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ROLE OF PLASMA D-DIMER LEVELS IN BREAST CANCER PATIENTS AND ITS CORRELATION WITH CLINICAL AND HISTOPATHOLOGICAL STAGE

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Abstract

Background: Breast cancer is a globally prevalent malignancy among women. Plasma D-dimer, a fibrinolytic degradation product, maybe a prognostic biomarker. This study aimed to evaluate the relationship between plasma D-dimer levels and clinical and histopathological parameters in patients with breast cancer. **Materials and Methods:** This prospective observational study included 50 patients with breast carcinoma admitted to GMKMCH, Salem, between July 2022 and June 2024. Clinical and demographic data, including menopausal status, tumour stage, histological grade, and ER/PR receptor status, were collected. Plasma D-dimer levels were measured preoperatively with standard laboratory techniques. **Result:** The mean age of the patients was 43.42±2.785 years, with 58% premenopausal and 42% postmenopausal. Most patients had invasive ductal carcinoma (86%) and Grade III tumours (40%). Lymph node involvement was observed in 68% of patients, and 78% were ER/PR-positive. Stage II breast carcinoma was the most common (60%). The mean plasma D-dimer level was 3.41±2.57. D-dimer levels showed a significant positive correlation with histological grade (r=0.727, p<0.001), tumour histology (r=0.490, p<0.001), lymph node involvement (r=0.661, p<0.001), ER/PR positivity (r=0.670, p<0.001), and tumour stage (r=0.660, p<0.001). Higher histological grades and lymph node involvement were associated with elevated D-dimer levels. **Conclusion:** Plasma D-dimer levels are a prognostic biomarker in breast carcinoma, significantly correlating with tumour grade, lymph node involvement, and disease stage. Elevated levels may indicate advanced disease and metastatic potential, highlighting their clinical utility in prognosis and management of the disease.

INTRODUCTION

Breast cancer is the most prevalent cancer in women and one of the leading causes of mortality in this population. In India, breast cancer is the second most frequent malignancy after cervical cancer, and its prevalence is on the rise (22.9%).[1] D-dimer is a biomarker that shows the activation of fibrinolysis and haemostasis. Hypercoagulability in patients with breast cancer leads to increased fibrin and fibrinolytic product production. Since D-dimer is one of the best fibrinolytic products, it is recognised as a possible prognostic indicator. It has been observed that people with breast cancer have significantly higher D-dimer levels than those without malignancy. D-dimer levels have been demonstrated to be higher in patients with breast cancer at the time of diagnosis and lower following surgical intervention during adjuvant treatment.

In cases of operable breast cancer, D-dimer levels have been linked to the clinical stage of the tumour, lymphovascular invasion, and involvement of the axillary lymph nodes. D-dimer may also be a biomarker for early tumour metastases.[2,3] In contrast, the increase in D-dimer as a byproduct of fibrin degradation is reported as a valuable biomarker to estimate the histological grading of BCs, considering its potential to indicate haemostasis activation, fibrinolysis, and estimate the enhancement of diffuse intravascular coagulation after the advancement of a tumour grading.[4,5] In this study, we aimed to assess the relationship between plasma D-dimer levels in patients with breast carcinoma and its significance in predicting lymph node metastasis and histopathological grading.

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MATERIALS AND METHODS

This prospective observational study included 50 patients with a clinical diagnosis of Breast Carcinoma in the General surgical ward and OP in the Department of General Surgery, GMKMCH, Salem, between July 2022 and June 2024. The study was conducted after receiving approval from the Institutional Ethics Committee, and informed consent was obtained from all patients.

Inclusion and Exclusion Criteria

Patients with breast carcinoma confirmed by fine-needle aspiration cytology (FNAC) and histopathological examination (HPE), regardless of age, were included. The exclusion criteria comprised cases of metastatic breast carcinoma and patients with conditions affecting coagulation, including those on warfarin therapy, with a history of thrombotic episodes, liver disease, major trauma, or major surgery within the past three months.

Methods

Demographic details were recorded, including age, socioeconomic status, and a detailed history of the presenting complaints with their duration. A thorough general and systemic examination was performed, and the patients were followed up until discharge and at periodic intervals. The clinical history included past medical conditions such as diabetes mellitus, systemic hypertension, tuberculosis, asthma, epilepsy, previous surgeries, and jaundice. Personal histories of smoking, alcohol consumption, and drug addiction were also documented.

The initial assessment involved recording vital parameters, including the pulse rate, blood pressure, respiratory rate, and temperature. A general examination assessed pallor, tongue and skin changes, icterus, cyanosis, and lymphadenopathy (LNs). Systemic examination covered the cardiovascular, respiratory, and central nervous systems, and the abdomen.

Investigations included haemoglobin percentage (Hb%)/packed cell volume (PCV), platelet count, total leukocyte count, blood grouping and typing, bleeding time/clotting time, random blood sugar, serum urea and creatinine, and D-dimer. Viral markers such as HBsAg, anti-HCV, and HIV were assessed, along with urine examination, electrocardiography (ECG), chest X-ray (PA view), and abdomen X-ray (erect). A detailed clinical examination of the breast and axillary lymph nodes was performed. The operative procedure was documented, including the type of anaesthesia used, patient positioning, incision, and surgical technique.

Statistical Analysis: Data are presented as mean, standard deviation, frequency, and percentage. The correlation between continuous variables was assessed using the Pearson correlation test. Significance was defined as $p < 0.05$ using a two-tailed test. Data analysis was performed using IBM SPSS version 21.0.

RESULTS

The mean age of the patients with breast carcinoma was 43.42 ± 2.785 years. The mean plasma D-dimer level in patients with breast carcinoma was 3.41 ± 2.57 [Table 1].

Table 1: Baseline characteristics.

	Mean ± SD
Age (years)	43.42 ± 2.785
Plasma D-dimer level scores	3.413 ± 2.579

Regarding menopausal status, the majority of patients, 29 (58%) were premenopausal. Regarding histological grade, most patients, 20 (40%) had grade III histology. The histological distribution showed that the majority 43 (86%) were diagnosed with invasive ductal carcinoma. Regarding lymph nodes, 34 (68%) patients had positive lymph nodes. For ER/PR receptor status, most patients 39 (78%) tested positive for both receptors. Regarding staging, the majority of patients who had stage II breast carcinoma were 30 (60%). In the analysis of plasma D-dimer levels, 24 (48%) patients had levels between 2 and 5 [Table 2].

Table 2: Clinical and pathological characteristics

		N (%)
Menopausal status	Premenopausal	29 (58%)
	Postmenopausal	21 (42%)
Histological grade	Grade I	12 (24%)
	Grade II	18 (36%)
	Grade III	20 (40%)
Histology	In situ	7 (14%)
	Invasive ductal carcinoma	43 (86%)
Lymph node	Positive	34 (68%)
	Negative	16 (32%)
ER/PR receptor	Positive	39 (78%)
	Negative	11 (22%)
Staging	I	8 (16%)
	II	30 (60%)

	III	12 (24%)
Plasma D-dimer levels	< 0.25	5 (10%)
	0.25–2	14 (28%)
	2–5	24 (48%)
	> 5	7 (14%)

The histological grade showed a positive correlation with r=0.727 and p=0.001, both significant. Histology demonstrated a positive correlation with r=0.490 and p=0.001, which were significant. Lymph nodes showed a positive correlation with r=0.661 and p=0.001, indicating significance. ER/PR receptor expression was positively correlated with r=0.670 and p=0.001, both significant. Staging was positively correlated with r=0.660 and p=0.001, which was also significant [Table 3].

Table 3: Correlations between plasma D-dimer levels

	r-value	P-value
Histological grade	0.727	0.001
Histology	0.490	0.001
Lymph node	0.661	0.001
ER/PR receptor	0.670	0.001
Staging	0.660	0.001

Plasma D-dimer levels and histological grade in breast carcinoma showed a significant positive correlation (r=0.727, p<0.001) [Figure 1].
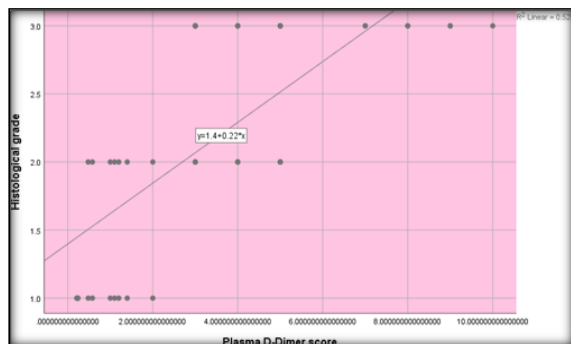

Figure 1: Correlations between plasma D-dimer levels and histological grade

The relationship between plasma D-dimer levels and histology in patients with breast carcinoma showed a significant positive correlation (r=0.490 and p<0.001) [Figure 2].
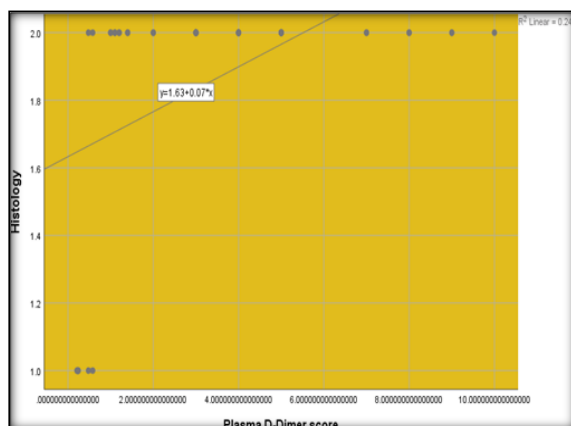

Figure 2: Correlations between plasma D-dimer levels and histology

The correlation between plasma D-dimer levels and lymph node involvement in patients with breast carcinoma showed a strong positive correlation (r=0.661, p<0.001) [Figure 3].
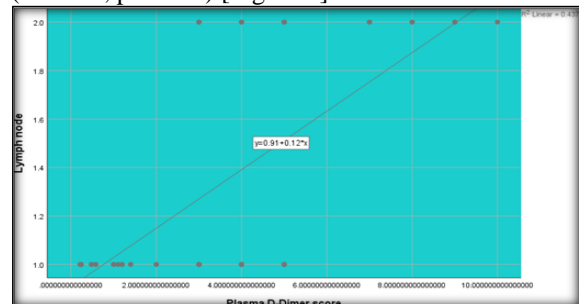

Figure 3: Correlations between plasma D-dimer levels and lymph node

The correlation between plasma D-dimer levels and ER/PR receptor status was significant. A positive correlation was observed (r=0.670, p<0.001) [Figure 4].
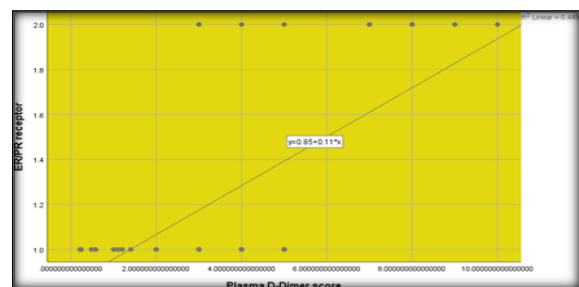

Figure 4: Correlations between plasma D-dimer levels and ER/PR receptor

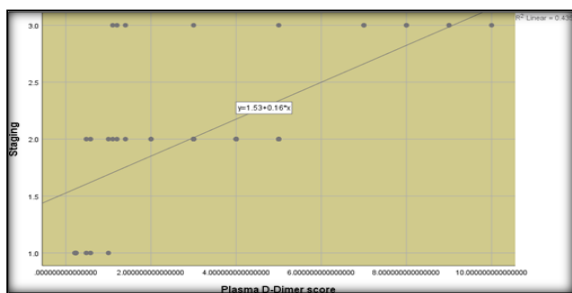Plasma D-dimer levels were significantly positively correlated with tumour staging (r=0.660, p<0.001) [Figure 5].

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Figure 5: Correlations between plasma D-dimer levels and staging

DISCUSSION

Our study assessed the relationship between plasma D-dimer levels in patients with breast carcinoma and its significance in predicting lymph node metastasis and histopathological grade. During the study period, 50 patients with a clinical diagnosis of breast carcinoma were enrolled. The mean age of the patients was 43.42 ± 2.785 years, and the menopausal status of breast carcinoma patients showed that the majority, 29 (58%) were premenopausal. Supporting results noted in a survey by Halugodu et al. showed that the age of patients ranged from 37 to 63 years, with a mean age of 51.9.[6] Sringeri et al., found that 46% of the patients were postmenopausal.[7]

Our study on the distribution of histological grades among patients with breast carcinoma found that the majority, 20 (40%), had a histological Grade III. Additionally, the study showed that 43 (86%) patients had invasive ductal carcinoma. Furthermore, 34 (68%) patients had positive lymph nodes. Our study aligns with Sringeri et al., who reported that thirty-eight (63.3%) patients had positive lymph nodes, whereas 22 (36.6%) had negative lymph nodes.[7]

In our study, the majority had 39 (78%) positive ER/PR receptor levels. Additionally, 30 (60%) participants were diagnosed with stage II breast carcinoma. We observed that 24 (48%) of the majority had 2–5 Plasma D-dimer levels. Furthermore, the mean plasma D-dimer level among patients with breast carcinoma was 3.41 ± 2.57. Supportive results from a study conducted by Halugodu et al. showed that the mean D-dimer level in patients with stage I breast cancer was 0.1. All patients in stage II (IIA and IIB) showed D-dimer values with a mean of 0.2, ranging from less than 0.2 to 0.5. The mean D-dimer was 0.3 in stage III B and 0.4 in stage III A. Additionally, 8.57% of the patients had D-dimer averages of 0.5 mg/l and 1.0 mg/l, categorising them in stages III C and IV. Therefore, D-dimer levels increased as the stage progressed and also increased significantly. Correlations were found between plasma D-dimer levels in breast carcinoma patients and their significance in predicting lymph node metastasis and histopathological grading.[6]

In our study, we found a positive correlation that was highly statistically significant. The histological grade showed a positive correlation with r=0.727 and p=0.001, which was highly significant. Histology results indicated a positive correlation with r=0.490 and p=0.001, which were highly significant. The lymph node showed a positive correlation (r = 0.661, p = 0.001), which was highly significant. ER/PR receptor showed a positive correlation with r=0.670 and p=0.001, which were highly significant. Staging indicated a positive correlation with r=0.660 and p=0.001, which were highly significant.

Our study agrees with that of Sringeri et al., who found that the amount of lymph node involvement and lymph vascular invasion were directly correlated with D-dimer levels among all the histopathological variables examined. The number of positive lymph nodes showed the strongest correlation between D-dimer levels and lymphovascular invasion, but not with tumour size, oestrogen receptor status, or progesterone receptor status. Elevated D-dimer levels and tumour size significantly predicted the presence of positive lymph nodes. No patients were in stages IIIB or IV. Based on histologic grade, there was a significant difference in D-dimer values (p=0.002).[7]

CONCLUSION

Plasma D-dimer levels serve as a strong predictor of prognosis in breast cancer and may also be a valuable marker for assessing disease progression, lymph vascular invasion, and metastasis. Activation of the coagulation and fibrinolysis systems in patients with cancer is associated with tumour stroma development and metastasis in various cancer types. A multidisciplinary approach involving surgeons, radiologists, pathologists, and medical oncologists is essential for the accurate diagnosis and treatment of breast cancer, with the illness stage at diagnosis playing a crucial role in determining the treatment strategy and prognosis. Lymph node metastasis is the most significant prognostic factor. This study demonstrates that patients with breast cancer have higher plasma D-dimer levels, with elevated concentrations serving as essential indicators of tumour metastasis, lymphovascular invasion, clinical stage, and lymph node involvement.

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