ORIGINAL ARTICLE

Change in D-dimer Levels due to Chemotherapy in Patients with Hematological Malignancies: An Observational Study

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ABSTRACT

Background: Elevated D-dimer levels are usually associated with a hypercoagulable state. Hematological malignancies are often associated with raised D-dimer but may not always be associated with altered coagulation. Chemotherapy may elevate D-dimer levels without clinically significant thrombosis. This study was conducted to evaluate pre- and post-chemotherapy D-dimer levels ie, its change with chemotherapy in patients with hematological malignancies and to explore associations with hematological parameter and socio-demographical factors.

Methods: This cross sectional observational study was conducted at the Department of Hematology, Shaheed Ziaur Rahman Medical College Hospital, Bogura, from December 2023 to November 2024. Fifty patients with newly diagnosed hematological malignancies were enrolled. D-dimer levels were measured before chemotherapy and on 3rd post-chemotherapy day. Statistical analysis was done using paired 't' test, ANOVA test and Pearson's correlation coefficient test; $p<0.05$ was considered as level of significance.

Results: The sample had a mean age of 35.7±22.8 years, predominantly male (58%), with T-ALL (44%) and B-ALL (32%) being the most common subtypes. Mean D-dimer increased slightly from 2.16±2.70 µg/ml pre-chemotherapy to 2.22±2.47 µg/ml post-chemotherapy ($p = 0.893$), indicating no significant overall change. Subgroup analyses showed the highest post-treatment D-dimer in T-ALL, though differences across disease groups were non-significant. Post-chemotherapy D-dimer change correlated significantly with pretreatment D-dimer ($p=0.028$). Pre-treatment D-dimer correlated positively with anemia severity ($r=0.29$, $p=0.041$) and negatively with platelet count ($r=–0.32$, $p=0.022$), while post-treatment levels correlated with age ($r=0.29$, $p=0.042$).

Conclusion: Hematological malignancies exhibit elevated D-dimer levels both before and after chemotherapy without clinically significant thrombosis. Chemotherapy significantly raised D-dimer levels. Correlations with anemia, platelet count, and age may highlight its potentiality as a biomarker of baseline disease state rather than immediate treatment response. So, raised D-dimer in hematological malignancies should be interpreted cautiously especially in absence of clinically significant thrombosis.

Keywords: D-dimer, hematological malignancy, chemotherapy, hypercoagulability, anemia, platelet count.

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INTRODUCTION

Hematological malignancies, including leukaemias, lymphomas, and multiple myeloma, are frequently accompanied by coagulation abnormalities. A key biomarker of such dysregulation is the elevation of D-dimer, a fibrin degradation product reflecting ongoing activation of coagulation and fibrinolysis [1,2]. In cancer patients, elevated D-dimer levels are associated with increased risk of thrombosis, poor prognosis, and reduced overall survival[3,4]. This abnormal biochemical result creates a confusion whether to start thrombolytic or not in critical thrombocytopenic patient or stable asymptomatic patient. It also to be remembered by the clinicians that pregnancy, trauma, malignancy, surgery, and liver disease can all cause elevations of the D-dimer[5].

In patients with hematological malignancies, the mechanisms contributing to D-dimer elevation are multifactorial. The malignant transformation of hematopoietic cells can promote a prothrombotic

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micro-environment through the release of cytokines, activation of endothelial cells, and expression of tissue factor. Additionally, bone marrow infiltration and systemic inflammation further exacerbate coagulation activation [1,2]. Chemotherapy can induce and exacerbate coagulation activation by inducing endothelial injury, triggering inflammatory cytokine cascades, and promoting tumor cell lysis, all of which contribute to elevated D-dimer levels during and after treatment [6]. Consequently, fluctuations in D-dimer concentrations before and after chemotherapy may reflect both disease burden and treatment-related physiological stress.

While previous studies have documented elevated D-dimer in solid tumors, data on pre- and post-chemotherapy changes in hematological malignancies remain limited. Furthermore, the relationship between D-dimer and patient-specific factors such as anemia, platelet count, age, and gender has not been comprehensively evaluated. Since anemia and thrombocytopenia are common in hematological malignancies, their interplay with coagulation activation warrants systematic investigation.

This study aimed at evaluating pre- and post-chemotherapy D-dimer status in (1) hematological malignancies, (2) chemotherapy-induced changes, (3) variations across different malignancy subtypes, and (4) correlations with anemia, platelet count, age, and gender.

METHODS & MATERIALS

Study Design and Population:
This cross-sectional observational study was conducted at the Department of Hematology of Shaheed Ziaur Rahman Medical College Hospital, Bogura, from December 2023 to November 2024. The study included 50 newly diagnosed cases of hematological malignancies, irrespective of age and gender who provided informed consent and on whom chemotherapy was initiated. Patients with a history of thromboembolic disease, or receiving anticoagulant therapy, or those with active infection, renal or hepatic impairment, pregnancy, or unwillingness to provide consent were excluded from this study.

Data Collection and Statistical Analysis:
Data were collected on patient demographics, including age and gender, along with relevant laboratory parameters such as platelet count, WBC count, blast cell, disease & cellular type, and D-dimer concentration. D-dimer levels were measured prior to the initiation of chemotherapy and subsequently repeated on day 3 (D3) of chemotherapy. Statistical analyses were performed to compare pre- and post-chemotherapy D-dimer values using paired *t*-test. Subgroup analyses were conducted to evaluate differences among various malignancy types utilizing analysis of variance (ANOVA). Correlation analyses between D-dimer levels and hemoglobin, platelet count, and age were assessed using Pearson's depending on data distribution. A *p*-value of <0.05 was considered statistically significant.

RESULTS

Baseline Profile: Age range of the patients was 3- 78 years with a mean±SD was 35.7±22.8 years; number of male (58%) was greater than female, reflecting the higher prevalence of hematological malignancies among males. (Table I)

Table I: Age & sex distribution of patients.

Variable	Values (N=50)
Age (years):	
≤10	8 (14.3%)
11-25	13 (23.2%)
26-40	7 (12.5%)
41-55	15 (26.8%)
>55	13 (23.2%)
Sex, n (%):	
Male	29 (58.0%)
Female	21 (42%)

Among study people T-ALL (44%) was the most common hematological malignancy, followed by B-ALL (32%) and AML (16%), while B-cell NHL, CLL, and HL were less frequent (2–4%). Overall, majority of cases are of lymphoid origin (60.7%), with myeloid malignancies accounts for 39.3% of patients. (Table II)

Table II: Disease types of the patients

Disease types, n (%)	
B ALL	16 (32.0%)
T ALL	22 (44.0%)
AML	8 (16.0%)
B cell NHL	1 (2.0%)
CLL	2 (4.0%)
HL	1 (2.0%)
Cellular origin of disease, n (%)	
Lymphoid	34 (60.7%)
Myeloid	22 (39.3%)

D-dimer level showed a slight, non-significant increase from 2.16±2.70 µg/ml pre-chemotherapy to 2.22±2.47 µg/ml post-chemotherapy (p=0.893), indicating that chemotherapy did not produce any significant change in D-dimer levels among the patients. (Table III)

Table III: D-dimer levels Pre & Post Chemotherapy

Status	D-dimer level mean ± SD µg/ml
Pre-chemotherapy	2.16 ± 2.70
Post-chemotherapy	2.22 ± 2.47

p (for paired 't' test) = 0.893

Subgroup Analysis by Disease Types

D-dimer changes varied by disease type. The highest chemotherapy induced changes were seen in AML patients (mean 1.30±1.67 µg/ml to 2.41±2.48 µg/ml), whereas B-ALL patients showed a mild decline after treatment (from 2.03±2.24 µg/ml to 1.55±1.81 µg/ml). (Table IV)

Table IV: Pre-chemotherapy & Post-chemotherapy D-dimer by Disease Type

Disease Type	Pre-chemo (µg/ml) mean ± SD	Post-chemo (µg/ml) mean ± SD
B cell ALL (n=16)	2.03 ± 2.24	1.55 ± 1.81
T cell ALL (n=22)	2.78 ± 3.37	2.81 ± 2.99
AML (n=8)	1.30 ± 1.67	2.41 ± 2.48
B cell NHL (n=1)	–	–
CLL (n=2)	0.72 ± 0.61	1.67 ± 0.014
HL (n=1)	–	–

Table V: ANOVA test of D-dimer after treatment against Diagnosis, Platelet & Anaemia

	'F' ratio	'p' value
Diagnosis	0.611	0.692
Platelet	0.960	0.390
Anaemia	0.463	0.710

Table V shows that post-treatment D-dimer levels did not differ significantly when compared across diagnosis (p=0.692), platelet count groups (p=0.390), or anaemia status (p=0.710), indicating no significant association between these clinical variables and D-dimer levels following chemotherapy.

Post-treatment D-dimer levels showed a significant association with D-dimer status before chemotherapy (p=0.028), suggesting that D-dimer levels significantly influenced by chemotherapy. No significant relationships were observed with cellular origin (p=0.54), gender (p=0.958), WBC status (p=0.247), or blast cell presence (p=0.899). (Table VI)

Table VI: 't' & 'p' values of D-dimer after treatment against cellular origin of disease, D-dimer status before chemotherapy (DDSBC) & blast cell.

	't' value	'p' value
Cellular Origin	0.622	0.54
DDSBC	2.26	.028
Gender	0.053	0.958
WBC	1.173	0.247
Blast cell	0.128	0.899

Correlations Analysis

Pre-chemotherapy D-dimer levels had a significant positive correlation with anaemia severity (p=0.041) and a significant negative correlation with platelet count (p=0.022), while post-chemotherapy D-dimer correlated significantly only with age (p=0.042), indicating that higher age and severity of anaemia were associated with elevated D-dimer levels. (Table VII)

Table VII: Correlation Matrix of Anemia, Platelet Count, and Age.

Variable	D-dimer Pre (r, p)	D-dimer Post (r, p)
Anemia (severity)	0.29, 0.041	0.25, 0.074
Platelet Count	-0.32, 0.022	-0.22, 0.119
Age	0.19, 0.188	0.29, 0.042

DISCUSSION

This study was conducted on clinically non-thrombotic hematological malignancy patients and evaluated the D-dimer status and changes in D-dimer levels after chemotherapy, as well as their associations with disease type, hematological parameters, and demographic

characteristics. The findings revealed that D-dimer levels were elevated in many patients before treatment and persisted after chemotherapy. Although in some cases D-dimer level was reduced, in most cases it was increased from the pretreatment level; the overall change following treatment was statistically insignificant. This suggests that coagulation activation is a common feature, even in clinically non thrombotic hematologic malignancies, chemotherapy itself significantly altered D-dimer levels within the short post-treatment interval studied.

Sociodemographic and Clinical Distribution

The patient cohort exhibited a mean age of 35.7 ± 22.8 years, with most participants aged 41–55 years, and a male predominance (58%). This demographic distribution aligns with prior studies indicating a higher prevalence of hematological malignancies, particularly acute leukemias, among males and middle-aged adults [7,8]. Regarding disease type, T-cell acute lymphoblastic leukemia (T-ALL) was the most frequent diagnosis (44%), followed by B-ALL (32%) and acute myeloid leukemia (AML) (16%). Such distribution is notable for the high proportion of T-ALL, which exceeds rates typically reported in Western populations [9,10]. But this is not the common distribution of hematological malignancies even in our countries. This study was carried out for a limited period of time with some inclusion and exclusion criteria. This may be the coincidence of multiple factors. Although seasonal and yearly variation of hematological malignancies was also seen [11].

Pre- and Post-Chemotherapy D-Dimer Levels

The mean D-dimer levels showed a slight increase from 2.16 ± 2.70 µg/ml pre-chemotherapy to 2.22 ± 2.47 µg/ml post-chemotherapy, though this difference was not statistically significant ($p = 0.893$). But post-treatment change D-dimer levels showed a significant association with D-dimer status before chemotherapy ($p = 0.028$), suggesting that D-dimer levels significantly influenced by chemotherapy. These findings indicate persistent fibrinolytic activity in patients with hematologic malignancies, consistent with the hypercoagulable state often reported in such diseases [12,4]. Elevated D-dimer levels before treatment may reflect tumor-induced activation of coagulation and endothelial dysfunction, while post-treatment persistence could be due to chemotherapy-related endothelial injury or delayed normalization of fibrinolytic pathways [13]. However, the lack of a significant difference suggests that the immediate post-chemotherapy phase may not capture longer-term coagulation changes.

Variation by Disease Type and Hematological Parameters

Subgroup analysis revealed that T-ALL patients had the highest post-chemotherapy D-dimer levels (mean 2.81 ± 2.99 µg/ml) as well as prechemo, while B-ALL patients showed a slight reduction after treatment. But highest chemotherapy induced changes were seen in AML patients (mean 1.30 ± 1.67 µg/ml to 2.41 ± 2.48 µg/ml), Despite these differences, ANOVA tests demonstrated no statistically significant variation in post-treatment D-dimer levels across diagnosis ($p = 0.692$), platelet count groups ($p = 0.390$), or anaemia status ($p = 0.710$). This suggests that D-dimer elevation occurs broadly across disease subtypes, independent of hematologic parameters or anemia severity. Previous literature similarly reports that while D-dimer levels tend to be higher in aggressive leukemias, their relationship with specific subtypes or blood counts remains inconsistent [14,15].

Predictors of Post-Treatment D-Dimer

A significant association was observed only between change in post-treatment D-dimer and baseline D-dimer levels ($p = 0.028$), implying that initial coagulation activation along with effect of chemotherapy strongly influences post-chemotherapy D-dimer. In contrast, no significant associations were noted with cellular origin, gender, WBC status, or blast presence. Similar findings have been observed in prior studies where pretreatment coagulation markers were predictive of thrombosis risk and overall survival, reflecting their potential as baseline prognostic indicators [16,17].

Correlations with Anemia, Platelet Count, and Age

Correlation analysis demonstrated that pre-chemotherapy D-dimer correlated positively with anaemia severity ($r = 0.29$, $p = 0.041$) and negatively with platelet count ($r = -0.32$, $p = 0.022$), indicating that patients with more severe anemia and lower platelet counts had higher D-dimer levels. These relationships reflect the systemic inflammatory and hematologic disturbances in malignancy that enhance coagulation activity. Furthermore, post-chemotherapy D-dimer showed a significant positive correlation with age ($r = 0.29$, $p = 0.042$), aligning with evidence that older patients often exhibit enhanced coagulation activation due to endothelial dysfunction and reduced fibrinolytic reserve [18,19].

Clinical Implications

Often there is a question, what to do with a raised D-dimer in clinically non-thrombotic hematological malignancy patient, whether to start thrombolytic or not in critical thrombocytopenic patient or stable patients

who are asymptomatic. Findings of this study collectively reinforce the role of D-dimer as a sensitive marker of coagulation but not always related to clinically significant hypercoagulation. Although chemotherapy significantly change D-dimer level, anti-thrombotic treatment may not require in asymptomatic patient.

Conclusion

Patients with hematological malignancies exhibit elevated D-dimer levels both before and after chemotherapy, reflecting persistent coagulation activation. And, chemotherapy significantly altered short-term D-dimer levels. Correlations with anemia, platelet count, and age highlight its potentiality as a biomarker of baseline disease state rather than immediate treatment response. So, raised D-dimer in hematological malignancies should be interpreted cautiously especially in absence of clinically significant thrombosis. Longitudinal monitoring may better define its prognostic and therapeutic relevance.

Limitations

The study's limitations include a single-center design, small sample size, and a single post-chemotherapy measurement, which may not reflect delayed hematologic recovery or longer-term coagulation trends. Additionally, the exclusion of thrombotic outcomes limits clinical correlation. Future research with larger cohorts and longitudinal sampling could clarify the dynamic relationship between D-dimer, chemotherapy response, and thrombotic risk in hematologic malignancies.

Conflict of interest

The authors declare no conflict of interest.

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