs caused by a single drug.

DRUGS	NO. OF REACTION	%
ASPIRIN	9	39.13%
ATORVASTATIN	1	4.34%
BISOPROLOL	2	8.69%
CLOPIDOGREL	3	13.04%
FUROSEMIDE	2	8.69%
GLIMEPIRIDE	2	8.69%

METFORMIN	1	4.34%
PANTOPRAZOLE	2	8.69%
ROSUVASTATIN	1	4.34%
TOTAL	23	100%

Predisposing Factors

In the present study, the concurrent interacting drugs was responsible for 45.23%, which was more predisposing factor for the ADR and 28.57% followed by 26.19% was responsible for age and polypharmacy respectively.

Table No: 8. Predisposing factors.

PREDISPOSING FACTORS	NO. OF OCCURENCE	PERCENT
AGE	12	28.57%
POLYPHARMACY	11	26.19%
INTERACTING DRUGS	19	45.23%
TOTAL	42	100%

Causality Assessment

There were 42 ADRs found among the 172 cases, among which severity, 30 (71.42%) were possible and 12 (28.57) were probable.

Table No: 9. Causality assessment.

CAUSALITY ASSESSMENT	SEVERITY	PERCENT
POSSIBLE	30	71.42%
PROBABLE	12	28.57%
TOTAL	42	100%

Management Of ADR

In the present study, the management of ADRs included Dose alteration (32%) followed by Drug withdrawal (64%) and Dose alteration + Drug withdrawal (4%).

Table No: 10. Management of

ADR.

MANAGEMENT	PERCENT
DOSE ALTERED	32%
DOSE ALTERED AND DRUG WITHDRAWN	4%
DRUG WITHDRAWN	64%

POLYPHARMACY

Out of 172 patients, 136 were above the age of 50. In these, 136 patients, 130 of them were prescribed with 5 or more drugs which eventually results in polypharmacy. The percent of patients having more than 5 drugs are at 76.47% which is quite high. The data collected are shown below.

Table No: Polypharmacy.

POLYPHARMACY	NO. OF PATIENTS	PERCENT
PATIENTS HAVING 5 OR MORE DRUGS WHO ARE ABOVE 50	130	76.47%

PATIENTS HAVING LESS THAN 5 DRUGS WHO ARE ABOVE 50	06	3.48%
TOTAL NO. OF PATIENTS ABOVE 50	136	79.06%
TOTAL NO. OF PATIENTS IN THE STUDY	172	100%

DISCUSSION

Among the 172 cases collected for our study, we found that majority of them were from the IPD (152) followed by OPD patients (20). It was also found that the majority were males (113) 65.69% and (59) 34.30% females (Table No:1). The average age group was 55-65. The result found to be consistent with the study conducted by Rajesh Hadia, *et al.* indicated that males were more susceptible to CVDs compared to females and the risk increases with the increasing age.

Out of 172 cases, 37.69 % (n=49) were diagnosed with IHD, 21.53% (N=28) CVA, 14.61% (N=19) cad, 10.76% (N=14) severe LV dysfunction, 5.38% (N=7) unstable angina, 5.38% (N=7) CAD-TVD, 4.61% (N=6) CCF (Fig No: 3).

Out of 172, 150 cardiovascular disease patients were assessed with co-morbid conditions whilst 22 were free of co-morbidities. In our study, the common co-morbidities related to cardiovascular diseases were 46.37% (N=96) hypertension, diabetes mellitus 35.74% (N=74), lower respiratory tract infection 5.79% (N=12), acute kidney injury 5.31% (N=11), hypothyroidism 3.86% (N=8), chronic kidney disease 2.89% (N=6) (Table No: 3) respectively.

The drug utilisation evaluation study helps to identify the behavior of the use of the medicines and helps in rational prescription of drugs. This type of drug utilisation pattern studies helps to determine the prescribing approach of the physicians. It also helps to provide efficient and cost effective treatment to the society and results in the enhancement of their quality of life and well being. Polypharmacy is also been observed in our study (Table No: 11). 172 prescriptions of patients suffering from various cardiovascular diseases were collected. 130 prescriptions of patients above 50 years of age had more than 5 drugs prescribed followed by 6 prescriptions had less than 5 drugs who were above 50 years of age constituting 3.48%.

Out of 1302 drugs prescribed, 303 antiplatelets were prescribed over the study period. Out of this 303, the most commonly prescribed drugs were T. Ecosprin (aspirin) 55.44% (N=168), followed by T. Clopilet (clopidogrel) 28.71% (N=87), T. Brilinta (ticagrelor) 6.27% (N=19), T. Pletoz (cilostazol) 3.30% (N=10) (Table No: 4).

Amongst all the patients who received antiplatelet agents, 93% of the prescribed were mono antiplatelet therapy followed by dual antiplatelet therapy prescribes to 7%. As per our study, the most commonly prescribed dual antiplatelet therapy was found to be T. Clopilet A (aspirin+clopidogrel) 6.27% (N=19) which was consistent with the study conducted by Rajesh Hadia, *et al.* The different classes of drugs prescribed among 172 cases collected were as follows: antihyperlipidemic 17.96% (N=148), followed by antihypertensives 15.89% (N=131), antacids 14.80% (N=122), antidiabetcs 12.74% (N=105), diuretics 8.85% (N=73), antibiotics 5.94% (N=49), bronchodialators 5% (N=44), antiemetic 5.09% (N=42), antianginal 4.97% (N=41), anticoagulants 4.73% (N=39), anticonvulsants 2.79% (N=23), antithyroid 1% (N=7) (Table No: 5).

The highest number of drugs prescribed other than antiplatelets include antihyperlipidemic like atorvastatin 10.70% (N= 98), rosuvastatin 2.73% (N=25). Antihypertensives like telmisartan 4.26% (N=39), metoprolol 3.39% (N=31), cilnidipine 2.07% (N=19). Antacids like pantoprazole 10.17% (N=93), esomeprazole 1.09% (N=10), rabeprazole 0.87% (N=8). Antidiabetcs included metformin 3.17% (N=29), human insulin 2.29% (N= 21), glimepiride 2.18% (N=20). Diuretics like furosemide 3.50% (N=32), torsemide 2.62% (N=24), spironolactone 0.76% (N=7). Antibiotics included were ceftriaxone 3.06% (N=28), piperacillin and tazobactam 1.64% (N=15), clindamycin 0.76% (N=7). Bronchodialators like levosalbutamol 1.96% (N=18), budesonide 1.85% (N=17), acebrophylline 0.54% (N=5) were found. Antiemetic like ondansetron 3.82% (N=35), domperidone 0.87% (N=8), metoclopramide 0.10% (N=1) were present. Antianginal included were isosorbide dinitrate 2.40% (N=22), nitroglycerin 1.53% (n=14), ivabradine 0.76% (N=7). Anticoagulants includes heparin sodium 3.50% (N=32), enoxaparin sodium 0.76% (N=7). Anticonvulsants like levetiracetam 1.20% (N=11), alprazolam 0.76% (N=7), escitalopram 0.54% (N=5) and antithyroid drugs like

levothyroxine 0.76% (N=7) were found to be prescribed.

The medication adherence was performed using the Morisky Medication Adherence Scale (containing questionnaires) with the score range between 1 to 8. 119 (69.18%) patients that have scored less than 6 were described as patients with low medication adherence followed by 44 (25.58%) patients scored between 6 to 8 are moderate and 9 (5.23%) patients scored 8 represents high adherence to the medicines (Table No: 6).

In our study, 23 adverse drug reactions were found to occur by single drugs like aspirin (39.19%), followed by clopidogrel (13.04%), bisoprolol (8.69%), furosemide (8.69%), glimepiride (8.69%), pantoprazole (8.69%), atorvastatin (4.34%), metformin (4.34%), rosuvastatin (4.34%) (Table No: 7). Commonly found predisposing factors of adverse drug reactions are age, gender, polypharmacy, multiple illness, intercurrent disease, history of ADR to the drug or drug class. In our study, the common category of predisposing factors during the study period were concurrent interacting drugs (45.23%), followed by age (28.57%) and polypharmacy (26.19%). The observed drug reactions were taken care either by drug withdrawal (64%), followed by dose alteration (32%) and both the dose alteration and drug withdrawal (4%). The causality assessment were found to be possible (71.42%) and probable (28.57%) which was found to be consistent with the study conducted by M. Reshma, *et al.*

CONCLUSION

An increase in the number of co-morbidities can significantly increase the utilisation of the drugs which can further lead to drug related problems like adverse drug reactions, medication adherence, polypharmacy, etc. Aspirin remains the cornerstone of therapy, although its increase in the adverse effects, clopidogrel and ticagrelor is beneficial in prevention as well as medical and interventional therapy of various cardiovascular disease.

In this study, individuals with drug related problems of cardiovascular diseases, it was found that males were more prone when compared with females due to various risk factors such as age, gender, co-morbidities, multiple drug use, concomitant use of drugs etc. The clinical pharmacist can help to alleviate the problems of various drug related problems and its consequence.

Patients must be provided with adequate information and knowledge in order to improve the medication adherence. Treatment must be tailored to the patient after careful consideration of harm versus benefit and a clear plan should be conveyed to patients and their health team.

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