Prevalence and Risk Factors for Cancer Associated Thrombosis (CAT) among Patients Seen in TASH Clinical Oncology Department in One Year, (Sept 11, 2018 - Sept 10, 2019).

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Thesis for Speciality Certificate in Clinical Oncology

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Abbreviations/Acronyms

CAT- cancer associated thrombosis

DVT- deep vein thrombosis

VTE- venous thromboembolism

PE- pulmonary embolism

PCTA-pulmonary computed tomography angiography

TASH- TikurAnbessa Specialized Hospital

USG- ultrasonography

NET-neutrophil extracellular traps

vWF-von Willebrand factor

TF-tissue factor

BMI- body mass index

MI-myocardial infarction

DIC-disseminated intravascular coagulation

VEGF-vascular endothelial growth factor

TNF-tumor necrosis factor

ESMO- European Society of Medical Oncology

ECOG- Eastern Cooperative Oncology Group

SVT-Splanchnic Vein Thrombosis

Abstract

Introduction: Cancer is prothrombotic. Thrombosis is common complication in patients with malignant disease.Cancer associated thrombosis is a major cause of mortality in cancer patients. It is the second leading cause of mortality in cancer patients. In a study done at Tikur Anbssa Specialized Hospital malignancy was number one cause of DVT.

Objective: To determine prevalence of thrombosis in the general cancer population and specific cancers, to determine type of CAT, to identify Causes of CAT, and associated factors among patients seen in TASH Clinical Oncology Department in One year

Methods: Retrospective descriptive analysis of CAT in all cancer patients seen in one year, from Sept 11, 2018_Sept 10, 2019 at TASH Clinical Oncology Department was conducted

Result: A total of 177 patients with CAT was identified. 61.5% of them were females, and 38.42% were males. The prevalence of CAT in cancer patients was 5.47. Prevalence of CAT in female cancer patients was found to be 5.53% while it was 5.39% in males. Females were twice more likely to develop CAT than males with odds ratio 2.5 (CI 1.8332—3.4179), P <0.0001. CAT was most prevalent in, HCC (30.68%), genitourinary cancers (10.78%), brain tumor (10.74%), thyroid cancer (9.8%), thoracic tumors (9.0%). The three most common type of cancers associated with CAT in our set up were gynecologic cancers (29.4%), HCC (15.3%), GIT cancers (14.7%). Limb DVT was the commonest type of CAT (58.8%) identified followed by PVT (17.5%).

Conclusion: The burden of CAT is significant in our cancer patients like it is all over the world. Gynecologic cancer, cervical cancer in particular was the most common type of cancer associated CAT cause of CAT. HCC was the second most common type of cancer associated with CAT. CAT was most prevalent in HCC. In this study it was found that there are significant number of incidentally detected portal vein thrombosis patients which were not treated nor on follow up for their thrombosis. Studies recommend that such patients should be managed similar to clinically detected patients.

Recommendation: Emphasis should be given on prevention and treatment of CAT in cancer patients. We recommend active identification of CAT cases on high risk cancer patients. Discussion is recommended on how to go about incidentally identified CAT cases in general and PVT cases in particular. We strongly recommend further preferably prospective studies to address this important cause of morbidity and mortality in cancer patients.

1.0. Introduction

1.1. Statement of the Problem

Cancer is prothrombotic. Thrombosis is a common complication in patients with malignant disease. First recognised by Bouillard in 1823 and later described by Trousseau in 1844, multiple studies have since provided considerable evidence for a clinical association between cancer and thrombosis. VTE and its treatment could impact the quality of life in cancer patients, delay cancer treatment, and have complications including recurrent VTE and/or bleeding.

Thrombotic complications in cancer can vary from arterial or venous thromboembolism to DIC. Cancer associated thrombosis is a major cause of mortality in cancer patients, the most common type being venous thromboembolism (1).It is the second leading cause of mortality in cancer patients(1).Occurrence of VTE in cancer patients increase likelihood of death 2--6 fold. VTE has been reported to be the most common cause of death at 30-day follow up among cancer patients underwent surgery.90% of patients with cancer have subclinical hemostatic abnormalities. Independent of the timing of cancer diagnosis (before or after the VTE), the life expectancy of cancer patients with VTE is relatively short, because of both deaths from recurrent VTE and the cancer itself (2).

Deep vein thrombosis (DVT) and pulmonary embolism (PE) are the most commonly encountered venous thrombotic complications, other vascular territories, such as the splanchnic veins and upper extremity venous system, can also be involved. Arterial events including stroke and MI can occur particularly with regimens containing antiangiogenic agents (4).

With the increasing age and cancer prevalence, enhanced detection of incidental thrombosis and greater thrombogenicity of multiagent chemotherapeutic regimens, it has been observed that there is a steady increase in the incidence of cancer-associated thrombosis during the past 2 decades(2).Cancer-associated venous thrombosis is a common condition, although the reported incidence varies widely between studies depending on patient population, start and duration of follow-up, and the method of detecting and reporting thrombotic events. Furthermore, as cancer is a heterogeneous disease, the risk of venous thrombosis depends on cancer types and stages, treatment measures, and patient-related factors. In general, cancer patients with venous thrombosis do not fare well and have an increased mortality compared with cancer patients without.

In a study done at Tikur Anbssa Specialized Hospital malignancy was number one cause of DVT with 30.9% of cases. The second most common cause was prolonged immobilization with only 19.8% of cases. (51)

The survey of the Spanish National Discharge Database found that, of those patients who suffered secondary pulmonary embolism during hospitalization for other reasons, the highest proportion were admitted because of cancer (21%), which was much more than the number admitted because of acute respiratory failure (11%), acute heart failure (6.4%), stroke (6.1%) or pneumonia (5.5%)(4).

According to clinical data prospectively collected on the population of Olmsted County, Minnesota, since 1966, the annual incidence of a first episode of DVT or PE in the general population is 117 of 100,000. The approximate annual incidence of VTE is 1 of 200 in a population of cancer patients (5).On the basis of long-term follow-up data on patients with thrombosis, those with cancer have a 4- to 8-fold higher risk of dying after an acute thrombotic event than patients without cancer. Furthermore, patients with cancer and thrombosis have a lower survival rate than those with cancer without thrombosis (6).

A large Danish cancer registry revealed the one-year survival of cancer patients with VTE is 12%, and against 36% in cancer patients without VTE. The mortality ratio associated with VTE was 2.2 for the 1-year follow-up period. This high mortality probably reflects deaths due to both thromboembolism and a more aggressive course of malignancies associated with VTE (7).

Autopsy series have reported increased rates of pulmonary embolism (PE) in cancer patients compared with patients without cancer. Furthermore, the risk of recurrence after a first episode of VTE is higher in cancer patients than in those without underlying malignancy (8). Individuals presenting with an unprovoked episode of VTE are more likely to have an underlying cancer than those with an identifiable risk factor for thrombosis. It is estimated consistently that: 20% to 30% of all first venous thromboembolic events are cancer associated (9-10).

White and coworkers used the California discharge data set to identify a cohort of 21,002 patients hospitalized with incident venous thrombosis in 1996. Of these patients, 20% (4368) were reported to have cancer-associated venous thrombosis (12). In another study, medical records of residents from the Worcester metropolitan area were obtained for a total of 1399 subjects with a confirmed episode of venous thrombosis. Of these patients, 29% had a recent or active malignant neoplasm (11). In a more recent registry, the RegistroInformatizado de EnfermedadTromboEmbolica (RIETE) ´registry, which included, 35 000 consecutive symptomatic venous thrombosis patients from 2001 to 2011, active cancer was reported in 6075 patients (17%)(9).Last, the Tromsø study is a population based prospective follow-up study of 26, 000 subjects. Participants were followed for venous thrombosis from 1994 to 2007. Of 462 patients with a first-ever venous thrombosis event, 106 had an active cancer (23%) (13).

Data on the occurrence of VTE in cancer patients is probably underestimated, judging by autopsy findings where pulmonary embolism or venous thrombosis is found in more than 50% of autopsies while VTE detection in lifetime only amounts to 15% of cases, indicating substantial shortcomings in diagnosis (14).

Despite the well known association between cancer and thromboembolic disease , the mechanism that promote thromboembolic events in cancer patients are not clear and appear to be multifaceted. Multiple mechanisms of CAT have been `identified, which could vary depending on the type of malignancy. A recent review has summarized this topic in detail. Traditionally, CAT is thought to represent the intersection of the “Virchow’s triad” with chronic disseminated intravascular coagulation (DIC) from malignancy, venous stasis from central venous catheter placement, and endothelial injury from antineoplastic chemotherapy. More recent translational research suggests that the vascular

microenvironment, including tissue factor, platelets, and neutrophils, explains a great deal of the prothrombotic tendencies (5).

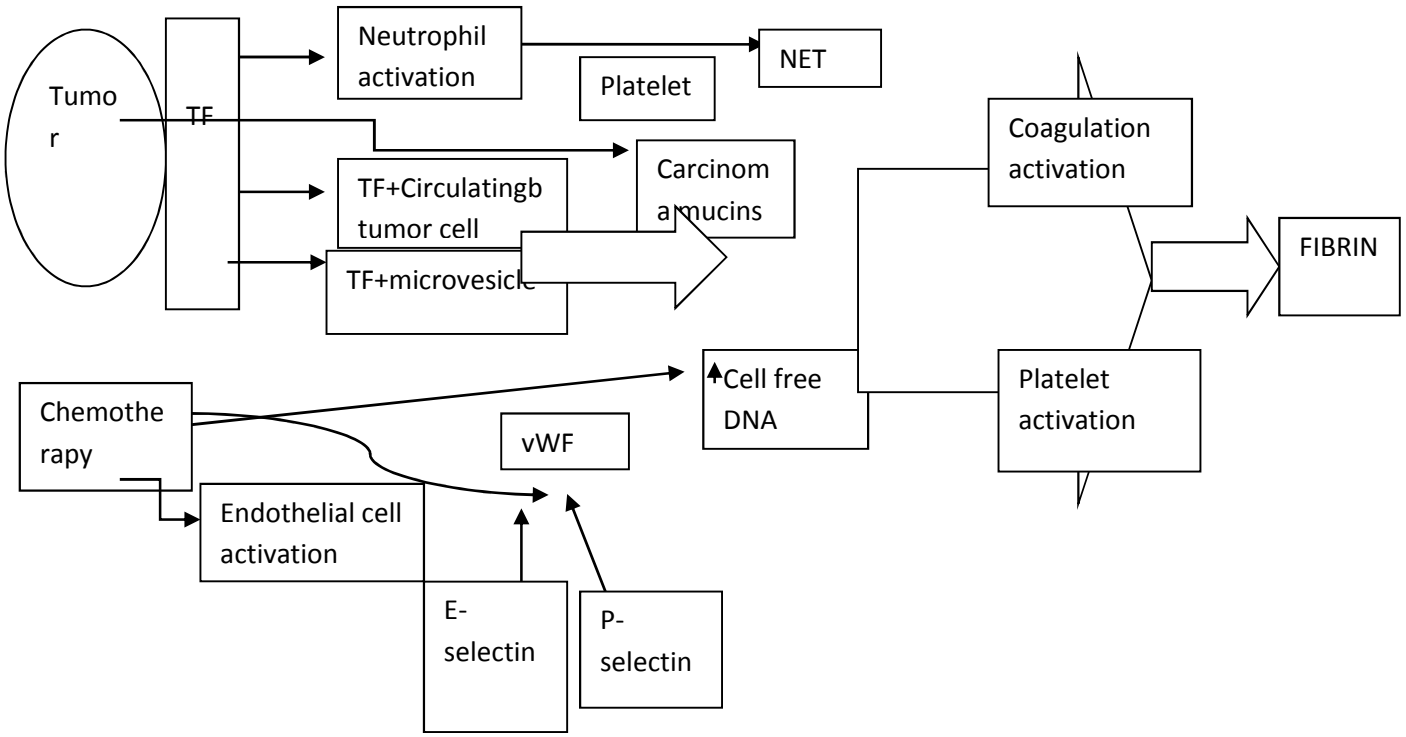

Figure-1-Mechanism of thrombosis in cancer. Diagram taken from DeVita textbook of oncology, 10TH Edition

Table 1: Prothrombotic Mechanisms in Cancer, Source; Scientific World Journal Volume 2014, Article ID 125706, 9 pages http://dx.doi.org/10.1155/2014/125706.

Proaggregation and procoagulant activity, increased platelet
Acceleration of thrombin production, overproduction of tissue factor, and other procoagulant factor
Cytokine production by tumor cells, production of TNF-1, interleukin-II, , and VEGF
Direct interactions between tumor cells and the endothelium of blood vessels, increased adhesiveness
Factors related to cancer treatment- surgery, radiotherapy, chemotherapy, and antiangiogenic treatment
Increased immobilization
Central venous catheters

Currently cancer and its treatments are well recognized risk factors for VTE. Evidence suggests that the absolute risk depends on the tumor type, the stage of the cancer, and the treatment with the antineoplastic agents. Furthermore, age, surgery, immobilization, and other comorbid features will also

influence the overall likelihood of thrombotic complications, as they do in patients without cancer. The most common malignancies associated with thrombosis are those of the breast, colon, and lung, reflecting the prevalence of these malignancies in the general population. When adjusted for disease prevalence, the cancers most strongly associated with thrombotic complications are those of the pancreas, ovary, and brain (19).

Table-2- risk factors for thrombosis in cancer patients

	Risk factors
Cancer related factors	Tumor site Histologic type Tumor stage Tumor grade Initial period after diagnosis
Treatment related factors	Surgery Radiotherapy Chemotherapy Antiangionic drugs Immunomodulatory drugs Hormonal therapy Therapy with erythropoiesis stimulating agents Blood transfusion Central lines
Patient related factors	Age BMI Mobility Comorbidity Sepsis Compliance with prophylaxis
Other risk factors	Leukocyte count Platelet count Anemia thrombophilia

Despite the problem posed by VTE in the setting of cancer, it is evident that a notable proportion of oncologists do not recognize the link between cancer, its treatment, and thrombogenesis. A small 2003 questionnaire survey, conducted in northern England, examined prophylaxis for VTE during treatment for cancer (20).

Among oncologists who responded, over 27% believed that their patients were not at risk for VTE. This response was independent of the type of tumor treated (20). It is noteworthy that over 60% of

respondents did not believe that hormone therapy or chemotherapy increased risk for VTE (20), and approximately 80% did not use thromboprophylaxis routines in chemotherapy or hormone therapy (20).

According to the European Society of Medical Oncology (ESMO), “most oncologists underestimate the prevalence of VTE and its negative impact on their patients” (21).

According to the UK Government`s All-Party Parliamentary Thrombosis Group, VTE is under-diagnosed to a large degree and only 54% of patients receiving chemotherapy are made aware of the associated risk of VTE. In the UK, only 41% of hospital trusts have a policy for managing cancer-associated VTE (22).

1.2. Significance of the Study

From the above discussion it is evident that CAT is a significant problem in cancer patients. However prevention and treatment of this problem is often overlooked one. In TASH Clinical Oncology Department we see a lot of patients with thrombosis may be because many of our patients are with advanced disease and even there are patients who present with thrombosis before diagnosis of cancer itself. So far to our knowledge there is no study that shows the magnitude of thrombosis in cancer patients in our hospital, so we believe that this study is a great input. This study tried to look into the magnitude of CAT in our cancer patients, its associated factors and gave recommendations depending on the findings.

1.3. Literature Review

Cancer associated thrombosis is a common complication in patients with malignant disease. Across all cancers, the risk for VTE is elevated 7-fold; in certain malignancies, the risk for VTE may be increased up to -28 fold (23).

A large, population-based, case–control study – the MEGA study – found that patients with cancer have a significantly increased risk for VTE, particularly during the first few months after diagnosis and in the presence of distant metastases (23). Among the cohort examined in this study, which comprised over 3200 patients with a first DVT of the leg, PE, or both, the overall risk for VTE was elevated by 7-fold in patients, with a malignancy (23), with the most profound increase risk seen in patients with hematological malignancies (28-fold increased risk), lung cancer (22-fold), gastrointestinal cancer (20-fold), or with distant metastases (19.8-fold) (23). The risk for VTE was 54-fold higher from 0 to 3 months after diagnosis, rapidly declining thereafter to 14-fold higher at 3 –12 months and 3.6 fold at 1 –3 years after diagnosis. Notably, however, the risk for VTE remained appreciably elevated up to 15 years after initial diagnosis (23).

Epidemiological studies suggest that hematological, lung, and gastrointestinal cancers, as broad diagnostic categories, is associated with a substantial risk for VTE. Significant efforts have been made to further delineate the cancer types that are associated with the highest risk for thrombotic events. In 1999, Levitan and colleagues assessed the rate of DVT/PE in a population of 41.2 million US Medicare patients (primarily aged X65 years) initially admitted with a malignancy (24). As shown in Table 1, malignancies associated with the highest incidence of DVT/PE include kidney, stomach, pancreas, brain,

and ovarian, as well as lymphoma. In contrast, cancers of the head and neck, bladder, breast, esophagus, uterus, and cervix are associated with relatively low rates of DVT/PE (24).

Table-3- Rates of DVT/PE in different malignancies

Sites	Rates OF DVT/PE per 10,000 patients
Head/neck	16
Bladder	22
Breast	22
esophagus	43
Uterus	44
Cervix	49
Prostate	55
Lung	61
Rectal	62
Liver	69
Colon	76
Leukemia	81
Renal	84
Stomach	85
Lymphoma	96
Pancreas	110
Brain	117
Ovary	120

An analysis of 41.2 million US Medicare (age X65) patients admitted to the hospital with a malignancy (Levitan et al, 1999).

In a study in Turkey, which involved one 123 female and 114 male patients (52% and 48%, respectively) were enrolled to study and the median age was 62 (range 25--89). Gastrointestinal tract cancers (colorectal, stomach, esophagus, and pancreatic cancers, respectively), lung cancer and breast cancer were the most common cancers in patients whom thrombosis detected on (25.7%, 19.7%, and 18.1%, respectively) (25). VTE was detected in 59 of 163 patients who underwent lower extremity venous Doppler USG and 35 of 104 patients who underwent PCTA (radiographic findings consistent with pulmonary thromboembolism-PTE). Eleven patients underwent both Doppler USG and PCTA. Totally, thrombosis was detected in 83 of 237 (35%) patients (25).

In this study, thrombosis was seen more often in males than females (60% vs. 40%, p ¼ 0.006). 54 patients were immobilized at the time of imaging and thrombosis was detected in 48% of immobilized patients, whereas thrombosis was detected in 30% of non-immobilized patients. Only 17.3% of the patients had undergone surgery within the last 6 months and thrombosis was detected in 56% of these patients. Thrombosis was detected in 47.3% of 55 patients who had a history of 4-day-long bed rest and

51% of the 45 patients who had anesthesia for at least 2 h. Finally, an association between increased risk of thrombosis and immobilization status (p ¼ 0.019), histories of surgery within the last 6 months (p ¼ 0.02), anesthesia for at least 2 h (p ¼ 0.012), 4-day-long bed rest (p ¼ 0.03) and hormonal treatment (p: 0.03) were found statistically significant. There was no relationship between thrombosis and the extent of disease, use of the central venous catheter, platinum-based chemotherapy, and anti-VEGF treatment in the study population. One hundred and eighty four patients' blood groups were detected. The relation between blood groups subtypes and thrombosis risk was evaluated. There was a statistically significant relationship between blood group subtypes and thrombosis (p: 0.011). Thrombosis was found more frequently in the non-O group than in O group (p: 0.024). When we stratified blood groups according to the presence of B antigens. It was shown that thrombosis was more frequent in B-group (p: 0.036) when patients were stratified as B group (B and AB group) and non-B group (A and O) (25).

The incidence of VTE in hospitalized patients with cancer increased sharply between 1979 and 1999(25). This increase has been substantially sharper than the rise in incidence observed among hospitalized patients who do not have cancer. These data suggest that improved diagnostic modalities are only partly responsible for changes over time in the incidence of VTE in patients with malignancies. Similarly a study, (3) found that there was a 36% increase in venous events among hospitalized neutropenic cancer patients between 1995 and 2002. Data also suggest that patients with cancer undergoing surgical procedures have an approximately two-fold increased risk for developing VTE compared with those without cancer (26).

UK data revealed a VTE incidence of 14/1000 people per year (95% CI 13 to 14) for all cancers. Regarding cancer type, the incidence of VTE is the highest for pancreatic cancer at 98/1000 people per year (95%CI 80 to 119), followed by lung cancer at 44/1000 (95% CI 39 to 48), stomach cancer at 37/1000 (95% CI 31 to 45), ovarian cancer at 31/1000 (95% CI 27 to 36), uterine cancer at 11/1000 (95% CI 9 to 14) and breast cancer at 9/1000 (95% CI 8 to 10)(29). Systematic review data show somewhat higher incidences for these cancer types: pancreatic cancer: 102/1000 (95% CI 70 to lung cancer: 52/1000 (95% CI 38 to 70); colorectal cancer: 33/1000 (95% CI 21 to 53); and breast cancer: 21/1000 (95% CI 10 to 41) (30). In Japanese autopsy data from 99000 patients (>65000 patients with cancer), the rate of pulmonary embolism (PE) was 2.3% (95% CI 2.2 to 2.4). The rate of PE for ovarian cancer was 5.4%, whereas rates for cancers of the pancreas, lung, digestive system, breast and uterus were 3.4%, 3.2%, 2.4%, 2.6% and 3.0%, respectively (32). The most common site of venous thrombosis leading to PE is a distal deep vein (33).

Among cancer patients with the same primary site, VTE rates seem to vary markedly based on grade and histology. Blom et al., for instance, showed that lung cancer patients with adenocarcinoma had a greater incidence of venous thrombosis as compared to those with squamous cell carcinoma (34). Indeed the stage of cancer is also important, with more advanced stages of cancers conferring ever increasing risk (35, 36). It appears that this risk is highest in the period immediately following cancer diagnosis. In a large case-control study, it was reported that the risk of VTE was highest in the first 3 months following the diagnosis of cancer [adjusted odds ratio (OR), 53.5; 95% confidence interval (CI), 8.6–334.3], subsiding gradually over a 15-year period to levels observed in the general population (23).

Other studies show that chemotherapy is associated with a two- to six fold increase in the risk of VTE compared to the general population and in patients starting new chemotherapy regimens, accounts for 9% of deaths (5, 37). These trends seem to be increasing over time, perhaps owing to the development of additional chemotherapeutic options. In hospitalized patients receiving chemotherapy, rates of VTE rose from 3.9 to 5.7% from 1995 to 2003, an increase of 47% (38). Some chemotherapy agents appear to confer greater risk than others. Patients with multiple myeloma receiving Thalidomide in combination with dexamethasone, for example, have DVT rates as high as 28% in some instances (39, 40). Additional predictors for Thalidomide associated VTE include its combined use with Doxorubicin (OR = 4.3), newly diagnosed disease (OR = 2.5), and Chromosome 11 abnormalities (OR = 1.8) (40). Another commonly used agent, Lenalidomide, has significant survival benefits in myeloma patients while also being associated with rates of VTE as high as 75% (40). Another agent, Bevacizumab (an anti-angiogenic in use for a variety of cancers) has been associated with increased risk of both arterial as well as venous events (41).

Even common and seemingly innocuous practices, such as the administration of erythropoiesis-stimulating agents (ESAs) to treat anemia, can be harmful in the cancer patient. In a systematic review of 57 trials on cancer patients, thromboembolic events were observed in 229 of 3,728 patients treated with Epoetin or Darbepoetin and in 118 of 3,041 untreated controls (RR = 1.7; 95% CI, 1.4–2.1)(42).

In hospitalized cancer patients, it is often necessary to transfuse blood and platelet products both of which are associated with an increased risk of thromboembolic events as well as mortality (43).

Central venous catheters are widely used in patients with cancer for the administration of chemotherapy. Verso et al. reported that the incidence of symptomatic catheter-related DVT in adults ranges from 0.3 to 28% while that of catheter-related DVT screened by venography ranges from 27 to 66%. (44).

Other treatment-related risk factors for VTE that have been described in the literature include hospitalization (2) and radiation (34).

2.0. Objective of the Study

2.1. General Objective; **Determine prevalence CAT in cancer patients**

2.2. Specific Objects

2.2.1. Determine prevalence of CAT in specific cancer diagnosis

2.2.2. Identify cancers commonly causing CAT in cancer patients

2.2.3. Identify types of CAT in cancer patients

2.2.3. Identify risk factors for CAT in cancer patients

3.0. Methods and Materials

3.1. Study Design-Retrospective analysis of prevalence, cause and type of CAT and risk factors of CAT in all solid and hematologic malignancy patients seen at TASH Clinical Oncology Department in one year was conducted for one year.

3.2. Study Area: This study was conducted in TASH. This hospital is the only hospital in Ethiopia where cancer patients are being treated .

3.3. Study Period: Sept 11, 2018 _ Sept 10, 2019

3.4. Source and Study Population

Source Population: For this study the source population was patients treated in TASH from Sept 11, 2018 _ Sept 10, 2019

Study Population: For this study the study population was all cancer patients treated in TASH from Sept 11, 2018 _ Sept 10, 2019

Study Unit: Charts of cancer patients

3.5. Inclusion and Exclusion Criteria:

All patients with age of 18 and above was included

Charts of patients with no adequate information for the study was excluded

3.6. Variables of the Study

Dependent Variables:

- Cancer Associated Thrombosis (CAT)

Independent Variables:

- Age
- Sex
- Diagnosis
- Performance Status-ECOG
- Stage
- Histology
- Baseline WBC Count
- Baseline Platelet Count
- Baseline Hgb Level
- Chemotherapy
- Radiotherapy
- Hormonal Therapy
- Anatomic Site
- Major Surgery
- Medical Comorbidity
- History of Transfusion
- Smoking
- Infection
- Admission
- BMI

3.7. Operational Definition

Thrombosis: The formation of a blood clot within a blood vessel, venous or arterial.

Cancer Patient: Solid or hematologic malignancy diagnosed by FNAC or biopsy, or clinically by physician

Admission: Admission to hospital other than for transfusion or for chemotherapy

Infection: Bacterial, fungal of viral infection diagnosed clinically, imaging, or by laboratory requiring treatment

Major Surgery: Surgery requiring general anesthesia, and done within 6 months before diagnosis of CAT.

CAT: Venous or arterial thrombosis, stroke, MI, PE, diagnosed with imaging.

Head and Neck Cancer: in this study head and neck cancer is all head and neck cancer except thyroid cancer.

GIT Cancer: in this study GIT cancer esophageal cancer, gastric cancer, biliary cancer, pancreatic cancer, colorectal cancer, and anal cancer.

Thoracic Cancers: In this study thoracic cancers are cancers of lung and thymus

3.8. **Sampling**: All CAT patients were included from all cancer patients seen in one year. So sampling was not required.

3.9. **Data Collection**: Data was collected for CAT patients from patients' charts by using structured format. All cancer patients seen at TASH in one year were counted and identified by cancer type and sex. Data was collected by oncology residents. Training was given for one day.

3.10. **Data Quality Assurance**: Data quality was assured during data collection, coding, entry, and analysis. Training was given for data collectors. Two supervisors was assigned. Card number was written on the data collection format so that card would be traced in case there was mistake during data collection.

3.11. **Data Management and Analysis Procedure**: Data was coded, entered and analyzed using SPSS version 16. Frequency tables and charts were produced. Linear regression and multinomial logistic regression tests were employed. Odds ratio was also employed.

4.0. **Limitation of the Study**: Incompleteness of charts was a problem to get all required information in this study. Significant number of CAT cases might have been missed at hematology department, because we were not able to access them. The study was retrospective and so did not include asymptomatic patients. Some cases of specific disease patients may not come to clinical oncology department, so this study might have underestimated prevalence of CAT in the general cancer population as well as in some specific cancer types.

5.0. **Ethical Consideration**: Ethical clearance was obtained from AAU health Science College Ethical committee.

6.0. **Dissemination of the Result**: The result of the study will be presented to AAU College of Health Science, Clinical Oncology department, school of public health. It will be sent to local journals and international journal for possible publication. Different governmental and other relevant supporter organizations working on cancer and thrombosis can have the access to get the results for their health care activities.

7.0. RSULT

7.1. General Information

We conducted a retrospective descriptive study on cancer associated thrombosis, CAT, on cancer patients who visited clinical oncology department in one year.

From Sept 11, 2018_Sept 10, 2019, in one year, a total of 3233 cancer patients were seen at TASH Clinical Oncology Department. Of these patients 1972(61%) were females and 1261(9%) were males.

835(26.54%) of patients were gynecologic cancer patients, most of which 773/858(90%) were cervical cancer patients. The second most common cancers were the GIT cancers excluding HCC (colorectal, esophageal, gastric, pancreatic, biliary tract cancers, anal cancers together) 619(19.14%). The third most common cancer was breast cancer patients, 541(16.73%).

Table 4: Number and Percentage of Cancer Patients Seen at TASH Clinical Oncology Department. Sept 11, 2018_Sept 10, 2019

Type of Cancer	Number	Percent
Gynecologic cancers	858	26.54
Breast Cancer	541	16.73
Head and Neck Cancer	336	10.39
GIT cancer other than HCC	619	19.14
Sarcoma	188	5.81
Thoracic tumors	111	3.43
Thyroid Cancer	102	3.15
HCC	88	2.72
CUP	74	2.28
Hematologic Malignancy	104	3.21
Brain Tumor	56	1.73
Genitourinary tumors	102	3.15
Non-melanoma skin cancer	30	0.92
Melanoma	16	0.50
others	8	0.25
total	3233	100

7.2. Prevalence of Cancer Associated Thrombosis, CAT

7.2.1. Prevalence in the general cancer patients

From 3233 cancer patients, there were 177 patients who were diagnosed with Cancer Associated Thrombosis, CAT. This means prevalence of cancer associated thrombosis, CAT in cancer patients seen at our center is 5.47%. Out of 177 patients diagnosed with cancer associated thrombosis, 109(61.58%) were females and 68(38.42%) were males. Prevalence of CAT in female cancer patients was found to be 109/1972 (5.53%) while it was 68/1261 (5.39%) in males.

Table 5: Prevalence of CAT among Cancer Patients Seen at TASH, Clinical Oncology Department, Sept 11, 2018 _ Sept 10, 2019

	Total number of cancer patients	Number of patients with CAT	percent
Male	1261	68	5.39
Female	1972	109	5.53
Total	3233	177	5.47

7.2.2. Prevalence in Specific Cancer Types

The highest prevalence of CAT was seen in patients with HCC 27/88(30.68%), followed by in genitourinary cancers 11/102(10.78%), brain tumors 6/56(10.74%), thyroid cancer 10/102(9.80%), thoracic tumors 10/11(9%).

Its prevalence was lowest in breast cancer and head and neck cancers with 4/541(0.73%), 1/337(0.30) respectively.

Table 6: Prevalence of CAT in Each Type of Cancer among Cancer Patients seen at TASH Clinical Oncology Department, Sept 11, 2018_Sept 10, 2019

Diagnosis	Number	Number of patients with CAT	Prevalence in each diagnosis
Gynecologic cancers Cancer	858	52	6.06
Breast Cancer	541	4	0.73
Head and neck cancer	336	1	0.30
GIT Cancer other than HCC	619	26	4.20
Sarcoma	188	15	7.98
Thoracic tumors	111	10	9.00
Thyroid cancer	102	10	9.80
HCC	88	27	30.68
Genitourinary cancer	102	11	10.78
CUP	74	6	8.11
Hematologic Cancer	104	9	8.65
Brain Tumor	56	6	10.74
Total		177	

7.3. Type of CAT

177 patients had CAT. Limb DVT was the most common type of CAT with 104 (58.76%), of cases. 27(15.25%) of them were PVT. 30(16.95%) of them had other vein thrombosis. 3 (1.7%) had arterial thrombosis. PTE was identified in 9(5.10%) of cancer patients.

Table 7: Type of CAT Seen Among Cancer Seen at TASH Clinical Oncology Department,

Sept 11, 2018 - Sept 10, 2019

Type of CAT	Freq.	Percent
LIMB DVT	104	58.8%
PVT	31	17.5%
OTHER VEIN THROMBOSIS	30	16.9%
ARTERIAL THROMBOSIS	3	1.7%
PTE	9	5.1
Total	177	100.0

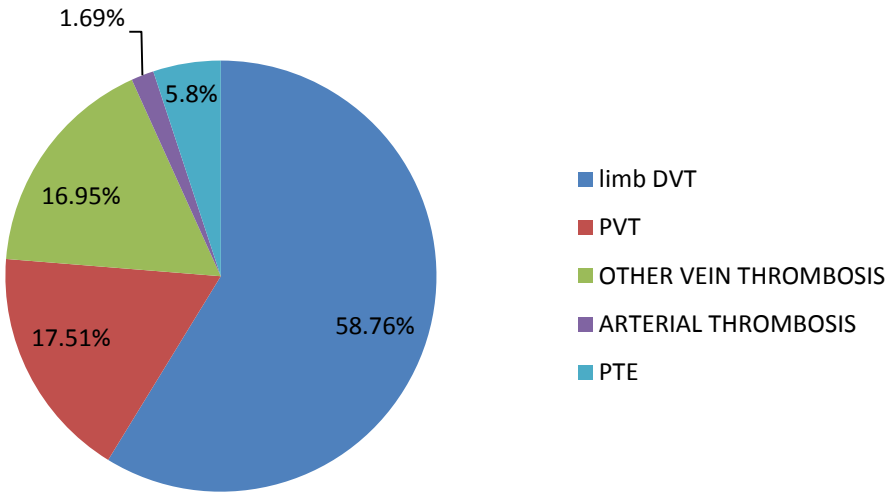

Figure 2: Type of CAT in Cancer Patients by Percent TASH, 2018 -

According to our data (linear regression), likelihood of developing Limb DVT was affected by anatomic site of cancer with p=0.000, and (95% CI: 0.102 and 0.35), and by anatomic site of surgey with p=02, (CI: 0.923 and 1.275). When type of cancer was taken into consideration likelihood of occurrence of limb DVT was significant for GIT cancer and gynecologic cancer with p=0.023, (CI: 1.172 and 8.735), p=0.000, (CI: 6.485 and 340.649) respectively. It was also significant for the pelvis and abdomen for location of tumor with p=0.000, (CI: 6.014 and 45.268), and p=0.048, (CI: 1.007 and 5.856) respectively. When site of surgery was taken in to consideration likelihood of occurrence of limb DVT was significantly higher for pelvis with p=0.001, (CI: 2.462 and 44.781). (Tables: 8, 9, 10, multinomial regression)

Table 8: Type of CAT with Type of Cancer among Cancer Patients Seen at TASH Clinical Oncology Department, Sept 11, 2018 - Sept 10, 2019

Type of CAT	Type of Cancer	Frequency	Percent	p-value	95% CI	
					Lower Bound	Upper Bound
limb DVT	Brain	6	5.8	.997	.000	.[b]
	Cup	4	3.8	.423	.366	10.919
	Genitourinary	7	6.7	.220	.603	9.023
	GIT	16	15.4	.023	1.172	8.735
	Gynecologic	47	45.2	.000	6.485	340.649
	HCC	2	2.0	1.000	.141	7.099
	Hematology	3	2.9	.657	.251	8.977
	Others	3	2.9	.998	.000	.[b]
	Sarcoma	10	9.6	.121	.784	7.971
	Thoracic	4	3.8	1.000	.250	3.998
	Thyroid	2	2.0	.118	.059	1.375
PVT	Brain	0	0	.	1.000	1.000
	Cup	0	0	.998	.000	.[b]
	Genitourinary	0	0	.997	.000	.[b]
	GIT	3	9.6	.484	.143	2.511
	Gynecologic	4	1.3	.215	.447	35.788
	HCC	22	71.0	.001	2.587	46.779
	Hematology	0	0	.996	.000	.[b]
	Others	2	6.4	.998	.000	.[b]
	Sarcoma	0	0	.996	.000	.[b]
	thoracic	0	0	.996	.000	.[b]
	Thyroid	0	0	.997	.000	.[b]
ARTERIAL	Brain	0	0	.	1.000	1.000

THROMBOSIS	Cup	0	0	.998	.000	.[b]
	Genitourinary	0	0	.997	.000	.[b]
	GIT	0	0	.994	.000	.[b]
	Gynecologic	0	0	.996	.000	.[b]
	HCC	1	33.3	.571	.045	5.514
	Hematology	2	66.7	1.000	.141	7.099
	Others	0	0	1.000	.000	.[b]
	Sarcoma	0	0	.996	.000	.[b]
	Thoracic]	0	0	.996	.000	.[b]
	Thyroid]	0	0	.997	.000	.[b]
PTE	Brain	0	0	.	1.000	1.000
	Cup	0	0	.998	.000	.[b]
	Genitourinary	1	11.1	.341	.035	3.205
	GIT	2	22.2	.273	.078	2.062
	Gynecologic	0	0	.996	.000	.[b]
	HCC	0	0	.996	.000	.[b]
	Hematology	2	22.2	1.000	.141	7.099
	Others	0	0	1.000	.000	.[b]
	Sarcoma	1	11.1	.215	.028	2.237
	Thoracic	2	22.2	.423	.092	2.730
	Thyroid	1	11.1	.069	.018	1.161

Table 9: Type of CAT with Site of Cancer among Cancer Patients Seen at TASH Clinical Oncology Department, Sept 11, 2018 _ Sept 10, 2019

Type of CAT	Site of Cancer	Frequency	Percent	P-value	95% CI	
					Lower Bound	Upper Bound
limb DVT	Pelvis	66	63.4	.000	6.014	45.268
	Abdomen	17	16.3	.048	1.007	5.856
	Thoracic	5	4.8	.410	.204	1.910
	Head & Neck	3	2.9	.067	.083	1.090
	Others	13	12.5	.013	1.701	99.375
PVT	Pelvis	5	16.1	.739	.336	4.655
	Abdomen	24	77.4	.004	1.477	7.957
	Thoracic	0	0	.998	.000	.[b]
	Head & Neck	1	3.2	.028	.013	.781
	Others	1	3.2	1.000	.063	15.988
ARTERIAL THROMBOSIS	Pelvis	0	0	.998	.000	.[b]
	Abdomen	2	66.7	.118	.059	1.375

	Thoracic	0	0	.998	.000	.[b]
	Head & Neck	1	33.3	.028	.013	.781
	Others	0	0	.	4.334E-009	4.334E-009
PTE	Pelvis	1	11.1	.215	.028	2.237
	Abdomen	4	44.4	.372	.167	1.952
	Thoracic	2	22.2	.080	.053	1.177
	Head & Neck	2	22.2	.038	.044	.913
	others	0	0	.	4.334E-009	4.334E-009

Table 10: Type of CAT with Site of Surgery among Cancer Patients Seen at TASH Clinical Oncology Department, Sept 11, 2018 _ Sept 10, 2019

Type of CAT	Site of Surgery	Frequency	Percent	P- value	95% CI	
					Lower Bound	Upper Bound
limb DVT	Pelvis	21	20.2	.001	2.462	44.781
	Abdomen	9	29.0	.177	.693	7.306
	Thoracic	2	6.4	.571	.181	22.056
	Others	3	9.6	.657	.251	8.977
	No Surgery	69	66.3	.000	2.016	5.355
PVT	Pelvis	2	6.4	1.000	.141	7.099
	Abdomen	5	16.1	.739	.336	4.655
	Thoracic	1	3.2	1.000	.063	15.988
	Others	0	0	.	3.011E-009	3.011E-009
	No surgery	23	74.2	.763	.606	1.979
ARTERIAL THROMBOSIS	Pelvis	0	0	.	3.862E-009	3.862E-009
	Abdomen	0	0	.997	.000	.[b]
	Thoracic	0	0	.998	.000	.[b]
	Others	0	0	.	3.011E-009	3.011E-009
	No Surgery	3	100	.002	.043	.479
PTE	Pelvis	0	0	.	3.862E-009	3.862E-009
	Surgery	2	22.2	.423	.092	2.730
	Thoracic	1	11.1	1.000	.063	15.988
	Others	0	0	.	3.011E-009	3.011E-009
	No Surgery	6	66.7	.007	.115	.708

7.4. Proportion of CAT Caused by Each Cancer Type

The commonest cancers associated with diagnosis of CAT were the gynecologic cancers 52/177 (29.38%), of these 42/52(81%) of patients were cervical cancer patients. The next most common one was HCC by 27/177(15.25%). The HCC patients were incidentally found to have portal vein thrombosis while worked up for liver mass. Only two patients were started on anticoagulation, others were neither started on treatment nor linked to hematology or emergency departments. CAT was seen in causes of 26/177 (14.70%), of GIT cancers, 15(8.47%) of sarcomas, 11/177(6.21%) of genitourinary cancers, 10/177(5.65%) of thoracic cancers, 10/177(5.65%) of thyroid cancers. Among the sarcoma patients, 9/10 (90%) were pelvic/abdominal soft tissue sarcomas. 10/11 (91%) of thoracic tumors were lung cancer patients, all NSCLC.

Table 11: Proportion of CAT Caused by Each Cancer Type among Cancer Patients Seen at TASH Clinical Oncology Department, Sept 11, 2018 - Sept 10, 2019

Cancer Type	Freq.	Percent
Gynecologic	52	29.4
Sarcoma	15	8.5
HCC	27	15.3
Thoracic	10	5.6
Thyroid	10	5.6
Hematology	9	5.1
Genitourinary	11	6.2
GIT	26	14.7
Brain	6	3.4
CUP	6	3.4
Others	5	2.8

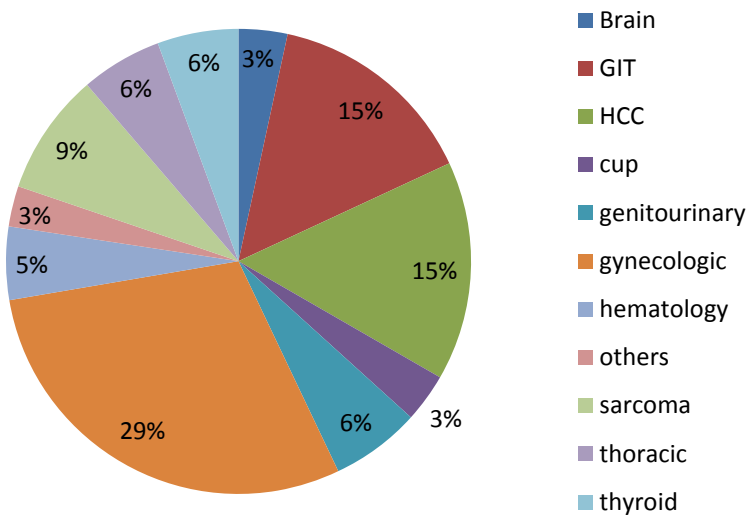

Figure 3: Proportion of Causes of CAT in Cancer Patients by Percent, TASH, 2018 - 2019

7.5. Risk Factors for CAT

7.5.1. Patient Related Risk Factors

109 (61.58%) patients were found to be females, 68/177 (38.42%) of patients were males. There were more patients in higher age groups; the highest number was in the above 60 age group, 51/177 (28.81%).

41/177 (23.16%) patients were found to have comorbidity. The commonest comorbidity identified was hypertension 18/177 (10.17%) of patients, followed by RVI 8/177 (4.50%) and type II DM 7/177 (3.95%) of patients respectively.

BMI was documented only for 29 patients. Only four patients were found to have BMI 35kg/m2 and above which is considered to be a risk for CAT in cancer patients.

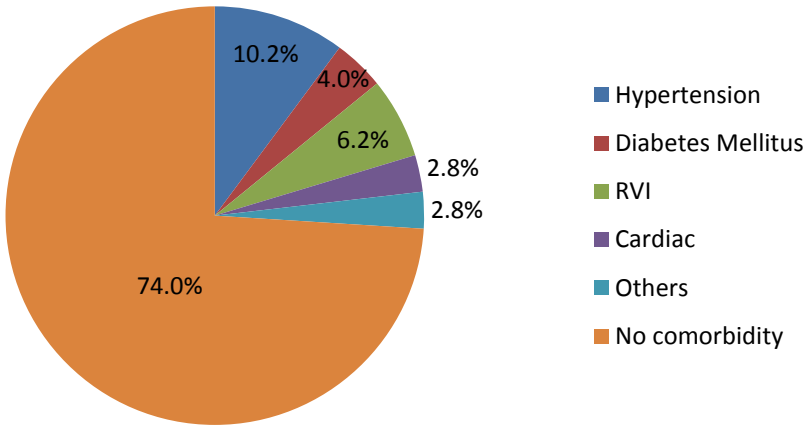

Figure 4: Medical Comorbidity with CAT in Cancer Patients, TASH, 2018 - 2019

13/177 (7.34%) of patients were found to have infection as a potential risk. 56/177(31.64%) of patients were found to have history of admission other than for routine administration of chemotherapy. Only 4 patients have history of smoking.

Table 12: Patient Related Factor for CAT among Cancer Patients with CAT Seen at TASH, Clinical Oncology Department, Sept 11, 2018 - Sept 10, 2019

Sex	**Count**	**%**
Male	68	38%
Female	109	62%
Age		
18 - 30	21	12%
31 - 40	26	15%
41 - 50	37	21%
51 - 60	43	24%
>60	50	28%
Comorbidity		
Hypertension	18	10%
RVI	11	6%
DM	7	4%
Cardiac	5	3%
Others	5	3%
No Comorbidity	131	74%
BMI		
>=35KG/M2	4	2%
<35KG/M2	23	13%

Not documented	150	85%
Infection		
Yes	14	8%
No	163	92%
Admission		
Yes	62	35%
No	115	0.649718
Smoking		
Yes	5	0.028249
No	172	0.971751
Performance Status (ECOG)		
1	40	22.6
2	70	39.5
3	48	27.1
4	19	10.7

7.5.2. Cancer Related Rrisk Factors

76(43%) of patients the location of the tumor was found to be in the pelvis. In 54(30.5%) of the patients it was in the abdomen. 17(9.6%), and 15(8.5%) of them were in the head and neck and the thorax. Most of the head and neck located tumors were the thyroid cancer patients. Others. 15(8.5%) of patients were brain, breast, etc.

The commonest histologies identified were SCC and adenocarcinoma both by 48(27.1%) of patients. The next most common histology was found to be HCC 27 (15.3%) of patients. 27(15.9%) of patients were patients with HCC. Third most common histology was sarcoma with 14 (7.9%) of patients.

102(57.6%) of patients were found to be stage IV. 61(34.5%) of patients were at stage III. 12(6.8%), and 2(1.1%) of them were at stage II and I respectively.

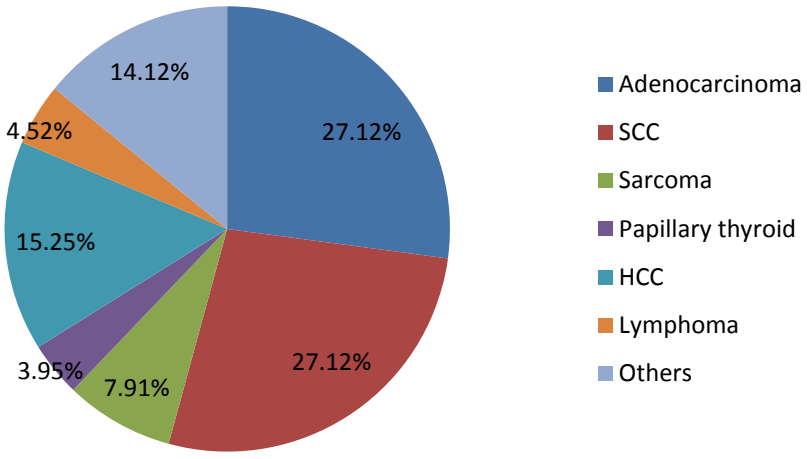

Figure 5: Histologies Identified in Cancer Patients with CAT, TASH, 2018 - 2019

Table 13: Cancer Related Factors for CAT among Cancer Patients with CAT among Cancer Patients Seen at TASH, Clinical Oncology Department, Sept 11, 2018 - Sept 10, 2019.

Tumor site	**Count**	**%**
Pelvis	76	43%
Abdomen	54	31%
Head & neck	17	10%
Thoracic	15	8%
Others	15	8%
Histologic type		
Adenocarcinoma	48	27%
SCC	48	27%
Sarcoma	27	15%
Papillary thyroid	14	8%
HCC	7	4%
Lymphoma	8	5%
Others	25	14%
Tumor stage		
I	2	1%
II	12	7%
III	61	34%
IV	102	58%

7.5.3. Treatment Related Risk Factors

55(31.1%) of patients had has history of surgery, out of which 25 (14.1%) were pelvic, 20(11.3%) were abdominal, 5(2.8%) were thoracic, and 5(2.8%) were other sites.

21(11.9%) of patients has history of transfusion as potential risk factors.

25(14.12%) of patients took chemotherapy. 20(11.30%) of patients took radiotherapy. 11(6.21%) of patients took hormonal treatment, most of which were thyroxine for differentiated thyroid cancer.

Table 14: Treatment Related Factors for CAT among Cancer Patients with CAT Seen at TASH, Clinical Oncology Department Sept 11, 2018 - Sept 10, 2019 .

Surgery	**Freq.**	**%**
Pelvis	25	14.12
Abdomen	20	11.3
Thoracic	5	2.82
Others	5	2.82
No surgery	122	68.93
Transfusion		
Yes	21	11.86
No	156	88.14
Chemotherapy		
Cisplatin + Paclitaxol	5	2.82
CHOP/VAC	7	3.95
Carboplatin + paclitaxol	6	3.39
Others	7	3.95
No chemotherapy	152	85.88
Radiotherapy		
Yes	20	11.3
No	157	88.7
Hormonetherapy		
Thyroxine	8	4.52
Anastrazole	3	1.69
No hormonal	166	93.79

7.5.4. Hematologic Risk Factors

48 (27.1%) of patients had leukocyte count greater than 11,000, 71 (40.1%) of patients had platelet count greater than 350,000, 26 (14.1%) of patients had Hgb level 9 and below. These are the values regarded as risk factors for CAT.

Table 15: Hematologic Risk Factors for CAT among Cancer Patients with CAT Seen at

TASH, Clinical Oncology Department, Sept 11, 2018 - Sept 10, 2019.

WBC	**Freq.**	**Percent**
<= 11,000	129	72.88
>11,000	48	27.12
Platelet Count		
<=350,000	106	59.89
>350,000	71	40.11
HgB		
9 and below	26	14.69
>9	151	85.31

8.0. Discussion

8.1. Prevalence in the General Cancer Patients

The general prevalence of CAT in our study was 5.53%. In a retrospective study of 17,284 patients, 12.6 percent of patients developed VTE compared with only 1.4 percent in the general population (46). Another study by Chew and colleagues found out 3775/235,149 patients, 1.6 percent were identified to have VTE (35). We didn't found a study on prevalence of thrombosis in Ethiopian general population. The risk of thrombosis in South African general population which may have similarity with Ethiopian population was found to be 0.10% (52). So the prevalence of thrombosis in our cancer population may be much higher than the Ethiopian general public. Studies show that approximately 4—20 percent of cancer patients will experience CAT at some stage. (38).The prevalence of CAT in our study was within the range of the studies mentioned and even much higher than the study by Chew and colleagues. Furthermore in our study, prevalence of CAT might be underestimated as the study was retrospective and involved symptomatic and already incidentally diagnosed patients, and we might have also missed patients who were linked to Hematology Department and not yet returned to oncology department.

The prevalence of CAT in male cancer patients was 68/1261 (5.39%), compared with its prevalence in female patients 109/1976 (5.53%). In this study females were twice more likely to develop CAT than males with odds ratio 2.5 (CI 1.8332—3.4179), P <0.0001.

There were more female cancer patients with CAT than males, 109 (61.58%) compared with 68(38.42%). In a study done at TASH on DVT paitents, out of which 31% are cancer patients, the ratio females to males was 2:1 (51). In a study in Turkey, thrombosis was seen more often in males than females (60% vs. 40%, p ¼ 0.006). (25). The reason for this difference may be due to the fact that we have cervical cancer as the most frequent cancer as it is true in many poor countries which may not be the case in Turkey which is a developed country.

8.2. Prevalence in Specific Cancer Types

In our study, the highest prevalence was seen in patients with HCC, 27/88 (30.68%). Genitourinary cancers 11/102 (10.78%) was with the next highest rate. Brain tumor 6/56 (10.74%), thyroid cancer 10/102 (9.8%), thoracic tumors 10/111 (9.0%) were with the next high rates. UK data revealed the incidence of VTE is the highest for pancreatic cancer at 98/1000 people, followed by lung cancer at 44/1000, stomach cancer at 37/1000, ovarian cancer at 31/1000, uterine cancer at 11/1000, and breast cancer at 9/1000. (29). In our study, when individual cancers are taken, brain cancers, ovarian cancers, NSCLC, rectal cancers are among with highest rates of CAT which is more or less similar to the studies mentioned. In an analysis of US Medicare patients admitted to hospital with malignancy, the cancers with the highest rates were ovary, brain, GIT, lymphoma, which does not contradict with our finding. In this US study among the cancers with lowest rates of CAT were head and neck and breast cancers which is the case in our study (24).

8.3. Proportion of CAT Caused by Each Cancer Type

The commonest type of cancer associated with diagnosis of CAT in our set up were gynecologic cancers 52/177 (29.4%), out of which 41/52 were cervical cancer patients. The next most common ones were was HCC 27/177 (15.3%). CAT was diagnosed in 26(14.7%) of GIT cancers, most of which 24/26(92%) were colorectal cancers. The most common causes of CAT in cancer patients found by Levitan et al were cancers involved the prostate, colon, lung, and brain in men, and the breast, lung, and ovary in women, in which lung cancer accounted for 21% of cases, colon cancer for 18%, and prostate cancer for 17%, this was because these were among the most prevalent cancers. (24). Both in our study and the study mentioned, the commonest causes of CAT were the most prevalent cancers in the respective setups. Among more prevalent cancers in our study breast cancer was among least common cause of CAT. Gynecologic cancer and GIT cancers were among the commonest causes of CAT and were among the commonest causes of cancer. HCC was the second commonest cause of CAT because it was with the highest rate with CAT.

8.4. Type of CAT

Limb DVT was the most common type of CAT identified in this study (58.8%). This is important to know because limb DVT is the one most commonly progress to PE (42). In general vein thrombosis contributed to 93.2% CAT. This was a similar finding in studies by Pradoni.P Ana Nobles, 94% of thrombosis cases were vein thrombosis (1, 2). According to our data (linear regression analysis), likelihood of developing Limb DVT was affected by anatomic site of cancer with p=0.000, and (95% CI: 0.102 and 0.35), and by anatomic site of surgey with p=02, (CI: 0.923 and 1.275). When type of cancer was taken into consideration likelihood of occurrence of limb DVT was significant for GIT cancer and gynecologic cancer with p=0.023, (CI: 1.172 and 8.735), p=0.000, (CI: 6.485 and 340.649) respectively. It was also significant for the pelvis and abdomen for location of tumor with p=0.000, (CI: 6.014 and 45.268), and p=0.048, (CI: 1.007 and 5.856) respectively. When site of surgery was taken in to consideration

likelihood of occurrence of limb DVT was significantly higher for pelvis with p=0.001, (CI: 2.462 and 44.781). We wanted to discuss more on limb DVT because it is the most common one, and it is the one which with high rate of complication.

In our study PVT contributed to 31 (17.5%) of cases. These were incidentally identified while worked up for liver mass and metastasis. Two of such patients were treated with anticoagulants. The rest of them were not started on treatment nor linked to emergency or hematology. A study by Dr. Nicoletta and colleagues on 177 patients with splanchnic vein thrombosis, (138(78%) were PVT, prognosis of incidentally detected splanchnic vein thrombosis is similar to that of clinically suspected vein thrombosis and suggest that similar treatment strategies should be applied. (49) Another study showed that incidental SVT is increasingly diagnosed in cancer patients with prevalence ranging from 2% to 20%.(46) A study showed that HCC patients had the highest incidence of incidental venous thromboembolism, and suggested active surveillance and administration of thromboprophylaxis in such patients.(50) We recommend a discussion what to do for such patients. PTE was identified in 9(5.1%) of patients. Three patients had arterial related CAT. It is known that cancer predispose patients to arterial events including stroke and MI can occur particularly in patients who are on antiangiogenic agents. (1).

8.5. Risk Factors

8.5.1. Patient Related Risk Factors

In a Turkish study the median age was 62, compared with the finding in our study, median age was 52. The cancer patients population in our country may be generally younger, because our population is generally younger than the population of more developed countries; otherwise we also found the highest rate of CAT to be in the 60 and above age group 28.81%). In retrospective cohort studies, cancer patients aged 65 and above years old have a greater likelihood of developing CAT. (48).

41 (23.16%) were found to have comorbidity. The commonest comorbidity identified was hypertension, 10.1%. RVI, DM, and cardiac diseases were identified in 11(6.2%), 7(4.0%), 5(2.8%) of patients respectively. Comorbid conditions such as renal failure, respiratory disease, heart disease, DM have been associated with an increased risk of CAT in cancer patients. (46).

In only 27(15.25%) of patients was BMI documented. Of these, only 4(2.3%) of patients had BMI in the known risk for CAT range, i.e. >35kg/m2. 14(7.9%) of patients had documented infection.

Only 5(2.8%), patients were smokers in cancer patients with CAT.

62(35.5%), of patients had history of admission other than for routine chemotherapy administration. Admission was a risk factor in a study done by Turan, Khorana. (25,38). In our study although significant number of patients with CAT had history of admission, it could not be concluded that history of admission was a risk factor in our patients because it was not compared in patients who had history of admission and did not develop CAT.

8.5.2. Cancer Related Risk Factors for CAT

The pelvis is the most common site of CAT, with 79(42.9%). The second most common site is the abdomen, with 54(30.5%), 30.4. The third most common site is head and neck, with 17(9.6%) percent of patients. These frequencies seem related to the causes of CAT in our setup; cervical cancer, rectal cancer, genitourinary-most are bladder cancers are among the most common cancers found associated with CAT in our study. However a study by Zhang showed that pelvis and then abdomen tumors were more important risk factors (53). The head and neck site as a third cause of CAT is due to thyroid cancer patients found in our setup. I didn't come across a study site as a predisposing factor for CAT.

SCC, Adenocarcinoma and HCC are the commonest histologies with, 48(27.48%), 48(27.48%), 27(15.3%) of patients respectively. Among cancer patients with the same primary site, VTE rates seem to vary markedly based on grade and histology. Blom et al., for instance, showed that lung cancer patients with adenocarcinoma had a greater incidence of venous thrombosis as compared to those with squamous cell carcinoma (34). In our case SCC is one of the commonest histology, may be because cervical cancer was the commonest cause of CAT. The other commonest cause is adenocarcinoma, which seems the commonest histology found in studies. HCC histology is the third commonest cause due to an incidental finding in patients with advanced liver disease patents found in our set up.

This study showed that the rate of CAT was higher in higher stages, this is in consistent with other study findings. In a Danish population based study, the risk of cancer patients developing CAT is increased with cancer stage, and calculated adjusted relative risks for stage I,II,III,IV were 2.9, 2.9. 7.5, and 17.1, respectively (7, 35, 36).

8.5.3. Treatment Related Risk Factors

55(31.1%) of patients had has history of surgery, out of which 25(14.1%) were pelvic, 20(11.3%) were abdominal, 5(2.8%) were thoracic, and 5(2.8%) were other sites. In a study by Turan, surgery within last 6 months was identified as a risk factor for CAT, p=0.02.pelvic and abdominal surgeries were the site of surgery that mostly related to thrombosis (25, 38).

Transfusion was given for 21(11.9%) of cancer patients with CAT. Studies showed that transfusion is a risk factor for CAT. In a study by Khorana and colleagues, among patients receiving RBC transfusions 7.2% developed VTE, and 5.2% developed ATE which was statistically significant in that study.(43)25(14.2%), of patients took chemotherapy. Chemotherapy is associated with a 2—6 fold increase in the risk of CAT (5,34).

20(11.35%) of patients with CAT took radiotherapy. Radiotherapy is mentioned as risk factor for thrombosis, I didn't find a specific study about radiotherapy as risk factor for CAT.

11(6.2%) of patients took hormonal treatment. 8(4.5%) of them took thyroxine, and 3 took ananstrazole. I didn't come across with a study that said that thyroxine treatment is pro-thrombotic. These patients were thyroid cancer patients who were on TSH suppressive treatment.

8.5.4. Hematologic Risk Factors

48(27.1%) of patients had base line leukocyte count of above 11,000, and the rest had 11,000 and below.

71(40.1%) of patients had platelet count of above 350,000.

26(14.7%) of patients had Hgb level of 9gm% and below

Studies show that, leukocyte count above 11,000, hgb level 9 and below, platelets count above 350,000 are risk factors for CAT.(38)

9.0. Conclusion

Prevalence of Cancer Associated Thrombosis, CAT is high in our cancer patients. Its true prevalence is even expected to be higher if the study was done in asymptomatic patients as well, and with standard imaging, and if missed patients at hematology were included. Studies show that the rate of thrombosis in asymptomatic patients range from 2% to 20%.

In conclusion the burden of CAT is significant in our patients like it is all over the world.

Gynecologic cancers, cervical cancer in particular was the most common cause of CAT.

HCC was cancer with the highest rate of CAT. In this study it was found that there are significant number of incidentally detected portal vein thrombosis which were not treated nor on follow up for their thrombosis. Studies mentioned on discussion part recommend that such patients should be managed similar to clinically detected patients.

Limb DVT was the most common type of CAT identified in our cancer patients which is the one most commonly progress to PE which is a life threatening complication.

In this study factors that are known to predispose cancer patients to CAT were described mainly in magnitude, association was not studied due to inadequacy of money and time.

BMI is an important parameter in the evaluation of cancer patients and more so in patients with thrombosis, but was not documented in most (84.7%) patients.

10.0. Recommendation

As the study showed that burden of CAT is significant in our set up, oncologists should be aware of this and give emphasis for this problem. Prevention by administering prophylaxis for patients with multiple risk factors should be emphasized to decrease burden of CAT in our cancer patients. Treatment of CAT should be emphasized and we recommend that the care should be given integrated to cancer care at our department rather than referral to other departments for the sake of patients' convenience and compliance. We recommend on adequate training on prevention and treatment of cancer associated thrombosis to oncology residents.

We also recommend a discussion on how to go about incidentally detected CAT patients, or should be treated similar to clinically detected patients as other studies recommendation.

It is our belief that this study can serve as a base line study for other future studies on this significant problem in cancer patients. We recommend that it should be studied in asymptomatic cancer patients as well. It is also our recommendation that CAT should be studied as a cause of mortality in our patients.

Association of risk factors should be studied in a case control fashion.

Factors such as BMI which are considered as risk factor for both cancer and thrombosis should be include and documented in patients' chart.

ANEX-1. Data collection Form

Data Collection Format; Retrospective Analysis of CAT among Cancer Patients in TASH.

Date of Data collection---------- Patient Card Number----------

1. Age----------

2. Sex----------

3. Diagnosis----------

4. Stage----------

5. Histology----------(adenocarcinoma, SCC, SARCOMA, Others)

6. Site---------- (H & N, thoracic, abdomen, pelvis, trunk, brain, extremity, others)

7. Medical comorbidity----------

8. Performance status (ECOG) ----------

9. BaselineWBC count----------

10. Base line platelets count----------

11. Base line HGB----------

12. Chemotherapy type a. yes b. no

13. If yes to 12, type of chemotherapy----------

14. Radiotherapy a. yes b. no

15. Hormonal therapies a, yes b. no

16. If yes to 15, type of hormonal therapy----------

17. Surgery a. yes b. no

18. If yes to 17, site of surgery; a. brain, b.Head and Neckc,c.thoracic,d. abdomen, e.pelvis, f.extremity,g. others

19. History of transfusion, a. yes b. no

20. Infection a. yes b. no

21. Smoking a. yes b. no

22. BMI ----------

23. History of admission other than for chemotherapy infusion a. yes b. no

24. Type of CAT----------

Data collector ----------sign----------Supervisor----------sign----------

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