

Deep Vein Thrombosis in Cancer Patients: A Pilot Study from Eastern India

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Abstract

Background: Patients with cancers are at higher risk of developing deep vein thrombosis (DVT) than others. This study determined the prevalence of DVT and analysed its association with disease subtypes and previously established risk factors. There are very few studies on DVT in cancer patients from our country and this is the first of its kind from the eastern part of India.

Methods: This retrospective cross-sectional study enrolled patients aged >18 years with cytologically or histopathologically confirmed malignancies. Medical history, demographic characteristics, comorbidities, cytological or histopathological subtypes of these cancers were noted at the presentation.

Results: Out of 147 patients, 11 (8.59%) had DVT and a female preponderance (72.7%) was noted. The mean age (years) of the patients with DVT was significantly lower than patients without DVT (48.64 versus 59.68; $p = 0.005$). A significant correlation between DVT and age of patients was observed ($p = 0.045$). Cancer patients < 55 years of age had DVT, that was 3.49 times more than prevalent in patients > 55 years of age (Odds ratio = 0.286; 95% CI: 0.079 - 1.035). Risk factors like gender, diabetes, and hypertension did not show any definite association with DVT prevalence ($p > 0.05$). Prevalence of DVT was highest amongst patients with underlying breast and gynaecologic cancers (36.4%, each). The subtypes of cancer did not show any significant association with occurrence of DVT ($p > 0.05$).

Conclusion: These are the observations about the prevalence of DVT in cancer patients in this eastern part of the country and their correlation with age of the patients. However, cancer site, subtype, and standard comorbidities did not have any statistically significant correlation with the prevalence of DVT. In this study DVT was mostly observed in younger female patients who had breast and gynaecological cancers.

Key words: Cancer subtype, chemotherapy, deep vein thrombosis, gynaecological cancers.

Introduction

Globally, cancer patients are at higher risk of developing deep venous thrombosis (DVT) and subsequent serious venous thromboembolism (VTE). This risk is 4 to 6 times higher in the cancer population as compared to non-cancer cohorts^{1,2}. The repercussions of malignancy on venous stasis, imbalance of blood coagulants, and vessel wall damage substantially contribute to the alterations in normal blood flow (rheology), thereby increasing thrombus formation³.

Development of thrombosis in cancer patients results in their poor prognosis and has been associated with increased mortality and morbidity^{7,8}. Prevalence of DVT in cancer patients in India is not uncommon and there is an underestimation of these risks as well as low levels of clinical awareness. Limited use of thrombo-prophylaxis with high fatality from VTE has made DVT a worldwide cause of concern for mortality of cancer patients. But there is a scarcity of published literature related to the prevalence of DVT in cancer patients in India, specially the lack of available

data from this part of the country. Therefore, the present retrospective cross-sectional study was designed to determine the prevalence of DVT in cancer patients at presentation in this tertiary referral centre of Eastern India. This study will help us to be aware of this very important and preventable complication of cancer that is not uncommon, but often overlooked even in this part of the subcontinent.

Methods

A retrospective cross-sectional study was conducted in a tertiary care multispeciality centre of Eastern India during the period of May 2017 to May 2018. The study protocol was approved by the Institutional Ethics committee and was in accordance with the principles of the Declaration of Helsinki. Patients >18 years of age with cytologically or histopathologically confirmed malignancies were enrolled in the study. The patients already on any anticoagulant or antiplatelet drugs were excluded from the study.

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The medical records were retrospectively reviewed for detailed medical history, demographic profile, site of cancer, presence of comorbidities like hypertension and diabetes mellitus, co-prescription of drugs, cytological or histopathological confirmation of malignancies and their subtypes in all the patients included in this study. Diagnosis of DVT was suspected if patients showed positive clinical signs and symptoms like localised oedema, pain, warmth, reddish-blue discoloration over limbs (especially when unilateral) and diagnosis was confirmed with Doppler ultrasonography.

Statistical analysis of data was done using SPSS version 23.0. Categorical data were expressed as number (percentages) and continuous data were expressed as mean (standard deviation (SD)). Correlation between different clinicopathological parameters and DVT prevalence was assessed using Pearson's chi-square test. Fisher's exact test was used for finding the correlation between risk factors and DVT. The p value < 0.05 was considered as statistically significant.

Results

Of the total 148 patients with confirmed malignancies and whose lower limb Doppler USG results were available (Table I), 11 patients (8.59%) were diagnosed with the presence of DVT and 117 patients (91.41%) were without DVT. The mean (SD) age of the study population was 58.72 years with 70 (54.6%) females and 58 (45.4%) males. The mean (SD) age (years) of the patients with DVT was significantly lower as compared to patients without DVT [48.64 (8.62)] versus [59.68 (12.45)]; $p = 0.005$. Although the prevalence rate of DVT in females ($n = 8, 72.7\%$) was higher than in males ($n = 3, 27.3\%$), this was not statistically significant ($p = 0.2$). A significant correlation between DVT prevalence and age of patients was observed ($p = 0.045$). Interestingly, it was found that DVT was 3.49 times more common in cancer patients <55 years of age (Odds ratio = 0.286; 95% CI: 0.079 - 1.035). Amongst patients with DVT, 36.4% of patients had hypertension and 27.3% had diabetes as comorbidities. Whereas, in patients without DVT, 16.2% of patients had hypertension and 17.9% had diabetes. However, this correlation with standard comorbidities was not statistically significant.

As tabulated in Table II, the highest DVT prevalence rate was observed in patients with breast cancers (36.4%) and gynaecologic cancers (36.4%) followed by patients with digestive tract cancers (18.2%) and lung cancers (9.1%). However, the type of cancer did not show any statistically significant association with DVT prevalence ($\div 2 = 12.911$; $p = 0.16$). Morphological subtyping of cancer also did not

show any significant association with DVT prevalence ($p = 0.3$).

Table I: Correlation of deep vein thrombosis (DVT) with clinical characteristics in cancer patients.

Parameters	Patients with DVT (n = 11)	Patients without DVT (n = 117)	Total (n = 128)	Odds Ratio (95% CI)	p-value
Age (years), mean (SD)	48.64 (8.62)	59.68 (12.45)	58.72 (12.54)	–	0.005
≤ 55 years	07 (63.6)	39 (33.3)	46 (36.2)	0.286	0.045*
> 55 years	04 (36.4)	78 (66.7)	82 (63.8)	(0.079 - 1.035)	
Sex					
Male	03 (27.3)	55 (47.0)	58 (45.4)	0.423	0.2
Female	08 (72.7)	62 (53.0)	70 (54.6)	(0.107 - 1.673)	
Hypertension					
Present	04 (36.4)	19 (16.2)	23 (18.3)	2.947	0.09
Absent	07 (63.6)	98 (83.8)	105 (81.7)	(0.785 - 11.067)	
Diabetes					
Present	03 (27.3)	21 (17.9)	24 (18.3)	1.714	0.45
Absent	08 (72.7)	96 (82.1)	104 (81.7)	(0.419 - 7.010)	

Data shown as n (%), unless otherwise specified. *Significance with $p < 0.05$

Table II: Correlation of deep vein thrombosis (DVT) with cancer-related parameters among the study population.

Parameters	Patients with DVT (n = 11)	Patients without DVT (n = 117)	Total (n = 128)	Odds ratio (95% CI)/ $\div 2$ test value	p-value
Type of cancer					
Lung	1 (9.1)	6 (5.6)	6 (5.9)	$\div 2 = 12.911$	0.16
Brain	0 (0.0)	1 (0.9)	1 (0.8)		
Breast	4 (36.4)	18 (16.7)	22 (18.5)		
Digestive	2 (18.2)	44 (40.7)	46 (38.7)		
Genitourinary	0 (0.0)	8 (7.4)	7 (6.7)		
Gynaecologic	4 (36.4)	10 (9.3)	14 (11.8)		
Haematopoietic	0 (0.0)	12 (11.1)	11 (10.1)		
Mouth	0 (0.0)	4 (3.7)	4 (3.4)		
Endocrine	0 (0.0)	2 (1.9)	2 (1.7)		
Others	0 (0.0)	3 (2.8)	3 (2.5)		
Morphology					
Adenocarcinoma	03 (100)	17 (73.9)	20 (71.4)	0.850	0.3
Squamous cell carcinoma	0 (0.0)	06 (26.1)	06 (28.6)	(0.707 - 1.022)	

Data shown as n (%); C: Chemotherapy; S: Surgery; R: Radiotherapy; Others: germ cell, pyriform sinus and sarcoma.

Discussion

The present retrospective cross-sectional study evaluated the prevalence of DVT in cancer patients registered with

this tertiary referral centre in eastern India and assessed the association of DVT with clinical characteristics, sites of malignancy, histopathological subtypes and comorbidities. A significant association between DVT prevalence and age of the patients was observed ($p = 0.045$). Although elderly age is in general risk factor for DVT, but interestingly in our study, younger patients (<55 years) had a higher prevalence. That maybe due to higher prevalence of breast and gynaecologic malignancies which are common in this particular age group. Gender, comorbidities like diabetes and hypertension did not show any statistically significant association with DVT. The site of cancer or histo-morphology also did not show any significant association with DVT prevalence in the present study.

A study by Lee *et al* has reported malignancy as a risk factor in 31% of Indian patients with DVT⁹. A recent study by Kamekar *et al* showed that 7% of patients with DVT had malignancy as a predisposing factor and genitourinary cancers had the highest incidence of DVT¹⁰. Interestingly, our study showed a higher prevalence rate of DVT than that reported in earlier studies^{7,10}. The present study reported 8.59% incidence of DVT in cancer patients with a mean age of 48.64 years and female (72.7%) preponderance. The mean age of cancer patients with DVT was significantly lower as compared to cancer patients without DVT ($p = 0.005$). This might be due to a relatively small number of cancer patients with DVT in this study than those without DVT (11 versus 117). A recent study by Fekri *et al* reported a DVT prevalence rate of 19.9% in cancer patients of which 21.2% were in males and 18.2% in females and there was no statistically significant correlation between gender and DVT prevalence ($P = 0.409$)¹¹. Similarly, the present study also reported no significant relationship between gender and DVT prevalence ($p = 0.2$). However, female preponderance observed in the present study is in concordance with the study done by Dutia *et al*¹³.

In the present study, a significant correlation between DVT prevalence and age of patients was observed ($p = 0.045$). Cancer patients with < 55 years of age were 3.49 times more prone to develop DVT than patients > 55 years of age (Odds ratio = 0.286; 95% CI: 0.079 - 1.035). The observations of a study done by Fekri *et al* showed that the patients between 40 to 65 and over 65 years of age had the highest DVT prevalence rate (21.6% and 20.1%, respectively); however, there was no significant correlation between age and DVT prevalence ($p = 0.459$) in that study also. Several other previous studies, have reported advanced age as an independent risk factor for VTE in hospitalised patients with cancer^{14,15}. However, 2 retrospective studies did not find that advanced age was associated with the risk of DVT^{13,16}. The variations in these observations in different studies can be attributed to the heterogeneity of different population

of cancer patients as far as size and timelines of their presentations were concerned.

This study reported no significant association between site of cancer or pathological subtype with DVT prevalence. DVT prevalence rate was highest in patients with breast cancers (36.4%) and gynaecologic cancers (36.4%) followed by patients with digestive tract cancers (18.2%) and lung cancers (9.1%). A study by Fekri *et al* showed that the DVT prevalence differs based on various pathological subtypes. Small cell carcinoma (42.5%), adenocarcinoma (26.9%), and squamous cell carcinoma (23.1%) were the malignancies with highest rates of DVT. Other previous studies have reported stronger association of DVT risk with adenocarcinoma than squamous cell carcinoma^{7,17}. The present study did not show any statistical correlation with histopathological subtype. This might be due to the smaller size of the patient population in the current study and their different timelines of presentation.

This study was a pilot study done with limited number of patients. The retrospective design of the study also limited the confirmation of the effect of risk factors on the prevalence of DVT. There were also biases of referral. Only Doppler USG was used to diagnose DVT and no further confirmatory methods were used.

Conclusion

This is a pilot study on DVT in different types of cancers, and the first of its kind in eastern India. Observations in the present study revealed 8.59% incidence of DVT in cancer patients. Interestingly, a significant association between age and DVT prevalence was observed. It reiterates that DVT is prevalent even in relatively younger populations with cancer, especially in breast and gynaecological malignancies. We should pro-actively search for it, irrespective of age, even in the absence of symptoms and comorbidities. In our study, other cancer-related parameters like site of disease, histological subtype or co-morbidities did not reveal any statistical correlation with the risk of DVT.

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