



Research article

Efficacy and safety of pharmacist-led vs. Physician-led anticoagulation care in Saudi hospital

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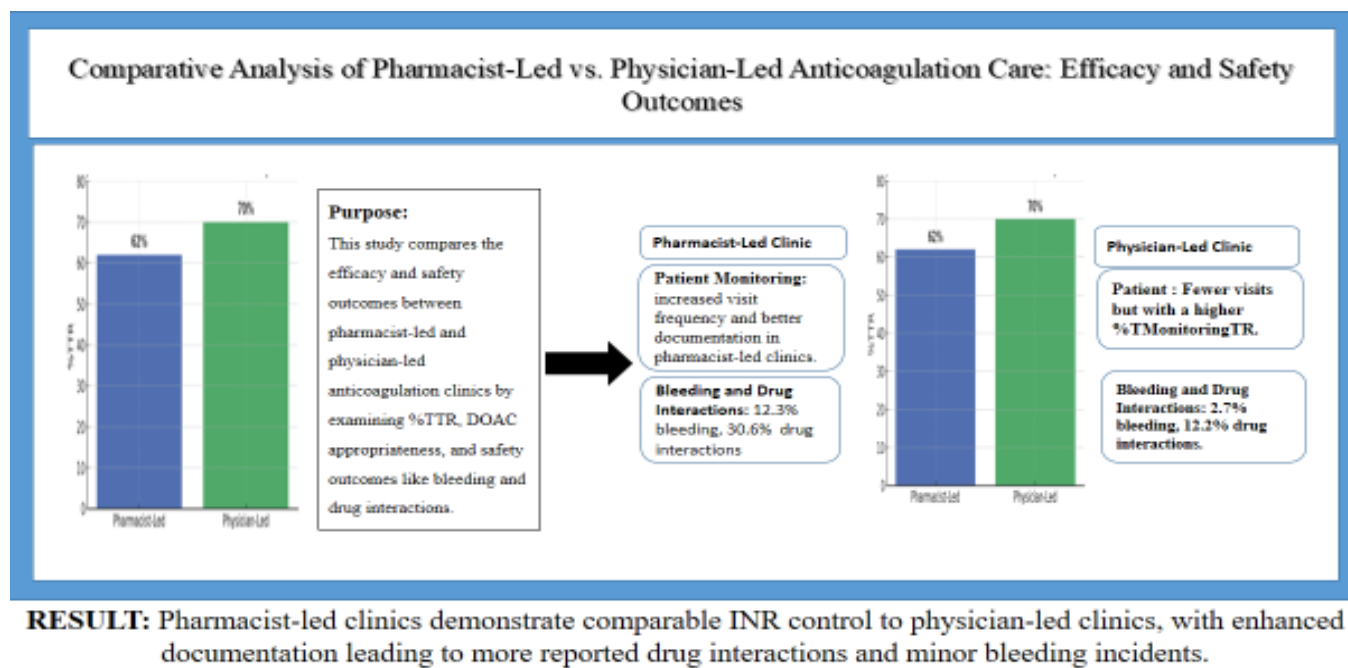
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ABSTRACT

The effective management of thromboembolic disorders heavily rely on oral anticoagulants. Attaining the best control, monitoring, and patient compliance with anticoagulation therapy is crucial for ensuring its safe and effective application. This study sought to compare the efficacy and safety outcome between clinics led by pharmacists and those led by physicians for anticoagulation management. The study evaluated two primary endpoints: the proportion of international normalized ratio values within the target range (%TTR) for warfarin treatment and the appropriateness of DOAC therapy. Secondary endpoints encompassed the percentage of time spent within the preferred INR range, occurrences of significant bleeding, and instances of thrombosis necessitating visits to the emergency department or hospitalisations. The primary endpoints were %TTR for warfarin and the appropriateness of DOAC therapy. Secondary outcomes assessed safety through bleeding and thrombotic events.



The pharmacist-led cohort demonstrated a %TTR of 62%, compared to 70% in the physician-led cohort ($P=0.073$). DOAC therapy showed no significant differences between the groups in terms of indication, dosage, and duration ($p=0.527$, $p=0.555$, and $p=0.627$, respectively). Minor bleeding was significantly higher in the pharmacist-led group (12.3% vs. 2.7%, $p<0.001$), as were drug interactions (30.6% vs. 12.2%, $p=0.004$), attributed to enhanced documentation. The pharmacist-led group had more frequent visits (25.3% vs. 4.5%, $p<0.001$), resulting in greater INR stability. The anticoagulation clinic led by pharmacists demonstrated comparable effectiveness to that led by physicians, exhibiting reduced INR fluctuation and enhanced documentation. This led to a statistically significant increase in the reporting of drug interactions and incidents of minor bleeding.

Keywords: Anticoagulants, Safety, International Normalized Ratio, Warfarin, Drug interactions.

INTRODUCTION

Thromboembolic disorders, condition occur when blood clot forms inside the blood vessel, block another vessel by traveling through the bloodstream [1]. This leads to critical complications depending on the location of lodged clot. Effective management and prevention of thromboembolic disorders such as stroke and venous thromboembolism (VTE), are essential in clinical practice, high mortality and morbidity is associated with these condition. oral anticoagulants are utilized for its management [2]. However, their safety and effectiveness hinge on achieving precise control, vigilant monitoring, and patient adherence [3]. Inadequate anticoagulation therapy can result in thromboembolic events, while excessive anticoagulation raises the risk of bleeding [4]. According to the American College of Chest Physicians (ACCP) guideline, it is advised to strive for optimal control of anticoagulation, characterised by a time within the therapeutic range (TTR) surpassing 70% for warfarin therapy [5].

The clinics that are led by the pharmacist are one of the possible models that can be used to improve anticoagulation management. Several researches and trials have evaluated the competency of pharmacists in managing anticoagulation clinics in comparison to physicians [6, 7]. Several of the findings highlighted maximum clinical effects and fewer complications, such studies by Manzoor et al. and Elewa et al., where pharmacist-led anticoagulation services presented higher control and a more significant %TTR [8, 9]. Furthermore, Ashijan et al. conducted a study stated that the use of direct-acting oral anticoagulant pharmaceutical care services by pharmacists improved patients' treatment appropriateness and treatment adherence compared to the standard care [10].

Pharmacist's expertise in drug interactions, pharmacodynamics, pharmacokinetics and counseling empower them in anticoagulation management [11]. This proficiency allows them to safely and effectively manage patients by adhering to protocols [12]. However, due to their role, there is a scarcity of evidence regarding the effectiveness of pharmacist-led anticoagulation clinics within Saudi Arabia and the Middle East. Furthermore, there is limited literature available concerning the impact of pharmacists in the management of Direct-Acting Oral Anticoagulants (DOACs) [13]

The purpose of this study is to address these gaps by

assessing the effectiveness and safety of pharmacist-led clinics of anticoagulation against the physician-led clinics by treating patients with Warfarin, apixaban, and Rivaroxaban.

Literature Review

Warfarin is referred to as Vitamin K antagonist (VKA) and is an anticoagulants drugs used for stroke prevention in patient with atrial fibrillation and mechanical heart valves. Alghadeer et al., 2020, carried out a study in Saudi Arabia showed that, patients under the care of pharmacists clinics had better anticoagulant control, 82 % of the patients achieved target INR as compared to 24% patient who were under physicians-led clinics [14]. Additionally, the Alshaiban et al. 2023's retrospective cohort study also underlined the gradual improvement of the target INR levels of patients managed by pharmacists from 36.46% at baseline to 85.42% by the fifth week of follow up. The findings of this study support the efficiency of the Pharmacist's Interception Service for anticoagulation with warfarin [15]. Moreover, patient safety was enhanced in pharmacist-led clinics as participants had less bleeding or hospitalization and less ADR occurrences some studies had no ADR reports in follow-up periods [15].

The other type of oral anticoagulant besides the conventional VKAs and the LMWH is the newer oral anticoagulant known as apixaban, a direct factor Xa inhibitor [16]. The study conducted by de Souza Brito et al., 2013 showed that pharmacist led services enhance the patient's compliance and overall patient outcome [17]. For instance, in a quality improvement intervention, the screening of apixaban by pharmacists enhanced medication access and follow-up care, identified dosing errors [18]. Pharmacist are also educated the patients on the medication use as well as any possible side. Moreover, a recent study by Zhang et al., 2024, indicated that the establishment of pharmacist-led clinics is cost-effective as healthcare costs are substantially lower than the physician-led clinics, making this model a feasible solution for healthcare networks [19].

Another direct factor Xa inhibitor, rivaroxaban, has also been approved for several indications including stroke prevention in nonvalvular atrial fibrillation and management of acute deep vein thrombosis (DVT) [20]. A comparative study by Mullen et al 2021, evaluated the effectiveness of pharmacist managed VTE clinic for patient on rivaroxaban after emergency department discharge did not show any variation in major bleedings or recurrent thromboembolism

between pharmacist's management & physician's management indicating that pharmacist managed care is equally safe as physician managed care [21]. Pharmacists also offered valuable information on rivaroxaban use, potential side effects, and the significance of compliance, resulting in increased medication compliance rate among the pharmacist group than the respective control group [22]. The findings of study by Aziz et al., 2011 demonstrated that pharmacist-managed clinics are cost-effective to manage anticoagulation, with total costs per patient-year being less than those of physician-managed clinics, which is an economic benefit [23].

This study aimed to address two specific research questions: First, what is the percentage of time in therapeutic range (TTR) of warfarin patients who enrolled in the pharmacist-led clinic and the physician-led clinics in a tertiary care hospital in Saudi Arabia? Second, does pharmacist-led anticoagulation management result in lower rates of bleeding incidents and hospitalizations than physician-led management? These questions are aimed to determine the efficiency and safety of the pharmacist-managed care in anticoagulation therapy.

MATERIAL AND METHOD

Study Setting

This study was carried at the anticoagulation clinic of King Faisal Specialist Hospital & Research Centre (General Organization) – KSA, Jeddah which is an internationally recognized and accredited healthcare organization with a 500 bedded general multi-speciality tertiary care hospital. This reputed hospital provides a wide range of very specialized care and therapy that range from cardiology, organ transplantation, oncology, hematological diseases, adult and children's critical care, neurology, pain management and other cares. The hospital is accredited from organizations such as the Joint Commission International (JCI) as well as the Saudi Central Board for Accreditation of Healthcare Institutions (CBAHI).

Study Design

This retrospective cohort study compared the Pharmacist-led anticoagulation clinics with Physician-led clinics and aimed at understanding the Pharmacist-led clinics role in the effectiveness and safety of the thromboembolic disorder management protocols. The chosen institution, with its distinguished reputation and specialised medical services, provided an ideal setting for this insightful investigation.

Participants

The sample consisted of all patients who attended the anticoagulation clinics during the study period between the March 1, 2018, and March 31, 2020. Specifically, the inclusion criteria comprised patients undergoing therapy with Warfarin, apixaban, or rivaroxaban, ensuring a comprehensive representation of relevant cases for thorough examination and analysis.

Eligibility Criteria

To be considered eligible for the study, patients had to meet the following specific criteria: Patients should be (i) at least 18 years old, (ii) referred to the anticoagulation clinic for monitoring within the described period, (iii) under anticoagulation therapy for at least one year, and (iv) received care from this clinic for at least four weeks. Exclusions were applied to patients who were pregnant or breastfeeding, exclusively on injectable anticoagulation or had initiated anticoagulation therapy through the pharmacist-led clinic. Additionally, INR values were omitted if they fell within the initial 30 days of warfarin initiation or hospital discharge, during any hospitalisation period, or temporary planned interruptions, defined as occurring from the first day warfarin was temporarily discontinued to two weeks after resuming the therapy. These rigorous criteria were implemented to ensure a robust and accurate assessment of the study's outcomes.

Study Endpoints

The main aims in this study involved the assessment of the quality of anticoagulation specifically in relation to warfarin treatment. This assessment was based on two key metrics: The first was the %TTR of INRs and the second was the appropriateness of DOAC therapy for patients.

The overall appropriateness of DOAC therapy was consisting of the utilisation of DOAC for intended indication, proper dosing for the specific indication, and dosing adjustment for reduced renal function or concurrent use of P-glycoprotein or CYP450 isoenzyme inhibitors or inducers.

Moreover, the study also addressed the secondary outcomes. These included the percentage of time during which INR values were maintained within the desired range, as well as the incidence of significant bleeding events or thrombotic occurrences necessitating visits to either the emergency department or hospitalisation. For this study, major bleeding events were precisely defined in accordance with the criteria established by the International Society on Thrombosis and Haemostasis (ISTH). This encompassed instances of symptomatic bleeding occurring in vital areas or organs, bleeding associated with a reduction in haemoglobin levels of ≥ 2 g/dL or necessitating the transfusion of ≥ 2 units of blood or packed cells, and ultimately, cases of fatal bleeding. These stringent measures were followed in order to maintain a comprehensive and valid assessment of the study's outcomes.

Data Collection and Analysis

A detailed demographic and clinic data was obtained periodically from the Integrated Compliance Information System (ICIS). These data were collected from the medical records kept in the anticoagulation clinic by a thorough analysis and examination of the medical charts. Among the variety of informations gathered

concerning the number of patients visits, the particularities of the indication for anticoagulation, the time period over which such treatment was administered, the targeted INR range, and the documented INR values during each visits. In addition, the dataset gathered comprehensive details of any adverse events such as bleeding events, thromboembolic events, hospitalisation, and emergency room visits. This volume of data was useful in creating a solid foundation on which thorough and comprehensive evaluation could be performed.

The statistical analysis procedure entailed the description of categorical data in terms of frequencies and percentages. On the other hand, continuous data was described by the mean with standard deviation (SD) or median with interquartile range (IQR) depending on the normal distribution of the data. Categorical variables were analyzed either by Chi-square test or Fisher's exact test. However, the continuous variables were evaluated by the student t test or Mann-Whitney test.

The progression of mean INR levels, instances of INR falling out of the desired range, and occurrences of missed doses were graphically represented against the corresponding visit numbers. A two-tailed p-value below 0.05 was established as the threshold for statistical significance. The analysis was executed using the statistical software SPSS (Version 25.0). The determination of time spent within the therapeutic range (TTR) was computed using the methodology outlined by Roosendaal and colleagues.

RESULTS

Patient Demographics

A total of 264 participants were enrolled in the study. Table 1 provides an overview of the patient's baseline characteristics. The average age was 53.2 years, and 66.7% of the participants were female. The most prevalent comorbidities included hypertension, diabetes, renal impairment, heart failure, and coronary artery disease. The primary reasons for anticoagulation therapy were deep vein thrombosis, pulmonary embolism, atrial fibrillation, antiphospholipid syndrome, and the presence of a mechanical mitral valve. Warfarin was the predominant anticoagulant utilised (64.8%), followed by direct oral anticoagulants (DOACs) such as rivaroxaban and apixaban (35.2%). Antiplatelet therapy was prescribed for fewer than 10% of the participants.

Comparison of Anticoagulation Management

The physician-led anticoagulation clinic was less likely to use DOACs compared to the pharmacist-led clinic. Additionally, it was associated with more frequent occurrence of the cases such as deep vein thrombosis, pulmonary embolism, and antiphospholipid syndroms. On the other hand, instances of atrial fibrillation, and patients with mechanical mitral or aortic valves were comparatively less frequent in the pharmacist-led clinic. The pharmacist-led clinic

also presented lower HAS-BLED score and a lower percentage of Antiplatelet therapy utilisation.

Quality of Anticoagulation and Clinical Outcomes

As presented in Table 2, the evaluation of study outcomes showed that most of the patients had a favourable percentage of TTR and the desirable INR level that has been recommended. Furthermore, it was observed that a significant number of patients stick to the indication for anticoagulants therapy, the dose and duration of therapy. Moreover, other remarkable findings comprised of case of minor bleeding stroke, major bleeding or thrombosis, experience of major bleeding, and myocardial infarction events, all of which contributed to give a holistic view of the study's findings and its relevancy for practice.

INR Variability and Drug Interactions

As seen in Figure 1, it is quite clear that the INR levels variability was higher in the physician-led clinics than in the pharmacist-led clinics. These differences in mean INR levels indicated a possibility of a more stable and better managed anticoagulation regime in the pharmacist-managed care.

In addition, Figure 2 gives a perspective over the percentage of the values of INR falling outside the therapeutic range. Although, there was a statistically significant increase in the variability of INR towards the end stage of the study in the pharmacist-managed clinic. However, it is important to note that this difference was based on a relatively small number of patients, warranting a cautious interpretation of this observation.

These subtle differences in INR patterns between the two clinical models reveal that it is not only the average INR values that should be taken into account in normalizing and maintaining positive anticoagulation outcomes but also the distribution of values and their outliers.

The Demographic and Clinical Characteristics of the Patients were carefully evaluated such as gender, age, existing diseases, indications for anticoagulation therapy, usage of anticoagulant and antiplatelet agents. This made possible to have an intensive comparison between the pharmacist-led anticoagulation clinic and the physician-led clinic.

Notably, serious differences were identified in specific characteristics such as age and comorbidities. Such variances highlighted the differences that the distinct patient profiles and medical histories that each clinical model catered to.

However, one of the most important findings of the study regarding epidemiology of drug interactions effecting 21.6% percent of the population. Fortunately, all the people who reported having such interactions claimed to have received an adequate response from their clinicians within a short time, which acknowledges the proactivity and efficiency of the clinical care teams.

Of significant interest, the pharmacist-led anticoagulation clinic exhibited a notably lower incidence of drug interactions in comparison to its physician-led counterpart, a finding of substantial clinical significance ($p=0.004$). This discrepancy highlights a

potentially enhanced level of expertise and vigilance in medication management within the pharmacist-led clinic, thereby contributing to the overall safety and effectiveness of anticoagulation therapy in that setting.

Table 1: (Demographic and Clinical Characteristics of the Patients)

	Pharmacist (N=154)	Physician (N=110)	Total (N=264)	P-value
Gender				
Male	47 (30.5%)	41 (37.3%)	88 (33.3%)	0.251
Female	107 (69.5%)	69 (62.7%)	176 (66.7%)	
Age in years, mean \pm SD	51.1 \pm 14.2	56.1 \pm 16.8	53.2 \pm 15.5	0.009
Age categories n (%):				
<45	53 (34.4%)	26 (23.6%)	79 (29.9%)	
45-65	78 (50.6%)	51 (46.4%)	129 (48.9%)	0.008
>65	23 (14.9%)	33 (30.0%)	56 (21.2%)	
Comorbidity				
Renal Impairment	19 (12.3%)	19 (17.3%)	38 (14.4%)	0.260
Liver Impairment	6 (3.9%)	3 (2.7%)	9 (3.4%)	0.739
Malignancy	5 (3.2%)	2 (1.8%)	7 (2.7%)	0.703
Diabetes	50 (32.5%)	47 (42.7%)	97 (36.7%)	0.088
Hypertension	54 (35.1%)	46 (41.8%)	100 (37.9%)	0.265
Coronary artery disease	8 (5.2%)	12 (10.9%)	20 (7.6%)	0.084
Heart failure	10 (6.5%)	25 (22.7%)	35 (13.3%)	<0.001
Immune thrombocytopenic purport	1 (0.6%)	0 (0.0%)	1 (0.4%)	>0.99
Others	88 (57.1%)	62 (56.4%)	150 (56.8%)	0.900
Indications				
Atrial Fibrillation	10 (6.5%)	53 (48.2%)	63 (23.9%)	<0.001
Deep vein thrombosis	92 (59.7%)	12 (10.9%)	104 (39.4%)	<0.001
Pulmonary embolism	55 (35.7%)	9 (8.2%)	64 (24.2%)	<0.001
Stroke	14 (9.1%)	4 (3.6%)	18 (6.8%)	0.083
Ant phospholipid syndrome	52 (33.8%)	7 (6.4%)	59 (22.3%)	<0.001
Mechanical aortic valve	4 (2.6%)	12 (10.9%)	16 (6.1%)	0.005
Mechanical mitral valve	12 (7.8%)	27 (24.5%)	39 (14.8%)	<0.001
Systemic lupus erythematous	18 (11.7%)	10 (9.1%)	28 (10.6%)	0.499
Others	10 (6.5%)	9 (8.2%)	19 (7.2%)	0.601
NVAF scores, median (IQR)				
CHA ₂ DS ₂ -VASC	3 (2-5)	3 (2-4)	3 (2-4)	0.855
HAS-BLED	0 (0-1)	2 (0-2)	1 (0-2)	0.026
Anticoagulation therapy				
Warfarin	89 (57.8%)	82 (74.5%)	171 (64.8%)	0.005
DOACs	65 (42.2%)	28 (25.5%)	93 (35.2%)	
Antiplatelet therapy				
None	146 (94.8%)	93 (84.5%)	239 (90.5%)	0.007
Aspirin	6 (3.9%)	15 (13.6%)	21 (8.0%)	
Clopidogrel	2 (1.3%)	2 (1.8%)	4 (1.5%)	
Drug interaction				
No	59 (69.4%)	72 (87.8%)	131 (78.4%)	0.004
Yes	26 (30.6%)	10 (12.2%)	36 (21.6%)	

Figure 1: (Mean INR level in different visits by the type of management of the anticoagulation clinic)

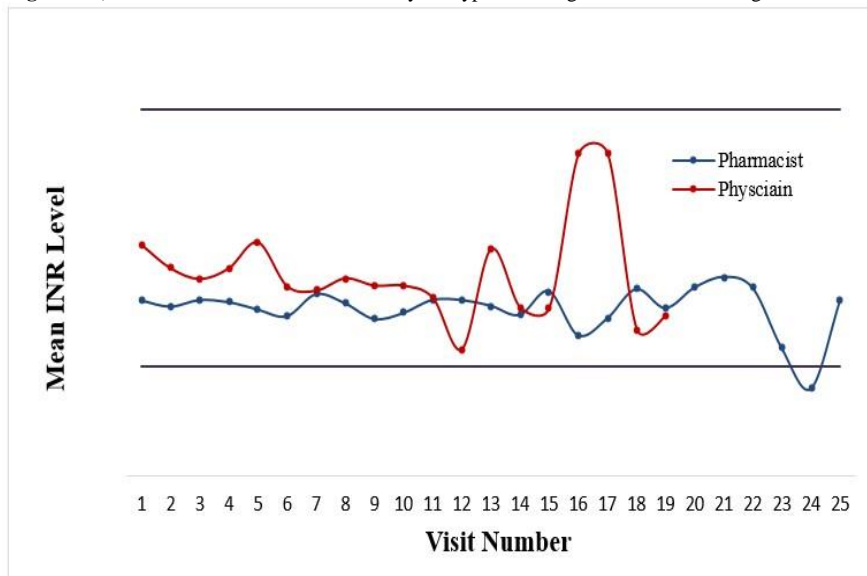
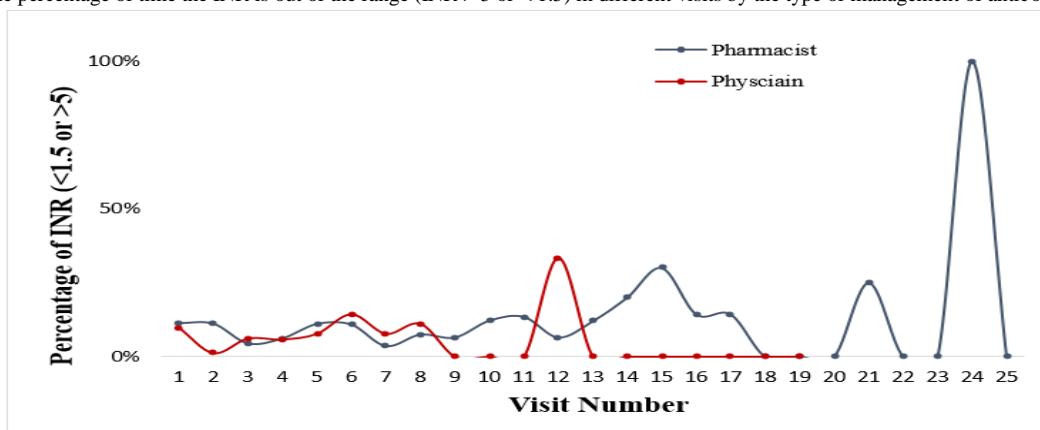


Table 2: (Outcomes by the type of management of anticoagulation clinic)

	Pharmacist (N=154)	Physician (N=110)	Total (N=264)	P-value
Warfarin Therapy				
% TTR, median (IQR)	62 (42-83)	70 (48-97)	65 (44-90)	0.073
% INR in range, median (IQR)	64 (40-80)	67 (50-75)	67 (45-78)	0.652
DOACs Therapy				
Appropriate indication				
No	18 (27.7%)	6 (21.4%)	24 (25.8%)	0.527
Yes	47 (72.3%)	22 (78.6%)	69 (74.2%)	
Appropriate indication, reason for no:				
FDA unapproved indication (Off label use)	3 (18.8%)	3 (50.0%)	6 (27.3%)	0.283
Not been used for this indication	13 (81.3%)	3 (50.0%)	16 (72.7%)	
Appropriate dose				
No	17 (26.2%)	9 (32.1%)	26 (28.0%)	0.555
Yes	48 (73.8%)	19 (67.9%)	67 (72.0%)	
Appropriate dose, the reason for no:				
Overdose	0 (0.0%)	3 (33.3%)	3 (11.5%)	0.032
Underdose	2 (11.8%)	0 (0.0%)	2 (7.7%)	
Not been used for this indication	15 (88.2%)	6 (66.7%)	21 (80.8%)	
Appropriate duration of therapy				
No	17 (26.2%)	6 (21.4%)	23 (24.7%)	0.628
Yes	48 (73.8%)	22 (78.6%)	70 (75.3%)	
The appropriate duration of therapy, the reason for no:				
Indefinite duration	2 (11.8%)	0 (0.0%)	2 (8.7%)	>0.99
Not been used for this indication	15 (88.2%)	6 (100.0%)	21 (91.3%)	
Other outcomes				
Major bleeding	0 (0.0%)	1 (0.9%)	1 (0.4%)	0.417
Minor bleeding	19 (12.3%)	3 (2.7%)	22 (8.3%)	0.005
Stroke	4 (2.6%)	2 (1.8%)	6 (2.3%)	>0.99
Thromboembolic events	0 (0.0%)	0 (0.0%)	0 (0.0%)	NA
Myocardial infarction	0 (0.0%)	1 (0.9%)	1 (0.4%)	0.417
Major bleeding or thrombosis	4 (2.6%)	4 (3.6%)	8 (3.0%)	0.723

Figure 2: (The percentage of time the INR is out of the range (INR > 5 or < 1.5) in different visits by the type of management of anticoagulation clinic)

DISCUSSION

Long-term anticoagulation therapy is important in the prevention of thromboembolic complications in patients with atrial fibrillation, deep vein thrombosis, or mechanical heart valves [24]. A well-coordinated management of anticoagulant therapy consists of the constant assessment and modification of the administered doses in order to avoid toxicity and at the same time ensure adequate anticoagulation is provided [25]. In the past, the role has primarily been played by physicians; however, in the current society, pharmacists are taking on more responsibility in this area because of their understanding of drugs and medications [26].

The purpose of this study was to assess the consequences of patient receiving warfarin and DOACs from pharmacist-led clinics compared to those who attended physician-led clinics in a tertiary care Saudi Arabian hospital. More precisely, the study intended to assess

disparities in TTR, thromboembolic and bleeding events, and appropriateness of the DOAC treatment under the two models of care.

Pharmacist-led clinics strongly exhibited superior standard care in anticoagulation quality, as defined by a higher TTR and significantly less thromboembolic and bleeding events. The TTR values exceeding the range of 68-70% offer a powerful support to the high quality management of warfarin therapy in case of patients within the clinics run by pharmacists. From the analysed outcomes, it was evaluated that the clinics run by pharmacist are more structured and bring a greater level of management in the handling of anticoagulant therapy.

These findings in line with previous studies conducted by Ballestri et al., 2023 and Hoffman et al. 2007, that have compared pharmacist-led anticoagulation clinics with conventional care which is more often provided by the physicians [24, 27]. In the systematic review

by Xu et al. , 2023 including randomised controlled trials and observational studies underscores the proposition that clinics practiced by pharmacists result in measurable improvement in anticoagulation care, higher than conventional models [28].

When comparing these findings with the previous studies, a similar trend emerges. For instance, a study conducted in Qatar yielded an impressive TTR of 81.8% in the pharmacist-led clinic, a notable improvement over the 69.8% achieved in the physician-led counterpart [29,30]. Likewise, a study conducted in Saudi Arabia by Shilbayeh, 2020 demonstrated a TTR of 59% in the pharmacist-led clinic, surpassing the 48% observed in the physician-led clinic [31]. These findings collectively reinforce the pivotal role of pharmacists in optimising anticoagulation therapy and underscore the potential for broader implementation of pharmacist-led care models in similar clinical contexts.

Furthermore, the study also assessed the appropriateness of Direct Oral Anticoagulant (DOAC) therapy, including indications, dosage, and duration; the results showed no significant differences between the pharmacist-led and physician-led groups, indicating that both groups demonstrated similar adherence to guidelines for DOAC therapy, this finding highlighted the expertise of pharmacists in managing DOAC therapy, which is crucial given the increasing use of these agents in clinical practice [32].

One noteworthy result is the higher reporting of minor bleeding and drug interactions in the pharmacist-led group, which was attributed to the pharmacist's enhanced documentation and use of standardised notes; the meticulous documentation practices in pharmacist-led clinics likely result in a more comprehensive record of adverse events, contributing to a better understanding of patient outcomes [33].

Moreover, this study addressed the necessity for further evidence on the efficacy of the pharmacist-led anticoagulation management in Saudi Arabia based tertiary care clinics. Previous research has shown that pharmacist-led clinics are effective [14], and the present study extends this line of research by confirming these effects in a particular and relevant clinical context.

The mean INR values were more stable in the pharmacist-led group due to frequent visits as compared to the physician-led group hence showing that clinics managed by pharmacists might be more rigid and closely monitored than the clinics under a physician [34, 35].

This study supports prior research by Alghadeer et al. , 2020; Qiu et al. , 2021 showed enhanced anticoagulation control and higher TTR established in pharmacist-managed clinics [14, 36]. This study adds to the growing body of evidence supporting the role of pharmacists in anticoagulation management.

However, this study highlighted the pharmacist role in anticoagulation management and suggested that the clinical outcomes can be improved when pharmacist is involved [37]. This suggestion provided a rationale for increasing pharmacist-led anticoagulation services in every healthcare settings.

CONCLUSION

In conclusion, the findings of this study support the effectiveness of pharmacist-led anticoagulation clinics compared to physician-led ones. It suggests potential benefits, such as reduced INR fluctuation and improved documentation. While the pharmacist-led group had slightly higher incidences of drug interactions and minor bleeding, this should be considered in context. The results strongly recommend adopting and expanding pharmacist-led anticoagulation management not only in Saudi Arabia and the Middle East, but also globally. Limitations include single-center data, retrospective design, small sample size, and lack of pre-post data. Nonetheless, spanning two years, the study underscores the effectiveness of pharmacist-led clinics, the first of its kind in the region, advocating for wider implementation in regional hospitals.

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Data Availability

The data used to support the findings of this study are available from the corresponding author upon reasonable request.

Ethical Approval

The study obtained Institutional Review Board (IRB) approval from the King Faisal Specialist Hospital & Research Centre (Gen. Org.) - Jeddah.

Consent

Informed consent was obtained from all subjects participating in the study.

Authors' Contributions

AM was responsible for the study's conceptualization, research, initial draft writing, and investigation. The investigation and methodology were the responsibility of MA. SA was in charge of the investigation, writing, and editing. AA, MO was in charge of conceptualization and investigation. It was AA-II's responsibility to write and edit. The final manuscript has been reviewed and approved by all authors.

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Conflicts of interest

The study authors declared no conflicts of interest.

REFERENCES

1. Harris V, Bavalia R, Mohamad T, et al, 2023. Life-threatening Coagulation Disorders. Radiologic Technology. 94(5), Pages 364-371.

2. Bavalia R, Mohamad T, Khan F, et al, 2020. Treatment of venous thromboembolism in special populations with direct oral anticoagulants. *Thromb Haemost.* 120(6), Pages 899-911.
3. Mohamad T, Khan F, Bungard TJ, et al, 2024. Thrombolysis vs Anticoagulation: Unveiling the Trade-Offs in Massive Pulmonary Embolism. *Cureus.* 16(1), Doi: 10.7759/cureus.52675.
4. Khan F, Bungard TJ, Lip GY, et al, 2021. Long-term risk for major bleeding during extended oral anticoagulant therapy for first unprovoked venous thromboembolism: a systematic review and meta-analysis. *Ann Intern Med.* 174(10), Pages 1420-1429. Doi: 10.7326/M21-1094.
5. Bungard TJ, Lip GY, Haché J, et al, 2009. Evaluation of a pharmacist-managed anticoagulation clinic: improving patient care. *Open Med.* 3(1), Pages e16-21.
6. Lip GY, Haché J, Elewa H, et al, 2018. Antithrombotic therapy for atrial fibrillation: CHEST guideline and expert panel report. *Chest.* 154(5), Pages 1121-1201. Doi: 10.1016/j.chest.2018.07.040.
7. Haché J, Elewa H, Manzoor BS, et al, 2021. Assessment of a pharmacist-led direct oral anticoagulant monitoring clinic. *Can J Hosp Pharm.* 74(1), Pages 7-14.
8. Elewa H, Manzoor BS, Ashjian E, et al, 2016. The first pharmacist-managed anticoagulation clinic under a collaborative practice agreement in Qatar: clinical and patient-oriented outcomes. *J Clin Pharm Ther.* 41(4), Pages 403-408. Doi: 10.1111/jcpt.12400. Epub 2016 May 4.
9. Manzoor BS, Ashjian E, Manirajan P, et al, 2017. Quality of pharmacist-managed anticoagulation therapy in long-term ambulatory settings: a systematic review. *Ann Pharmacother.* 51(12), Pages 1122-1137. Doi: 10.1177/1060028017721241.
10. Ashjian E, Manirajan P, Shields MR, et al, 2017. Evaluation of a pharmacist-led outpatient direct oral anticoagulant service. *Am J Health Syst Pharm.* 74(7), Pages 483 - 489. Doi: 10.2146/ajhp151026.
11. Manirajan P, Shields MR, Generalova D, et al, 2024. A Pharmacist Perspective on Optimizing Pharmacotherapy among Older Adults—A Review. *F1000Res.* 13: 748. Doi: 10.12688/f1000research.152996.1.
12. Shields MR, Generalova D, Alghadeer S, et al, 2022. Pharmacogenomics in Pharmacy Practice. *ERA.* Doi: <https://doi.org/10.7939/r3-yg17-mw10>.
13. Generalova D, Alghadeer S, Alshaiban A, et al, 2020. Investigating prescribers' experiences of direct-acting oral anticoagulants for the management of nonvalvular atrial fibrillation. Doi: <https://doi.org/10.48526/rgu-wt-1447131>.
14. Alghadeer S, Alshaiban A, Fredenburgh JC, et al, 2020. Anticoagulation control of warfarin in pharmacist-led clinics versus physician-led clinics: a prospective observational study. *Risk Manag Healthc Policy.* Pages 1175-1179. Doi: 10.2147/RMHP.S248222.
15. Alshaiban A, Fredenburgh JC, de Souza Brito F, et al, 2023. Impact of Clinical Pharmacist Running Anticoagulation Clinic in Saudi Arabia. *J Clin Med.* 12(12), Pages 3887. Doi: 10.3390/jcm12123887.
16. Fredenburgh JC, de Souza Brito F, Uppuluri EM, et al, 2021. New anticoagulants: Moving beyond the direct oral anticoagulants. *J Thromb Haemost.* 19(1): Pages 20-29. Doi: 10.1111/jth.15126. Epub 2020 Nov 3.8.
17. De Souza Brito F, Uppuluri EM, Zhang X, et al, 2013. The safety and efficacy of apixaban: where do we stand in 2013? *Expert Opin Drug Saf.* 12(4): Pages 559-567. Doi: 10.1517/14740338.2013.799663.
18. Uppuluri EM, Zhang X, Aziz F, et al, 2020. Implementation of a direct oral anticoagulation screening service at a large academic medical center provided by a pharmacist-managed antithrombosis clinic as a method to expand antithrombotic stewardship efforts. *J Pharm Pract.* 33(3), Pages 271-275. Doi: 10.1177/0897190018799200.
19. Zhang X, Aziz F, Mullen D, et al, 2024. Knowledge, attitudes, and practices of primary healthcare practitioners regarding pharmacist clinics: a cross-sectional study in Shanghai. *BMC Health Serv Res.* 24(1), Pages 677.
20. Aziz F, Mullen D, Veale EL, et al, 2021. Rivaroxaban: expanded role in cardiovascular disease management—a literature review. *Cardiovasc Ther.* 2021(1), Pages 8886210. Doi: 10.1155/2021/8886210.
21. Mullen D, Veale EL, Biskach E, et al, 2021. Case Report: Possible Rivaroxaban Failure in Patient with Nephrotic Syndrome Discussing Anticoagulation in Nephrotic Syndrome. *Clin Case Rep Int.* 5, Pages 1206.
22. Veale EL, Biskach E, Tadesse TA, et al, 2024. Pharmacy-Led Management of Atrial Fibrillation: Improving Treatment Adherence and Patient Outcomes. *Integr Pharm Res Pract.* 13, Pages 101-114. Doi: 10.2147/IPRP.S397844.
23. Aziz F, Biskach E, Hoffman GM, et al, 2011. Anticoagulation monitoring by an anticoagulation service is more cost-effective than routine physician care. *J Vasc Surg.* 54(5), Pages 1404-1407. Doi: 10.1016/j.jvs.2011.05.021.
24. Ballestri S, Hoffman GM, Xu Y, et al, 2023. Risk and management of bleeding complications with direct oral anticoagulants in patients with atrial fibrillation and venous thromboembolism: a narrative review. *Adv Ther.* 40(1), Pages 41-66. Doi: 10.1007/s12325-022-02333-9.
25. Buchbender M, Xu Y, Qiu S, et al, 2021. Management of anticoagulated patients in dentoalveolar surgery: a retrospective study comparing bridging with heparin versus unpaused vitamin K antagonist medication. *BMC Oral Health.* 21, Pages 1-8.
26. Elewa H, Egunsola O, Tadesse TA, et al, 2016. Evaluation of pharmacist-based compared to doctor-based anticoagulation management in Qatar. *J Eval Clin Pract.* 22(3): 433-438. Doi: 10.1111/jep.12504.