IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 22, Issue 5 Ser.6 (May. 2023), PP 51-57
www.iosrjournals.org

A Prospective Study To Determine The Correlation Of D-Dimer With Axillary Lymph Node Metastasis In Carcinoma Breast

PARSHANT KUMAR,
Resident Doctor, Department of General Surgery, SMS Medical College and attached hospital, Jaipur
AMIT JAIN,
Professor, Department of General Surgery, SMS Medical College and attached hospital, Jaipur
SACHIN KALSAN,
Resident Doctor, Department of General Surgery, SMS Medical College and attached hospital, Jaipur
GUNJAN KUMAR UIKEY,
Resident Doctor, Department of General Surgery, SMS Medical College and attached hospital, Jaipur

ABSTRACT
Background- *Lymph node metastasis has been one of the most prognostic markers of the carcinoma breast. Search for a marker to predict the metastasis to lymph nodes in clinically negative axilla has been a matter of research for long. The aim of study was to determine the association of D-dimer value as a predictive marker of lymph node metastasis in breast cancer and to correlate D-Dimer levels with the staging of breast cancer.*
Methods - *A prospective study was conducted in the Department of general surgery at SMS medical college and attached hospital in Jaipur (INDIA), from December 2021 to November 2022. The study uses clinical staging, histopathological diagnosis & grading, and axillary lymph node metastasis as variables.*
Results- *There is statistically significant highly positive correlation present between axillary lymph node metastasis and D dimer levels. As the D dimer values increases, axillary lymph node metastasis is more common.*
Conclusions - *D-dimer alone or in combination with other biomarkers may provide an alternative to conventional sentinel node biopsy in node negative breast cancer.*

Date of Submission: 08-05-2023 Date of Acceptance: 18-05-2023

I. INTRODUCTION

The most frequent malignant neoplasm in females is breast cancer, which is a diverse group of tumors with variable behavior and variable response to treatment. The importance of biological markers, hormonal state, histological grade and subgroup status, tumor size, and lymph node embroilment in determining the most suitable treatments may be seen.[1]

Even though clinical and experimental studies have shown a connection between cancer and hemostasis, the precise mechanism is still not entirely known. Therefore, systemic activation of the coagulation and hemostatic systems in all cancer patients lacking thromboembolism has been a subject of ongoing research.[2] Hypercoagulation and cancer are related, and patients with cancer typically experience global hemostasis activation. Tumor cell angiogenesis, progression, metastatic spread has been associated with systemic activation. Increased levels of d-dimer, which is created when cross-linked fibrin is degraded, show that hemostasis and fibrinolysis have been activated globally.[3] Elevated plasma d-dimer levels are associated with either distant metastasis or metastases to the axillary lymph nodes in breast cancer.[4] Remodeling and fibrin deposition in the extracellular matrix of the tumor are the primary steps in tumor spread. A tumor must go through numerous coercive processes, be transported via the bloodstream, and establish viability in the base tissues to successfully metastasize from its original site.[5] Cross-linked fibrin provides a robust framework in the extracellular matrix for angiogenesis during the invasion and migration of tumor cells by endothelial cells.[6] Angiogenesis in tumors is primarily mediated by extracellular fibrin remodeling, and the patient plasma contains activated intravascular fibrin formation and dissolution.[7] Furthermore, angiogenesis, tumor development, tumor cell stealth, and metastatic spread have all been linked to the activation of the coagulation system, minute thrombin generation, and fibrin configuration and breakdown.[8] The key enzyme in the process of blood coagulation, thrombin, causes fibrinogen to change into fibrin, which is the last product of blood coagulation and ultimately results in the development of a fibrin clot. The standard for systemic adjuvant therapy in patients with node-negative, 1 cm

breast cancer may be D-dimer and factor VII. In clinically node-negative breast cancer, D-dimer may show to be a reliable biomarker that can be used in conjunction with traditional sentinel node biopsy to evaluate outcomes. Significant postoperative drops in D-dimer and factor VIII may offer objective standards for approving surgical procedures. Large multicenter prospective trials with long-term follow-ups are required to validate these findings.

Hence, we have attempted to determine the association of D-dimer value as a predictive marker of lymph node metastasis in breast cancer.

AIMS AND OBJECTIVES

The aims and objectives of the study were to determine the association of D-dimer value as a predictive marker of lymph node metastasis in breast cancer and to correlate D-Dimer levels with the staging of breast cancer.

II. MATERIAL AND METHOD

A prospective study was conducted in the Department of general surgery at SMS medical college and attached hospital in Jaipur (INDIA), from December 2021 to November 2022.

Study population

Forty-five randomly selected patients with diagnosed carcinoma breast, admitted to the Department of general surgery at SMS medical college and attached hospital, after proper consent were included in the study. Patients suffering from any severe blood coagulation disorders and Conditions known to increase coagulation marker levels like disseminated intravascular coagulation, myocardial infarction, sickle cell disease with Vaso-occlusive crisis, thrombo-embolic events, and mechanical valve repair.

Various variables were studied, namely TNM staging, clinical staging, D-dimer levels, mammography findings, histopathological diagnosis, histological grades, and axillary lymph node metastasis.

D-dimer levels were measured before starting any treatment and axillary lymph node status was confirmed using the histopathological reports.

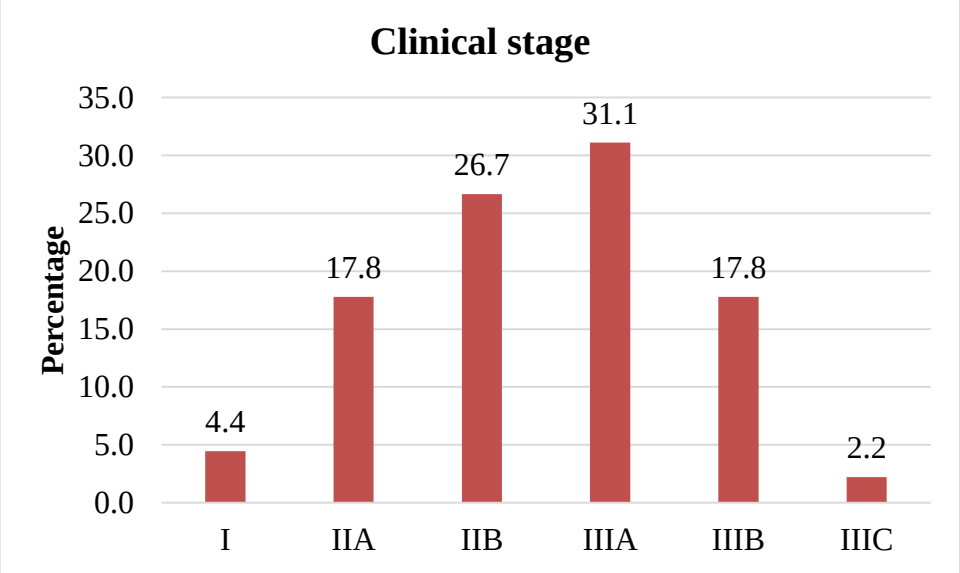
Statistical analysis

Data were analysed using SPSS version 23. Descriptive statistics for categorical data were expressed as numbers and percentages, while mean ± standard deviation and median (minimum-maximum) were used to express continuous data based on the normal distribution. Descriptive statistics, Paired t-test, and chi-square test were done for inter-duration comparison.

III. OBSERVATIONS AND RESULTS

A total of 45 patients were analyzed.

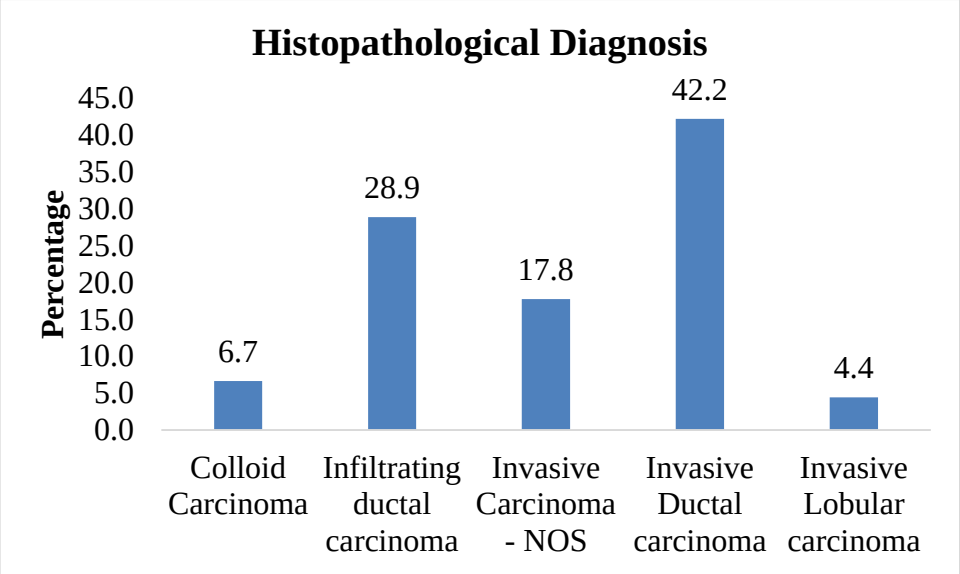
Figure 1: Bar diagram showing Clinical stage



In this study as per clinical staging, out of the total patients, two patients belonged to clinical stage I, eight patients belonged to clinical stage IIA, twelve patients belonged to clinical stage IIB, fourteen patients

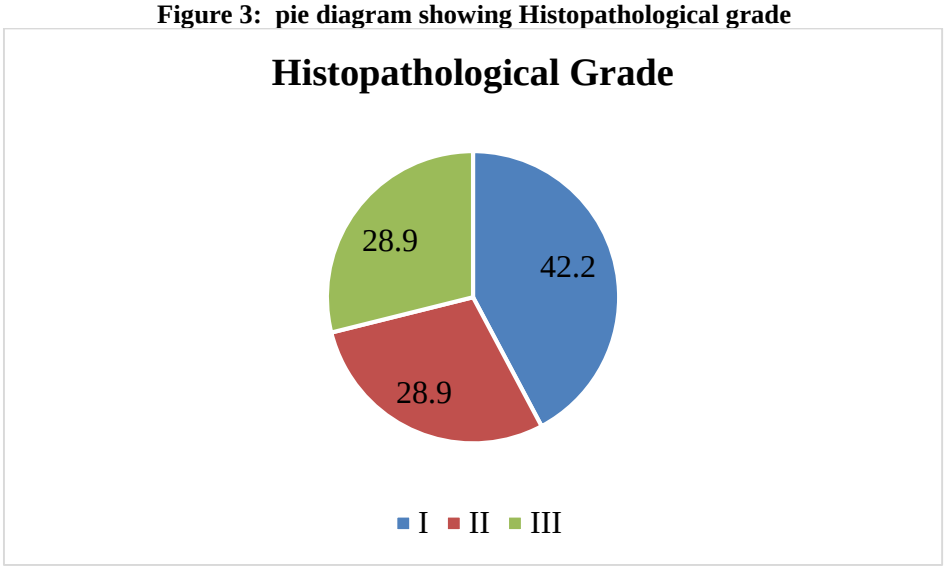
belonged to clinical stage IIIA, eight patients belonged to clinical stage IIIB, one patient belonged to clinical stage IIIC.

Figure 2: Bar diagram showing Histopathological Diagnosis



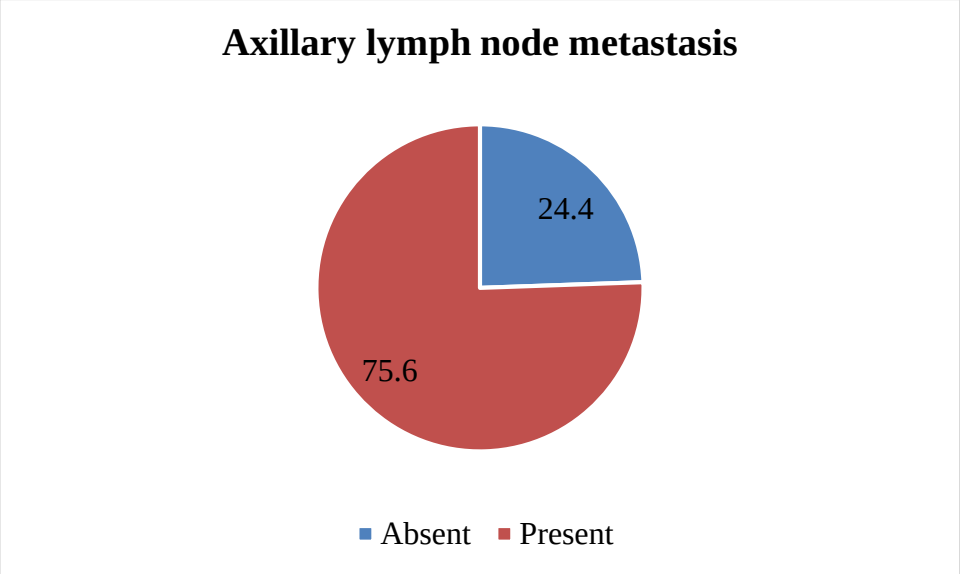
In this study as per Histopathological Diagnosis, out of the total patients three patients had Colloid Carcinoma, thirteen patients had Infiltrating ductal carcinoma, eight patients had Invasive Carcinoma – NOS, nineteen patients had Invasive Ductal carcinoma, and two patients had Invasive Lobular carcinoma.

Figure 3: pie diagram showing Histopathological grade



In this study as per Histopathological grade, out of forty-five patients nineteen patients belonged to grade I, thirteen patients belonged to grade II, thirteen patients belonged to grade III.

Figure 4: pie diagram showing Axillary lymph node metastasis



In this study as per Axillary lymph node metastasis, out of total patients eleven patients showed no lymph node metastasis while thirty-four patients showed lymph node metastasis.

Table 1: Comparison of Clinical stage with D Dimer levels

STAGE	N	Minimum	Maximum	Mean	Std. Deviation	F value	P value
I	2	104	142	123.00	26.870	13.448	<0.001**
IIA	8	98	1478	668.63	476.514		
IIB	12	145	1875	871.00	563.145		
IIIA	14	384	2547	1728.07	565.764		
IIIB	8	1324	3141	2256.13	621.113		
IIIC	1	2945	2945	2945.00			

**-Highly significant (p<0.001)

There is statistically significant difference between D Dimer values at various clinical stages. As the stage increased D Dimer values increases

Figure 5: Bar diagram showing co-relation between Clinical stage with D Dimer levels

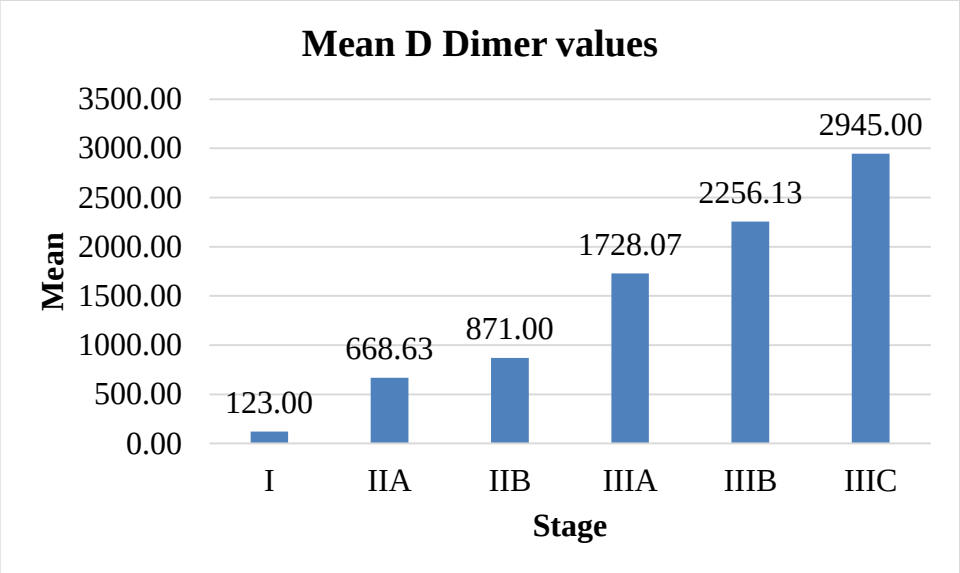


Table 2: Comparison of D Dimer Values in various histopathological grades

GRADE	N	Minimum	Maximum	Mean	Std. Deviation	F value	P vale
I	19	98	3141	1301.74	855.58	0.077	0.926 NS
II	13	104	2945	1390.77	997.70		
III	13	145	2578	1417.00	779.27		

NS- Not significant (p>0.05)

D-dimer levels did not vary as per histological grades.

Figure 6: Bar diagram showing correlation between D Dimer Values in various histopathological grades.

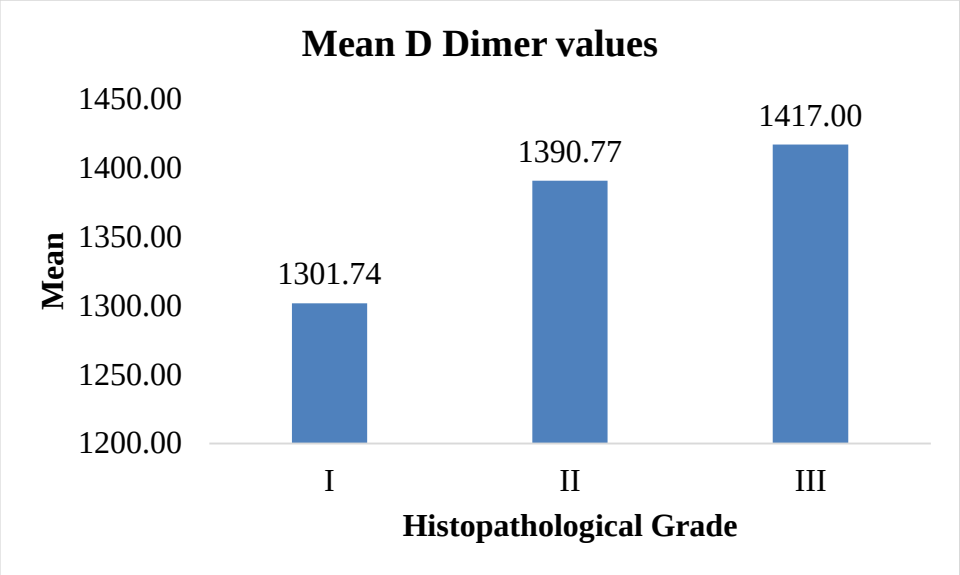


Figure 7: Bar diagram showing correlation between axillary lymph node metastasis and D Dimer levels

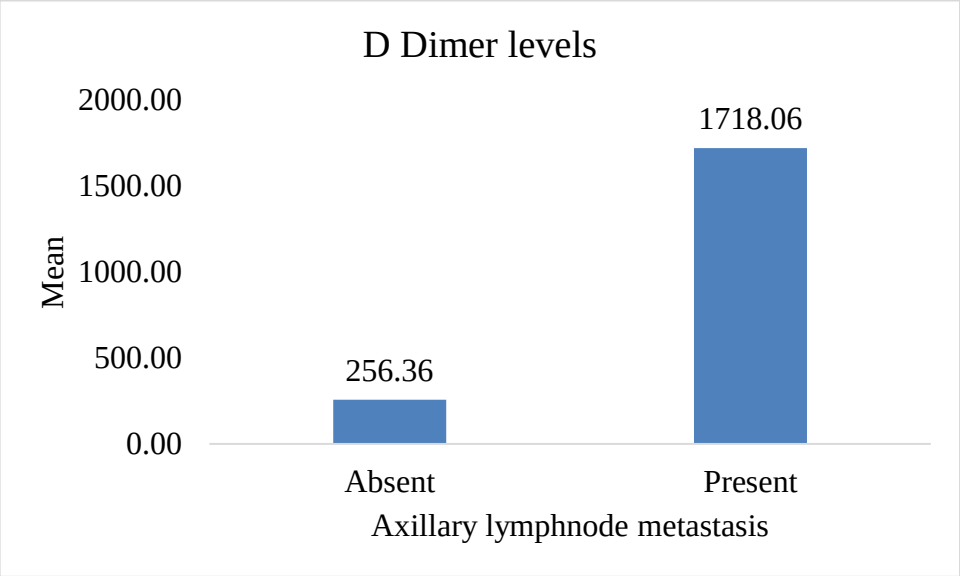


Table 3: Correlation between axillary lymph node metastasis and D dimer levels

Parameter	Statistics	AXILLARY LYMPH NODE METASTASIS	D-DIMER
AXILLARY LYMPH NODE METASTASIS	Pearson Correlation	1	.739**
	Sig. (2-tailed)		<0.001**
	N	45	45
**. Correlation is significant at the 0.01 level (2-tailed).			

There is statistically significant highly positive correlation present between axillary lymph node metastasis and D dimer levels. As the D dimer values increases, axillary lymph node metastasis is more common.

IV. DISCUSSIONS

Breast cancer continues to be one of the most feared diseases affecting people today despite centuries of theoretical rambling and scientific investigation. Prognostic variables have significant effects on both the breast cancer patient and her attending physician. The interrelationships and relative relevance of prognostic factors are the main points of contention. The numerous clinical and pathological characteristics of a group of breast cancer patients can be statistically analysed to identify prognostic markers. There is some variation in the relative weight given to prognostic factors among studies, but most of them highlight the importance of axillary nodal disease, tumor size, and differentiation.

Only if statistical analysis of a prospective study demonstrates that a new factor exhibits clinical utility above and beyond the norms will merit its inclusion as standard care. The hunt for predictive characteristics that will determine the tumor most likely to benefit from a particular therapy is taking precedence over the study of prognostic factors at this time. For the assessment of the prognosis of breast cancer and the prediction of therapeutic response, including the selection of the best feasible treatment modality, newer molecular markers are being looked for and studied.

A currently under investigation yet potentially key biomarker to predict lymphatic invasion status and early growth metastases in confirmed breast cancer is fibrin metabolism and control, as characterized by D-dimer level in plasma. A functioning marker should be taken into consideration to support the initial workup of breast cancer, or at least represent how active a malignancy was, even though the role of the other breast carcinoma predictive factor, such as estrogen and/or progesterone receptor (ER/PR) expressivity, human-epidermal receptor (HER)-2 status, tumor size, and histopathological investigations (HPE), is unquestionably essential in establishing the most anticipated course of the disease.

The clinical stage and D Dimer values show a statistically significant positive connection. D-Dimer readings rise with increasing clinical stage, and vice versa.

Other studies also discovered a strong correlation between high d-dimer levels and a positive axillary lymph node status.

D-dimer concentrations were not affected by histological grade in our study. The rise in the mean value of D-dimer with increasing histological grade was found to be minimal in previous studies as well.

In this study, 11 of them had no axillary lymph node metastasis, while 34 of them had it. A statistically significant and strong positive connection exists between D dimer levels and axillary lymph node metastases. Metastasis to the axillary lymph nodes is more frequent when the D dimer concentrations rise.

In a similar study, the increase in the mean value of D-dimer with an increase in LN status was shown to be significant. The results of investigations conducted in various other studies further support the findings of our study. It is safe to offer D-dimer levels as prognostic indicators because axillary lymph node involvement is the most significant prognostic factor. Additionally, these parameters may be employed in patients who are node negative for a personalized assessment and systemic therapy.

Though our study, in a first attempt, and a prior study indicated a strong association of D-dimer to predict lymph node metastasis, undoubtedly inspires optimism and underscores the necessity for sizable prospective trials to corroborate these findings.

In clinically node-negative breast cancer, D-dimer may prove to be a safe, practical, and easily accessible biomarker that can be used in conjunction with traditional sentinel node biopsy to identify the axillary metastatic disease and lessen false-negative results. In addition, D-dimer offers an alternative to traditional sentinel node biopsy for evaluating axillary metastatic illness.

It is reasonable to believe that increased D-dimer levels reflect fibrin by-product breakdown may eventually be influenced by a perceivably higher grade or expansion of a malignant focus because the subsequent results of those cancer pathophysiologic aspects are an increase in fibrin degradation rate. D-dimer essentially reflected the dysregulation of a person's physiologic coagulation function and fibrinolysis activity.[9-11]

Since we discovered a discernible link between high D-dimer and ALN metastatic positive and because its diagnostic performance was at a level that was generally considered to be suitable for routine use, those results are therefore consistent with our findings.

This study shows that D-dimer, appears to be a promising biomarker in this patient population. However, more prospective studies with long-term follow-ups are necessary before any recommendations can be made.

V. CONCLUSIONS

This study was conducted to determine the association of D-dimer value as predictive marker of lymph node metastasis in breast cancer. The clinical stage and D Dimer values show a statistically significant positive connection. D-Dimer readings rise with increasing clinical stage, and vice versa. D-dimer concentrations were not affected by histological grade. A statistically significant and strong positive connection exists between D-dimer levels and axillary lymph node metastases. Metastasis to the axillary lymph nodes is more frequent when the D-dimer concentrations rise. In addition, D-dimer alone or in combination with other biomarkers may also provide an alternative to conventional sentinel node biopsy in node negative breast cancer. A significant postoperative drop in D-dimer could serve as an objective criterion for determining whether surgery was successful. D-dimer may prove to be a safe, practical, and easily accessible biomarker that can be combined with conventional sentinel node biopsy in clinically node negative breast cancer to assess metastatic disease in axilla and reduce false negative results. There is a need to conduct frequent screening programs at each health care facility level to monitor the changing trends of these carcinomas. D-dimer levels as a biomarker can be utilised at these programs. This can help us in formulating evidence informed guidelines to effectively manage further.

REFERENCES

[1]. D. Cabuk, G. Basaran, M. Teomete, et al., Clinical outcome of Turkish metastaticbreast cancer patients with currently available treatment modalities–single centerexperience, Asian Pac. J. Cancer Prev. APJCP 15 (2014) 117–122.
[2]. K. Turgut, Y. Birsen, B. Seher, M.M. Celasun, N. Seker, Babacan, The prognosticvalue of high pretreatment plasma d-dimer levels in nonmetastatic breast cancerpatients with absence of venous thromboembolism, Int. J. Hematol. Oncol. 26 (3)(2016).
[3]. H.F. Dvorak, L.F. Brown, M. Detmar, et al., Vascular permeability factor/vascularendothelial growth factor, microvascular hyperpermeability, and angiogenesis, Am.J. Pathol. 146 (1995) 1029–1039.
[4]. L. Knowlson, S. Bacchu, S. Paneesha, et al., Elevated D-dimers are also a marker ofunderlying malignancy and increased mortality in the absence of venous throm-boembolism, J. Clin. Pathol. 63 (2010) 818–822.
[5]. Falanga, F.R. Rickles, Pathophysiology of the thrombophilic state in cancer pa-tient, Semin. Thromb. Hemost. 25 (1999) 173–182.
[6]. D. Green, K. Maliekel, SushkoE, Akhtar R, SoffGA. Activatedprotein-C resistance incancer patients, Haemostasis 27(1997) 112–118.
[7]. W.P. Mielicki, M. Tenderenda, P. Rutkowski, K. Chojnowski, Activation of bloodcoagulation and the activity of cancer procoagulant (EC 3.4.22.26) in breast cancerpatients, Cancer Lett. 46 (1999) 61–66.
[8]. Mz Khan, M.S. Khan, F. Raziq, A.M. Khattak, Fibrinogen degradation products andD-Dimer in patients with breast carcinoma, Gomal J. Med. Sci. 5 (2007) 9–12.
[9]. Harish S, Raxith SR, Sarath CP. Role of Plasma D-Dimer Levels in Breast Cancer Patients and Its Correlation with Clinical and Histopathological Stage. Indian J Surg Oncol. 2018;9(3):307–311.
[10]. Siddiqui NA, Malik M, Wijeratne Fernando R, Sreekantan Nair A, Illango J, Gor R, et al. D-Dimer: A Potential Solution to Problems of Cancer Screening, Surveillance, and Prognosis Assessment. Cureus. 2021;13(5):4–9.
[11]. Langer F, Bokemeyer C. Crosstalk between cancer and haemostasis: Implications for cancer biology and cancer-associated thrombosis with focus on tissue factor. Hamostaseologie. 2012;32(2):95–104.