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Research Article

Patient factors impacting on oral anticoagulation therapy among adult outpatients in a Kenyan referral hospital

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Background: Patients' factors such as knowledge on warfarin use are important in achieving desirable anticoagulation outcomes.

Objective: To assess the patient factors impacting on oral anticoagulation control among adult outpatients taking warfarin at Kenyatta National Hospital.

Methodology: A cross-sectional survey of 147out-patients on warfarin at Kenyatta National Hospital was carried out between March and April 2015. Data were collected using a pre-designed interviewer administered questionnaire. The data included patient characteristics such as indication and duration of anticoagulation; knowledge on anticoagulation; and international normalized ratio tests. The Oral Anticoagulation Knowledge test was used with a score of ≥75% indicating sufficient knowledge. Logistic regression was used to determine independent variables associated with anticoagulation control.

Results: Females were majority (74.9%) while optimal anticoagulation control was at 43.5%. Only 10.1% had sufficient knowledge on anticoagulation. Anticoagulation knowledge scores were associated with marital status (p=0.015), education level (p=0.014) and indication (p=0.032). Independent predictors of poor anticoagulation were female gender (p=0.011) and lower education level (p=0.005). Optimal anticoagulation control was, however, not associated with knowledge on anticoagulation (p=0.794).

Conclusion: Knowledge and control of anticoagulation among the patients are poor. Female gender and lower education level were predictors of poor anticoagulation. Provision of information on anticoagulation to patients on was warfarin is recommended.

Key words: Knowledge, Warfarin, Anticoagulation, International normalized ratio

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1. Introduction

Oral anticoagulants are indicated for prophylaxis and treatment of deep vein thrombosis, pulmonary embolism, atrial fibrillation in those who are at risk of embolization and in mechanical prosthetic heart valves to prevent emboli developing on the valves (Dipiro et al, 2008). Vitamin K antagonists (VKAs), especially warfarin are the oral anticoagulants of choice due to their ease of administration and low cost. Warfarin has a narrow therapeutic index and has been associated with a number of complications, mostly re-thrombosis and bleeding (Ansell et al, 2008). This necessitates frequent international normalized ratio (INR) monitoring to maintain optimal anticoagulation control and prevent adverse effects.

The annual incidence of major bleeding ranges from 1% in carefully managed patients to >10% in those not appropriately managed (Ansell et al, 2008).One study

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showed that the relative risk of venous thromboembolism (VTE) recurrence was higher in those patients who spent a longer duration in markedly sub-therapeutic INR values during the first ninety days of treatment after the acute VTE episode (Palareti et al, 2005a). In a survey of the epidemiology of sub-therapeutic INR in the United States, more than one in five thromboembolic events occurred during a period of low INR (Rose et al, 2009).

Maintaining adequate anticoagulation using warfarin has proved to be a challenge. Past studies have estimated that patients on warfarin may be in the therapeutic range as little as one-third of the time (Ogendo, 2000; Ageno et al, 2012). Multiple factors have been associated with anticoagulation instability including drug and food interactions, presence of other disease states and genetic differences in warfarin metabolism (Ageno et al, 2012). Patient-related factors such as lack of knowledge about anticoagulation therapy (Tang et al, 2003), and social factors such as stress, family support, relationship with prescribers, and the inconvenience of regular clinic appointments, may also contribute to poor anticoagulation control (Davis et al, 2005).

This study sought to explore the patient factors affecting anticoagulation control among adult outpatients taking warfarin at Kenyatta National Hospital (KNH).

2. Methodology

2.1 Study design, site and population

This was a cross sectional study that was carried out in March and April 2015 at the cardiac, hemato-oncology and cardiothoracic clinics of Kenyatta National Hospital. The target population was adult out-patients coming for review of their anticoagulation management.

2.2 Inclusion and exclusion criteria

Out-patients on warfarin, and over 18 years who consented to the study were included. Patients with a documented evidence of psychiatric illness, and those unwilling to participate were excluded.

2.3 Sample size and sampling procedure

The sample size was calculated using the formula for comparing proportions (Fleiss et al, 2003). The calculated sample size was 147 based on the finding that 55% of patients with satisfactory knowledge on anticoagulation had a therapeutic INR compared to 20% of those who had unsatisfactory knowledge (Khudair et al, 2010). Knowledge as a factor was chosen in this determination because it was the only documented patient factor impacting on oral anticoagulation control.

Participants were recruited by consecutive sampling during the clinic days after being seen by the doctors until the required sample size was achieved. All adult out-patients on warfarin who met the criteria were invited to participate.

2.4 Data collection

Data was collected through an investigator administered pre-tested questionnaire in a face to face interview with the patients and analysis of their blood samples for INR. Data recorded included patient characteristics such as demographics, duration of warfarin use, indication, co-morbidities, and INR values. Knowledge on anticoagulation was assessed using 15 multiple choice questions adapted from the Oral Anticoagulation Knowledge (OAK) test (Zeolla et al, 2006). These captured the knowledge of patients on important aspects of anticoagulation such as monitoring therapy, food and drug interactions, effect of missing a dose, when to seek medical attention, among others. For each question, a score of one was awarded for a correct answer and zero for a wrong answer.

2.5 Data analysis

All data collected was entered in a Microsoft Excel spreadsheet (Microsoft office 2013) then exported to IBM SPSS version 20 software for analysis. Continuous variables were summarized as the mean and standard deviation of the mean, or as the median and the ranges. Categorical variables were summarized as frequencies and proportions. Knowledge scores for each patient were computed as one's total score divided by 15 then converted to a percentage. Bivariate analysis was carried out to correlate the independent variables such as patient characteristics to knowledge and the level of anticoagulation control (INR values). Chi-square tests were adopted to determine the association of dependent variables with nominal factors, and analysis of variance (ANOVA) tests to characterize association of the dependent variables with continuous variables. Stepwise backward logistic regression analysis to determine independent variables associated with INR was then carried out. P-values of 0.05 or less were considered statistically significant.

2.6 Ethical considerations

Authorization to conduct the study was sought from the Kenyatta National Hospital/ University of Nairobi Ethics and Research Committee and a letter reference number **KNH-ERC/A/34** dated 2nd February, 2015 was provided.

Informed consent from the study participants who met the inclusion criteria was sought. Confidentiality was maintained by using study serial numbers instead of participants' names.

Immediately after administering the questionnaire, the study participants were given information regarding anticoagulation, with emphasis on the aspects that they least understood. They were given a chance to ask questions.

3. Results

3.1 Characteristics of the study participants

The study participants were mainly female 109 (74.9%) and had a median age [range] of 41[18-74] years (**Table 1**).

Those aged between 38 and 57 years constituted 81 (56.3%) of the participants. Venous thromboembolism (VTE) was the most prevalent indication for oral anticoagulation therapy (OAT) making up 71 (48.6 %) of the study participants

Table 1: General characteristics of the study participants

Variable	n (%)
Sex	
Male	38(25.9)
Female	109(74.1)
Age (median, years [range])	(41 [18-74])
Age group (years)	
18-37	51(35.4)
38-57	81(56.3)
> 57	12(8.3)
Marital status	
Single	42(28.1)
Married	93(63.7)
Separated	5(3.4)
Divorced	7(4.8)
Level of education	
Informal	1(0.7)
Primary	46(31.3)
High school	64(43.5)
College	36(24.5)
Monthly Income (KSh)	
<10,000	63(42.6)
10,000-30,000	67(45.9)
>30,000	17(11.5)
Indication for OAT	
Heart disease	26(17.8)
VTE	71(48.6)
Heart valve replacement	50(33.6)
Duration of OAT	
< 3 months	12(8.2)
3 months – 1 year	33(22.4)
> 1 year	102(69.4)

3.2 Knowledge on anticoagulation

Knowledge on anticoagulation was determined by administering fifteen questions adapted from the OAK test (Zoella et al, 2006).The aspects tested by the questions are shown in **Table 2** below.

The mean score on knowledge on anticoagulation was 57% ± 16. Only 15 (10.1%) attained the pass mark of ≥75% and were graded as having adequate knowledge on anticoagulation. We chose a pass mark of 75% as an average of pass mark set in other documented studies (Davis et al, 2005; Yahaya et al, 2009). A substantial number 90 (60.8%) had fairly good knowledge as they answered 50-74% of the questions correctly while about a quarter of the participants scored below average. A very small fraction of the participants 5 (3.4%) scored less than 25%.

Figure 1 gives a breakdown of how the participants faired in the Zeolla et al, 2006 questions testing knowledge on oral anticoagulation. The best answered questions (over 80% correct scores) were those examining indication and action of warfarin (question 1); significance of the INR test (question 2); effect of alcohol on warfarin therapy (question 5); and the action to be taken in case one missed a dose of warfarin (question 14).

Patients' knowledge in the aspects of interacting medication was below average (questions 7 and 10). Their deficiency in knowledge was also seen with respect to the effect of diet on anticoagulation (questions 8 and 9); the vitamin involved in anticoagulation (question 6) and the symptoms or events necessitating seeing a doctor (question 15). In these three aspects, less than a third of the respondents answered correctly.

Table 2: Aspects of knowledge on anticoagulation tested by OAK test

Question	Aspect tested
1	Indication for warfarin use.
2	Significance of the INR test.
3	Effect of having an INR below patient's goal range.
4	Frequency of INR testing once one is stabilized.
5	Effect of alcohol on anticoagulation therapy.
6	The vitamin that interacts with warfarin.
7	Effect of taking a medication containing aspirin or other pain killers such as ibuprofen while on warfarin.
8	Effect of occasionally eating a large amount of leafy green vegetables while taking warfarin.
9	The ideal diet of a person taking warfarin.
10	Time when one can safely take medication that interacts with warfarin.
11	Effect of having an INR above the patient's goal range.
12	When to monitor for signs of bleeding.
13	Effect of missing one dose of warfarin.
14	What to do if you miss a dose of warfarin.
15	When a person on warfarin should seek medical attention.

INR – International normalized ratio, OAK – Oral anticoagulation knowledge

3.3 Factors associated with knowledge on anticoagulation

Good anticoagulation knowledge was associated with marital status (p=0.003), level of education (p=0.046) and indication for oral anticoagulation therapy (p=0.007) (**Table 3**).

On multivariate analysis, independent predictors of higher knowledge on anticoagulation were marital status (OR 2.462 [1.192-5.085] p=0.015, level of education (OR 2.836 [1.231-6.534] p=0.014 and indication for OAT (OR 2.733 [1.093-6.832] p=0.032.

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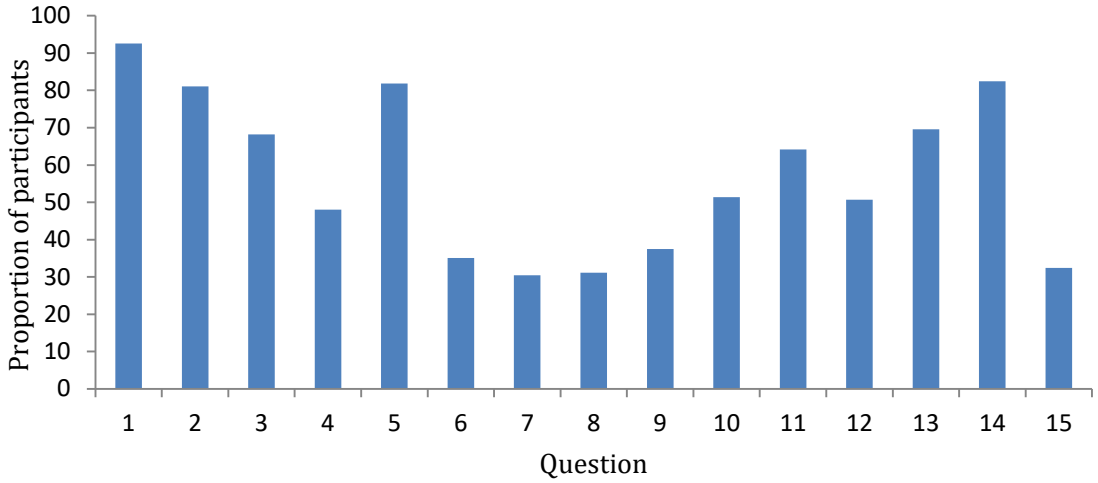

Figure 1: Proportion of participants that answered correctly each of the individual questions testing knowledge on anticoagulation

Table 3: Association between patient factors and knowledge on anticoagulation

Variable		Knowledge score		P value
		<75% n (%)	≥75% n (%)	
Age group (years)	18-37	47(32.6)	4(2.8)	0.269
	38-57	70(48.6)	11(7.6)	
	> 57	12(8.3)	0(0.0)	
Gender	Male	36(24.5)	2(1.4)	0.227
	Female	96(63.3)	13(8.8)	
Marital status	Single	39(26.5)	3(2.0)	**0.003**
	Married	85(57.8)	8(5.4)	
	Separated	2(1.4)	3(2.0)	
	Divorced	6(4.1)	1(0.7)	
Level of education	Informal level	1(0.7)	0(0.0)	**0.046**
	Primary	46(31.3)	0(0.0)	
	High school	58(39.5)	6(4.1)	
	College	30(20.4)	6(4.1)	
Monthly Income (Kenya shillings)	<10,000	57(38.7)	6(4.1)	0.455
	10,000-30,000	60(40.8)	7(4.8)	
	>30,000	14(9.5)	3(2.0)	
Indication for OAT	Heart disease	26(17.7)	0(0.0)	**0.007**
	VTE	63(42.9)	8(5.4)	
	Valves replacement	42(28.6)	8(5.4)	
Duration of OAT	< 3 months	10(6.8)	2(1.4)	0.640
	3 months – 1 year	29(19.7)	4(2.7)	
	> 1 year	93(63.3)	9(6.1)	
Last anticoagulation clinic visit	< 1 month ago	50(35.0)	5(3.5)	0.162
	1- 2 months ago	19(12.9)	5(3.5)	
	> 2 months ago	63(42.9)	5(3.5)	
Smokes	Yes	3(2.0)	0(0.0)	0.554
	No	129(87.8)	15(10.2)	
Alcohol consumption	Yes	8(5.4)	0(0.0)	0.325
	No	124(84.3)	15(10.2)	

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3.4 Anticoagulation control among the participants

Less than half of the study participants, 64 (43.5%) had an optimal INR, as per their condition. Patients with sub-therapeutic INRs, accounted for 58 (39.5%) of the study participants, whereas only 25 (17.0%) had above normal range values (**Figure 2**).

3.5 Patient factors affecting anticoagulation control

Gender, level of education, and indication for anticoagulation therapy were associated with level of anticoagulation as measured by INR values. Of the psychosocial factors, patients who had family support achieved a therapeutic INR (**Table 4**). On multivariate analysis, the independent patient factors associated with poor anticoagulation control were female gender [OR 2.782 (1.263-6.128)] p=0.011; and lower education level [OR 1.935 (1.214-3.084)] p=0.005. Being of female gender was about three times more likely to present with poor anticoagulation control than being a male. Patients with lower education level were twice as likely to have poor anticoagulation control as those with higher education.

4. Discussion

The patient's knowledge on anticoagulation has previously been shown to be a determinant of anticoagulation control (Tang et al, 2003). Our study showed that only 10.1% had good knowledge of anticoagulation therapy. Inadequate knowledge on anticoagulation has been demonstrated in similar studies. Only 37% and 39% of patients in the studies by Davis et al, 2005 and Hu et al, 2006 respectively reported sufficient knowledge on anticoagulation. The proportion of patients with good knowledge on anticoagulation from these two studies, though low, is still higher than that which our study showed and can be attributed to differences in the set pass marks and information received by patients during and after hospitalization. In one of these studies, a lower pass mark of 70%was used compared to that in our study which was 75% (Davis et al, 2005). In the other study, patients had received warfarin education sessions conducted by clinical pharmacists and nurses at the time when they were in-patients and some reported receiving post discharge community counseling from pharmacists, general practitioners and other sources such as the internet (Hu et al, 2006).

The knowledge scores from studies in The Far East compare well to those from our study as sufficient knowledge was found in less than 20% of the patients (Tang et al, 2003; Yahaya et al, 2009; Matalaqah et al, 2013). The latter study revealed that only 11.2% had adequate knowledge and tallies with our findings (Matalaqah et al, 2013). This is possibly due to the fact that the study design was similar to ours and that they also used the OAK test by Zeolla et al, 2006.

On the contrary, three studies have illustrated a substantial proportion of patients having adequate knowledge on anticoagulation (Khudair et al, 2010; El-Naby et al, 2014; Mayet et al, 2015). In one of these, 76% of the patients had satisfactory knowledge before the implementation of an education program (El-Naby et al, 2014). However, the pass mark was quite low at 60% and if we applied the same to our study, we may get a similar picture. This study also used in-patients who had undergone cardiac surgeries, while in our study, participants had varied indications for the use of warfain. The other two studies used fewer questions to test knowledge while we used fifteen. In addition, 83% of patients in one of these studies had received previous warfarin education (Khudair et al, 2010).

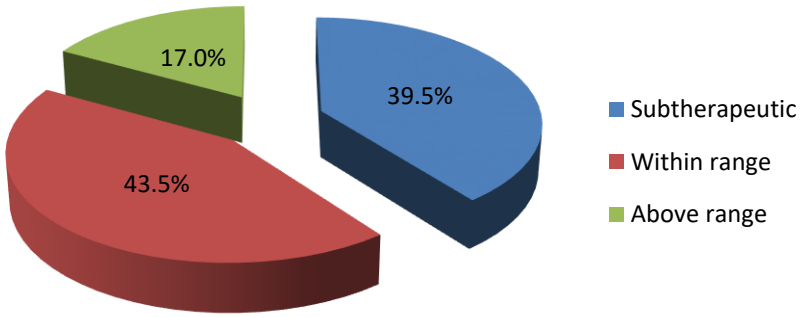

Figure 2: Proportion of participants with subtherapeutic, therapeutic or supratherapeutic INR values

Table 4: Association between patient factors and level of anticoagulation control

Variable		INR values		P value
		Out-of- range; n (%)	In range; n (%)	
Age group (years)	18-37	29(19.7)	22(15.0)	0.748
	38-57	44(30.0)	37(25.2)	
	> 57	8(5.4)	4(2.7)	
Gender	Male	15(10.2)	23(15.6)	**0.014**
	Female	68(46.3)	41(27.9)	
Marital status	Single	20(13.6)	22(15.0)	0.384
	Married	55(37.4)	38(25.9)	
	Separated	4(2.7)	1(0.7)	
	Divorced	3(2.0)	4(2.7)	
Level of education	Informal level	0(0.0)	1(0.7)	**0.001**
	Primary	29(19.7)	17(11.6)	
	High school	43(29.3)	21(14.3)	
	College	10(6.8)	26(17.7)	
Monthly Income (Kenya Shillings)	<10,000	32(21.8)	31(21.1)	0.294
	10,000-30,000	39(26.5)	28(19.0)	
	>30,000	6(4.1)	11(7.5)	
Indication for OAT	Heart disease	16(10.9)	10(6.8)	**0.035**
	VTE	46(31.3)	25(17.0)	
	Valves replacement	20(13.6)	30(20.4)	
Duration of OAT	< 3 months	7(4.8)	5(3.4)	0.081
	3 months – 1 year	24(16.3)	10(6.8)	
	> 1 year	51(34.7)	50(34.0)	
Knowledge score	≥ 75%	57(38.8)	76(51.7)	0.794
	< 75%	7(4.8)	7(4.8)	
Adherence	High	35(23.8)	42(28.6)	0.834
	Medium/Low	32(21.8)	38(25.9)	
Smokes	Yes	1(0.7)	2(1.4)	0.412
	No	83(56.5)	61(41.5)	
Alcohol consumption	Yes	5(3.4)	3(2.0)	0.727
	No	79(53.7)	60(40.8)	
Stressed recently	Yes	39(26.5)	23(15.6)	0.191
	No	45(30.6)	40(27.2)	
Family members supportive	Yes	66(44.9)	61(41.5)	**0.025**
	No	16(10.9)	4(2.7)	
Feel therapy is/will be helpful	Yes	77(52.4)	61(41.5)	0.461
	No	4(2.7)	5(3.4)	
Financial implications of therapy	Not serious	10(6.8)	6(4.1)	0.734
	Manageable	39(26.5)	30(20.4)	
	Very costly	33(22.4)	29(19.7)	

VTE – venous thromboembolism; OAT – oral anticoagulation therapy

Patients in our study generally understood the effect of warfarin in the management of their conditions, the significance of INR testing, the effect of alcohol on anticoagulation treatment and the action to be taken in case one missed a dose. The most frequently failed questions covered drug and food interactions, effect of missing a dose, interpretation of INR values and recognition of symptoms of over or under dosing warfarin. A similar pattern in knowledge has been documented in other studies whereby the highest scores were recorded in the indication for warfarin and the least scores recorded in interaction of warfarin and detection and management of adverse effects (Taylor et al, 1994; Yahaya et al, 2009; Khudair et al, 2010; Mayet et al, 2015). It can be interpreted that these least understood aspects are more scientific in nature and unless these are explained to patients in a structured way such as through booklets or warfarin education

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sessions, the patients may not be informed. These poorly understood aspects represent potential starting points for re-education of patients and primary education for new patients seen at our hospital. Pharmacists, being the drug experts, should be encouraged to take up this role and provide this information during medication counseling.

Our study found that having higher formal education resulted in higher warfarin knowledge scores. This is consistent with previous studies that concluded that illiteracy is associated with inadequate knowledge on treatments received by patients, and consequently to challenges in receiving high-quality care (Hu et al, 2006; Yahaya et al, 2009; Khudair et al, 2010; Matalaqah et al, 2013; Mayet et al, 2015). Therefore, as the country develops and more people get access to tertiary education, we expect individuals to be more informed about their health status.

In our study, indication for warfarin was statistically significantly associated with knowledge on anticoagulation. Those who were taking warfarin for prophylaxis of thromboembolism after undergoing heart valve replacement were the most knowledgeable. This finding could be due to the fact that in KNH, it is only this sub-group of patients on anticoagulation that had a warfarin diary. This booklet had brief information about warfarin and spaces to record their INR value whenever a patient came for a clinic appointment. This suggests that this group of patients were more informed as they were more involved in their healthcare by virtue of having a documented indicator of their progress.

In our study, patients that had been previously married were more likely to have higher knowledge than those that were currently married or never been married at all. This finding is in contrast to a previous study that reported married patients to have higher knowledge (Matalaqah et al, 2013). In that study however, only patients with atrial fibrillation were used while in our study, patients with all indications for anticoagulation were included. It could also be that in our set up, having a spouse hinders one from informing oneself through reliance on the partner. That the freedom or the need to survive and make it after separation pushes individuals, to enlighten themselves on matters that would otherwise have been left in the hands of their spouses.

We found that 43.5% of patients on warfarin at KNH had therapeutic INRs. Although this figure is still low, it represents an improvement from a previous study done in this hospital (Ogendo, 2000). The reason for this is most likely the fact that we used the cross-section-of-the-files method in calculating time in therapeutic range (TTR) with each patient having only one INR value used, while the other study used the Rosendaal method that has been reported to underestimate TTR (Schmitt et al, 2003). It could also be that the awareness brought forth by theis study led to an improved approach in managing patients on warfarin. Our finding contrasts some other studies which showed that more than 75% of their study participants had poor anticoagulation control (Davis et al, 2005; Yahaya et al, 2009). These studies however had far much smaller sample sizes. Two studies which employed a similar study design to ours had results consistent to ours with 41% and 33% of their patients, respectively, having INRs within range (Khudair et al, 2010; Mayet et al, 2015).

Independent predictors of poor anticoagulation control in our study were female gender and lower education. There is limited support for these observations in literature. One study reported female gender as being associated with over anticoagulation (Cadiou et al, 2008). Patient knowledge was not found to contribute to poor anticoagulation control. Previous studies that have examined the relationship between knowledge and anticoagulation control have yielded conflicting results. Small positive correlations between knowledge and number of INRs in range were observed in two studies (Tang et al, 2003; Matalaqah et al, 2013). In another study however, no association was found between knowledge and optimal anticoagulation control (Mayet et al, 2015). In a case-control study in Italy, the odds ratio of INR instability was significantly higher in those who had poor comprehension of anticoagulation therapy (Palareti et al, 2005b). Another study reported improved INR values after education sessions, but this study was conducted only in the elderly (Khan et al, 2004). The comparability of each of these studies is limited because each one utilized a unique study design, patient population and instruments to evaluate knowledge and TTR.

The key limitation to our study was that we measured only one INR value per patient to determine anticoagulation control. Secondly, we relied mostly on patients' self-reports and as common with cross-sectional interviewing studies, participants may over or under-state their experiences.

5. Conclusion

Anticoagulation control in KNH is inadequate, and female gender and lower education level were predictors of poor anticoagulation. Further studies are needed to confirm our observations.

Knowledge on anticoagulation therapy in patients on warfarin at KNH is poor. The identified weak areas should form potential starting points for patients' education on anticoagulation.

Conflict of Interest Declaration

The authors declare no conflict of interest.

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