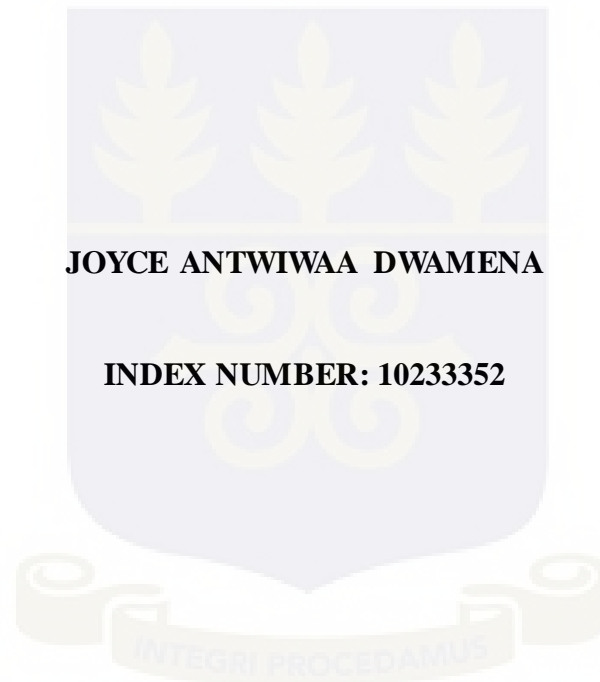


**UNIVERSITY OF GHANA, LEGON  
COLLEGE OF HEALTH SCIENCES  
SCHOOL OF NURSING**

**KNOWLEDGE LEVEL AND ANTICOAGULATION CONTROL AMONG PATIENT ON  
WARFARIN THERAPY AT THE NATIONAL CARDIOTHORACIC  
CENTER, KORLE BU TEACHING HOSPITAL**



**This dissertation is submitted to the University of Ghana, Legon in partial fulfillment of the requirement for the award of MSc Nursing degree.**

**JULY, 2012**

**DECLARATION**

I declare that except for references to literature sources which have been duly acknowledged, this work is entirely the outcome of my own research, and that it has not been partly or wholly presented elsewhere for another degree.

Name of student: Joyce Antwiwaa Dwamena

Signature: .....

Date: .....

We the under listed accept this Dissertation as conforming to the required standard.

Name of Supervisor: Mrs. Cecilia Eliason

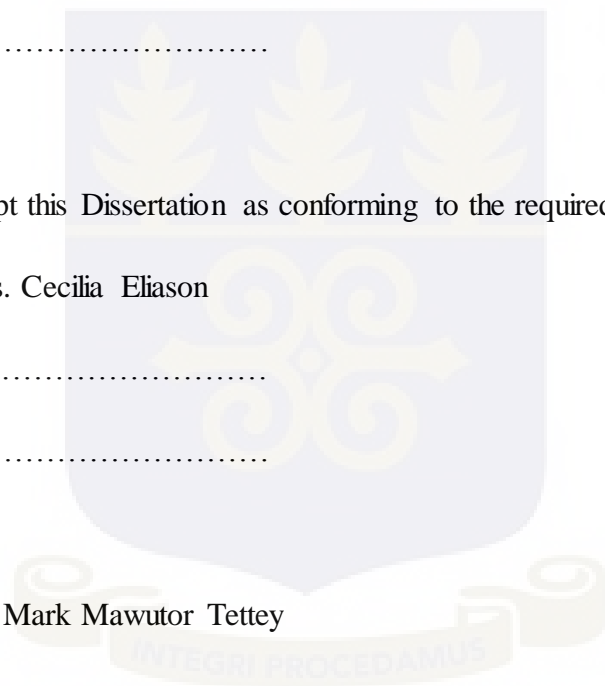
Signature: .....

Date: .....

Name of Supervisor: Dr. Mark Mawutor Tettey

Signature: .....

Date: .....



## **DEDICATION**

This work is dedicated to my sweet mother Mrs. Grace Dwamena, for her great love and support.



## ACKNOWLEDGEMENT

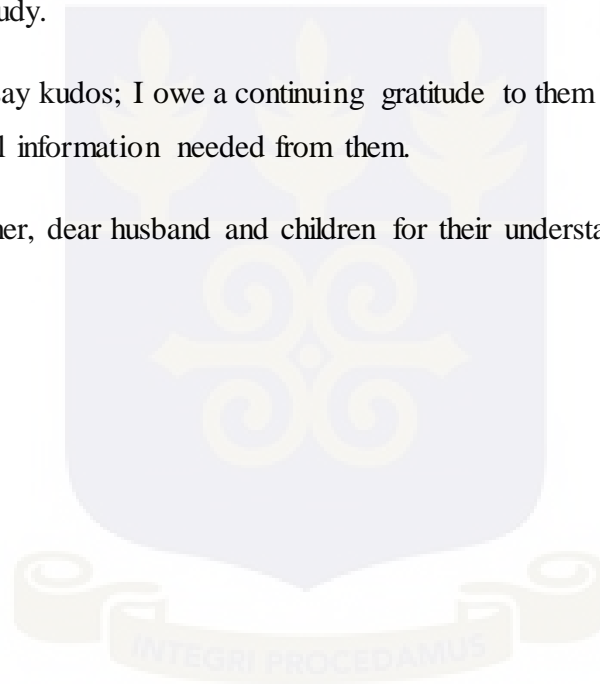
I thank the God for the wisdom and strength giving me to go through this study. My appreciation also goes to Dr. Mrs. Patience Aniteye, of the school of Nursing, for the instructions and guidance given before the commencement of this research.

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To all the respondents I say kudos; I owe a continuing gratitude to them for their endurance and willingness to disclose all information needed from them.

Finally, to my elder brother, dear husband and children for their understanding, support, and care. I say thank you.



**TABLE OF CONTENTS**

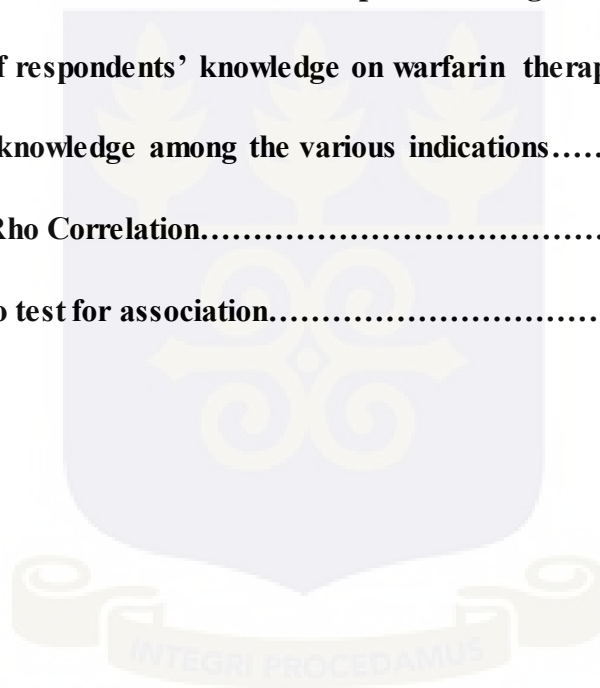
<b>Declaration:</b> .....	<b>i</b>
<b>Dedication:</b> .....	<b>ii</b>
<b>Acknowledgement:</b> .....	<b>iii</b>
<b>Table of Contents:</b> .....	<b>iv</b>
<b>Lists of Tables:</b> .....	<b>vi</b>
<b>Abstract:</b> .....	<b>ix</b>
<b>CHAPTER ONE- INTRODUCTION</b> .....	<b>1</b>
1.0 Background Information .....	1
1.1 Problem Statement .....	4
1.2 Purpose of the study .....	4
1.3 Objectives of the study .....	4
1.4 Research questions .....	5
1.5 Relevance of the Study .....	5
1.6 Operational definitions .....	5
<b>CHAPTER TWO- LITERATURE REVIEW</b> .....	<b>7</b>
2.0 Introduction.....	7
2.1 Definition of the Warfarin Therapy.....	7
2.2 Clinical Practices of Warfarin Therapy.....	8

2.3 Patients Knowledge on Anticoagulation with Warfarin.....	12
2.4 Challenges faced by patients on warfarin therapy.....	14
2.5 Patient warfarin knowledge and anticoagulation control.....	14
2.6 Education Strategies for Improving Patients’ Knowledge about Warfarin.....	16
2.7 Conclusions.....	17
<b>CHAPTER THREE- METHODOLOGY .....</b>	<b>18</b>
3.0 Introduction .....	18
3.1 Research design .....	18
3.2 Research setting .....	18
3.3 Target population .....	20
3.4 Sample size and sampling technique .....	20
3.5 Data gathering tool .....	20
3.6 Analysis of data .....	21
3.7 Reliability and Validity.....	22
3.8 Ethical consideration .....	22
3.9 Limitation to the study.....	23
<b>CHAPTER FOUR-ANALYSIS OF DATA.....</b>	<b>24</b>
4.0 Introduction.....	24
4.1 Demographic information of respondents.....	24

4.2 Information received by respondents.....	26
4.3 Source of information.....	28
4.4 Respondents knowledge about anticoagulation.....	29
4.5 Correlation of knowledge and INR control.....	30
4.6 Test of Associations .....	37
<b>CHAPTER FIVE-DISCUSSION OF FINDINGS.....</b>	<b>38</b>
5.0 Introduction.....	38
5.1 Demographic information of respondents.....	38
5.2 Information received by respondents.....	39
5.3 Source of information.....	40
5.4 Respondents knowledge about anticoagulation.....	41
5.5 Summary and conclusion.....	43
5.6 Implications of findings for nursing practice.....	43
5.7 Recommendations.....	44
<b>REFERENCES.....</b>	<b>46</b>
<b>APPENDIX A INFORMATION SHEET.....</b>	<b>55</b>
<b>APPENDIX B CONSENT FORM.....</b>	<b>57</b>
<b>APPENDIX C QUESTIONNAIRE.....</b>	<b>59</b>
<b>APPENDIX 11 LETTER OF PERMISSION.....</b>	<b>65</b>

**LIST OF TABLES**

<b>Table 1---Demographic characteristics.....</b>	<b>25</b>
<b>Table 2---Clinical details and general health status.....</b>	<b>27</b>
<b>Table 3---Reponses on information received and source.....</b>	<b>29</b>
<b>Table 4—Responses of knowledge on warfarin therapy.....</b>	<b>30</b>
<b>Table 5—Responses of conditions associated with poor anticoagulation control.....</b>	<b>31</b>
<b>Table 6—Correlation of respondents’ knowledge on warfarin therapy.....</b>	<b>32</b>
<b>Table 7—Responses of knowledge among the various indications.....</b>	<b>34</b>
<b>Table 8—Spearmans’ Rho Correlation.....</b>	<b>35</b>
<b>Table 9---Chi- square to test for association.....</b>	<b>36</b>



## LIST OF ACRONYMS

**INR: ---International normalizes ratio**

**AF:--Atrial fibrillation**

**OPD;--Out-patient Department**

**SPSS: ----Statistical package for social sciences**



## ABSTRACT

Warfarin (vitamin K antagonist) is effective for the management of thromboembolic disorders. However, continued use of warfarin is challenged by its complex pharmacology and inherent risk of adverse outcomes which needs drug monitoring to ensure safe and effective therapy. The purpose of the study is to examine the knowledge of anticoagulation and its relationship with international normalized ratio control among patients, after discharge from hospital. A cross sectional survey was conducted at the National Cardiothoracic Center and one hundred and seventy-five (175) respondents were randomly selected. Data was analyzed using SPSS version 16.0. Questionnaires were administered to determine the demographic characteristics, clinical details and knowledge of warfarin therapy. Medical records were reviewed to determine anticoagulation control over a period of six weeks. Findings revealed that 51% of respondents were females and 42.9% were males, with a mean age of  $37.6 \pm 7.5$  years. Eighty eight point six percent of the respondents had been on warfarin for more than four months. Fifty one point two percent had good knowledge on how warfarin works whilst more than 80% of the respondents knew about the side effects of warfarin therapy. There was a significant correlation between level of knowledge and anticoagulation control. In conclusion, the study revealed that respondents had adequate knowledge on warfarin and it was related to international normalized ratio control. There were concerns about cost of regular blood test and medications.

## CHAPTER ONE

### INTRODUCTION

#### 1.1 Background

Warfarin, a Vitamin K antagonist is currently the most widely prescribed oral anticoagulant in the world and remains the main oral anticoagulation medications for the prevention and treatment of various cardiac, thrombotic conditions and hypercoagulable diseases (Cabral, Ansell & Hylek, 2011).

It has been the mainstay oral anticoagulant agent for the last several decades despite its narrow therapeutic index and difficulties in its use (Nutescu & Wittkowsky, 2004). Warfarin has become a successful agent for the medical management of thromboembolic diseases such as chronic atrial fibrillation, mechanical heart valve replacement, deep vein thrombosis, pulmonary embolism, and valvular heart disease, among others (Stephanie, Panayiotis et al. 2003). This has led to a dramatic increase in the number of patients receiving warfarin therapy and those who are referred to anticoagulation clinics (Yahaya, Hassali, Awaisu & Shafie 2009).

Warfarin was initially introduced in 1948 as a pesticide against rats and mice and is still popular for this purpose although more potent poisons such as brodifacoum have since been developed. In the early 1950s warfarin was found to be effective and relatively safe for preventing thrombosis and embolism in many disorders. It was approved for use as a medication in 1954 and has remained popular ever since; warfarin is the most widely prescribed oral anticoagulant drug in North America (Holbrook, Pereira, Labiris et al. 2005).

Although alternative agents have recently become available for the management of thromboembolic complications, they are not without risks and are associated with significant treatment cost, which is why warfarin remains a primary therapeutic option (Mannucci & Franchini, 2011). The continued use of warfarin is challenged by its complex pharmacology and inherent risk of adverse outcomes when dosage is not regulated. It has become necessary that routine therapeutic drug monitoring is undertaken to ensure safe and effective therapy (Mannucci and Franchini, 2011).

Warfarin has a narrow therapeutic window and requires frequent monitoring and dose adjustments to maintain its optimal anticoagulation effect through monitoring of the patient's international normalized ratio (INR) (Nutescu, Chuatrisorn & Hellenbart, 2011).

Warfarin therapy is aimed at decreasing clotting tendency of blood, but not to prevent clotting completely. Therefore, the coagulability of blood must be carefully monitored when a person is on warfarin. The dose of warfarin is adjusted, based on the results of periodic blood tests, to maintain the clotting time within a target range (Gage, Fihn, & White 2000).

The most commonly used test to measure the effect of warfarin is the prothrombin time (PT). It is particularly sensitive to the clotting factors affected by warfarin. PT is also used to compute a value known as the INR (or International Normalized Ratio). The INR expresses the PT in a standardized way; this ensures that results obtained by different laboratories can be reliably compared (Gage, Fihn, & White 2000).

The longer it takes the blood to clot, the higher the PT and INR. The target INR range depends upon the clinical situation. In most cases the target INR range is between 2 to 3, although higher or lower values may be used depending on special circumstances (Ansell, Jacobson, Levy, et al. 2005)

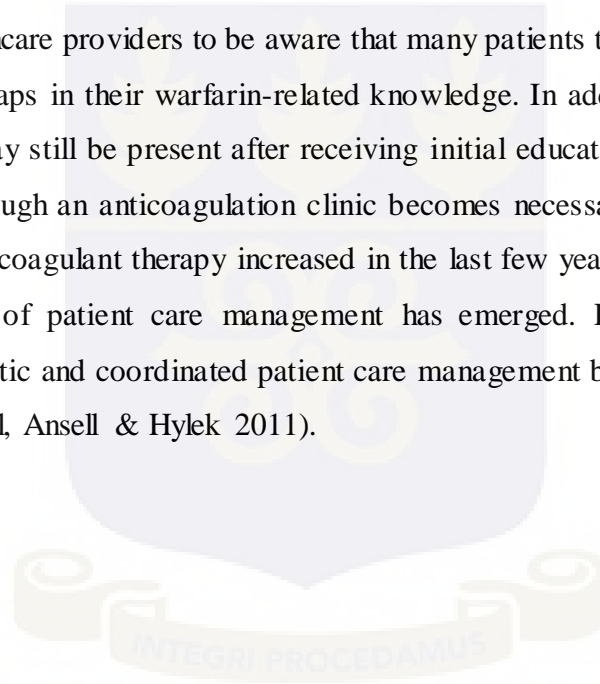
If the INR is below the target range (under-anticoagulated), there is a risk of clotting. If, on the other hand, the INR is above the target range (over-anticoagulated), there is an increased risk of bleeding.

In healthy people, the INR is about 1.0. For most patients on warfarin therapy, the INR range is between 2.0 and 3.0 and patients with mechanical heart valves on Warfarin, the range is between 2.5 and 3.5. These ranges are general recommendations. The aim of monitoring the patient's international normalized ratio (INR) is to minimize the risk of thromboembolic events without increasing the risk of bleeding complications (Fang et al., 2006). Serious adverse events are most likely to occur when the INR is outside the therapeutic range. Factors contributing to such fluctuations in INR are patient non-compliance and warfarin-drug interactions (Tang Lai, Lee, Wong, Cheng, Chan, et al., 2003).

Wysowski, Nourjah and Swartz (2011) reported that warfarin is among the top (ten) 10 drugs with the largest number of serious adverse events reported during the last two decades. It has become very necessary for patients on warfarin to be counselled and educated on its adverse

effects as to ensure safe and effective treatment. Besides, patient education is also one of the principal patient's rights. Tang, Lai, Lee, Wong, Cheng, Chan, et al. (2003) suggested that patient's knowledge on warfarin therapy has an important impact on anticoagulation control. As such, patients who use warfarin should receive an educational session at the beginning of the therapy to ensure that the medication is taken correctly. Barcellona, Contu & Marougm (2002) illustrated that adequate education concerning anticoagulation therapy resulted in a more effective and stable treatment. Pirmohamed, James, Meakin, Green, Scott, Walley et al. (2004) confirmed that adherence to medical treatment is enhanced by the knowledge and understanding of the medication, its benefits, and side-effects.

It is important for healthcare providers to be aware that many patients taking oral anticoagulants might have significant gaps in their warfarin-related knowledge. In addition, patients may have unsafe beliefs, which may still be present after receiving initial education on warfarin therefore frequent monitoring through an anticoagulation clinic becomes necessary (Khudair & Hanssens, 2010). As the use of anticoagulant therapy increased in the last few years, the need for advanced educational preparation of patient care management has emerged. Effective anticoagulation therapy requires systematic and coordinated patient care management by trained anticoagulation therapy providers (Cabral, Ansell & Hylek 2011).



### **1.1 Problem Statement**

Patients who were on long term anticoagulation with warfarin were often faced with issues regarding their treatment. The continued use of warfarin was challenged by the complex pharmacology and inherent risk of adverse outcomes hence adequate knowledge on warfarin was very important. Patients who were on warfarin had to be counselled on the ‘do’s and ‘don’ts’ of the medication. This necessitated the attachment of a clinical pharmacist to the National Cardiothoracic Center to ensure that patients had adequate knowledge prior to warfarin treatment before discharge. The education given was ultimately to prevent any complication that might occur as a result of warfarin use.

Nonetheless, some patients who were managed on warfarin from 2007 to 2011 were observed to have reported with clotted valve, bleeding, missed abortion, cerebrovascular accident and recurrent of embolism which was an indication of non-compliance or adherence to the warfarin treatment.

The periodic blood test done to adjust the dose of warfarin and to maintain the clotting time within the target range was observed not to be carried out by some of the patients leading to complications such as bleeding from over coagulation or thrombosis from under coagulation. Although the warfarin education was well established in the center, there is no information related to the determinants of this knowledge after discharge.

The study was therefore designed to determine the knowledge of warfarin treatment and compare with anticoagulation control among patients on warfarin after discharge.

### **1.2 Purpose of the Study**

The purpose of this study is to examine anticoagulation knowledge and its relationship with international normalized ratio (INR) control among patients on warfarin after discharge.

### **1.3 Objectives of the study**

- To determine the level of knowledge of patients on warfarin therapy.
- To determine the effectiveness of warfarin education on anticoagulation control of patients.
- To determine the relationship between patient warfarin knowledge and anticoagulation control.

- To identify the challenges patient faced.

#### 1.4 Research Questions

- What is the level of knowledge of patients on warfarin therapy?
- What is the effectiveness of education given to patients on warfarin therapy?
- What is the relationship between patient's knowledge and anticoagulation control?
- What are the challenges faced by patients on warfarin?

#### 1.5 Significance of the Study

The study added to the body of knowledge of patients on warfarin and evaluates current patient knowledge as a first step to improve the quality of anticoagulation therapy and patient care.

In the long term be a document for the source of information on the level of knowledge of patient who is on warfarin, to encourage a new approach, and focus attention on interventions to promote patients knowledge and improve adherence to warfarin therapy and to prevent complications.

#### 1.6 Operational definition

**Anticoagulants:** are usually administered to patients with myocardial infarction, venous thrombosis, prosthetic valve, peripheral arterial emboli and pulmonary emboli. They have been used to prevent transient ischemic attacks and to reduce the risk of recurrent myocardial infarction.

**Warfarin:** (also known under the brand names Coumadin, Jantoven, Marevan, Lawarin, Waran, and Warfant) is an anticoagulant normally used in the prevention of thrombosis and thromboembolism.

**International Normalized Ratio (INR):** A calculation made to standardize prothrombin time and this is based on the ratio of the patient's prothrombin time and the normal mean prothrombin time.

**Therapy:** (in Greek: θεραπεία), or treatment, is the attempted remediation of a health problem, usually following a diagnosis. In the medical field, it is synonymous with the word "treatment".



## CHAPTER TWO

### LITERATURE REVIEW

#### 2.0 Introduction

The study reviewed previous studies worldwide in relation to the subject matter. Literature was also reviewed from scientific databases such as Pubmed, Science Direct, Hinari, Biomed Central, JSTOR and Oxford Journal. Keywords and phrases such as Warfarin Therapy; clinical practices of warfarin therapy, patients knowledge on anticoagulation with warfarin, challenges faced by patients on warfarin therapy and the role of patients' knowledge in improving the anticoagulation control on the Warfarin therapy were used. Results of the search were then used in discussing the literature review.

#### 2.1 Definition of the Warfarin Therapy

Warfarin, a vitamin K antagonist, is an oral anticoagulant indicated for the prevention and treatment of venous thrombosis and its extension and the prevention and treatment of the thromboembolic complications associated with atrial fibrillation.

Warfarin has also been used to decrease the tendency for thrombosis or as secondary prophylaxis in those individuals that have already formed a blood clot. Warfarin treatment can help prevent formation of future blood clots and help reduce the risk of embolism (American Society of Health System Pharmacist 2011), thromboembolism or in those with atrial fibrillation (AF) or prosthetic heart valves. The type of anticoagulation for which warfarin has been best suited, is that of slowly-flowing blood, such as in veins and pooled in dysfunctional cardiac atria. Common clinical indications for warfarin use are atrial fibrillation, the presence of artificial heart valves, deep venous thrombosis, and pulmonary embolism. Warfarin is also used in antiphospholipid syndrome and has been used occasionally after heart attacks (myocardial infarctions), but is far less effective at preventing new thromboses in coronary arteries. Prevention of clotting in arteries is usually undertaken with antiplatelet drugs, which act by a different mechanism from warfarin (Hirsh, Fuster, Ansell & Halperin 2003).

Despite its effectiveness, treatment with warfarin has several shortcomings. Many commonly used medications and some foods (fresh plant-based foods containing vitamin K) interact with warfarin. The activity of the drug is monitored by using the international normalized ratio (INR) results from the laboratory to ensure an adequate and safe dose (Ansell, Hirsh, Poller, Bussey, Jacobson & Hylek 2004). A high INR predisposes to a high risk of bleeding, while an INR below the therapeutic target indicates that the dose of warfarin is insufficient to protect against thromboembolic events.

The International Normalized Ratio (INR) is the indorsed method for reporting results for the control of anticoagulation (Baglin, Keeling, Watson, 2005). The management of deep vein thrombosis, pulmonary embolism and patients with one or more mechanical heart valves and other heart related diseases involves the use of anticoagulants, which have the potential for complications such as bleeding and heparin- induced thrombocytopenia (Haines, 2008).

## **2.2 Clinical Practices of Warfarin Therapy**

Beginning warfarin therapy is challenging, since the pharmacodynamics response is delayed and hard to predict. Because prothrombin has a half-life of around 50 hours, loading doses of warfarin are of limited value (Dager, Branch, King, White, Quan, Musallam & Albertson, 2000). Prior to initiating warfarin treatment, it is important considering contraindications which are relative to a patient's risk for thrombosis then weighed against the risk for bleeding while on vitamin K antagonist anticoagulation therapy. This is closely followed by using International Normalized Ratio, which forms the bases of drug administration. (Burnett et. al, 2009).

According to (Holbrook, Pereira, Labiris, et al. 2005) dosing of warfarin is complicated by the fact that it is known to interact with many commonly-used medications and even with chemicals that may be present in certain foods, and stated that, these interactions may enhance or reduce warfarin anticoagulation effect. In addition, (Hirsh, Fuster, Ansell & Halperin 2003) noted that in order to optimize the therapeutic effect without risking dangerous side effects such as bleeding, close monitoring of the degree of anticoagulation is required by blood testing (INR). During the initial stage of treatment, checking may be required daily; intervals between tests can be lengthened if the patient's therapeutic INR level remains stable on an unchanged warfarin dose.

Ansell, Hirsh, Hylek, et. al., 2008, showed that, the optimal maintenance dose for warfarin to enable a therapeutic INR differs from patient to patient and at different times in the same patient and there is no maximal or minimal dose to maintain a therapeutic range.

Linkins, Choi and Douketis (2003) draws our attention to attaining optimal anticoagulation which is clearly important in protecting patients against hemorrhagic and thromboembolic events and this is especially important during the first few months of anticoagulant therapy when the risk of hemorrhagic complications is considered greatest.

Baglin, Keeling and Watson (2006) pointed out that, when initiating warfarin therapy, the doctor decides how strong the anticoagulant therapy needs to be. The target INR level vary from case to case depending on the clinical indicators, but tends to be between 2–3 in most conditions and in particular, target INR may be between 2.5–3.5 (or even 3.0–4.5) in patients with one or more mechanical heart valves.

Many dosing procedures for the initiation of warfarin therapy have been developed and in the UK, the most widely published regimen was described by Lenzini, Grice, Milligan, et al. (2008). Other studies suggest using less strong loading doses to avoid dangerous over anticoagulation but even then this may be extreme in over 80% of elderly (>70 years) patients (Garcia, Regan, Crowther, Hughes & Hylek ,2005).

According to Warfarin diet (2011) the maintenance dose of warfarin can fluctuate significantly depending on the amount of vitamin K in the diet. Keeping vitamin K intake at a stable level can prevent these fluctuations. Leafy green vegetables tend to contain higher amounts of vitamin K and typically green vegetables, cabbages, and lettuces are high in vitamin K. Certain vegetable oils have high amounts of vitamin K. Foods that are low in vitamin K include roots, bulbs, tubers, some fruits and fruit juices. Cereals, grains and other milled products are also low in vitamin K. Warfarin is contraindicated in pregnancy, as it passes through the placental barrier and may cause bleeding in the fetus; warfarin use during pregnancy is commonly associated with spontaneous abortion, stillbirth, neonatal death, and preterm birth (Macina, Orest, Schardein & James, 2007). Warfarin is also a teratogen; they are known to cause birth defects. The incidence of birth defects in infants exposed to warfarin in utero appears to be about 5%, although higher figures (up to 30%) have been reported in some studies. Depending on when exposure occurs

during pregnancy, two distinct combinations of congenital abnormalities can arise are deformation of the face (depressed nasal bridge) and bones (stippled epiphyses) Macina, Orest, Schardein & James, 2007.

The only common side effect of warfarin is hemorrhage (bleeding). The risk of severe bleeding is small but definite (a median annual rate of 0.9 to 2.7% has been reported by (Hylek, Evans-Molina, Shea, Henault & Regan, 2007) and any benefit needs to outweigh this risk when warfarin is considered as a therapeutic measure. Risk of bleeding is augmented if the INR is out of range (due to accidental or deliberate overdose or due to interactions), and may cause hemoptysis, excessive bruising, bleeding from nose or gums, or blood in urine or stool.

The risks of bleeding is increased when warfarin is combined with antiplatelet drugs such as Clopidogrel, aspirin, or other nonsteroidal anti-inflammatory drugs ( Hylek , Evans-Molina , Shea , Henault & Regan 2007) and the risk may also be increased in elderly patients on hemodialysis (Delaney , Opatry, Brophy & Suissa,2007).

Warfarin interacts with many commonly used drugs, and the metabolism of warfarin varies greatly between patients. Some foods have also been reported to interact with warfarin (Holbrook, Pereira, Labiris, et al. 2005). Apart from the metabolic interactions, highly protein bound drugs can displace warfarin from serum albumin and cause an increase in the INR (Gage, Fihn, White 2000). This makes establishing the correct dosage difficult, and accentuates the need of monitoring. When initiating a medication that is known to interact with warfarin (e.g. simvastatin), INR checks are increased or dosages adjusted until a new ideal dosage is found.

Many commonly used antibiotics, example metronidazole and the macrolides greatly increase the effect of warfarin by reducing the metabolism of warfarin in the body. Other broad-spectrum antibiotics can reduce the amount of the normal bacterial flora in the bowel, which produce significant quantities of vitamin K, thus potentiating the effect of warfarin (Juurlink, 2007). Several mechanisms have been proposed for this effect, including changes in the rate of breakdown of clotting factors and changes in the metabolism of warfarin (Holbrook, Pereira, Labiris, et al. 2005)

Excessive use of alcohol is also known to affect the metabolism of warfarin and can elevate the INR (Weathermon & Crabb, 1999). Patients are often cautioned against the excessive use of alcohol while taking warfarin.

Warfarin also interacts with many herbs and spices some used in food (such as ginger and garlic) and others used purely for medicinal purposes (such as ginseng and Ginkgo biloba). All may increase bleeding and bruising in people taking warfarin; similar effects have been reported with borage (starflower) oil or fish oils ( Information Pharmacists' news 2008) St.John's Wort, which is sometimes recommended to help with mild to moderate depression, also reduces the effectiveness of a given dose of warfarin by inducing the enzymes that break down warfarin in the body, causing a reduced anticoagulant effect (Barnes 2002).

The effects of warfarin can be reversed with vitamin K, or, when rapid reversal is needed (such as in case of severe bleeding), with prothrombin complex concentrate—which contains only the factors inhibited by warfarin—or fresh frozen plasma (depending upon the clinical indication) in addition to intravenous vitamin K (Crowther, Douketis, Schnurr , et al. 2002)

A separate resource guide, including patient information sheets, is available and should be discussed with the patient at the initiation of warfarin therapy; it is recommended that the prescriber discusses the following with the patient when possible:

- the reason for prescribing warfarin and duration of treatment
- the need to adhere to recommended warfarin dosage
- the importance of monitoring and the patient's target INR
- the need to take their warfarin once a day, preferably at the same time in the evening, and to have their INR test performed in the morning
- side effects, signs of bleeding and potential need for blood products
- set-up an agreed system of communication when side effects or changes occur
- when to call the doctor or seek urgent attention at an emergency facility
- strongly encourage wearing Medic Alert bracelets or necklaces to assist with care in an emergency
- review of current medications (prescription & non-prescription), herbal supplements and diet for potential interactions
- the need for caution when initiating or stopping other medications (including ASA), herbs or supplements
- the use of a daily pill box to assist with improving patient compliance with warfarin therapy
- the importance of consistent vitamin K content in the diet

- the need to avoid heavy or variable alcohol consumption
- the importance of avoiding pregnancy while taking warfarin if applicable
- the importance of not changing brands of warfarin
- the need to avoid intramuscular injections (for flu shots – physicians are recommended to apply firm, prolonged pressure for several minutes after a deltoid injection)

(Adapted from: Baker, Coughlin, Gallus, et al 2004)

### **2.3 Patients Knowledge on Anticoagulation with Warfarin**

Warfarin is more likely to be used safely by a patient who has knowledge on the potential for drug and diet interactions, understands the need for monitoring, and can recognize the signs of over- and under- anticoagulation (Baker, Coughlin, Gallus, et al 2004).

A study by Barcellona, Contu et al. (2002) showed that, good knowledge and understanding of warfarin therapy underpins optimum therapeutic outcomes and a reduction of warfarin related-adverse drug events. In another study, Ansell, Hirsh et al. (2001) found that 85% of patients with good understanding of warfarin had a well controlled and stable INR, compared to 63% in the poor –understanding group. Several studies have revealed that a significant relationship exists between the patients' literacy level and warfarin knowledge (Barcellona, Contu et al.2003, Estrada, Martin-Hryniewicz et al.2004, Wilson, Raane et al.2003).Furthermore, previous studies on evaluation of anticoagulation knowledge resulted in undesirable pass rates. Tang et al. (2003) used a novel survey containing 7 open-ended questions in their study and found out that only 18% of patients achieved a passing score of at least 70%. Davis et al. found that 37% of patients achieved a passing score of at least 70% on a novel 18- question multiple- choice test. Additionally, using a previously created 20- question true or false questionnaire, Hu et al. (2006) found a 39% pass rate, defined as a score of at least 80%. However, using the anticoagulation knowledge assessment (AKA) questionnaire in Alvin C. York anticoagulation Clinic, Baker, Pierce Casey (2011) defined a passing score of at least 72.4% (21 of 29) of questions answered correctly and found out that 74.1% of the patients achieved a passing score. Various studies have been done on knowledge of the complications of warfarin and till now, only few studies have shown an association between the outcomes of anticoagulation therapy and health literacy, anticoagulation and patient education, and anticoagulation and knowledge of warfarin therapy

with mixed results (Barcellona, Contu et al.2003, Estrada Martin-Hryniewicz et al.2004, Wilson, Raane et al.2003).Several studies identified that patients who have been prescribed warfarin often have deficiencies in their warfarin knowledge (Cheah and Martins 2003; Lambert and Wynne 2003; Roche- Nagle, Chambers et al. 2003; Tang, Lai et al.2003).

The aforementioned studies with the exception of Baker et al. (2011) used a different instrument which was not validated to measure the patients' knowledge of warfarin therapy. The challenge has been a suspicion of patients' lack of knowledge of warfarin therapy thereby causing non-adherence and compromising patient safety. Patients taking warfarin may have significant knowledge gaps, particularly concerning drug-drug and drug-food interactions. Kimmel et al (2007) identified that even in anticoagulation clinics where adherence is stressed repeatedly throughout the therapy` poor adherence was exhibited by patients. More importantly, they observed that poor adherence to warfarin therapy was significantly influencing anticoagulation control.

For Davies et al (2005), the frequent blood test monitoring to measure INR may have a negative impact on the quality of life of patients and promote non adherence, and suggested this to be strong challenge in most African settings where the culture of hospital attendance is not a practice and where the patient is too weak to carry himself around without a caregiver. He said patients may stay long at the clinic for their INR measurements, consultation with the physician and dispensing their prescription. For patients with a therapeutic INR, the duration of the prescription may even be longer and may be accompanied by longer clinic visits which may result in reducing overall hospital service load and cost. Rewiuk, Bednarz, Faryan and Grodzkki (2007) in their study also pointed out that, necessity of systematic blood checks, fear of complications caused by treatment, cost of medication and the necessity of taking the medicine everyday were the concerns of the inconveniences associated with chronic anticoagulation.

In lieu of the above factors, Levi et al (2009) advocated for self-testing and self-management of one's warfarin dose. This will allow home testing and might be an alternative for anticoagulation clinics for improving adherence. However, this is only possible in well educated and adherent patients. Currently, the country has no such provisions. Moreover, illiteracy and low educational backgrounds among most settings as well as unbearable cost might frustrate such arrangement.

Notably, the educational level of patients seems to predict a patient's knowledge on anticoagulation therapy.

#### **2.4 Challenges faced by patients on warfarin therapy**

According to Tang et al. (2003), sufficient time between the patient and the healthcare provider is essential to reveal and solve any therapy related inquiry the patient might have. A busy clinic like those in the public hospitals may not allow time for proper counseling. An added factor is patient information retention about warfarin therapy. Fang et al. (2006) reported that with increasing complexity of medical care involving poly-pharmacy and complicated cases, physicians are concerned with lack of time to provide adequate patient education for patients using warfarin. Therefore, failure on the part of the clinics to offer a refreshing educational session completed with handouts to patients on warfarin often may facilitate non-adherence (Fang et al. 2006).

Kagansky, Knobler, Rimon, Ozer and Levy (2004) revealed that counseling patients with respect to their anticoagulant treatment is vital and significantly improves patient's knowledge and quality of anticoagulation.

Baglin, Cousins, Keeling, Perry and Watson (2007) pointed out that, verbal and written information should be provided at the start of the therapy, when patient is discharged from hospital and on the first anticoagulant clinic appointment. In addition, Erban (1999) stated that, booklets aimed at patient education are made available and they are useful supplement to the healthcare provider's advice.

#### **2.5 Patient warfarin knowledge and anticoagulation control**

A survey study by Tang, Lai et al. (2003) to evaluate patients' knowledge on warfarin and its relationship to anticoagulation control showed a positive correlation between patients' warfarin knowledge the number of INR values that was within the target range in the four most recent clinic visits ( $r = 0.20; p = 0.024$ ). However, in a cross-sectional study of patients aged 80 years or older, Kagansky et al (2004) found that, the percentage of INRs within the therapeutic range was

highest among patients with perceived satisfactory education (45%) compared to with those who perceived their education as insufficient (34.9%) or received no education (20.0%,  $P < 0.001$ ). Furthermore, with survey study which sampled 122 patients attending a warfarin clinic, Tang et al. (2003) discovered a positive Pearson correlation between patient knowledge about warfarin therapy and the percentage of INR values within therapeutic goal range ( $r=0.20$ ,  $p= 0.024$ ). Davis et al. (2005) claims that adherence to warfarin therapy was significantly associated with anticoagulation control. Only 14% of patients in the study by Davis et al. (2005) achieved good anticoagulation control, defined as more than 70% of INR values within therapeutic range. Lambert and Wynne (2003) in their study showed that 35% of respondents were aware of alcohol's potential to increase international normalized ratio, whilst 88% knew of the interaction with alcohol.

In a study by Fang, Machtinger et al., (2006), Sixty-one percent of participants had scores indicative of insufficient knowledge of warfarin therapy (score  $\leq 80\%$ ). Age was negatively related to warfarin knowledge scores ( $r = 0.27$ ,  $P = .007$ ). Patients with family incomes greater than \$25,000, who had greater than a grade 8 education, and who were employed or self-employed had significantly higher warfarin knowledge scores ( $P = .007$ ,  $P = .002$ , and  $P = .001$ , respectively). Gender, ethnicity, and warfarin therapy before surgery were not related to warfarin knowledge scores. None of the in-hospital teaching practices significantly influenced knowledge scores, but receiving post discharge community counseling significantly improved knowledge scores ( $P = .001$ ). Multivariate regression analysis revealed that understanding the concept of International Normalized Ratio, knowing the acronym, age, and receiving community counseling after discharge were the strongest predictors of warfarin knowledge. Accessing post discharge counseling resulted in significantly improved warfarin knowledge scores. Because improved knowledge has been associated with improved compliance and control, findings supported the need to develop a comprehensive post discharge education program or at least to ensure that patients have access to a community counselor to compliment the in-hospital education program. This study did not state the design used but the current study used cross-sectional survey. A cross-sectional study by Hassan, Shamala, Basariah et al., (2011) with 156 randomly sampled patients from physician- (non-medication therapy adherence clinic [non-MTAC]) and pharmacist (MTAC)-run anticoagulation clinics using a validated interviewer-administered questionnaire.

Patients' INR readings from 2008 to 2010 were recorded. The results showed that, patients on warfarin scored an average of  $66.5\% \pm 36.0\%$  for their knowledge on how warfarin works  $42.9\% \pm 44.9\%$  for interaction between warfarin and alcohol, and  $49.2\% \pm 21.1\%$  for adverse effects. No significant differences were found between MTAC and non-MTAC patients on their knowledge. There was a negative correlation between patients' knowledge and age ( $P = .001$ ,  $r_s = -.293$ ) and a positive correlation between patients' knowledge and education level ( $P = .001$ ,  $r_s = .365$ ). MTAC patients were found to have better INR control than non-MTAC when compared for mean percentage days in range ( $63.4\% \pm 18.9\%$  vs.  $52.5\% \pm 18.2\%$ ;  $P = .006$ ) and mean percentage visits in range ( $58.8\% \pm 17.9\%$  vs.  $46.8\% \pm 18.6\%$ ;  $P = .001$ )

## **2.6 Education Strategies for Improving Patients' Knowledge about Warfarin**

In recognition of the reported knowledge deficits, several structured and interventional education strategies (for example individualized face-to-face verbal consultations, group-based patient education and other) about warfarin have been evaluated and reported in literature. (Khan, Kamali, Kesteven, Avery, Wynne, 2004).

Interventions and strategies to advance the education of patients taking warfarin have, to date, largely focused on providing individual face-to-face counseling by key healthcare professionals within their respective practice settings (Tang, Lai, Lee, Wong, Cheng, Chan, 2003). This mode of education is most often used because it is convenient, easy to deliver and allows the educator to target the patient's individual requirements (Newall, Monagle, Johnston, 2005)

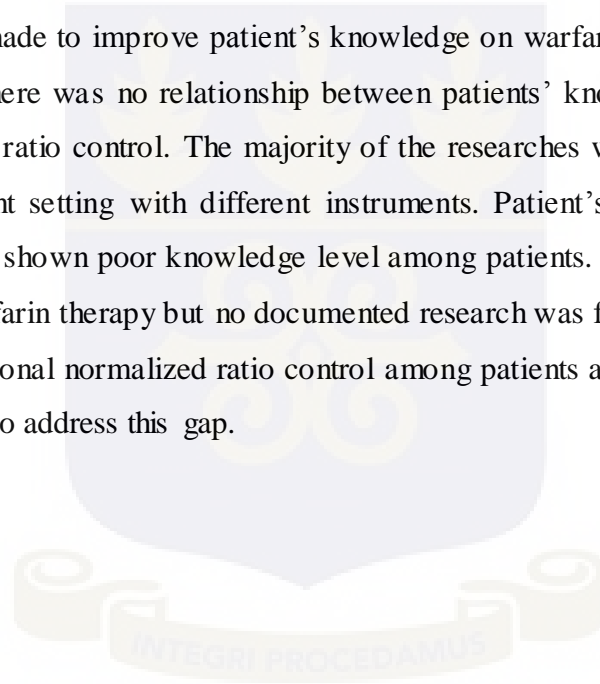
Various literature identified that written warfarin information resources, available as both printed materials and via the internet, could not be read or understood by between 50% to 88% of the older patient population (Estrada, Hryniewicz, Higgs, Collins, Byrd, 2000).

Bajorek, Ogle, Duguid, Shenfield, Krass (2007) further reported that both health professionals and patients perceived existing written information materials to be suboptimal in terms of content regarding day-to-day warfarin management issues, such as interactions with other drugs or foods. Given the suboptimal nature of existing warfarin related written information materials various approaches have been suggested in literature to improve the comprehensibility and usability of these materials (Bajorek et al, 2007).

The use of specially designed written materials that contain relevant figures or images, pictograms, larger font or page size and other formatting elements which could improve the comprehensibility of written materials, especially for older patients, have all been proposed in literature (Estrada, Hryniewicz, et al., 2000).

## **2.7 Conclusions**

From the literature reviewed, many studies were quantitative and explored patient's knowledge on warfarin, and international normalized ratio control. The general conclusion of all these researches has shown deficiencies in patient's knowledge on warfarin therapy. Various suggestions have been made to improve patient's knowledge on warfarin therapy. Some studies have also shown that, there was no relationship between patients' knowledge on warfarin and international normalized ratio control. The majority of the researches were done in the Western countries and in different setting with different instruments. Patient's knowledge on warfarin therapy and results have shown poor knowledge level among patients. A few studies were done in Ghana relating to warfarin therapy but no documented research was found on knowledge level on warfarin and international normalized ratio control among patients after discharge .The study adopted a questionnaire to address this gap.



## **CHAPTER THREE**

### **METHODOLOGY**

#### **3.0 Introduction**

The means of conducting this research are presented in this chapter. These include the research design, study setting, the target population, sampling technique and procedure, sources of data and data collection, quality considerations, data analysis and ethical issues.

#### **3.1 Research Design**

According to Cooper and Schindler (2001), research design is a strategy or plan that promotes systematic management of data collection. Research design also describes how a study is conducted to maximize control over factors that could interfere with the desired outcome of a study (Burns & Grove, 2005). This research is quantitative and it employed a cross-sectional design using a survey. This method was chosen as data was collected on study population at a particular point in time. It is also a descriptive survey because it is designed to measure certain phenomena in a population of interest at a point in time (Bowling, 2009).

The research explored and described the patients' knowledge on warfarin and its relationship with the control of international normalized ratio. It was therefore appropriate to use the descriptive research design to achieve the objectives of the research.

#### **3.2 Research Setting**

The study was conducted at the National Cardiothoracic Centre, Korle-Bu Teaching Hospital. The hospital is located in the Nation's capital, Accra, specifically in the Ablekuma Central Sub - metro District and is 0.5 km from the Korle- Lagoon. It covers an area of about 441 acres. The hospital is the premier and leading national referral hospital. It serves as the foremost training facility for healthcare professions within its various branches including the Nursing and Midwifery Training Colleges, the Public Health School, Peri-operative and Critical Care Nursing

School, Ophthalmic Nursing School, School of Medical Laboratory Technology, the Medical and Dental Schools and School of Allied Health Sciences, Radiography Department.

Korle-Bu Teaching Hospital (KBTH) has a bed capacity of 1,700 with staff strength of 3,500 made of 390 doctors and dentists, 1035 nurses, 40 pharmacists, a number of health service administrators, laboratory technicians and technologists, and biostatisticians and other category of staff. KBTH out-patient average daily attendance is 1,000 patients and average admission is 120 patients. It has 17 clinical departments and centers. These are Obstetrics and Gynaecology, Surgery, Medicine, Radiology as well as Ear, Nose and Throat departments. The others are Hematology, Microbiology, Eye Clinic, Reconstructive Plastic Surgery and Burns, and National Cardiothoracic Centre. The Mission of the Hospital is to provide quality tertiary health care, teaching, research and outreach services.

The National Cardiothoracic Centre is a national resource of excellence for thromboembolic diseases and artificial valve replacement care and training. The National Cardiothoracic Centre was established in 1989 at the Surgical 3<sup>rd</sup> floor and commissioned in 1992. It is situated in the southern part of the hospital. The Centre has various units including, theatre, Intensive Care, ward, diagnostic unit, dialysis unit and the out-patient unit where we have the anticoagulation clinic. The anticoagulation clinic is currently staffed with two cardiologists, four physicians, six cardiothoracic surgeons, seven laboratory technicians and technologists, and ten licensed practicing nurses. The centre runs ambulatory services on Tuesday and Friday by the cardiologists and physicians and on Thursdays by the cardiothoracic surgeons. The unit's average daily Out Patient Department attendance is about 120 old cases and 10 new cases with those on warfarin forming about 40 %. To facilitate care delivery, laboratory services are carried on the premises of the National Cardiothoracic Centre. The testing is performed by staff of the laboratory. This centre is ideal for this study because most of the diseases that require anticoagulation are managed with good results.

### 3.3 Target Population

A target population is the complete totality of all subjects (Polit & Hungler, 2003). The population was the different categories of patients from almost all the regions in Ghana who are on warfarin for more than one month and attended clinic during data collection at the National Cardiothoracic Centre (NCTC). Patients with at least (ten) 10 INR readings from the National Cardiothoracic laboratory prior to the consent date met the inclusion criteria.

### 3.4 Sample Size and Sampling Technique

Systematic sampling was used in data collection. Systematic sampling was easy to use and every member of the population had an equal chance to be chosen (Hunt & Tyrrell, 2001). The sample size was determined by computing the average number of monthly attendance at the anticoagulation clinic into a computerized system. Roasoft sample size calculator was use in calculating the sample size. The size of population was 300; expected frequency was 10%, margin of error  $\pm 5\%$ , confidence level of 95% and response distribution of 50%. This gave a sample size of 169 and 10 was added to make up for errors and non submitted questionnaires giving a new sample size of 179. After the first person was picked, every fifth person after consultation who met the inclusion criteria and agreed to participate was selected and interviewed as participant for the study.

### 3.5 Data Gathering Tool

A previously validated questionnaire by Taylor et al., (1994) was adopted and adapted and used for data collection. The questionnaire had five sections. **Section A** focused on the demographic data of the respondents. **Section B** had questions on clinical details and health status; **Section C** was on admission details. **Section D** was on information patients received on anticoagulant treatment and had yes and clear, or yes but not clear, and no options for patient to tick; and **Section E** contained multiple choice questions in which patients are asked to tick the true or false, and don't know options. Patient's medical records were reviewed for their ten most recent INR readings.

### **3.5.1 Data Gathering Procedure**

Permission was sought from the in-charge of the out-patient department, and the purpose of my visit was explained to her. After seeking informed consent from each participant the questionnaires were self administered and explanations were given where respondents had some difficulties understanding some areas. Thus, oral instructions were given as well as written instructions on the questionnaire, on how to provide responses. Data was collected on Tuesdays, Thursdays and Fridays after patients had gone through their routine checks and had seen the doctor. Each day, a maximum of twelve eligible patients were given questionnaires to complete at the center. Patients who could not read English were assisted by the researcher, informing them in; Twi, Ewe and Ga and those who could not write were also assisted by the researcher. The data was collected over a period of six weeks.

### **3.5.2 Response Rate**

A total of one hundred and seventy five respondents completed and returned questionnaires the same day out of one hundred and seventy nine questionnaires distributed, giving it approximately ninety-eight percent response rate.

### **3.6 Analysis of Data**

Descriptive statistics such as frequency, percentages, means and standard deviations were used to summarize findings from data collected. Association between the independent variables and passing versus failing score, were measured as a binomial, and was assessed using Pearson Chi-Square to test for categorical variables.

The independent variable was level of knowledge and was determined by the score of the questionnaire. The knowledge information profile was made up of 30 true or false questions that are scored as; correct (1point), incorrect (0), or don't know (0). Correctly answering 17 questions or more was needed for determination of adequate knowledge of anticoagulation therapy (passing score).

The dependent variable was INR control, and was defined using 3 different methods, (a) the count of the 10 most recent INR values within the therapeutic goal range (0,1,2,3,), (b) their therapeutic range (TTR) calculated using the Rosendal method and(c) anticoagulation stability measured as the standard deviation (SD) of INR values.

Spearman's Rho correlation analysis was used to assess the relationships between each of the 3 measures of INR control and both measures of anticoagulation knowledge. All statistical analysis was performed using Statistical Package for Social Sciences (SPSS version 16.0). P-value less than 0.05 were interpreted as significant in the study. Content analysis was done to identify themes arising from the open-ended responses and these were paraphrased.

### **3.7 Reliability and Validity**

To ensure reliability and validity a pre-test was done using ten (10) in- patients who were on warfarin therapy at the Medical Department. They were given the questionnaire to provide responses. Minor modifications were done to the questionnaire based on their responses with (reliability coefficient = 0.80).

### **3.8 Ethical Consideration**

Approval of the topic was sought from a committee in the School of Nursing. Again, permission was sought from the Director of Nursing services and the Deputy Director in-charge of the National Cardiothoracic Center of the Korle-Bu Teaching Hospital before the commencement of the study. Verbal informed consent was sought from each respondent. They were given the opportunity to ask questions for further clarification. No coercion was used and the participants were assured of confidentiality.

### **3.9 Limitations of the study**

The researcher was faced with time constraint because it was difficult getting the proposed sample size within a stipulated time, leading to the extension of the period of data collection. Some of the respondents wanted to talk more but there was no interview. Although the measures of knowledge were based on issues highly relevant to warfarin therapy and adapted from previous warfarin study, more in-depth qualitative interviews may provide greater insights into the degree of knowledge and concerns on warfarin therapy.



## CHAPTER FOUR

### 4.0 Introduction

This chapter presents the findings of the study in the form of graphs and tables where appropriate. It has five main sections. The demographic characteristics of patients, their general health status on the anticoagulant treatment, time spent in the ward (National Cardiothoracic Centre), information given to patients on anticoagulant treatment and patients' knowledge on anticoagulant treatment and problems they encounter. Correlation between scores and INR are presented as the final findings.

### 4.1 SECTION A: DEMOGRAPHICS

A total of 179 respondents were selected for the study, with 175 responding to all the study questionnaires (98 % response rate). 100 (57.1%) were females and male to female ratio of participants of the study was 1:33. The mean age  $\pm$  SD of the respondents was  $37.6 \pm 7.5$  years with most of them in 31-45 year-old category. Fifty eight (33.1%) participants were from Volta region forming the majority of the respondents. 115 (65.7%) were full time workers, 23(13.1%) were students and the least 19(10.9%) were retired. Sixty (34.2%) had secondary school education and 23 (13%) had no formal education.

The detailed patient's characteristics are presented in Table 4.1

**Table 4.1: Demographic characteristics**

<b>Patients' characteristics</b>		<b>N=175</b>
<b>Age (years)</b>		
Mean(=SD)	37.6±7.5 years	
< 16	19	9.7%
16-30	35	20.0%
31-45	54	30.9%
46-60	35	20.0%
61-70	31	17.7%
>70	3	1.7%
<b>Gender</b>		
Male	75	42.9%
Female	100	57.1%
<b>Region</b>		
Ashanti	25	14.3%
Brong Ahafo	3	1.7%
Greater Accra	54	30.9%
Volta	58	33.1%
Western	2	1.1%
Eastern	14	8%
Central	12	6.9%
Upper East	1	0.6%
Northern	6	3.4%
<b>Employment</b>		
Full time	115	65.7%
Part time	4	2.3%
Unemployed	8	4.6%
Sick leave	6	3.4%
student	23	13.1%
Retired	19	10.9%

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**Education**

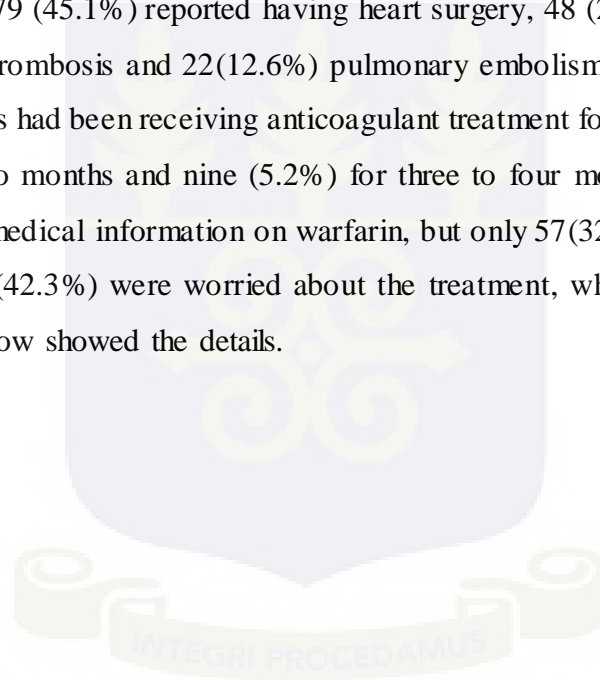
No formal education	23	13.1%
Primary	45	25.8%
Secondary	60	34.2%
Tertiary	47	26.9%

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Field source data: 2012

**4.2 SECTION B: Clinical Details**

Of the 175 participants, 79 (45.1%) reported having heart surgery, 48 (27.4 %) atrial fibrillation, 26 (14.9%) deep vein thrombosis and 22(12.6%) pulmonary embolism. One hundred and fifty-five (88.6 %) participants had been receiving anticoagulant treatment for more than four months. 11 (6.3%) for one to two months and nine (5.2%) for three to four months. Sixty two (35.4%) would have liked more medical information on warfarin, but only 57(32.6%) were able to obtain medical information. 74(42.3%) were worried about the treatment, while 101 patients (57.7%) were not. Table 4.2.1 below showed the details.



**Table 4.2.1 Patients' Clinical details and general health status on anticoagulant treatment (n=175)**

<b>Clinical details &amp; Health status</b>		
<b>status</b>	<b>Frequency</b>	<b>Percentage</b>
<b>Indication for treatment</b>		
Deep Vein Thrombosis	26	14.9
Pulmonary Embolism	22	12.6
Atrial Fibrillation	48	27.4
Heart Surgery	79	45.1
<b>Duration of warfarin therapy</b>		
1-2 months	11	6.3
3-4 month	9	5.2
> 4month	155	88.5
<b>General health status</b>		
Improved	168	96
Worsened	1	0.6
Stayed the same	6	3.4
<b>Desire to seek advice</b>		
Yes	62	35.4
No	113	64.6
<b>Able to seek advice</b>		
Yes	57	32.6
No	118	67.4
<b>Worry about treatment</b>		
worry	74	42.3
Not at all	101	57.7

Field source data: 2012

One question was about the inconvenience associated with warfarin therapy. Of the total number of patients (74) who were worried about warfarin treatment, 24 of the patients (32.4%) stated cost of regular blood tests to monitor warfarin as their main problem, Twenty three (31.1%), taking one drug daily, 15(20.3%), worry about bleeding while taking warfarin, 7 (9.7%) felt they were young when counselled on the drug and 5 (6.7%) missed abortion. This is presented in Table 4.2.2 below.

**Table 4.2.2 Patients' concerns about anticoagulant treatment**

<b>Concerns</b>	<b>No of (%) patients</b>
Cost of regular blood tests to monitor warfarin	24 (32.1%)
Taking one drug at a particular time daily	23 (31.1%)
Worry about bleeding while taking warfarin	15 (20.6%)
Missed abortion	5 (6.7%)
Felt were young when counselled	7 (9.5%)
<b>Total</b>	<b>74</b>

**Field source data: 2012**

#### **4.3 SECTION C: Admission details**

Of all the participants, 133(76%) had been admitted at the study Unit, four (2.3%) at another hospital, six (3.43%) from another department within the hospital and 32(18.3%) were from the study's centre outpatient department.

The 133(76%) were given a red card "Information on anticoagulant treatment". 66 of the patients (49.6%) indicated that the information in the book was just right as presented in the Table 4.3 below.

**Table 4.3 Primary facility of diagnosis and commencement of warfarin therapy (n=175)**

<b>Admission details</b>	<b>No (%) of patients</b>
Admitted at CTU	133 (76)
Admitted at another Hospital	4 (2.3)
From department within the KBTH	6 (2.43)
From Out-patient(CTU)	32 (18.3)
<b>Anticoagulant information booklet</b>	
Given Red card	133(76.0)
Not given red card	42 (24.0)
<b>Status of information in red card</b>	
Too complicated	23(13.1)
Too simple	77 (44.0)
Just right	75 (42.9)
<b>Field source data: 2012</b>	

#### **4.4 SECTION D: Patients' Information Received**

Most patients received clear information on each of the five items. All the 133 in-patients (76%) in the study hospital received clear advice from the clinical pharmacist.

17 (9.7%) of the patients received information from doctors at the anticoagulation clinic and 25(14.3%) from doctors on the ward. This is presented in the Table 4.4 below

**Table 4.4 Patients who received education on aspects of warfarin therapy (n=175)**

<b>Items</b>	<b>No (%) of patients</b>
How warfarin works	152 (86.9)
Action in bleeding/bruising occurs	122 (69.7)
Problems with anticoagulant treatment	143(81.7)
Drugs to avoid	153(87.4)
Alcohol	160(91.4)
<b>Source of information</b>	
Doctors at anticoagulation clinic	17(9.7)
Doctor at the ward	25(14.3)
Pharmacists on the ward	133(76)

**Field source data: 2012**

#### **4.5 KNOWLEDGE ON ANTICOAGULANT TREATMENT**

Most of the patients 90 (51.2%) had accurate knowledge that warfarin “thinned” the blood,

72 (41.1%) of the patients correctly reported that a new treatment could affect anticoagulant treatment, and only 45 (25.7%) of the patients knew that changing the dose of concurrent treatment could also affect anticoagulation. Of the 160 patients (91.4%) that received clear advise on alcohol, 78 (44.5%) knew it could interact with warfarin, 50 (28.6%) could correctly identify an excessive level of alcohol consumption, and 32 (18.3%) patients indicated that alcohol does not affect anticoagulant treatment. This is presented in Table 4.5 below

**Table 4.5 Patient's Knowledge on warfarin therapy (n=175)**

Knowledge domain	Correct Answer N (%)
How warfarin works	90 (51.2%)
Effects of starting new treatments	72 (41.1%)
Effects of changing dose of concurrent treatment	45 (25.7%)
Alcohol	
Alcohol does not affect anticoagulant treatment	30 (17.1%)
Alcohol must be avoided totally	78 (44.5%)
8 units of alcohol a night is ok	2(1.14%)
1 unit of alcohol a night is ok	50(28.6%)
Drugs to avoid	39 (22.3%)

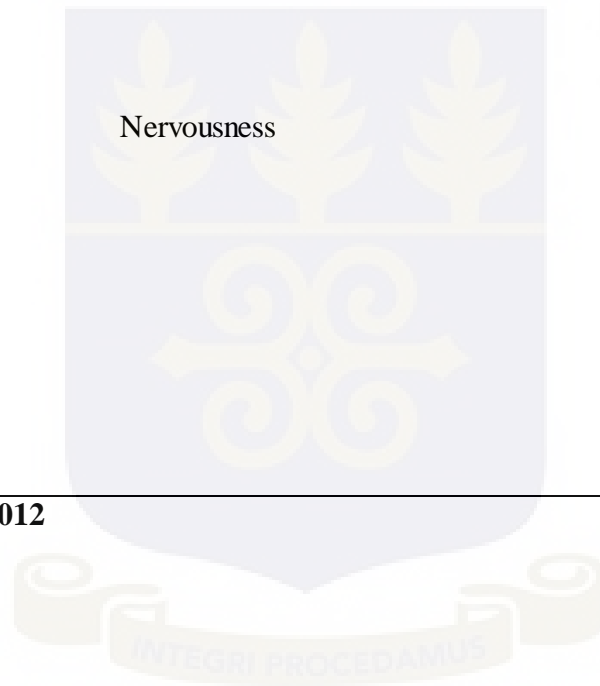
**Field source data: 2012**

Patient's knowledge of the possible side effects of poor control of anticoagulant treatment was generally average and majority 110 (62.8%) could identify nose bleeding, 102 (58.3%) prolonged bleeding and 125 (71.4%) blood clot from the lists of conditions associated with poor control and 35(20.4%) chose one or more of the seven unrelated conditions as presented in Table 4.6 below

**Table 4.6 Patients identified conditions associated with poor control of anticoagulant treatment (n=175)**

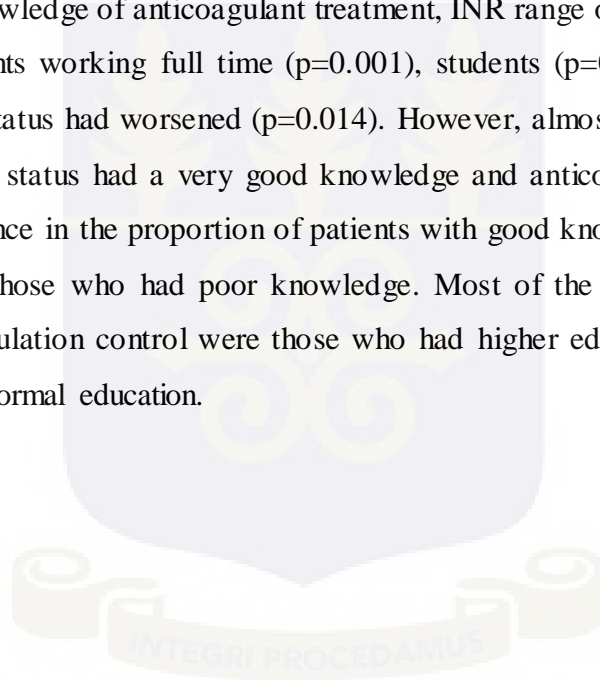
Conditions	No (%) of patients
<b>Associated effects</b>	
Blood in stools	60(34.3)
Nose bleeding	110 (62.8)
Prolonged bleeding	102 (58.3)
Bruising	52 (29.7)
Blood in urine	48 (27.4)
Blood clot	125(71.4)
<b>Non-associated effects</b>	
Nervousness	20 (11.4)
Sleeplessness	12 (6.8)
Weakness	17 (9.7)
Loss of appetite	5 (2.9)
Ringling in the ears	35 (20)
Nausea	3 (1.7)
High blood pressure	6 (3.4)

**Field source data: 2012**



#### **4.5.1 Distributions for knowledge of participants on anticoagulant treatment**

Test of two proportions was used to test for significant difference in the proportion of patients who have adequate knowledge and those who do not have adequate knowledge among selected variables. The findings of the study revealed that patients had a mean INR of  $2.43 \pm 0.62$  and 112 (64%) have good knowledge on anticoagulant treatment. A p-value less than 0.05 were interpreted as statistically significant. There was statistically significant difference in the proportion of participants with good knowledge compared with that of those without good knowledge in terms of males ( $p=0.001$ ), females ( $p=0.001$ ) however more males (58.9%) had better knowledge compared to females (41.1%). 73% of the patients with controlled INR goal range had very good knowledge of anticoagulant treatment, INR range of 2.0-3.0 ( $p=0.004$ ), 2.5-3.5 ( $p=0.010$ ), participants working full time ( $p=0.001$ ), students ( $p=0.038$ ), retired ( $p=0.008$ ) and participants whose status had worsened ( $p=0.014$ ). However, almost all patients 95.5% with improved general health status had a very good knowledge and anticoagulation control. There was a significant difference in the proportion of patients with good knowledge on anticoagulant treatment compared to those who had poor knowledge. Most of the patients with very good knowledge and anticoagulation control were those who had higher education while those with poor knowledge had no formal education.



**Table 4.8 Knowledge of participants on anticoagulant treatment**

	<b>Passed Patients n (112)</b>	<b>Failed Patients N (63)</b>	<b>P- value</b>
<b>Gender</b>			
Male	66 (58.9 %)	9 (14.3%)	0.001
Female	46 (41.1 %)	54 (85.7%)	0.001
<b>INR Goal Range</b>			
2.0-3.0	82 (73.1 %)	25 (39.6%)	0.004
2.5-3.5	22 (19.6 %)	25 (39.6%)	0.010
Other	8 (7.3%)	13 (20.8%)	0.001
<b>Employment</b>			
Full Time	88 (78.6 %)	27 (42.8%)	0.001
Part Time	2 (1.8 %)	2 (3.2%)	0.676
Unemployed	3 (2.7%)	5 (7.9%)	0.137
Sick Leave	2 (1.8%)	4 (6.3%)	0.164
Student	10 (8.9%)	13 (20.6%)	0.038
Retired	7 (6.3%)	12 (19.0%)	0.008
<b>Treatment Status</b>			
Improved	107 (95.5%)	61 (96.8%)	0.736
Worsened	1 (0.9%)	0 (0.0%)	0.014
Stayed the same	4 (3.6%)	2 (3.25)	1.000
<b>Educational level</b>			
None	3 (2.8%)	20 (31.7%)	0.001
Primary	10 (8.9%)	35 (55.65)	0.001
Secondary	55 (49.1%)	5 (7.9%)	0.001
Tertiary	44 (39.2%)	3 (4.85%)	0.001

**Field source data: 2012**

#### 4.5.1 Correlation of Patients' knowledge on warfarin

112 (64%) have good knowledge on anticoagulant treatment. Statistically, there was a significant difference in the proportion of participants with good knowledge compared with that of those without good knowledge in terms of male ( $p=0.001$ ), female ( $p=0.001$ ), INR range of 2.0-3.0 ( $p=0.004$ ), 2.5-3.5 ( $p=0.010$ ), others ( $p=0.001$ ), participants working full time ( $p=0.001$ ), students ( $p=0.038$ ), retired ( $p=0.008$ ) and participants whose status had worsened ( $p=0.014$ ).

**Table 4.8 Knowledge of participants on anticoagulant treatment**

	<b>Passed Patients n (112)</b>	<b>Failed Patients N (63)</b>	<b>P- value</b>
<b>Gender</b>			
Male	66 (58.9)	9 (14.3)	0.001
Female	46 (41.1)	54 (85.7)	0.001
<b>INR Goal</b>			
<b>Range</b>			
2.0-3.0	82 (73.1)	25 (39.6)	0.004
2.5-3.5	22 (19.6)	25 (39.6)	0.010
Other	8 (7.3)	13 (20.8)	0.001
<b>Employment</b>			
Full Time	88 (78.6)	27 (42.8)	0.001
Part Time	2 (1.8)	2 (3.2)	0.676
Unemployed	3 (2.7)	5 (7.9)	0.137
Sick Leave	2 (1.8)	4 (6.3)	0.164
Student	10 (8.9)	13 (20.6)	0.038
Retired	7 (6.3)	12 (19.0)	0.008
<b>Treatment Status</b>			
Improved	107 (95.5)	61 (96.8)	0.736
Worsened	1 (0.9)	0 (0.0)	0.014
Stayed the same	4 (3.6)	2 (3.2)	1.000

**Field source data: 2012**

#### 4.5.2 Knowledge levels of patients among the various indications for anticoagulant treatment

68 (60.0%) of all patients who passed the knowledge test had had heart surgery, followed by atrial fibrillation 24 (21.4%) while the least proportion of 8.9% came from those with Deep Vein Thrombosis and Pulmonary Embolism.

**Table 4.9 Knowledge of patients among reasons for anticoagulant treatment**

Reasons	Knowledge		
	Passed n=112	Failed n=63	Total N=175
<b>Deep Vein Thrombosis</b>	10 (8.9)	16 (25.4)	26 (14.9)
<b>Pulmonary Embolus</b>	10 (8.9)	5 (7.9)	15 (8.6)
<b>Atrial Fibrillation</b>	24 (21.4)	31 (49.2)	55 (31.4)
<b>Heart Surgery</b>	68 (60.0)	11 (17.5)	79 (45.1)
<b>Stroke</b>	0 (0.0)	0 (0.0)	0 (0.0)
<b>Total</b>	112 (64.0)	63 (36.0)	175 (100)

Field source data: 2012

#### 4.5.3 Spearman's Rho Correlation Analysis of Anticoagulant knowledge with INR control

Spearman's Rho correlation (rho) analyses showed significant correlations between total knowledge of participants on anticoagulant and any of the three (3) measures of INR controls in terms of INR values within goal range (rho= 0.346; p=0.013), TTR (rho=0.076; p=0.028), and (rho=0.087; p=0.037) . In sensitivity analyses limited to selected items relevant to INR control, there was a significant correlation between number of correct responses and INR control (rho= 0.456; p=0.021), TTR (rho=0.097; p=0.022), and (rho=0.123; p=0.041)

**Table 4.10 Spearman's Rho Correlation**

	Number Range	in Time Range	in Therapeutic Standard Dev
<b>Total Score</b>	0.346 (0.013)	0.076 (0.028)	0.087 (0.037)
<b>Relevant Score</b>	0.456 (0.021)	0.097 (0.022)	0.123 (0.041)

**Field source data: 2012****4.6 Test of Associations**

Chi-square analysis was performed to establish the existence of any association between selected variables and knowledge level of patients on anticoagulant treatment.

**Table 4.13 Chi-square analysis to test for association between variables and knowledge**

Variables	X <sup>2</sup>	P-value
Sex	2.31	0.894
Age group	11.83	0.034
Educational level	15.41	0.027
Employment Status	1.42	0.926
General Health Status	12.38	0.021
Length on treatment	3.28	0.634
Reasons for treatment	14.76	0.025

Significant at 5%

**Field source data: 2012**

The study revealed statistically significant associations between knowledge on anticoagulant treatment and age group (p=0.034); educational level (0.027); general health status (p=0.021) and reasons for treatment (p=0.025)

## CHAPTER FIVE

### DISCUSSION

#### 5.0 Introduction

The study sought to determine the knowledge level and anticoagulation control of patients on Warfarin Therapy at the Cardiothoracic Centre of the Korle-Bu Teaching Hospital. The study investigated the indication for anticoagulant treatment, general health status of the patients on warfarin, information received on anticoagulant treatment and knowledge of patients on the treatment modalities.

Data was captured from one-hundred and seventy five (175) out patients who met the inclusion criteria and had consented to the study. The patients answered questions pertaining to all the five sections of the questionnaire. Their medical records were also reviewed to access the 10 most recent INRs readings. The study sampled more females (57%) compared to males and the age group with the highest proportion of patients (30.9%) found in the age group 31-45 years and the least (1.7%) was reported in age group above seventy (70) years. Majority of the patients (65.7%) were full time workers. The findings of the study showed that approximately 112(64%) of the participants scored 70% for knowledge and mean INR of  $2.43 \pm 0.62$ . Furthermore, a significant correlation was found between the knowledge level of patients on warfarin treatment and anticoagulation control.

#### 5.1 Patients' clinical details and General Health Status on Anticoagulant Treatments

Patients' knowledge level on anticoagulant treatment in relation to clinical outcome was also determined in this study. Patients reported on their health status since they started treatment, how long they had been on treatment, indications for the treatment and whether they were worried about the treatment they received at the unit. Majority of the respondents (96%) reported that their health status had improved since they started the treatment. However, 1 (0.6%) reported that their health status had worsened. This may be attributed to the fact that majority of the patients (88.6%) had been on treatment for more than four (4) months and had benefited from the

treatment. Similarly, the study revealed that the average number of years the respondents had been on treatment was a  $9\pm 8.2$  year which was enough for a patient to experience the effect of anticoagulation treatment. The patients who reported that their health status had remained the same or worsened could be attributed to the fact that they had just started the treatment (less than four months). Non compliance and treatment pluralism could also be factors. Almost half (45%) of the respondents reported Heart Surgery as the indication of being on the coagulation treatment while (27.4%) was due to Atrial Fibrillation. This may be attributed to the fact that the study was conducted at the cardiothoracic centre where most of the indications for anticoagulation are compulsory for patients who had native valve replacement with prosthetic valve. Only (35.4%) of the patients reported that they had the desire to approach someone for medical advice on anticoagulant treatment out of which about (32.6%) had been able to seek sufficient medical advice on the treatment. That had buttressed the fact that most of the patients had adequate knowledge on coagulation treatment because warfarin education was given in the language they understood. It was also not surprising that only 42.2% of the patients had some concerns about the treatment. The concerns reported were; (32.4%) cost of regular blood tests to monitor warfarin, (31.1%) taking one drug daily at the same time, (15%) bleeding while taking warfarin, 5(6.7%) missed abortion and those who felt they were young when they had surgery and did not understand most of the things they were told (9.5%). Those were findings consistent with previous study by Rewiuk, Bednarz, et al, (2007) which pointed out that, the necessity of systematic blood checks, fear of complications caused by the treatment, cost of medication and the necessity of taking medicine everyday, were the concerns of inconvenience associated with chronic anticoagulation.

## **5.2 Patients 'admission details**

Majority of the patients (76%) in this study were inpatients from the ward (National Cardiothoracic Centre). The study investigated the extent of effectiveness of warfarin education given to them and the extent of preparation for their discharge and self management. All the inpatients reported that they were provided with "red cards" after counseling on the treatment. The "red card" is a leaflet which contains advice for patients on anticoagulant treatment. The

effectiveness of the “red card” depends on the ability of the patients to read and understand the information it contains and apply the advice. Surprisingly, half of the respondents (67%) reported that they were satisfied with the contents of the leaflet and did not have any problems with the booklet. However, 10% lost their booklets several times and 23% were not told the importance of the booklet. Similar studies have reported that verbal and written information should be provided at the start of the therapy, in hospital after discharge and on the first anticoagulant clinic appointment (Baglin, Cousins, Keeling, Perry, Watson, 2007). Various literature identified that written warfarin information resources, available as both printed materials and via the internet, could not be read or understood by between 50% to 88% of the older patient population (Estrada, Hryniewicz, Higgs, Collins, Byrd, 2000). The use of specially designed written materials that contain relevant figures or images, pictograms, larger font or page size and other formatting elements could improve the comprehensibility of written materials, especially for older patients (Estrada, Hryniewicz, Higgs, Collins, Byrd, 2000). This may help the 10% in this study that lost their booklet often and 23% who were not told of the importance of the booklet. Yahaya, Hassali et al., (2009) were of the view that better levels of the knowledge of the patient may also be achieved if the information is reinforced by simple measures such as repetition or use of written materials. The fact that 13.1% of the patients in this study reported that the content of the leaflet was complicated and difficult to understand requires that the leaflet be re-examined.

### **5.3 Information Received on Anticoagulant Treatment**

Patients’ knowledge, drug compliance and anticoagulation control all improved after patient education became part of patients’ management plan. Adequate information ensures better quality of life. Patients reported receiving clear information on how warfarin works action to take if bleeding or bruising occurs, problems with anticoagulation treatment, drugs to avoid and alcohol consumption. Although large proportion of the patients (87%) reported receiving clear information on all the five items, there were gaps in their knowledge. Twenty-two percent of respondents had poor knowledge on drugs to avoid, and (25.1%) on the effects of changing dose of concurrent treatment. Several studies identified that patients who are on warfarin often have deficiencies in their warfarin knowledge (Cheah and Martins 2003; Lambert and Wynne 2003;

Roche- Nagle, Chambers et al. 2003; Tang, Lai et al.2003). One hundred and sixty (91%) admitted they were advised on alcohol intake while (44.5%) this to be avoided totally. This is similar to the findings by Lambert, Wynne (2003) in which (35%) of respondents were aware of the potential of alcohol to increase international normalized ratio. A study by Hassan, Shamala et al (2011) also reported patients who on warfarin had poor knowledge in the interaction between warfarin and alcohol.

This study showed that information was provided to some of the patients (24%) by doctors at the anticoagulant clinic and doctors on the ward but the majority of patients (76%) were given information by the pharmacists on the various aspects of warfarin treatment. Results of the comparison of the knowledge levels on warfarin education among the various indications revealed that, those who had heart surgery passed (60.0%) more than those without surgery (21.4%). Participants who received counseling from pharmacists had higher warfarin knowledge scores compared with those who received counseling from doctors. Roche, Chambers Nanra et al., (2003) noted that the availability of a non-physician counselor such as a clinical pharmacist or a nurse practitioner had also been shown to increase the patient's knowledge about medical treatment.

#### **5.4 Knowledge on Anticoagulant Treatment**

When patients are provided with adequate knowledge on anticoagulant treatment it impacts on their INR levels. Baker, Coughlin, Gallus , et al (2004) reported in their study that, Warfarin is more likely to be used safely by a patient who had knowledge on the potential for drug and diet interactions, understands the need for monitoring, and could recognize the signs of over and under- coagulation. The ultimate goal of anticoagulant treatment is to bring INR levels to the accepted level. Findings of this study showed that most patients 64% had accurate knowledge on anticoagulant treatment. There was a significant difference in the proportion of patients with accurate knowledge compared to those without accurate knowledge in relation to gender. Males with accurate knowledge were (58.1%) compared to that of females 41.1%. There was also a significant difference in the proportion of patients who had accurate knowledge of anticoagulant treatment, and that of those with INR. Among the patients with accurate knowledge of

anticoagulant treatment 73% had the desired INR level of 2.0-3.0. Kagansky, Knobler, Rimon, Ozer, Levy, (2004) in their study reported that, counseling patients with respect to their anticoagulant treatment is vital and significantly improves patient's knowledge and quality of anticoagulation. Of all those who had accurate knowledge, 86% were full time workers and 95.5% have had their general health status improved. It was therefore not surprising that majority of patients with accurate knowledge on the treatment, 60% had undergone heart surgery. A correlation analysis was performed to determine the correlation between the knowledge level of patients and INR control in this study. Significant positive correlations were found between the total knowledge level of patients and the control of all three measures of INR controls in this study. Thus patients with high accurate knowledge on anticoagulant treatment had better INR controls. The study showed significant associations between knowledge on anticoagulant treatment and the following: (1) age of respondents ( $p=0.034$ ); (2) education level of patients ( $p=0.027$ ), (3) indications for treatment ( $p=0.025$ ) and (4) general health status of patients ( $p=0.021$ ). In agreement with the study, Hassan, Shamala et al (2011) in their study to assess the anticoagulation knowledge and international normalized ratio (INR) control, reported a negative correlation between patients' knowledge and age ( $P = .001$ ,  $r (s) = -.293$ ) and a positive correlation between patients' knowledge and education level ( $P = .001$ ,  $r (s) = .365$ ). Tang et al. (2003) also discovered a positive Pearson correlation between patient knowledge about warfarin therapy and the percentage of INR values within therapeutic goal range ( $r=0.20$ ,  $p= 0.024$ )

In the study, patients' knowledge on various knowledge domains showed scores indicative of sufficient knowledge of warfarin but knowledge in bruising (29.7%) and blood in urine (27.4%) were low among patients. Also, knowledge level in the other effects of warfarin was average and that explained the good anticoagulation control among patients used for the study. A similar study by Hassan, Shamala et. al., (2011) reported that patients on warfarin scored an average of  $66.5\% \pm 36.0\%$  for their knowledge on how warfarin works, and  $49.2\% \pm 21.1\%$  for adverse effects.

## **5.5 Summary and Conclusion**

The study was on knowledge level on warfarin and international normalized ratio among patients at National Cardiothoracic Center, Korle-Bu. The researcher used questionnaires to collect data from 175 respondents. Findings from the study indicated that respondents had adequate knowledge on warfarin and a relationship was between knowledge and international normalized ratio control. The research also revealed that, respondents who had surgery had better knowledge than the physician cases. Patients were able to identify how warfarin works, the side effects of warfarin and the effects of starting new drug. The existing policies of educating patient before initiation of warfarin and discharge from hospital and issuing warfarin information booklet has shown to have had a positive impact on the general knowledge of patients. Patients admitted to the wards were seen to be more knowledgeable and had better controlled INR levels compared to patients who came to the OPD direct and were educated by the doctors. An integrated multidisciplinary education program may improve patient's knowledge and enhance compliance.

## **5.6 Implications for nursing**

The outcome of the study has implications for nursing and these are presented in four areas of nursing: management, research, education and practice.

### **5.6.1 Nursing management**

Nurses in the various wards/units especially the OPD should be well trained in educating patients regularly on anticoagulation treatment. Nurses need to be knowledgeable in the anticoagulation protocol to be able to advise and answer patient questions to improve patient's knowledge level on their medication.

### **5.6.2 Nursing Research**

There's the need for more research to be done on control and management of anticoagulant treatment. Nurses are known to spend most of their time with patients. The current research brings to light the need for qualified and knowledgeable personnel to be available to give good counsel to patients. Workshops and in-service training must be regular for nurses and other health workers for them to be abreast with standard practices worldwide to enhance the quality of service given at the centre.

### **5.6.3 Nursing Education**

Nurses and specialist in cardiology must be well equipped with the necessary skills to cater for these patients. There should be avenues for continuous education to keep knowledge and skill up to date.

### **5.6.4 Nursing Practice**

There is more understanding and compliance from patients when the counseling is done by the nurses as nurses spend more time with the patients on the ward.

## **5.7 Recommendations**

Every health worker should be equipped with the basic knowledge in anticoagulant treatment to be able to identify those who need anticoagulation and help reduce morbidity and mortality of venous thromboembolic conditions.

Anticoagulant treatment must be incorporated into the National Health Insurance Scheme to alleviate the burden of cost on patients.

Despite the adequate level of knowledge among patients at the National Cardiothoracic Center, more research should be carried out, especially qualitative study to know more about patient experiences on their anticoagulant treatment.

Nurses and pharmacists should team up at the OPD on clinic days to reinforce education given to patients on warfarin therapy after discharge.



## REFERENCES

- Ansell, J., Hirsh, J., Hylek, E., Jacobson, A., Crowther, M. & Palareti, G. (2008). Pharmacology and management of the Vitamin K antagonists: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest*; 133(6 Suppl):123S-131S
- Ansell, J., Jacobson, A., Levy, P., Poller, L. & Hasenkam, B. (2005). Guidelines for implementation of patient self-testing and patient self-management of oral anticoagulation. International consensus guidelines prepared by International Self-Monitoring Association for Oral Anticoagulation. *International Journal of Cardiology*, 99: 37–45.
- Ansell, J., Hirsh, J., Poller, L, Bussey, H., Jacobson, A., & Hylek, E. (2004). The pharmacology and management of the vitamin K antagonists: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest*, **126**(3 Suppl):204S-233S.
- Ansell, J., Hirsh, J., Dalen, J., Anderson, DR., Poller L., Bussey, H., Ansell, J. & Deykin, D. (2001). Managing oral anticoagulant therapy. *Chest*. Jan; 119 (1 Suppl):22S-38S.
- Arnsten, J H., Gelfand, J.M., & Singer, D.E. (2007). Determinants of compliance with anticoagulation: a case control study. *American Journal of Medicine*, 103: 11–17.
- Ansell, J., Hirsh, J., Poller, L., Bussey, H., Jacobson, A., & Hylek, E. (2004). Pharmacology and management of vitamin K antagonists. *Chest*; 126: 2045-335
- Baglin, T.P., Keeling, D.M. & Watson, H.G. (2006). Guidelines on oral anticoagulation (warfarin): third edition 0 2005 update *British Journal of Haematology* 132(3): 277-85
- Baglin, T.P., Cousins, D., Keeling, D.M., Perry, D.J. & Watson, H.G. (2007). Recommendations

- from the British Committee for Standards in Haematology and National Patient Safety Agency. *British Journal of Haematology*, 136: 26–29
- Bajorek, B.V., Ogle, S.J., Duguid, M.J., Shenfield, G.M. & Krass, I. (2007). Management of warfarin in atrial fibrillation; views of health professionals, older patients and their careers. *Journal of American Geriatrics Society*, 53:1912-20
- Baker, R I., Coughlin, P.B., Gallus, A.S., Harper, PL., Salem, HH. & Wood, EM. (2004). Warfarin reversal: consensus guidelines, on behalf of the Australasian Society of Thrombosis and Haemostasis, *Medical Journal Australia*;181:492-497.
- Barcellona, D., Contu, P. & Marongiu, F. (2002). Patient education and oral anticoagulant therapy. *Haematologica*; 87: 1081-1086.
- Barnes, J.O. (2002). Working group on complementary medicine. Herb-medicine interactions: S John's Wort (*Hypericum perforatum*) Useful information for pharmacist. Lambeth High Street, London SE1 7JN: Royal Pharmaceutical Society of Great Britain pp. 5
- Bowling, A. (2009). 3<sup>rd</sup> Ed., *Research Methods in Health: investigating health and health services*. UK, pp.225-226
- Burnett, B., et al., (2009). Institute for Clinical Systems Improvement. Health Care Guideline Supplement. Anticoagulation Therapy Supplement. *Genet Med* 13(6):509-518
- Burn, S.N. & Grove, S.K. (2005). *The practice of nursing research: conduct critique and utilization* (5<sup>th</sup> Edition), Texas: Lippincott. 72 (2), pp.233-235.
- Cabr al, K. P., Ansell, J. & Hylek, E. M. (2011). Future directions of stroke prevention in atrial fibrillation: the potential impact of novel anticoagulants and stroke risk stratification. *J Thromb Haemost*; 9:441-9.

Cheah, G.M. & Martens, K.H. (2003). Coumadin knowledge deficits: do recently hospitalized patients know how to safely manage the medication? *Home Healthcare Nurse*; **21**:94-100

Crowther, M.A., Douketis, J.D., Schnurr, T., Steidl, L., Mera, V., Ultori, C., Venco, A &

Agno, W. (2002). "Oral vitamin K lowers the international normalized ratio more rapidly than subcutaneous vitamin K in the treatment of warfarin-associated coagulopathy. A randomized, controlled trial"(PDF). *Ann. Intern. Med.***137** (4): 251–4.

Dager, W.E., Branch, J.M., King, J.H., White, R.H., Quan, R.S., Musallam, N.A.& Albertson,

T.E. (2000). Optimization of inpatient warfarin therapy: impact of daily consultation by a pharmacist-managed anticoagulation service. *Ann Pharmacother*; 34:567–572.

Davis, N.J., Billett, H.H., Cohen, H.W. & Arnsten, J.H. (2005). Impact of adherence, knowledge, and quality of life on anticoagulation control. *Ann Pharmacother* 39(4):632–636.

Delaney, J.A., Opatry, L., Brophy, J.M. & Suissa, S. (2007)."Drug drug interactions between antithrombotic medications and the risk of gastrointestinal bleeding".*CMAJ***177** (4): 347–51

Erban, S. (1999). Initiation of warfarin therapy: recommendations and clinical pearls. *Journal of Thrombosis and Thrombolysis*, 7: 145.

Estrada, C.A., Hryniewicz, M.M., Higgs, V.B., Collins, C. & Byrd, J.C. (2000). Anticoagulant patient information material is written at high readability levels. *Stroke*.31:2966–70.

Estrada, C.A., Martin-Hryniewicz, M., Peek, B.T., Collins, C. & Byrd, J.C. (2004). Literacy and numeracy skills and anticoagulation control. *AM J Med Sci*. 328:88–93.

Fang, M.C., Chang, Y., Hylek, E.M., Rosand, J., Greenberg, S.M., GO, A.S. & Singer, D.E. (2004).

Advanced age, anticoagulation intensity, and risk for intracranial hemorrhage among patients taking warfarin for atrial fibrillation. *Ann Intern Med.*; 141:745–52.

Fang, M.C., Machinter, E.L., Wang, F. & Schillinger, D. (2006). Health Literacy and

anticoagulation-related outcomes among patients taking warfarin. *J Gen Intern Med*, 21:841-846.

Gage, B.F., Boechler, M., Doggette, A.L., Fortune, G., Flaker, G.C., Rich, M.W. & Radford, M.J.

(2000). adverse outcomes and predictors of underuse of antithrombotic therapy in Medicare beneficiaries with chronic atrial fibrillation. *Stroke*, 31:822-827

Gage, B.F., Fihn, S.D. & White, R.H. (2000). "Management and dosing of warfarin therapy".

*Am. J. Med.* 109 (6): 481–8

Gandolfo, C., Balestrino, M., Burrone, A., Del Sette, M. & Finocchi, C. (2008). Stroke due to

atrial fibrillation and the attitude to prescribing anticoagulant prevention in Italy *J Neurol* 2008; 255:796-802.

Garcia, D., Regan, S., Crowther, M., Hughes, R.A. & Hylek, E.M. (2005). Warfarin maintenance

dosing patterns in clinical practice: implications for safer anticoagulation in the elderly population. *Chest*, 127: 2049–2056.

Haines, S.T. (2008). Challenges in managing venous thromboembolism and acute coronary

syndrome: case studies of the use of antithrombotic and antiplatelet therapies. *Am J Health-System Pharm.*; 65 (Suppl 7):S3-4

Hassan, S. S., Shamala, R., Syed, I. A., Bassariah, N., Chang, D.W.K., Mei, T.K.. & Chin H.O.

(2011). factors Affecting Warfarin-Related Knowledge and INR Control of Patient Attending Physician and Pharmacist Managed Anticoagulation Clinics. *Journal of pharmacy practice*, 2012 (25):111-112.

Heneghan, C., Alonso-Coello, P., Garcia-Alamino, J.M., Perera, R., Meats, E. & Glasziou, P.

(2006). Self-monitoring of oral anticoagulation: a systematic review and meta-analysis. *The Lancet*, 367: 404–411.

Hirsh, J., Fuster, T., Ansell, J. & Halperin, J.L. (2003). `American Heart Association American

College of Cardiology, Foundation guide to warfarin therapy`. *Journal of American College of Cardiology* 41(9): 1633-52

Holbrook, A.M., Pereira, J.A., Labiris, R., McDonald, H., Douketis, JD., Crowther, M. & Well,

PS. (2005). Systematic overview of warfarin and its drug and food interactions. *Archives of Internal Medicine* 165(10) 1095- 106

Hu, A., Chow ,C.M., Dao, D., Errett. L. & Keith, M. (2006). Factors influencing patient

knowledge of warfarin therapy after mechanical heart valve replacement. *J Cardiovasc Nurs*, **21**:169-175

Hunt, N., Tyrrell, S. (2001). systematic sampling; Coventry University.

Hylek, E.M., Evans-Molina, C., Shea, C., Henault, L.E. & Regan, S. (2007). "Major hemorrhage

and tolerability of warfarin in the first year of therapy among elderly patients with atrial fibrillation". *Circulation* **115** (21): 2689–96.

"Information Pharmacists' news" (2008). *Information Centre Bulletin*. 1 Lambeth High Street,

London SE1 7JN: Royal Pharmaceutical Society of Great Britain.

- Juurlink, D.N. (2007). Drug interactions with Warfarin: What Clinicians need to know. *CMAJ*; 177(4): 369-71
- Kagansky, N., Knobler, H., Rimon, E., Ozer, Z. & Levy, S. (2004). Safety of anticoagulation therapy in well-informed older patients. *Archives of Internal Medicine*, 164: 2044–2050.
- Khan, T.I., Kamali, F., Kesteven, P., Avery, P. & Wynnes, H. (2004). The value of education and self-monitoring in the management of warfarin therapy in older patients with unstable control of anticoagulation. *Br J Haematol* 126:557-567
- Kimmel, SE., Chen, Z., Price, M., Parker, CS., Metlay, JP. & Christie, JD., (2005). The influence of patient adherence on anticoagulation control with warfarin: results from the International Normalized ratio adherence and Genetics (IN-RANGE) study. *Arch Intern Med*; 167: 229-235.
- Khudair, I.F. & Hanssens, Y.I. (2010). Evaluation of patients' knowledge on warfarin in outpatient anticoagulation clinics in a teaching hospital in Qatar. *Saudi Med J*; 31(6):672-7.
- Lambert, H., Wynne, H. (2003). Patients' understanding of anticoagulation therapy. *Journal of the Royal Society of Medicine* 96 (11):572
- Lenzini, P.A., Grice, G.R., Milligan, P.E., *et al.*, (2008). "Laboratory and clinical outcomes of pharmacogenetic vs. clinical protocols for warfarin initiation in orthopedic patients". *Journal of Thrombosis and Haemostasis* 6: 1–8.
- Levi, M., De Porter, O.R. & Kamphuisen, P.W. (2009). Management strategies for optimal control of anticoagulation in patients with atrial fibrillation, *Semin Thomb Homost*; 35: 560-567.

- Linkins, L.A., Choi, P. T. & Douketis, J.D. (2003). Clinical impact of bleeding in patients taking oral anticoagulant therapy for venous thromboembolism: a metaanalysis. *Annals of Internal Medicine*, 139: 893–900.
- Macina, O. T. & Schardein, J. L. (2007). "Warfarin". *Human Developmental Toxicants*. Boca Raton: CRC Taylor & Francis. pp. 193–4. ISBN 0-8493-7229-1.
- Mannucci, P.M. & Franchini, M. (2011). Old and new anticoagulant drugs: A minireview. *Ann Med* ; 43:116-23.
- Matchar, D.B. (2000). Relationship between test frequency and outcomes of anticoagulation: a literature review and commentary with implications for the design of randomized trials of patient self management. *Journal of Thrombosis and Thrombolysis*, 9: 283–292. Self Anticoagulation Management Servicea GP.
- Matchar, D.B. (2003). Do anticoagulation management services improve care? Implications for the design of randomized trials of patient self management. *Journal of Thrombosis and Thrombolysis*, 8: 273–282. Self Anticoagulation Management Servicea GP.
- Newall, F., Monagle, P. & Johnston, L. (2005). Patient understanding of warfarin therapy: a review of education strategies. *Hematology* 10:437-442.
- Nutescu, E., Chuatrisorn, I. & Hellenbart, E. (2011). Drug and dietary interactions of warfarin and novel oral anticoagulants: an update. *J Thromb Thrombolysis*; 31:326-43.
- Nutescu, E.A.& Wittikowsky, A.K. (2004). Direct thrombin inhibitors for anticoagulation: *Ann pharmacotherapy*; 35:99-109.
- Pirmohamed, M., James, S., Meakin, S., Green, C., Scott, A.K., Walley, T.J., Farrar, K. & Park, BK. (2004), Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients. *BMJ*; 329: 15-19.

- Polit, D.F. & Hungler, B.P. (2003). *Nursing Research, Principles and Methods Appraisal and utilization*. (7<sup>th</sup> edition.) Philadelphia, Lippincott.pp.293-295
- Rewiuk, K., Bednarz, S., Paryan, P. & Grodzkiki, T. (2007). Knowledge of antithrombotic prophylaxis among patients with atrial fibrillation. *Cardiology Journal* vol.14 pp.44-49
- Roche-Nagle, G., Chambers, F., Newra, J., Bouchier, H. & Young, S. (2003). Evaluation of Patients' knowledge regarding oral anticoagulant; *Iris Medical journal*.96 (7):211-213
- Stephanie, H., Panayotis, F., James, L.O., Ryan, J.L. & Terese, H.,(2003). Clinical outcome of patients undergoing non-cardiac surgery in the two months following coronary stenting. *JAM Coll Cardiol*, 42: 234-40.
- Tang, E.O., Lai, C.S., Lee, K.K., Wong, R.S., Cheng, G. & Chan, T.Y. (2003). Relationship between patient's knowledge and anticoagulation control. *Ann Pharmacother*; 37:34-39.
- Taylor, F.C., Ramsay, M.E., Tan, G., Gabby, J. & Cohen, H. (1994).Evaluation of patients' knowledge about anticoagulant treatment. *Qual Health Care*.3 (2):79-85.
- Warfarin diet: What foods should I avoid?". Mayoclinic.com.  
<http://http://www.mayoclinic.com/health/warfarin/AN00455>. Retrieved 2011-08-09.
- Weathermon, R. & Crabb, D.W. (1999). "Alcohol and medication interactions". *Alcohol Res Health* 23 (1): 40–54.
- Wilson, F.L., Racine, E., Tekieli, V. & Williams, B. (2003). Literacy, readability and cultural barriers: critical factors to consider when educating older African Americans about anticoagulation therapy. *J Clin Nurs*, 12:275-282.

Wysowski, D.K., Nourjah, P. & Swartz, L. (2011). Bleeding complications with warfarin use:

a prevalent adverse effect resulting in regulatory action. *Arch Intern Med*; 167:1414-1419.

Yahaya, A H M., Hassali, M A A., Awaisu, A. & Shafie, A A. (2009). Factors associated

with warfarin therapy knowledge and anticoagulation control among patients attending a warfarin clinic in Malaysia. *Journal of Clinical and Diagnostic Research*. (3)1663-1670



## APPENDIX A

### PARTICIPANT INFORMATION SHEET

**Title:** KNOWLEDGE LEVEL AND ANTICOAGULATION CONTROL AMONG PATIENTS ON WARFARIN THERAPY AT THE NATIONAL CARDIOTHORACIC CENTER, KORLE-BU.

**Principal Investigator:** Joyce Antwiwaa Dwamena (Msc. Student)

**Address:** School of Nursing, College of Health Sciences, University of Ghana, Legon.

#### General Information about Research

**Objectives of the Research:** To determine the knowledge level of patients on warfarin therapy.

To determine the effectiveness of warfarin education among patients.

To determine the knowledge of warfarin and its relationship with international normalized ratio control among patients after discharge.

**Purpose of the Study:** The purpose of this study is to find out whether patient's knowledge on warfarin therapy has a relationship with anticoagulation control.

**Study Procedures:** You will be asked to fill a questionnaire for approximately fifteen minutes and it will be collected the same day.

**Possible Risks and Discomforts:** I do not expect that you will be harmed by being in the study; however, if in the course of filling the questionnaire, any aspect upsets you, I will assist you to obtain the help you need.

**Possible Benefits:** Your participation will help improve counseling given to patients who are started on anticoagulation. It might also let your relatives and significant others understand you better and give you the necessary support.

**Confidentiality:** Your name will not be needed. Code number will be given and at the end of the study, the analysis will be reviewed only by my supervisor and me. The results of this study may be published or presented at conferences but your name and any information that may give your identity will not be included.

**Voluntary Participation and Right to Leave the Research:** You are free to refuse or participate, or to withdraw from the study at anytime. You do not have to give any reason and it will not affect you in any way.

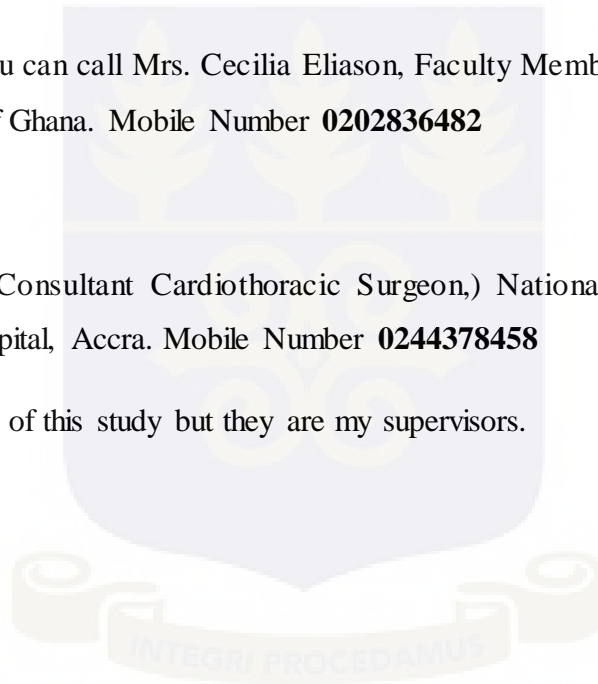
**Contacts for Additional Information:** If you have any question you can phone me on **0208537689**.

If you have concerns, you can call Mrs. Cecilia Eliason, Faculty Member (Adult Health, School of Nursing, University of Ghana. Mobile Number **0202836482**

OR

Dr. Mark .M. Tettey, (Consultant Cardiothoracic Surgeon,) National Cardiothoracic Center, Korle –Bu Teaching Hospital, Accra. Mobile Number **0244378458**

These people are not part of this study but they are my supervisors.



**APPENDIX B**

**INFORMED CONSENT FORM**

Title of research study: knowledge level and anticoagulation control among patients at National cardiothoracic Center, Korle-Bu Teaching Hospital.

Researcher: Joyce A Dwamena, Msc. Student, School of Nursing, College of health Sciences, University of Ghana, Legon.

Purpose of the Study: this study is to examine patient knowledge on warfarin and its relationship with international normalized ratio control after discharge.

**CONSENT**

**Please tick or circle your answers**

- a. Do you agree to be in this research? Ye s[ ] No [ ]
- b. Do you understand the information sheet? Ye s[ ] No [ ]
- If you agree to be in the study it will include the following.
- c. The research will ask you various questions. Ye s[ ] No [ ]
- d. At most 15 minutes will be used in answering the questions. Ye s[ ] No [ ]
- e. Are you aware that you will not be given any money or item when you take part in the study? Ye s[ ] No [ ]
- f. Do you understand that you are free to pull out from the study at anytime? Ye s[ ] No [ ]
- g. Do you understand that you will not be castigated in anyway if you opt out of the study, and information given will be confidential? Ye s[ ] No [ ]

h. have you had the opportunity to ask questions about the study Yes [ ] No [ ]

The research purpose was explained to me by .....

I agree to take part in the research.

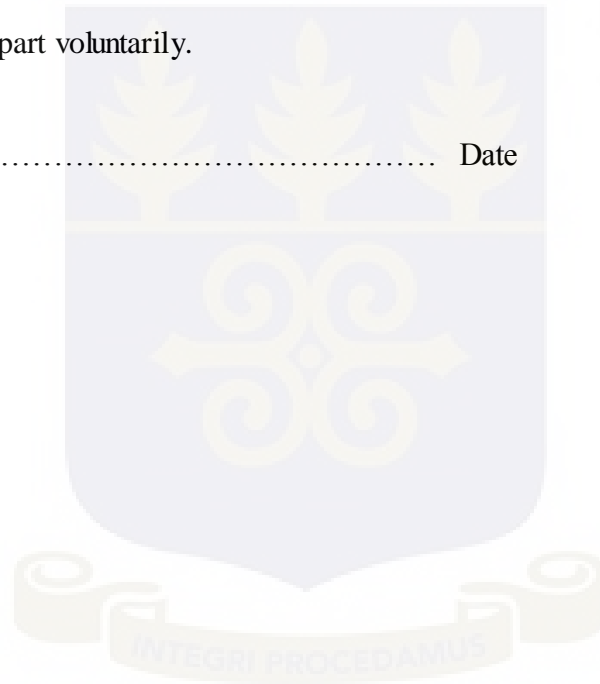
Signature of Participant/Thumb print .....

Name

Date

I believe that the participant signing/thumb printing this form understands what this form is about and agrees to take part voluntarily.

Signature of Researcher..... Date



**APPENDIX C**

**QUESTIONNAIRE**

**UNIVERSITY OF GHANA**

Dear Participant,

The purpose of this questionnaire is to solicit information on the knowledge of warfarin and its relationship with international normalized ratio control after discharge. Anonymity and confidentiality of the information given is assured.

Your candid response to the questions will be very much appreciated. Thank you.

**Please tick or circle the correct answer.**

**Section A**

**Demographic Data**

a. Are you

Male  Female

b. Which of the following age groups do you fall?

Under – 16

• 16 – 30

• 31 – 45

• 46 – 60

• 61 – 70

• 71 – and over

c. Which of the following best describes your employment status?

Employed full time  Employed part time

Unemployed  Long term sick leave or benefit

Student  Retired

d. Which region do you coming from?.....

e. What is your educational Level?

No formal education  Primary education

Secondary education  Tertiary education

**Section B: this section is about your general health and the anticoagulant treatment (for example, warfarin) that you are now receiving.**

1. Since starting anticoagulant treatment, would you say that your general health has:

*(Please tick)*

a. Improved

b. Worsened

c. Stayed the same

2. How long ago was your present anticoagulant treatment started?

a. Less than 1 month

b. Between 1-2 months

c. Between 2-4 months

d. More than 4 months

If more than 4 months, please state how long \_\_\_\_\_

3. As far as you know, which of the following are reasons for your present anticoagulant treatment? *(please tick Yes, No, or Not sure for each item)*

	Yes	No	Not sure
a. Deep venous thrombosis (DVT) – blood clot in the leg vein	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

b. Pulmonary embolus (PE) – blood clot in the lung	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
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- c. Atrial Fibrillation
- d. Heart surgery
- e. Stroke

Anything else? \_\_\_\_\_

4. About your present anticoagulant treatment:
- a. Have you wanted to approach anyone for medical advice?  
Yes  No
  - b. Have you been able to?  
Yes  No

If Yes, who? \_\_\_\_\_

5. Do you worry about being on anticoagulant treatment?

A lot  A little  Not at all

If so, what are your concerns? \_\_\_\_\_

**Section C: The questions in this section are about the time you spent as a patient at the National Cardiothoracic ward at the Korle-Bu Teaching Hospital.**

1. Were you recently in-patient at the National Cardiothoracic Ward?  
Yes  No

*Please answer question 2 only if you started anticoagulation treatment while in the ward at National Cardiothoracic Centre.*

- 2.
- a. When you left the ward were you handed a Red Card “Advice for patients on anticoagulant treatment”?  
Yes  No  Not sure
  - b. Was the information on the card:  
Too complicated?   
Too simple?

Just right? [ ]

c. Please state any problems you had with the red card:

---

**Section D: The questions in this section are about the information you may have been given about your anticoagulant treatment**

1.

a. Were you told how anticoagulant treatment works, and was this clear to you?

Yes and clear [ ]      Yes but not clear [ ]      No [ ]

b. Who told you?

Doctor in the anticoagulant clinic [ ]      Doctor in the ward [ ]      Pharmacist [ ]

Who else (for example, nurse, and other clinic staff)... Please state \_\_\_\_\_

2.

a. Were you told of the *problems with anticoagulant treatment*, and was this clear to you?

Yes and clear [ ]      Yes but not clear [ ]      No [ ]

b. Who told you?

Doctor in the anticoagulant clinic [ ]      Doctor in the ward [ ]      Pharmacist [ ]

3.

a. Were you told what to do if you *have a nose bleeding or are bruising*, and were this clear to you?

Yes and clear [ ]      Yes but not clear [ ]      No [ ]

b. Who told you?

Doctor in the anticoagulant clinic [ ]      Doctor in the ward [ ]      Pharmacist [ ]

4.

c. Were you told what *drugs to avoid*, and was this clear to you?

Yes and clear [ ]      Yes but not clear [ ]      No [ ]

d. Who told you?

Doctor in the anticoagulant clinic [ ]      Doctor in the ward [ ]      Don't know [ ]

5.

e. Were you given *advice on drinking alcohol*, and was this clear to you?

Yes and clear [ ]      Yes but not clear [ ]      No [ ]

f. Who told you?

Doctor in the anticoagulant clinic [ ]      Doctor in the ward [ ]      Don't know [ ]

**Section E: This section is a mini quiz to find out how well patients have been informed about anticoagulant treatment and the problems it may cause**

1. How does warfarin work?

*(Please tick Yes or No for each statement)*

a. Warfarin does not affect the blood      Yes[ ]      No[ ]

b. Warfarin thin the blood      Yes[ ]      No[ ]

c. Warfarin thickens the blood      Yes[ ]      No[ ]

2. Could starting a new treatment or any other preparation affect your anticoagulant treatment?      Yes [ ]      No [ ]      Don't know [ ]

3. Could changing the dose of a treatment you are already taking affect your anticoagulant treatment?      Yes [ ]      No [ ]      Don't know [ ]

4. The following are statements about any patient drinking alcohol when receiving anticoagulant treatment.

*(Please tick Yes or No for each statement)*

• Alcohol does not affect anticoagulant treatment      Yes[ ]      No[ ]

• Alcohol must be avoided totally      Yes[ ]      No[ ]

• 8 units of alcohol a night is OK (*e.g. 4 pints of beer or 8 glasses of wine*)      Yes[ ]      No[ ]

• 1 unit of alcohol a night is OK (*e.g. 1/2 pint of beer or 1 glass of wine*)      Yes[ ]      No[ ]

5. Of the list below, which drugs should be avoided when receiving anticoagulant treatment? Please do not be alarmed, some of the drugs listed should not be avoided.

*(Please tick True, False, or Don't know for each item)*

	Don't know	True	False
Aspirin	[ ]	[ ]	[ ]

Cough medicines	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Iprobrufen	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Antacids (for example, Rennie, Settlers)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Optrex (eye solution)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Garlic capsules	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
TCP/Dettol	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Vitamin C tablets	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Throats lozenges	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Herbal preparations	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

6. Which of the following could be possible side effects of taking the wrong (too little or too much) amount of anticoagulant treatment? Please do not be alarmed, some the items are wrong. *(Please tick True, False, or Don't know for each item)*

	Don't know	True	False
Blood in stools	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Nose bleeds	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Sleeplessness	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Prolonged bleeding	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Bruising without injury	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Weakness	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Loss of appetite	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Ringing in the ears	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Nausea	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Blood in urine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Nervousness	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Blood clot	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
High blood pressure	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>