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Original Article

Plasma D-Dimer as a Disease Progression Marker in Operable Breast Cancer

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Abstract

Background: Identifying reliable prognostic markers is crucial for early intervention and improved survival in breast cancer. Plasma D-dimer, a fibrin degradation product, has been implicated in cancer progression and metastasis. This study was conducted to evaluate the significance of plasma D-dimer as a disease progression marker in Bangladeshi women with operable breast cancer, and its correlation with tumor size, histological grade, lymph node status, and hormone receptor profile.

Methods: An observational cross-sectional study was conducted at Dhaka Medical College Hospital between July and December 2018. Fifty women aged 20–60 years with operable breast cancer were enrolled using systematic random sampling. Clinical, radiological, and histopathological evaluations were performed. Plasma D-dimer levels were measured and analyzed against clinicopathological variables using SPSS v20.

Results: The mean age of patients was 46.2±14.2 years. The majority (42%) were aged 41–50 years. Left breast involvement predominated (58%), and 52% presented with diffuse whole-breast disease. Most tumors were ≥T3 stage (76%). Elevated D-dimer levels correlated significantly with larger tumor size (mean 3.22 mg/ml for T4), higher histological grade (2.67 mg/ml for grade III), lymphovascular invasion (2.5 mg/ml vs. 0.5 mg/ml, $p<0.05$), lymph node involvement (2.78 mg/ml vs. 0.54 mg/ml, $p<0.05$), and hormone receptor negativity (2.41 mg/ml vs. 1.64 mg/ml, $p<0.05$).

Conclusion: Plasma D-dimer levels reflect tumor burden and correlate with aggressive pathological features in operable breast cancer. D-dimer may serve as a cost-effective and accessible prognostic marker in low-resource settings, though larger multicentric studies with long-term follow-up are warranted.

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Introduction

Breast cancer is the most frequently diagnosed malignancy in women globally and remains a leading cause of cancer-related death, particularly in developing countries.[1] In Bangladesh, breast cancer poses a major public health burden, often presenting at advanced stages due to limited screening and awareness.

The biological behavior of breast cancer is heterogeneous, and prognosis is influenced by factors such as tumor size, nodal involvement, histological

grade, and hormone receptor status[1]. However, these parameters do not always predict disease progression reliably. Increasing evidence links cancer progression with hypercoagulability and fibrinolytic activation[2]. D-dimer, a degradation product of cross-linked fibrin, is an established marker of coagulation activity and has been associated with poor prognosis in several malignancies[3-5].

This study aimed to investigate the role of plasma D-dimer as a marker of disease progression in operable breast cancer and explore its association with other prognostic variables.

Materials and Methods

Study design and setting: An observational cross-sectional study was carried out in the Department of Surgery, Dhaka Medical College Hospital, from July to December 2018.

Study population: Fifty women aged 20–60 years with operable breast carcinoma were enrolled. Patients with distant metastasis, chronic illnesses (e.g., diabetes, hypertension, connective tissue disorders), or unwilling to consent were excluded. Systematic random sampling was applied.

Data collection: After informed consent, detailed clinical history and examination were recorded. Imaging (ultrasonography, mammography), histopathology, and hormone receptor assays were performed. Plasma D-dimer levels were measured preoperatively using immunoturbidimetric assay.

Statistical analysis: Data were analyzed with SPSS v20. Mean, SD, and percentages were calculated. Associations between D-dimer levels and clinicopathological factors were assessed, with $p<0.05$ considered statistically significant.

Ethical approval was obtained from the institutional review board.

Results

The mean age of patients was 46.2±14.2 years. The majority (42%) were aged 41–50 years. Left breast involvement predominated (58%), and 52% presented with diffuse whole-breast disease. Most tumors were ≥T3 stage (76%). Elevated D-dimer levels correlated significantly with larger tumor size (mean 3.22 mg/ml for T4), higher histological grade (2.67 mg/ml for grade III), lymphovascular invasion (2.5 mg/ml vs. 0.5 mg/ml, $p<0.05$), lymph node involvement (2.78 mg/ml vs. 0.54 mg/ml, $p<0.05$), and hormone receptor negativity (2.41 mg/ml vs. 1.64 mg/ml, $p<0.05$).

Table I : *Plasma D-dimer levels (n=50)*

D-dimer level (mg/ml)	Number	Percentage (%)
<0.25	5	10
0.25–2.0	10	20
2.1–5.0	23	46
>5.0	12	24

Mean plasma D-dimer = 3.75 ± 2.51 mg/ml.

Table II : *Tumor size and corresponding mean plasma D-dimer levels*

Tumor size	Number of patients	Mean D-dimer (mg/ml)
T1 (<2 cm)	1	1.00 ± 0.0
T2 (2–5 cm)	11	1.44 ± 0.15
T3 (>5 cm)	20	3.20 ± 0.21
T4 (extension beyond breast)	18	3.22 ± 0.41

D-dimer increased proportionally with tumor size.

Table III : *Histopathological grade vs. plasma D-dimer levels*

Grade	Number of patients	Percentage (%)	Mean D-dimer (mg/ml)
I	6	12	0.33 ± 0.08
II	28	56	0.46 ± 0.05
III	16	32	2.67 ± 0.98

D-dimer levels rose with increasing histological grade.

Table IV : *Lymphovascular invasion vs. plasma D-dimer levels*

Lymphovascular invasion	Number	Percentage (%)	Mean D-dimer (mg/ml)	p-value
Present	16	32	2.50 ± 0.76	<0.05
Absent	34	68	0.50 ± 0.02	

Lymphovascular invasion was strongly associated with elevated D-dimer.

Table V : *Lymph node involvement vs. plasma D-dimer levels*

Lymph node involvement	Number	Percentage (%)	Mean D-dimer (mg/ml)	p-value
Yes	29	58	2.78 ± 0.83	<0.05
No	21	42	0.54 ± 0.03	

Table VI : *Hormone receptor status vs. plasma D-dimer levels*

Hormone receptor status	Number	Percentage (%)	Mean D-dimer (mg/ml)	p-value
Positive	36	72	1.64 ± 0.09	<0.05
Negative	14	28	2.41 ± 0.61	

Receptor-negative tumors showed significantly higher D-dimer values.

Correlation with prognostic factors

- Tumor size: Mean D-dimer rose from 1.0 mg/ml in T1 to 3.22 mg/ml in T4.
- Histological grade: Mean D-dimer increased from 0.33 mg/ml in grade I to 2.67 mg/ml in grade III.
- Lymphovascular invasion: Present in 32% with mean D-dimer 2.5 mg/ml vs. 0.5 mg/ml in absence (p<0.05).
- Lymph node involvement: Seen in 58%, mean D-dimer 2.78 mg/ml vs. 0.54 mg/ml without involvement (p<0.05).
- Hormone receptor status: Higher D-dimer in receptor-negative tumors (2.41 mg/ml) than positive (1.64 mg/ml, p<0.05).

Discussion

This study demonstrates that plasma D-dimer levels are elevated in Bangladeshi women with operable breast cancer and correlate with established prognostic factors. Elevated D-dimer levels may be explained by tumor-associated activation of coagulation and fibrinolysis, increased angiogenesis, and vascular invasion[2,6].

Our findings align with earlier reports by Blackwell and Patel, which showed significant associations between D-dimer levels and lymph node involvement, histological grade, and lymphovascular invasion[5,6]. Other studies also documented higher D-dimer levels in advanced disease[3,7].

Although D-dimer cannot independently predict nodal status due to low negative predictive value, combining it with conventional parameters could enhance prognostic accuracy.

Limitations: The study was limited by small sample size, single-center design, and short follow-up. Larger, multicentric prospective studies with serial D-dimer measurements are needed to confirm these results.

Conclusion

Plasma D-dimer is a promising adjunct prognostic marker in operable breast cancer. Its elevation correlates with tumor size, histological grade, lymphovascular invasion, lymph node involvement, and hormone receptor negativity. Integration of D-dimer testing with traditional prognostic parameters could improve risk stratification and clinical decision-making, especially in low-resource settings.

References

1. Carter CL, Allen C, Henson DE. Relation of tumor size, lymph node status, and survival in 24,740 breast cancer cases. *Cancer*. 2009;63:181–7.
2. Dirix LY, Salgado R, Weytjens R, Colpaert C, Benoy I, Huget P. Plasma fibrin D-dimer levels correlate with tumour volume, progression rate and survival in patients with metastatic breast cancer. *Br J Cancer*. 2002;86:389–95.
3. Batschauer AP, Bueno EC, Riberio MA, Carvalho GP. D-dimer level as possible prognostic marker in operable breast carcinoma. *Ann Oncol*. 2009;21:1267–72.
4. Engin Y, Guzin G, Idris Y, Mehmet T. Relation between hemostatic parameters and prognostic factors in breast carcinoma. *Eur J Med*. 2008;19:602–8.
5. Blackwell K, Haroon Z, Broadwater G, Berry D, Harris L, Iglehart JD, et al. Plasma D-dimer levels in operable breast cancer patients correlate with clinical stage and axillary lymph node status. *J Clin Oncol*. 2000;18(3):600–8.
6. Patel S, Rashmi C, Harish S. D-dimer levels in breast carcinoma: a clinico-pathologic study. *Ann Pathol Lab Med*. 2018;5(3):75–80.
7. Ghadhban BR. Plasma D-dimer level correlated with advanced breast carcinoma in female patients. *Ann Med Surg*. 2018;36:75–8.
8. Khan MZ, Khan MS, Raziq F, Khattak AM. Fibrinogen degradation products and D-dimers in patients with breast carcinoma. *Gomal J Med Sci*. 2007;5(1): 9–12.
9. Rakha EA, El-Sayed ME, Green AR, Paish EC, Lee AH, Robertson JF, et al. Prognostic markers in triple-negative breast cancer. *Cancer*. 2007;109:25–32.
10. Waks AG, Winer EP. Breast cancer treatment: a review. *JAMA*. 2019;321(3):221–5.