

Original Research Article

The evaluation of demographic factors, clinicopathological characteristics and plasma D-dimer levels among breast cancer patients

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Received: 17 July 2026

Revised: 20 August 2026

Accepted: 23 September 2026

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ABSTRACT

Background: Breast cancer is the most common malignancy among women worldwide. Activation of coagulation and fibrinolysis is linked to tumor progression and metastasis. Plasma D-dimer, a fibrin degradation product, may serve as a biomarker of disease severity in breast cancer. The objectives of the study is to assess the association of plasma D-dimer levels with demographic and clinicopathological characteristics of breast cancer patients.

Methods: This cross-sectional study was conducted in the Department of Pathology, Mymensingh Medical College, from September 2022 to October 2023. Eighty-six histopathologically confirmed breast cancer patients were enrolled. Data were collected using a structured questionnaire. Plasma D-dimer was measured and categorized as elevated or normal by laboratory reference values. Associations were analyzed using Chi-square and ANOVA tests; $p < 0.05$ was considered significant.

Results: Mean age was 49.57 ± 9.96 years; invasive ductal carcinoma predominated (95.3%). Elevated D-dimer was found in 55 (64.0%) patients. Mean D-dimer rose significantly from 0.57 ± 1.08 $\mu\text{g/ml}$ in T1 to 3.47 ± 1.33 $\mu\text{g/ml}$ in T4 tumors ($p < 0.001$), and from 0.57 ± 1.09 $\mu\text{g/ml}$ in N0 to 3.54 ± 1.35 $\mu\text{g/ml}$ in N3 disease ($p < 0.001$). Elevated D-dimer was significantly associated with advanced tumor stage ($p = 0.00002$) and lymph node metastasis ($p < 0.001$), but not with lymphovascular invasion ($p = 0.158$) or histological subtype ($p = 0.407$).

Conclusions: Plasma D-dimer was significantly associated with larger tumor size and greater nodal involvement, suggesting it may be a useful non-invasive biomarker of tumor progression. Larger prospective studies are needed to validate its prognostic value.

Keywords: Breast cancer, D-dimer, Tumor size, Lymph node metastasis, Lymphovascular invasion, Prognostic biomarker

INTRODUCTION

Breast cancer is the most frequently diagnosed cancer among women worldwide and remains a leading cause of cancer-related mortality. According to the Global Cancer

Observatory, approximately 2.3 million new cases and 670,000 deaths from breast cancer were reported globally in 2022, making it a major public health concern.¹ In Bangladesh and other low- and middle-income countries, the burden of breast cancer continues to rise because of

population aging, urbanization, lifestyle changes, and delayed diagnosis.²

Breast cancer progression is a complex process involving tumor growth, angiogenesis, invasion, and metastasis. Increasing evidence suggests that malignant tumors activate the coagulation and fibrinolytic systems, resulting in a hypercoagulable state that contributes to cancer progression.³⁻⁵ This hypercoagulable state also increases the risk of venous thromboembolism in cancer patients.^{6,7} Among the biomarkers reflecting this process, D-dimer, a degradation product of cross-linked fibrin, has gained attention as a routinely available laboratory test.⁸ Elevated plasma D-dimer levels indicate increased fibrin formation and fibrinolysis and have been associated with tumor burden, metastatic spread, and poor clinical outcomes in various malignancies.^{9,10}

Several studies have demonstrated that patients with breast cancer exhibit significantly higher D-dimer levels than healthy individuals.^{11,12} Elevated D-dimer concentrations have been linked to larger tumor size, lymph node metastasis, advanced clinical stage, and reduced survival.^{13,14} Furthermore, D-dimer has been proposed as a cost-effective and readily available biomarker that may assist clinicians in assessing disease progression and treatment response.¹⁵

Despite growing international evidence, data regarding the association between plasma D-dimer levels and clinicopathological characteristics of breast cancer remain limited in Bangladesh. Understanding this relationship may improve risk stratification and provide additional information regarding disease severity. Therefore, the present study aimed to evaluate the association of plasma D-dimer levels with demographic and clinicopathological characteristics, including tumor size, lymph node involvement, lymphovascular invasion, and histological subtype among patients with breast cancer.

METHODS

This cross-sectional study was conducted in the Department of Pathology, Mymensingh Medical College, Bangladesh, over a period of 12 months, from September 2022 to October 2023. A total of 86 histopathologically confirmed breast cancer patients were enrolled using purposive sampling. Patients diagnosed with primary breast carcinoma and willing to participate in the study were included, whereas patients with known coagulation disorders, active infections, thromboembolic diseases, chronic liver disease, or those receiving anticoagulant therapy were excluded.

Sociodemographic information, including age, body mass index (BMI), menopausal status, and family history of breast cancer, was collected using a structured data collection form. Clinicopathological data, including histological subtype, tumor size, lymphovascular invasion (LVI), and lymph node involvement, were obtained from

pathology reports and clinical records. Tumors were staged according to the TNM classification system.

Venous blood samples were collected from all participants under aseptic conditions prior to initiation of treatment. Plasma D-dimer levels were measured using a standardized immunoassay method in the pathology laboratory. Based on the laboratory reference range, D-dimer levels were categorized as normal or elevated.

Statistical analysis

Data were entered, cleaned, and analyzed using Statistical Package for Social Sciences (SPSS) version 26.0. Continuous variables were expressed as mean $\pm$ standard deviation (SD), while categorical variables were presented as frequencies and percentages. Associations between plasma D-dimer status and categorical clinicopathological variables were assessed using the Chi-square test. Differences in mean D-dimer levels across tumor and nodal stages were evaluated using one-way analysis of variance (ANOVA). A p-value of less than 0.05 was considered statistically significant.

RESULTS

Among the 86 breast cancer patients, the majority belonged to the 40–50 years age group (40.1%), followed by 50–60 years (32.6%). Only 8.2% of patients were younger than 40 years. The mean age of the study population was 49.57 ± 9.96 years, with an age range of 25–80 years (Table 1). These findings indicate that breast cancer was predominantly diagnosed among middle-aged and older women in this cohort.

Half of the study participants (50.0%) had a normal BMI, while 31.4% were obese and 11.6% were overweight. Only 7.0% of patients were underweight (Figure 1). The relatively high proportion of overweight and obese individuals suggests that excess body weight may be a common characteristic among patients with breast cancer.

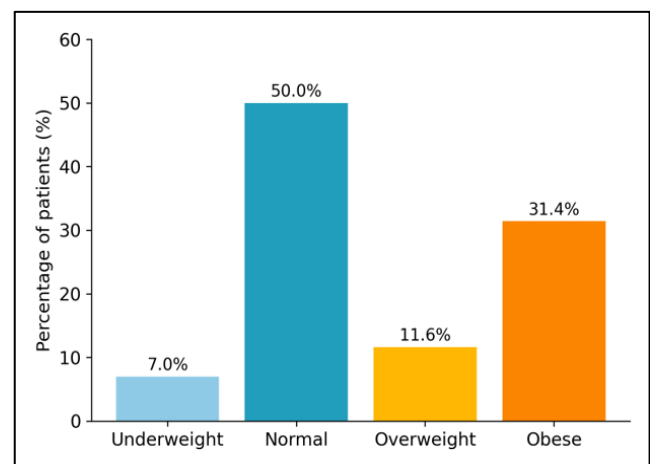


Figure 1: BMI distribution of the study population.

A positive family history of breast cancer was reported by only 3.5% of the participants, whereas 96.5% had no known family history (Figure 2). This indicates that the vast majority of breast cancer cases in the present study occurred sporadically.

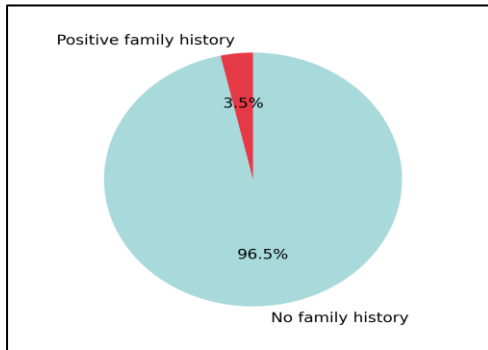


Figure 2: Family history of breast cancer in the study population.

Among the study participants, 47.7% were postmenopausal, while 52.3% were premenopausal (Figure 3). The nearly equal distribution indicates that breast cancer affected women across different reproductive stages, with a slightly higher proportion of premenopausal patients.

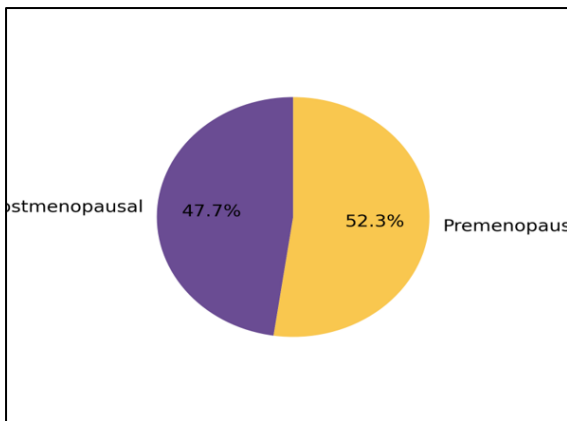


Figure 3: Distribution of menopausal status of the study population.

All patients were diagnosed with invasive carcinoma, while no cases of in situ carcinoma were identified. Invasive ductal carcinoma (NOS) was the predominant histological subtype, accounting for 95.3% of cases. Invasive lobular carcinoma and invasive breast carcinoma with medullary pattern represented only 3.5% and 1.2% of cases, respectively (Table 2).

Elevated plasma D-dimer levels were observed in 64.6% of patients with invasive ductal carcinoma, 33.3% of those with invasive lobular carcinoma, and all patients with medullary-pattern carcinoma. However, the association between D-dimer status and histological subtype was not statistically significant ($p=0.407$) (Table 3).

Lymphovascular invasion (LVI) was present in 48.8% of patients and absent in 51.2%. Patients with LVI demonstrated a higher mean plasma D-dimer level (1.77 ± 1.56 $\mu\text{g/ml}$) compared with those without LVI (1.59 ± 1.50 $\mu\text{g/ml}$) (Table 4). Among patients with lymphovascular invasion, 71.4% exhibited elevated plasma D-dimer levels compared with 56.8% among those without LVI; however, this difference did not reach statistical significance ($p=0.158$) (Table 4).

Mean plasma D-dimer levels increased progressively with advancing tumor size, from 0.57 ± 1.08 $\mu\text{g/ml}$ in T1 tumors to 3.47 ± 1.33 $\mu\text{g/ml}$ in T4 tumors, a highly significant difference (ANOVA, $p<0.001$) (Table 5). The proportion of patients with elevated plasma D-dimer levels increased markedly with tumor stage, rising from 25.0% in T1 tumors to 100% in T4 tumors (χ^2 test, $p=0.00002$) (Table 5).

Mean plasma D-dimer levels increased steadily with greater lymph node involvement, from 0.57 ± 1.09 $\mu\text{g/ml}$ in patients without nodal metastasis to 3.54 ± 1.35 $\mu\text{g/ml}$ in those with N3 disease (ANOVA, $p<0.001$) (Table 6). Elevated plasma D-dimer levels were observed in 94.5% of patients with lymph node metastasis, compared with only 5.5% of patients without nodal involvement ($p<0.001$) (Table 7). These findings suggest that elevated D-dimer may serve as a useful marker of nodal metastasis and disease progression in breast cancer.

Table 1: Distribution of the studied patients by demographic variables (n=86).

Demographic variables	Number of patients	Percentage
Age <40 years	7	8.2
Age 40-50 years	35	40.1
Age 50-60 years	28	32.6
Age ≥ 60 years	16	18.6
Mean $\pm$ SD	49.57 ± 9.96	
Range (min-max)	25-80	

Table 2: Distribution of studied patients by morphologic types of breast carcinoma (n=86).

Types of breast carcinoma	Number of patients	Percentage
In situ carcinoma	0	0
Invasive carcinoma	86	100
Invasive ductal carcinoma (NOS)	82	95.3
Invasive lobular carcinoma (NOS)	3	3.5
Invasive breast carcinoma (NST) with medullary pattern	1	1.2

Table 3: Association between plasma D-dimer and morphologic types of breast carcinoma (n=86).

D-dimer	Invasive ductal carcinoma	Invasive lobular carcinoma	Medullary pattern	Total
Elevated	53 (64.6%)	1 (33.3%)	1 (100%)	55
Normal	29 (35.4%)	2 (66.7%)	0 (0%)	31
Total	82	3	1	86

P value reached from chi-square test.

Table 4: Distribution of the studied patients, mean plasma D-dimer level and D-dimer status by lymphovascular invasion (n=86).

LVI	Frequency (%)	Mean D-dimer (µg/ml)	Elevated D-dimer, N (%)	Normal D-dimer, N (%)
Present	42 (48.8)	1.77±1.56	30 (71.4)	12 (28.6)
Absent	44 (51.2)	1.59±1.50	25 (56.8)	19 (43.2)
Total	86	—	55	31

P value (LVI vs mean D-dimer, independent t-test): not statistically significant; p-value (LVI vs D-dimer status, chi-square)=0.158.

Table 5: Distribution of the studied patients, mean plasma D-dimer level and D-dimer status by tumor size (n=86).

Tumor Size (T)	Frequency (%)	Mean D-dimer (µg/ml)	Elevated D-dimer, N (%)	Normal D-dimer, N (%)
T1	24 (27.9)	0.57±1.08	6 (25.0)	18 (75.0)
T2	33 (38.4)	1.49±1.32	21 (63.6)	12 (36.4)
T3	15 (17.4)	2.34±1.35	14 (93.3)	1 (6.7)
T4	14 (16.3)	3.47±1.33	14 (100)	0 (0)
Total	86	—	55	31

P value (tumor size vs mean D-dimer, ANOVA) <0.001; p value (tumor size vs D-dimer status, chi-square) = 0.00002. T1=tumor size ≤20 mm; T2=>20 mm but ≤50 mm; T3=>50 mm; T4=tumor of any size with direct extension to the chest wall.

Table 6: Distribution of the studied patients and plasma D-dimer level by lymph node involvement (n=86).

Lymph node involvement	Frequency (%)	Mean D-dimer (µg/ml)
N0	23 (26.7)	0.57 ± 1.09
N1	34 (39.5)	1.51 ± 1.11
N2	23 (26.7)	2.66 ± 1.73
N3	6 (7.0)	3.54 ± 1.35
P value	<0.001 (ANOVA)	

P value reached from ANOVA test. N0 = no regional lymph node metastasis; N1 = metastasis in 1-3 axillary lymph nodes; N2 = metastasis in 4-9 axillary lymph nodes or clinically detected internal mammary lymph nodes without axillary involvement; N3 = metastasis in ≥10 axillary lymph nodes, infraclavicular nodes, clinically detected ipsilateral internal mammary nodes with ≥1 positive axillary node, or ipsilateral supraclavicular lymph nodes.

Table 7: Association between plasma D-dimer and lymph node involvement (n=86).

D-dimer	Nodal metastasis present	Nodal metastasis absent	Total
Elevated	52 (94.5%)	3 (5.5%)	55
Normal	11 (35.5%)	20 (64.5%)	31
Total	63	23	86

P value reached from chi-square test.

DISCUSSION

The present study evaluated the association between plasma D-dimer levels and demographic as well as clinicopathological characteristics among patients with breast cancer.

The mean age of the study participants was 49.57 ± 9.96 years, with the majority belonging to the 40–50-year age group. Similar age distributions have been reported in South Asian breast cancer populations, where middle-aged women constitute the largest proportion of cases.^{16,17} Elevated D-dimer levels were observed in 64.0% of patients, suggesting activation of coagulation and fibrinolytic pathways in breast cancer.

A key finding of this study was the significant increase in D-dimer levels with advancing tumor size. Mean D-dimer concentrations increased progressively from T1 to T4 tumors ($p < 0.001$), indicating a strong relationship between tumor burden and coagulation activity. This observation is consistent with previous studies that demonstrated higher D-dimer levels in patients with larger and more advanced tumors.^{11,12} Tumor progression promotes fibrin formation, angiogenesis, and extracellular matrix remodelling, leading to increased fibrinolysis and D-dimer production.¹⁵

Similarly, D-dimer levels showed a significant association with lymph node involvement. Patients with nodal metastasis exhibited substantially higher D-dimer levels than those without metastasis ($p < 0.001$). This finding agrees with reports by Harish, Chandra and Sringeri and Mego et al who identified elevated D-dimer as a marker of metastatic potential and lymphatic spread.^{18,13} The progressive rise in mean D-dimer levels from N0 to N3 disease further supports its role as an indicator of tumor dissemination.

Although patients with lymphovascular invasion demonstrated higher mean D-dimer levels, the association did not reach statistical significance. Similar findings have been reported by Lu et al who suggested that the relationship between D-dimer and lymphovascular invasion may vary according to sample size and tumor characteristics.¹⁴ Furthermore, no significant association was observed between D-dimer levels and histological subtype, likely due to the overwhelming predominance of invasive ductal carcinoma in the study population, although some studies have suggested D-dimer may assist histopathological grading in larger, more balanced cohorts.¹⁹

Overall, the findings indicate that plasma D-dimer is closely associated with tumor burden and nodal metastasis and may serve as a simple, cost-effective biomarker for assessing disease progression in breast cancer patients.

CONCLUSION

The present study demonstrated a significant association between plasma D-dimer levels and important clinicopathological characteristics of breast cancer. Elevated D-dimer levels were significantly correlated with larger tumor size and greater lymph node involvement, indicating increased disease burden and metastatic potential. Although higher D-dimer levels were observed in patients with lymphovascular invasion, the association was not statistically significant. No significant relationship was found between D-dimer levels and histological subtype. These findings suggest that plasma D-dimer may serve as a simple, inexpensive, and readily available biomarker for assessing disease progression in breast cancer patients. Further multicenter studies with larger sample sizes are recommended to validate its clinical utility and prognostic significance.

ACKNOWLEDGEMENTS

The authors express gratitude to the Department of Pathology, Mymensingh Medical College, for their support during data and sample collection, and the patients who participated in this study.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Tabassom T, Adhikary L, Saha N, Chowdhury G, Kabir MJ, Liza FA. The evaluation of demographic factors, clinicopathological characteristics and plasma D-dimer levels among breast cancer patients. *Int J Res Med Sci* 2026;14:4971-6.