


Assessment of prescribing pattern and adverse drug reaction in patients receiving anticoagulant therapy: A prospective observational study

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Abstract

Introduction: Cardiovascular diseases (CVD) are the leading cause of death worldwide as well as a major blockade to sustainable human development. It is among the leading causes of morbidity and mortality. Anticoagulants are among the most essential life-saving drugs that are generally used in cardiology for the prevention and treatment of many CVD.

Objectives: To assess the prescribing pattern and adverse drug reaction (ADR) in patients receiving anticoagulant therapy for cardiac diseases.

Methodology: This was a Prospective Observational study conducted in the Department of Cardiology, SRM Medical College Hospital and Research Center, Kattankulathur including 88 patients for 6 months.

Results: Out of the 88 patients, the majority were males (73%) compared to females (27%), and the prevalence of CVD was found to be higher in patients above 40 years of age. Various categories of drugs prescribed to the patients were antiplatelets (14.88%), anticoagulants (8.79%), antianginal (13.82%), antihypertensives (15.7%), antihyperlipidemic (7.83%), thrombolytics (0.68%), Ionotropic agents (2.13%), antibiotics (5.31%), and other miscellaneous drugs (36.61%). The anticoagulant dosage regimens prescribed to the patients were categorized into monotherapy (9%), combinational therapy with antiplatelets (38%), and triple therapy (53%). The most commonly prescribed anticoagulant to the patients was Heparin (93.41%), followed by Warfarin (5.49%) and lastly Rivaroxaban (1.10%) respectively. From the details of the prescriptions analyzed, the average number of drugs per patient (prescription) was found to be 11.7.

Conclusion: Heparin was found to be the most commonly used anticoagulant, Combination therapy of antiplatelets and antihypertensives was observed in most of the prescriptions, which is more effective than a single therapy. Polypharmacy was encountered in the study with an average number of 11.7 drugs per prescription. Several anticoagulant-related drug interactions were identified and there were two

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adverse drug reactions with Heparin. The prescribing pattern can be improved by reducing the number of drugs prescribed.

KEYWORDS

adverse effects, anticoagulants, drug therapy

1 | INTRODUCTION

Cardiovascular diseases (CVD's) are among the leading cause of death worldwide as well as a major blockade to sustainable human development.¹ According to the world health organization (WHO), it is among the leading causes of morbidity and mortality in India with an estimated 17.7 million deaths per year.² Anticoagulants are among the most essential life-saving drugs that are generally used in cardiology for the prevention and treatment of many CVD such as ischemic heart disease, left ventricular dysfunction, acute coronary syndrome, valve abnormalities, Atrial fibrillation, deep vein thrombosis, and pulmonary embolism. These drugs prevent thrombus extension and embolic complications by reducing the rate of fibrin formation.³⁻⁵ These drugs are either used orally (mostly for long-term therapy) or Parenterally (for the prevention and initiation of treatment of thrombosis as well as other surgical procedures) and are among the most frequently implicated medications that cause ADRs in hospitalized patients, mostly elderly patients are at high risk to suffer from anticoagulant-associated ADRs such as ecchymosis, epistaxis, hematuria, gastro intestinal (GI) bleeding, thrombocytopenia, osteoporosis on long term use and hypersensitivity reactions.⁶⁻⁹

The present study was aim to evaluate and understand the drug use pattern of oral and Injectable anticoagulants. This prospective study will be helpful to improve current prescription patterns and give insights to minimize the drug therapy problems associated with anticoagulant therapy.

2 | MATERIALS AND METHODS

2.1 | Study design

Prospective Observational Study.

2.2 | Site of study

Cardiology department: Cardiovascular Intensive Care Unit (CV-ICU) and Coronary Care Unit (CCU) SRM Medical College Hospital & Research Center, Kattankulathur.

2.3 | Study period

6 months.

2.4 | Inclusion criteria

Patients with cardiovascular disease admitted to Cardiology department: CV-ICU and CCU receiving both oral and parenteral anticoagulant treatment.

2.5 | Exclusion criteria

Patients who were not willing to participate in the study were excluded from the study.

Alcoholics and patients with a medical history of peptic ulcers were also excluded from the study.

2.6 | Sources of data

Patient's case sheets.

Medication charts.

Lab data reports.

2.7 | Study procedure

The study was approved by the Institutional Ethics Committee of SRM medical college hospital and research center. Data collection form was designed and information including patients' socio-demographic data (age, gender, family history, place of stay, smoking status, alcohol consumption, allergy, and diet assessment), therapeutic data (drug name, dosage form, route of administration, frequency, and laboratory investigation including anticoagulation profile) and principle investigation was obtained and analyzed. Drugs were categorized into various classless and presented as percentages.

Possible drug-drug interactions were assessed using Medscape and the anticoagulant-associated ADRs were assessed and reported using Naranjo's ADR probability scale.

2.8 | Sample size calculation

Sample Size Calculated using Raosoft sample size calculator software.

Estimated sample size at 95% CI (confidence interval), 4.99% margin of error and

15% of contingency: 86.

Observed sample size: 125 with a 5% margin of error and 15% of contingency.

3 | RESULTS AND DISCUSSION

Anticoagulant usage in patients with CVD is almost unavoidable, appropriate measures are necessary before initiating therapy to avoid nonadherence to standard clinical guidelines. The main aim of this study was to assess the prescribing pattern of anticoagulants in cardiovascular disease patients alongside evaluating possible anticoagulants-related drug–drug interactions and ADR in the prescriptions. A total number of 88 patients receiving anticoagulant therapy were included in the study among which (73%) were males and (27%) were females, the incidence of cardiovascular disease was more common in males. The patients were divided into 4 different age groups with an age gap of 10 years and the mean age group was found to be 57 which indicates the prevalence of CVD among the age group 40–59. The prevalence of CVD was found to be higher in patients above 40 years of age. Results were found to be similar to the study conducted by Sam et al.¹⁰

The majority of the patients were diagnosed with Acute Coronary Syndrome including Anterior ST-Elevation Myocardial Infarction (38.64%), Inferior ST-Elevation Myocardial Infarction (21.59%), non-ST-Elevation Myocardial Infarction (10.23%), and Unstable Angina (21.59%). among others were Rheumatic Heart

Disease (5.68%), sinus tachycardia, and dilated cardiomyopathy (1.14%) respectively, as shown in. From the prescription assessed, the most common comorbid conditions associated with an increased risk of CVD were hypertension (47.72%) and diabetes mellitus (45.45) as well as dyslipidemia (9%), COPD (8%), hypothyroidism (2.3%), CKD (1.13%), and Leprosy (1.13%) among others which are in accordance with the studies conducted by Nair et al.¹¹ and Sam et al.¹⁰

In our study, various categories of drugs prescribed to the patients were antiplatelets (14.88%), anticoagulants (8.79%), anti-anginals (13.82%), antihypertensives (15.7%), antihyperlipidemics (7.83%), thrombolytics (0.68%), Ionotropic agents (2.13%), antibiotics (5.31%), and other miscellaneous drugs (36.61%) This shows similar trends in the studies conducted by Nair et al., Thomas et al., and Narayanan et al.^{12–14} The miscellaneous drugs prescribed to the patients with those associated with different comorbidities includes proton pump inhibitors (PPI) (15.30%), Laxatives (12.93%), antipsychotics (12.66%), NSAID's (8.44%), Vitamins and electrolytes (11.08%), other GI agents (6.86%), antidiabetics (10.03%), mucolytics (3.69%), bronchodilators (2.37%), H2 receptor blockers (10.6%), antiepileptic (0.53%), Antithyroid (0.53%), and Antibiotics (14.51%) respectively. The most commonly prescribed PPI was Pantoprazole; laxative was sodium Picosulfate and antipsychotic was Alprazolam, Antibiotics was Ceftriaxone administered intravenously (Figure 1).

In the study conducted by Nair et al.¹¹ the most commonly prescribed anticoagulant to the patients was Heparin (92.23%) and

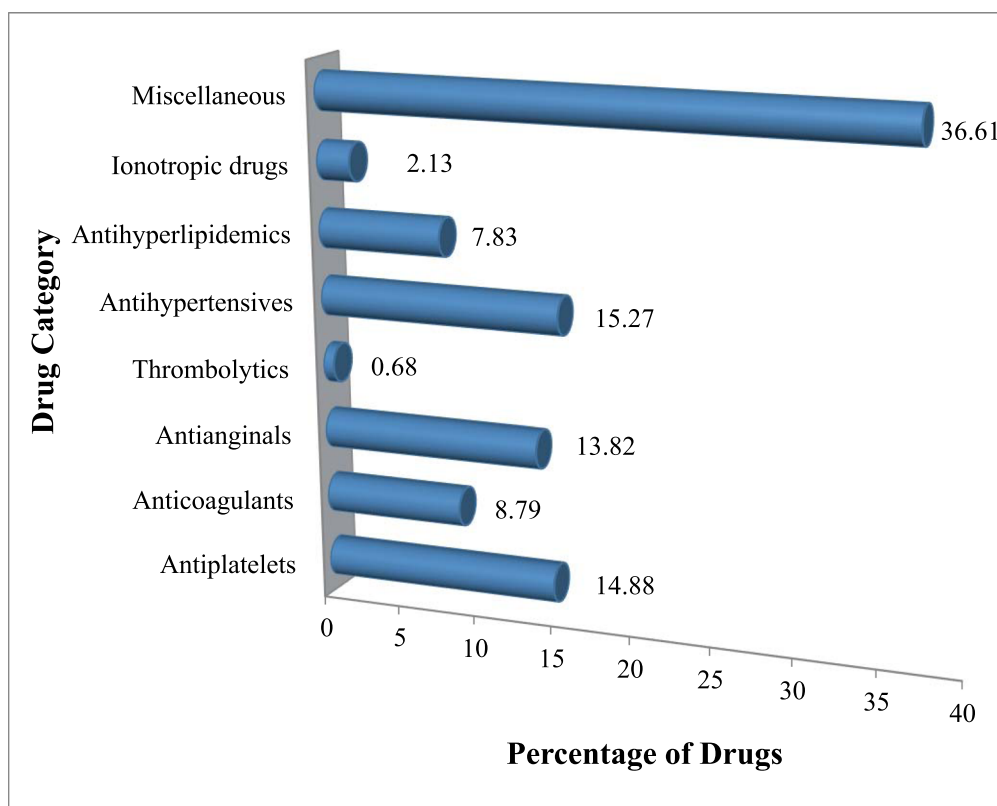


FIGURE 1 Prescribing pattern of drugs in CVD. CVD, cardiovascular diseases.

Anticoagulants	Dose	Frequency	No. of drugs (N = 91)	Percentage (%)
Heparin	2500–5000 IU	Q6H	85	93.41
Warfarin	2 mg	OD	5	5.49
Rivaroxaban	10 mg	OD	1	1.10

TABLE 1 Prescribing pattern of anticoagulants

TABLE 2 Dosage Regimen of Anticoagulant

Regimen	No. of patients (N = 88)	Percentage (%)
Monotherapy	8	9
Combinational therapy with antiplatelets	47	53
Triple therapy	33	38

this was in accordance with our study with Heparin (93.41%) as the major anticoagulant prescribed to the patients administered in the form of injection followed by Warfarin (5.49%) and lastly Rivaroxaban (1.10%) respectively both administered orally as shown in the table below (Table 1).

In our study, the anticoagulant dosage regimen prescribed to the patients was categorized into monotherapy, combinational therapy with antiplatelets, and triple therapy using dual antiplatelet therapy, the anticoagulant prescribing pattern was more in triple therapy (53%) and combinational therapy with antiplatelets (38%) which is more effective than a monotherapy (9%) in the initial and long term management of acute coronary syndrome (ACS) despite it may cause an increased risk of bleeding to the patients (Table 2).

Antiplatelets were generally prescribed to the patients, to reduce further clot formation and cardiovascular mortality in coronary artery disease. In our study, the antiplatelets prescribed to the patients were Aspirin (31.82%), Clopidogrel (12.99%) a combination of Aspirin and clopidogrel (26.62%) ticagrelor (25.97%), and prasugrel (2.60%) respectively. Aspirin was the commonly prescribed antiplatelet followed by a combination of aspirin Clopidogrel and Ticagrelor. This is in accordance with the study conducted by Thomas et al.¹²

Thrombolytics prescribed were Streptokinase (71.43%) and Tranexamic acid (28.57%). Streptokinase was the most commonly prescribed thrombolytic drug to the patients.

Antihypertensives are unavoidable in the prescriptions as hypertension is among the major comorbid condition in this study, various antihypertensive drugs prescribed to the patients includes diuretics (34.81%), beta-adrenergic blockers (31.65%), ACE inhibitors (12.66%), calcium channel blockers (9.49%), ARBs (6.96%), beta and alpha-adrenergic blockers (3.16%) and lastly, other cardiovascular agents (1.27%). In this study Diuretics and beta-adrenergic blockers were the two most commonly prescribed anti-hypertensives which shows a similar pattern in the studies conducted by Thomas et al.¹² and Narayanan et al.¹³ Diuretics prescribed to the patients were Furosemide (54.55%) and Spironolactone (45.45%). Beta-adrenergic blockers prescribed were Metoprolol (80%) and Bisoprolol (20%).

TABLE 3 WHO prescribing indicator

Prescribing indicator	Number
Total number of drugs prescribed	1035
Average number of drugs per prescription	11.7
Number of injections prescribed	267
Number of oral drugs prescribed	768
Number of drugs prescribed in generic name	215
Number of drugs prescribed in brand name	820

Abbreviation: WHO, world health organization.

ACE inhibitors prescribed were Ramipril (80%) and Enalapril (20%). The Angiotensin receptor blockers prescribed include Telmisartan (45.45%), Valsartan (18.18%), Losartan (18.18%) and Olmesartan (18.18%) respectively. Among other classes, calcium channel blockers prescribed to the patients were Amlodipine (60%), Nifedipine (26.67%), and Verapamil (13.33%). Carvedilol was the only mixed adrenergic blocker prescribed in the study.

Antihyperlipidemic drugs prescribed to the patients were Atorvastatin (76.54%) and Rosuvastatin (23.46%). Atorvastatin was the most commonly prescribed lipid-lowering drug which shows similar trends in the studies conducted by Nair et al., and Rakesh et al.,^{11,14}

The antianginals drugs prescribed to the patients include Nitrates (38.46%), Trimetazidine (37.06%), Nicorandil (13.99%), Ranolazine (2.80%), and Ivabradine (7.69%). The most commonly prescribed Nitrates were Isosorbide dinitrates and glyceryl trinitrates. In our study, the three most commonly prescribed antianginals drugs were Nitrates, Trimetazidine and Nicorandil. This shows similar trends in the studies conducted by Rakesh et al.¹⁴ and Thomas et al.¹² Lastly, Ionotropic agents prescribed to the patients include Dopamine (36.36%), Noradrenaline (22.73%), Adrenaline (4.55%), Digoxin (13.64%), Amiodarone (18.18%), and Atropine (4.55%) respectively. Dopamine and Noradrenaline were the two most commonly prescribed Ionotropic agents to the patients.

From the details of the prescriptions analyzed as per the WHO prescribing indicators the total number of drugs prescribed were 1035 and the average number of drugs per patient (prescription) was found to be 11.7 which was found to be higher in the present study, compared to other studies conducted by Narayanan et al., and Rakesh et al.,^{13,14} The number of injections prescribed was 267 and the number of oral drugs prescribed was 768. Similarly, the number of drugs prescribed in generic name versus brand name was found to be 215 versus 820. (Table 3).

TABLE 4 Adverse drug reactions in patients treated with anticoagulants

Drug	ADR/ADE	Naranjo's score	Casualty assessment
Heparin	Hematuria	3	Possible
Heparin	Gum bleeding	3	Possible

Out of the 88 cases, 188 potential drug-drug interactions were identified related to anticoagulants. Among which (19%) major, (67%) moderate, and (14%) minor. The most severe interaction was between Heparin-Ceftriaxone (15.43%) followed by Heparin-Warfarin (5.66%) and the least severe interaction was Warfarin-Ceftriaxone (0.53%). Heparin-Aspirin (25.53%) was the most frequently encountered interaction in our study. The most common interacting effects were the risk of bleeding.

Among the 88 prescriptions, two patients have been found with ADR associated with Heparin and were assessed using Naranjo's ADRs probability scale as shown in the table below (Table 4).

Inappropriate anticoagulant dosing increases the risk of developing significant bleeding and failing to produce a therapeutic effect. The incorporation of a clinical pharmacist can help check the rationality of high-alert medications and correct medication errors related to anticoagulation dosing.

4 | CONCLUSION

In this study, CAD was more frequent in males than in females among the age group of 40–60 years. The most common comorbid conditions are hypertension, diabetes mellitus, and dyslipidemia which is also been a major risk factor associated with CAD. The most commonly prescribed drug categories were antihypertensives, antiplatelets, antianginals, anticoagulants, and antihyperlipidemic among others. Among the anticoagulants prescribed, Heparin was found to be the most commonly used anticoagulant followed by warfarin and rivaroxaban respectively. Combination therapy of antiplatelets and antihypertensives was observed in most of the prescriptions which is more effective than a single therapy. Polypharmacy was encountered in the study with an average number of 11.7 drugs per prescription and only 31 prescriptions were having coagulation profile. Several potential anticoagulant-related drug interactions were identified and the effect was mostly related to an increased risk of bleeding. Two ADRs with Heparin were assessed spontaneously using the WHO casualty assessment scale. In conclusion, the coagulation profile should be checked in patients receiving anticoagulants at both the time of admission and discharge and the prescribing pattern can be improved by reducing the number of drugs prescribed to reduce economic burden and avoid further health complications in so doing improving the patient's quality of life.

AUTHOR CONTRIBUTIONS

Thangavel Mahalingam Vijayakumar: Conceptualization. Priyadharshini Ananthathandavan: Methodology; writing—review and editing. Basiru A. Zago: Data curation; writing—original draft.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data supporting the findings of this study are available with the corresponding author upon reasonable request.

ETHICAL STATEMENT

Data used in this article were collected after, the study was approved by the institutional ethics committee. In addition, participants' consent was obtained orally before collecting their data.

TRANSPARENCY STATEMENT

The lead author (Basiru Ahmad Zago) affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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REFERENCES

- Roth GA, Johnson C, Abajobir A, et al. Global, regional, and national burden of cardiovascular diseases for 10 causes, 1990 to 2015. *J Am Coll Cardiol*. 2017;70(1):1-25.
- Chauhan S, Aeri BT. Prevalence of cardiovascular disease in India and its economic impact—a review. *Int J Sci Res Publ*. 2013;3(10):1-5.
- Ansell J, Hirsh J, Hylek E, Jacobson A, Crowther M, Palareti G. Pharmacology and management of the vitamin K antagonists: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th edition). *Chest*. 2008;133:160S-198S.
- Di Nisio M, Middeldorp S, Buller HR. Direct thrombin inhibitors. *N Engl J Med*. 2005;353:1028-1040.
- Raj G, Kumar R, McKinney WP. Long-term oral anticoagulant therapy: update on indications, therapeutic ranges, and monitoring. *The American Journal of Medical Sciences*. 1994;307(2):128-1321994.
- Agno W, Gallus AS, Wittkowsky A, Crowther M, Hylek EM, Palareti G. Oral anticoagulant therapy: antithrombotic therapy and prevention of Thrombosis, 9th ed: American college of chest physicians Evidence-Based clinical practice guidelines. *Chest*. 2012;141:e44S-e488.
- Garcia DA, Baglin TP, Weitz JI, Samama MM. Parenteral anticoagulants: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012;141:e24S-e243.

8. Amaraneni, A, Tadi, P, Rettew, AC. "Anticoagulation Safety" [updated 2019 Sep 10]. *StatPearls [Internet]*. StatPearls Publishing; 2020.
9. Piazza G, Nguyen TN, Cios D, et al. Anticoagulation-associated adverse drug events. *Am J Med*. 2011;24(2):1136-1142.
10. Sam V, Shravya G, Mounika DS, et al. A prospective study on prescribing pattern of anticoagulants in cardiovascular disease. *Ijppr Human*. 2020;17(3):482-494.
11. Nair SS, Pooja P, Kumar CD, et al. A prospective observational study on prescribing pattern of myocardial infarction in a tertiary care hospital. *Asian J Pharm Health Sci*. 2019;9(3):2126-2131.
12. Thomas BR, TJ C, Sabu N, et al. Prescribing pattern of cardiovascular drugs—a prospective observational study. *Indian J Phar Pract*. 2017;10(4):287-292.
13. Narayanan S, Bhaskaran K, Vinod AP. A prospective study of prescription pattern in patients with coronary artery disease in a tertiary care centre. *Int J Recent Trends Sci Technol*. 2016;19(2): 272-277.
14. Rakesh B, Suresha BS, Himaj J, et al. Assessment of prescribing pattern in coronary artery disease. *Int J Allied Med Sci Clin Res*. 2016;4(4):698-715.

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