

**A SURVEY OF EXTENT OF VENOUS THROMBOEMBOLISM
PROPHYLAXIS AMONG MEDICAL IN-PATIENTS IN KENYATTA
NATIONAL HOSPITAL**

**A dissertation submitted in partial fulfillment for Masters Degree of University of Nairobi
(Clinical Pharmacy).**

By

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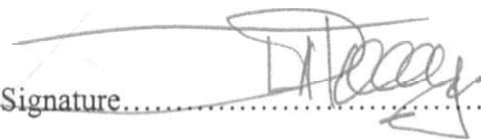
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DEDICATION

I dedicate this dissertation to my paternal uncle Mr. William O. Atungulu, who instilled a sense of discipline and hard work in my academic life and who taught me the virtues of standing tall in whatever I undertake.

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First, I would like to thank the almighty God who has enabled me to go through this academic journey. I wish to extend my sincere thanks to my wife Lydia, sons Einstein, Timothy and daughter Merkel for the understanding and encouragement I got from them.

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ABBREVIATIONS

VTE	Venous Thrombo Embolism
PE	Pulmonary Embolism
ACCP	American College of Chest Physicians
UFH	Unfractionated Heparin
LMWH	Low Molecular Weight Heparin
KNH	Kenyatta National Hospital
DVT	Deep Venous Thrombosis
PIOPED	Prospective Investigation of Pulmonary Embolism Diagnosis
THRIFT	Thrombo embolic risk Factors
RR	Risk ratio
CI	Confidence interval
ICU	Intensive care unit
RFUT	Radio labeled Fibrin-Uptake Test
OR	Odds Ratio

DEFINITION OF TERMS

Thrombosis:	Condition in which the blood changes from liquid to a solid state and produces a blood clot
Embolism:	The condition in which an embolus becomes lodged in an artery or vein and obstructs its blood flow.
Embolus:	material, such as a blood clot, fat, air, amniotic fluid, or a foreign body that is carried by blood from one point in the circulation to lodge at another point.
Prophylaxis:	Putting measures in place to prevent an occurrence of an event.
Coagulation:	Process by which blood changes to a jelly like mass (solid state)
Coagulation factors:	A group of substances present in blood plasma that under certain conditions, undergo a series of chemical reactions leading to a solid state of blood.
Vein	Blood vessel conveying blood towards the heart, they carry deoxygenate blood except pulmonary vein.

ABSTRACT

Background: Venous thromboembolism comprises both deep venous thrombosis (DVT) and pulmonary embolism (PE). It accounts for approximately 10% of deaths in hospitals and has been identified as the most preventable cause of death during hospitalization. Along with the mortality associated with venous thromboembolism, long term complications, such as post thrombotic syndrome, affect a patient's quality of life and result in significantly increased health care costs, morbidity and mortality.

Objective: The main purpose of this study was to carry out a baseline survey of extent of venous thromboembolism prophylaxis among medical in-patients in Kenyatta national Hospital.

Setting: Kenyatta National Hospital, which is the largest teaching and referral centre in Kenya.

Study design: The study was a cross sectional study.

Methodology: The target population was the medical in-patients with high risks of developing venous thromboembolism. One hundred and sixty eight (168) patients were selected by purposive sampling from medical in patients. Data was collected using venous thromboembolism prophylaxis risk assessment tool, and analysed by SPSS

Results: Of the 168 patients studied, (40%) were not given prophylaxis, (52%) got prophylaxis and 8% had contraindications to chemical prophylaxis. Prevalence of VTE was 18.5% and the gender ratio was similar 1:1. The drugs used were heparin (65.6%), enoxaparin 18.3%, warfarin 9.7%, warfarin and heparin concurrently used were 6.5%. No patient was put on non pharmacological prophylaxis.

Conclusion: The prevalence of venous thromboembolism in Kenyatta National Hospital which stands at 18.5% is higher than in the ones documented in literature that is 10-13%. The extent of provision of VTE prophylaxis is still low at 52%. Of the population that required prophylaxis only 52% were given while a big proportion 40% were left out. There are no non pharmacological interventions being given to patients having contraindications to chemical prophylaxis this left them prone to development of VTE. Active bleeding and uncontrolled hypertension were the major contraindications to pharmacological prophylaxis

INTRODUCTION

1.1 Study Background

Venous thromboembolism (VTE) comprises both deep venous thrombosis and pulmonary embolism (PE) and affects approximately 30 million Americans annually. Pulmonary embolism accounts for approximately 10% of deaths in hospitals and has been identified as the most preventable cause of death during hospitalization. Along with the mortality associated with VTE, long-term complications, such as post thrombotic syndrome, affect a patient's quality of life and result in significantly increased health care costs.^[4] The risk of developing a second VTE after a first-time event increases by up to 14%, making a prior VTE a risk factor for VTE identified by the American College of Chest Physicians (ACCP).^[2,4] A 2001 report assessing patient safety practices identified VTE prophylaxis as the number-one preventive strategy to improve patient safety.^M

The silent nature of VTE is also of concern, with asymptomatic disease in up to 70% of VTE cases.¹⁰¹ Reliance on patient-reported symptoms is a faulty strategy for managing VTE, since the first event may in fact be a fatal PE. However, it is not realistic or recommended to screen each hospitalized patient for VTE with venous Doppler ultra sonography.^{^21} Therefore, assessment of risk factors and the appropriate choice of prophylaxis continue to be the recommended strategies for VTE prevention in hospitalized medical patients. American college of chest physicians (ACCP) recommends that every hospital develop a formal strategy to address the prevention of VTE.^[2]

Prophylaxis for VTE often is overlooked.^{17,81} The ACCP recommends specific prevention regimens in a variety of populations, such as patients undergoing general and orthopedic surgery and those with trauma, acute myocardial infarction, and ischemic stroke, and recommends that every hospital develop specific strategies for implementing prophylaxis.^[9] In the heterogeneous group of medical patients, two options for prevention are suggested:

low-dose subcutaneous unfractionated heparin (UFH) 5000 U 2 or 3 times/day, or subcutaneous low-molecular-weight heparin (LMWH). Determining when and how to administer prophylaxis in the medically ill is difficult due to many limitations in VTE prevention trials. Sample characteristics and sizes, results, and conclusions vary. Critical evaluation of strengths and limitations in the literature is essential for determining which method produces the best outcomes.

1.2. Pathophysiology

Patients with venous trauma, venous stasis, or hyper coagulability are predisposed to formation of VTE.^[10] Medically ill patients, therefore, are often at substantial risk. A venous thromboembolism occurs when the natural anticoagulation and fibrinolytic systems are overcome by a procoagulant setting. Trauma or damage to vascular endothelium can lead to release of tissue factor, which initiates the extrinsic clotting cascade by activating factor VII [ii, 12] Ca^{2+} factor-VIIa complex, with Ca^{2+} , leads to activation of factor X and the common pathway of the clotting cascade. Factor Xa then converts prothrombin (II) into the potent procoagulant thrombin (IIa), which in turn converts fibrinogen into fibrin, which stabilizes the clot.^[11,14] During this process, areas of vascular injury expose proteins such as collagen and von Willebrand factor, which are responsible for platelet adhesion.^{115,161} Once platelets adhere to the area of injury they are activated, leading to expression of glycoprotein IIb-IIIa receptors. Fibrinogen links platelets by binding glycoprotein IIb-IIIa receptors on different platelets, resulting in platelet aggregation.^{17,183} Unlike arterial thrombus, which is heavily composed of platelets, venous thrombus incorporates mainly fibrin and red blood cells, with platelets playing a smaller role.^[19,20]

Medically ill patients are often immobile for several days. Immobility is a known risk factor for development of VTE since it promotes venous stasis and impairs venous return from the lower extremities. Venous stasis also causes endothelial hypoxia at the site of stasis,

which damages endothelium and activates intrinsic and extrinsic clotting cascades.^{1,11}
Decreased venous return from the legs also leads to local accumulation of clotting factors that may trigger thrombogenesis.^{1,21}

When the body's natural defense mechanisms, such as proteins C and S, antithrombin, and tissue factor pathway inhibitor, are overwhelmed, procoagulant factors promote formation of VTE.^[23,26] Because of fibrin's predominant role in VTE, the natural fibrinolytic system is an important protective mechanism. This protection may be limited by secretion of plasminogen activator inhibitor from the thrombus, which prevents conversion of plasminogen into the proteolytic enzyme plasmin. Plasmin that is produced can be inhibited by α_2 -antiplasmin.^[27,29] With less production and increased inhibition of plasmin, there is less fibrin breakdown and therefore more fibrin incorporated into the clot.

Venous thrombosis usually occurs in the cusp of a venous valve. As a thrombus forms around it, the valve is damaged irreversibly, potentially leading to chronic venous insufficiency or postphlebotic syndrome.^{^01} The damaged valve is an attractive environment for future thrombosis, increasing the risk for recurrent VTE.^{[9, j01} This makes prevention of initial DVT critical.

LITERATURE REVIEW

2.1 Introduction

Until the 1990s, venous thromboembolism (VTE) was viewed primarily as a complication of hospitalization for major surgery (or associated with the late stage of terminal illness)[2]. However, recent trials in patients hospitalized with a wide variety of acute medical illnesses have demonstrated a risk of VTE in medical patients comparable with that seen after major general surgery. In addition, epidemiologic studies have shown that between one quarter and one half of all clinically recognized symptomatic VTEs occur in individuals who are neither hospitalized nor recovering from a major illness. This expanding understanding of the population at risk challenges physicians to carefully examine risk factors for VTE to identify high-risk patients who could benefit from prophylaxis [3].

2.2. Epidemiology

Data from the Worcester DVT study indicate that the annual incidence of VTE is 1/1000 individuals.²¹ The incidence increases with age, with a 200-fold increase between ages 20 and 80 years. In this study, 12% of patients who experienced their first episode of VTE died while hospitalized. The risk of in-hospital mortality increased with advancing age; only 2% of patients younger than 40 years died, compared with 16% of those older than 80. Mortality was greatest within the first 12 months, approaching 20% at 1 year. The actual incidence of VTE may have been underestimated because patients from long-term care facilities and rehabilitation centers were not included in the analysis, and a low autopsy rate may have underestimated VTEs' contribution to in-hospital mortality.

Other investigations confirmed the increased frequency of VTE and the climb in short-term and long-term mortality risks associated with advancing age.¹⁰⁴¹ The risk of PE more than doubled (relative risk [RR] 2.29, 95% confidence interval [CI] 2.09-2.51) in patients aged 85-89 years compared with those aged 65-69 years, whereas the risk of DVT almost doubled

(RR 1.73, 95% CI 1.59-1.88) in these groups.¹ In another study, the diagnosis of PE increased the risk of 30-day mortality that further was amplified in the elderly.^{1,41} The prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) determined that the risk of mortality 1 year after PE doubled for patients older than 60 years.^{1,51} Observation of VTE trends across 25 years indicate a decrease in the occurrence of PE, but a steady increase in the frequency of all VTEs in the aging population.¹ Extrapolation of these data suggests that the absolute number of VTEs is expected to rise as a country's population ages. Therefore, it is not unrealistic to anticipate an increased risk of VTE in hospitalized patients and to expect an increased need for prevention as the medically ill age.

2.3. Risk factors for VTE

Several risk factors have been suggested to contribute towards the occurrence of thromboembolism^[31]. Some of these are outlined in table 1.

Table 1: Risk factors for venous thromboembolism[31,62]

Age	<p>Exponential increase in risk with age. In the general population:</p> <p>< 40 years - annual risk 1/10,000</p> <p>60-69 years - annual risk 1/1,000</p> <p>> 80 years - annual risk 1/100</p> <p>May reflect immobility and coagulation activation</p>
Obesity	<p>3 times risk if obese (body mass index ≥ 30 kg/m²)</p> <p>May reflect immobility and coagulation activation</p>
Varicose veins	<p>1.5 times risk after major general / orthopaedic surgery</p> <p>But low risk after varicose vein surgery</p>
Previous VTE	<p>Recurrence rate 5% / year, increased by surgery</p>
Thrombophilias	<p>Low coagulation inhibitors (antithrombin, protein C or S)</p> <p>Activated protein C resistance (e.g. factor V Leiden)</p> <p>High coagulation factors (I, II, VIII, IX, XI)</p> <p>Antiphospholipid syndrome</p> <p>High homocysteine</p>
Other thrombotic states	<p>Malignancy 7 times risk in the general population</p> <p>Heart failure</p> <p>Recent myocardial infarction / stroke</p> <p>Severe infection</p> <p>Inflammatory bowel disease, nephrotic syndrome</p> <p>Polycythaemia, paraproteinaemia</p> <p>Bechet's disease, paroxysmal nocturnal haemoglobinuria</p>
Hormone therapy	<p>Oral combined contraceptives, HRT, raloxifene, tamoxifen-3 times risk</p> <p>High-dose progestogens 6 x risk</p>
Pregnancy, Puerperium	<p>10 times risk.</p>
Immobility	<p>Bedrest > 3 days, plaster cast, paralysis, 10 x risk; increases with duration</p>
Prolonged travel	<p>Especially air travel.</p>
Hospitalisation	<p>Acute trauma, acute illness, surgery 10 x risk</p>
Anaesthesia	<p>2 times general vs spinal / epidural</p>

2.3.1. Age

A number of studies support an association between increasing age and a higher incidence of VTE [2,12,44] Patients >40 years of age are at significantly increased risk compared with younger patients, and risk approximately doubles with each subsequent decade. Venous thromboembolism is rare in children,[45,46] and young patients with venous thrombosis usually have strong predisposing factors, such as multiple trauma, leg fractures, or indwelling central venous lines.[47,48]

2.3.2. Obesity

Obesity has long been cited as a risk factor for VTE.[49] but a number of studies have found no association with excess weight.[50] Studies of morbidly obese individuals suggest that the risk of VTE based on obesity alone is low.[51] Overweight individuals, whether defined by weight or body mass index, may be at increased risk.

2.3.2 Varicose Veins

The importance of varicose veins as an independent risk factor for VTE is controversial, because assessment of varicose vein severity is subjective, and the number of studies is small. A population-based case-control study by Heit *et al.* found that the risk of VTE associated with varicose veins decreases with age: odds ratios 4.2 at 45 years, 1.9 at 60 years, and 0.9 at 75 years. [50] On balance, varicose veins are a weak risk factor for VTE [7, 9].

2.3.3 Prior VTE

Patients with a previous episode of VTE are at greatly increased risk for recurrence, particularly when exposed to high-risk conditions (like major surgery, prolonged immobility, or serious illness).

The risk of recurrent VTE grows with time, ranging from 17.5% 2 years after the first VTE to

30 3% after 8 years.^[3b] Recurrent VTE will manifest as PE in 20% of patients, of which half will be fatal. The remaining 80% will experience DVT.^[1o] Therefore, prevention of an initial thromboembolic event in those at risk is crucial.

2.3.4 Immobility

Medically ill patients are often immobile for several days. Immobility is a known risk factor for development of VTE since it promotes venous stasis and impairs venous return from the lower extremities.^{^21} Venous stasis also causes endothelial hypoxia at the site of stasis, which damages endothelium and activates intrinsic and extrinsic clotting cascades.^[2?] Decreased venous return from the legs also leads to local accumulation of clotting factors that may trigger thrombogenesis.^{'''}

2.3.5 Oral Contraceptives

As oral estrogen compounds became widely available in the late 1960s; early reports suggested an alarming incidence of VTE in young and otherwise healthy women taking oral estrogen to prevent conception. [62]

Like women receiving estrogens for contraception or menopause, men receiving estrogen therapy for prostate cancer are also at increased risk for VTE. [70]

2.3.6 Pregnancy and the Puerperium

Fortunately, the absolute risk of developing clinically important VTE during pregnancy or postpartum is low.[57] Despite the low incidence, however, PE is a leading cause of maternal death after childbirth, with approximately « clinically recognized PE per 1,000 births and one fatal PE per 100,000 births.[58,59] The greatest risk occurs during the postpartum period. Carter *et al* found that the incidence of DVT was similar for pregnant and non pregnant women of similar age, but the incidence was 20 times higher during the postpartum period

compared with an age-matched cohort of non pregnant women.[60] The risk of VTE in pregnant women is increased by smoking, prior VTE, and inherited thrombophilias^{1]}

2.3.7 Congestive Heart or Respiratory Failure

Patients with congestive heart or respiratory failure are also at risk of venous thrombo embolic complications [39, 40].

2.3.8 Myocardial Infarction

Myocardial infarction (MI) is associated with DVT. The VTE risk of patients hospitalized with acute MI is comparable with that of moderate-risk general surgical patients («*20% overall and 2% symptomatic). [40]. Among medical diseases, those reported to confer the highest independent risk of VTE in a population-based, case-control study with multivariate analyses were malignant neoplasms with and without chemotherapy (odds ratio [OR], 6.5 and **4.1**, respectively), prior superficial vein thrombosis (OR, 4.3), and neurologic disease with extremity paresis (OR, 3.0).^{(62]} Among hospitalized nonsurgical patients, VTE risk is especially high among the critically ill.

The most feared consequence of DVT is PE. Once a thrombus has formed in the deep veins of the legs, portions of it may embolize and flow upstream into the central circulation. The embolus will travel through the right side of the heart and lodge in the pulmonary vasculature, causing PE. Twenty percent of untreated DVTs progress to clinically significant PE.^{137]} The consequences of PE can be catastrophic. Alveolar dead space and altered blood flow impair gas exchange, decrease pulmonary compliance, and may result in pulmonary infarction. This process can lead to acute hemodynamic compromise and even death. Patients who survive the first event may have increased pulmonary vascular resistance and increased right ventricular after load, which may lead to pulmonary hypertension and right ventricular heart failure.^[37-38]

Factors that promote venous stasis, result in vascular endothelial damage, or promote hyper coagulability contribute to the risk of VTE. Both ACCP and the Thrombo embolic Risk Factors (THRIFT) consensus group established similar risk factors^[9, j9] Hospitalized patients often have many risk factors, and they appear cumulative.^{ij1} In addition to those listed, both groups acknowledge inherited thrombophilias (antithrombin, protein C, protein S, Factor V Leiden deficiencies), the presence of phospholipid antibodies, and hyper homocysteinemia as risk factors.

Providing prophylaxis is a priority in patients with established risk. In those undergoing major orthopedic surgery (total hip replacement, total knee replacement, hip fracture surgery), prevention is a necessity. In orthopedic patients not receiving postoperative VTE prophylaxis, DVT and PE occur at a rate of 40-84% and 0.7-30%, respectively.^[9] Prevention of VTE is not as well studied in hospitalized medical patients as in surgical patients. Risks for and the need to prevent VTE are easily identified in the latter because those patients are well defined with regard to type of surgical procedure and demographics. In the medically ill, however, the heterogeneity of demographics, acute illnesses, and co-morbidities make determining the risk challenging. Some medical conditions, however, have been identified as high risk and require aggressive prophylaxis.

The frequency of DVT in patients experiencing acute myocardial infarction or acute ischemic stroke is high. In these disorders, 24% and 55% of patients, respectively, developed DVT in the absence of antithrombotic therapy.^[40n44] Cancer also carries a high risk of VTE, which is attributed to surgery, chemotherapy, radiotherapy, central venous catheters, and hyper coagulability associated with malignancy. The risk of postoperative DVT is doubled in patients with cancer compared with those without malignancy undergoing similar procedures.¹⁴⁵¹ Treatment of cancer alone increased the risk of DVT (RR 1.6) and PE (RR

3.0), and VTE risk declined after discontinuation of therapy.^{46]} Despite identification of high risk in these homogeneous medical patients, the risk of VTE and need for prophylaxis in other medically ill patients receive little attention.

Evidence providing a solid estimation of the frequency of VTE in patients with acute medical illness is limited. Trials lack consistency in terms of sample size and methodology, and the primary diagnosis and coexisting risk factors in trials of prophylaxis vary. From available data, the frequency of VTE in medical illness is 10-26%.^{[4/00i}

Although a consistent definition does not exist, one trial defined immobility as unassisted ambulation of less than 10 MJ¹¹ Based on this definition, most hospitalized patients who are restricted to their rooms do not ambulate far enough to offset the risk. Most trials use 3-7 days of immobilization to define risk, but it is often difficult to predict at admission which patients will experience prolonged immobility.

Other data identify the risk of VTE in a variety of medical illnesses by primary diagnosis. In a small study, 26% of 46 patients hospitalized for chronic obstructive pulmonary disease (age > 40 yrs) and requiring bed rest for at least 3 consecutive days developed DVT confirmed by venography.^[50]

Heart failure and chronic lung disease are predictors of death 1 year after PE.^[35] Although PE was the actual cause of death in 2.5% of all patients, the risk of mortality at 1 year was higher in those with heart failure (RR 2.7, 95% CI 1.5-4.6) and chronic lung disease (RR 2.2, 95% CI 1.2-4.0). A DVT was detected by ultrasound in 33% of 100 medical intensive care unit patients; nearly half had acute respiratory distress syndrome or pneumonia.^[2]

According to autopsy reports from various medical services in a Swedish hospital, VTE was confirmed at a rate of 26-36% of internal medicine and infectious disease patients, with fatal

PE the confirmed cause of death in up to 9% and 11%, respectively.^[53] This suggests a substantial risk in the medically ill, especially those with cardiopulmonary disorders.

2.4. Diagnosis and Clinical Confirmation

Once thrombogenesis has occurred, it is difficult to detect DVT and PE accurately since many patients are asymptomatic. If signs and symptoms do occur, their evolution may occur over hours to weeks. Clinical manifestations are often nonspecific, making the differential diagnosis extensive. Confirmation requires complete clinical assessment of patient and risk factors, and objective testing^[406]

One of the most frequently encountered shortcomings of trials of VTE prophylaxis is selecting the objective method to determine prophylaxis efficacy. Contrast venography is the only method that retains both sensitivity and specificity to diagnose DVT definitively in asymptomatic patients^[55], all other noninvasive methods do not retain their diagnostic value.

Many existing trials in medical illness adopted ultra sonography as the method to detect asymptomatic DVT. The sensitivity of both Doppler and duplex ultra sonography is 40-60% in these patients^[58,60].

Other studies used the Radiolabeled Fibrinogen-Uptake Test (RFUT) as the screening method of choice, but it also loses sensitivity in asymptomatic patients (< 50%).^[5,7] Contrast venography remains the gold standard for DVT diagnosis in these patients, but venography and screening of asymptomatic patients are uncommon in clinical practice. Perhaps many episodes of VTE in the medically ill are overlooked because they often occur without symptoms, and only half of asymptomatic episodes are detected by ultrasonography.

Since a connection between asymptomatic disease and patient outcomes has not been

identified, screening for asymptomatic VTE remains controversial. However, retrospective evaluation of autopsies and medical records reveal that clinical suspicion of VTE before death is low.^[61] Of 195 pulmonary emboli confirmed at autopsy, only 38 patients (19%) experienced a clinically suspected DVT, indicating that asymptomatic VTE is accompanied by an impressive mortality rate. Since symptoms are not clinically reliable and asymptomatic VTE is difficult to diagnose, medical patients with risk factors must be identified so that appropriate prophylactic measures are employed.

2.5. Administration of Prophylaxis

Despite ACCP consensus guidelines for VTE prevention, prophylaxis remains under administered.^[7,91] Investigation of more than 2000 inpatient records revealed that only 32% of patients with several risk factors for VTE received appropriate prophylaxis.^{^1} Adequate preventive therapy was defined as prophylaxis (pharmacologic, mechanical, device placement) provided for at least 24 hours in patients with at least three risk factors. Prophylaxis was given more frequently in teaching than in non- teaching hospitals (44% vs 19%, $p < 0.001$) and in surgical than in medical patients (34% vs 30%, $p < 0.001$). These data may underestimate the actual administration of prophylaxis since the investigation was near completion when the National Institutes of Health released its first consensus statement on VTE prevention. However, prevention may be overestimated because of clinical and research interests in VTE in the geographic area in which the study was conducted.

A more recent retrospective evaluation identified cases of preventable VTE and examined reasons for inadequate prophylaxis.^[8] Thrombo prophylaxis was adequate if the regimen was recommended in the 1995 ACCP guidelines, was given regularly for 7 days or until patient discharge or ambulation, or if it was started within 24 hours of a risk-defining event.

A VTE was defined as preventable if it occurred in a setting in which prophylaxis was

indicated, but omitted or inadequate. One of six cases of all VTEs was potentially preventable and 66% of VTEs for which prevention was indicated occurred without adequate prophylaxis. Omission was the most frequent reason for inappropriate prophylaxis; this occurred in almost half (47.7%) of patients. Other reasons for inadequate prophylaxis were delay in starting it and inappropriate drug, dosage, or duration. The most frequently missed indication for prevention in medical patients was admission for pneumonia or stroke with lower limb paralysis.

Potential barriers to appropriate VTE prophylaxis should be considered. In some cases, lack of awareness regarding the risk may be present. Prophylaxis may be easily overlooked at the time of admission because attention is focused on more acute problems. Clinicians may have concerns regarding the safety of prophylaxis regimens, patient comfort with many daily injections, and cost, especially LMWH. Regardless, much improvement is necessary in starting thromboprophylaxis, and literature is available to guide clinicians in reducing VTE risk in the medically ill.

In studies utilizing periodic screening (for example, venography) to detect asymptomatic thrombosis, DVT has been estimated to develop within the first week in more than 30% of patients who are admitted to intensive care units (ICUs) and do not receive prophylaxis.¹⁶⁴¹

High risks of DVT in the absence of antithrombotic therapy have also been documented among patients with acute myocardial infarction (about 24%) and those with ischemic stroke and a paralyzed lower extremity (pooled risk of 55%).¹⁶⁴¹ It is important to note that these high rates of DVT are based on screening and that the great majority of thromboses so identified would remain undiagnosed in clinical practice. For example, in a randomized placebo-controlled trial of enoxaparin prophylaxis among acutely ill medical patients at increased risk of VTE, the rate of DVT among those receiving placebo was 14%, but of 42

cases documented by screening (almost all by venography), only 2 (5%) were symptomatic⁶³¹

On the basis of well-established risks and the demonstrated efficacy of prophylaxis with anticoagulants, VTE prophylaxis is recommended and widely prescribed for many types of surgery.^[64] The risks of VTE among medical patients have been less well studied and there have been many fewer trials of antithrombotic therapy for VTE prophylaxis in this patient population. Consequently, VTE prophylaxis is believed to be underutilized for medical patients compared with those undergoing surgery^[64].

Patients with acute myocardial infarction, ischemic cerebrovascular disease, and atrial fibrillation are exceptions to this statement, as they usually receive antithrombotic therapy; the primary motivation for such therapy is prevention of arterial thrombosis, however. Prevention of VTE is a secondary benefit. Information on the risks of clinical VTE in hospitalized medically ill patients undoubtedly would highlight the benefits of prophylaxis in this patient population^[63].

This study confirms findings of earlier studies that the risk of clinical VTE in hospitalized medically ill patients, while less than that among patients undergoing major surgery, is not negligible^[47]. The findings also suggest that VTE risk may persist following hospital discharge. Patients with a history of recent VTE or surgery, those who are admitted to the ICU, those with an admitting diagnosis of heart failure, and those with active cancer are at especially high risk of VTE and deserve increased consideration for prophylaxis ^[47, 48],

2.6. Contraindications to VTE prophylaxis

It should be noted that there are cases where VTE prophylaxis should not be given. These may be considered as either chemical or mechanical prophylaxis.

Table 2 Contraindications in use of VTE prophylaxis

Chemical prophylaxis	Mechanical prophylaxis
Active bleeding	Severe peripheral arterial disease
High risk of bleeding e.g. Haemophilia, thrombocytopenia (platelet count <50 x10 ⁹ /L), history of GI bleeding	Severe peripheral neuropathy
Severe hepatic disease (INR >1.3)	Severe leg deformity
Adverse reaction to heparin	Recent skin graft
On current anticoagulation	Other (please state):

2.7. Regional studies on venous thromboembolism (VTE)

Several studies on VTE have been carried out in the region with results comparable to the **global** picture.

In an Eritrean study by Goitom *et al.* at Orotta National referral hospital, Asmara, Eritrea it **was** found that VTE prophylaxis was underutilized by physicians. For all the ICU patients **studied** none had got prophylaxis against venous thromboembolism (VTE). There were **previous** reported DVT cases of only 3 % due to limited diagnostic tools available in the **country** [66].

At Mulago hospital in Kampala Uganda, A study by Mangeni *et al.*, (2003)', found a VTE **prevalence** of 13.2%, with a male to female ratio of 1:1 and age peaks of 21-30 years. This **showed that** VTE is a major problem to hospitalized patients.[67].

Table 2 Contraindications in use of VTE prophylaxis

ChemkaLnn?P ^{hv,axis} -	Mechanical DroDhvlaxis
Active bleeding	Severe peripheral arterial disease
High risk of bleeding e.g. Haemophilia, thrombocytopenia (platelet count <50 x10 ⁹ /L), history of GI bleeding	Severe peripheral neuropathy
Severe hepatic disease (INR >1.3)	Severe leg deformity
Adverse reaction to heparin	Recent skin graft
On current anticoagulation	Other (please state):

2.7. Regional studies on venous thromboembolism (VTE)

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An earlier study at Kenyatta National Hospital by Bonass, B G, established that DVT and PE are under diagnosed. Only 42.1% of patients were positively diagnosed as having DVT and 57.9% were missed out. This indicated low clinical suspicion of the problem. The majority of the patients 76.6% were female and only 23.4% were male. This further indicated the higher risk females have of developing DVT and PE.[68].

2.7 Statement of the Problem

Data from western countries indicate that the annual incidence of venous thromboembolism (VTE) is high (1/1000 individuals) [2]. And the extent of VTE prophylaxis is low. Failure to give prophylaxis could lead to increased morbidity and mortality. Local data on VTE prophylaxis is scanty but it's probably much lower than the western countries rate of prophylaxis. It is with this that the study endeavored to establish the extent of venous thromboembolism and the rate of VTE prophylaxis in Kenya.

2.8 General Objective

The purpose of this study was to determine the extent of venous thromboembolism prophylaxis among medical in-patients.

2.8.1 Specific Objectives

The objectives of this study were to:

- i) Determine the extent of:
 - a) Venous thromboembolism among the medical in-patients at KNH.
 - b) Venous thromboembolism prophylaxis among medical in-patients at KNH
- ii) Establish the pharmacological interventions being used in venous thromboembolism prophylaxis at KNH.
- iii) Find out the non pharmacological measures being used in venous thrombolism prophylaxis at KNH
- iv) Establish the considered contraindications of venous thromboembolism prophylaxis in medical in-patients in KNH

2.9 Research Questions

The main research questions of this study were:

- i) What is the extent of:
 - a) Venous thromboembolism among the medical in-patients at KNH?
 - b) Venous thromboembolism prophylaxis among the medical in-patients at KNH?
- ii) What are the pharmacological interventions being used in the VTE prophylaxis among the medical in patients at KNH?
- iii) What are the non pharmacological measures being used in the VTE prophylaxis at KNH?
- iv) What are the contraindications to VTE prophylaxis in medical in-patients in KNH?

2.9 Study Justification

Venous thrombo embolism is an established global problem that is associated with increased morbidity and mortality to hospitalized patients, but there is very little information on VTE in Kenya and KNH in particular. Furthermore in the VTE prophylaxis there has been bias towards surgical patients who are routinely covered for VTE. This prompted the investigator to want to find out more about the prophylaxis of VTE in medical patients.

2.10 Study Limitations

Patients who had poorly recorded information and bad hand writing by the clinicians that was illegible presented a challenge to the researcher. Some members of staff were uncooperative and reluctant to offer some vital information to the researcher. This was minimized by establishing good working relationship with the members of staff and reassuring them that the information given will be kept confidential and will not be used

for any other purpose other than for the research work.

METHODOLOGY

3.1 Study Setting

This study was carried out in medical wards at Kenyatta National Hospital (KNH). Kenyatta national Hospital is the largest teaching and referral hospital in east and central Africa. It's the main referral hospital for Kenya

3.2 Study Design

The study was a crossing sectional study on patient's hospital records, who were still admitted in the medical wards.

3.3 Target Population

The study targeted medical in-patients with high risks of developing venous thromboembolism that were admitted into the eight medical units of KNH during the period Jan 2010 to June 2010. The study targeted patients that were still in the wards so that the current practice in the prevention of development of thrombosis while in the hospital could be assessed (audited).

3.3.1 Inclusion Criteria

The following patients were included in the study:

- Adult patients (more than 18 yr) admitted in medical wards and had the risk factors for developing venous thromboembolism.
- Patients who had stayed for at least four days after admission and whose baseline investigations had been done.

3.3.2 Exclusion Criteria

The following was the exclusion criteria:

- Less than 18 years of age.
- Newly admitted patients, before baseline investigations were done were not included in the study.

3.4. Sample Size and Sampling Procedure.

There being no previous studies carried out on the VTE prophylaxis at KNH, local data on the prevalence of venous thromboembolism among medical patients was not available.

Convenient sampling was used to get the ²⁰ patient files. For purposes of sample size

calculation, the prevalence for America which is at 10 per cent as per the ACCP (2, 3) was assumed and used.

3.4 Sample size estimation

The prevalence (p) of VTE among medical in- patients is approximately 10%. The standard error (S.E) of this measure estimated to be * 5%. The sample size is calculated using the given formula:

$$\begin{aligned} N &= P (1-P)/S.E^2 \\ &= 0.1 \times 0.9 / (0.025^2) \\ &= 0.1 \times 0.9 / 0.025 \times 0.025 \\ &= 144. \end{aligned}$$

All the patients who were admitted in all the eight medical wards in KNH between January 2010 to June 2010 and who satisfied the inclusion criteria were recruited into the study. This generated a universal sample of 168 patients. Purposive sampling was used to identify patient files that qualified in the inclusion criteria and it resulted into 168 patients being recruited. The increase in patient numbers from the calculated minimum of 144 was to help improve validity and also to take care of any loss of data (patient attrition) during the study. Hence, a total of 168 patient files were recruited for the study.

3.5. Ethical Considerations and Informed Consent

The investigator sought and was granted approval to carry out the study from The Kenyatta National Hospital and University of Nairobi Ethics and Research Committee.

Given the study involved only information captured from patients' files, a consent waiver was sought and granted from the ethics committee because the investigator was not to interview the patients.

3.6. Confidentiality

The patients whose files were used were coded. Patient names were not entered into data collection forms. The data extracted from the patient files were stored securely under lock and key. The raw data will be destroyed once the study findings have been compiled into the research dissertation.

3.7. Study Benefits

It is anticipated that future patients will benefit from study findings, as the need for developing a VTE prophylaxis protocol in the hospital may become a reality. This protocol will help reduce the morbidity and mortality associated with the venous thromboembolism.

The findings of the study will be shared with the health care providers in KNH namely Physicians, Medical postgraduate students (Registrars), postgraduate clinical pharmacy students, medical officers, various interns and nurses. They may be able to improve on the venous thromboembolism prophylaxis to high risk patients.

The hospital management may also use the findings from the study to know the extent of venous thromboembolism prophylaxis done to medical in patients. This information will help the Hospital management lay out strategies of improving on venous thromboembolism prophylaxis in medical in-patients, thus reduce the morbidity and mortality associated with venous thromboembolism in the hospital. Future researchers in this area may also replicate the study in other settings.

3.8. Risk Involved

There were no risks involved to the patients as information was obtained from the patient files.

3.9 Data Collection Method

All medical in-patients' files were obtained from the medical wards and perused through all

of them to determine patients with risk factors for venous thromboembolism. Those patients with risk factors for VTE and who met inclusion criteria were then identified. The identified files were then separated from the rest of files. A Thorough study was carried out on each patient's medical record using the VTE risk assessment tool to determine if the patient received prophylaxis for VTE and if not why.

3.10 Data Analysis Procedure

The data collection tool was piloted before use by randomly perusing 20 VTE high risks medical in-patients records. The data collection tool was then adjusted and reformatted accordingly.

The data collected was coded and edited for accuracy and completeness. The data was transferred from the data collection tool into a Microsoft Access database and analyzed using SPSS version 13.0 software.

The descriptive data was analyzed quantitatively using descriptive statistics and was presented using tables, graphs, charts and summary derived from the data.

RESULTS AND DISCUSSION

4.1 Age Distribution

A total of 168 files of patients with risk factors for developing venous thromboembolism were studied. Of the 168 cases, the ages ranged from 18 to 98 years with a peak of age 31-40 years (30.1 %) as presented in fig. 1.

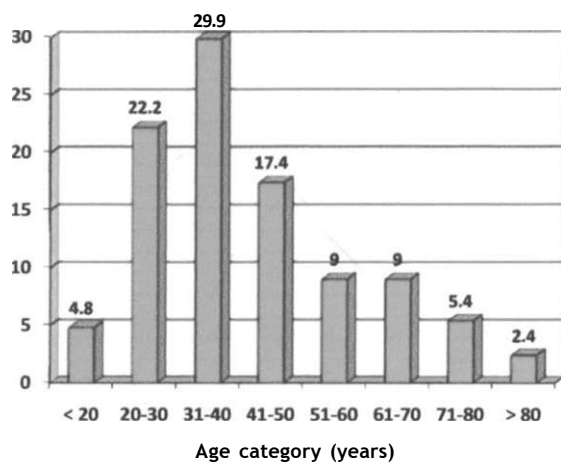


Figure 1. Age distribution

In a previous study by Bonass at Kenvatta National Hospital (KNH) [68], the age distribution ranged between 13 to 82 years with a peak of 41 -45 years. This age peak was much higher compared to this study. In a similar study done by Mangeni at Mulago National Hospital, Uganda [67], the age range was from 12 to 81 years which was similar to this study. In a retrospective study by Goitom at Orotta National hospital Asmara, Eritrea [66] that looked at DVT in intensive care patients the age range was 20 to 99 years and had age peak at 30- 39 years. This age peak was also similar to one in this study.

From the above studies its thus apparent that the age groups (31-40) affected in the African set up tends to be much lower compared to the western figures of 40 years and above[1].

4.2. GENDER

Of the 168 patients evaluated, 49.4% were males while 50.6% were females giving a male to female ratio of 1:1 similar to a study by Mangeni at Mulago National hospital [67]. In a retrospective study by Goitom at Orotta National hospital Asmara, Eritrea [66] had male to female ratio of 1:1 while prospective study by Bonass at KNH [68] showed a ratio of 1:3 where the researcher reported the use of hormonal contraceptives as being a major contributory to the increased female ratio. Other previous studies report approximate 1:1 male to female ratio when female factors like pregnancy and contraceptives are not considered.

4.3. Prevalence of VTE

Out of the total population of 168, 18.5% had either a history of venous thromboembolism (VTE) or a current VTE. From this study, the prevalence of VTE in medical patients at KNH stands at 18.5 %.

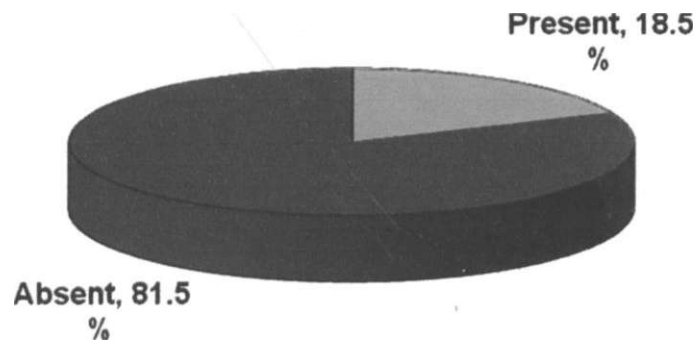


Figure 2: Prevalence of VTE

A study by Mangeni at Mulago National hospital Uganda [67], reported a prevalence of 13.5% which is comparable to the findings in this study. In a retrospective study by Goitom at Orotta National hospital Asmara, Eritrea [66] that looked at DVT in intensive care patients the prevalence of DVT was 8%. The low percentage was explained by the author as having been due to the limited diagnostic capacity of the hospital [66].

4.4. Risk factors for venous thromboembolism.

A presumptive conclusion of the risk factors associated with VTE is presented here in table 1; a clear picture could only be shown in a prospective study. The commonest risk factor was immobility (>4 days, stroke and paralysis of legs) which had 39% of the total patients analyzed. This was followed by increasing age >40 years which had 66 cases representing 21% of the total risks. Heart failure is an important risk factor as it was third commonest having 40 (13%) of the cases. Other factors that are important in VTE development are previous venous thromboembolism which had 8%, malignancy which had 5% and nephrotic syndrome having 3%.

TABLE 3. Risk Factors for developing VTE

Factor	Frequency	Percentage
Immobility *> 4 days) stroke, paralysis of the legs	122	39
Increasing age > 40 years	66	21
Heart failure	40	13
Previous venous thromboembolism	26	08
Malignancy (pelvic, abdominal, metastatic)	20	06
Nephrotic syndrome	16	5
Burns and sepsis	11	3
Indwelling central venous catheters	5	2
Trauma (pelvic, hips, legs)	2	1
Recent myocardial infarction	2	1
Obesity BMI > 25	1	0.3
Pregnancy and ^postpartum	1	0.3
Recent CNS surgery	1	0.3
Total	313	100

In a similar study done by Mangeni at Mulago National Hospital, Uganda [67], it reported immobility or prolonged bed rest as the highest risk at 52.6% of the VTE cases followed by previous DVT at 13.2% and then malignancy and cardiac diseases at 5.3%. It is therefore evident that the biggest risk to hospitalized patients for developing VTE is immobility or prolonged bed rest.

Pregnancy, postpartum and hormonal contraceptive uses are known risk factors for VTE in women [57-62]. In this study, the above factors did not come out clearly because clinicians in the medical wards either did not inquire about them or were not recorded. Such very important information was missing in the patient files. Other known factors such as varicose veins [50], were not recorded in the patient records, which means that clinicians did not consider them important.

Obesity has long been cited as a risk factor for VTE [49-51]. Obesity as an independent risk factor did not come out well in this study because most patients in the wards not have their weight taken. Lack of weight as part of patient's bio data made it impossible to consider obesity as a contributing risk factor. This factor can easily be demonstrated if prospective study is done.

4.5. Number of risk factors

The table 4 shows the number of patients who had one or more risk factors. Of the 168 patients studied, 31.1% had only one risk factor, while most patients 47.3% had combination of two risk factors. Those who had three risk factors or more were 21.6%. This shows that VTE is a result of a combination of several factors.

Table 4. Patients Combined risk factors

Number of risk factors	Frequency	Percentage
1	52	31.1
2	79	47.3
3	36	21.6
Total	167	100

Table 5: Prophylaxis use in patients with multiple risk factors

No of risks	Missed prophylaxis	Received prophylaxis	Contraindicated prophylaxis	Total (%)
1	17(33.3%)	31(60.8%)	3(5.9%)	51(100%)
2	32(40.5%)	37(46.8%)	10(12.7%)	79(100%)
j	17(47.2%)	18(50.0%)	1(2.8%)	36(100%)

Table 5 above shows how the various patients who had one or more risk factors for developing VTE received VTE prophylaxis. Of those patients who had only one risk factor 33.3% missed out on prophylaxis, 60.8% received prophylaxis while 5.9% were contraindicated to pharmacological prophylaxis. Those with two risk factors 40% were left out of prophylaxis 46.8% received the prophylaxis while 12.7% had contraindications to chemical prophylaxis.

Patients with three or more risk factors 47.2% missed prophylaxis, 50% received prophylaxis while one (2.8%) were contraindicated to prophylaxis.

4.5 Methods of diagnosing venous thromboembolism VTE

The table 6 below shows the methods of diagnosis and confirmation used in the determining the cases of VTE. Some were used singly while some in combination.

Table 6. Methods of VTE diagnosis

Mode of diagnosis	Frequency	Percentage
Clinical manifestation, ultrasonography	18	62.1
Clinical manifestation, contrast venography	7	24.1
Clinical manifestation, contrast venography, ultrasonography	3	10.3
Clinical manifestation	1	3.4
Total	29	100

Majority of patients were diagnosed and confirmed using clinical manifestation and ultrasonography 62.1%. A study by Mangeni at Mulago National hospital [67] showed that 60% of the suspected VTE patients are diagnosed using ultrasonography. Ultrasonography has become the first line imaging modality because of its advantages such as safety, availability, low cost, ability to detect other pathology other than DVT and PE and has ability to directly visualize a thrombus.

Out the 29 patients with VTE, 24.1% were diagnosed using the clinical manifestation and contrast venography. Contrast venography is taken as the gold standard for diagnosis of DVT despite its disadvantages, which include invasiveness, exposure to radiation, adverse

reactions to contrast agent and is costly compared to ultrasonography.

A combination of three diagnostic tools namely; clinical manifestation, ultrasonography and contrast venography were used in only 10.3% patients. This could have been due to increased cost and increased adverse reactions.

Only one patient is reported to have been diagnosed using only clinical manifestation of VTE. This is because clinical diagnosis of VTE is reported to be unreliable [57, 66, and 67].

4.6. Drugs used in VTE prophylaxis

Out of 93 patients put on VTE prophylaxis 65.5% were on heparin. The second commonly used drug was enoxaparin which was used in 18.3% of the cases while warfarin was used in only 9.7% of the cases. The least used was a combination of heparin and warfarin which was used in 6.5% of the patients [Table 7 & figure 3].

Table 7: Drugs used in VTE prophylaxis

Drug	Frequency	Percent
Heparin 5000 IU SC 8 hourly BD	61	65.6
Enoxaparin 40 units SC daily	17	18.3
Warfarin 5mg orally daily	9	9.7
Heparin 5000, Warfarin 5mg orally daily	6	6.5
Total	93	100

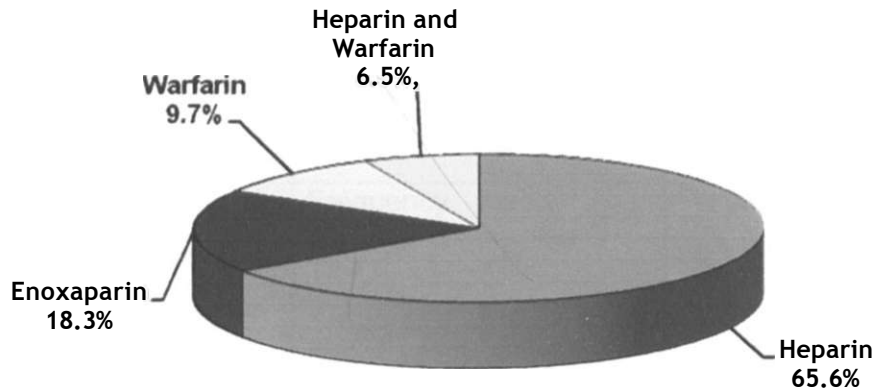


Figure 3: Drugs used In VTE prophylaxis

Heparin was commonly used because its more affordable compared to enoxaparin. Even though enoxaparin has less side effects and requires less monitoring compared to heparin, its cost is still prohibitive. Warfarin, the only orally active anticoagulant available in the hospital (KNH) was used mainly in stable patients requiring anticoagulation therapy for long-term

Newer anticoagulants (low molecular weight heparins) e.g. enoxaparin, pentasaccharides (fondaparinux) have reduced side effects and require less monitoring compared to the parent heparin. The only other orally active anticoagulant (Dabigatran) is still new in the market hence not yet used in the hospital.

4.6 Extent of VTE prophylaxis

Of the 168 patients studied, 52.1% received the prophylaxis while 8.4% did not receive prophylaxis. While 8.4% did not receive prophylaxis because they had contraindications

against it. Of greater concern are 39.5% of patients who required prophylaxis but were left out. About 40 % of the patients that qualified for prophylaxis are left out at the KNH.

Table 8: Patients who got and those who missed prophylaxis.

	Frequency	Percent
Patient did not receive prophylaxis and qualifies for prophylaxis	66	39.5
Patients did not receive prophylaxis, did not qualify for prophylaxis	14	8.4
Patient did receive prophylaxis and qualifies for prophylaxis	87	52.1
	167	100



KEY A: Patients who received VTE prophylaxis

B: Patients who missed VTE prophylaxis

C: patients who were contraindicated to chemical prophylaxis

Figure 4. Status of patient prophylaxis

In a retrospective study by Goitom at Orotta National hospital Asmara, Eritrea [66], prophylaxis against VTE was highly underutilized by physicians, indeed it was not provided to any patient in his study. Given the morbidity and mortality associated with VTE, it would be appropriate if every patient that needs prophylaxis gets it. This will help reduce increased hospitalization costs and mortalities associated with VTE.

4.7 Contraindications to chemical prophylaxis

The documented contraindications to pharmacological prophylaxis were: Active bleeding which constituted 75% of those with contraindications. This was determined to be the major contraindication. This was followed by uncontrolled hypertension which had 17% of the cases and then lastly was recent CNS surgery that constituted 8% of the patients.

Other causes of contraindication to chemical prophylaxis such as hypersensitivity and history of heparin induced thrombocytosis (HIT) were either absent or were not documented. The researcher took it that they were absent.

4.8 Non pharmacological prophylaxis

From literature there are non pharmacological VTE prophylaxis measures such as use of compression stockings and intermittent pneumatic chest compression [7, 9]. Interestingly there was no patient put on them. Patients in KNH who have contraindications to pharmacological prophylaxis are left without any other form of prophylaxis. Compression stockings are widely used especially for patients having varicose veins. Curiously both varicose veins and graduated compression stockings were not recorded anywhere that patients were having them. There is also no record that patients use intermittent pneumatic compression in the wards. Therefore patients in KNH are left with only one Option of prophylaxis that is use of pharmacological interventions or none. This presents a very bad scenario for those patients who are contraindicated to chemical prophylaxis.

5.1 CONCLUSION

From the study it is clear that the prevalence of venous thromboembolism in Kenyatta National Hospital which stands at 18.5% is higher than 10-13% documented in literature [2, 3, 67]. The extent of provision of VTE prophylaxis is still low. Of the population that required prophylaxis only 52% were given while a big proportion 40% were left out.

The drugs used in providing prophylaxis are heparin 65.5 % followed by enoxaparin 18.3% and warfarin 9.7%. The newer anticoagulants are not widely used despite the fact that they have fewer side effects and do not require frequent monitoring unlike unfractionated heparin, this could be due to their high cost compared with the older anticoagulants.

There were no non pharmacological interventions being given to patients having contraindications to chemical prophylaxis this left them prone to development of VTE. Active bleeding and uncontrolled hypertension were the major contraindications to pharmacological prophylaxis.

Prophylaxis against VTE was highly under utilized by the physicians, indeed it was not provided to 40% of the patients who required it. These findings are anticipated to stimulate more interest in future studies of VTE. The availability of diagnostic tools would help in the prompt diagnosis of DVT and pulmonary embolism.

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5.2 RECOMMENDATIONS

This study highlights the significance of detecting associated risk factors (of VTE) to determine high-risk patient groups and providing prophylaxis to those who deserve. This would help reduce high morbidity and mortality associated with venous thromboembolism.

1. There should be emphasis on the need to aggressively implement VTE risk stratification strategy and provide prophylaxis unless contraindicated
2. The medicines and therapeutic committee of KNH should develop VTE prophylaxis protocol to help improve the level of prophylaxis
3. There is need to carry out continuous medical education (CME) especially to clinicians working in the medical wards concerning risk identification and prophylaxis of VTE
4. Medical personnel working in wards should be sensitized on need to provide mechanical prophylaxis to those patients having contraindications to chemical prophylaxis.
5. Patients should be encouraged to have early mobility as much as possible avoid prolonged immobility (bed rest).
6. Other studies are needed to define the clinical course, natural history and optimum approach for the work up and management of VTE.

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- Platelet less than 100,000
- Documented uncontrolled Hypertension
- Hypersensitivity
- History of heparin induced thrombocytopenia
- Recent CNS surgery
- Other
- Active bleeding

Please select ANY of the following

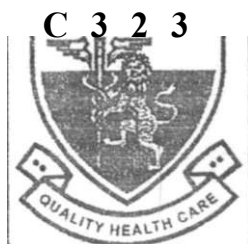
- Patient received VTE prophylaxis
- Heparin 5000 IU S.C. 8 hourly
- Graduated compression stockings
- Enoxaparin 40 units s.c daily
- Intermittent pneumatic compression
- Warfarin 5mg orally daily
- Other
- Fondaparinux 5mg s.c. daily

Conclusion

Patient did not receive prophylaxis and qualifies for prophylaxis

Patient did not receive prophylaxis, did not qualify for prophylaxis

Patient did receive prophylaxis and qualifies for prophylaxis



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Ref: KNH-ERC/ A/459

15th April 2010

Dr. Linus Makokha Wafula
Dept. of Pharmaceutics & Pharmacy Practice
School of Pharmacy
University of Nairobi

Dear Dr. Wafula

RESEARCH PROPOSAL: "SURVEY OF EXTENT OF VENOUS THROMBOEMBOLISM PROPHYLAXIS AMONG MEDICAL IN-PATIENTS IN KENYATTA N. HOSPITAL" (P309/11/2005)

This is to inform you that the KNH/UON-Ethics & Research Committee has reviewed and approved your above revised research proposal for the period 15th April 2010 to 14th April 2011.

You will be required to request for a renewal of the approval if you intend to continue with the study beyond the deadline given. Clearance for export of biological specimens must also be obtained from KNH/UON-Ethics & Research Committee for each batch.

On behalf of the Committee, I wish you a fruitful research and look forward to receiving a summary of your research findings upon completion of the study.

This information will form part of the data base that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Yours sincerely

PROFAN GUANTAI
SECRETARY, KNH/UON-ERC

W I t E R s . i T y U F
M e o / c a l ^ i n o B f

c.c. Prof. K. M. Bhatt, Chairperson, KNH/UON-ERC
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« The Dean, School of Pharmacy, UON
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