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International Normalized Ratio Control in a Warfarin Anticoagulation Clinic: A Cross-Sectional Study

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ABSTRACT

Background: Warfarin is an effective anticoagulant with a narrow therapeutic index. It requires frequent, careful dose adjustment and patient monitoring. This study assesses the International Normalized Ratio (INR) control among patients attending pharmacists-led anticoagulation clinics (ACCs).

Methods: An observational cross-sectional study was conducted in ACCs from January to April 2022. INR control was assessed by calculating the proportion of the patient's time in the therapeutic range (TTR) for the previous three months using the traditional method. The patient's warfarin knowledge level was assessed using a patient knowledge questionnaire. Spearman correlation analysis investigated the association between questionnaire scores and the demographics.

Results: Out of 211 approached patients, 200 patients were included (response rate 94.8%). TTR for all the patients was 68.7%. Out of 200, 113 (56.5%) patients had their INR within therapeutic range. Most patients (n=180, 90%) reported adherence to warfarin. Despite a relatively high mean patient knowledge score (76.1%), one-quarter of patients had poor TTR (TTR < 60%). A weak correlation existed between patients' knowledge scores and older age (Rs=-0.203, p= 0.004). No significant correlation was observed between patient knowledge scores and other factors (gender or current INR). In multivariable logistic regression, patients having a higher INR showed a 36% increase in the odds of poor TTR (OR = 1.36, 95% CI [0.71, 2.61]).

Conclusions: Most patients attending ACCs had within normal TTR and acceptable medication knowledge. Older patients had lower knowledge scores. More attention and close monitoring should be given to older patients and those with poor TTR.

Keywords: Anticoagulation Clinics, International Normalized Ratio Control, Patient Knowledge, Time in Therapeutic Range, Warfarin Adherence.

Introduction

Warfarin is a vitamin K antagonist that has historically been the most commonly used oral anticoagulant worldwide, even with the availability of new direct oral anticoagulants (NOACs). Warfarin is prescribed for various indications as it has efficacy to prevent and reduce the thromboembolic events in patients with high risk of thromboembolism, such as those with deep vein thrombosis (DVT), pulmonary embolism (PE), atrial fibrillation (AF), heart valve replacement, recurrent myocardial infarction (MI), especially among AF patients after stroke (1, 2). Warfarin is a drug with a narrow therapeutic index. Warfarin dose must be defined for each patient according to the condition being treated, the target International Normalized Ratio (INR) and laboratory readings for the patient's INR (3). Warfarin has a delayed onset of action, complex dosing with genetic variances, potential drug-food and or herbal interactions, and the needs for routine monitoring of INR along with patient dosage adjustment. Moreover, warfarin has a high chance of causing adverse effects such as bleeding, hemorrhagic stroke, and even death (4). However, warfarin will remain the exclusive anticoagulant choice for many patients with prosthetic heart valves (5). Warfarin has a long half-life of about 40 hours, which gives superiority for many patients who miss or skip doses compared with NOACs. Moreover, frequent coagulation monitoring and patient education will allow early detection of nonadherent patients. Further, warfarin has been used for more than 70 years, and experts have enough experience in the long-term safety and efficacy profile compared to NOACs (6,7).

The dose-response relation of warfarin is highly variable between patients and depends on multiple factors such as genetics, drug metabolism, the amount of vitamin K in diet, comorbidities, protein binding, drug-drug interactions, and patient adherence (8). Some patients uncommonly hit consistent INR readings, whereas many patients find difficulties to reach target INR and need continuous warfarin dose adjustment (9). Therefore, healthcare providers and anticoagulant clinics (ACCs) should recognize the importance of counselling and patient education to guarantee safe and effective treatment with warfarin so that patients can reach their target INR

smoothly. A retrospective study assessed the anticoagulation services offered to patients by a pharmacist during hospitalization. This study highlighted the crucial role of pharmacists in improving the compliance, efficacy, and safety of warfarin and increasing the time within the target INR range (10). A systematic review indicated a positive association between pharmaceutical care, target INR control, patient education and warfarin adherence (11).

This study aims to assess INR control among patients attending pharmacists-led ACC. The specific objectives of this study were to determine patients' current INR values, measure their time in the therapeutic range (TTR) for the previous three months, evaluate patients' knowledge regarding warfarin use, and identify the major factors contributing to sub-therapeutic or supra-therapeutic INR range. We also sought to define patients' comorbidities, warfarin indications, concurrent medications, supplements, or herbs taken among warfarin users, in addition to assessing patients' warfarin adherence.

Methods

Study Design and Setting

A descriptive cross-sectional study was conducted over three months from January to April, 2022, with patients receiving warfarin therapy at the ACCs in Queen Alia Heart Institution (QAHI) and Royal Medical Services (RMS), in Amman, Jordan. QAHI is a center that is responsible for the treatment of patients with cardiac diseases. The first ACC was established in this center in 2013 and is managed by clinical pharmacists and dietitians. ACCs are considered the only referral ACCs in RMS. The ACCs accept patient referrals from RMS hospitals from all over the country. The ACCs run two days a week (Monday and Tuesday) with an average of 25-30 patients per clinic day. Before the initiation of warfarin therapy, a clinical pharmacist creates a new medical record for new patient in the computer system to set the initial dose and desired INR, which is ordered by a specialist. The pharmacist then gives a 30-minute verbal education session alongside a dietitian. In addition, a clinical pharmacist also provides patients or caregivers with an educational booklet in Arabic. In general, appointments are determined according to INR values, and more frequent appointments are given to patients who need close monitoring.

Prothrombin time (PT) and partial thromboplastin time (PTT) measurements were done in the QAHI laboratory using an STA Compact Max® 2 analyzer from Stago. INR values were measured during each patient's visit. According to the INR value, a clinical pharmacist manages the warfarin dose. The ACC's protocol for dosage adjustment for a target therapeutic INR of either 2-3 or 2.5-3.5 is prepared through consensus between specialists and clinical pharmacists and approved by the higher medical committee of RMS. According to the anticoagulation protocol, the target range of INR at the time of the study was 2.5-3.5 for heart valve replacement patients and 2–3 for other indications. However, there was a specific target INR range for some patients, depending on their risk factors and indication.

TTR is a reflection of the overall quality and adequacy of anticoagulation with warfarin in clinical trials and is commonly calculated by three methods. The first is the traditional method, the second is the cross-sectional method, and the third is the Rosendaal method (12). In this study, the traditional method was used to measure TTR in the last three months, by which the number of within-range INR values is divided by the total number of INR values. This method was selected because the study was based on routinely collected retrospective clinical data, with a limited number of INR measurements available over the study period. Under these circumstances, the traditional method provides a simple and practical measure of anticoagulation control in retrospective studies.

In practical experience, TTR is expected to be lower than in a clinical research setting. Therefore, in this study, TTR ≥ 60% was defined as good TTR to achieve better outcomes, such as reduced rates of stroke, major bleeding events, and death. TTR < 60% was defined as poor TTR (13).

Sample size calculation

Using the clinic's historical data, it was estimated that 372 patients on warfarin therapy visited the chosen ACCs. The sample size was calculated as 190 participants (at a 95% confidence level with a 5% margin of error) by using Openepi.com (https://www.openepi.com). The target sample size was increased to 200 participants.

Study procedure

Over three months (from January to April, 2022), all patients who visited the clinic for follow-up and met the inclusion criteria were asked to participate in the study. The inclusion criteria were patient age of 18 years and above, taking warfarin for more than 3 months, and having three INR values available from the last three months. The exclusion criteria were pregnant and lactating women, glomerular filtration rate (GFR) < 30 ml/min, liver cirrhosis, patients who were disoriented or not cooperative, and difficulties with communication. Patients who consented to participate in the study were invited to a face-to-face interview involving questions related to demographic information and other patient-related details. In addition, the participants filled out a patient knowledge questionnaire. The questionnaire underwent expert review by Professor in clinical pharmacy and pharmacy practice to assess its content and face validity before data collection. The questionnaire was reviewed by a clinical pharmacist and a dietitian at the ACC. Furthermore, pilot study representing 5% of the target sample was done to ensure accuracy; ten patients were asked to fill the questionnaire during interview and to give feedback or comment if there were any unclear questions or if the order of questions was confused. The data of the pilot were excluded from the final analysis. The interview took 10-15 minutes.

Data collection instrument

The first part of the questionnaire included demographic information, adherence, concomitant over-the-counter medication, supplements, and any type of herbal product used. Clinically relevant information was obtained from the patients and their electronic health record. The second part included the patient knowledge questionnaire. The questionnaire was constructed in Arabic and contained 17 questions, which were based on the contents of the warfarin education booklet and related literature (14, 15). Three questions (questions 11, 16, and 17) were excluded from scores as they were considered part of the patients' information. All 14 other questions had the same three answer options: "true," "false," and "I do not know." The patient had to select one option. Each correct answer was scored as 1. Scores of 0-5 indicated a low level of knowledge, 6-10 indicated an interme-

mediate level of knowledge, and 11-14 indicated a high level of knowledge [see supplemental material].

Ethics approval and consent to participate

An informed consent form for participation in the study was read, approved, and signed by all eligible patients.

Statistical analysis

Data were analyzed using IBM Statistical Package for Social Sciences (IBM SPSS®23 software). Categorical variables were expressed as frequencies and percentages, while continuous variables were expressed as the mean ± standard deviation (SD). Spearman correlation analysis was used to assess the correlation between the score on the patient-knowledge questionnaire and the independent variables (gender, age, and current INR). Furthermore, multivariable logistic analysis regression was conducted to evaluate independent variables of anticoagulation stability. The dependent variable was poor TTR (TTR < 60.00%) and the independent variable were (age, gender, controlled INR, comorbidities and herbal use). A P value <0.05 was considered significant.

Results

A total of 274 patients visited the AACs in QAHI during the study period, but 63 patients were excluded because they were treated with warfarin for less than three months. Out of 211 patients who met the inclusion criteria, 11 patients were not enrolled in the study for different reasons. Five patients were referred to the emergency department due to either high INR (higher than 5.50) or low INR (lower than 1.70) among patients who underwent mitral heart valve replacement. Furthermore, two patients had operations and were prepared for admission, two patients were instructed to stop taking warfarin after reversion of sinus rhythm (cardioversion procedure), and two patients refused to as they did not have time. Ultimately, the response rate of the questionnaire was 94.80%.

The mean age of patients was 56±14.85 years, and 111 (55.50%) patients were males. About 75.00% of patients had concurrent comorbidities, of which the most common was coronary artery disease. Forty-two (21.00%) patients were current smokers (**Table 1**).

Table 1. Demographic and clinical characteristics of participating patients using warfarin (N=200)

Patient Characteristics	N (%)
Age in years (mean=55.60 years; SD =14.86 years)	
18-39	32 (16.00)
40-60	83 (41.50)
61-74	66 (33.00)
≥ 75	19 (9.50)
Gender	
Male	111 (55.50)
Female	89 (44.50)
Residence (City)	
Amman	132 (66.00)
Others [a]	68 (34.00)
Indication	
Atrial fibrillation	76 (38.00)
Mechanical Mitral Heart Valve	51 (25.50)
Mechanical Aortic Heart Valve	32 (16.00)
Mechanical Aortic and Mitral Heart Valve	5 (2.50)
Mechanical Mitral Heart Valve + Atrial fibrillation	5 (2.50)
DVT + recurrent DVT	12 (6.00)
PE	3 (1.50)
PE + DVT, Recurrent DVT + PE	8 (4.00)
Others [b]	8 (4.00)

Table 1, Cont. Demographic and clinical characteristics of participating patients using warfarin (N=200)

Patient Characteristics	N (%)
INR goal	
2.0–3.0	125 (62.50)
2.5–3.5	73 (36.50)
2-2.5	1 (0.50)
2.5-3	1 (0.50)
Smoking Status	
Non-smoker	158 (79.00)
Smoker (cigarettes)	38 (19.00)
Smoker (hookah)	4 (2.00)
Herbal use [c]	
Yes	98 (49.00)
No	102 (51.00)
Insurance	
Military	115 (57.50)
Others [d]	85 (42.50)

[a] Zarqa, Salt, Jarash, Irbid, Ajloun, Madaba Fuheis, Mahis, Karak.

[b] Cardiac device thromboembolism, apical clot, Senning procedure, portal vein thrombosis, ectatic coronaries, Marfan syndrome and Bentall procedure.

[c] These herbs included: anise, artemisia, chamomile, cumin, germanders, sage, thyme, green tea, mint, rosemary, cinnamon, cardamom, purslane, malva and clove.

[d] Ministry of Health, Royal Court exemptions, Yarmouk University, Prime Minister Office.

At the time of the clinic visit, it was found that the lowest INR reading was 1.19, the highest was 5.50, and 113 patients (56.50%) had an INR within the therapeutic range. There were 87 patients (43.50%) with an INR that was out of range, of which 44.80% were aged 40-60 years. TTR was calculated for the last three months for all patients. A total of 600 INR values were recorded, and 412 INRs were in the therapeutic range (68.70%). The greatest TTR percentage was 74% for the last month. Moreover, 150 patients (75.00%) had good TTR (≥60.00%) while 50 patients (25.00%) had poor TTR (<60.00%). The characteristics of patients who had poor TTR included male gender (56%) and age of 40-60 years (56.00%). Moreover, about half (48.00%) of patients with poor TTR were receiving warfarin because they underwent mechanical valve replacement.

Warfarin weekly dose for all targets ranged from 8.75 to 125 mg. The majority of patients (n=170, 85.00%) took warfarin in the evening. Of these, 57.60% of patients had INR within the therapeutic range. Among the 30 patients (15.00%) who took warfarin in the morning, 46.60% had INR within the therapeutic range. Most patients (n=180, 90.00%) reported that they were adherent to their medication. The assessment of adherence in the present study indicated that 11 patients (6.10%) depended on an alarm on their phones or a home pill organizer to take their doses. There were 20 patients (10.00%) who reported that they had missed one or more warfarin doses during the last week (**Table 2**). It was found that 28.70% (25 out of 87 patients) took different doses on different days of the week. For example, a patient may take 2.50 mg alternating with 5 mg or 5 mg alternating with 7.50 mg, and more than half of the patients in the study (53.00%) needed dose adjustment.

Table 2. Clinical data of participating patients (N=200).

Parameter	N (%)
Indication	
Mechanical heart valve replacements	88 (44)
Male	53 (60.20)
Female	35 (39.80)
Atrial fibrillation	76 (38.00)
Male	39 (51.30)
Female	37 (48.70)

Table 2, Cont. Clinical data of participating patients (N=200).

Parameter	N (%)
DVT, recurrent DVT, PE, (PE+DVT), Recurrent (DVT+PE)	23 (11.50)
Atrial fibrillation + Mechanical Mitral Heart Valve	5 (2.50)
Others [a]	8 (4.00)
INR tests	
INR tests within therapeutic range at the time of clinic visit	113 (56.50)
Male	62/113 (54.90)
Female	51/113 (45.10)
Sub-therapeutic INR at the time of clinic visit	46 (23.00)
Male	29/46 (63.00)
Female	17/46 (37.00)
Supra-therapeutic INR at the time of clinic visit	41 (20.50)
Male	20/41 (48.80)
Female	21/41 (51.20)
INR tests within the therapeutic range for INR target of 2-3	73 / 127 patients (57.50)
INR tests within the therapeutic range for INR target of 2.5-3.5	40 / 73 patients (54.80)
INR Mean ± SD	2.70 ± 0.80
Time of administration	
Morning	30 (15.00%)
Evening	170 (85.00%)
Adherence	
No missed doses	180 (90.00%)
One or more missed doses	20 (10.00%)
Average and range of doses (Mg/week)	
Average for current warfarin dose	37
Average warfarin dose for INR 2-3	35.60
Average warfarin dose for INR 2.5-3.5	39.10
Dose range for 2-3 target INR	8.75-87.50
Dose range for 2.5-3.5 target INR	17.50-125.00
TTR for the three most recent INR readings	412/600 (68.70%)
TTR ≥60 %	150 (75.00)
TTR < 60 %	50 (25.00)

[a] Cardiac device thromboembolism, apical clot, Senning procedure, portal vein thrombosis, ectatic coronaries, Marfan syndrome and the Bentall procedure.

Several possible causes that interfere with INR control in patients out-of-INR range could be concluded upon reviewing patient data. In 53.00% of patients, no possible causes were found, 13.80% reported missed doses, and 10.30% reported low vitamin K intake (**Figure 1**). The respondents used about 86 medications that may interact with warfarin (**Figure 2**), including amiodarone. One patient had just started taking amiodarone, and her INR reached 5.50. For another patient, reducing the dose of amiodarone led to an INR of 1.19. These medications have interactions with warfarin, and patients who need to start therapy with one of these drugs require close monitoring.

About half of the patients used herbal products, and the herbs were consumed either as soaked or added as flavor to drinks, few patients used fresh garlic cloves or capsules in the morning. Herbs included anise, artemisia, chamomile, cumin, germander, hibiscus, sage, thyme, green tea, mint, rosemary, cinnamon, cardamom, and

clove. Moreover, one patient had an INR of 4.40 as a result of drinking cinnamon tea for 4 days consecutively, while another patient had an INR of 3.70 due to taking cinnamon frequently during a week, leading to sudden fluctuations in INR. Although some herbs may interact with warfarin, the evidence for these interactions varies depending on the specific herbal product, and the clinical significance of these interactions depends on the specific herb and available evidence.

Two hundred patients completed the 14-item patient knowledge questionnaire, and the mean percentage of correct answers was 76.10%. The mean score for the patient knowledge questionnaire was 10.65 ± 2.08 with a range of 4 -14 points. All patients were able to answer two questions correctly (questions 2 and 10). Patients scored the lowest on question 13, for which the rate of correct answers was 25.00%, as well as question 9, for which the rate of correct answers was 27.00%. There was a significant but weak inverse correlation be-

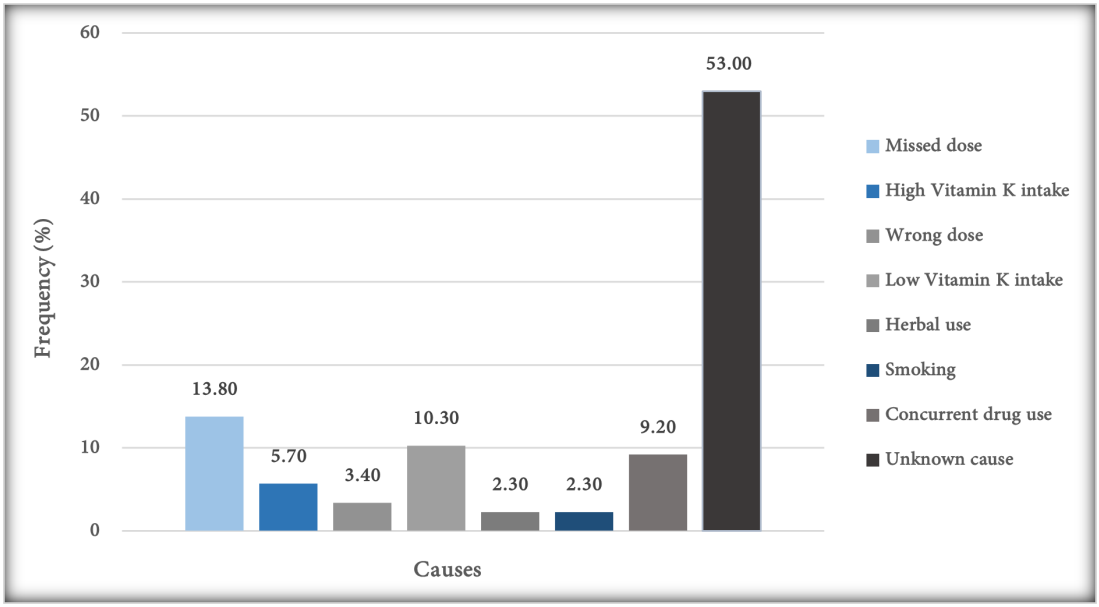

Figure 1. Possible causes that interfere with INR control among patients with out-of-range INR.

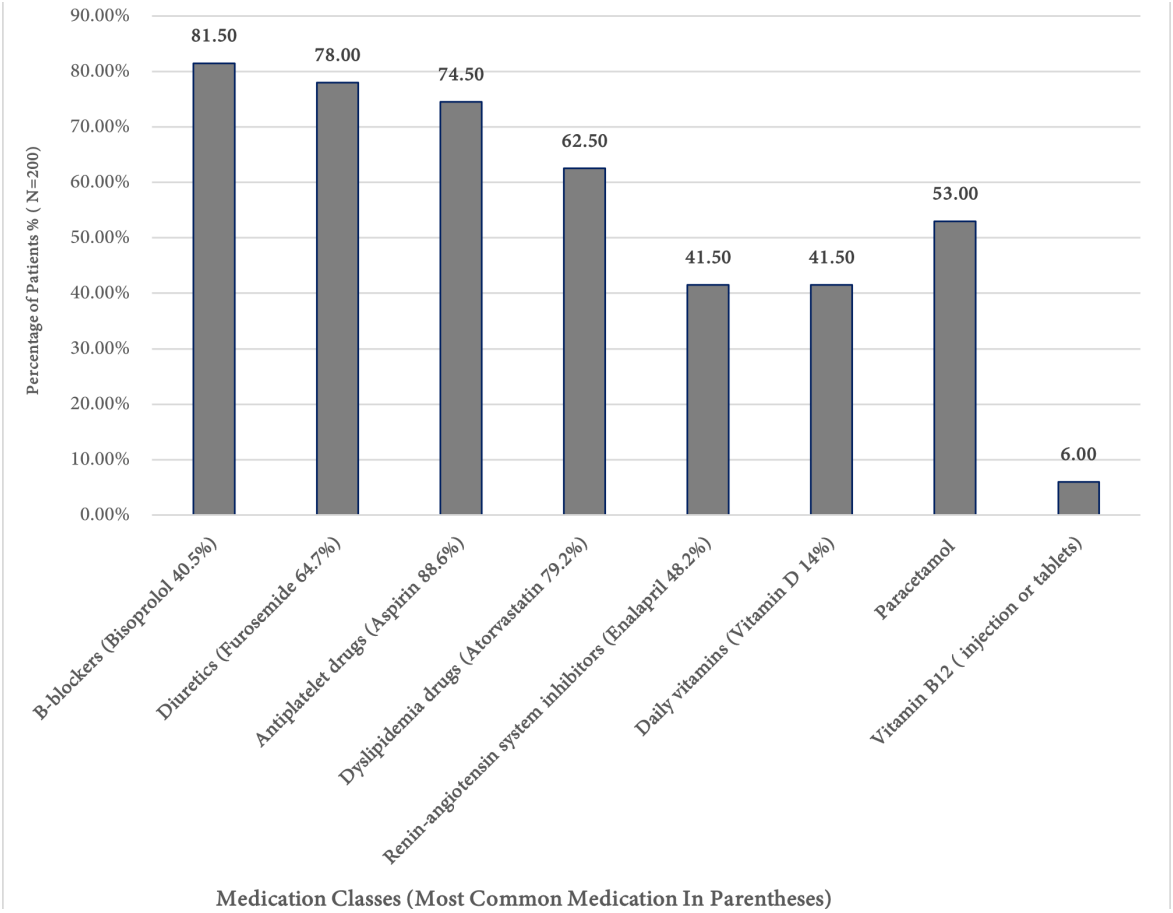

Figure 2. Concurrent medications among warfarin users.

Note: Values above the bars represent the percentage of all warfarin users (N = 200) receiving each medication class. Percentages in parentheses next to medication names represent the percentage of patients within each medication class receiving the specified medication.

tween older age and the patient knowledge scores (Rs = -0.203, p = 0.004). p = 0.004). No significant correlations were found between gender or current INR and patient knowledge scores.

A multivariable logistic regression was conducted to assess the concurrent impact of age, gender, controlled INR, comorbidities and herbal use on the likelihood of experiencing poor TTR control (<60.00%). Following analysis, none of the variables reached independent statistical significance (p > 0.05 for all variables). Specifically, the baseline odds of poor TTR control were not independently altered by advancing age (OR=1.007) or female gender (OR=0.95). Patients who had comorbidities demonstrated a 31.00% increase in the odds of experiencing poor TTR (OR = 1.31, 95% CI [0.46, 2.79]). Similarly, patients having a non-standard or higher target INR showed a 36.00% increase in the odds of poor TTR (OR = 1.36, 95% CI [0.71, 2.61]). However, neither of these predictors reached statistical significance (p = **0.79** and p = 0.354, respectively; Table 3).

Table 3. Multivariable logistic regression analysis of predictors for poor TTR,60%.

Predictor Variable	Odds Ratio (OR)	95% CI for OR [a]	*p*-value
Age	1.007	0.980-1.033	0.623
Gender	0.95	0.492-1.833	0.877
Comorbidities	1.31	0.458-2.790	0.790
Target INR	1.36	0.710-2.607	0.354
Herbal Use	1.049	0.547-2.013	0.886

[a] CI: confidence interval

Discussion

Our INR analysis showed that more than half of the patients had INR within the therapeutic range, while 23.00% had a supra-therapeutic INR, and 20.50% had a sub-therapeutic INR. TTR for the last three months was found to be 68.70%. Our results are similar to those of an observational cohort study of AF patients receiving warfarin in four European countries, including the United Kingdom (UK), which found that the greatest TTR was 65.40%. The authors explained their results in the UK by patients being treated by expert physicians in warfarin clinics, where INR is measured routinely, and doses of warfarin are adjusted (16). In disagreement with the previous, some authors stated that keeping INR control for patients on warfarin therapy is a global problem. For example, in Poland, a multi-center cross-sectional study showed that INR below, within, and over therapeutic range were 30.90%, 54.70%, 14.40%, respectively. TTR was 55.00% (17). Another cross-sectional study conducted at the Security Forces Hospital ACC in Saudi Arabia indicated that 47.50% of patients had good to moderate INR control and 52.50% had poor control (18).

Our study supports the data from other studies indicating factors that contribute to disrupting INR control, including concurrent medication use like amiodarone and use of herbals like cinnamon, in addition to other factors like lack of balance in dietary vitamin K intake, noncompliance, comorbid diseases, malabsorption, genetic polymorphism, and alcohol intake (19).Other complicating factors include patients using the wrong dosage, especially in alternative dose schedules within days of a week, and smoking cigarettes or hookah. Tobacco smoking has a high prevalence in Jordan, and tobacco consumption increased remarkably from 2003 to 2013. Therefore, Jordan's Ministry of Health adopted a strategy to reduce tobacco use by 30.00% by 2023 (20). Notably, 21.00% of patients in our study were smokers. Smoking affects INR control by increasing warfarin clearance (21,22). In addition, a few patients in this study consumed fresh garlic cloves or capsules in the morning. Garlic can be used for its benefits in preventing thrombosis (23).

Regarding the time of warfarin administration, 85.00% of patients took warfarin in the evening, of which 57.60% had INR within the target range. This matches the recommendations of clinical practice guides regarding the administration time of anticoagulation therapy (24). However, a randomized controlled trial concluded that there was no statistically significant or clinically important effect of administration time (morning vs. evening) on the INR control. The study also encouraged patients to take warfarin at any time that increases their adherence (25). The assessment of adherence in the present study indicated that 11 adherent patients (6.10%) depended on an alarm on their phones or a home pill organizer to remember their doses. We suggest using these tools, especially among previously non-adherent patients in the warfarin clinic. Our findings demonstrated that about two-thirds of patients had a high level of knowledge. A pilot study conducted in England to test knowledge of patients receiving warfarin treatment before and after a short educational intervention showed that awareness increased from 52.00% before the intervention to 70.00% (26). Furthermore, a scoping review was conducted, which revealed that maintaining the existing pharmacist-led patient education is effective and crucial in cases of patients on warfarin (27).

In our study, a multivariable logistic regression analysis adjusting concurrently for independent variables revealed that age (OR= 1.007), gender (OR=0.95), comorbidities (OR=1.31), target INR (OR=1.36), and herbal use (OR=1.049) were not independent predictors of poor TTR control. This lack of independent statistical significance strongly implies that anticoagulation stability is driven by highly complex, overlapping clinical factors rather than single, isolated

drivers. These findings suggest that clinical efforts to optimize TTR should focus on global, comprehensive patient monitoring systems rather than targeting isolated demographic or clinical markers.

Our findings indicated a significant weak correlation between age and patient knowledge scores, whereas other factors, such as gender and current INR, did not affect scores. These findings are supported by another study conducted in the warfarin clinic of the Prince of Wales Hospital in Hong Kong. That study found a positive relationship between patients' warfarin knowledge and the number of INR values within the target range (r 0.20; p = 0.024), as well as an inverse correlation between the knowledge score of the patient and age (r – 0.43; p < 0.001) (28).In summary, the mixed results regarding correlations may be due to different elements such as INR fluctuations (due to concurrent comorbidity and medications), age, gender, and the nature of the education session.

Limitations

Study limitations. This study has several limitations, similar to studies based on face-to-face interviews, this study is susceptible to the Hawthorne effect and recall bias. Additionally, the single-center setting may limit the generalizability of the findings, and the cross-sectional design precludes the causal relationships. The absence of a control group further limits the interpretation of the results. Finally, the use of the traditional TTR method, based on a limited number of INR measurements, may have yielded a less precise estimate of anticoagulation control than the Rosendaal method.

Conclusion

This study supports the potential value of pharmacist-led anticoagulation monitoring in public and private hospitals to optimize anticoagulation management. The findings suggest that such services may contribute to improved therapeutic outcomes, enhanced patient education, and reduced risks associated with anticoagulation therapy, including bleeding and thrombosis. The study also highlights the importance of identifying patients with poor time in therapeutic range (TTR), who may benefit from closer monitoring. Furthermore, it emphasizes the role of the clinical pharmacist in assessing medication adherence, changes in medications or supplements, dietary intake of vitamin K-containing foods, herbal product use, comorbidities, and previous warfarin doses, together with INR evaluation, before making warfarin dose adjustments.

Ethical approval

Ethical approval to perform the study was obtained from the Committee for Clinical and Pharmaceutical Research, Studies, and Professional Ethics at RMS (approval number: TF3/1/ Ethics 12467).

Conflict of interest

The authors declare that they have no competing interests in this research.

Authors' contributions

Conception; AB, RA. **Design;** AB, RA. **Formal Analysis;** AB, RA. **Writing;** AB, RA. All authors have approved the final submitted article.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Supplemental Material

See Appendix Supplemental Material for the complete patient knowledge questionnaires used in this study.

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List of abbreviations

Anticoagulation Clinics (ACCs)

Glomerular Filtration Rate (GFR)

Informed Consent Form (ICF)

International Normalized Ratio (INR)

Milligram (mg)

New Direct Oral Anticoagulants (NOACs)

Partial Thromboplastin Time (PTT)

Prothrombin Time (PT)

Queen Alia Heart Institution (QAHI)

Royal Medical Services (RMS)

Standard Deviation (SD)

Time in Therapeutic Range (TTR)

United Kingdom (UK)

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Appendix

Patient knowledge questionnaire

Table. Percentages of correct responses to 14 questions in the patient knowledge questionnaire (N=200).

#	Questions	Frequency of correct answers (%)
1	The physician prescribed warfarin for anticoagulation.	99.50
2	The patient has to perform periodic INR test to ensure the efficacy of recommended dose.	100.00
3	Every patient has defined target INR, either 2-3 or 2.5-3.5.	94.00
4	Some drugs affect the efficacy of warfarin such as cardiac, thyroid disease drugs, analgesics and antibiotics.	79.00
5	Foods that contains high vitamin K such as leafy vegetables affect the efficacy of warfarin.	98.50
6	Some of vitamins, medical herbs and supplements containing garlic and ginger affects the efficacy of warfarin.	75.50
7	Bleeding is one of the adverse effects of warfarin.	86.50
8	Rash is one of the adverse effects for warfarin.	43.50
9	Severe headache is one of the adverse effects of warfarin.	27.00
10	The patient has to contact a physician or an emergency room immediately for any abnormal bleeding.	100.00
11	Smoking has an effect on efficacy of warfarin.	74.50
12	The patient has to inform a physician or a pharmacist if he/she wants to increase or decrease the number of cigarettes.	73.50
13	If the patient forgets to take his/her dose then he /she can take it within 8 hours of time of dose.	25.00
14	It is necessary to inform a surgeon, a dentist, a specialist or any other health care worker that you take warfarin before you do any operation or any procedure.	89.00
Patient knowledge questionnaire scores		**Frequency (%)**
Low level of knowledge (0-5)		2.00
Intermediate level of knowledge (6-10)		36.50
High level of knowledge (11-14)		61.50