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Evaluation of warfarin management in primary health care centers in Qatar: A retrospective cross-sectional analysis of the national dataset

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ABSTRACT

Background: Warfarin management is associated with severe complications, highlighting the critical need to evaluate the quality of its administration.
Objectives: To evaluate the quality of warfarin management for patients managed in primary healthcare centers by measuring the percentage of Time in Therapeutic Range (TTR) and the proportion of extreme out-of-range international normalized ratio (INR) values.
Methods: This is a cross-sectional study. Data was extracted from a national dataset retrieved from the largest primary healthcare provider in Qatar. TTR was calculated using the traditional method. Inferential and descriptive analyses were performed as appropriate.
Results: Four hundred ninety-four patients met the inclusion criteria. The mean (SD) TTR was 45.3 % (17.5). This was significantly lower than the recommended cutoff value ($P<0.001$). Extreme out-of-range INR accounted for 24.7 % of total INR readings.
Conclusions: The management of patients taking warfarin in Qatar is inadequate. More effective strategies are warranted to ensure safe and effective therapy.

Introduction

Warfarin has been used for decades to treat and prevent thromboembolic complications in patients with various medical conditions.[1] It is recommended over direct oral anticoagulants (DOACs) for patients with mechanical valves, Hughes syndrome, and patients with severe renal dysfunction.[2–4] However, because of its narrow therapeutic ratio, warfarin is associated with dosing challenges, which necessitate appropriate management to prevent thromboembolic complications. Such management involves a comprehensive process of dosage adjustment, patient education, regular follow-up, and frequent testing of the international normalized ratio (INR) to achieve high-quality anticoagulation control.[5]

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Effective anticoagulation control is characterized by improved efficacy and safety of warfarin therapy.[6] A commonly used method for evaluating the quality of warfarin management is the percentage of time that patients spend within their therapeutic INR range.[7–9] Studies have demonstrated a negative correlation between Time in Therapeutic Range (TTR) and major bleeding and thromboembolic events. A previous analysis of retrospective studies found that an increase of 6.9 % and 11.9 % in TTR in patients with atrial fibrillation was associated with a reduction of one major bleeding and thromboembolic event per 100 patient years, respectively.[10] Additionally, analysis of 2300 patients with Venous Thromboembolism (VTE) showed that patients with a TTR of less than 45 % were at a higher risk of major bleeding and thromboembolic events than with patients who achieved a TTR of more than 65 % (RR 2·8, 1·9–4·3, $P<0·001$).[11] Hence, several guidelines define achieving a TTR greater than 70 % as indicative of high-quality warfarin management.[7,12]

Primary care is an important component of the healthcare process. Delivering services within such community settings provides greater accessibility and continuity of care.[13,14] However, studies have reported low-quality warfarin management in such settings.[15–17]

In Qatar, the management of patients taking warfarin is provided through different models of care. Warfarin is initiated by a secondary and tertiary care provider. Patients taking warfarin are often monitored in specialized anticoagulation clinics in hospital-based settings. In addition, patients taking warfarin may present to primary care centers for medication refills, drawn by the accessibility and convenience offered by these facilities. Primary care centers provide point-of-care INR measurement and refill services for patients taking warfarin to adjust the doses according to the patient's INR and any other changes that may be recognized during the visit. Despite the introduction of DOACs, warfarin is the most commonly prescribed oral anticoagulant in Qatar.[18] However, no study has assessed the quality of warfarin management in primary care settings. Therefore, this study aimed to evaluate the quality of warfarin management in the primary care settings in Qatar.

Methods

Study design and setting

A cross-sectional study was conducted at one of Qatar's main healthcare institutions, the Primary Health Care Corporation (PHCC).[19] PHCC is the leading provider of primary healthcare services and operates in more than 31 centers nationwide. It delivers a comprehensive array of preventive, curative, and rehabilitative services to more than 1.7 million individuals. The current role of PHCC in warfarin management is to support secondary care by providing warfarin refills, education, and opportunistic monitoring of INR levels based on the patient's clinical condition and preferences.

Population and sampling

Participants' data were extracted from the electronic medical record system of the PHCC. All adult patients ($\geq$18 years old) on warfarin with a predefined INR target who had at least one INR reading between January 2018 and July 2023 were included in the study. The universal sampling technique was adopted to extract data from the entire population meeting the study inclusion criteria.[20]

Outcome assessment

TTR was used as the primary outcome measure and was calculated using the traditional method.[21] INR values were derived from both point-of-care (POC) testing and venous withdrawal. A precise INR target range, rather than an expanded target range, was considered therapeutic INR. The mean TTR for the included population was then compared with the recommended 70 % cut-off value.[7,12]

The secondary outcome was the proportion of extreme out-of-range INR values. Extreme INR values were defined as subtherapeutic (INR $\leq$ 1.5) and supratherapeutic (INR $\geq$ 4.0), a definition previously used by Sood et al. [22]

Data analysis

Statistical analyses were performed using the IBM SPSS@ software v29.0 (IBM Corp. Released 2022. IBM SPSS Statistics for Windows, version 29.0. Armonk, NY: IBM Corp). The Kolmogorov–Smirnov test was used to assess the normality of the variables. Normally distributed continuous data are presented as means and standard deviations (SD). Categorical variables are presented as frequencies and proportions. An independent t-test was used to compare the population TTR with the recommended cutoff. To compare the mean TTR and INR categories (subtherapeutic and supratherapeutic) across age, sex, indication for warfarin, region, and nationality, chi-square, and one-way ANOVA with post hoc analysis were used as appropriate. The association between achieving the given TTR cutoff and patient variables was analyzed using binary logistic regression. Statistical significance was set at $P \leq 0.05$.

Ethical consideration

The research proposal was reviewed and approved by the Institutional Review Boards (IRB) of PHCC (BUHOOTH-D-23-00011) and Qatar University (QU-IRB 1945-EA/23). The research was conducted in strict adherence to the principles of good research practice and ethical standards and guidelines established by the institutions.

Results

Nine hundred forty-two patients on warfarin were identified from electronic health records, and more than half of them had a predefined INR target (53.2 %, *n*=501). Four hundred forty-one patients (46.8 %) were excluded from the study as they did not have a clearly defined INR target. Six patients received warfarin without prior INR readings, and one patient was under 18 years of age. Therefore, 494 patients were included in this study. Table 1 presents the clinical and demographic characteristics of the study population.

The mean age (SD) of the included patients was 66 (17) years. The majority of the population consisted of Arabs (83 %, *n*=410). Among these, Qatari patients represented 46.6 % (*n*=191) of the total population. The main indication for warfarin use was atrial fibrillation (AF) (60.9 %, *n*=301), followed by DVT (15.8 %, n=75). Most patients had an INR target of 2–3 (99.4 %, *n*=491). The mean number of visits per patient during the study period was 86.

The mean (SD) TTR of the included patients was 45.3 % (17.5). This was significantly lower than the recommended cut-off value of 70 % ($p < 0.001$, 95 % CI: -26.22, -23.12). Only thirty-four (6.9 %) patients achieved a TTR of > 70 % (i.e., high-quality warfarin management), and 46.4 % (*n*=229) had a TTR between 45 % and 70 %. Two hundred thirty-one (46.8 %) patients had a TTR of less than 45 %. Patients aged > 65 years achieved a higher TTR than those aged less than 65 years (46.6 vs. 43.4 %, respectively; $p = 0.049$). The patients with AF had a mean TTR of 47.86 %. This was significantly higher than that in patients with DVT, who had a TTR of nearly 41 % ($p = 0.018$). Overall, there were no statistically significant differences in TTR across sex, region, and country of origin (Table 2).

Binary logistic regression analysis was conducted to examine the relationship between age, sex, indication for warfarin, and achievement of a TTR exceeding the recommended cutoff of 70 %. No statistically significant factors were identified.

The second outcome was the percentage of extreme out-of-range INR. Based on 42,413 INR values retrieved from the record, the mean (SD) INR was 2.35 (1.02). Subtherapeutic INR accounted for 18.9 % (*n*=8,014) of the total INR readings, and 5.8 % (n=2,456) were supratherapeutic. Patients aged < 65 years had a higher percentage of subtherapeutic INR (20.0 %, *n*=2,563) and supratherapeutic INR (6.3 %, $n = 804$) than those in the older group (18.4 %, n=5,451 and 5.6 %, *n*=1,652, respectively, $P< 0.001$). Female subjects had a lower percentage of subtherapeutic INR than male subjects (17.7 % vs. 20.4 %, $P<0.001$). However, the percentage of supratherapeutic INR readings was higher in females than that in males (6 % vs. 5.5 %; $P<0.001$). Asian patients (i.e., South Asia and West Asia) had a higher rate of subtherapeutic (20.2 %, *n*=912) INR values than Arab patients (18.6 %, *n*=6,883) ($P<0.001$). Similarly, the percentage of supratherapeutic INR was higher among Asian patients (6.9 %, *n*=312) than among Arab patients (5.7 %, *n*=2,215) ($P<0.001$). Table 3 presents the INR readings according to patient characteristics.

Discussion

The aim of this study was to evaluate the quality of warfarin management in primary health care. The findings identified gaps in the management of warfarin within PHCC, necessitating targeted interventions to ensure safe and effective use of warfarin. Both outcome

Table 1
Patient demographic and clinical characteristics.

Patient characteristic	Frequency (%)
Age category	
< 65	197 (39.9)
≥ 65	297 (60.1)
Gender	
Male	255 (51.6)
Female	239 (48.4)
Region	
Arab	410 (83.0)
Asia*	73 (14.8)
Other	11 (2.2)
Country of origin	
Qatari	191 (38.7)
Non-Qatari	303 (61.3)
Indication for warfarin	
AF	301 (60.9)
DVT	75 (15.2)
PE	41 (8.30)
APL	22 (4.6)
Others	55 (11.1)
INR target	
1.5-2.5	3 (00.6)
2-3	491 (99.4)

Abbreviations: AF, atrial fibrillation; DVT, deep vein thrombosis; PE, pulmonary embolism; APL, antiphospholipid syndrome; INR, international normalized ratio.
* South Asia/ West Asia

Table 2
Comparisons of TTR among patient characteristics.

Patient characteristic	TTR% mean (SD)	P-value
Gender		
Male	45.00 (18.17)	P=0.666**
Female	45.68 (16.82)	
Region		
Arab	45.81 (17.38)	P=0.183***
Asia*	42.05 (18.72)	
Others	49.19 (12.08)	
Country of origin		
Qatari	45.04 (17.29)	P=0.771**
Non-Qatari	45.51 (17.69)	
Age		
< 65	43.42 (18.22)	P=0.049**
≥ 65	46.60 (17.0)	
Indication of warfarin		
AF	47.86 (17.26)	P=0.02***
DVT	40.94 (18.35)	
PE	43.71 (17.51)	
APL	41.21 (19.27)	
Others	40.32 (14.71)	

Abbreviations: TTR, time in therapeutic range; SD, standard deviation; IQR, interquartile range; AF, atrial fibrillation; VTE, venous thromboembolism; APL, antiphospholipid syndrome.
* South Asia/ West Asia
** Calculated using independent T test.
*** Calculated using one-way ANOVA test.

Table 3
Analysis of INR among patient characteristics.

Patient characteristic	Subtherapeutic INR n (%)	INR <1.5 and >4.0 n (%)	Supratherapeutic INR n (%)	P-value*
Gender				
Male	3,705 (20.4)	13,415 (74.0)	999 (5.5)	P< 0.001
Female	4,309 (17.7)	18,528 (76.3)	1,457 (6.0)	
Region				
Arab	6,883 (18.6)	28,080 (75.7)	2,215 (5.7)	P< 0.001
Asia**	912 (20.2)	3,290 (72.9)	312 (6.9)	
Others	219 (26.7)	573 (69.8)	29 (3.5)	
Country of origin				
Qatari	3,756 (19.0)	14,872 (75.3)	1,128 (5.7)	P=0.707
Non-Qatari	4,258 (18.8)	17,071 (75.3)	1.328 (5.9)	
Age				
<65	2,563 (20.0)	9,478 (73.8)	804 (6.3)	P< 0.001
≥ 65	5,451 (18.4)	22,465 (76.0)	1,652 (5.6)	

Abbreviations: INR, international normalized ratio.
* Calculated using Chi-square test
** South Asia/ West Asia

variables, TTR and percentage of extreme INR values, indicated inadequate control of warfarin management in Qatar. The mean (SD) percentage of TTR for the included population was significantly lower than the recommended target.[7,12] A previous study linked achieving a TTR of less than 45 % to a higher rate of bleeding and thromboembolic events.[11] In this study, just under half of the study population achieved a TTR of less than 45 %.

The results of this study are consistent with those of previous studies conducted in other countries that showed low-quality warfarin management within primary care settings.[15–17,23] Insufficient resources for anticoagulation monitoring, perceived inadequacies in expertise among primary care physicians, and unclear documentation of therapeutic plans can contribute to this issue.

In this study, slightly less than half of the population was excluded from the analysis primarily because of unclear indications for warfarin. Notably, a significant proportion of the excluded individuals were patients who had undergone heart valve replacement. The absence of well-defined target INR values for these patients is particularly noteworthy, given that the target INR is determined based on the specific type of valve used. This lack of clarity in defining target INR values for patients taking warfarin underscores a critical gap in current anticoagulation management practices.

The healthcare setting in which patients receive anticoagulation management plays a pivotal role in influencing the control of anticoagulation. A systematic review of 67 studies highlighted the significant influence of care settings on anticoagulation control.[15] The review found that patients under the care of their community physicians experienced an absolute decrease in TTR compared to those receiving supervision in dedicated clinic-based settings.

The pharmacist-led anticoagulation model demonstrated lower minor bleeding events, warfarin-related hospitalizations, and higher TTR levels than usual care.[24,25] A previous study conducted in Qatar showed a mean TTR of 81.8 % for patients managed in a pharmacy-led clinic in a hospital-based setting.[26] Shifting this model to the primary care setting may offer better accessibility and greater continuity of care, while providing anticoagulation care in a systematic and timely manner. In addition, establishing a clear referral system between primary and secondary care settings, the integration of POC testing with the electronic health record system, and the dissemination of patient education materials can further contribute to enhancing patient outcomes.[27,28] The holistic implementation of these interventions may overcome the gap in the care provided to patients on warfarin.

Study strengths and limitations

This study had several notable strengths. First, owing to the utilization of advanced electronic medical records, we managed to capture data from a national dataset of 31 primary health centers in the country. This leads to better data accuracy. Second, the quality of warfarin management was assessed in a diverse patient population to evaluate the effects of the patients' clinical and demographic characteristics.

Nevertheless, this study had some limitations. Some medical records were incomplete, mainly information about the INR target. For this reason, patients who had undergone heart valve replacement were excluded. Additionally, the POC system was not integrated into electronic medical records, contributing to the potential for manual entry inaccuracies. Furthermore, it was difficult to access hospital-based records to collect clinical data such as hemorrhage and thromboembolic events. Therefore, we were unable to assess the long-term consequences of warfarin management at PHCC.

Study implications

The findings of this study highlight a substantial gap in achieving optimal anticoagulation control in patients on warfarin in Qatar. This emphasizes the urgent need for more advanced evidence-based interventions aimed at enhancing patient safety and improving overall health outcomes. Addressing these issues is crucial for ensuring the effectiveness of anticoagulation therapy and minimizing associated risks in patients managed in primary care settings.

Conclusions

In conclusion, the findings of this study highlight a concerning gap in the management of patients on warfarin. A notable proportion of patients did not maintain their INR values within the desired therapeutic range, indicating suboptimal care. TTR was found to be significantly lower than the recommended target, and patients had a high proportion of extreme out-of-range INR values. This finding indicates a significant need for more evolved evidence-based interventions to improve patient safety and improve health outcomes.

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CRediT authorship contribution statement

Safaa Alshihab: Conceptualization, Methodology, Writing – review & editing, Formal analysis, Investigation, Data curation, Writing – original draft. **Mohamed Izham Mohamed Ibrahim:** Conceptualization, Methodology, Writing – review & editing, Formal analysis, Investigation, Supervision. **Muhammad Abdul Hadi:** Conceptualization, Methodology, Writing – review & editing, Formal analysis, Investigation, Supervision. **Abdullah Syed:** Conceptualization, Methodology, Writing – review & editing, Formal analysis, Investigation. **Abdulrahman Arabi:** Conceptualization, Methodology, Writing – review & editing, Formal analysis, Investigation. **Awad Al-Qahtani:** Conceptualization, Methodology, Writing – review & editing, Formal analysis, Investigation. **Hanan Almujalli:** Conceptualization, Methodology, Writing – review & editing, Formal analysis, Investigation. **Ihsan Rafie:** Conceptualization, Methodology, Writing – review & editing, Formal analysis, Investigation. **Mohamed Gaith Al-Kuwari:** Conceptualization, Methodology, Writing – review & editing, Formal analysis, Investigation. **Mujeeb Kandy:** Data curation. **Manal Al-Zaidan:** Conceptualization, Methodology, Writing – review & editing, Formal analysis, Investigation, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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