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**Prevalence of Deep Venous Thrombosis in Cancer Patients
Admitted to the Medical Wards at the Kenyatta National
Hospital****Amina Habib¹, Andrew Odhiambo², N.A Othieno-Abinya² & MD Maina³**¹PGY3 Internal Medicine Resident, University of Nairobi, Kenya²Faculty, Department of Clinical Medicine and Therapeutics, University of Nairobi, Kenya³Kenyatta National Hospital**ABSTRACT**

Venous thromboembolic events in cancer are quite common and are a leading cause of morbidity, delays in care and death. As cancer is a heterogeneous disease, the risk of DVT depends on cancer types and stages, treatment measures, and patient-related factors. The objectives of this study were to establish the prevalence of DVT in cancer patients at KNH medical and oncology wards, to describe patient characteristics of those with DVT vs those without and compare rates of DVT in different types of cancer. This was a cross-sectional descriptive study carried out at the Kenyatta National Hospital general medical wards and oncology wards. Patients were interviewed and examined. Patients' records were perused for information relevant to the study. Patients with history and physical examination findings suggestive of a thrombotic event were screened by compression sonography to confirm a DVT. A total of 266 patients with a diagnosis of cancer were studied, 29 (10.9%) had DVT. Among the patients who were found to have DVT, 13 (44.8%) had gynaecological cancers, 3 (10.3%) breast cancer, 3(10.3%) prostate cancer, 3(10.3%) gastric cancer, 2(6.9%) patients had lymphoma and a patient (3.4%) each in the multiple myeloma, adenocarcinoma, squamous cell carcinoma and pancreatic cancer groups. Some significant patient characteristics in the patients who had a DVT were female sex (P value 0.014), presence of comorbidities (P 0.004) and ECOG scores of 3 and 4 (P 0.04, 0.001). Some common risk factors known for DVT were analysed and some were found to be significant in our patient group. Of the significant risk factors, presence of comorbid condition, female sex and higher ECOG scores were noted.

Keywords: DVT, VTE, ECOG, Comorbidities, Kenyatta National Hospital

1. INTRODUCTION

Venous thromboembolism is a common occurrence in cancer patients putting them at a four to seven-fold risk of developing venous thromboembolic events(1). In a retrospective analysis, VTE occurred in 12.6% (2170/17 284) of ambulatory cancer patients receiving chemotherapy compared to 1.4% (237/17 284) of matched controls without cancer (2). Cancer-associated thrombosis results in increased morbidity, mortality, and cost of care with actual mortality from fatal VTE being 3 times more common in cancer patients than in patients without cancer (3). Overall, cancer patients with VTE do not fare well.

Many risk factors for cancer-associated thrombosis have been identified, including patient-related, cancer-related and treatment-related factors (4).

2. Research Methods

The study was a cross-sectional descriptive study carried at the KNH medical and oncology wards where an approximate 5000 patients are admitted with a primary diagnosis of cancer. Participants were patients admitted to the said inpatient units with a histologic diagnosis of cancer. After approval from KNH/UoN Ethical Review Committee, consent was sought from patients meeting eligibility criteria. Patients' files were reviewed. A brief history was taken with focus on the objectives of the study. A directed physical examination was also conducted. Patients with a confirmatory Doppler study were documented directly into the data capture tool, those with no Doppler study, one was done for confirmation or to rule out a diagnosis of DVT where history and/or physical examination were suggestive.

All of the Doppler ultrasound studies were done on the lower limbs except one. This was based on guidance from the patients' medical history and clinical findings. A single patient with a diagnosis of breast cancer was identified to have a DVT of the upper limb. This was confirmed by a Doppler ultrasound after a suggestive history and clinical findings.

3. Results

A total of 272 patients with a histologic diagnosis of cancer were screened for eligibility, 6 declined consent. From the review of the remaining 266 patients who consented to the study, 52 had an indication for an ultrasound study. Patients found positive for DVT were 29, 28 had lower limb DVT and 1 upper limb DVT. The gender distribution within the 266 subjects was 145(54.5%) female vs 121(45.5%) male. The mean age was 50.25 (15.2) with most patients falling in the above 45 (72.9) years age group. The youngest patient was 13 years old and the oldest 86 years. The socio-demographic characteristics are as shown in table 1.

A significant number of patients had gynaecological malignancies; these included uterine cancer 6 (2.6%), ovarian cancer 10 (3.6%), vulva cancer 1(0.4%) and cervical cancer 29 (10.9%) which had the largest number of patients in the study. Following closely were the gastrointestinal tract adenocarcinomas; gastric cancer was the most prevalent 25(9.4%) followed by large bowel tumors 17 (6.4%). Esophageal cancer had a significant prevalence at 26 (9.7%). The acute leukemias 20 (7.5%), breast cancer 20 (7.5%) and lymphoproliferative disorders 15 (5.6%) then followed in prevalence. The rest of the malignancies had comparably small number of patients and are grouped as others. A comprehensive table on all the site-specific cancers screened in this study can be found in Appendix 1.

Most of the patients in this study were distributed in stage 3, 129(48.5%) and stage 4, 92(34.6%) in comparison to those who had stage 2 disease 34(12.8%) and unfortunately a few 11(4.1%) whose stage was unknown. No patient in our study was found to be in Stage 1 disease. More than half of the patients had comorbidities, 154 (57.9%). Only 10 (3.8%) patients in study population had a significant history of a previous thrombosis. Most of the patients had received some form of anti-cancer treatment at the time of this screening; 136 (51.1%)

radiotherapy and 120 (45.1%) chemotherapy. Of the total subjects, 10(3.8%) patients had a central venous catheter. All the patients in this analysis save one had an ECOG score above 1. The sickest patients with a functional status of 4 were 32 (12%), patients with ECOG 3 score were 97(36.5%), ECOG 2 group were 114 (42.9%) and ECOG 1 had 22 (8.3%) patients.

Table 1: Socio-demographic Characteristics

Variable	Frequency (%)
Gender	
Female	145 (54.5)
Male	121 (45.5)
Mean age (SD)	50.25 (15.2)
Age group	
<25	26 (9.8)
25-34	12 (4.5)
35-44	34 (12.8)
>45	194 (72.9)

Of the subjects screened, 29 patients (10.9%, CI 7.2-15.0) had DVT vs 237 (89.1%, CI 85.0-92.8) that did not.

Table 2: Prevalence of DVT in Cancer patients

Variable	Frequency (%)	95% CI
VTE		
Present	29 (10.9)	7.2-15.0
Absent	237 (89.1)	85.0-92.8

Among the patients who were found to have DVT, a good number of them had gynaecological malignancies and by extension, pelvic malignancies when considering the female patients. 7 (24.1%) patients had cervical cancer, 3(10.3%) uterine cancers while 3 (10.3%) had ovarian cancer. Of the males, 3(10.3%) had prostate cancer. Moreover, 3 (10.9%) patients had a primary diagnosis of gastric cancer while 3 (10.3%) had breast cancer. For the rest of the patients, each had a different cancer diagnoses, i.e. Glioblastoma Multiforme, Multiple myeloma, Non-Hodgkin's lymphoma, Hodgkin's lymphoma, Squamous cell carcinoma, Adenocarcinoma and Pancreatic adenocarcinoma respectively (Table 3).

Table 3: Site of Cancer in Patients with DVT

Site of Cancer	Rate of DVT in all patients (%) N=266	Rate of DVT in specific cancer groups %	No DVT in specific cancer group %
Cervix	7(2.6)	24.1	75.8
Breast	3(1.1)	15	85
Ovary	3(1.1)	30	70
Uterus	3(1.1)	50	50
Stomach	3(1.1)	12	88
Prostate	3(1.1)	30	70

Non- Hodgkin's lymphoma	2(0.8)	13.3	86.7
Pancreas	1(0.4)	25	75
Multiple myeloma	1(0.4)	20	75
Adenocarcinoma of unknown origin	1(0.4)	50	50
Nasopharyngeal carcinoma	1(0.4)	50	50
GBM	1(0.4)	100	-

Most of the patients 22(75.9%) with a DVT diagnosis were in the older age group of above 44 years. Incidence of VTE was found to be higher in the female patients 22(75.9%) vs the male patients 7(24.1%) where it was lower, (P value 0.014). The stage of disease distribution of patients who had DVT was 13(44.8%) patients in stage 3, 12(41.4%) in stage 4 and only 2(6.9%) patients each in Stage 2 disease and patients whose stage was unknown. Half the patients had received radiotherapy 12 (41.3%) vs 17(58.6%) who had not and only a few, 9(31.0%) received chemotherapy while 20(69%). More than half of the study participants had a comorbid condition and this was reflected in the DVT group 16(55.2%) as well, (P value 0.004). A statistically significant characteristic was the ECOG score above 4 in patients found to have a DVT. Most of the patients with a DVT clustered within ECOG 3, 13(44.8%) and ECOG 4, 10 (34.5%). Patients in ECOG 2, 6(20.7%) were the least in number while there was no patient with a functional grade 0 or 1.

4. Discussion

All age groups were fairly well represented but majority of the patients fell above the 45 years and older age group. This is in keeping with most cancer diagnosis which occurs later in life. The female patients were slightly more than the males (54.5% vs 45.5%). This female predominance was also seen in the cancer incidence rates in the regional cancer registry (5) in a similar heterogeneous distribution of cancers. Relevant in our study, aside from other predisposing factors, this gender distribution could be due to the high prevalence rates of genitourinary malignancies.

Majority of our patients had advanced (stage 3 and stage 4) stage disease, this trend is due to majority of the patients presenting late in the course of the disease when it is more likely to be symptomatic which could be due to the challenges met while accessing health care. Of the patients who had a DVT, only two had stage 2 disease, epidemiologic studies which have also shown patients with metastatic disease were at a significant risk of getting thromboembolic event (6) in comparison to early disease. This is because of multiple risk factors being present at metastatic disease in comparison to early cancer including longer hospital stays, obstruction of venous return due to large tumors and metastatic lymph nodes and a high tumor burden which increases the secretion of procoagulant and other prothrombotic factors from tumor cells.

Studies done have clarified that most thromboembolic events tend to occur soon, often within a year after diagnosis of cancer when most interventions are attempted (7), that would be chemotherapy, surgical procedures or blood product transfusion all of which pose a significant risk for VTE. This holds for our setting as well as the major interventions that pose as an increased risk are done soon after diagnosis, however late our diagnosis takes.

Over half of the patients had co-morbidities besides the primary diagnosis. This finding was statistically significant as a characteristic of patients who had a DVT in comparison with those who did not. This was important as certain co-morbidities have been associated with the occurrence of VTE in cancer patients (7).

In this prevalence study, 10.9% of the population was reported to have DVT. Sites of cancer with the highest rates of DVT included genitourinary malignancies, breast cancers, lymphomas and gastric cancers. This trend is almost

duplicated in other epidemiological studies done(8). A notable difference from most of the previous studies done is the predominance of the genitourinary cancers with DVT especially cancer of the cervix. In similar studies, it had been concluded that adenocarcinoma was the most frequent histopathological type associated with an increased VTE risk (9). As cervical cancer has squamous cell histology, it can safely be assumed, the obstructive nature of the disease to the venous flow in the pelvic and inguinal region especially at its later stages compounded with other traditional risk factors would be the cause of this local trend. Another significant difference of this study from most of other papers is the high incidence of VTE in pancreatic cancer found in the Western papers. We only had four patients with a primary diagnosis of pancreatic adenocarcinoma, of these, one had a DVT. It impossible to analyze this small group and form a trend based on this study alone, a recommendation though might be a prevalence study with this group only and for a longer duration so as to arrive at numbers that would eventually help in clinical decisions. The incidence of DVT in other malignancies was comparable to other similar epidemiological studies (4). Some significant clinical characteristics when comparing the patients who had DVT vs those who did not are female patients, presence of comorbidities and ECOG scores of 3 and 4. These are known risk factors for DVT without an additional diagnosis of cancer. The female patients are particularly significant in this study due to the increased incidence of genitourinary cancer and hence this would make a useful consideration in clinical decision making when managing this group of patients.

5. Strength, Limitation and Recommendations

This study is the first one of this kind, with an ample sample size done amongst cancer patients in our setting. This study serves as a benchmark for future studies around this topic that need evaluation.

Some limitations are that the study was limited to inpatient patients only hence missing the patients on outpatient follow up with a possible DVT diagnosis, especially patients who come for outpatient chemotherapy. An important limitation is also that compression sonography were done on lower limbs only, this means missing a DVT in any other region of the body if patient was not symptomatic and also not all patients had compression ultrasounds done; subclinical thrombi could easily have been missed. As a follow up to this study we recommend DVT risk assessment in all cancer patients admitted to the wards. In particular groups of cancers that have shown a high incidence of DVT. Validated risk score calculators should be used to stratify patients and appropriately preempt any VTE event. A follow up study recommendation would be to look at chemotherapy drugs and regimens most associated with DVT so as to best manage these patients as chemotherapy is widely administered in our setting.

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APPENDIX 1: Distribution of Types of cancer

Type of Cancer	Frequency	Percentage (%)	DVT rate (%)
Cervical cancer	29	10.9	2.6
Esophageal Cancer	26	9.8	-
Gastric Cancer	25	9.4	1.1
Breast Cancer	20	7.5	1.1
Colorectal Cancer	17	6.4	-
Non-Hodgkin's Lymphoma	15	5.6	0.8
Acute Lymphoblastic Leukemia	11	4.1	-
Ovarian Cancer	10	3.6	1.1
Prostate Cancer	10	3.6	1.1
Lung Cancer	10	3.6	-
Acute myeloid Leukemia	9	3.4	-
Hepatocellular cancer	8	3.0	-
Squamous cell Carcinoma; Skin	8	3.0	-
Hodgkin's Lymphoma	6	2.6	-
Chronic Myeloid Leukemia	6	2.6	-
Uterine Cancer	6	2.6	1.1
Bladder cancer	6	2.6	1.1
Multiple Myeloma	5	1.9	0.4
Chronic Lymphocytic Leukemia	4	1.5	-
Pancreatic Cancer	4	1.5	0.4
Squamous cell Carcinoma	4	1.5	-
Osteogenic sarcoma	3	1.1	-
Cholangiocarcinoma	2	0.8	-
Adenocarcinoma	2	0.8	0.4
Malignant Melanoma	2	0.8	-
Kaposi sarcoma	2	0.8	-
Oropharyngeal carcinoma	2	0.8	-
Fibrosarcoma	2	0.8	-
Spindle cell sarcoma	2	0.8	-
Undifferentiated Sarcoma	2	0.8	-
Nasopharyngeal Carcinoma	2	0.8	0.4
Vulva cancer	1	0.4	-
Renal cell Cancer	1	0.4	-
Glioblastoma Multiforme	1	0.4	0.4
Ameloblastoma	1	0.4	-
Rhabdomyosarcoma	1	0.4	-
Retinoblastoma	1	0.4	-
	266	100.0	