# **ORIGINAL ARTICLE**

# Prevalence of Deep Vein Thrombosis in Cancer Patients in Hospitals of Rawalpindi

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# **ABSTRACT**

**Background and Aim:** Carcinoma/Cancer patients are more susceptible to venous thromboembolism compared to common disease patients. Regardless of chemotherapy, venous thromboembolism risk increases by 5-6 fold. The aim of the present study was to evaluate the prevalence of deep vein thrombosis in Fauji Foundation, Holy Family and Benazir Bhutto Hospital of Rawalpindi.

**Materials and Methods:** This cross-sectional study was carried out on 434 carcinoma/cancer patients presented to the Department of Medical Oncology, Fauji Foundation, Holy Family and Benazir Bhutto Hospital of Rawalpindi from May 2020 to July 2021. Malignancy patients of age range from 5 years to 65 years with deep vein thrombosis clinical signs and symptoms were investigated. All patients had to have a biopsy to prove they had cancer. All patients underwent routine baseline investigations, which included a complete blood picture ECG, biochemistry, and X-rays.

**Results:** Of the total 434 carcinoma/cancer patients, 23 (5.3%) malignant patients had deep vein thrombosis. The overall mean age of 23 patients was  $34.56 \pm 8.71$  years with an age range from 5 years to 65 years. Out of 23 patients, 14 (60.9%) were male and 9 (39.1%) were females. The prevalence of primary cancer (tumors) and hematological malignancies were 11 (47.8%) and 12 (52.2%) respectively. Enoxaparin injections of 1mg/kg/day were prescribed to these patients for 5 days to 7 days duration followed by 6 months of warfarin.

**Conclusion:** Our study found that the prevalence of deep vein thrombosis was 5.3%. Antithrombotic agents lower the risk of venous thromboembolism in cancer patients undergoing chemotherapy. Low dose warfarin and Low molecular weight heparins can both prevent and treat cancer-related thrombosis. Venous thromboembolism be treated with either unfractionated heparin (UFH) or low molecular weight heparin (LMWH) before starting Warfarin therapy as per guidelines.

Keywords: Prevalence, Deep vein thrombosis, Warfarin

### INTRODUCTION

Carcinoma/Cancer patients are more susceptible to venous thromboembolism compared to common disease patients. Regardless of chemotherapy, venous thromboembolism risk increases by 5-6 fold [1]. It has been well known since the 19th century that patients with cancer have an increased risk for venous thromboembolism (VTE), compared with those without cancer1. Active cancer with and without chemotherapy increases the risk of venous thromboembolism by 5-6 fold. Overall, cancer patients constitute 15-20% of the patients diagnosed with VTE [2]. Furthermore cancer associated thrombosis is linked with poor prognosis. It is the second leading cause of death in cancer patients [3]. The deep vein thrombosis prevalence is associated with centrally inserted venous catheters has ranged from 11% to 50% in studies [4]. A higher risk of venous thromboembolism (VTE) has been observed in patients with cancer than in those who do not have cancer [5]. The deep vein thrombosis risk is raised with active cancer regardless of chemotherapy [6]. About 15% to 20% of cancer cases had deep vein thrombosis [7]. Additionally, poor prognosis is correlated with thrombosis of malignancy. Deep vein thrombosis is the second most common of mortality among cancer patients [8].

A previous study reported a venous thromboembolism prevalence of 12.4/1000 cases within six months of a cancer diagnosis. In cancer patients, the incidence of venous thromboembolism (VTE) is increasing, and VTE significantly participates in mortality and morbidity [9].

Breast, prostate, lung, and colorectal are various common cancer types present with vein thrombosis [10]. Life expectancy is reduced when VTE is diagnosed concurrently. With an increase of venous thrombosis, mortality risk increases by 40-47 times. The fatal pulmonary embolism increases the mortality rate but reflects advanced stages of cancer and patients' aggressive tumor biology. The cancer patients' VTE risk varies depending on specific factors of disease such as stage, cancer types, and location [11-13]. As a result, there is an unmistakable need for thromboprophylaxis in surgical patients [14]. Therefore, the prevalence of venous thromboembolism relative risks among cancer patients were evaluated in the present study. The VTE and cancer correlation could be clarified partially by the hypercoagulable state induced by cancer cells, which aids metastasis and cancer growth [15]. The vitamin K antagonist's administration and heparins of low molecular weight are used to treat VTE [16].

#### MATERIAL AND METHODS

This cross-sectional study was carried out on 434 carcinoma/cancer patients presented to the Department of Medical Oncology, Fauji Foundation, Holy Family and Benazir Bhutto Hospital of Rawalpindi from May 2020 to July 2021. Malignancy patients of age range from 5 years to 65 years with deep vein thrombosis clinical signs and symptoms were investigated. All patients had to have a biopsy to prove they had cancer. All patients underwent routine baseline investigations, which included a complete

blood picture ECG, biochemistry, and X-rays. A Magnetic Resonance Venogram was used to confirm the presence of cerebral venous thrombosis. Inj. Enoxaparin1mg/Kg body weight hypodermically twice daily for 5-7 days was the treatment protocol for DVT patients. Based on underlying malignancy and thrombus non-resolution can affect the Warfarin long-term effect when started from a similar time. SPSS version 24 was used for data analysis. Quantitative variables such as age, tumors types, and Hematological Cancer were expressed as frequency and percentage.

# **RESULTS**

Of the total 434 carcinoma/cancer patients, 23 (5.3%) malignant patients had deep vein thrombosis. The overall mean age of 23 patients was 34.56 ± 8.71 years with an age range from 5 years to 65 years. Out of 23 patients, 14 (60.9%) were male and 9 (39.1%) were females. The prevalence of primary cancer (tumors) and hematological malignancies were 11 (47.8%) and 12 (52.2%) respectively.

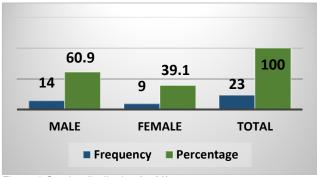


Figure-1 Gender distribution (n=23)

Enoxaparin injections of 1mg/kg/day were prescribed to these patients for 5 days to 7 days duration followed by 6 months of warfarin. Hepatic vein thrombosis was confirmed in two patients with polycythemia rubravera using Doppler USG of the abdomen. A patient with cerebral venous thrombosis was suffering from severe headaches, and a

fundoscopy revealed bilateral papilledema. Four patients with underlying polycythemia rubra Vera and hepatic vein thrombosis presented with severe abdominal pain. Tender hepatomegaly with ascites was discovered during the examination. Table-1 and 2 demonstrate the types of malignancies distribution.

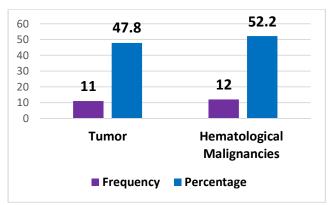


Figure-2 prevalence of tumors and hematological malignancies

Table-1 Tumor's patients distribution (n=11)

Table-1 Tullion's patients distribution (II-11)	
Tumor's Types	Frequency n (%)
Oesophagus	2 (18.2)
Ovary	3 (27.2)
Colon	1 (9.1)
Prostate	1 (9.1)
Osteosarcoma	1 (9.1)
Rhabdomyosarcoma	1 (9.1)
Breast	2 (18.2)

Table- Hematological Malignancies patients distribution (n=12)

Hematological Cancer	Frequency n (%)
Burkitt's lymphoma	2 (16.7)
Non-hodgkin's lymphoma	3 (25)
Acute myeloid leukemia	2 (16.7)
Multiple Myeloma	1 (8.3)
Polycythaemia rubra vera	2 (16.7)
Myelofibrosis	1 (8.3)
Chronic Myeloid Leukemia	1 (8.3)

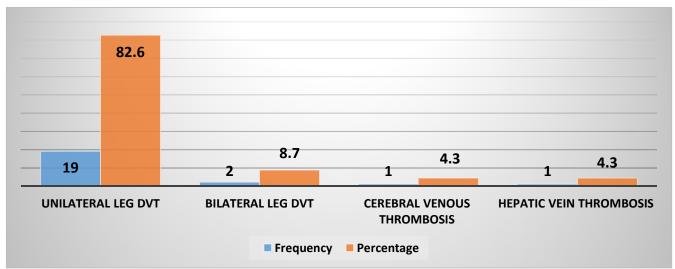


Figure-3. Vein Thrombosis Site

# **DISCUSSION**

Venous thrombosis, which includes deep vein thrombosis and pulmonary embolism, affects approximately 1 in 1000 adults each year [16]. Cancer patients are at an even higher risk [17]. The prevalence of cancer patient complications in the West is higher than in our population, with estimates ranging from 15 to 20% versus 5.3 %in our population [18]. These findings are supported by clinical trials, which show that the Asian community has a significantly lower incidence of thromboembolic disease. Recently, in Singapore, the incidence of sonographic evidence of DVT was found to be only 3% in the control group of patients undergoing colorectal surgery without any form of prophylaxis [19]. Similarly, in another study conducted reported that only one out of a hundred patients had sonographic evidence of DVT. They did not receive any form of prophylaxis [20].

Other potential risk factors for deep vein thrombosis are hyperosmolar solutions infusion [21], transfusion of blood product [22], peripherally inserted central catheters insertion in cephalic veins [23], and too large catheter utilization in vein through which it is inserted. We found no statistically significant relationship between these possible factors and outcome in our study, but this could be due to the small number of patients in our study who had similar risk factors to those listed above. Another study [24] conducted at PIMS Hospital, Islamabad in order to evaluate the incidence of DVT in femur, posttraumatic hip, and knee surgery. On compression sonography performed between the third and tenth postoperative days, three patients out of 100 were found to have positive evidence.

With INR within range of 2.5 to 3, no patient experienced significant bleeding. Our findings contradict Western reports, which show a 2-6 times bleeding complications higher than cancer patients gone through anticoagulant therapy [25]. Because our study lasted 1.5 years, the number of patients with deep vein thrombosis was limited. The decision to discontinue, take a lower dose, or continue warfarin was indicated by a prolonged INR, which was later reintroduced at a lower dose. The location of the thrombus corresponded to world literature. In polycythemia rubra Vera, we discovered two patients with hepatic vein thrombosis. There is a link between active cancer and intraabdominal DVT [26]. DVT is thought to be less common in Asian populations [27]. One patient had a cerebral venous thrombosis. He had underlying CML and complaining of severe headaches. papilledema was discovered via fundoscopy. The diagnosis was confirmed by a CT brain scan followed by an MRV.

Deep vein thrombosis is notoriously difficult to diagnose clinically. Before exposing patients to the risk of long-term anticoagulation, confirmation is required. Ascending venography was the gold standard for diagnosing DVT, but it is invasive and has side effects. As a result, venous duplex ultrasonography has become the standard initial evaluation for DVT. Ultrasonography or impedance plethysmography is sensitive and specific for the diagnosis of proximal occult venous thrombosis. An abnormal result almost always confirms the diagnosis, allowing treatment to begin. Serial testing is recommended if a normal result is obtained but clinical suspicion remains

high. As a result, Duplex and Color Doppler Sonography is currently the technique of choice for DVT diagnosis [27].

D-dimers products and Fibrin degradation are thought to be useful in thrombosis diagnosis. However, the evidence for diagnosing thrombosis with fibrin-related products is lacking [28]. We chose duplex ultrasound for diagnosis of femoro-popliteal and intra-abdominal thrombosis because of its high sensitivity and specificity, as well as its positive and negative predictive value. The diagnosis of cerebral venous thrombosis was confirmed using the gold standard, Magnetic Resonance Venogram [29].

## CONCLUSION

Our study found that the prevalence of deep vein thrombosis was 5.3%. Antithrombotic agents lower the risk of venous thromboembolism in cancer patients undergoing chemotherapy. Low dose warfarin and Low molecular weight heparins can both prevent and treat cancer-related thrombosis. Venous thromboembolism be treated with either unfractionated heparin (UFH) or low molecular weight heparin (LMWH) before starting Warfarin therapy as per guidelines.

#### REFERENCES

- Takada T, van Doorn S, Parpia S, de Wit K, Anderson DR, Stevens SM, Woller SC, ten Cate-Hoek AJ, Elf JL, Kraaijenhagen RA, Schutgens RE. Diagnosing deep vein thrombosis in cancer patients with suspected symptoms: An individual participant data meta-analysis. Journal of Thrombosis and Haemostasis. 2020 Sep;18(9):2245-52.
- Alipanahzadeh H, Ghulamreza R, Shokouhian M, Bagheri M, Maleknia M. Deep vein thrombosis: a less noticed complication in hematologic malignancies and immunologic disorders. Journal of thrombosis and thrombolysis. 2020 Aug;50(2):318-29.
- Becattini, C.; Cohen, A.T.; Agnelli, G.; Howard, L.; Castejón, B.; Trujillo-Santos, J.; Monreal, M.; Perrier, A.; Yusen, R.D.; Jiménez, D. Risk stratification of patients with acute symptomatic pulmonary embolism based on presence or absence of lower extremity DVT: Systematic review and meta-Analysis. Chest 2016, 149, 192–200.
- Streiff MB, Agnelli G, Connors JM, Crowther M, Eichinger S, Lopes R, et al. Guidance for the treatment of deep vein thrombosis and pulmonary embolism. J Thromb Thrombolysis. 2016 Jan;41(1):32–67.
- Medicine JHUa. Coronavirus resource center https://coronavirus.jhu.edu/map.html. 2020.
- Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020; 395: 1054- 1062.
- Landrigan CP, Parry GJ, Bones CB, Hackbarth AD, Goldmann DA, Sharek PJ. Temporal trends in rates of patient harm resulting from medical care. N Engl J Med. 2017; 363: 2124- 2134.
- Alikhan R, Cohen AT, Combe S, et al. Risk factors for venous thromboembolism in hospitalized patients with acute medical illness: analysis of the MEDENOX Study. Arch Intern Med. 2014; 164: 963- 968.
- Yang F, Shi S, Zhu Jiling, Shi J, Dai K, Chen X. Clinical characteristics and outcomes of cancer patients with malignancy. Journal of Medical Virology. 2020. http://dx.doi.org/10.1002/jmv.25972
- Hutten BA, Prins MH, Gent M, Ginsberg J, Tijssen JG, Buller HR. Incidence of recurrent thromboembolic and bleeding

- complications among patients with venous thromboembolism in relation to both malignancy and achieved international normalized ratio: a retrospective analysis. J Clin Oncol. 2020; 18: 3078- 3083.
- Decousus H, Tapson VF, Bergmann JF, et al. Factors at admission associated with bleeding risk in medical patients: findings from the IMPROVE investigators. Chest. 2017; 139: 69-79.
- Kaatz S, Ahmad D, Spyropoulos AC, Schulman S. Subcommittee on Control of A. Definition of clinically relevant non-major bleeding in studies of anticoagulants in atrial fibrillation and venous thromboembolic disease in nonsurgical patients: communication from the SSC of the ISTH. J Thromb Haemost. 2015; 13: 2119- 2126.
- Campigotto F, Neuberg D, Zwicker JI. Biased estimation of thrombosis rates in cancer studies using the method of Kaplan and Meier. J Thromb Haemost. 2018; 10: 1449-1451.
- Khorana AA, Francis CW, Culakova E, Fisher RI, Kuderer NM, Lyman GH. Thromboembolism in hospitalized neutropenic cancer patients. J Clin Oncol. 2016; 24: 484-490.
- Patell R, Rybicki L, McCrae KR, Khorana AA. Predicting risk of venous thromboembolism in hospitalized cancer patients: Utility of a risk assessment tool. Am J Hematol. 2017; 92: 501-507.
- Alikhan R, Cohen AT, Combe S, et al. Prevention of venous thromboembolism in medical patients with enoxaparin: a subgroup analysis of the MEDENOX study. Blood Coagul Fibrinolysis. 2013; 14: 341- 346.
- Varga Z, Flammer AJ, Steiger P, et al. Endothelial cell infection and endotheliitis in COVID-19. Lancet. 2020; 395: 1417-1418
- Fujiwara R, Numao N, Ishikawa Y, Inoue T, Ogawa M, Masuda H, Yuasa T, Yamamoto S, Fukui I, Yonese J. Incidence and predictors of deep vein thrombosis in patients with elevated serum D-dimer prior to surgery for urologic malignancy. Urologia internationalis. 2020;104(1-2):16-21.
- Bosch F, Nisio MD, Büller HR, van Es N. Diagnostic and therapeutic management of upper extremity deep vein thrombosis. Journal of Clinical Medicine. 2020 Jul;9(7):2069.
- Houghton DE, Billett HH, Gaddh M, Onadeko O, George G, Wang TF, Oo TH, Feng M, Dasgupta M, Jaglal M, Streiff

- MB. Risk of pulmonary emboli after removal of an upper extremity central catheter associated with a deep vein thrombosis. Blood Advances. 2021 Jul 27;5(14):2807-12.
- Houghton DE, Key NS, Zakai NA, Laux JP, Shea TC, Moll S. Analysis of anticoagulation strategies for venous thromboembolism during severe thrombocytopenia in patients with hematologic malignancies: a retrospective cohort. Leuk Lymphoma. 2017;58(11):2573-2581.
- Samuelson Bannow BT, Lee A, Khorana AA, et al. Management of cancer-associated thrombosis in patients with thrombocytopenia: guidance from the SSC of the ISTH. J Thromb Haemost. 2018;16(6):1246-1249.
- Debourdeau P, Farge D, Beckers M, et al. International clinical practice guidelines for the treatment and prophylaxis of thrombosis associated with central venous catheters in patients with cancer. J Thromb Haemost. 2013;11(1):71-80.
- Joffe HV, Kucher N, Tapson VF, Goldhaber SZ, Deep Vein Thrombosis FSC; Deep Vein Thrombosis (DVT) FREE Steering Committee. Upper-extremity deep vein thrombosis: a prospective registry of 592 patients. Circulation. 2004;110(12):1605-1611.
- Muñoz FJ, Mismetti P, Poggio R, et al; RIETE Investigators. Clinical outcome of patients with upper-extremity deep vein thrombosis: results from the RIETE Registry. Chest. 2008;133(1):143-148.
- Grant JD, Stevens SM, Woller SC, et al. Diagnosis and management of upper extremity deep-vein thrombosis in adults. Thromb Haemost. 2012;108(6):1097-1108.
- Rokosh RS, Ranganath N, Yau P, et al. high prevalence and mortality associated with upper extremity deep venous thrombosis in hospitalized patients at a tertiary care center. Ann Vasc Surg. 2020;65:55-65.
- Baumann Kreuziger LGM, Onadeko O, George G, et al. Wide variation in duration of anticoagulation after catheterrelated thrombosis: a venous thromboembolism network US multicenter retrospective cohort study. Blood. 2018;132(suppl 1):1248.
- Kreuziger LB, Gaddh M, Onadeko O, et al. Treatment of catheter-related thrombosis in patients with hematologic malignancies: a Venous ThromboEmbolism Network US retrospective cohort study. Thromb Res. 2021;202:155-161.