International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 32, Issue 11, November 2026 ijppr.humanjournals.com ISSN: 2349-7203

Drug Utilization Pattern of Anticoagulants among Inpatients of St. Philomena's Hospital

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Received: 15 September 2026 Revised: 30 September 2026 Accepted: 16 October 2026

ABSTRACT

PURPOSE: To study the drug utilization pattern of anticoagulants; to assess patterns of anticoagulant use and evaluate the rationality of prescriptions; to monitor and document anticoagulant-induced adverse drug reactions (ADRs); to identify drug–drug interactions; and to assess patients' adherence to anticoagulant therapy. **METHODS** A prospective, hospital-based observational study was carried out for six months at a tertiary care hospital in Bangalore. Inpatients of both genders and all age groups who received anticoagulants were recruited. The research student attended ward rounds daily and collected the cases that met the inclusion criteria**. : RESULTS:** During the six-month study period, 184 patients were enrolled from the inpatient wards of the hospital. Female patients outnumbered male patients (54.9% vs 45.1%), and most patients were aged 60–80 years. Anticoagulants were mainly prescribed in surgical cases, followed by cardiovascular disorders, and most patients received them as prophylaxis. Enoxaparin was the most commonly prescribed anticoagulant for both treatment and prophylaxis (80.61% of 196 prescriptions), and the parenteral route was used more widely than other routes. ADRs occurred in 13 patients (7.07%).**CONCLUSION:** Enoxaparin administered by the parenteral route was the most commonly used anticoagulant. Although the international normalized ratio (INR) and other parameters were not assessed in all patients, the choice of therapy was evidence-based or guided by expert opinion.

Keywords: Anticoagulant, Enoxaparin, Prophylaxis, Drug utilization

1. INTRODUCTION

A thrombus is a blood clot that forms within the circulatory system and stays attached to its site of formation, obstructing blood flow; it may develop when an artery, a vein or the surrounding tissue is damaged.[1] If a fragment breaks away and travels in the bloodstream, it is called an embolus, a dangerous and potentially fatal complication of thrombosis, particularly when it reaches the heart, lungs or brain.[1] Thrombosis is thus the formation of a clot within a blood vessel that disrupts the normal flow of blood through the circulation.[2]

1.1 Anticoagulants and Their Classification

Anticoagulants are drugs that interfere with the blood coagulation process. They inhibit thrombus formation and prevent clots from forming too readily, and are therefore often called blood thinners. They may be classified as follows:

1. Used in vivo

A. Parenteral anticoagulants

(i) Indirect thrombin inhibitors: Heparin, Low-molecular-weight heparins (LMWHs), Fondaparinux, Danaparoid

(ii) Direct thrombin inhibitors: Lepirudin, Bivalirudin, Argatroban

B. Oral anticoagulants

(i) Coumarin derivatives: Bishydroxycoumarin (dicumarol), Warfarin sodium, Acenocoumarol (Nicoumalone), Ethylbiscoum acetate

(ii) Indandione derivative: Phenindione.

(iii) Direct factor Xa inhibitors: Rivaroxaban

(iv) Oral direct thrombin inhibitors: Dabigatran etexilate

2. Used in vitro

A. Heparin: 150 U to prevent clotting of 100 mL blood.

B. Calcium complexing agents:

Sodium citrate: 1.65 g for 350 mL of blood (used to keep blood fluid for transfusion)

Sodium oxalate: 10 mg for 1 mL blood (used in blood taken for investigation)

Sodium edetate: 2 mg for 1 mL of blood (used in blood taken for investigation).[3]

1.2 Evaluation of Therapeutic Outcomes

Patients should be monitored for resolution of symptoms, recurrent thrombosis, post-thrombotic syndrome and treatment-related adverse effects.

Hemoglobin, hematocrit and blood pressure should be monitored closely to detect bleeding during anticoagulant therapy.

Baseline coagulation tests, namely activated partial thromboplastin time (aPTT), prothrombin time (PT) and international normalized ratio (INR), should be obtained before therapy begins to guide subsequent anticoagulation.

In outpatients taking warfarin, adherence, bleeding symptoms, thromboembolic complications and any change in concurrent medication should be reviewed at every visit.[4]

1.3 Review of Literature

Gitter et al. (1995) carried out a population-based study to estimate the incidence of, and risk factors for, hemorrhage and thromboembolism during long-term anticoagulant therapy. Malignancy and a history of peptic ulcer were significantly associated with major or minor hemorrhage, and malignancy was also significantly associated with thromboembolism.[5]

Toss et al. (1999) studied the influence of sex and smoking habits on anticoagulant activity during low-molecular-weight heparin treatment of unstable coronary artery disease in Sweden. Minor bleeding was more frequent in women than in men, and in non-smokers than in smokers.[6]

Lee (2007) studied the prevention of deep vein thrombosis (DVT) in cancer patients and reported that LMWHs and oral vitamin K antagonists are the anticoagulants most commonly used for primary prevention, although adherence to consensus guidelines is poor.[7]

Khalili et al. (2010) evaluated anticoagulant utilization in a teaching hospital in Iran. Of the patients, 55% received anticoagulants as DVT prophylaxis and 2.8% as therapy, and anticoagulants were ordered inappropriately in some cases.[8]

Nathisuwan et al. (2011) performed a systematic review and meta-analysis of the interaction between smoking and warfarin. Smoking was associated with a 12.13% increase in warfarin dose requirement, an additional 2.26 mg per week compared with non-smokers.[9]

1.4 Aim

The present study was undertaken to study the drug utilization pattern of anticoagulants among inpatients of a tertiary care hospital.

1.5 Objectives

The primary objectives were to assess the pattern of anticoagulant use and to evaluate the rationality of anticoagulant prescribing. The secondary objectives were to monitor and document adverse drug reactions (ADRs) induced by anticoagulants, to identify the drug–drug interactions most commonly associated with anticoagulants, and to assess medication adherence among patients with a past history of anticoagulant use.

2. MATERIALS AND METHODS

2.1 Study Materials

Patient case sheets, personal interviews with patients or their attendants, and personal interviews with resident doctors or consultants.

2.2 Study Design and Setting

A hospital-based, prospective observational study was carried out over six months at St. Philomena's Hospital, a tertiary care hospital in Bangalore.

2.3 Study Population and Eligibility Criteria

The study population comprised inpatients of both genders and all age groups who were receiving anticoagulants. Patients were enrolled on the basis of predefined inclusion and exclusion criteria: those of either gender and any age receiving an anticoagulant were included, whereas patients who were unwilling to participate and those with known bleeding disorders were excluded.

2.4 Data Collection

The research student attended ward rounds daily and recruited patients who fulfilled the inclusion criteria. Data were collected from patient case sheets and through direct interaction with patients, consultants and resident doctors. Prescribing patterns were checked against the medication charts, and the case sheets were analysed for drug-related problems.

3. RESULTS

3.1 Demographic Profile: Gender Distribution

A total of 184 patients who met the inclusion criteria were recruited from the inpatient wards of St. Philomena's Hospital. Of these, 83 (45.1%) were male and 101 (54.9%) were female (Figure 1).

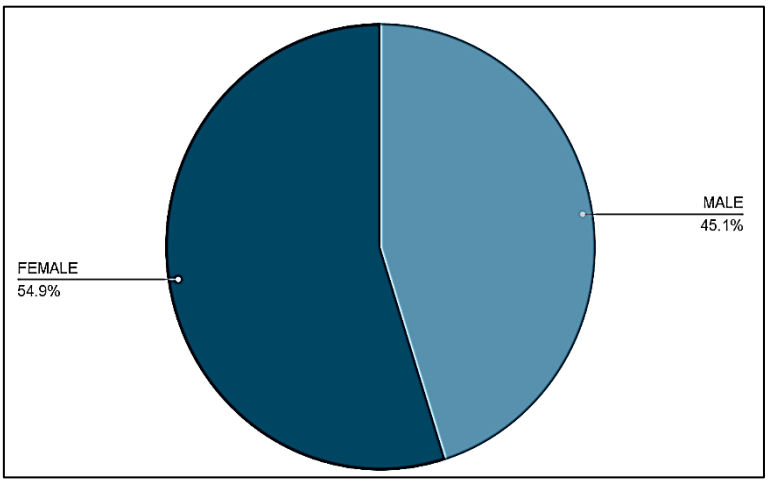


FIGURE 1. PERCENTAGE DISTRIBUTION OF PATIENTS BASED ON GENDER

International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 32, Issue 11, November 2026 ijppr.humanjournals.com ISSN: 2349-7203

3.2 Anticoagulants Prescribed

A total of 196 anticoagulant prescriptions were recorded for the 184 patients (some patients received more than one anticoagulant). Enoxaparin was the most frequently prescribed, accounting for 158 prescriptions (80.61%), followed by fondaparinux with 11 (5.61%). Rivaroxaban was the least prescribed, with 1 prescription (0.51%) (Table 1).

TABLE 1. DISTRIBUTION OF ANTICOAGULANTS PRESCRIBED

S. NO.	TYPE OF ANTICOAGULANT	NO. OF PRESCRIPTIONS	PERCENTAGE (%)
1	Heparin	5	2.55
2	Enoxaparin	158	80.61
3	Dalteparin	6	3.06
4	Dabigatran	5	2.55
5	Acenocoumarol	10	5.10
6	Fondaparinux	11	5.61
7	Rivaroxaban	1	0.51
Total		**196**	**100**

3.3 Prophylactic versus Therapeutic Use and Age Distribution

Of the 184 patients, 144 (78.3%) received anticoagulants prophylactically and 40 (21.7%) received them as treatment. In both the prophylactic and the treatment groups, the most common age group was 60–80 years (Figure 2).

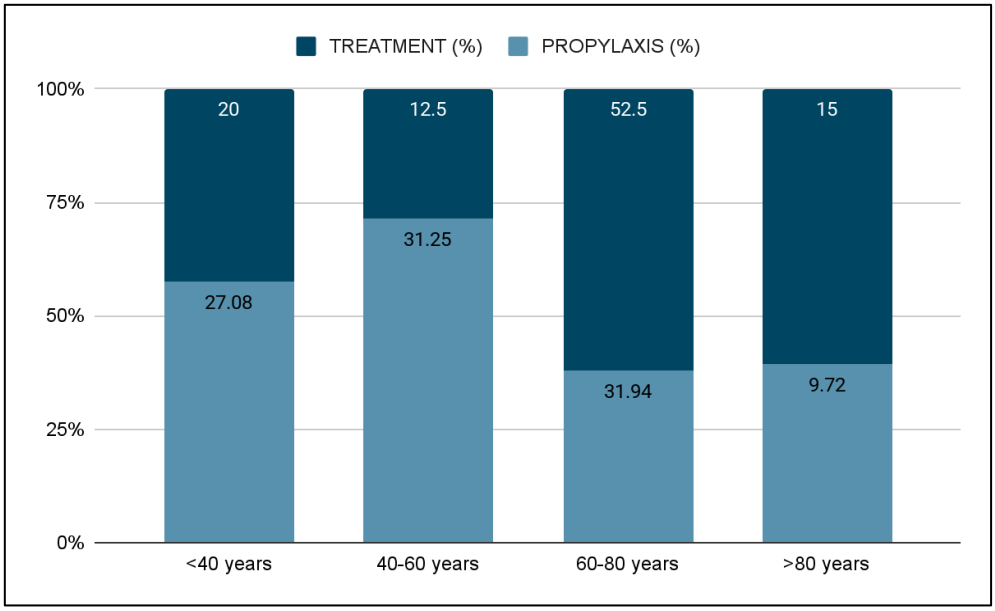


FIGURE 2. PERCENTAGE OF ANTICOAGULANT PRESCRIBED FOR DIFFERENT REASON AND AGE GROUPS

3.4 Reasons for Prophylactic Prescribing

Among the 144 patients who received prophylaxis, the most common reason was the post-operative state (73 patients; 50.69%), followed by other reasons (61 patients; 42.36%). Pre-operative prophylaxis was recorded in 7 patients (4.86%), and 3 patients (2.08%) received it for both pre- and post-operative purposes (Figure 3).

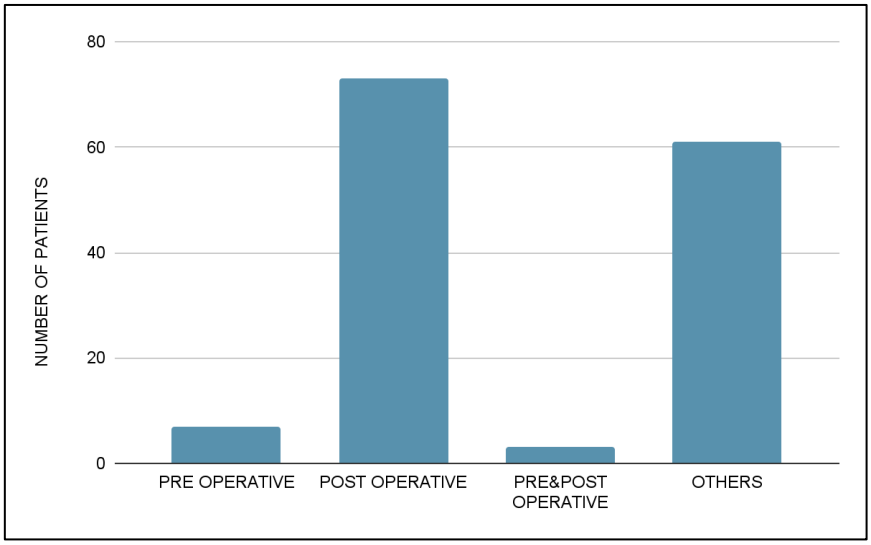


FIGURE 3. REASON FOR PROPHYLACTIC PRESCRIBING

3.5 Anticoagulant-Related Drug–Drug Interactions

Medication charts were screened for anticoagulant-related drug–drug interactions. Enoxaparin was the anticoagulant involved in all the interactions identified, with aspirin, acenocoumarol and fondaparinux as the interacting drugs (Table 2).

TABLE 2. DRUG–DRUG INTERACTIONS ASSOCIATED WITH ANTICOAGULANTS

DRUG	INTERACTING DRUG	CLINICAL EFFECT	FREQUENCY
Enoxaparin	Aspirin	Hemoptysis	1
Enoxaparin	Aspirin	Epistaxis	1
Enoxaparin	Acenocoumarol	Increased INR	2
Enoxaparin	Fondaparinux	Hypokalemia	1
Total			**5**

3.6 Adverse Drug Reactions

Of the 184 patients, 13 (7.07%) experienced ADRs attributable to anticoagulant therapy.

A total of 15 ADRs were observed in these 13 patients. The most common were erythematous rash over the body, hemoptysis and thrombocytopenia, each occurring twice (13.3%) (Table 3).

TABLE 3. ADVERSE DRUG REACTIONS (ADRs) OBSERVED

DRUG	ADVERSE EFFECTS	FREQUENCY	%
Enoxaparin	Bilateral subconjunctival hemorrhage	1	6.7
Enoxaparin	Bleeding	1	6.7
Acenocoumarol	Chronic cerebral microhemorrhage	1	6.7
Dabigatran	Decreased serum creatinine	1	6.7
Enoxaparin	Erythematous rash all over the body	2	13.3
Enoxaparin	Hematuria	1	6.7
Enoxaparin	Hemoptysis	2	13.3
Enoxaparin	Hemorrhagic infarct	1	6.7
Enoxaparin	Hyperkalemia	1	6.7
Acenocoumarol	Increased PT	1	6.7
Enoxaparin	Increased serum creatinine	1	6.7
Enoxaparin	Thrombocytopenia	2	13.3
Total		**15**	**100.0**

4. DISCUSSION

This prospective observational study evaluated the utilization of anticoagulants among 184 inpatients over six months. The major findings were that enoxaparin was by far the most commonly prescribed anticoagulant (158 of 196 prescriptions; 80.61%); that most patients (144; 78.3%) received anticoagulants as prophylaxis, mainly in the post-operative setting; and that patients aged 60–80 years formed the largest group in both the prophylaxis and treatment groups. ADRs occurred in 13 patients (7.07%), and five drug–drug interactions were identified, all of which involved enoxaparin.

Female patients (54.9%) outnumbered male patients (45.1%). This is similar to the findings of RC Anakwul et al.but differs from those of Khalili et al.[8] and Singh et al.[10], which may reflect differences in population characteristics or hospital admission trends.

The predominance of enoxaparin reflects a strong preference for LMWHs in the inpatient setting, probably because of their favorable pharmacokinetic profile, ease of dosing and reduced need for routine laboratory monitoring compared with unfractionated heparin or warfarin.

Prophylactic anticoagulation is widely used to reduce the risk of hospital-acquired DVT in medical and surgical patients, whereas therapeutic anticoagulation is the mainstay of treatment for thromboembolic disease. Among patients receiving prophylaxis, the most common indication was the post-operative state, followed by other conditions associated with immobility or an increased risk of venous thromboembolism (VTE). The predominance of prophylactic use is similar to the finding of Khalili et al.[8]

All the drug interactions identified involved enoxaparin, a pattern similar to that reported by Singh et al.[10] These results show the importance of vigilant monitoring, particularly in older patients who are often on multiple medications, and support the role of pharmacist intervention in minimizing drug-related problems.

Adverse drug reactions may occur with any anticoagulant, and the risk increases with advanced age, high comorbidity, impaired renal function and polypharmacy. In this study, 13 patients (7.07%) experienced 15 ADRs, which are known complications of anticoagulant therapy and can range from mild to life-threatening. Although the incidence was relatively low, ADRs can prolong hospital stay and increase healthcare costs.

The study is limited by its single-center design and short duration, and INR and other monitoring parameters were not assessed in all patients. Overall, the findings emphasize the crucial role of anticoagulants in the prevention and treatment of thromboembolic disorders in hospitalized patients.

5. CONCLUSION

During the six-month study period, 184 inpatients of St. Philomena's Hospital were enrolled in the study.

Female patients outnumbered male patients, and most patients were aged 60–80 years. Anticoagulants were mainly prescribed in surgical cases, followed by cardiovascular disorders, and most patients received them as prophylaxis.

Enoxaparin was the most commonly prescribed anticoagulant for both treatment and prophylaxis. Fifteen ADRs were observed in 13 patients; the most common were erythematous rash, hemoptysis and thrombocytopenia. Drug interactions were observed in five patients, and enoxaparin was the anticoagulant most prone to interact with other drugs.

In conclusion, enoxaparin administered by the parenteral route was the most commonly used anticoagulant. Although INR and other parameters were not assessed in all patients, the choice of therapy was evidence-based or guided by expert opinion.

ACKNOWLEDGMENT

The authors express their sincere gratitude to Dr. Vithya T, Professor and Head of the Department of Pharmacy Practice, Al Ameen College of Pharmacy, Bangalore, for her constant support, valuable inputs and motivation throughout the study. They also thank Al Ameen College of Pharmacy for its continued support.

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How to cite this article:
Vithya Thirumoorthi et al. Ijppr.Human, 2026; Vol. 32 (11):91-98.
Conflict of Interest Statement: All authors have nothing else to disclose.

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