# Evaluation of Practice of Prescribing and Monitoring Anticoagulants Among Hospitalized Iraqi Patients

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## Abstract

**Background:** Anticoagulant drugs are lifesaving agents that are prescribed for millions of patients annually. It is essential in the treatment of atrial fibrillation, acute myocardial infarction, as well as deep venous thrombosis. Inaccuracies of their use will lead to life-threatening complications such as bleeding. This study was designed to evaluate and explore the prescribing practice of anticoagulants in the internal medicine ward of Al-Sadr Medical City, Al-Najaf governorate, Iraq.

**Materials and Methods:** The present study is a prospective, survey-based, that was carried out in the wards of internal medicine at Al-Sadr Medical City, during the period from October/2020 to April/2021.

**Results:** 20% of the patients admitted to the ward, were treated with anticoagulants and the rate of their prescribing in respect to all medications administered by the patients was 13%, enoxaparin is being the most commonly prescribed anticoagulant (51%), then unfractionated heparin (40%) and least one was the oral anticoagulant warfarin (9%). Most cases used the anticoagulant drug as monotherapy (92%), and only 8% used combined anticoagulants. The dose range of enoxaparin was about (4000 IU - 6000 IU) and the most frequent dose of enoxaparin reached was (10000 IU), the dose of heparin was about (5000 IU) and for warfarin was 5mg per day. The monitoring of the anticoagulant agents' activity was found to be very rare (8%).

**Conclusion:** The most prescribed anticoagulant was the low molecular weight heparin, and the monitoring of anticoagulants was poor.

**Keywords:** heparin, enoxaparin, warfarin, monitoring, activity, anticoagulants

## Introduction

Throughout healthy homeostasis, the body keeps a steady balance between thrombosis and thrombolysis. This balance is sustained by a multifaceted collaboration between vascular endothelium, platelets, fibrinolytic system, and normal coagulation pathways [1-3]. The normal coagulation cascade (fig-1) encompasses an interface between the tissue factor (extrinsic pathway) and the contact activation mechanism (intrinsic pathway). These dual pathways apparently independent result to the transformation of "factor X" to active "factor Xa" that is the beginning of the common coagulation pathway. The latter pathway transforms prothrombin to active "thrombin", which is then catalyzes fibrin formation and constantly stabilize the aggregated platelets to form a final stable clot.

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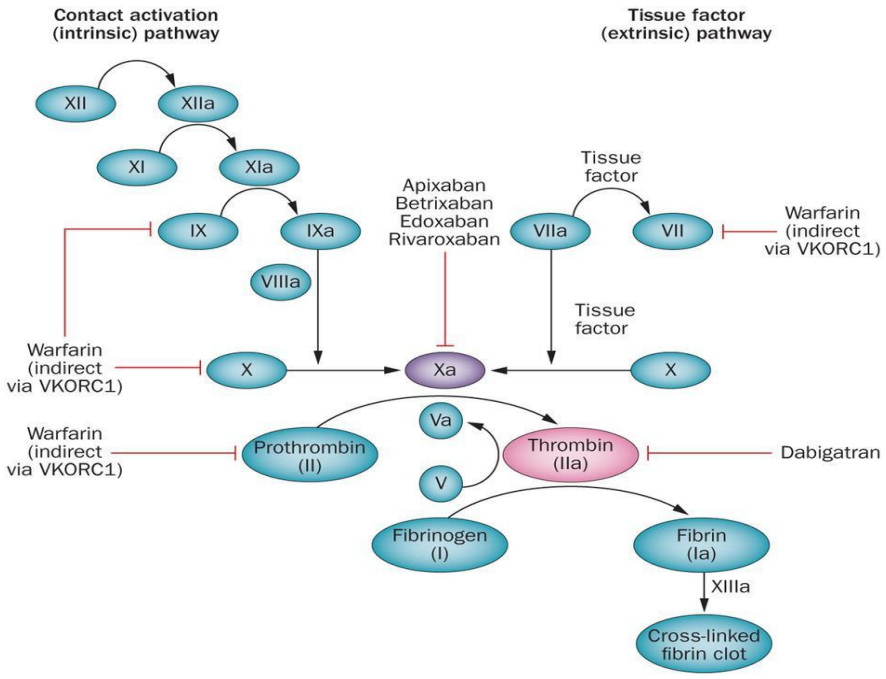


*Fig 1: Normal coagulation cascade (extrinsic and intrinsic pathways) (1)*

[4], and it has been predicted that over 65,000 subjects in U.S. EDs are treated for "warfarin-related hemorrhage. Owing to this bleeding, besides the "narrow therapeutic index" of warfarin and the requirement for repeated monitoring, it is essential to obtain more safe anticoagulant that requires no specific monitoring. Thus, many novel anticoagulant agents created, including direct thrombin inhibitors (dabigatran), factor Xa inhibitors (rivaroxaban, apixaban) and developed to target diverse steps of the coagulation mechanism (fig-1)[2, 5]. Warfarin act by blocking the "vitamin K-epoxide reductase", leading to prevent the synthesis of the "vitamin K-dependent" clotting factors [6, 7]. The recommendations for anticoagulant prescription of "Federal Drug Administration" advocate long-term anticoagulants after any thrombosis or for preventing thrombotic event in high-risk subjects, such as atrial fibrillation, postoperative conditions, and those with artificial cardiac valves [4]. The oral doses of warfarin normally range from 5-10mg/day, adjusted according on the "international normalized ratio (INR)", which is the common global monitoring-index deepened on prothrombin time. The cytochrome P450 system is the main metabolic pathway for [8]. Inhibition or induction of the isozymes that occurred with the metabolism of warfarin can possibly enhance the INR considerably. In addition to that, changes in oral vitamin K intake can develop significant variations in the INR (9). Alternatively, "unfractionated heparin (UFH)" can binds to and enhances the activity of antithrombin-III by causing conformational changes in factor Xa, which inhibit IIa/Xa in a ratio of 1:1 (10). As well, UFH causes some inhibitory effects on factors IXa, XIa, and XIIa [9].

## Materials and methods

### Study design

The present study was a prospective survey-based, carried out in Al-Sadr Medical City, in the internal medicine ward from October/2020 to April/2021.

### Patients

We collect the data for 60 patients taking anticoagulants depending on their records out of 303 total patients who are admitted to the hospital. Thirty-five of them were females and 25 were males. There was a lack of electronic documentation for the data in the hospital. The data were collected from the patient that is why the process takes time to collect these data manually based on the questionnaires, which included (patient personal history, past medical history, diagnosis, type of anticoagulant use, dose regimen, duration, monitoring parameters of prescribed anticoagulant).

### Statistical analysis

The research descriptive statistics mainly used the count and the percentage of anticoagulant use, anticoagulant prescription, and their combination in a pure descriptive statistic. The collected data were summarized and the result was calculated by Microsoft excel.

## Results

## Anticoagulant use and prescribing rate

Out of the total 303 admitted patients, around 20% were receiving anticoagulants (fig-2).

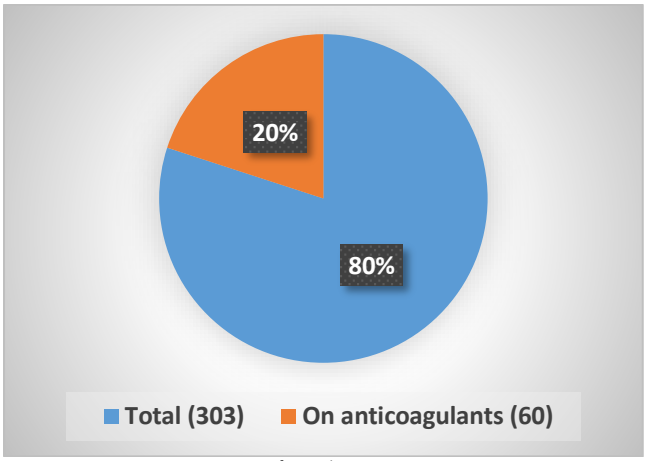


*Figure-2: Percent of those were receiving anticoagulants out of the total admitted patients (N-303)*

### Anticoagulant prescribing rate

Anticoagulants were prescribed in about a 13% ratio out of the total drugs prescribed to admitted patients (fig-3).

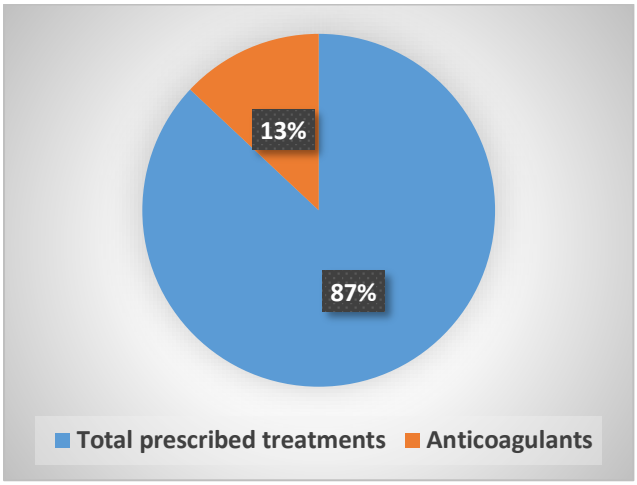


*Figure-3: Anticoagulant prescribing rate out of the total drugs prescribed to the admitted patients*

In general, females receive anticoagulants more than males, 58% of the anticoagulants were prescribed for female patients, while 42% were prescribed for males (fig-4).

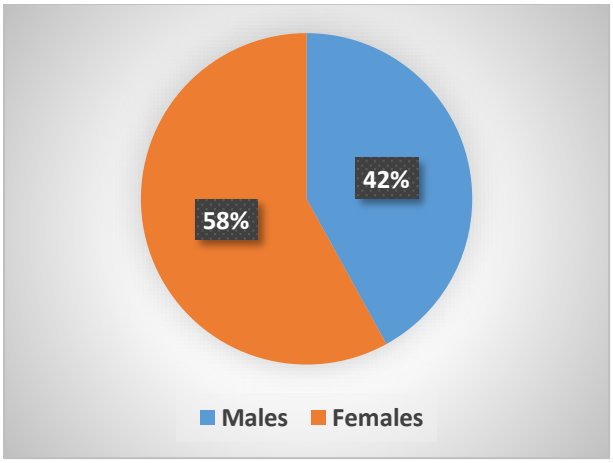


*Figure-4: Ratio of female to male receiving anticoagulants among the total included patients*

### Type of prescribed anticoagulants

Enoxaparin was the most prescribed anticoagulant (51%), heparin was the second one (40%), and warfarin was the least prescribed one (9%), (fig-5).

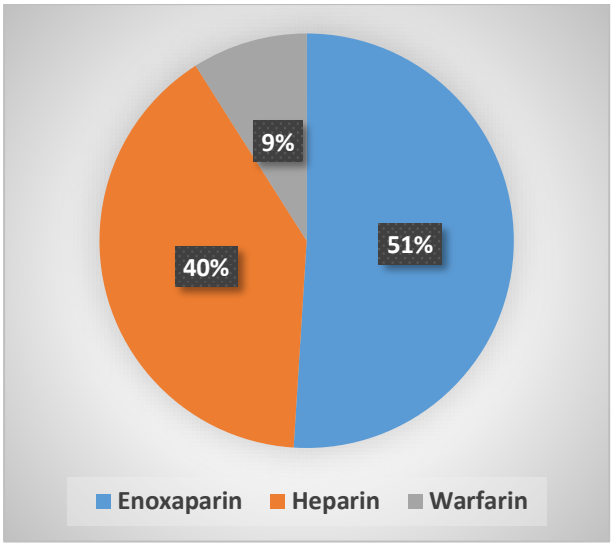


Figure-5: Type of prescribed anticoagulants among all admitted patients

### Combined therapy

Most cases were using monotherapy anticoagulants (92%), and only (8%) of the cases used combined anticoagulants (fig-6).

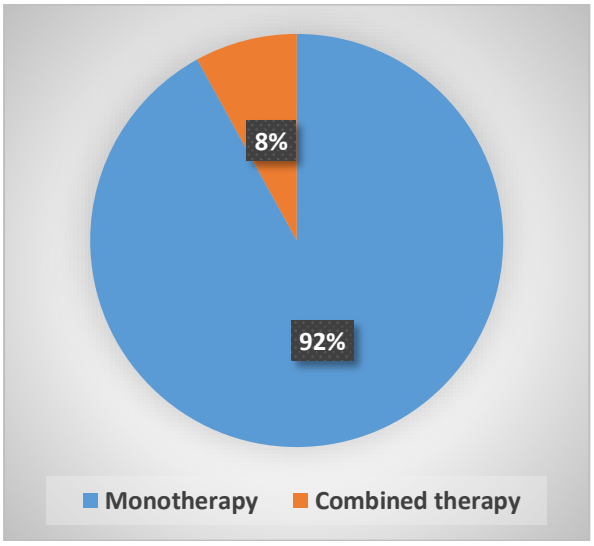


*Figure-6: Percent of using combined anticoagulants to monotherapy anticoagulant among admitted patients*

### Clinical diagnosis of patients underwent anticoagulant therapy

Out of the total, 35% were on anticoagulants for ischemic heart diseases, 21.6% for heart failure, and 13.3% as part of deep vein thrombosis management or cerebrovascular accidents (fig-7). The remaining were on anticoagulants for treatment of pulmonary embolism (6.7%) or atrial fibrillation and infections (5%).

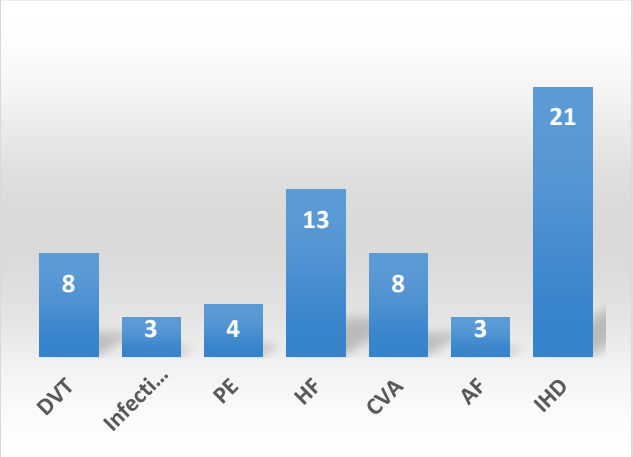


*Figure-7: Clinical diagnosis of the patients that were under anticoagulant therapy*

**Therapeutic indications of anticoagulants among the studied patients**

Out of the total, 45% (27) were on anticoagulants as primary prophylaxis. 32 (19) were on anticoagulants as treatment and 23% (14) as secondary prophylaxis (fig-8).

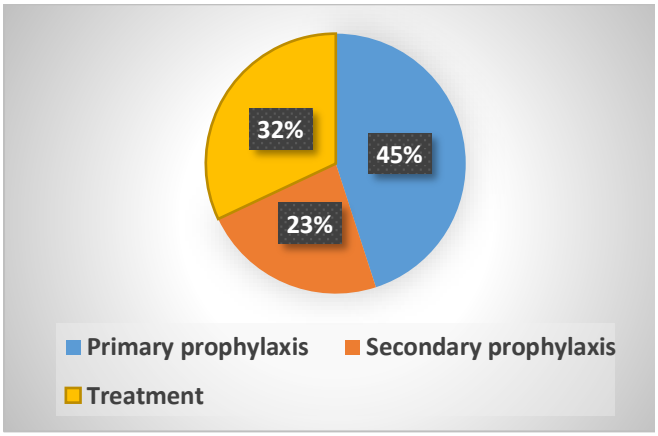


*Figure-8: Therapeutic indications of anticoagulants among the studied patients*

Figure-9 revealed the distribution of the patients according to the usage of the three main anticoagulant therapy based on their therapeutic indications among the included patients. 45%. were using anticoagulants as primary prophylaxis, and the remaining 55% were using them either as treatment or secondary prophylaxis (21 and 17), respectively.

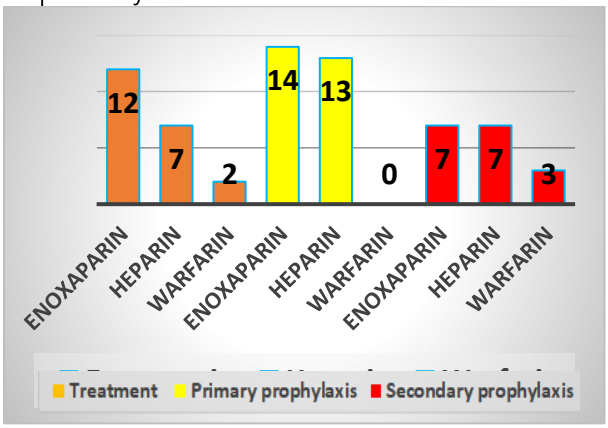


*Figure-9: Usage of the three main anticoagulant therapy according to their therapeutic indications among the included patients*

## Monitoring of the therapy

In about 92% of the patients (fig-10), there was poor monitoring of the activity of anticoagulant agents, this can subsidize further complications.

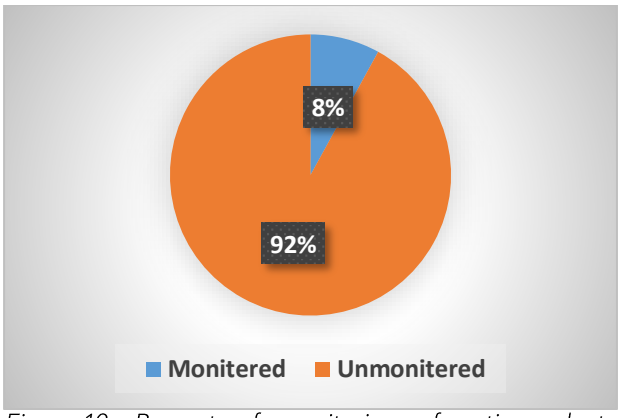


*Figure-10: Percent of monitoring of anticoagulant therapy among included patients*

Figure-11 revealed the total daily administered dose of Enoxaparin/IU and Heparin/IU for the admitted patients.

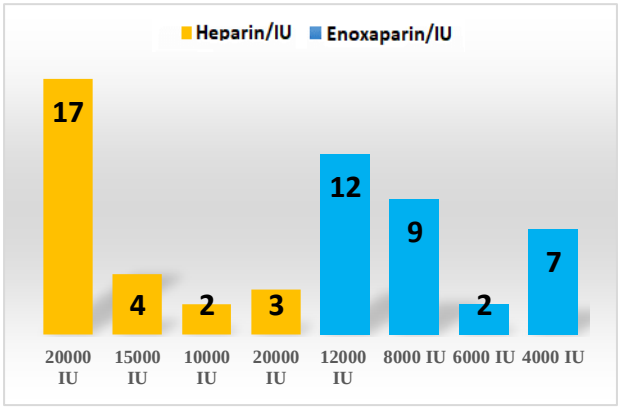


*Figure-11: Total daily administered dose of Enoxaparin/IU and Heparin for the admitted patients*

## Discussion

To the best of our knowledge, we did not find any previous research concerning anticoagulant prescribing practice in our Iraqi situation. Anticoagulants are life-saving drugs that are prescribed to many patients annually, they are very important in the treatment of deep venous thrombosis [10] , acute myocardial infarction [6, 11-13], and atrial fibrillation [14]. Mistakes of their use lead to life-threatening complications like hemorrhage that is why the objective of the current study is to estimate how anticoagulants are practically prescribed, to which patients are usually prescribed, which dose is used, and how it is monitored [9]. We found that about 20% of the patients admitted to the medical ward are treated

with anticoagulants and the prescribing rate of anticoagulant among all medications taken by the patient is 13%, with the low molecular weight heparin (enoxaparin) is being the most prescribed anticoagulant (51%), followed by heparin (40%) and to a lesser extent the oral anticoagulant warfarin (9%). These findings explain the fact which states that low molecular weight heparins are usually preferred because they have a and are effective [15]. The standard prophylactic regimen does not require anticoagulant monitoring [16, 17]. The low molecular weight heparins duration of action is longer than that of heparin (unfractionated) and subcutaneous administration once-daily is possible for some indications, rendering them convenient to use [18]. While warfarin less commonly used has many restrictions due to dosing is variable and its slow onset of action, because its activity is affected by dietary intake of vitamin K and the requirement for frequent and specific monitoring and inherent variability in response with time, the ability for changing the INR potential for causing mistakes in laboratory test values [19].

Most cases use anticoagulants as monotherapy (92%), and only 8% of the cases use a combination. The most frequent dose of enoxaparin reached (10000 IU) and the dose range was about (4000-6000IU). While for heparin the dose was about 5000 IU and for warfarin was 5mg. Anticoagulants are characterized by heterogeneous mechanisms of action and are also different in their effect on coagulation assays [20]. Therefore; an array of assays is required to monitor the activity of anticoagulant drugs which we obtained to be very rare (8%). Such an absence of monitoring can lead to further complications. We observed that in some cases, there is a lack of monitoring even for the critical cases, like patients that take warfarin. Meanwhile, monitoring was observed for less critical cases, such as patients receiving enoxaparin.

Studies have shown that when initiating therapy with warfarin, physicians should leave loading dosages that may increase the INR very high [21]. As a substitute, warfarin must be started with initial dose of 5mg, and in very elderly started with 2-4mg dose, not increase in the initial 24hours, unless in sporadic cases who will continually need quiet small doses (0.5-2.0mg) per day [22]. The adjustment of warfarin dose at a steady-state deepened on the clinical factors and calculated INR measures. The dosage does not require adjustment for a specific INR that is marginally out of range. As well, modifications should adjust the weekly entire dose by 5-20% [23]. The INR requires a frequent monitoring (e. g., 2-4 times/weekly) directly after beginning of warfarin; the intervals between INR measures subsequently, can be extended step by step (reaching to 4-6 weeks) in cases sustained stable INR readings. cases who have a raised INR tests will necessitate more frequent analysis as well as vitamin K1 supplement [8].

A prior study in Paris revealed that anticoagulant, low molecular weight heparin was used routinely [24]. This study obtained that low molecular weight heparin was prescribed incorrectly to13% of the patients and in only 26.8% of the patients who are given low molecular weight heparin were fully compliant with all criteria of proper therapeutic use (treatment duration, indications, patient's age, monitoring and renal creatinine clearance).

The findings of the present study were comparable with the outcomes of the reports of the "Public Health Insurance System" in France, which revealed an over-all rate of incorrect anticoagulants prescribing of 47.4% at 1999 [24].

## Conclusions

In the internal medicine ward, the anticoagulant prescription is 13% of the total drugs prescribed to patients, and 20% of the patients admitted were receiving anticoagulants. In general, females receive anticoagulants more than males, 58% of the anticoagulants are prescribed for female patients, while 42% are prescribed for male Enoxaparin is the most prescribed one (51%), heparin is the second one (40%), and warfarin is the least prescribed one (9%). Most cases use anticoagulants as monotherapy (92%), and only (8%) of the cases use a combination. There is a lack of monitoring of the activity of anticoagulant agents and this can lead to further complications.

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