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FACTORS INFLUENCING WARFARIN DOSE AND RESPONSE AMONG KENYAN PATIENTS ON LONG-TERM ANTICOAGULATION THERAPY

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ABSTRACT

Background: Warfarin dosing is challenging because of its narrow therapeutic range and large between patient dose-response variability. **Main Objective:** To assess the factors influencing warfarin dosing and response among Kenya patients on long-term anticoagulation therapy. **Methods:** This was a descriptive cross-sectional study. Sociodemographic and clinical information on primary diagnosis, warfarin doses, duration of therapy and medication history were collected from 180 adult patients on long-term (≥28days) warfarin therapy. Data analysis was done using IBM statistical package for social sciences version 23 computer software at $p \leq 0.05$. **Results:** The main clinical indication of warfarin treatment was venous thrombosis at 56.6%. The mean initial and maintenance daily warfarin doses were 6.03mg (±4.90) and 6.17mg (±2.75), respectively. For every unit increase in the initial warfarin dose, participants with spouses were receiving 0.749 higher dose than those without spouses (β=0.749; 95% CI: 0.078 to 1.420, p=0.0287). Participants suffering from cardio-embolic diseases required statistically significant lower initial warfarin doses than those presenting with other clinical indications of anticoagulation (β=-1.15; 95% CI: -2.203 to -0.099, p=0.0320). In addition, half of the male patients were adequately anticoagulated and almost 70% of the females had out-of-range international normalized ratios (p=0.0173). The odds of females being therapeutically anticoagulated was 0.408 (OR=0.408; 95% CI: 0.188 to 0.883; p=0.0229). **Conclusion:** Warfarin dose and response among Kenyan patients is influenced by sex, marital status and clinical diagnosis of anticoagulation. Large prospective studies are required to find out other factors such as the impact of genetic polymorphisms among patients on warfarin dose and response.

KEYWORDS: Warfarin response, Warfarin dose, International Normalized Ratio, Kenyan patients.

1. INTRODUCTION

Owing to its proven efficacy and affordability, warfarin is the most commonly preferred and widely used oral anticoagulant particularly in resource-poor countries.[1,2] Warfarin has been shown to be effective in the prevention of thromboembolism events in patients with atrial fibrillation,[3] prosthetic heart valves, venous thrombosis as well as prevention of death in patients with acute myocardial infarction.[4,5]

Warfarin treatment is challenging because of its narrow therapeutic index and large inter-individual and between population dose-response variability.[6] The internationally recommended initial daily dose of warfarin is 10mg as has been suggested from studies in the Western communities,[4] but patient-specific factors such as age, comorbidities, nutritional status, and drug interactions should be taken into consideration prior to deciding a commencing dose.[7–9] Previous studies indicated age[10] and body mass index[11] as important determinants of warfarin dose requirements.[7–11] Literature has indicated the importance of ethnicity in determining warfarin dose requirements partly due to genetic variations,[12,13] with black patients requiring the highest daily dose, Whites requiring intermediate daily dose while Asians requiring the lowest daily dose of warfarin.[14,15]

Factors that influence warfarin dose-response are well characterized in Asians, European ancestry and African Americans and, a well-defined and validated population-specific warfarin dosing algorithms have been established for maintenance dose prediction,[16–19] but data from sub Saharan African population is scarce. The limited available reports from Africa indicate relatively poor anticoagulation outcomes,[19–22] which is continuing, when compared to European countries.[23,24] This has resulted in suggested ways forward including development and validation of warfarin monitoring tools.[25]

Anticoagulation therapy remain an unmet clinical need in Sub-Saharan Africa due to challenges in monitoring warfarin dose-response[22,25] and the high cost of the alternative non–vitamin K oral anticoagulants.[26–28] The present study was therefore, aimed at characterizing clinical characteristics of patients and their relationship with the warfarin dose requirements and INR levels among adult outpatients on long-term anticoagulation management in the leading hospital in Kenya. The objective being to provide future guidance to improve anticoagulation among patients in Kenya and wider community. If there are problems at this leading hospital in Kenya, these will be echoed in other clinics throughout Kenya. This study also builds on previous publications in Kenya[29–31] as well as across Africa including Botswana, Namibia, South Africa and Uganda.[19,21,22,32]

2. MATERIALS AND METHODS

2.1. Study Area and Site

This was a descriptive cross-sectional study. It was undertaken at Kenya's largest tertiary health facility, Kenyatta National Hospital (KNH). Study participants were enrolled from three specialized anticoagulation clinics: cardiothoracic, hemato-oncology and cardiac as well as the Central Health Records Department. The anticoagulation clinics were the main entry point for patients requiring anticoagulation services in the country. The cardiac clinic served participants suffering from cardiac problems including atrial fibrillation while the hemato-oncology centre served patients suffering from malignancies and thrombotic events. The cardiothoracic clinic attended to participants who underwent cardiac valve corrective surgery and required long-term oral anticoagulation therapy.

2.2 Study Population

This involved outpatients aged ≥18 years that underwent long-term anticoagulation management at KNH. Patients were eligible if they had been on warfarin for at least one month, without contraindications such as peptic ulcer disease or uncontrolled hypertension. Both males and females were eligible but participants had to sign a written informed consent to participate. Pregnant mothers and participants with mental health issues were excluded. Pregnant mothers were not invited to participate because they were presumed not to be taking warfarin due to the possible teratogenicity in the first semester and risk of haemorrhagic complications during delivery. Patients with mental health issues were not included because it could have required the consent of the caregivers and participants were expected to provide self-informed consent for the study.

2.3 Sample Magnitude and Selection Method

The major study outcome was response to warfarin as measured by INR values (2-3). For the present study, we defined INR of 2-3 as therapeutic because related studies had also used similar therapeutic ranges.[31,33] Furthermore, similar local studies had indicated that the commonest clinical indications of warfarin anticoagulation were venous thromboembolic disorders whose target INR is 2-3.[30,34] Previous studies had indicated that approximately 14 % of the patients on anticoagulation therapy were able to maintain therapeutic INR.[35] In another study, therapeutic INR values were maintained by 10% patients on warfarin.[33] Using the average (12%) of proportions from the two studies, and the Cochran formula for epidemiological surveys, we estimated the least sample size of 162 patients. A sample size of 162, would allow us to detect 12% of the participants in the population who achieve INR target, with 5% precision and 95% confidence. However, to provide for data losses and those who may fail to respond, a 10% was added to make approximately 180 participants who were used for the study.

All participants who met the inclusion criteria had an equal chance of being included in the study and therefore, random sampling procedure was used. On the morning of the clinic day, the files for booked patients were retrieved from the Central Health Records and Information Department of the hospital to identify patients that met the study inclusion criteria. These files were then tagged with coloured stickers for ease of identification and tracking to avoid loss or duplication of data. There were approximately 3-9 eligible participants each day and random selection was made by tossing the coin such that only those who got the tails participated in the study. This sampling procedure continued till the estimated sample was attained.

2.4 Study Methods

Study authorization was sought and acquired from KNH/University of Nairobi-Ethics and Research Committee (KNH/UoN-ERC) vide reference number **KNH-ERC/A/569**. Raw data was extracted into structured tool in a one-on-one interview with patients and review of medical records. Every data collection tool had a distinct alphanumeric number to avoid confusion and duplication of data. The questionnaire was organized in sections capturing demographic data including age, gender, height, weight, marital status, highest level of academic achievement, employment status, and recreation activities. The second part of the questionnaire comprised of details of warfarin use such as duration of warfarin therapy, initial and maintenance doses, clinical indications of anticoagulation and concomitant medications. This was based on previous related studies.[29–31]

Participants who signed the consent declaration form and successfully taken through the questionnaire were escorted to the KNH bleeding centre for the blood sample collection for the determination of INR. Approximately 4mL of blood was drawn aseptically, put in citrate laced bottles (Chengdu Rich Science Industry Co. Ltd, Germany) and taken to the Department of Hematology and Blood Transfusion, UoN, Laboratory for the determination of INR.

2.5 Statistical Analysis

A database was created into the IBM Statistical Package for Social Sciences (IBM SPSS) version 23 computer software where all the data entry, cleaning and analyses were done. Descriptive statistics were used to survey the general distribution of the hypothesized factors. The outcomes were also examined by calculating the means, median, standard deviations and range for continuous variables and frequencies for categorical data.

The exposure variables in our analysis were predictor variables contained in the questionnaire. Consequently, all the sociodemographic variables including the marital status of patients were analyzed to find whether they influenced warfarin dose and INRs. Exploration of data was undertaken to ascertain the distribution of the study variables as well as detect outliers or abnormally entered values. In addition, computations of proportions were performed for categorical variables. This analysis revealed that BMI could be dichotomized into ≤25 and above 25 based on the reasonable proportions of participants falling into each category. The same was undertaken for the participants' ages, including those falling into ≤50 years and >50 years.

For ease of determining any the relationships between the predictor and outcome variables, patients were grouped into two categories according to their clinical indications for warfarin anticoagulation. Patients suffering from rheumatic heart disease, atrial fibrillation or who had corrective valve surgery were all grouped as "heart diseases". Participants suffering from venous thromboembolic events including deep vein thrombosis and pulmonary thrombotic events were all grouped as "Venous Thromboembolic Events (VTEs)". Only 2 patients had transient ischemic attacks and were left out during inferential statistics. The association between the outcome variables (Warfarin Dose and INRs) and predictor variables including marital status and clinical conditions were conducted by statistical tests of analysis of variance (ANOVA), student-t-tests, Pearson's chi square or Fischer's exact tests.

In order to adjust for potential confounders impacting on the outcome variable, and to identify independent determinants of dose and response to warfarin therapy, variables significant at bivariate analysis were subjected to multivariate regression, achieved using generalized linear models. For outcomes measured in a continuous scale (Dose and INR), the models used an identity link while for those with binary measures, a logit link was used. Beta (β) coefficients and odds ratios (ORs) were computed to determine the strengths of associations investigated. For all data analyses the confidence limit was set at 95%.

3.0: RESULTS

A total of two hundred and seventeen patients were screened for the study. However, thirty-seven patients were ineligible because of various reasons including age below 18 years/declined to participate (n=9), had contraindications to warfarin therapy (n=6), and were not regularly using warfarin as required (n=7). Fifteen patients were left out because they had no data in the records. Data from 180 participants were subsequently analyzed. Table 1 shows the demographics of the study patients.

Patients were aged 43.4 (±13.2) years, with a range of 19-87 and more than half (55.5%) were aged between 31-50 years. Almost three-quarters of the study participants were females, two-thirds were married and half had body mass indices above >25. Patients had been on warfarin for a median duration for approximately two years. The mean commencing dose of warfarin was 6.03mg (±4.90). The maintenance dose was 6.17mg (±2.75) (**Table 1**).

Table 1: Socio-demographics of the study participants (N=180)

Variable	Category	Frequency (N=180)	Percentage (%)
Sex	Males	42	23.0
	Females	**138**	**77.0**
Age categories(years)	19-30	31	17.2
	31-50	**100**	**55.5**
	51-64	37	20.6
	65 and above	12	6.7
Body Mass Index	≤25	58	32.2
	>25	90	50.0
Marital status	Single	39	22.0
	Married	**118**	**66.0**
	Divorced	11	6.0
	Widowed	12	7.0
Employment status	Unemployed	55	31.0
	Salaried	53	**29.0**
	Self employed	**64**	**36.0**
	Student	8	4.0

Highest academic level	College/ University	35	**19.0**
	Secondary	**81**	**45.0**
	Primary	41	23.0
	Non-formal	23	13.0
Denomination	Protestant	86	**48.0**
	Catholic	84	**47.0**
	Muslim & others	10	5.0
Co-Prescribed Drugs	Yes	81	**45.0**
	No	99	55.0
Warfarin Prescribed (mg)	Mean commencing dose	6.03 (SD±4.90)	
	Mean maintenance dose	6.17 (SD±2.75)	
Duration of Warfarin Therapy(Days)	Median (range)	753 (SD 31-11433)	
Key: SD- Standard Deviation			

Figure 1 shows the clinical indications for warfarin anticoagulation therapy. Over half (54.4%) of participants were using warfarin due to deep vein thrombosis and 33.3% had undergone major surgeries. Other patients were using warfarin because of rheumatic heart disease (9.4%), atrial fibrillation (5.6 %) pulmonary embolism (2.2 %) and stroke (1.1%) (**Figure 1**).

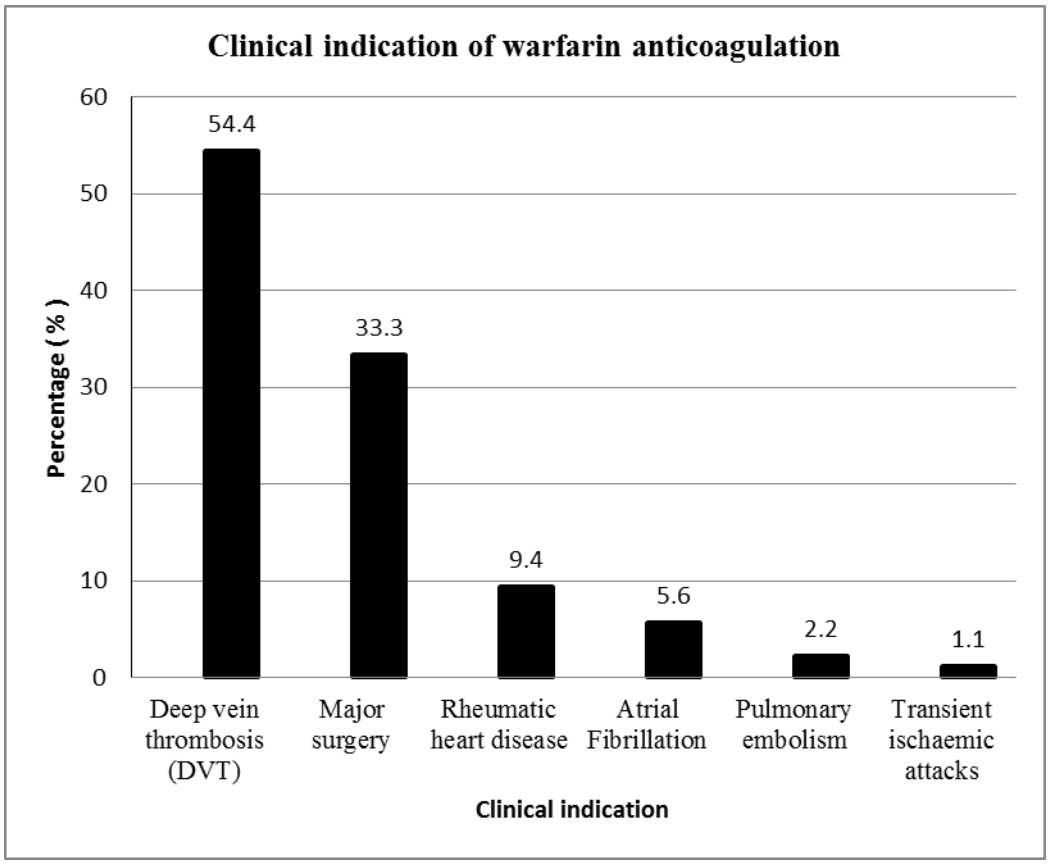

Figure 1: Clinical indications for warfarin therapy among the study participants (N=180)

**Major surgeries included heart surgery such as aortic, mitral or double valve replacement. Atrial fibrillation included the associated conditions such as thrombus in the heart, dilated cardiomyopathy, constrictive pericarditis, ischemic heart disease and heart failure.*

Associations between the sociodemographic variables and determined INRs are shown in **Table 2**.

Table 2: Relationship between demographic features and the level of INR.

Variable	Category	INR; In-range	INR; Out- of-Range	Group differences
		n (%)	n (%)	
Sex	Male	20(51.3)	19(48.7)	$\chi^2_{(1, 164)}$=5.67; P=0.0173
	Female	38(30.4)	87(69.6)	
Age	≤ 50 years	41(34.7)	77(65.3)	$\chi^2_{(1, 164)}$=0.07; P=0.7902
	>50 years	17(37.0)	29(63.0)	
Body mass index	Underweight/Normal	16(32.0)	34(68.0)	$\chi^2_{(1, 134)}$=1.24; P=0.2650
	Overweight/Obese	35(41.7)	49(58.3)	
Marital status	Without Spouse	16(26.7)	44(73.3)	$\chi^2_{(1, 164)}$=3.13; P=0.0768
	With Spouse	42(40.4)	62(59.6)	
Employment status	Non-Regular Income	46(38.7)	73(61.3)	$\chi^2_{(1, 164)}$=2.05; P=0.1519
	Regular Income	12(26.7)	33(73.3)	
Highest academic level	Below Secondary	19(31.7)	41(68.3)	$\chi^2_{(1, 164)}$=0.57; P=0.4517
	Secondary and Above	39(37.5)	65(62.5)	
Denomination	Christian	54(35.1)	100(64.9)	$\chi^2_{(1, 164)}$=0.10; P=0.7518
	Muslim and Others	4(40.0)	6(60.0)	
Tobacco use	No	55(35.0)	102(65.0)	$\chi^2_{(1, 159)}$=1.07; P=0.3007
	Yes	0(0.0)	2(100.0)	
Alcohol Use	No	50(34.0)	97(66.0)	$\chi^2_{(1, 158)}$=0.59; P=0.4423
	Yes	5(45.5)	6(54.5)	

Key: INR-International Normalized Ratio

Half of the male patients had therapeutic anticoagulation responses and almost 70% of the females had poor responses (out-of-range INRs) to warfarin therapy (p=0.0173). Similar proportions of patients with out-of-range INRs were observed in those aged ≤ 50 years and the older counterparts. Approximately two-fifths of patients either living with their spouses, or who were obese/overweight, had therapeutic INR response; however, this was not statistically significant. In addition, three-fifths of non-regular income earners, and those who were educated from secondary level and above, had poor responses to warfarin therapy (**Table 2)**. In addition, compared to males, there were higher proportions of females with sub-therapeutic and supra-therapeutic levels of INRs (**Table 3**).

Table 3: Association between participants' sociodemographic characteristics and warfarin response as measured by INRs.

Variable	Category	INR Level			Group Differences
		<2	2-3	>3	
		n (%)	n (%)	n (%)	
Sex	Male	16(41.0)	**20(51.3)**	3(7.7)	$\chi^2_{(2, 164)}$=6.45; **P=0.0398**
	Female	64(51.2)	38(30.4)	23(18.4)	
Age	50 and Below years	59(50.0)	41(34.7)	18(15.3)	$\chi^2_{(2, 164)}$=0.27; P=0.874
	Above 50 Years	21(45.7)	17(37.0)	8(17.4)	
Body mass index	Underweight/Normal	29(58.0)	16(32.0)	5(10.0)	$\chi^2_{(2, 134)}$=4.78; P=0.092
	Overweight/Obese	33(39.3)	35(41.7)	16(19.0)	
Marital status	Without Spouse	32(53.3)	16(26.7)	12(20.0)	$\chi^2_{(2, 164)}$=3.45; P=0.178
	With Spouse	48(46.2)	42(40.4)	14(13.5)	
Employment status	Non-Regular Income	55(46.2)	46(38.7)	18(15.1)	$\chi^2_{(2, 164)}$=2.06; P=0.358
	Regular Income	25(55.6)	12(26.7)	8(17.8)	
Highest academic level	Below Secondary	31(51.7)	19(31.7)	10(16.7)	$\chi^2_{(2, 164)}$=0.57; P=0.753
	Secondary and Above	49(47.1)	**39(37.5)**	16(15.4)	
Denomination	Christian	74(48.1)	54(35.1)	26(16.9)	χ^2 (2, 164)=2.03; P=0.363
	Muslim and Others	6(60.0)	**4(40.0)**	0(0.0)	
Tobacco use	No	78(49.7)	55(35.0)	24(15.3)	χ^2 (2, 159)=2.21; P=0.331
	Yes	1(50.0)	0(0.0)	1(50.0)	
Alcohol Use	No	73(49.7)	50(34.0)	24(16.3)	χ^2 (2, 158)=0.76; P=0.684
	Yes	5(45.5)	5(45.5)	1(9.1)	

Key: INR-International Normalized Ratio

The covariates of initial and maintenance warfarin doses prescribed are shown in **Table 4**.

A significant relationship was found between the mean initial warfarin doses prescribed and the patients' marital status. Furthermore, for every unit increase in the initial warfarin dose, participants with spouses were receiving 0.749 higher dose than those without spouses (β=0.749; 95% CI: 0.078 to 1.420, p=0.0287)**.** Similarly, participants suffering from heart diseases required statistically significant lower initial warfarin doses than those presenting with other clinical indications of anticoagulation (β=-1.15; 95% CI: -2.203 to -0.099, p=0.0320) (**Table 4**).

Table 4: Covariates of warfarin doses among the study population.

Variable `	Category	Maintenance Doses of Warfarin(mg)				Initial Doses of Warfarin(mg)			
		Bivariate Analysis		Multivariate analysis		Bivariate Analysis		Multivariate Analysis	
		Beta Coefficient (95% C.I)	p-value	Beta Coefficient (95% C.I)	p-value	Beta Coefficient (95% C.I)	p-value	Beta Coefficient (95% C.I)	P-value
Sex	Male	Ref.		Ref.		Ref.			
	Female	-0.681(-1.513 to 0.151)	0.1088	-0.864(-1.823 to 0.095)	0.0774	-0.281(-1.043 to 0.481)	0.4701		
Age	50 years and Below	Ref.				Ref.			
	Above 50 Years	-0.108(-0.904 to 0.688)	0.7905			-0.154(-0.883 to 0.576)	0.6800		
Body mass index	Underweight/Normal	Ref.		Ref.		Ref.			
	Overweight /Obese	0.597(-0.230 to 1.424)	0.1572	0.548(-0.347 to 1.442)	0.2304	0.015(-0.717 to 0.747)	0.9672		
Marital status	Without Spouse	Ref.		Ref.		Ref.			
	With Spouse	0.702(-0.038 to 1.441)	0.0628	0.578(-0.275 to 1.434)	0.1862	0.749(0.078 to 1.420)	**0.0287**	0.640(-0.032 to 1.311)	0.0620
Employment status	Non-Regular Income	Ref.				Ref.			
	Regular Income	0.357(-0.423 to 1.138)	0.3698			0.086(-0.626 to 0.799)	0.8120		
Education Level	Below Secondary	Ref.				Ref.			
	Secondary and Above	0.111(-0.632 to 0.855)	0.7691			0.106(-0.569 to 0.781)	0.7581		
Religion	Christian	Ref.				Ref.			
	Muslims and Others	-0.427(-2.051 to 1.197)	0.6063			0.262(-1.218 to 1.742)	0.7287		
Tobacco use	No	Ref.				Ref.			
	Yes	-1.019(-4.416 to 2.377)	0.5565			1.505(-1.531 to 4.540)	0.3313		
Alcohol Use	No	Ref.				Ref.			
	Yes	-0.290(-1.722 to 1.143)	0.6919			-0.065(-1.348 to 1.219)	0.9214		
Comorbidities	No	Ref.				Ref.			
	Yes	0.021(-0.707 to 0.748)	0.9558			0.304(-0.357 to 0.966)	0.3673		
Heart Diseases	No	Ref.				Ref.			
	Yes	-0.558(-1.270 to 0.155)	0.1250	-0.437(-1.314 to 0.440)	0.3290	-0.821(-1.463 to -0.179)	0.0122	-1.151(-2.203 to -0.099)	0.0320
Venous Thromboembolic Events	No	Ref.				Ref.			
	Yes	0.293(-0.465 to 1.051)	0.4483			0.503(-0.184 to 1.191)	0.1511	-0.580(-1.693 to 0.533)	0.3072

Co-prescribed medications	None	Ref.				Ref.			
	≥1 drug	-0.020(-0.734 to 0.694)				-0.031(-0.680 to 0.619)	0.9267		

Key: CI-Confidence interval

The study further sought to find the associations between the clinical variables and warfarin response as shown in **Table 5.**

Table 5: Covariates of therapeutic anticoagulation among the study population.

Variable	Category	INR value(in-range)			
		Bivariate analysis		Multivariate analysis	
		O.R(95% C.I)	p-value	O.R(95% C.I)	p-value
Sex	Male	Ref.		Ref.	
	Female	0.415(0.199 to 0.865)	0.0189	0.408(0.188 to 0.883)	0.0229
Age	50 years and Below	Ref.			
	Above 50 Years	1.101(0.542 to 2.236)	0.7903		
Body mass index	Underweight/Normal	Ref.			
	Overweight/Obese	1.518(0.727 to 3.168)	0.2662		
Marital status	Without Spouse	Ref.		Ref.	
	With Spouse	1.863(0.931 to 3.727)	0.0787	1.803(0.866 to 3.756)	0.1153
Employment status	Non-Regular Income	Ref.		Ref.	
	Regular Income	0.577(0.271 to 1.230)	0.1545	0.459(0.203 to 1.038)	0.0616
Highest academic level	Below Secondary	Ref.			
	Secondary and Above	1.295(0.660 to 2.539)	0.4522		
Denomination	Christian	Ref.			
	Muslims and Others	1.235(0.334 to 4.565)	0.7521		
Tobacco use	No	Ref.			
	Yes	0.000(0.000 to 0.000)	0.9997		
Alcohol Use	No	Ref.			
	Yes	1.617(0.470 to 5.558)	0.4458		
Comorbidities	No	Ref.		Ref.	
	Yes	0.659(0.335 to 1.299)	0.2285	0.633(0.307 to 1.305)	0.2154
Heart Diseases	No	Ref.		Ref.	
	Yes	1.452(0.763 to 2.763)	0.2554	1.382(0.691 to 2.765)	0.3606
Venous Thromboembolism Disorders	No	Ref.			
	Yes	0.906(0.464 to 1.770)	0.7729		
Co-prescribed medications	None	Ref.			
	≥1 drug	1.217(0.640 to 2.314)	0.5484		

Key: CI-Confidence interval; O.R-Odds ratio

A statistically significant relationship was exhibited between sex and therapeutic INRs, with more females likely to have out-of-range INRs. The odds of females presenting with therapeutic INR was approximately 0.4 times that of males (OR=0.415; 95% CI: 0.199 to 0.865, p=0.0189). On multivariate analysis, compared to males, the odds of females being therapeutically anticoagulated was 0.408 (OR=0.408; 95% CI: 0.188 to 0.883; p=0.0229) (**Table 5**).

4.0: DISCUSSION

The present study has characterized the clinical characteristics that influence warfarin dose and response among Kenyan patients on oral anticoagulation therapy. The study population comprised of married (66.0%) and relatively middle-aged patients; mean age of 43.4(±13.2) years receiving anticoagulation therapy, with female preponderance at 77.0%. Related local studies on anticoagulation using Vitamin K antagonists have yielded similar findings of middle-aged persons and female majority.[29–31,36,37] African studies have yielded similar findings of young persons and female predominance.[19,21,22] Western countries have revealed a female preponderance as well as a more elderly population.[38] This is probably due to differences in the clinical indications of anticoagulation between European and African countries. The finding may be suggest that being of female gender predisposes patients to developing thrombotic disorder than the male counterparts as has been found in related studies[39] and the young population may warrant more investigation and care because it is the economically productive age group.

Significant relationship was revealed between marital status and initial doses of warfarin prescribed, with

patients living with spouses receiving higher warfarin doses compared to those without spouses (p=**0.0287**). The present study observed that majority (~75%) of patients with spouses had diagnoses of VTEs and as such, required higher doses than those with heart diseases. It has been established in other related studies that a diagnosis of VTEs was associated with higher warfarin dose requirements.[40] Furthermore, patients suffering from heart diseases received a statistically significant lower initial warfarin doses than other participants (p=0.0122). Importantly, for every unit of warfarin dose required by patients with VTEs, participants with heart diseases required 1.15 times less (β= -1.151; 95% CI: -2.203 to -0.099, p=0.0320). This finding is supported by a study among the Egyptians patients suffering from pulmonary embolism who were found to receive statistically significant higher warfarin maintenance doses.[41]

Bivariate analysis on factors impacting on adequate anticoagulation revealed that the proportion of males who were adequately anticoagulated was statistically significantly more than females (51.3% vs. 30.4%; p=0.0173). Furthermore, the odds of females who were therapeutically anticoagulated was 0.4 times that of males (OR=0.408; 95% CI: 0.188 to 0.883; p=0.0229). Although there is scarce scientific explanation to this finding, related studies have indicated that female patients are a risk factor for over-anticoagulation using vitamin K antagonists.[38,42] In addition, our findings corroborate another Kenya study which has shown that there were statistically significant proportions of females who are either over-anticoagulated[30] or with out-of-therapeutic ranges INRs.[31,36,43] Previous related studies on the outcome of management of coagulation disorders among the South African communities have indicated that males have better outcome than females.[20] Other related studies have also indicated that females are less likely to be therapeutically anticoagulated.[44]

A greater proportion of participants (BMI>25) were therapeutically anticoagulated compared to those with BMI≤25 (41.7% vs. 32.0 %). In contrast, one study indicated that higher BMI values are associated with under-anticoagulation.[45] This finding suggests that there were other factors such as knowledge and adherence as suggested in related studies[25,30,36] that are associated with INR within the therapeutic range.

The major limitation was that the INRs were measured only once and given how variable it can be, one measurement may not be a good measure of whether a person is in therapeutic range or not. Another constraint of the present research was the cross-sectional nature and therefore, what was observed at the time of study may not be occurring throughout the year. In addition, for unclear reasons, some participants declined to be interviewed even after consenting to participate into the study.

5.0 CONCLUSION

Health care workers should be aware that warfarin dosing and response among Kenyan patients on anticoagulation therapy may be influenced by gender, marital status, body mass index and clinical indications. Therefore, Kenya, like any other country requires validated protocols to improve on warfarin anticoagulation. However, we recommend other studies on the role the genetic variability in warfarin dosing and response among Kenyans.

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Author's Contribution

The idea was conceived by DGN who wrote the protocol with the help of GOO, ANG and EA. Data was collected and analysed by DGN and ANG. ANG and GOO participated in interpretation of the data. All authors reviewed and approved the final manuscript for publication.

Conflict of interest

There is no conflict of interest among the authors.

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