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D-Dimer Values in Carcinoma Breast: A Useful Prognostic and Diagnostic Parameter

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ABSTRACT

INTRODUCTION

Worldwide breast cancer is the most common cancer in women, accounting about 25.4% of total number of new cases of cancer in women diagnosed in 2018. [1] Progression of Cancer have close association with inflammatory response, thromboembolism and hypercoagulability in host. . Because of hypercoagulability in breast cancer more fibrin formation occurs and so more fibrinolytic products occurs. One of the best fibrinolytic product is D-Dimer.D-Dimer is a biomarker which indicates activation of hemostasis and fibrinolysis. D-Dimer plays an important role in activation of coagulation, angiogenesis, progression and invasion of tumour. [2, 3] D-Dimer is accepted as potential prognostic marker. [4, 5]

AIMS AND OBJECTIVES

To study clinicopathological profile of patients of breast carcinoma and establish any association of D-Dimer levels with tumour size, TNM stage, histopathologicalgrading, lymphnode status and receptor status (ER,PR,HER2neu)

MATERIAL AND METHODS

Histopathologicaly proven 30 cases of breast carcinoma were selected for this study. D-Dimer was measured in those patients twice, first before surgery and second after 14 days (2 weeks) of surgery and also other parameters like histopathological features, estrogen receptors, progesterone receptors, HER-2/neu status were studied in carcinoma breast patients.

RESULTS

Strong association seen between D-Dimer levels and TNM stage (p value 0.00941), Tumour size (p value 0.04536), histopathological grade (p value 0.00153), lymphovascular invasion (p value 0.0001), pathological lymphnode status (p value 0.0001), clinically palpable lymphnodes (p value 0.000155). After operative intervention D-Dimer levels decreased which was due to decrease in tumour load (p value <0.00001). But there was no association with ER (p value 0.104), PR (p value 0.061), HER2neu (p value 0.378) status.

CONCLUSION

Measurement of D-Dimer is a safe and easily available biomarker as diagnostic tool to predict early metastasis in breast cancer patients. It can be also used as prognostic tool in carcinoma breast patients.

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I. BACKGROUND

Worldwide breast cancer is the most common cancer in women, accounting about 25.4% of total number of new cases of cancer in women diagnosed in 2018. [1] Progression of Cancer have close association with inflammatory response, thromboembolism and hypercoagulability in host. There are evidences that in cancer biology and angiogenesis, components of coagulation and fibrinolytic system play an important role. D-dimer plays an important role in activation of coagulation, angiogenesis, progression and invasion of tumour. [2, 3] D-Dimer is a biomarker which indicates activation of hemostasis and fibrinolysis. Because of hypercoagulability in breast cancer more fibrin formation occurs and so more fibrinolytic products occurs. One of the best fibrinolytic product is D-Dimer, so D-Dimer is accepted as potential prognostic marker. [4, 5] D-Dimer levels have been found to be significantly increased in patients with breast cancer when compared with patients without carcinoma. [6, 7] In patients with breast cancer, D-Dimer levels have been shown to be elevated at the time of diagnosis and to be decreased after operative intervention during adjuvant chemotherapy. [6, 8] D-Dimer levels have been found to be correlated with clinical stage of tumour, lymphovascular invasion and axillary lymphnodes involvement in operable breast cancer and D-Dimer is suggested to be a biomarker for predicting early tumour metastases. [8, 9]

AIMS AND OBJECTIVES

To study Clinicopathological profile of patients of Breast Carcinoma.

To study Plasma D-Dimer levels in Carcinoma Breast patients preoperatively and postoperatively on day 14 (2 weeks after surgery).

To correlate plasma D-Dimer levels with Tumour Size, clinical stage of tumour, Histopathological Grading and lymph node status.

To evaluate plasma D-Dimer values in molecular basis of carcinoma breast.

II. MTERIAL AND METHODS

STUDY POPULATION AND SAMPLE SIZE:-

All patients with breast lump were admitted in MMIMSR hospital, Mullana, Ambalafrom September 2018 to 2020 and detailed history with clinical examination was carried out. All the findings were recorded in proforma. All these patients were investigated based on triple assessment by clinical examination, radiology (Ultrasound of breast/Mammography) and histopathological studies (FNAC/Biopsy) of breast lump. Histopathologicaly proven 30 cases of breast carcinoma who gave their consent were selected for this study

SAMPLING PROCEDURE AND DATA COLLECTION:-

The baseline parameters like D-Dimer was measured in those patients twice, first before surgery and second after 14 days (2 weeks) of surgery and also other parameters like histopathological features, estrogen receptors, progesterone receptors, HER-2/neu status were studied in carcinoma breast patients. 5ml blood sample was taken and centrifuged within 4 hours of blood withdrawal from vein. This centrifuged plasma was stored at -80^0C until assays were run. Quantitative D-Dimer levels were measured. D-Dimer level <0.50microgram/ml FEU (Fibrinogen Equivalent Units) was considered to be normal.

STUDY DESIGN :-

Surgically removed breast cancer tissues were studied for Histopathological features and grading. Tumour, Node, Metastasis Staging (TNM staging) was used for clinical staging of tumour. ER, PR, HER2neu receptors status were checked by IHC testing of sample and their correlation with D-Dimer levels were established.

STATISTICAL ANALYTIC PLAN:-

Statistical analysis was done by using One Way ANOVA and Student T test.

Inclusion criteria :

All the cases of Carcinoma Breast Diagnosed by triple assessment method and operated in MMIMSR.

Patient of any age group, both sex will be included in this study.

Exclusion criteria :

All the cases of Breast carcinoma Operated outside the MMIMSR.

All the cases of breast carcinoma who have procured chemotherapy/radiotherapy in the past.

Other concurrent conditions known to increase D-Dimer levels like DVT (Deep Vein Thrombosis), pregnancy, carcinoma of lung, prostate, cervix and colon, will be excluded from the study.

III. RESULTS

TABLE 1: Age wise distribution of patients of Carcinoma Breast.

Age (years)	Number of Patients	Percentage (%)
<35 years	1	3 %
35 – 45 years	14	47%
46 – 55 years	11	37%
56 – 65 years	1	3%
>65 years	3	10%
TOTAL	30	100 %

In this study age of patients ranged between 34-74 years with mean age of 47.9 years. Highest number of patients were in age group of 35-45 year 47% (14 out of 30) and lowest in age group < 35 year 3% (only one patient). In our study minimum age of diagnosed carcinoma breast was 34 year and maximum age was 74 year.

Groups	D-Dimer level (mg/l)	No. of PreoperativeCa. breast patients	No. of Postoperative Ca. breast patients.
I	< 0.25	1	1
II	≥ 0.25 – ≤ 0.5	6	6
III	>0.5 – ≤ 1	8	10
IV	>1 – ≤ 2	12	11
V	>2	3	2
	TOTAL	30	30

TABLE 2: Levels of D-Dimer in Carcinoma Breast patients (preoperative and postoperative)

In our study minimum value of plasma D-Dimer was 0.22 mg FEU/l and maximum value was 2.66 mg FEU/l (seen in stage IV metastatic disease). Maximum number of patients were in the bracket having D-Dimer levels of > 1 - ≤ 2 (Preoperatively 12 out of 30 and postoperatively 11 out of 30).

DIAGRAM 3: Distribution of carcinoma breast patients in various TNM stages of breast cancer

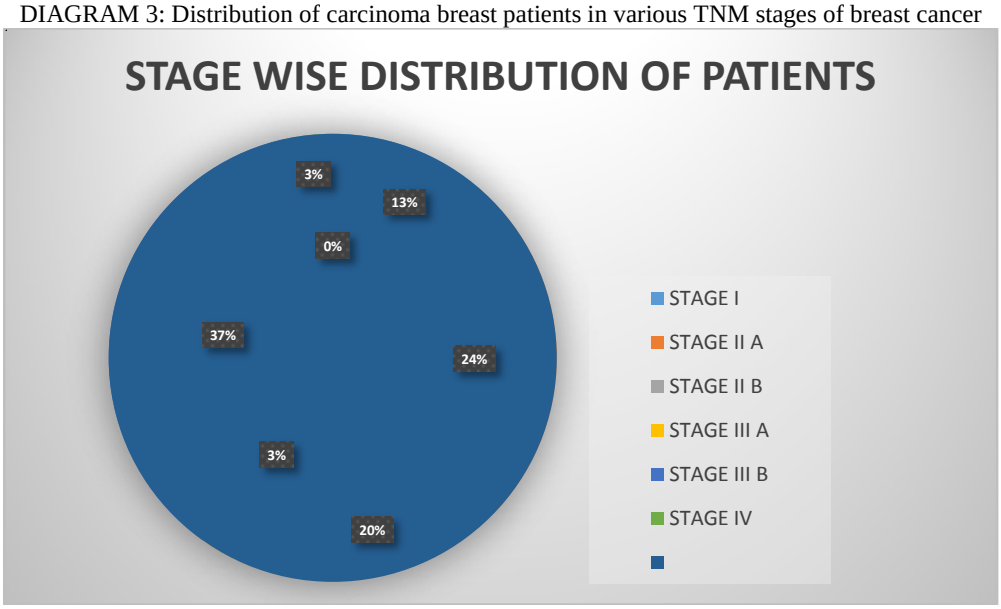


Diagram 3 shows that maximum number (11) of carcinoma breast patients were in stage III B at the time of presentation which accounted approximately 36.67 % of all patients with carcinoma breast included in this study.

TABLE 4A: Comparison between clinical stage of tumour (TNM) & mean values of preoperative/postoperative plasma D-Dimer levels.

Stage of disease	Number of patients (%)	Mean of D-Dimer level (mg/l) Preoperative	Standard Deviation of preoperative D-Dimer Levels	Mean of D-Dimer level (mg/l) Postoperative	Standard Deviation of postoperative D-Dimer levels
Stage I	4 (13.33%)	0.3675	0.138	0.355	0.148
Stage IIA	7 (23.33%)	0.95571	0.346	0.864286	0.284
Stage IIB	6 (20%)	1.045	0.436	0.965	0.360
Stage III	12 (40%)	1.2933	0.511	1.21167	0.508
Stage IV	1 (3.33%)	2.66	-	2.58	-
F value		4.763034		4.727954	
p value (< 0.05)		0.00941**		0.00954**	

In our study plasma D-Dimer levels increased with advancement/progression of stage of disease and this result was statistically significant with p value 0.00941 ($p < 0.05$, significant).

DIAGRAM 4: Mean of preoperative and postoperative D-Dimer levels distributed according to the clinical stage of disease.

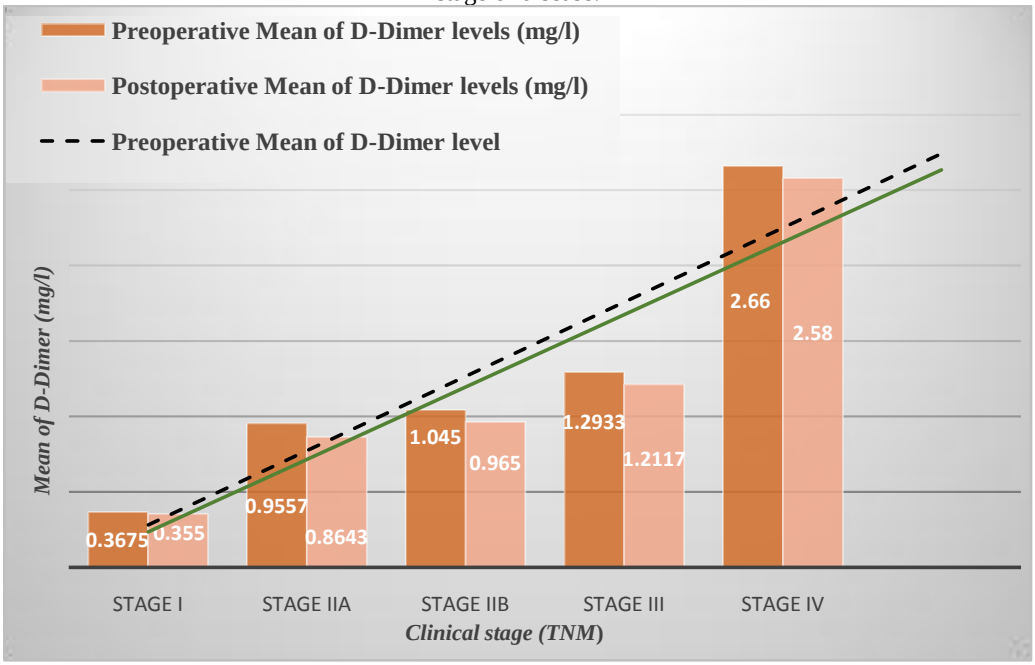


Diagram 4 showed increment in D-Dimer levels with progression of clinical stage. After operative intervention levels of D-Dimer showed decreasing trend.

TABLE 4B: Comparison between mean values of preoperative & postoperative D-Dimer levels in each stage of tumour individually.

Stage of disease	Number of patients	Mean of D-Dimer level (mg/l) Preoperative	Mean of D-Dimer level (mg/l) Postoperative	t-score	P-Value (< 0.05)
I	4	0.3675	0.355	1.987	0.141
II	13	0.9969231	0.9107692	4.041	0.002**
III	12	1.2933	1.21167	3.819	0.00142**
IV	1	2.66	2.58	-	-
TOTAL	30	1.135	1.10167		

TABLE 5A: Comparison between increasing size of tumour and mean values of D-Dimer levels preoperatively/postoperatively.

Tumour size	Number of patients	Percentage (%)	Mean of D-Dimer (mg/l) Preoperative	Mean of D-Dimer (mg/l) Postoperative
T_1 (< 2cm)	5	16.67 %	0.516	0.4860
T_2 (2-5cm)	9	30 %	1.07	0.9688
T_3 (> 5cm)	5	16.67 %	1.052	0.9880
T_4(Any size, direct extension to chest wall/ skin)	11	36.66 %	1.3763	1.2981
p value (< 0.05)			0.04536**	0.04661**

TABLE 5B: Comparison between mean value of Preoperative and Postoperative D-Dimer levels in each T stage of tumour individually.

Tumour size (Number Of patients)	Mean of D-Dime (mg/l) Preoperative	Std. deviation of D-Dimer (mg/l) Preoperative	Mean of D-Dimer (mg/l) Postoperative	Std. deviation of D-Dimer (mg/l) Postoperative	t-score	P-value (< 0.05)
T_1 (5)	0.516	0.353	0.486	0.31958	1.6514	0.087
T_2 (9)	1.07	0.3855	0.9689	0.3232	3.7448	0.00283**
T_3 (5)	1.052	0.6420	0.9880	0.6021	2.371	0.384**
T_4 (11)	1.3763	0.6235	1.2981	0.6215	3.3598	0.00362**

Table 5A and 5B showing that with increasing size of tumour, mean values of Pre/Post operative D-Dimer levels increased and after removal of tumour, D-Dimer levels decreased in T_2, T_3, T_4tumour but not in T_1 as there was no lymphovascular invasion in T_1. This result was statistically significant with p value <0.05

DIAGRAM 5: Mean values of preoperative and postoperative D-Dimer levels distributed according to the size (T) of tumour.

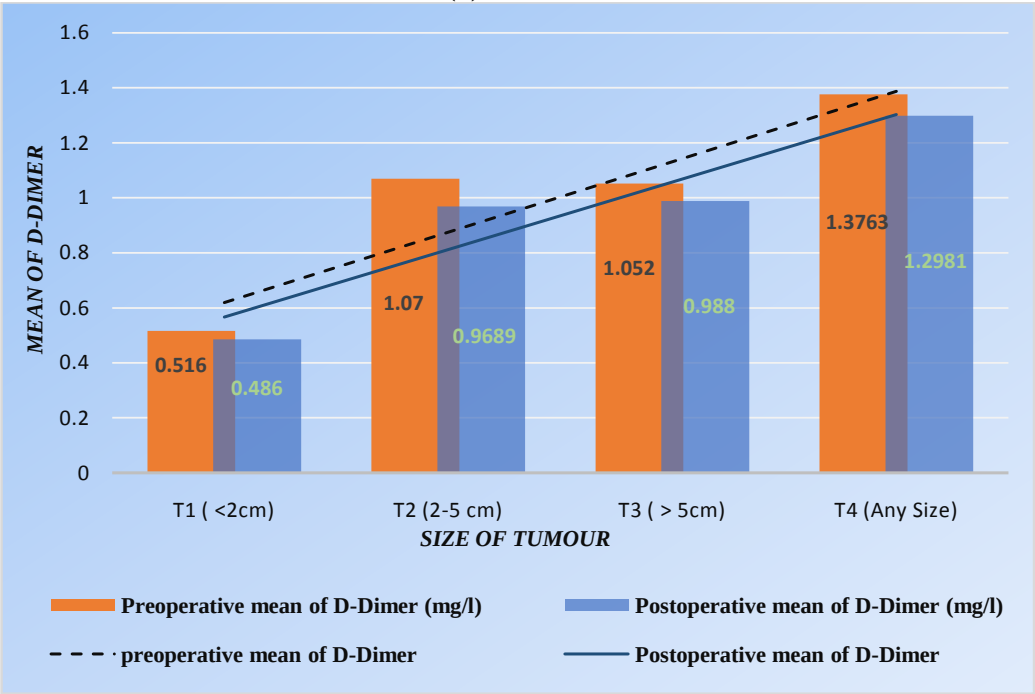


Diagram 5 showing that Mean values of preoperative D-Dimer levels rose with increasing size of tumour (in cm) and after surgery levels decreased due to decrease in tumour load.

TABLE 6A: Standard deviation and mean values of preoperative and postoperative D-Dimer levels distributed according to the histopathological grade of tumour.

		N	Mean	Std.Deviation	F-value	p value
Preoperative	Grade I	8	0.510	0.277	8.3238	0.00153**
	Grade II	13	1.241	0.425		
	Grade III	9	1.378	0.647		
Postoperative	Grade I	8	0.486	0.248	7.231	0.003**
	Grade II	13	1.158	0.385		
	Grade III	9	1.271	0.668		

In Table 6A we could find out correlation between increase in histopathological grading and D-Dimer values. Values increased with the increasing histopathological grading of tumour which was statistically significant with p value < 0.05.

TABLE 6B: Comparison between mean value of preoperative & postoperative D-Dimer levels in each grade of tumour individually.

Mean of D-dimer levels (mg/l)	Grade I (8)	Grade II (13)	Grade III (9)
Preoperative	0.51	1.24	1.38
Postoperative	0.49	1.16	1.27
t score	1.7438	4.2763	4.0722
p value (<0.05)	0.06236	0.00054**	0.00179**

DIAGRAM 6: Mean values of preoperative and postoperative D-Dimer levels distributed according to the histopathological grade of tumour.

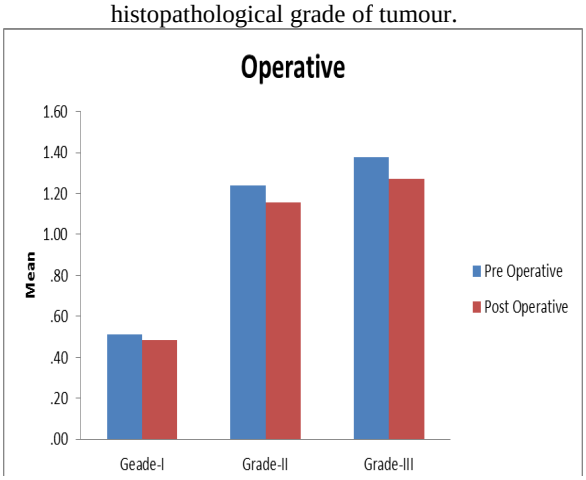


Diagram 6 showing that D-Dimer level decreases in postoperative period in all grade of tumour.

TABLE 7A: Comparison between Lymphovascular invasion of tumour on histopathology report and mean values of Pre/Post Operative D-Dimer levels.

Lymphovascular invasion		N	Mean	Standard Deviation	t value	p value (<0.05)
Preoperative	Yes	21	1.315	0.486	5.294	0.0001**
	No	9	0.470	0.147		
Postoperative	Yes	21	1.253	0.483	4.841	0.0001**
	No	9	0.452	0.142		

Table 7A showing that both pre and post operative mean values of plasma D-Dimer levels were found raised in patients with lymphovascular invasion of tumour cells on histopathology report. This was statistically highly significant with p values 0.0001 for both.

TABLE 7C: Comparison between mean values of pre & postoperative D-Dimer levels according to lymphovascular invasion of tumour.

Lymphovascular invasion	Mean of D-dimer levels		Mean difference	t score	p value (<0.05)
	Preoperative	Postoperative			
Yes (21)	1.35	1.253	-0.1	6.2504	0.000002**
No (9)	0.470	0.452	-0.02	2.3985	0.02164**

D-Dimer levels decreased postoperatively in both the groups. However p value was statistically highly significant (0.000002) in group with lymphovascular invasion.

TABLE 7D: Comparison between clinically palpable lymphnodes (cN) status and mean values of preoperative plasma D-Dimer levels.

Lymphnode status (N)	Number of patients	Percentage (%)	Mean of D-Dimer Preoperative(mg/l)
Positive (clinically palpable)	15	50%	1.45067
Negative (clinically not palpable)	15	50%	0.72333
t score	4.37026		
p value	0.000155**		

Mean value of preoperative plasma D-Dimer levels was higher in Ca. breast patients with clinically palpable lymphnodes which was statistically significant with p value 0.000155.

DIAGRAM 7: Lymphovascular invasion of tumour and mean value of D-Dimer levels preoperative and postoperative

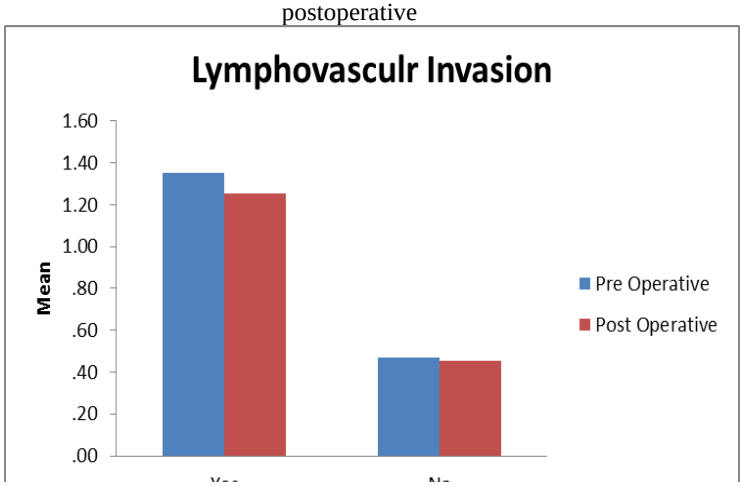


TABLE 8A: Comparison between oestrogen receptor status and mean value of D-Dimer levels preoperatively/postoperatively.

ER Status		N	Mean	Mean difference	Standard Deviation	t-value	p value (< 0.05)
Pre Operative	Positive	25	1.010	0.464	0.518	1.683	0.104
	Negative	5	1.474		0.780		
Post Operative	Positive	25	0.940	0.434	0.491	1.648	0.111
	Negative	5	1.374		0.759		

TABLE 9A: Comparison between progesterone receptor status and mean value of D-Dimer levels preoperatively/postoperatively.

PR Status		N	Mean	Std. Deviation	t-value	p-value (< 0.05)
Preoperative	Positive	24	0.988	0.533	1.948	0.061
	Negative	6	1.482	0.646		
Postoperative	Positive	24	0.920	0.502	1.910	0.066
	Negative	6	1.382	0.640		

We could infer from the above tables (8A & 9A) that patients with negative ER, PR status showed higher mean values of D-Dimer levels in comparison to ER, PR positive patient and this pattern continued even in postoperative patients. But it was not found statistically significant. Similar finding we could see in the bar diagram. (cf diagram 8, 9)

TABLE 8B: Comparison between mean values of pre & postoperative D-Dimer levels according to oestrogen receptor status.

ER Status	Mean of D-dimer levels		Mean Difference	t score	p value (<0.05)
	Preoperative	Postoperative			
Positive	1.010	0.940	-0.07	4.7197	0.00004**
Negative	1.474	1.374	-0.1	3.4711	0.01278**

TABLE 9B: Comparison between mean values of pre & postoperative D-Dimer levels according to progesterone receptor status.

PR Status	Mean of D-dimer levels		Mean Difference	t score	p value (<0.05)
	Preoperative	Postoperative			
Positive (24)	0.988	0.920	-0.07	4.46012	0.00009**
Negative (6)	1.482	1.382	-0.1	4.25115	0.00404**

This tables (8B & 9B) showing that plasma D-Dimer levels decreased after operative intervention in both ER/PR positive and negative patients, which was statistically significant (P values for ER positive 0.00004, ER negative 0.01278 and for PR positive 0.00009, PR negative 0.00404). It was highly significant in ER & PR positive patients. Similar finding we could see in the bar diagram. (cf diagram 8, 9)

DIAGRAM 8: Comparison between oestrogen receptor status and mean value of D-Dimer levels preoperatively and postoperatively.

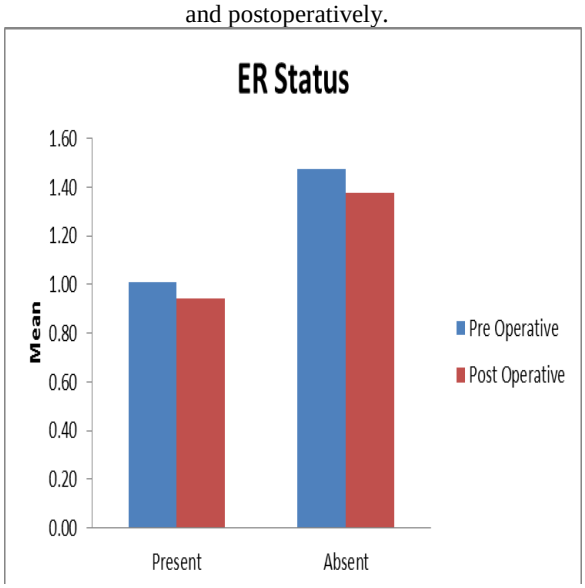


DIAGRAM 9: Comparison between progesterone receptor status and mean value of D-Dimer levels preoperatively and postoperatively.

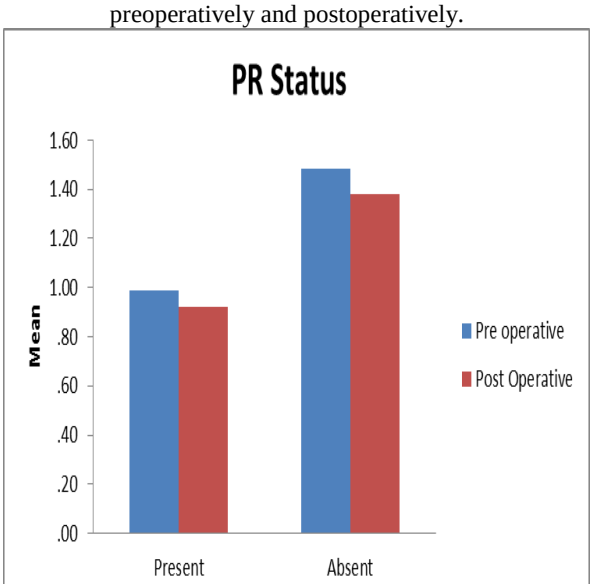


TABLE 10A: Comparison between HER-2/neu status and mean values of D-Dimer levels preoperatively/postoperatively.

HER-2neu Status		N	Mean	Standard Deviation	t-value	p-value
Preoperative	Positive	14	0.985	0.565	0.897	0.378
	Negative	16	1.176	0.598		
Postoperative	Positive	14	0.895	0.513	1.094	0.283
	Negative	16	1.116	0.582		

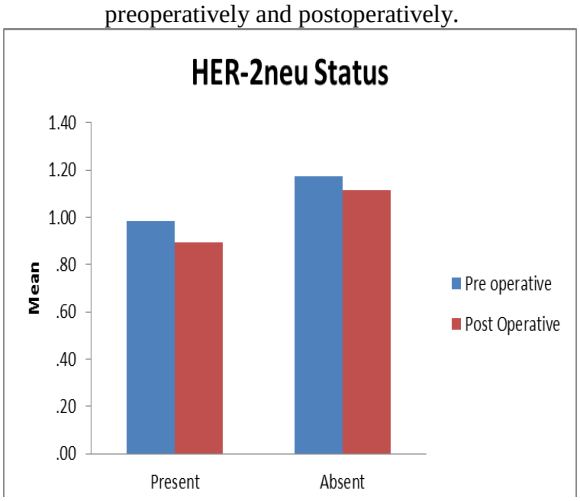
There was no direct correlation between HER-2/neu status and D-Dimer values in patients with carcinoma breast.

TABLE 10B: Comparison between mean values of pre & postoperative D-Dimer levels according to HER-2/neu receptor status.

HER-2/neu Status	Mean of D-dimer levels		Mean Difference	t score	p value
	Preoperative	Postoperative			
Positive (14)	0.985	0.895	-0.09	3.77223	0.00116**

Negative (16)	1.176	1.116	-0.06	4.72599	0.00014**

DIAGRAM 10: Comparison between HER-2neu receptor status and mean value of D-Dimer levels preoperatively and postoperatively.



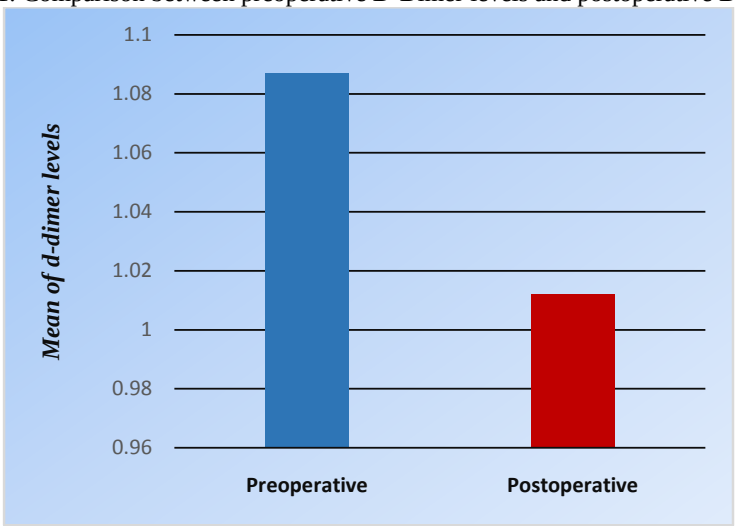
Value of D-Dimer decrease in both HER-2/neu positive and negative status patients postoperatively, but patient with HER-2/neu negative status had statistically higher significant (0.00014) changes in comparison with HER-2/neu positive patients (0.00116).

TABLE 11: Comparison between mean value preoperative D-Dimer levels and postoperative D-Dimer levels.

	Mean of D-Dimer levels	Mean difference	T score	p-value (<0.05)
Preoperative	1.087	0.075	5.6698	0.00000198**
Postoperative	1.012			

This table shows that 2 weeks after operative intervention D-Dimer levels decreased significantly with p value <0.00000198. (cf diagram 11)

DIAGRAM 11: Comparison between preoperative D-Dimer levels and postoperative D-Dimer levels.



IV. Discussion:

30 patients of histologically proven breast carcinoma were selected for this study. Purpose of this study was to investigate significance of plasma D-Dimer level as diagnostic and prognostic tool in carcinoma breast patients. In this study we measured plasma D-Dimer levels preoperatively and postoperatively on day 14 (2 weeks after surgical intervention) in those 30 patients and did statistical analysis to establish any correlation of

preoperative and postoperative plasma D-Dimer levels with other variables like clinical stage of tumour, size of tumour, hisopathological grading, lymphnode status and biomolecular markers (ER, PR, HER2/neu status).

In our study plasma D-Dimer levels increased with advancement/progression of stage of disease and this result was statistically significant with p value 0.00941 ($p < 0.05$, significant). This result was in accordance with studies done by Srivastava V et al (p value 0.006) [10], Choudhary GS et al (p value 0.016) [11], DrSumita A Jain et al (p value 0.0025) [12], Rajendran G et al (p value 0.029) [13], Harish et al (p value 0.002) [14], Bhavesh D et al (p value 0.011) [16], Dirix LY et al (p value 0.0001) [15]. All these studies concluded that plasma D-Dimer level would increase with progression of the stage of disease.

Plasma D-Dimer levels increased with increasing size of tumour which was statistically significant with p value 0.04536 ($p < 0.05$) in our study. Same result was observed in studies done by Choudhary GS et al (p value 0.014)[11], Bhavesh D et al (p value 0.023) [16], Blackwell et al (p value 0.008) [17].

There was an elevation in plasma D-Dimer levels with increasing histopathological grading of tumour, which was statistically significant with p-value 0.00153 ($p < 0.05$). Similar result is seen in various studies conducted by Choudhary GS et al (p value 0.007) [11], Sapna P et al (p value 0.015)[18], Harish S et al (p value 0.001) [14], Bhavesh D et al (p value 0.002) [16], Dirix LY et al [15], Blackwell et al [17], all these studies concluded that there was significant correlation between elevated plasma D-Dimer levels and histopathological grades of breast cancer. So a patient with high preoperative D-Dimer level have strong possibility to have high grade tumour and axillary lymphnode involvement with poor overall survival. Thus Carcinoma breast patient with high grade tumour and axillary node metastasis have poor overall survival. Preoperative quantitative D-Dimer measurement can be a good marker to predict high grade tumour and axillary lymphnode involvement preoperatively and to denote overall survival rate after operative intervention.

In our study out of 30 patients 21 had lymphovascular invasion and positive lymphnodes on histopathology of surgical specimen. A mean value of preoperative D-Dimer levels were high in patients with lymphovascular invasion and pathologically positive lymphnodes (1.315) than patients without lymphovascular invasion and pathologically negative lymphnodes (0.470) which falls within normal limit of plasma D-Dimer level (< 0.50 mg FEU/l).So we can say that plasma D-Dimer levels increased with lyphovascular invasion and lymphnode involvement by tumour cells which was statistically significant with p value 0.0001 for both ($p < 0.05$). This result was supported by various studies conducted by Srivastava V et al (p value 0.001) [10], Choudhary GS et al (p value 0.0004) [11], Rajendran G et al (p value 0.018) [13], Blackwell et al (p value 0.0002) [17], Harish S et al (p value 0.02 for lymphovascular invasion, p value 0.001 for lymphnode involvement) [14], Bhavesh D et al (p value 0.00017) [16]. All these studies concluded that high preoperative plasma D-Dimer is strongly associated with lymphnode metastasis and lymphovascular invasion.

In our study out of 30 patients 15 patients had clinically palpable lymphnodes with mean value of preoperative D-Dimer levels 1.45067 which was higher than mean value of preoperative D-Dimer levels of patients without clinically palpable lymphnodes (0.7233). The difference was statistically highly significant with p value 0.00015 ($p < 0.05$). This result showed strong association between high preoperative D-Dimer level and possibility of lymphnode involvement just on basis of blood investigation report.This result was in accordance with studies done by Sapna P et al (p value 0.003) [18], Blackwell et al (p value 0.0001) [17], Known et al (p value 0.027) [11], Xu G et al ($p < 0.01$) [19], Liu et al (Spearman correlation coefficient 0.389, $p<0.001$) [20], Harish S et al (p value 0.005) [14].

We analysed our patients who had proven lymphovascular invasion and positive lymphnodes on histopathological examination and compared with radiological and clinical findings and we found out that only 15 out of 21 patients had clinically palpable axillary lymphnodes and incidentally those 15 cases showed axillary lymphadenopathy on radiological investigations. All those 15 patients had high preoperative plasma D-Dimer levels with a mean value 1.45067. Remaining 6 patients had no clinically palpable axillary lymphnodes (cN) and no axillary lymphadenopathy on radiological investigation but they had raised preoperative D-Dimer levels (0.94 mg FEU/l, 0.96 mg FEU/l, 1.28 mg FEU/l, 1.39 mg FEU/l, 1.13 mg FEU/l, 0.92 mg FEU/l).

Thus we could conclude that D-Dimer has good diagnostic value for prediction of lymphovascular invasion preoperatively irrespective of lymphnodes status on clinical examination and radiological investigations without doing sentinel lymphnode biopsy

We can combine D-Dimer value with sentinel lymphnode biopsy to reduce false negative results. So D-Dimer could be used to pick up even micro-metastasis of cancer cells.

We had observed in our study that high preoperative plasma D-Dimer levels were strongly associated with high possibility of lymphovascular invasion, lymphnode metastasis and high grading of tumour.

In our study we could not establish any correlation between D-Dimer level and hormonal receptors status(ER, PR, HER2/neu status).

Mean value of Preoperative plasma D-Dimer levels was 1.0857 and postoperative plasma D-Dimer levels was 1.012, mean difference 0.075, t score 5.6698, p value 0.00000198 ($p < 0.05$). This result showed that after operative intervention D-Dimer level decreased which might be due to decrease in tumour load and no more lymphovascular invasion after surgery.This result in accordance with a various studies conducted by Sapna et al[18], Xu G et al [19], Rajendran G et al[13], Srivastava V et al[10].

V. Conclusion:

From the observations we got in our study showed clearly that D-Dimer value can be safely utilised for diagnostic and prognostic implications in cases of carcinoma breast. As the disease progresses in form of size of the tumour, palpability of lymphnodes, histological presence of lymphovascular invasion and metastatic lymphnodes and poor histopathological grading of tumour, direct correlation of increased plasma D-Dimer levels were observed in all the parameters in our study which is in accordance with the different studies done elsewhere.In case of hormonal status (ER, PR, HER-2/neu) no linear direct correlation could be observed.A significant finding of our study was fall in the levels of D-Dimer after surgery (2 weeks) which was found to be highly significant statistically with p value < 0.0001.

So we can safely conclude that D-Dimer should be made as a part of routine workup of the patients of Ca. breast which may guide us about the prognosis right in the begining.D-Dimer is a good biomarker to assess the status of Ca. breast particularly lymphovascular invasion but it requires further studies and long term follow up to make it as a standard diagnostic/prognostic tool.

Bibliography:

[1]. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians. 2018 Nov;68(6):394-424.

[2]. Rickles FR, Edwards RL. Activation of blood coagulation in cancer: Trousseau's syndrome revisited.1983:14-31.

[3]. Dvorak HF, Brown LF, Detmar M, Dvorak AM. Vascular permeability factor/vascular endothelial growth factor, microvascular hyperpermeability, and angiogenesis. The American journal of pathology. 1995 May;146(5):1029-39.

[4]. Nagy Z, Lővey J, Szántó A, Végső G. Biomarkers in solid tumors. MagyOnkol. 2013 Feb 10;57(1):56-62.

[5]. Khan MZ, Khan MS, Raziq F, Khattak AM. Fibrinogen degradation products and d-dimers in patients with breast carcinoma. Gomal Journal of Medical Sciences. 2007 Jun 30;5(1):9-12.

[6]. Ay C, Vormittag R, Dunkler D, Simanek R, Chiriac AL, Drach J, Quehenberger P, Wagner O, Zielinski C, Pabinger I. D-dimer and prothrombin fragment 1+ 2 predict venous thromboembolism in patients with cancer: results from the Vienna Cancer and Thrombosis Study. Journal of Clinical Oncology. 2009 Sep 1;27(25):4124-9.

[7]. Ay C, Pabinger I. Test predictive of thrombosis in cancer. Thromb Res. 2010;125(Suppl2):S12-5.

[8]. Ahmed T, Ahmed RS, Basharat MU, Mushtaq MH, Gill SS, Khawaja AR, Khan MF, Khan A. Comparative study to access coagulation abnormalities in breast cancer. Advancements in Life Sciences. 2014 Feb 25;1(2):96-103.

[9]. Khangarot SS, Gupta N, Goswami B, Hadke NS, Lal P, Gupta N, Khurana N. Correlation of D dimer and factor VIII levels with histopathology in patients with breast carcinoma. Cancer Biomarkers. 2010 Jan 1;7(6):305-14.

[10]. Srivastava V, Rai N, Ahmad S, Singh V, Kumar S. Correlation of coagulation markers with axillary lymph node metastasis in breast malignancy: a tertiary care centre study in North India. International Surgery Journal. 2020 Mar 26;7(4):1045-50.

[11]. Choudhary GS, Bairwa MS, Choudhary A, Singodia R. Correlation of coagulation markers with axillary lymph node metastasis in carcinoma breast. Journal of Evolution of Medical and Dental Sciences. 2017 Nov 27;6(91):6449-54.

[12]. DrSumita A Jain, DrAtulAmeta, DrMohitBudhgurjar, Dr Harish Chand choudhary, DrMohd. Irfan, DrLaxman Agarwal, D–Dimer : A helping tool in determining the prognosis in Breast Carcinoma, INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH : Volume-7 | Issue-9 | September-2018

[13]. Rajendran G, Aravind D, Venkatesh P, Anandan H. Correlation of coagulation markers with axillary lymph node metastasis in carcinoma breast. International Surgery Journal. 2018 Mar 23;5(4):1394-8.

[14]. Harish 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 Sep 1;9(3):307-11.

[15]. Dirix LY, Salgado R, Weytjens R, Colpaert C, Benoy I, Huget P, Van Dam P, Prove A, Lemmens J, Vermeulen P. Plasma fibrin D-dimer levels correlate with tumour volume, progression rate and survival in patients with metastatic breast cancer. British journal of cancer. 2002 Feb;86(3):389-95.

[16]. Bhavesh D, Kapil Dev N, Sudershan S, Jaswal S. Evaluation of plasma D-Dimer level as a predictve marker of advanced carcinoma breast. J Clin Case Rep. 2015;5(547):2.

[17]. 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. Journal of Clinical Oncology. 2000 Feb 1;18(3):600-608.

[18]. Patel S, Rashmi C, Harish S. D-Dimer Levels In Breast Carcinoma: A Clinico-Pathologic Study. Annals of Pathology and Laboratory Medicine. 2018 Mar 22;5(3):A221-227.

[19]. Xu G, Zhang YL, Huang W. Relationship between plasma D-dimer levels and clinicopathologic parameters in resectable colorectal cancer patients. World Journal of Gastroenterology. 2004 Mar 15;10(6):922.

[20]. Liu L, Zhang X, Yan B, Gu Q, Zhang X, Jiao J, Sun D, Wang N, Yue X. Elevated plasma D-dimer levels correlate with long term survival of gastric cancer patients. PloS one. 2014 Mar 11;9(3):e90547.

XXXXXXXXX, et. al. "D-Dimer Values in Carcinoma Breast: A Useful Prognostic and Diagnostic Parameter." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 22(1), 2023, pp. 41-51.