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FREQUENCY OF THROMBOEMBOLISM IN PATIENTS WITH HEMATOLOGICAL MALIGNANCIES

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ABSTRACT

Objective: To identify the frequency of thromboembolism among hematological malignancy patients.
Material and Methods: This cross-sectional study was carried out in the Department of Clinical Hematology and Bone Marrow Transplantation, Shifa International Hospital, Islamabad, and over a period of three months. The sample size of 142 patients was calculated with the WHO sample size calculator and non-probability consecutive sampling was used to enroll patient's admitted with hematological malignancies. The objective imaging (duplex ultrasonography of deep vein thrombosis and computed tomography pulmonary angiography of pulmonary embolism) was used to diagnose thromboembolism. Imaging was only done to clinically suspected patients. Binary logistic regression was conducted to detect associated factors, and adjusted odds ratios (ORs) with 95% confidence intervals (CIs). A p-value <0.05 was considered statistically significant.
Results: Among 142 patients (mean age 49.8 ± 17.6 years; 62.0% male), the frequency of thromboembolism was 9.9% (14/142; 95% CI: 5.5%–16.2%). The most frequent presentation was the presence of deep vein thrombosis (64.3%), and pulmonary embolism (35.7%). On multivariable analysis, age >50 years (OR 2.89; 95% CI: 1.04–8.01; p=0.041), BMI ≥30 kg/m² (OR 3.75; 95% CI: 1.12–12.52; p=0.032), and diabetes mellitus (OR 3.12; 95% CI: 1.01–9.67; p=0.048) were significantly associated with thromboembolism.
Conclusion: One of the complications that is rather frequent among patients with hematological malignancies is thromboembolism. Elderly age, obesity, and diabetes mellitus are major risk factors.

KEYWORDS: Body Mass Index; Hematologic Neoplasms; Pulmonary Embolism; Venous Thrombosis.

INTRODUCTION

Venous thromboembolism (VTE) is a significant complication among patients with malignancies, and it is a significant cause of morbidity and mortality in cancer populations. A national study conducted by Khamis et al. [1] indicated a high burden on cancer-related VTE in hospitalized patients with solid and hematological malignancies. On the same note, Dave and Khorana [2] stressed that active cancer is one of the most powerful acquired risk factors of VTE and there are some complex clinical issues in the management.

Evidence in the population also contributes to the fact that thrombotic events are observed in an oncology environment. A total of 10,500 cancer patients were followed in a large cohort study by Mulder et al. [3] who showed that a significantly increased risk of venous thromboembolism was present in cancer patients compared to the general population. Moreover, Mahajan et al. [4] have reported that cancer-related thrombosis has been on the rise over time, which is indicative of better cancer cure, intense therapy, and exposure of patients to thrombogenic treatments.

In the healthcare systems, the same patterns have been witnessed in different groups of people. Martens et al. [5] outlined the epidemiological patterns in the Veterans Affairs system, which established that a population of solid and hematologic malignancies had a high burden of VTE. The Lecumberri et al. [6] study found that, although hematological malignancies are linked to VTE, their outcome might be better than solid tumors.

Mechanistic and clinical understandings are in a state of development. Monegatti et al. [7] emphasized the mechanisms of hypercoagulability driven by cancer and therapy implications, especially highlighting the

variability of malignancy. The study by Girardi et al. [8] also updated the evidence on the pathogenesis and management of cancer-associated thrombosis, which further supports its multifactorial nature.
Outcomes also depend on socioeconomic and healthcare access factors. Da Costa et al. [9] showed the difference in risks of VTE, treatment, and outcomes between uninsured and vulnerable cancer populations, and it is essential to provide care in an equal manner. Moreover, Sadiq et al. [10] have also found high VTE risk and poor outcomes variability even in pediatric patients, especially in low- and middle-income countries.
On the whole, venous thromboembolism is a severe complication of all types of cancer and it has been recently found that there are peculiarities in the development of hematological cancers.
Although an increasing amount of evidence exists on cancer-associated thrombosis, there is a lack of consolidated data specifically on the rate and the clinical profile of thromboembolism in patients with hematological malignancies. This research assessed the rate and clinical presentation of thromboembolic events in hematological malignancy patients and determined the risk patterns.

MATERIAL AND METHODS

This study was carried out as a cross-sectional descriptive study, in Department of Clinical Hematology and Bone Marrow Transplantation, Shifa International Hospital, Islamabad, over a span of 3 months after the study synopsis was approved. The study started after the IRB of Shifa International Hospital gave ethical approval. Informed consent was given to all participants or their legal guardians (in the case of minors) after explaining to them the objectives of the study, the measures of confidentiality, and the voluntary nature of participation.
The sample size of 142 patients was calculated with the WHO sample size calculator and was assumed to have a 95% confidence level, an expected thromboembolism frequency of 9.8% among patients with the hematological malignancies and a precision of 4.9%. Non-probability consecutive sampling technique was used. [10].
They included patients of 18-60 years of age and gender with established hematological malignancies (including leukemia, lymphoma, and multiple myeloma, as per operational definitions) who had undergone relevant radiological imaging during the study period and had complete medical records. The patients who had incomplete data, patients who left against medical advice, and patients who had previous history of thrombosis were excluded.
After patients were enrolled, data were gathered using a structured and pre-designed proforma. The baseline demographic and clinical variables were age, gender, duration of malignancy, body mass index (BMI), occupation, residence, and comorbid conditions (diabetes mellitus, hypertension, and smoking status). Where possible, additional clinical variables, like chemotherapy status, presence of central venous lines, recent hospitalization, and use of thromboprophylaxis were documented, although incompleteness of these variables was admitted as such limitation.
The objective imaging modalities were used to diagnose thromboembolism. Deep vein thrombosis (DVT) was diagnosed with duplex ultrasonography and PE by computed tomography pulmonary angiography demonstrating intraluminal filling defects. It is significant to mention that imaging was performed only on the clinically suspected patients which can introduce selection bias. This was noted as the status of thromboembolism. The frequency of thromboembolism was calculated. Hematological malignancies were classified into subtypes (e.g., leukemia, lymphoma, multiple myeloma), and where sample size allowed, frequency of thromboembolism was stratified by malignancy subtype. Causality cannot be determined because of the cross-sectional design.
The SPSS version 25.0 was used to analyze the data. Depending on the distribution of data, continuous variables (e.g., age, BMI, duration of malignancy) were summarized by use of mean ± standard deviation or median with interquartile range, respectively. Frequencies and percentages were used to display categorical variables with well-defined denominators. To conduct inferential analysis, binary logistic regression was conducted to determine the related factors of thromboembolism. Adjusted odds ratio (ORs) with 95% confidence intervals (CI) and p-values were provided. The multivariate model also incorporated potential confounders, such as age, BMI, diabetes mellitus, high blood pressure, smoking status, and length of malignancy. The p-value of less than 0.05 was taken to be statistically significant. Where necessary confidence intervals were reported to enhance the accuracy of the estimates.

RESULTS

A total of 142 patients with hematological malignancies were included in the study. The mean age was 49.8 ± 17.6 years, with a predominance of males (88/142, 62.0%). Most participants were from urban areas (81/142, 57.0%). The mean body mass index (BMI) was 26.1 ± 4.8 kg/m², and the median duration of malignancy was 24 months (IQR: 8–48). Comorbid conditions included diabetes mellitus in 18/142 (12.7%) patients, hypertension in 24/142 (16.9%), and smoking history in 27/142 (19.0%). **Table 1**

Table 1: Baseline demographic and clinical characteristics (n = 142)

Variable	Value
Age (years)	49.8 ± 17.6
Male gender	88 (62.0%)
Urban residence	81 (57.0%)
BMI (kg/m²)	26.1 ± 4.8
Duration of malignancy (months)	24 (IQR: 8–48)

Diabetes mellitus	18 (12.7%)
Hypertension	24 (16.9%)
Smoking	27 (19.0%)
Malignancy type	**Frequency (%)**
Multiple myeloma (including kappa myeloma, POEMS)	15 (10.6%)
AML (including therapy-related & MDS → AML)	9 (6.3%)
ALL (B-ALL + T-ALL/T-LL)	7 (4.9%)
CLL	2 (1.4%)
CML	2 (1.4%)
Lymphomas (all subtypes combined)	13 (9.2%)
Other (aplastic anemia, none)	2 (1.4%)

Table 2 shows the overall frequency of thromboembolism was 14/142 (9.9%; 95% CI: 5.5%–16.2%). Among these cases, deep vein thrombosis (DVT) was the most common presentation (9/14, 64.3%), followed by pulmonary embolism (PE) (5/14, 35.7%).

Table 2: Frequency and types of thromboembolism

Variable	Value
Thromboembolism present	14/142 (9.9%; 95% CI: 5.5%–16.2%)
Deep vein thrombosis (DVT)	9/14 (64.3%)
Pulmonary embolism (PE)	5/14 (35.7%)

Hematological malignancies included leukemia, lymphoma, and multiple myeloma. Due to limited sample size within subgroups, stratified analysis of thromboembolism frequency by malignancy subtype was performed descriptively, but no statistically robust comparisons could be made.

On univariate analysis, higher age (>50 years), elevated BMI (≥30 kg/m²), and presence of diabetes mellitus showed significant associations with thromboembolism. Gender, hypertension, and smoking status were not significantly associated.

To further evaluate these relationships, binary logistic regression analysis was performed adjusting for potential confounders (age, BMI, diabetes mellitus, hypertension, smoking status, and duration of malignancy). After adjustment, age >50 years, BMI ≥30 kg/m², and diabetes mellitus remained significantly associated with thromboembolism. **Table 3**

Table 3: Multivariable logistic regression analysis of associated factors of thromboembolism

Variable	Adjusted Odds ratio	95% CI	p-value
Age >50 years	2.89	1.04–8.01	0.041
Male gender	1.08	0.39–3.01	0.871
BMI ≥30 kg/m²	3.75	1.12–12.52	0.032
Diabetes mellitus	3.12	1.01–9.67	0.048
Hypertension	1.41	0.49–4.03	0.529
Smoking	1.98	0.67–5.85	0.218

DISCUSSION

VTE in cancer patients is a complex phenomenon with both inherited and acquired risk factors. Suhail et al. reported that acquired and thrombophilia-related coagulopathy abnormalities play a significant role in the development of thrombosis, adding to the multifactorial nature of VTE in our study where age, BMI and diabetes mellitus were significant factors [11].

A major challenge in the field of risk assessment in hemato-oncology is still open. Given the differences in thrombotic risk per type of hematologic cancer and patient characteristics, -structured risk stratification is important in patients with these cancers, Sanfilippo noted. In a similar way, Gonzalez Diaz et al. found clinically significant thrombotic events in patients with hematologic nephromas in a dedicated cancer centre, confirming the high frequency of thrombosis seen in our cohort (9.9%) [12]. This study observed that the frequency of thromboembolism among patients with hematological malignancies is 9.9%, which is higher than the generally reported level of less than 5% for general internal medicine inpatients. This gap arises from the inherent prothrombotic state of this type of malignancy, as well as multiple disease- and treatment-related risk factors. These patients should therefore be classified as an extremely high-risk group, to receive standardized risk assessment and appropriately adapted thrombosis prevention strategies. [13].

Pathophysiological mechanisms involved in cancer associated thrombosis have been well described. Canonico et al. underscored the importance of inflammation, endothelial injury and coagulation activation in malignancy associated hypercoagulability [14]. These mechanisms will support our findings of the importance of metabolic comorbidities, obesity and diabetes mellitus, in significantly increasing the risk for thromboembolism.

Cohen et al. showed that different populations have different characteristics and outcomes associated with venous thromboembolism, and that age and comorbid conditions are important factors, confirming our results that age >50 years is an independent risk factor for thromboembolism [15]. Furthermore, Shah et al. reported the poor VTE risk assessment and prophylaxis practices in hospitalized medical patients, especially in resource-limited settings as one of the possible reasons for the burden of VTE found in our study population [16].

Saad et al. noted the rise in cancer associated thrombosis and mortality in the elderly population and confirmed that age is an important risk factor for thrombosis, in line with our multivariable regression findings [17]. Moreover, Adelborg et al. showed that patients with haematological malignancies have a continuously high risk for developing thromboembolic and bleeding events in a large population-based cohort and our observed frequency of VTE was 9.9% [18].

Thrombotic risk is also known to vary with the different types of disease. Morsia et al. showed that there were different frequencies of VTE in patients with multiple myeloma and aggressive lymphomas, suggesting that there is variation in thrombotic risk across hematological malignancies [19]. In our study, however, small numbers of patients meant that statistically valid comparisons between malignancy subtypes could not be made with a subgroup analysis.

Lastly, the meta-analysis performed by Jiang et al. has validated the association of venous thromboembolism with several clinicopathological features among patients with lymphoma, such as age and metabolic disorders, which is in keeping with our observations of venous thromboembolism being significantly associated with age, BMI, and diabetes mellitus [20].

In conclusion, our results corroborate the high prevalence of VTE as a complication related to a patient with hematological malignancy, and that patient related factors play a strong role in the risk. The lack of a universally agreed risk stratification model underscores the need for standardized tools to identify high-risk patients and guide choice of prophylaxis in this patient population.

Limitations of study: There are a number of limitations that ought to be taken into account when interpreting these findings. To begin with, this was a single centre study, which can reduce the generalisability. Second, the sample size is not very large and, therefore, it might not be the best measure of the diversity of hematological malignancies. The use of non-probability consecutive sampling may lead to selection bias. Furthermore, imaging was performed only in clinically suspected patients, and the exclusion of patients with a previous history of thrombosis may have omitted a high-risk group. These factors might have led to an underestimation of the actual frequency of thromboembolisms because of the absence of imaging in asymptomatic patients. In addition, the multivariate regression analysis should be interpreted with caution because the number of thromboembolic events was limited relative to the number of variables included in the model. The time frame of the study was restricted to three months and this could have missed delayed thromboembolic events especially in patients undergoing long term treatment. Critical clinical variables, including chemotherapy exposure, central venous catheter use, hospitalization status, and thromboprophylaxis were not completely available and could not be fully analyzed. Also, inherited thrombophilia and elaborate coagulation profiles have not been evaluated. Lastly, the cross-sectional design makes it impossible to infer causality, and impossible to draw any temporal conclusion between the associated variables and thromboembolism.

The main strength of this research is that it uses objective imaging to verify thromboembolism and has a rich group of hematological malignancies, which makes it possible to identify the significant risk factors, including age, obesity, and diabetes mellitus. Nonetheless, bigger multicentre studies are suggested to enhance generalizability. It should be done with routine risk assessment and early screening and correct thromboprophylaxis in high-risk patients and future studies are required to determine longitudinal outcome and incorporate coagulation and genetic profile to help in better risk stratification.

CONCLUSION

Thromboembolism is a significant complication in patients with hematological malignancies, and has a reported frequency of 9.9% in this study. Deep vein thrombosis presentation was the most common. The factors associated with thromboembolism included older age, high body mass index, and diabetes mellitus. These results underscore the need to evaluate risks early on, closely monitor, and consider preventive measures in higher-risk patients.

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