International Surgery Journal
Rajpoot PS et al. Int Surg J. 2025 Feb;12(2):183-186
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: https://dx.doi.org/10.18203/2349-2902.isj20250142

Original Research Article

Exploring the relationship between coagulation profiles and histopathological diagnosis of breast lumps: a case control study from Vindhya region, India

Parul S. Rajpoot*, Priyanka Agrawal, Suresh K. Sutrakar, Lokesh Tripathi, Shambhavi

Department of Pathology, Shyam Shah Medical College, Rewa, Madhya Pradesh, India

Received: 12 December 2024
Accepted: 17 January 2025

***Correspondence:**
Dr. Parul S. Rajpoot,
E-mail: drparulsinghssmc@gmail.com

ABSTRACT

Background: Breast cancer is the most common cancer among women in India. The country is on the verge of a potential breast cancer epidemic in the coming decade, driven by lifestyle changes such as delayed marriage and childbirth, influenced by Western trends. Hypercoagulable state is one of the adverse complication seen in cases of breast cancer, according to recent study. Therefore, the purpose of this study was to evaluate the coagulation anomalies in breast cancer patients.
Methods: The study was a prospective, case control study carried out with patients presenting with complaints of lump in the breast which were confirmed to be malignant by histopathological examination.
Results: Values of PT and aPTT were found to be comparable in patients with breast cancer when compared with controls. D-Dimers were found to be significantly elevated in patients with breast cancer when compared with controls. D-Dimers were also elevated in cases with high histological grade of cancer and lymphovascular invasion.
Conclusions: Elevated levels of plasma D-dimer may offer some insight for the diagnosis breast lump.

Keywords: aPTT, Breast lump, D-Dimer, PT

INTRODUCTION

With an anticipated 2.3 million new cases (11.7%) worldwide, breast cancer is currently one of the most common malignancies to be diagnosed and the fifth leading cause of cancer-related deaths. These statistics come from the GLOBOCAN 2020 data.[1,2] Patients with cancer have an imbalance in the coagulation and fibrinolytic systems. The high expression of tissue factor and the microparticles that cancer cells form from it, along with an increase in anticoagulant proteins, changes to platelet function, the production of malignant procoagulants and an increase in the release of microparticles expressing these substances, could all be contributing factors to this phenomenon.[3,4] It has long been known that increased coagulation system activation in breast cancer patients is linked to a higher incidence of systemic venous thromboembolism (VTE) and lower patient survival.[5,6] A hypercoagulable state with elevated tissue factor, fibrinogen, prothrombin time (PT) and activated partial thromboplastin time (aPTT) has also been observed in earlier research on breast cancer.[7] This hypercoagulable state is exacerbated and contributed to by breast cancer treatments, such as hormone therapy, chemotherapy and surgery.[8]

Thrombocytosis, elevated levels of fibrin degradation products such as D-dimer, elevated levels of factors V, VII, VIII, IX and XI and decreased levels of antithrombin III have all been reported to be observed in cancer patients. It has been demonstrated that the plasma of breast cancer patients activates the synthesis and breakdown of intravascular fibrin, which is necessary for angiogenesis in tumors.[9] This case-control study aims to

assess the correlation between the coagulation profile and the histopathological diagnosis of breast lumps.

METHODS

This prospective case control study was conducted for 5 months from August 2023 to November 2023 in the Department of Pathology, Shyam Shah Medical College, Rewa. The study received ethical clearance from the Institutional Ethics Committee (S.No/IEC/ M.C./2022/19704).

Inclusion criteria

All the cases of breast lumps sent for Fine Needle Aspiration Cytology (FNAC) and subsequent histopathological examination (HPE) in the Department of Pathology will be included in this study.

Exclusion criteria

Cases of metastatic breast carcinoma. Condition altering the coagulation profile such as warfarin therapy, thrombotic episodes, disorders of coagulation, liver diseases, pregnancy, major trauma within 3 months, recent surgery within 3 months and any autoimmune disease.

Study design

All patients presenting with breast lumps were first subjected to fine needle aspiration cytology (FNAC) for provisional diagnosis. Blood samples were collected in citrate vacutainers and stored under appropriate conditions for further analysis.

Cytology results were classified according to the IAC Yokohama system for reporting breast cytology. Simultaneously, coagulation tests including D-Dimer, prothrombin time (PT) and activated partial thromboplastin time (aPTT) were conducted. Patients were subsequently monitored and histopathological specimens, obtained through lumpectomy, wide local excision (WLE) biopsy or modified radical mastectomy (MRM), were collected from the Department of Surgery for further examination.

The histopathological specimens underwent routine grossing, slide preparation and microscopic evaluation. The histopathological findings were then correlated with the patients' coagulation profiles (D-Dimer, PT, aPTT). Statistical analysis was performed using unpaired t-tests and ANOVA to assess the relationship between the histopathological and coagulation findings.

Data analysis

All the coagulation studies were done using Erba ECL 105 Semi-automated Single Channel Coagulation Analyzer which performs clotting assays by light scatter at 640 nm and Immunoturbidimetric assays at 800 nm. The data collected was first entered in Microsoft® Excel® 2019 MSO (Version 2407 Build 16.0.17830.20056). Descriptive statistics such as mean, frequency and percentages and analytical statistics such as the unpaired T-test and ANOVA test were used to test the significance level and a probability value (P)<0.05 was considered statistically significant using Graph Pad Prism 10.2.3 (403).

RESULTS

A total of 40 patients were included in the study which were divided into group 1 (cases) confirmed malignant on histopathology consisting of 20 subjects and group 2 (controls) confirmed benign on histopathology consisting of 20 subjects. For malignant lesions, additional assessments were done which included histological grading using the modified Bloom-Richardson system, lymph node (LN) status i.e. N-stage, T-stage and lymph vascular invasion.

In group 1 subjects (malignant lesions) the ranges for PT, aPTT and plasma D-dimer were 11.2–16.78 seconds, 28.1–40.12 seconds and 293.1–1783 ng/ml respectively. In group 2 subjects (benign), the observed ranges for PT, aPTT and plasma D-Dimer were 11.09–14 seconds, 29.78–39.6 seconds and 7.04–782.3 ng/ml, respectively. The comparison of coagulation tests between benign and malignant breast lesions revealed a statistical difference in D-Dimer value ($p<0.0001$) whereas PT and aPTT showed no correlation ($p>0.05$) (Table1).

In group 1 subjects additionally coagulation studies were also compared across different histological grades, T-stages, N-stage and the presence or absence of lymphovascular invasion. Statistical analysis revealed a significant association between elevated D-Dimer levels and increased histological grade and the presence of lymphovascular invasion ($p<0.05$). No significant correlations were observed for the values of PT and aPTT with all four pathological parameters of malignant breast lesions (Table 2).

Table 1: Correlation of mean PT, mean aPTT and mean D-Dimer values of benign and malignant breast lesions.

	Mean PT (sec)	Mean aPTT (sec)	Mean D-dimer (ng/ml)
Group 1 (malignant lesions)	13.19	33.75	803.17
Group 2 (benign lesions)	12.78	32.69	121.86
P value	0.25	0.27	<0.0001
Statistical significance	Not significant	Not significant	Significant

Table 2: Correlation of mean PT, mean aPTT and mean D-Dimer values with histological grade, T-stage, N-stage and Lymphovascular invasion of the malignant lesions.

Variables	N (%)	Mean PT (sec)	Mean Aptt (sec)	Mean D-Dimer (ng/ml)
Histological grade				
I	8 (45%)	13.006	32.015	582.576
II	10 (50%)	13.03	35.256	794.39
III	2 (5%)	15.255	37.475	1729.45
P value		0.077	0.06	0.0004
Statistical significance		Not significant	Not significant	Significant
T-Stage				
T1	2	15.255	37.475	1076.8
T2	9	12.863	32.817	763.39
T3	6	13.32	35.403	798.45
T4	3	12.893	33.633	749.533
P value		0.139	0.319	0.808
Statistical significance		Not significant	Not significant	Not significant
N-Stage				
N0	5	13.98	33.66	634.12
N1	6	12.82	34.27	745.75
N2	7	13.42	34.88	1092.47
N3	2	12.3	32.78	385.49
P value		0.39	0.90	0.059
Statistical significance		Not significant	Not significant	Not significant
Lymphovascular invasion				
Seen	2	12.04	36.31	1339.06
Not seen	18	13.37	33.94	708.6
P value		0.1925	0.39	0.041
Statistical significance		Not significant	Not significant	Significant

DISCUSSION

Over a century has passed since the initial description of the connection between blood coagulation activity and cancer. An increasing amount of data points to the coagulation system as a potential mediator of the development and spread of malignant tumors as molecular biology research on tumors continues to advance.[10,11]

The smallest of the breakdown products that arise from plasmin's proteolytic activity on fibrin, D-dimer has distinct properties whereas the coagulation factor content and activity in internal and exterior coagulation pathways are shown by aPTT and PT, respectively.[12,13]

In our study, there was a slight increase in the mean values of PT and aPTT of malignant cases as compared to benign cases but this increase was statistically not significant ($p>0.05$), whereas the mean value of plasma D-dimer for malignant breast lesions was significantly raised as compared to benign breast lesions ($p<0.05$). Previous research on lung cancer and gynecologic cancer types has also verified elevated D-dimer levels as a predictor of tumor overload.[14,15] Our findings between benign and malignant cases were also in line with the study conducted by Manjunath et al, on coagulation abnormalities in breast malignancy, in which it was found the levels of PT and aPTT were comparable for both benign and malignant cases whereas D-dimer levels were significantly elevated in malignant cases ($p<0.05$).[16]

Huang et al, in their study on coagulation abnormalities in laryngeal carcinoma, demonstrated that the PT level was significantly raised with the T-stage of the tumor ($p<0.05$) whereas no correlation was found with histological grade, N-stage and lymphovascular invasion and in the same study a significant correlation was also found in the value of aPTT and lymphovascular invasion.[17]

In another study done by Tas et al, on breast carcinoma patients, a significant correlation was found between PT value and the histological grade of the tumor ($p<0.05$).[18]

So far, we could not find significant correlation of PT and aPTT value with the histological grade, T-stage, N stage and lymphovascular invasion of the tumor. In previous studies, significant correlations were identified between plasma D-dimer levels and factors such as lymph node involvement, clinical stage and the number of metastatic nodules, which are essential for determining clinical stage and treatment.[19] In one of the study conducted by Rajendran et al, a significant relation was found between D-dimer and the T-stage, N-stage and lymphovascular invasion ($p<0.05$), we found a significant relation between plasma D-dimer level and histological grade and presence of lymphovascular invasion ($p<0.05$).[20]

The study only included cases from the SGMH tertiary hospital in Rewa and it was carried out over the course of five months. To draw conclusions on the relevance of coagulation profile in breast lump prediction and prognosis, larger multicentric research are required.

CONCLUSION

Breast cancer is one of the leading causes of death and illness in the globe. In developing nations, breast cancer is spreading rapidly, imposing significant financial and psychological burdens on families and the country as a whole. While there is no definitive way to prevent breast cancer, combining effective screening with risk-reduction strategies offers a practical approach to alleviating this growing health challenge.

Screening aids in detecting early noninvasive cancers, enabling treatment before they progress. D-Dimer detection could provide a differential analysis for DIC in comparison to other laboratory techniques. And therefore, plasma D-dimer levels can provide a basis to predict whether the tumor is benign or malignant.

Whether other coagulation profiles such as PT and aPTT along with D-Dimer levels can be used as a marker or guide to assess the invasive potential and poor prognosis of the disease needs to be evaluated by further large-scale studies.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209-49.
2. Łukasiewicz S, Czeczelewski M, Forma A, Baj J, Sitarz R, Stanisławek A. Breast Cancer-Epidemiology, Risk Factors, Classification, Prognostic Markers and Current Treatment Strategies-An Updated Review. Cancers (Basel). 2021;13(17):4287.
3. Han X, Zha H, Yang F, Guo B, Zhu B. Tumor-derived tissue factor aberrantly activates complement and facilitates lung tumor progression via recruitment of myeloid-derived suppressor cells. International journal of molecular sciences. 2017;18(1):22.
4. Leppert U, Eisenreich A. The role of tissue factor isoforms in cancer biology. International journal of cancer. 2015;137(3):497503.
5. Caine GJ, Stonelake PS, Rea D, Lip GY. Coagulopathic complications in breast cancer. Cancer. 2003;15:1578–86.
6. Chew HK, Wun T, Harvey DJ, Zhou H, White RH. Incidence of venous thromboembolism and the impact on survival in breast cancer patients. J Clin Oncol. 2007;15:70–6.
7. Saki N, Javan M, Shokouhian M, Bagheri M, Moghimian-boroujeni B. A review of the interaction between the coagulation system and cancer. Iranian Journal of Blood and Cancer. 2023;15(1):71-9.
8. Lal I, Dittus K, Holmes CE. Platelets, coagulation and fibrinolysis in breast cancer progression. Breast Cancer Res. 2013;15(4):207.
9. Sringeri R R, Chandra P S. Role of plasma D-dimer levels in breast cancer patients and its correlation with clinical and histopathological stage. Indian Journal of Surgical Oncology. 2018;9:307-11.
10. Tinholt M, Sandset PM, Iversen N. Polymorphisms of the coagulation system and risk of cancer. Throm Res. 2016;140:49-54.
11. Singh AK, Malviya R. Coagulation and inflammation in cancer: Limitations and prospects for treatment. Biochimica et Biophysica Acta (BBA)-Reviews on Cancer. 2022;1877(3):188727.
12. Liu L, Zhang X, Yan B, Gu Q, Zhang X, Jiao J, et al. Elevated plasma D-dimer levels correlate with long term survival of gastric cancer patients. PloS one. 2014;9(3):90547.
13. Lei Z, Guo D. Significant difference between coagulation parameters and clinicopathological characteristics in breast cancer. Blood Coagul Fibrinol. 2021;32(8):572-7.
14. Unsal E, Atalay F, Atikcan S, Yilmaz A. Prognostic significance of haemostatic parameters in patients with lung cancer. Respir Med. 2004;98:93–8.
15. Rella C, Coviello M, Frenza ND. Plasma D-dimer measurement as a marker of gynecological tumors: comparison with CA 125. Tumori. 1993;79:347–51.
16. Procedure280 AF. of IACTS, February 2018. Indian J Thor Cardiovas Surg. 2018;34(2):181-331.
17. Huang Q, Chen J, Huang Y, Xiong. The prognostic role of coagulation markers in the progression and metastasis of laryngeal squamous cell carcinoma. Research Square (Research Square). 2023;9:123-8.
18. Tas F, Kilic L, Duranyildiz D. Coagulation tests show significant differences in patients with breast cancer. Tumor Biol. 2014;35(6):5985–92.
19. Blackwell K, Haroon Z, Broadwater G, Berry D, Harris L, Iglehart JD, Dewhirst M, Greenberg C. Plasma D-dimer levels in operable breast cancer patients correlate with clinical stage and axillary lymph node status. J Clin Oncol. 2000;18(3):600-9.
20. Rajendran G, Aravind D, Venkatesh P, Anandan H. Correlation of coagulation markers with axillary lymph node metastasis in carcinoma breast. Int Surg J. 2018;5:1394-8.

Cite this article as: Rajpoot PS, Agrawal P, Sutrakar SK, Tripathi L, Shambhavi. Exploring the relationship between coagulation profiles and histopathological diagnosis of breast lumps: a case control study from Vindhya region, India
Int Surg J 2025;12:183-6.