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# A Prospective Observational Study to Evaluate the Adverse Drug Reactions and Drug Interactions in Patients with Acute Coronary Syndrome

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## Abstract

**Background:** Acute Coronary Syndrome (ACS) is one of the major causes of morbidity and mortality in developing countries. The patients with ACS receive multidrug therapies which is likely to develop adverse reactions and potential drug interactions. **Aim:** The aim of our study is to evaluate the occurrence of adverse reactions and drug interactions in patients with Acute Coronary Syndrome. **Materials and Methods:** A prospective observational study for a period of 6 months was conducted in the cardiology and cardiothoracic departments of a tertiary care hospital. The sample size was determined by using Rao software and percentage of the data was calculated using Microsoft Excel 2007. **Results:** A total of 270 patients were enrolled in the study, out of which 54 patients developed adverse drug reactions and most of them belonged to the age group of 60 – 69 years. ADR caused by antiplatelets dominated and Ramipril, Atorvastatin, Frusemide were the most offending drugs. The highest rate of ADRs reported in the study was increase in serum creatinine level (14.8%), followed by hematuria (11.1%), dyspnoea (9.2%) and hyperkalaemia (7.4%). About 58.47% of prescriptions were found to have DAPT – Anticoagulants as the major DDI pair. **Conclusion:** This study highlighted the need of intense monitoring of patients prescribed with cardiovascular drugs as they are more susceptible to serious health hazards associated with adverse drug reactions and drug – drug interactions.

**Keywords**
Acute Coronary Syndrome, Drug interactions, Adverse drug reactions, Monitoring, Therapeutic benefit.

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## INTRODUCTION

Coronary Artery Disease is a condition in which there is an inadequate supply of blood and oxygen to a portion of the myocardium, which occurs due to an imbalance between myocardial oxygen supply and demand. The most common cause of myocardial ischemia is the atherosclerosis of an epicardial coronary artery, leading to a local decrement in the myocardial blood flow and deficient perfusion of the myocardium supplied by the involved coronary artery. Coronary Artery Disease can often lead to Acute Coronary Syndrome (ACS) which takes account of three types of life-threatening clinical conditions encompassing Unstable angina (UA), ST-Elevation Myocardial Infarction (STEMI) and Non-ST Elevation Myocardial Infarction (NSTEMI).[1]

Prescribing the medications based on practice guidelines from the American College of Cardiology and American Heart Association (ACC/AHA) has improved in recent years to promote the proper therapeutic management for secondary prevention of Coronary Artery Diseases. The recommended medications for ACS patients include Statins, Dual Antiplatelet agents, Angiotensin-converting enzyme inhibitors (ACEIs) or Angiotensin receptor blockers (ARBs), Beta-blockers and Nitroglycerin.[2]

### Adverse Drug Reactions

Adverse drug reactions refer to undesirable drug effects, excessive therapeutic effects, or allergic reactions to medicine. ADR has a major impact on public health by imposing a considerable financial burden on society and the already stretched healthcare system. Cardiovascular drugs have been reported to account for 9% of medication-related visits to clinics. Cardiac patients have shown that the ADR rate is high as 24% with severe ADRs, accounting for about 22%. 7% were potentially preventable.

Adverse effects and the monitoring parameters of the various cardiovascular drugs are as follows:

1. Antiplatelets
   - Aspirin – Gastrointestinal ulcer, hemorrhage, tinnitus, exudative age-related macular degeneration, bronchospasm, angioedema and Reye's syndrome.
   - Clopidogrel – Hemorrhage, coronary artery stent thrombosis, pancytopenia, Thrombotic thrombocytopenic purpura (TTP) and hypersensitivity reactions.
   - Prasugrel – Hypertension, hyperlipidemia, epistaxis, headache, backache, atrial fibrillation, bradyarrythmia, leukopenia and TTP.
   - Ticagrelor – Dyspnoea, raised serum creatinine, haemorrhage and bradyarrythmia.
   - Monitoring – Clinical signs of bleeding, baseline CBC, every 6 months
2. Anticoagulants
   - Unfractionated heparin – Heparin induced thrombocytopenia (HIT), increased liver aminotransferase level and haemorrhage.
     Monitoring – aPTT, until target / change in dose. CBC, HIT if indicated.
   - Enoxaparin – Anemia, thrombocytopenia, haemorrhage, diarrhoea, fever and nausea.
     Monitoring - CBC & S.cr, HIT if indicated. Avoid if CrCl<15
   - Fondaparinux – Injection site reactions, rashes, fever, anemia, haemorrhage and thrombocytopenia.
     Monitoring – CBC & S.cr
   - Abciximab, Tirofiban, Eptifibatide – Bleeding and acute profound thrombocytopenia
     Monitoring - Baseline S.cr & CBC (with emphasis on platelet count), 4hrs after intiation
3. Beta-blockers
   Bronchospasm, bradycardia, peripheral vasospasm, neurological-weakness, fatigue, vivid dreams, nightmares, hallucinations, reduced glucose tolerance, mask signs of hypoglycaemia, increased triglycerides, impotence.
   Monitoring - Monitor BP, HR, blood glucose and liver function
4. Calcium channel blockers (CCBs)
   - Dihydropyridines (Nifedipine, Amlodipine) – Tachycardia, headache, dizziness, peripheral edema, flush, gingival hyperplasia
     Monitoring – Monitor patient carefully for BP, cardiac rhythm and output while adjusting drug to therapeutic dose; use special caution if patient has CHF.
   - Non-dihydropyridines (Diltiazem, Verapamil) – Bradycardia, AV block, constipation, Gingival hyperplasia, headache, flushing, edema
     Monitoring – Continue periodic monitoring of electrolytes specially potassium.
5. ACEIs - First dose hypotension, cough, hyperkalemia, renal failure, angioedema

Monitoring – Monitor $K^+$, S.cr within 4 weeks of initiation or dose increase, BP, BUN.

6. Diuretics
   - Thiazide diuretics and Thiazide like diuretics – ↓$K^+$, $Mg^{2+}$, $Na^+$ , ↑uric acid, gout attack, ↑$Ca^{2+}$, ↑LDL, rashes, pancreatitis, photosensitivity
   - Loop diuretics – ↓$K^+$, ↓$Mg^{2+}$, ↓$Na^+$, ↓$Ca^{2+}$ , Ototoxicity, hyperuricemia, dizziness
   - $K^+$ sparing diuretics – Hyperkalaemia, hyponatremia, gynacomastia, weakness, fatigue, dizziness

     Monitoring – Monitor BP, BUN, S.cr, Serum electrolytes ($K^+$, $Mg^{2+}$, $Na^+$), uric acid (for thiazides), renal and hepatic function and blood glucose.
7. ARBs – Hyperkalemia, first dose orthostatic hypotension, pharyngitis, insomnia, muscle cramps

   Monitoring – Monitor serum $K^+$, BP, BUN, S.cr
8. Statins – Rhabdomyalgia, rhabdomyolysis, renal impairment, raised transaminases

   Monitoring – Monitor liver function, creatine kinase level, blood glucose level, LDL & other lipids.
9. Nitrates – Throbbing headache, postural hypotension, facial flushing, tachycardia

   Monitoring – Monitor HR & BP
10. Reteplase and Tenecteplase - Bleeding especially intracranial haemorrhage

    Monitoring - Clinical signs of bleeding, CBC with platelets, INR.

**Drug Interactions**

Drug-drug interaction is a pharmacological answer to the concomitant administration of 2 or more drugs that are divergent from the response caused by these drugs when used alone. Initial and long-term treatment of patients suffering from ACS, involves multidrug therapy, including Anticoagulants, Antiplatelet agents (Aspirin in combination with Clopidogrel), Beta-blockers, Nitrates, and ACEIs/ARBs. In many instances, other treatments should also be prescribed because of comorbidities such as hypertension and diabetes. Most of these drugs have to be prescribed for the long term, so attention must be paid to possible interactions that can limit the efficacy of certain drugs and compromise both outcome and the therapeutic benefit.

Potential drug-drug interactions (PDDI) describes interaction between drugs from a previously known and documented medical prescriptions, but they can occur or not, requiring clinical and lab monitoring. According to the intensity level we can classify the PDDI as:

- Major, contraindication, important or serious (when the interaction represent risk to life and/or request medical intervention to reduce or avoid serious effects) eg:- Clopidogrel & Omeprazole DDI, which may increase thrombosis risk due to reduction of Clopidogrel active metabolite formation.
- Moderate or significant (when the interaction exacerbates the patient health problem and/or require a pharmacotherapy change) eg:- Aspirin & Atenolol DDI reduces the antihypertensive effects.
- Minor or secondary (when the interaction results in limited clinical effects. The manifestations can include an increase in the frequency or intensity of adverse effects, but generally, they do not require a major pharmacotherapy change)

The various drug interactions associated with cardiovascular drugs are as follows:

1. Verapamil/Diltiazem ↔ Beta blockers – Additive effects on slowing HR; Avoid combining or monitor HR closely.
2. Clopidogrel ↔ Omeprazole – Concomitant use reduces levels of the clopidogrel active metabolites and reduces platelet inhibition when either given concomitantly or 12 hours apart; avoid concomitant use of both the drugs.
3. (Aspirin, Clopidogrel, Ticagrelor, Prasugrel) ↔ (Warfarin, Dabigatran, Rivaroxaban, Apixaban) – Doubling of bleeding risk; avoid combination or where not possible (eg:-high risk MI patients with mechanical valve or intracardiac thrombus), use combination for shortest time possible and reduce risk by ensuring BP control.
4. Statins ↔ Fibrates (gemfibrozil, fenofibrate) – Increased risk of myalgia; risk is small and usually outweighed by benefits in patients requiring this combination.
5. ACEIs/ARBs ↔ Loop diuretics – Increased risk of renal impairment and when initiating there is an increased risk of severe hypotension due to volume depletion. Closely monitor renal function and be very cautious in patients with hypovolaemia. Withhold loop diuretic (or reduce dose) for at least 24 hrs before starting and begin with a low dose of ACEI.
6. Beta blockers ↔ Other medicines that reduce BP, cardiac contractility and conduction – May cause additive hypotension, HF or bradyarrhythmia. Monitor BP, cardiac function and HR closely.

Our study aims to provide a significant collaboration to define the prevalence pattern of ADR and DDI in prescriptions for ACS.

## METHODOLOGY

### Study Design

A prospective observational study was conducted in the Cardiology and Cardiothoracic Departments to determine the adverse drug reactions and drug interactions among various cardiovascular drugs prescribed to the patients diagnosed with ACS from the time of admission between February1, 2018-June 31, 2018.

### Inclusion Criteria

- Male and female patients
- All patients admitted with symptoms of ACS (UA, STEMI and NSTEMI)
- Patients diagnosed with ACS

### Exclusion Criteria

- Pregnant women
- Outpatients
- Patients admitted with other heart diseases (Endocarditis, Rheumatic heart disease, arrhythmias and cardiac tumours)

### Study Population

- Sample size – 270

### Study Period

- 6 months (February1, 2018-July 31, 2018)

### Statistical Analysis

The information collected during hospitalization of the patients with ACS was recorded in a structured proforma. Data was computed in MS excel.

### Data Collection

The data were collected from the patient medical records which include patient demographics**,** past medical and medication history, diagnosis**,** laboratory investigations and drug chart.

## RESULTS AND DISCUSSION

In the present study, we have randomly collected 270 prescriptions of the inpatients who were admitted in a tertiary care hospital using a structured proforma. Mean age of 270 patients was found to be 59.08. The patients between ages of 60-69 years constituted the higher number followed by 50-59 and 40-49 years (Figure 1) which was found to be correlated to the to the study conducted by Siddaruda Malleshappa Biradar *et al.*[3] This shows that risk of ACS is common in older age groups. Out of the total patients enrolled in the study, 219 (81.12%) patients were males and 51 (18.89%) were females (Figure 2), where males dominate than females. This shows that the incidence of ACS is higher among the males than females.

Some of the risk factors may contribute to the progression of ACS by altering the normal mechanisms of the body. Diabetes (62.96%) constituted the dominant risk factor followed by Hypertension (54.81%) and Smoking (35.92%). Dyslipidaemia (34.07%), family history of CAD (14.45%) and obesity (4.45%) were weakly related to ACS risk (Figure 3), which is in contrast to the study conducted by Avula Naveen *et al,*[4] in which obesity constituted the dominant risk factor for ACS. In our study, majority of ACS were of the patients of Myocardial Infarction, 222 in number of this 135 were STEMI, 87 cases were NSTEMI and others (48 cases) were of Unstable angina, as observed by Avula Naveen *et al,*[4] (Figure 4).

Among 270 prescriptions analysed, 269(99.6%) were prescribed with antiplatelets, 200 (74.07%) received anticoagulants, 33 (12.2%) received thrombolytics, 262 (97.03%) received statins, 254 (94.07%) received beta blockers, 112 (41.4%) received nitrates, 36 (13.3%) were prescribed with CCBs, 206 (76.2%) and 38 (14.07%) received ACEIs & ARBs respectively (Table 1).

The frequency of ADRs in the present study was 54/270 (20%). The rate is much higher than the previous study performed in hospitalised patients in cardiac care unit in which 44 (5.95%) out of 740 inpatients developed 1 cardiovascular adverse drug reaction. Most of the patients presented with ADRs belonged to the age group of 60 – 69 years (Table 2). This is different from the study conducted by Kheirollah Gholami *et al.,*[5] in which the patients with ADRs mostly belonged to the age group of 51 – 60 years. This leads to a conclusion that older people are more likely to experience an ADR. About 12 patients were presented with adverse reactions induced by antiplatelets which constituted the highest number, followed by ACEIs and anticoagulants (Table 3). This was compared to a study conducted by Tom Mjorndal *et al.,*[6] in which the highest number of ADRs were constituted by beta blockers, followed by ACEIs and diuretics.

Ramipril, Atorvastatin and Frusemide were the most offending cardiovascular drugs in the current study which induced adverse reactions in 7, 5 and 4 patients respectively. It was compared with the study conducted by Iman Karimzadeh *et al,*[7] in which digoxin, atenolol and streptokinase were the drugs with highest ADR. The highest rate of ADRs reported in the study was increase in serum creatinine level (14.8%), followed by hematuria (11.1%), dyspnoea (9.2%) and hyperkalaemia (7.4%) (Table 4). These results were contrary to the study conducted by Mohebbi *et al.,*[8] in which headache, dizziness, nausea and vomiting were the highly reported ADRs.

Urinary system (40.7%), central and peripheral nervous system (11.1%), gastrointestinal system (11.1%) and respiratory system (11.1%) were considered to be the most frequent affected organ systems (Table 5). This was contradictory to the study conducted by Lia Amalia *et al.,*[9] in which cardiovascular system (20.41%), electrolyte systems (20.41%), gastrointestinal system (18.37%) and hematology (18.37%) were the most frequent affected organ systems.

On the causality assessment, certain (48.1%), probable (40.7%) and possible (11.1%) ADRs were observed (Table 6). Preventive strategies such as development of ADR surveillance centre in hospitals, instructive health team professionals especially doctors and nurses regarding detecting and reporting ADRs, participation of clinical pharmacists in drug prescription, dispensing, administration and patient follow-up, using computer-based prescription systems and regular level monitoring of drugs with narrow therapeutic index could considerably reduce the rate of ADR occurrence in medical settings.

The patients were prescribed with many cardiovascular drugs along with some non-cardiovascular drugs. Already, several studies have shown that polypharmacy increase the chance of drug interactions. Table 7 & 8 shows the possible major and moderate DDI pairs found on this survey. Most frequent major DDI pair found in major DDI was DAPT – Anticoagulants, which was nearly 58.47%, followed by Diuretics – Aspirin (47.4%) and Metformin – Aspirin (46.7%). Among the moderate drug interactions, Beta blockers – Aspirin pair was found in almost 85.5% of prescriptions, which was followed by Hypoglycemics – Beta blockers pair constituting about 51.1% of prescriptions. This was compared to the study conducted by Mohammad Borhan Uddin *et al.,*[10] in which Clopidogrel – Omeprazole DDI pair constituted the highest percentage.

**Figure 1: Age wise distribution of ACS patients**

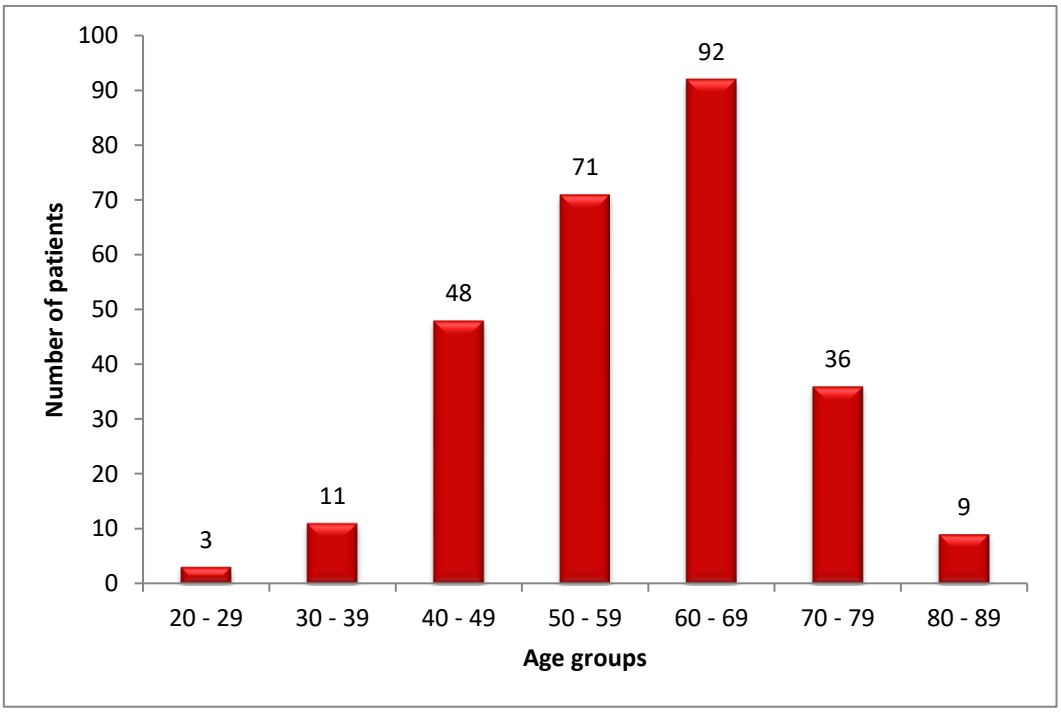

**Figure 2: Gender-wise distribution of ACS patients**

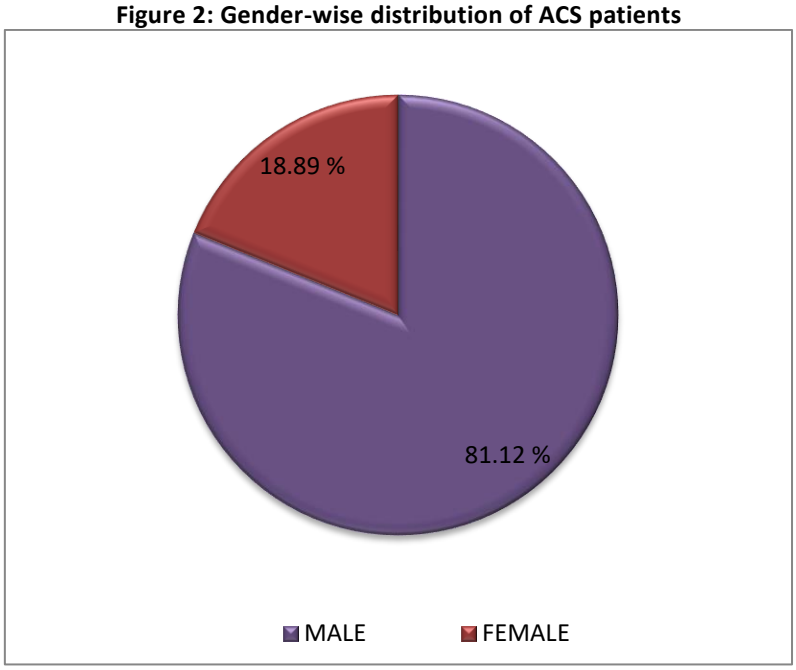


**Figure 3: Distribution of selected risk factors in ACS patients**

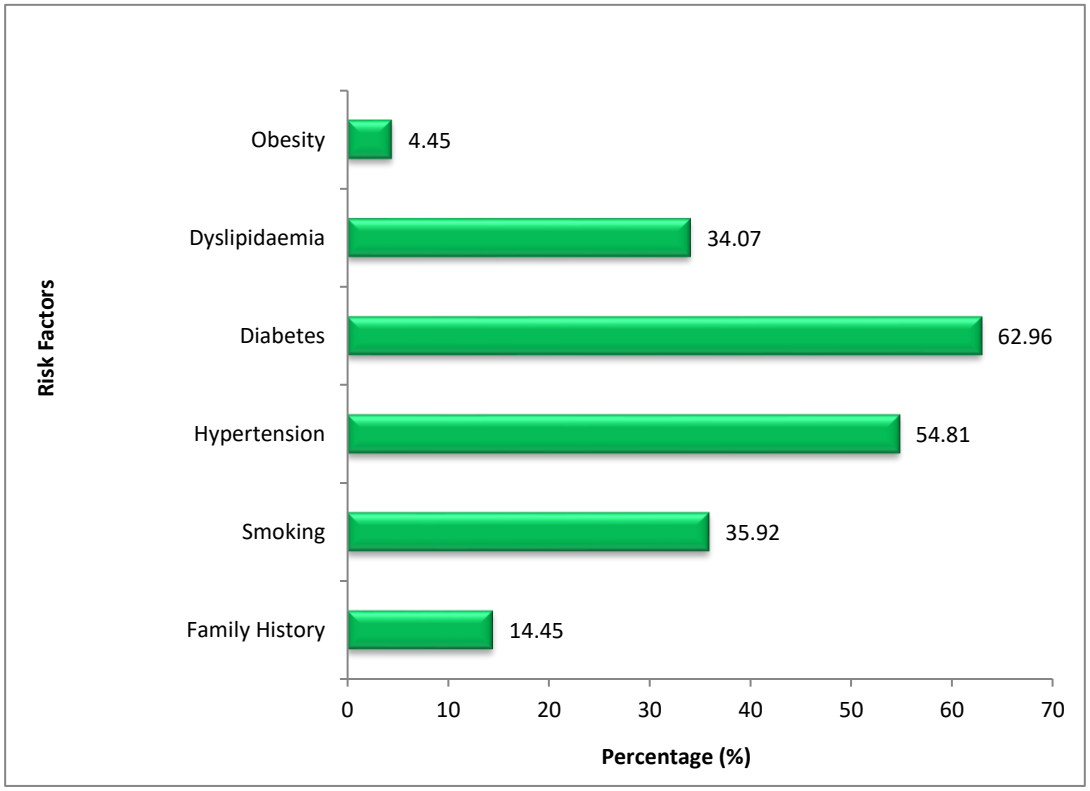

**Figure 4: Distribution of types of ACS**

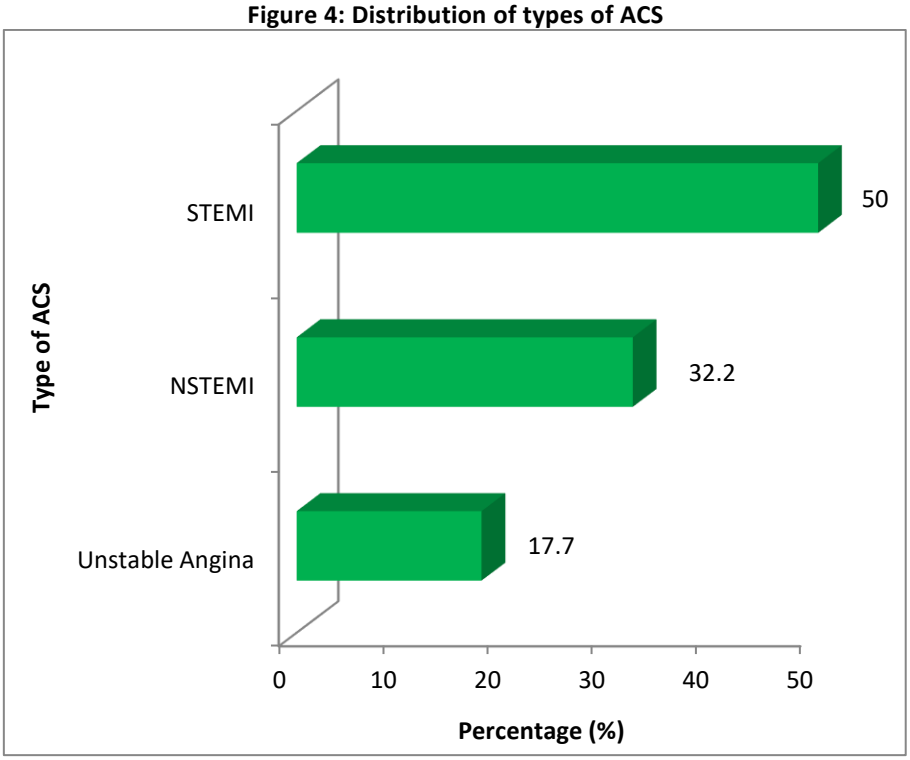


**Table 1: Pattern of Cardiac drugs prescribed to the patients with ACS**

| Class of drugs | No. of patients (n=270) | Percentage (%) |
|---|---|---|
| Anticoagulants | 200 | 74.07 |
| Antiplatelets | 269 | 99.6 |
| Thrombolytics | 33 | 12.2 |
| Statins | 262 | 97.03 |
| Beta blockers | 254 | 94.07 |
| ACEIs | 206 | 76.2 |
| Nitrates | 112 | 41.4 |
| CCBs | 36 | 13.3 |
| ARBs | 38 | 14.07 |

**Table 2: Number of adverse drug reactions in different age groups**

| Age groups | Patients with ADRs (%) | Patients without ADRs (%) | Total (%) |
|---|---|---|---|
| 20-29 | 0 | 3(100%) | 3 (100%) |
| 30-39 | 2 (18.1%) | 9 (81.9%) | 11 (100%) |
| 40-49 | 9 (18.75%) | 39 (81.25%) | 48 (100%) |
| 50-59 | 8 (11.2%) | 63 (88.8%) | 71 (100%) |
| 60-69 | 16 (17.3%) | 76 (82.7%) | 92 (100%) |
| 70-79 | 14 (38.8%) | 22 (61.2%) | 36 (100%) |
| 80-89 | 3 (33.3%) | 6 (66.7%) | 9 (100%) |

**Table 3: Number of ADRs induced by different classes of cardiovascular agents**

| Pharmacologic classification | Patients with ADRs (%) | Patients without ADRs (%) | Total (%) |
|---|---|---|---|
| ACEIs | 11 (4.1%) | 258 (95.9%) | 269 (100%) |
| Beta – blockers | 1 (0.4%) | 253 (99.6%) | 254 (100%) |
| CCBs | 0 | 36 (100%) | 36 (100%) |
| Nitrates | 0 | 111 (100%) | 111 (100%) |
| Antiplatelets | 12 (4.5%) | 257 (95.5%) | 269 (100%) |
| ARBs | 1 (0.5%) | 231 (99.5%) | 232 (100%) |
| Thrombolytics | 2 (1.3%) | 164 (98.7%) | 166 (100%) |
| Anticoagulants | 9 (4.5%) | 192 (95.5%) | 201 (100%) |
| Statins | 5 (2%) | 257 (98%) | 262 (100%) |
| Loop diuretics | 8 (15%) | 45 (85%) | 53 (100%) |
| Potassium sparing diuretics | 4 (7.1%) | 53 (92.9%) | 57 (100%) |
| Vasodilators | 6 (5.3%) | 91 (94.7%) | 97 (100%) |

**Table 4: Clinical manifestations, frequency, sex ratio and cardiovascular drugs suspected of causing adverse reactions (n=54)**

| Type of ADR | n (%) | M/F | Suspected drug (n) |
|---|---|---|---|
| Increase in serum creatinine | 8(14.8%) | 7/1 | Ramipril(7), Telmisartan(1) |
| Increase in uric acid | 6(11.1%) | 6/0 | Torasemide (2), Frusemide(4) |
| Hematuria | 6(11.1%) | 5/1 | Enoxaparin(3), Fondaparinux(2), Aspirin/ticagrelor(1) |
| Increase in SGOT | 5(9.2%) | 5/0 | Atorvastatin(5) |
| Dyspnea | 5(9.2%) | 4/1 | Ticagrelor(5) |
| Hyperkalemia | 4(7.4%) | 3/1 | Eplereone(1), Spironolactone(3), |
| Headache | 3(5.5%) | 3/0 | Nicorandil(1), Isosorbide dinitrate(2) |
| Bloody stools | 2(3.7%) | 2/0 | Dalteparin(1), Aspirin/clopidogrel(1) |
| Renal dysfunction | 2(3.7%) | 2/0 | Ramipril(2) |
| Hematoma | 2(3.7%) | 1/1 | Enoxaparin(2) |
| Malena | 2(3.7%) | 2/0 | Ecospirin(1), Ticagrelor/aspirin(1) |
| Ecchymosis | 1(1.85%) | 0/1 | Enoxaparin(1) |
| Rigors | 1(1.85%) | 1/0 | Streptokinase(1) |
| Cough | 1(1.85%) | 1/0 | Ramipril(1) |
| Constipation | 1(1.85%) | 1/0 | Frusemide(1) |
| Diarrhoea | 1(1.85%) | 1/0 | Carvedilol(1) |
| Hypokalemia | 1(1.85%) | 1/0 | Frusemide(1) |
| Hypotension | 1(1.85%) | 1/0 | Streptokinase(1) |
| Nausea | 1(1.85%) | 0/1 | Aspirin/clopidogerl(1) |
| Syncope | 1(1.85%) | 1/0 | Isosorbide dinitrate(1) |

**Table 5: Different Organ-system Classes affected by ADRs**

| Organ system class | Frequency | Percentage (%) |
|---|---|---|
| CNS and PNS disorders | 6 | 11.1% |
| Gastrointestinal system disorders | 6 | 11.1% |
| Urinary system disorders | 22 | 40.7% |
| Respiratory system disorders | 6 | 11.1% |
| Body as a whole - general disorders | 1 | 1.8% |
| Platelet, bleeding and clotting disorders | 2 | 3.7% |
| Endocrine disorders | 5 | 9.2% |
| Skin and appendages disorders | 1 | 1.8% |
| Increase/decrease in blood serum | 5 | 9.2% |

**Table 6: Causality Assessment of Detected Adverse Drug Reactions (n=54)**

| Causality | n (%) |
|---|---|
| Certain | 26 (48.1%) |
| Probable | 22 (40.7%) |
| Possible | 6 (11.1%) |
| Unlikely | 0 |

**Table 7: Major Drug Interactions occurred in patients with ACS**

| DDI-pair | Number (n) | Percentage (%) | Effects |
|---|---|---|---|
| Clopidogrel/Aspirin – Heparin/Enoxaparin/ Fondaparinux/Dalteparin | 160 | 59.2 % | Increased risk of bleeding by additive effects |
| Metformin/Glimepiride – Aspirin | 151 | 56 % | Increased risk of hypoglycemia by increased effectiveness of oral hypoglycaemic agent |
| Spironolactone/Eplerenone - Aspirin | 78 | 28.9 % | Increase the risk of renal toxicity, may reduce the diuretic effectiveness, hyperkalaemia by decreased prostaglandin synthesis |
| Ramipril – Spironolactone/ Eplerenone | 24 | 8.9 % | Hyperkalaemia due to increased potassium retention secondary to lowered aldosterone levels |
| Clopidogrel - Amlodipine | 20 | 7.4% | Decrease the effect of clopidogrel on platelet inhibition, increasing the risk of antithrombotic events by inhibition of $CYP_3A$-mediated clopidogrel activation by amlodipine |
| Clopidogrel - Fluconazole | 3 | 1.1% | Reduced clopidogrel active metabolite concentration and reduced platelet inhibition by inhibition of $CYP_2C_{19}$-mediated clopidogrel metabolism to its active metabolite by fluconazole |
| Frusemide/ Hydrochlorthiazide – Aspirin | 50 | 18.5 % | Reduced diuretic effectiveness by decreased renal prostaglandin synthesis |
| Metformin - Levofloxacin | 3 | 1.1% | Changes in blood glucose and increased risk of hypoglycemia or hyperglycemia |
| Ondansetron - Clarithromycin | 2 | 0.74% | Increased risk of QT interval prolongation,by inhibition of $CYP_3A_4$-mediated Ondansetron metabolism by clarithromycin |
| Ramipril – Potassium Chloride | 2 | 0.74% | Hyperkalemia due to decreased renal clearance |
| Morphine - Carvedilol | 9 | 3.3% | May result in increased morphine exposure and increase the risk of adverse effects, including respiratory and CNS depression by unknown mechanism |

**Table 8: Moderate Drug Interactions occurred in patients with ACS**

| DDI pair | Number (n) | Percentage (%) | Effect |
|---|---|---|---|
| Carvedilol/Nebivolol/ Metoprolol - Aspirin | 231 | 85.5 % | Decreased antihypertensive efficacy due to decreased production of prostaglandins |
| Metformin/Glimepiride/ Insulin – Metoprolol/ Carvedilol/Nebivolol | 138 | 51.1 % | Increase or decrease blood glucose lowering effect & decrease signs and symptoms of hypoglycaemia |
| Insulin/Metformin - Ramipril | 51 | 18.9 % | Increased risk of hypoglycaemia |
| Insulin – Aspirin/ Metformin | 80 | 29.6 % | Increased risk of hypoglycaemia |
| Ticagrelor – Enoxaparin/ Fondaparinux | 69 | 25.5 % | Increased risk of bleeding by additive effects |

| | | | |
|---|---|---|---|
| Spironolactone - Ramipril | 21 | 7.78% | Hyperkalaemia due to increased potassium retention secondary to lowered aldosterone levels |
| Frusemide - Morphine | 12 | 4.44% | Induce antidiuretic hormone release and reduced efficacy of the diuretic |
| Ramipril - Aspirin | 72 | 26.66% | Decreased ramipril effectiveness by inhibition of prostaglandin synthesis |
| Ramipril - Frusemide | 12 | 4.44% | Increase the risk of renal toxicity, may reduce the diuretic effectiveness & hyperkalaemia by decreased prostaglandin synthesis |
| Levothyroxine - Pantoprazole | 18 | 6.67% | Pantoprazole causes low stomach acid, decrease levothyroxine absorption and affect intragastric pH |

## CONCLUSION

This study highlighted the need of intense monitoring of patients prescribed with cardiovascular drugs as they are more susceptible to serious health hazards associated with adverse drug reactions and drug – drug interactions. The study also revealed that the major PDDIs can often aggravate the medical condition, lead to prolonged hospitalization, develop comorbid conditions and moreover, reduce the therapeutic effectiveness of the prescribed drugs. This implies the imperative need of a clinical pharmacist to oversee the prescribed medicines, to cross-check the adherence to the treatment guidelines and most importantly, to reduce the occurrence of adverse reactions and drug interactions to a great extent.

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## CONFLICTS OF INTEREST

None

## ABBREVIATIONS

ACS – Acute Coronary Syndrome, STEMI – ST segment Elevation Myocardial Infarction, NSTEMI – Non-ST segment Elevation Myocardial Infarction, UA – Unstable Angina, ACEIs – Angiotensin Converting Enzyme Inhibitors, ARBs – Angiotensin II Receptor Blockers, CCBs – Calcium Channel Blockers.

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