RESEARCH ASSIGNMENT

THE PROFILE OF HIV/AIDS PATIENTS ADMITTED WITH DEEP VENOUS THROMBOSIS (DVT) AT NELSON MANDELA HOSPITAL IN MTHATHA, SOUTH AFRICA.

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DECLARATION

I, **Dr Oludayo Olufemi Olubanwo**, hereby declare that this dissertation is my own idea and the result of my own original research; that it has not been submitted for any degree or examination at any other University, and that all the sources I have used or quoted have been indicated and acknowledged with complete references.

DR OLUDAYO OLUFEMI OLUBANWO

ABSTRACT

BACKGROUND

It has been found that HIV infection predisposes to a hypercoagulable state and that the risk of venous thromboembolism is about 10times that expected among people without HIV. Deep vein thrombosis (DVT) has been reported to be more common among HIV infected people in several parts of the country. No formal research has been published to confirm or refute this observation within the South African context. There has thus been the need to determine the true prevalence of deep vein thrombosis among patients with HIV infection in the medical ward of Nelson Mandela Hospital, Mthatha, South Africa.

AIM;

To determine the risk profile and prevalence of Deep Venous Thrombosis (DVT) in patients admitted with HIV/AIDS at the Nelson Mandela Hospital.

OBJECTIVES;

The main objectives of this study were:

- To determine the proportion of patients admitted with DVT who also had HIV/AIDS.
- To obtain a profile of the risk factors associated with DVT in patients requiring admission for DVT.
- To describe the association of DVT and HIV/AIDS in subgroups of patients with different degrees of immunosuppression.

METHODS

We conducted a study in which we collected data retrospectively on all DVT cases admitted over a year period. Detailed information was collected about HIV status,CD4 count, and other risk factors for DVT.

RESULTS

A total of 102 DVT cases were admitted over the period of one year and data was extracted from the charts. A total of 81 (79.4%) of the DVT cases were HIV infected (HIV positive) while 21 cases(20.6%) were HIV negative. Among the other risk factors for DVT considered, 42(41.2%) of the DVT cases were also on treatment for Tuberculosis. Only a small percentage of the DVT cases had co morbidities like obesity,smoking,cancer,diabetes, immobility, kidney disease etc.It was found that 70(68.6%) of DVT cases were < 40yrs of age. Among patients with known CD4 counts, 29(70.7%) had a CD4 count<200 while 12 (29.3%) had a CD4 count ≥ 200. In univariate analysis, HIV (OR = 11.571;95% CI = 4.888 – 27.392) and TB (OR = 1.667.CI = 1.420 – 1.956) had significant association with DVT.When subjected to multiple logistic regression, only HIV (OR = 13.2, 95% CI = 5.3 – 32.3;p = <0.0001) and Age < 40yrs (OR = 2.7, 95%CI = 1.1 – 6.7; p = 0.034) were statistically significantly associated with DVT.A total of 650 HIV related cases were admitted over the same year period which gave a cumulative period prevalence of DVT of 12.5% among the HIV infected population.

CONCLUSION

The prevalence of DVT at the Nelson Mandela hospital Mthatha was 12.5% for the year 2009 and is clearly above the average reported in other studies. HIV infection and age were the risk factors with a statistically significant association with DVT in this study. As this was an observational cross-sectional study, a more definitive prospective longitudinal design would assist in establishing the incidence of DVT in HIV infected patients, as well as the magnitude of the relationship between HIV and DVT.

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GLOSSARY OF ABBREVIATIONS

DVT (Deep vein thrombosis)

TB (Tuberculosis)

HIV (Human immunodeficiency virus)

AIDS (Acquired immunodeficiency syndrome)

OR (odds ratio)

CI (Confidence Interval)

VCT (Voluntary counseling and testing)

CHAPTER ONE

INTRODUCTION AND MOTIVATION

There is reason to believe that the number of patients being admitted with Deep Vein Thrombosis in our hospital recently has increased compared with past records. Many patients have also been admitted with pulmonary embolism some of which were actually diagnosed at autopsy.

Of note is that most of these patients admitted either with DVT or thrombosis at other sites are also infected with Human Immunodeficiency Virus (HIV). Although some of them have other risk factors for thrombosis like obesity, infections (e.g. Tuberculosis) etc, the relationship between thrombosis and HIV infection has been documented by many researchers. It has been documented that HIV infection predispose to a hypercoagulable state which increases their risk of developing thrombosis.[1]

The advent of Highly Active Antiretroviral Therapy (HAART) means that more people who are infected with HIV will be living longer on antiretroviral treatment. This may increase the prevalence of DVT in the population. This apparent increased incidence and prevalence of thrombotic episodes among the HIV infected population has a lot of implications for the health system e.g. in terms of morbidity, mortality and cost. It is also a source of psychosocial problems for the patients who have to be admitted during the acute stage and have to present to follow up clinics for many months after discharge.

Not many studies have been conducted to determine the prevalence of DVT among the HIV infected population in South Africa and especially in my own part of the country. Such a study would therefore be of fundamental importance to determine the true prevalence of DVT in the HIV infected population who present to the Nelson Mandela hospital.

From anecdotal experience in the medical ward of Nelson Mandela Hospital, there is a tendency to offer HCT to patients with DVT so as to utilize the opportunity to start them on ARV treatment in case they are HIV infected, but this is not enough. A study conducted to

establish the true prevalence of DVT among the HIV infected population may give us a scientific basis to offer VCT routinely to patients admitted with DVT.
Almost all past studies are retrospective and are able to demonstrate only association between HIV and thrombosis with very few formal studies on DVT. A study to establish the prevalence of DVT among HIV infected population might stimulate people to conduct a prospective study to formally investigate the relationship between DVT and HIV.

With the rising cost of health in the country, it means that any efforts at developing effective prophylaxis against DVT and thrombosis at other sites will help reduce the cost of health especially when you consider the population of HIV infected people and the high cost involved in Antiretroviral drugs and TB treatment. A study to establish the prevalence of DVT among HIV infected people might be useful as a basis to advise our HIV/AIDS patients on the need to avoid and be aware of risk factors of thrombosis like oral contraceptives pills etc.

This study may serve as a stimulus for more definitive research seeking to establish the association between DVT and HIV/AIDS. Following on such research, formal randomized clinical trials might be done to investigate possible effective prophylaxis against DVT as in the case of aspirin used as prophylaxis against acute myocardial infarction (AMI) and Cerebrovascular Accident (CVA) [23].

CHAPTER TWO

LITERATURE REVIEW

A review of the literature revealed that hematological abnormalities are among the most common manifestations of human immunodeficiency virus [HIV] infection and acquired immune deficiency syndrome [AIDS]. Saif and Greenberg [1] in their review article reported thromboembolic disease among HIV patients who had no clear cut general risk factors such as surgery, trauma, stasis, nephritic syndrome, pregnancy, or other medical conditions associated with thrombus formation. In addition, various abnormalities leading to a hypercoagulable state have been detected in HIV patients who had thrombotic disease. [1; 2; 3; 4;5;6;7] Such abnormalities consistent with a hypercoagulable state include: presence of antiphospholipid antibodies and lupus anticoagulant, increased levels of von Willebrand factor and d-dimer, deficiencies of protein C , protein S, antithrombin,and heparin cofactor II, Disorders of plasmin;increased levels of plasminogen activator inhibitor has been reported in HIV–infected patients, predisposing to thromboembolism. These abnormalities correlate with the severity of HIV associated immunosuppression as evidenced by the CD4 cell counts.

However, there are other factors that can predispose HIV/AIDS patients to thrombosis such as:

- HIV related nephropathy; presents with nephrotic syndrome with associated disorders of hemostasis resulting in thrombotic events. [1]
- Immobilization in HIV patients who are sick and confined to bed [1]
- Immunologic diseases; HIV associated autoimmune hemolytic anemia has been associated with an increased risk of thromboembolism. The underlying mechanism is unclear. [1]
- The presence of protease inhibitors; [1]
- HIV –associated malignancy and myeloproliferative disorders.
- Patients who develop deep venous thrombosis with no identifiable risk factors may have an underlying occult malignancy. [1; 8]
- AIDS –related malignancies include KS,NHL[B cell], anal carcinoma and cervical carcinoma

Numerous investigators have proposed various mechanisms to explain the thromboembolic events in HIV/AIDS patients. These include:

[i] Endothelial injury. [1; 9]As evidenced by increased levels of von Willebrand factor and total antigenic protein S in the blood of HIV/AIDS patients.

[ii] Endothelial cell infection by HIV 1 may contribute to vascular disease by causing vascular thrombosis and endothelial proliferation. [1; 8]

[iii] Low –grade DIC; [1; 9]. This is supported by elevated levels of d-dimers and decreased levels of both functional and antigenic protein C

[iv] Protease inhibitors:It is hypothesized that protease inhibitors may interfere with hepatic regulation of the thrombotic proteins, leading to a prothrombotic state in some patients. [1; 8]

Many aspects of acquired immunodeficiency syndrome [AIDS have been described in detail in the literature. However, there has been very few articles on the phenomenon of Deep Vein Thrombosis [DVT] in the lower extremities of human immunodeficiency virus [HIV/AIDS] infected patients. Thrombosis in general remains uncommon [10] and arterial thrombosis occurs much rarer although it has been described in patients with HIV/AIDS infection. [11]

Of note is a retrospective study conducted by Saber AA et al [5] to record the incidence of DVT in HIV/AIDS patients and the risk of development of embolic events and to emphasize the need for prevention and for the vigorous treatment of this complication.From the study, they concluded that HIV/AIDS infection is a considerable risk for the development of DVT in the lower extremity. Also, statistically, DVT in HIV/AIDS is approximately 10 times greater than in the general population.

Saif MW. et al [8] in their article" AIDS and Thrombosis: Retrospective study of 131 HIV-Infected patients" aimed to study the incidence of thrombosis in patients infected with HIV , and to assess the correlation of thrombosis with the degree of immunosuppression as well as the association with active illnesses and neoplasm. The result of this study suggests that AIDS appear to predispose to thrombosis. It also revealed a significant correlation between thrombotic disease and CD4 counts(less than 200/mm3) as well as the presence of opportunistic infections, AIDS related- neoplasm, or autoimmune disorders associated with HIV such as AIHA. In addition Jacobson MC et al, [9] in their article " Thrombotic complications in patients infected with HIV in the Era of Highly Active Anti retroviral

Therapy (HAART): A Case Series", concluded that patients in this series were characterized by a relatively young age at the time of thrombosis, a predominance of elevated levels of lipids, a history of malignancy, and an advanced CDC HIV classification but not by a low CD4 cell count or an elevated HIV load.

A study by Levine et al [12] sought to determine if advancing stages of HIV were associated with coagulation abnormalities that could predispose to venous thrombosis .They found progressive decreases in protein S and step wise increases in factor VIII with advancing stages of HIV. Thus providing a possible biologic mechanism for the increased prevalence of venous thrombosis in HIV. Similar study by Matthias E et al [13] found deficiencies of protein S and protein C in patients with opportunistic infections, which later improved with treatment of the opportunistic infections.

Bayer et al [14] in their study reported a case of bilateral subclavian vein thrombi which developed in the presence of a Groshong catheter in a patient with AIDS and disseminated cytomegalovirus infection. Similar to this is the case of cerebral venous thrombosis and dual primary infection with human immunodefiency virus and cytomegalovirus reported by Rouzioux C et al (1989) [15].They found an elevated Anti HIV IgG in the CSF of patients with cerebral venous thrombosis. In addition the blood to CSF ratio of anti HIV1 IgGtitres further suggests that HIV1 may be the causative agent.

An interesting study was conducted by Lijfering et al [16] to determine the absolute risk of venous and arterial thrombosis in HIV infected patients and effects of combination antiretroviral therapy. They found that overall, the absolute risk of venous thrombosis in their patients group was 6.5 times higher than reported in the general population, while the absolute risk of venous thrombosis in patients not using combination antiretroviral therapy was still approximately 6 fold higher compared to the general population. Micieli E et al [17] conducted a case control study to compare the prevalence of thromboembolic events between HIV-positive and HIV–negative individuals. Their results lead to a hypothesis that HIV–positive patients have an increased risk of thromboembolic disorders.

Another interesting case report was written by Ronald A et al [18].They documented the case of a 35 year old African woman with HIV infection and Systemic lupus erythematosus who developed recurrent episodes of DVT(4 episodes) and pulmonary embolism in the presence

of antiprothrombin antibodies. They concluded that immunological reconstitution in HIV infected patients contributes to the appearance of multiple autoimmune conditions including SLE and Anti phospholipids syndrome.

In a case control study to investigate the prevalence of established risk factors for venous thromboembolism and other risk factors among cohort of HIV infected patients in JohnsHopkins university AIDS service, it was found that the incidence of VTE was 0.54% which is similar to what other researchers have reported [2]. They also found that patients with VTE had lower CD4 counts. Also independent risk factors for VTE that was found includes age and hospitalization in the past three months. Of importance is the fact that they did not find any association between use of highly active antiretroviral therapy and VTE.- Ahonkhai AA et al. [19]

Fadi M, AbdoYY and Paul DS [20] conducted a study to determine the incidence of VTE in patients with HIV infection and those without HIV infection. Theyanalyzed data from the National hospital discharge survey from 1990 through 2005.Among hospitalized patients with HIV infection, they found that the incidence of pulmonary (PE) was 0.4%,deep venous thrombosis(DVT), 1.4% and VTE,1.7%.They also found that the relative risks compared with all hospitalized non – HIV patients of PE,DVT and VTE were 0.91, 1.26 and 1.21 respectively. That will support the observation that HIV in a way predisposes infected people to thromboembolic events.

Although many authors have mentioned many factors as predisposing to thromboembolic events in HIV infected patients, the study done by Lijfering WM et al [21] demonstrated how progression from HIV infection to AIDS actually affect the level of the commonly mentioned risk factors like factor C and factor S deficiency etc.In their study, they recruited 109 consecutive HIV infected patients in their study. The patients were tested twice for currently known thrombophilic abnormalities at an interval of at least 3 months.Repeated measurements established protein C deficiency in 9% of the patients, increased factor VIII concentration in 41%, high fibrinogen concentrations in 22%, and free protein S deficiency in 60%. In addition they found that median factor VIII concentrations were higher in patients with AIDS than in patients with a non – AIDS defining illness whereas median free protein S concentrations were lower. They concluded that multiple acquired and persistent thrombophilic abnormalities are more frequently observed in HIV infected patients than in

the healthy population. The frequencies of these thombophilic abnormalities increase with the progression to AIDS and these findings may contribute to the high prevalence of venous and to a lesser extent arterial thrombosis in HIV infected patients. [21]

LijferingWM [16] also pointed to the fact that the combination of high factor VIII and fibrinogen concentrations and decreased free protein S concentrations has been reported in patients with systemic lupus erythromatosus and other autoimmune diseases, in patients with cytomegalovirus infection and in patients with the nephritic syndrome which are all conditions that are associated with an increased risk of venous and arterial thrombosis. Also the finding that the development of AIDS was associated with increasing thrombophilic abnormalities may have clinical relevance. This is because since HAART is used for long term immunologic reconstitution, it may improve these thrombophilic abnormalities and lead to a decreased risk of venous and arterial thrombosis.

According to Eyal A and Veller M [22],the first isolated case report of the association between venous thromboembolism(VTE) and HIV infection started to appear in the late 1980s. Over the years, the association has now been conclusively proven by a large number of studies. They mentioned the first significant study by Hassell et al (1994) which reported an incidence of deep vein thrombosis (DVT) of 18% in a group of 60 HIV positive patients. A systematic review published in 2005 found an incidence ranging from 0.19% to 18%.This is said to be in excess of what one will expect in a non infected population where the average risk of developing DVT is reported to be approximately 5/10000. Eyal A and Veller M [22] mentioned an audit performed at Johannesburg hospital South Africa in which 84% of patients who presented with DVT were found to be HIV positive. This is of importance in South Africa when we consider the high burden of HIV in the country. They referred to the study by Laing et al (1996) which found that the incidence of DVT was twice as high in patients with AIDS as in those with HIV infection without manifestations of AIDS.

Deep vein thrombosis (DVT) has been reported to be more common among HIV infected people in several parts of the country. No formal research has been published to confirm or refute this observation within the South African context. There has thus been the need to determine the prevalence of deep vein thrombosis among patients with HIV infection in the medical ward of Nelson Mandela Hospital, Mthatha, South Africa.

CHAPTER THREE

AIM

To determine the prevalence of Deep Vein Thrombosis (DVT) among patients with HIV/AIDS at Nelson Mandela Academic Hospital in Umtata, South Africa and their risk profile.

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OBJECTIVES

The main objectives of this study are:

- To determine the proportion of patients admitted with DVT who also had HIV/AIDS
- To obtain a profile of the risk factors associated with DVT in patients requiring admission for DVT.
- To describe the association of DVT and HIV/AIDS in subgroups of patients with different degrees of immunosuppression.

METHODS

Setting of the study

The study was conducted in the medical ward of Nelson Mandela Academic Hospital, Mthatha, Eastern Cape, South Africa. Umtata is the capital of the Transkei region of the Eastern Cape Province in South Africa with an estimated population of about one million people. Nelson Mandela Academic hospital is a tertiary hospital and renders specialist services to other district hospitals and clinics in the area. It has about 600 beds and large population of doctors which range from interns to specialists in various fields. It also renders services in other health related fields like physiotherapy, speechtherapy, occupational therapy etc.

Study design:

The study design most appropriate for this research is an observational cross-sectional study.

Inclusion and exclusion criteria

Inclusion criteria:

(1) All DVT cases diagnosed by Doppler who were admitted over the past one year (2009)
(2) All patients who were recorded as being diagnosed HIV positive and admitted over the past one year (2009)
(3) DVT affecting only the lower limbs

Exclusion criteria:

(1) Patients with only clinical diagnosis of DVT.

Ethical consideration

Permission to conduct the study was obtained from the Nelson Mandela Academic Hospital authority. (Annexure 3).

Method of data collection

HIV is a major predisposing factor to DVT, as is documented in the literature review, but there are also other significant factors that could cause DVT either independently or in association with HIV. HCT is being done in our medical ward routinely for patients admitted with DVT as part of the screening process for the possible aetiology of the DVT in an attempt to ensure that effective and appropriate treatments are administered to patients on an individual basis. The health practitioners want to get HIV patients at early stage before they develop serious complications of AIDS. An attempt is therefore made to offer HCT to our patient as long as there is an indication whether it is serious or not.

All DVT cases were diagnosed by Doppler study which has high sensitivity and specificity for diagnosing thrombosis. HIV was diagnosed using the Elisa+ Antigen method, which significantly reduces the window period in HIV. It has high reliability and validity

Other variables such as age, immobility, pregnancy and pueperium, medication like oestrogen, previous DVT, family history etc were obtained from the admission files but the reliability cannot be ensured. See checklist Annexure 1. Other variables like the presence of obesity, varicose veins, infections, malignancy, recent myocardial infarction, nephrotic syndrome, haematological abnormalities etc, were also obtained from physical examination and laboratory investigations recorded in the files. See checklist and data extraction schedule, annexure 1 and 2 respectively.

Pilot study

A pilot study was conducted on 5-10 patients' charts in the ward in an attempt to clarify ambiguity and improve on the logistics and layout of the research instrument.

Collection of data

The researcher collected all data mostly from the patients' case notes on the ward, Annexure 2. All DVT patients were formally diagnosed by Doppler studies and HIV tested voluntarily using Elisa + Antigen method. All new DVT admissions are normally assessed on a daily basis until discharge. Even after discharge from the ward, they are normally referred to the hematology clinic where the effectiveness of anticoagulation agent ismonitored. A total number of 102 DVT cases were collected which were admitted over a one year period.

Statistical Analysis

Data were analyzed by a statistician at the Walter Sisulu University using appropriate descriptive statistics. Two main groups of DVT in HIV negative patients and DVT in HIV positive patients were analyzed to determine proportions and frequencies and to conduct further subgroup analysis as indicated in the objectives of the study.

CHAPTER FOUR

RESULTS AND ANALYSIS

A total no of 102 DVT cases were collected from the chart review over the past one year. A total of 81 (79.4%) of the DVT cases were also HIV infected while 21 (20.6%) of the DVT cases were HIV negative. It is of importance to note that most of the DVT cases 86(84.3%) were females while only 16 (15.7%) were males. Only 41(50.6%) of the HIV positive cases had their CD4 counts recorded in the charts. Out of these 41 cases, 29 (70.7%) cases had CD4 counts < 200 while 12 (29.3%) had CD4 counts ≥ 200. A total of 56 DVT cases had their full blood counts results recorded in the charts. Out of these,47 (83.9%) had platelets ≥ 150 000 while only 9 (16.1%) cases had platelets counts < 150 000.Out of the 81 cases of DVT with HIV infection, only 25 (30.9%) of them were on HAART.When we consider the data on other risk factors for DVT, only TB had a significant number of people,42 (41.2%) being co infected. We also found that most of the people with DVT, 70 (68.6%) are < 40yrs while only 32 (31.4%) are ≥ 40yrs.See Table 1.

TABLE 1

CLINICAL CHARACTERISTICS OF PATIENTS WITH DVT (n = 102)

Characteristic	n(%) or Median (Range)
Sex	
Male	16 (15.7%)
Female	86 (84.3%)
Leg	
Right	44 (43.1%)
Left	58 (56.9%)
HIV	
Positive	81 (79.4%)
Negative	21 (20.6%)
CD4 count	
< 200	29 (70.7%)
≥ 200	12 (29.3%)
Platelets	
< 150 000	9 (16.1%)
≥ 150 000	47 (83.9%)
HAART	
Yes	26 (32.1%)
No	55 (67.9%)
Obesity	
Yes	7 (6.9%)
No	95 (93.1%)
Smoking	
Yes	4 (3.9%)
No	98 (96.1%)
Tuberculosis	
Yes	42 (41.2%)
No	60 (58.8%)
Pregnancy	
Yes	10 (9.8%)
No	92 (90.2%)
Immobility	
Yes	6 (5.9%)
No	96 (94.1%)

Contraceptives	
Yes	4 (3.9%)
No	98 (96.1%)
Diabetes	
Yes	8 (7.8%)
No	94 (92.2%)
Hypertension	
Yes	8 (7.8%)
No	94 (92.2%)
Cancer	
Yes	3 (2.9%)
No	99 (97.1%)
Cardiac	
Yes	4 (3.9%)
No	98(96.1%)
Kidney	
Yes	1 (1.0%)
No	101 (99%)
Age	
< 40yrs	70 (68.6%)
≥ 40yrs	32 (31.4%)

The data was analyzed using SPSS software, version 18. Chi square test was used as test of hypothesis and unconditional logistic regression was used to adjust for the effect of confounding factors.

From the analysis, when individual risk factors were considered separately, people < than 40yrs which constituted 68.6% of DVT cases had OR = 1.979 (95% CI = 0.936 – 4.4.183); X^2 = 3.247 (p = 0.072). HIV is the single most important risk factor for DVT in this study. A consideration of the association between HIV and DVT yielded a X^2 = 36.959 (p = < 0001) and OR = 11.571 (4.888 – 27.392) which shows that HIV infected people have more chance of having DVT than those who are HIV negative. People with platelets ≥ 150 000 accounted for 83.9% of DVT cases with known platelets counts but with X^2 = 0.096 (P= 0.756) and OR = 0.814 (95% CI = 0.221 – 2.992), there is no association between platelets level and DVT.Obesity is one of the risk factors for DVT but found in only 6.9% of the DVT cases, X^2 = 2.887(P = 0.089), OR = 1.421 (CI = 1.274 – 1.585). Hypertension is found in 7.8% of DVT cases but there is no association between DVT and hypertension, X^2 = 0.749 (p = 0.387);OR

= 0.596 (95% CI = 0.183 – 1.944).Cancer is an important risk factor for DVT but only found in 2.9% of the DVT cases. Although the OR = 1.404 (95% CI = 1.263 – 1.561) suggests slight increase in the risk of DVT with cancer, the result is not statistically significant, X^2 = 1.202 (p = 0.273).People with cardiac disease as co morbidity accounted for 3.9% of DVT cases but there is no association between DVT and cardiac disease, X^2 = 0.785 (p= 0.376); OR = 0.503 (95% CI = 0.107 – 2.358). Kidney disease was found in only 1% of DVT cases and there is no association between kidney disease and DVT from the analysis, X^2 = 2.245 (p = 0.134);OR = 0.188 (95% CI = 0.017 – 2.135). (Table 2)

We have mentioned that females accounted for 84.3% of DVT cases but when subjected to statistical analysis, sex did not show any association with DVT,X^2 = 1.666(P = 0.197),OR = 0.558 (95% CI = 0.229 – 1.363).From the results, despite the fact that smoking is found in only 3.9% of DVT cases, with X^2 = 19.544 (p = < 0.0001) and OR = 0.095 (95% CI = 0.028 – 0.318), the result is statistically significant. As has been mentioned before, 41.2% of the DVT cases were also co infected with Tuberculosis. The analysis showed that people with TB have higher chance of developing DVT than others with X^2= 23.388 (P = < 0.0001) and OR = 1.667 (95% CI = 1.420 – 1.956).Not many of the DVT cases were immobile before they developed DVT (5.9%).Although the OR = 1.417(95% CI = 1.271 – 1.579) suggest slight risk of developing DVT when immobile, the result is not statistically significant, X^2 = 2.457 (P = 0.117).Diabetes was found in 7.8% of DVT cases but there was no association between Diabetes and DVT,X^2 = 1.656 (P = 0.198); OR = 0.482 (95% CI = 0.156 – 1.491).(table 2)

TABLE 2

UNIVARIATE ANALYSIS RESULTS

Variable	X^2 (p value)	OR (Confidence Interval)
< 40yrs	3.247 (0.072)	1.979 (0.936 – 4.183)
HIV	36.959 (0.000)	11.571(4.888 – 27.392)
Platelets>150000	0.096 (0.756)	0.814 (0.221 – 2.992)
Obesity	2.887 (0.089)	1.421 (1.274 – 1.585)
Hypertension	0.749 (0.387)	0.596 (0.183 – 1.944)
Cancer	1.202 (0.273)	1.404 (1.263 – 1.561)
Cardiac	0.785 (0.376)	0.503 (0.107 – 2.358)
Kidney disease	2.245 (0.134)	0.188 (0.017 – 2.135)
Sex	1.666 (0.197)	0.558 (0.229 – 1.363)
Smoking	19.544 (0.000)	0.095 (0.028 -0.318)
Tuberculosis	23.388 (0.000)	1.667 (1.420 – 1.956)
Immobility	2.457 (0.117)	1.417 (1.271 – 1.579)
Diabetes	1.656 (0.198)	0.482 (0.156 – 1.491)

LOGISTIC REGRESSION

When the effects of confounding factors were analyzed by logistic regression,HIV infection was identified as the most significant and independent determinant of the presence of DVT after adjusting for TB, sex,age,obesity,diabetes,cancer and immobility. Thus the risk of DVT was multiplied by 12 (OR = 11.6,95% CI = 4.9 – 27.3); p = < 0.0001; Beta coefficient = 2.449; Standard error = 0.440 and Wald chi square = 31.016. Also age < 40years showed as significant and independent determinant of DVT with OR = 2.7 (95% CI = 1.1 - 6.7); p = 0.034. (Table 3)

TABLE 3

SIGNIFICANT AND INDEPENDENT DETERMINANTS OF DVT

	B coefficient	**Standard Error**	**Wald chi square**	**OR (95% CI)**	**P value**
Independent variables					
Age groups					
Age< 40 yrs	0.989	0.466	4.509	2.7 (1.1-6.7)	0.034
HIV positive	2.574	0.462	30.984	13.2 (5.3-32.3	< 0.0001
Constant	1.021	0.438	5.434		0.020
After adjusting for sex, obesity, immobility, diabetes and cancer Y = 1.021 + 2.574 HIV + 0.989 Age group					

Out of the 650 HIV related cases admitted in the medical department over a year period according to the records, 81 were documented DVT and HIV cases which gave a prevalence of DVT = 12.5%. This is above the average of 1% to 2% normally reported in most studies [19; 20]. But, some studies have reported incidence as high as 18% among HIV population. [22]

CHAPTER FIVE

DISCUSSION

HIV predisposes to hypercoagulable state and the prevalence of DVT among HIV population at Nelson Mandela Hospital of 12.5% together with the results of OR and chi square for DVT and HIV further confirm the association between HIV and DVT recorded in various studies. This is in agreement with what researchers [22] have mentioned. Eighty one (79.4%) of the DVT cases also had HIV.This is close to the proportion of 84% found at Johannesburg hospital. [22] Various researchers [8; 12; 21] have also mentioned that progression to AIDS or lower CD4 counts also makes patients more susceptible to DVT.This is also confirmed in our study which found that among the 41 people whose CD4 counts were known, 70.7% of them have CD4 counts less than 200 and 29.3% have CD4 counts more than 200.This is important when prophylaxis measure to prevent DVT in HIV population is being considered. In the study, females were more affected than males 86 vs. 16.This could be attributed to the fact that females are more at risk of HIV infection from heterosexual relationship and also are the only one prone to unique risk factors like oral contraceptives pills and pregnancy. Though in our study, only 4 females were on contraceptives. It is expected that higher platelets counts will predispose to DVT but despite the fact that 47 people(out of 56 people with known platelets) had platelets count ≥ 150 000, there was no association between platelets counts and DVT in both univariate and multivariate analysis. Of importance is the fact that most of the people with DVT are <40yrs (70 people).These are generally the age group with the highest risk of HIV transmission. Studies such as [8] also found that thrombosis is more common in younger age group. This could be attributed to the fact that common risk factors for DVT like HIV, pregnancy, oral contraceptives pills etc are more common in this age group (Table 1).

From the analysis, when individual risk factors were considered separately, people < than 40yrs which constituted 68.6% of DVT cases had OR = 1.979 (95% CI = 0.936 – 4.4.183); X^2 = 3.247 (p = 0.072).Although the OR suggests that people < 40yrs have almost double the risk of having DVT compared with those ≥ 40yrs, the result is not statistically significant when you consider the CI and the p values.

Tuberculosis is the most common opportunistic infection among HIV infected population and also a risk factor for DVT. [8] It is therefore not surprising that 42 of the patients were also on TB treatment. In univariate analysis, TB predisposed to DVT, X^2 = 23.388 (p = < 0.0001), OR = 1.667 (95% CI = 1.420 – 1.956) but in multiple logistic regression, it did not show any association with DVT. However, as it has been mentioned above just as HIV infection predisposes to TB, Tuberculosis also worsens HIV infection leading to reduction in CD4 counts. This might be important when considering which patients are candidates for DVT prophylaxis. Only 3.9% of the DVT cases were smokers. Considering the fact that most of the DVT cases (79.4%) were HIV infected, they could have stopped smoking when their health condition deteriorated from AIDS. Also since most of the patients were females, this could have reduced the prevalence of smoking in the study since there are more smokers among males than females. From the results, despite the fact that smoking is found in only 3.9% of DVT cases, with X^2 = 19.544 (p = < 0.0001) and OR = 0.095 (95% CI = 0.028 – 0.318), smoking seems to have protective effect against DVT and the result is statistically significant. This is the opposite of what is expected with respect to smoking and DVT. Because of the age group of < 40yrs mostly having DVT, diseases like Diabetes and Hypertension are less prevalent and hence did not show any association with DVT. Immobility was found in only 5.9% of the DVT cases. Although the OR = 1.417 (95% CI = 1.271 – 1.579) showed that people who were immobile had higher chance of developing DVT, the result was not statistically significant (p = 0.117).This means that the result could be a chance finding. But we should also consider that fact that because of recall bias, many of the patients might not have remembered accurately if they had a few days of physical inactivity prior to the onset of DVT or not. In addition because these patients are now used to being less physically active because of their health condition, they might not recognize it as an abnormality that could be responsible for the DVT.

Out of 81 cases of DVT with HIV infection, only 25(30.9%) were on HAART.When we consider the fact that 70.7% of 41 cases with known CD4 counts had CD4≤ 200, there is thus the possibility that more of those patients with DVT who are HIV infected could have benefitted from HAART.However, one will also need to consider why those on HAART (30.9%) also had DVT since HAART is expected to improve the CD4 counts and reduce the occurrence of conditions like DVT, tuberculosis, etc. In this regard, the issue of compliance, treatment failure, associated risk factors for DVT etc will need to be considered. Furthermore,

we did not have information on when the patients started HAART and the initial CD4 counts. Also we are not sure of what regimen they were on and at what dosage since it has been found that not all medical practioners (especially general practioners) have adequate training in prescribing HAART.

Obesity is one of the risk factors for DVT but found in only 6.9% of the DVT cases, X^2 = 2.887(P = 0.089), OR = 1.421 (CI = 1.274 – 1.585).There is really no significant association between DVT and obesity although the OR suggest there is a small risk of DVT with obesity. This means that the association could have been a chance finding.With 79.4% of the DVT cases being HIV infected, weight loss would probably have being a more prominent feature. People with HIV/AIDS tend to have chronic diarrhea, loss of appetite etc.Sometimes when they don't have jobs and they are not on grants, they have little or no food to eat.
Out of the 650 HIV related cases admitted in the medical department over a year period according to the records, 81 were documented DVT and HIV cases which gave a prevalence of DVT = 12.5%.This is above the average of 1% to 2% normally reported in most studies [19; 20]. But, some studies have reported incidence as high as 18% among HIV population. [22]. However, it is important to know that because of poor record keeping, the number of HIV related admissions could have been under reported and which could be responsible for the higher than average prevalence of DVT in the hospital.

Clinical Outcomes:

Overall, there was no mortality due to complications of DVT (i.e. pulmonary embolism) among all the 102 patients admitted with DVT over the 12 months period while they were on admission. Most of the patients were discharged within two weeks of admission unless they had other co morbidities which necessitated longer stay on the ward.

RECOMMENDATIONS

It was found from the study that the risk for DVT among HIV/AIDS patients is approximately 12 times higher than that of the general population. With the advent of HAART, more people with HIV/AIDS will survive into old age and that means that the rate of thromboembolic episodes will further increase. So there is need to identify the common

pathway to thrombosis in this population from all the various risk factors identified. When the pathway is understood, it can then be possible to develop or administer appropriate prophylaxis measures for at risk patients either within the hospital set up (e.g. heparin) or for high risk out patients (e.g. anti – inflammatory or anti platelets agents).

During this study, the researcher discovered that our DVT cases were not adequately investigated especially in terms of biochemical tests. Hence information about protein C, protein S, antithrombin III, CMV infection etc were not available. These deficiencies were due to limited financial support from the government which limits health practitioners to ordering only the most essential investigations needed for patients' care. It is therefore important for government to make money and other resources available for detailed research into issues related to HIV in order to be able to offer the best management to our HIV patients. This is important when one consider the million of South Africans who are HIV infected and the bulk of which are in the productive age groups.

There is need for proper record keeping in our health institutions so that we can have data that are as accurate as possible in order for them to produce results that can be useful for the population when they are used for research.

Finally from our study, we found that most of the people with CD4 less than 200 (14) but who were not on HAART were referred from the clinics and district hospitals without ARV facility. Therefore it is important for the government to make ARVs available in all the health institutions.

CONCLUSION

The prevalence of DVT at the Nelson Mandela hospital Mthatha was 12.5% for the year 2009 and is similar to that reported in other studies although above the average reported. HIV infection and age were the risk factors with a statistically significant association with DVT in this study. As this was an observational cross-sectional study, a more definitive prospective longitudinal design would assist in establishing the incidence of DVT in HIV infected patients, as well as the magnitude of the relationship between HIV and DVT.

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ANNEXURE 1 (CHECKLIST)

- Age:

- Gender:

M	F

- Obesity:

YES	NO

-Height:

-Weight:

-Body Mass Index (BMI):

- Varicose veins:

YES	NO	UNSURE

- Surgical treatment of varicose veins:

YES	NO	UNSURE

- Opportunistic infections:

  - Confirmed Tuberculosis:

	YES	NO	UNSURE
X-ray findings			
Sputum			
Cerebrospinal fluid			

Abdominal Ultrasound			
Tissue biopsy			
On treatment			

- Confirmed Pneumocystis carinii pneumonia:

	YES	NO	UNSURE
X-ray findings			
Clinical diagnosis			
On treatment			

- Confirmed Malignancy:

	YES	NO	UNSURE
History			
Pathology report			

- Type of malignancy:

- Smoking:

YES	NO

-Severity of smoking:

Less than 10 /day	10-20 /day	More than 20 /day

- Confirmed recent myocardial infarction:

	YES	NO	UNSURE
Troponin T			
ECG findings			
History			

- -Time of diagnosis of myocardial infarction:

Less than 2 weeks	2weeks-1 month	1 month – 3 months	More than 3 months

- Confirmed Nephrotic syndrome:

-Proteinuria:

None	Trace/ 1+	2+	3+	4+

- -Others:

	YES	NO	UNSURE
Clinical findings			
On treatment			

- Confirmed Diabetes Mellitus:

	YES	NO	UNSURE
Blood sugar			
On treatment			

- HbA1c:

Less than 7	7- 10	More than 10

- Confirmed Hypertension:

	YES	NO	UNSURE
Hypertension			
On treatment			

- Systolic blood pressure:

	140-160 mmHg	161-180 mmHg	More than 180 mmHg
Systolic			

- Diastolic blood pressure:

	90-100 mmHg	101-110 mmHg	More than 110 mmHg
Diastolic			

- Immobility:

	YES	NO

-Duration of Immobility:

1- 4 days	5 days- 1 week	1-2 weeks	2-4 weeks	More than 4 weeks

- Hormone replacement therapy:

	YES	NO

-Duration of Hormone replacement therapy:

Less than 1 month	1-3 months	4-6 months	more than 6 months

- Oral contraceptives:

	YES	NO

-Duration of Oral contraceptives:

Less than 1 month	1-3 months	4-6 months	more than 6 months

- Pregnancy and Pueperium:

	YES	NO

- Previous Deep Vein Thrombosis: (DVT)

	YES	NO

- Family history of Deep Vein Thrombosis: (DVT)

	YES	NO

ANNEXURE 2 (EXTRACTION SCHEDULE)

Code number:

Date:

Height (meters):

Weight (kg):

Main complaints:

Risk factors from annexure 1:

Doppler findings:

Positive;	Negative	Unsure

HIV result:

	YES	NO	UNAVAILABLE
HIV			

CD4 counts:

	Normal	200-500	Less than 200

FBC:

MCV	WCC	Hb	Platelets

Blood sugar:

Troponin T:

ECG findings:

Urinalysis:

ANNEXURE 3: LETTER OF APPROVAL

DEPARTMENT OF HEALTH

EASTERN CAPE

NELSON MANDELA ACADEMIC COMPLEX

PRIVATE BAG X 5014
UMTATA 5100
TEL: (047) 502 4126
FAX (047) 5024126

Incorporating the Nelson Mandela Academic Hospital, Umtata General Hospital, and Bedford Orthopedic Hospital

1st September,2010

Dear Sir,

TO WHOM IT MAY CONCERN
RE : DR OLUBANWO OLUDAYO

This is to inform the authority concerned that the above named person has been granted permission to collect data for his study " The prevalence of deep vein thrombosis(DVT) among patients with HIV/AIDS at Nelson Mandela Hospital" in order to satisfy the requirement for the MMED (Family Medicine) programme.

This permission has been granted in accordance with rules and regulations governing good ethical practice at Nelson Mandela Hospital, Umtata.
Thanks.

Prof Awotedu
Head of department
Internal Medicine