ORIGINAL ARTICLE

FIBRINOGEN DEGRADATION PRODUCTS AND D-DIMERS IN PATIENTS WITH BREAST CARCINOMA

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ABSTRACT

Background: Many patients with cancer are complicated by disseminated intravascular coagulation. This study was aimed to determine the level of Fibrinogen Degradation Products and D-Dimers at various stages in patients suffering from breast carcinoma.

Material and Methods: This was a cross-sectional study conducted in the Department of Pathology, Postgraduate Medical Institute, Lahore, Pakistan, from June 2003 to June 2004. Sampling method was by convenience. Two groups were taken; Group-1 including 50 patients with breast carcinoma and Group-2 comprising of 25 healthy controls. Fibrinogen Degradation Products and D-Dimer levels were estimated in the blood and the results compared.

Results: Out of 50 patients, 28 (56%) had Fibrinogen Degradation Products >40 μg/ml; 13 (26%) in stage-III and 15 (30%) in stage-IV. 15 (30%) patients had levels between 5-40μg/ml; 8 (16%) in stage-II and 7 (14%) in stage-III. Only 7 (14%) had levels <5μg/ml; 3 (6%) in stage-II and 4 (8%) in stage-III. Similarly, 8 (16%) patients had D-Dimers level 1000-2000·g/ml; 1 (2%) in stage-III and 7 (14%) in stage-IV. 11 (22%) patients had D-Dimers level 500-1000·g/ml; 6 (12%) in stage-III and 5 (10%) in stage-IV. 30 (60%) had D-Dimers level 250-500·g/ml; 9 (18%) in stage-II, 18 (36%) in stage-III and 3 (6%) in stage-IV. Only 1 (2%) patient had D-Dimer level <250·g/ml.

Conclusion: Levels of Fibrinogen Degradation Products and D-Dimers are elevated in breast carcinoma, especially in those with distant metastasis.

Key words: Fibrinogen Degradation Products, D-Dimer, Carcinoma Breast.

INTRODUCTION

The relationship between malignancy and thrombosis is known for over 100 years. Thromboembolism is present in almost half of cancer patients at autopsy and there is a higher incidence of occult malignancy in patients with deep vein thrombosis. Thrombosis in cancer often is migratory and may involve superficial veins and relatively unusual sites. The hypercoagulable state of malignancy is due to a complex interaction of tumor cells and their products with the host cells leading to various degrees of impairment of the normal defense mechanisms that ordinarily protect the host against thrombogenesis. Tumor cells can activate directly the blood clotting cascade and cause thrombosis or can induce pro-coagulant properties and inhibit the anticoagulant ones of the vascular endothelial cells, platelets, monocytes and macrophages. In the setting of the local and systemic effects of cancer, this basic pathophysiology conspires to make cancer, perhaps the best example of "acquired thrombophilia.[1]

In laboratory, the evidence of intravascular coagulation can be readily obtained. These patients may have thrombocytopenia, falling fibrinogen levels and raised fibrinogen degradation products (FDP) but these represent only the decompensated form of disseminated intravascular coagulation (DIC), while a larger proportion of patients have evidence of compensated DIC. Thrombocytosis with functional defects such as reduced adhesion, aggregation and clot retraction may also be observed.[2,3]

Most patients with cancer are complicated by acute DIC having elevated FDPs and D-Dimers levels. The likelihood of increased FDPs is greater in patients with metastases as compared to localized disease and may have prognostic value. Detection of FDPs and D-Dimers are useful for the rapid diagnosis of DIC.[3]

Plasma D-Dimers are the specific derivatives of cross-linked fibrin, which are produced when fibrin is degraded by plasmin and concentrations are raised by thrombolysis. Plasma D-Dimers esti-

mation is a significant advancement over the historic assay for FDPs. It identifies specifically, the presence of cross-linked fibrin derivatives without interference from fibrinogen and non-cross-linked fibrin and therefore identifies intravascular thrombosis and fibrinolysis as distinct from fibrinogenolysis. Because of high specificity of D-Dimers, monoclonal antibodies can be used on plasma samples, thereby differentiating fibrinolysis from fibrinogenolysis and conferring an advantage over the standard assay for FDPs.[4,5]

D-Dimer is the only test that directly addresses both thrombin and plasmin generation i.e. generation of thrombin resulting in a cross-linked fibrin clot and of plasmin resulting in the lysis of cross-linked fibrin clot.[6] The use of a rapid and sensitive D-Dimer test for the diagnosis and follow-up during the treatment of DIC and thrombolytic therapy may give a better understanding of the formation and dissolution of fibrin in thrombotic disease.[7] Detection of fragment D-Dimer therefore offers a unique advantage over other laboratory tests for DIC because it addresses both dimensions of DIC.[1,6,8] D-Dimer is a molecular marker of tumor growth and metastasis in breast cancer patients. Patients with lymph mode metastasis have D-Dimer level greater than those with localized disease.[9] Estimation of D-Dimers and FDPs are very useful for the rapid diagnosis of DIC.[10]

The aim of this study was to assess the levels FDPs and D-Dimers in patients with breast carcinoma at different stages.

MATERIAL AND METHODS

This cross-sectional study was conducted in the Department of Pathology, Postgraduate Medical Institute, Lahore, Pakistan, from June 2003 to June 2004. Sampling method was by convenience. Two groups were taken; Group-1 including 50 patients with breast carcinoma and Group-2 including 25 normal healthy controls. Patients with breast carcinoma were staged according to the standard TNM sstem.

Four milliliters of blood was taken from the antecubital vein; 1.8 ml mixed with 0.2 ml of sodium citrate for D-Dimers analysis and 2.0 ml transferred to the collection tube for FDPs estimation. The D-Dimer and FDPs analyses were performed by commercially available kits obtained from Biopool International Sweden and Remel, UK respectively, using positive and negative controls. The results obtained were analyzed.

RESULTS

Out of 50 patients, 7 (14%) had FDPs level <5 μg/ml with 3 (6%) in stage II and 4 (8%) in stage III but none in stage IV disease. Fifteen (30%) patients had FDPs levels between 5-40 μg/ml with 8 (16%) having stage II and 7 (14%) stage III disease. 28 (56%) patients had FDPs >40 μg/ml with 13 (26%) patients in stage III and 15 (30%) in stage IV but none in stage II disease. (Table-1 & 2)

In respect to D-Dimers, only 1 (2%) had D-Dimer level <250 ·g/ml. Thirty (60%) patients had levels between 250-500 ·g/ml with 9 (18%) in stage II, 18 (36%) in stage III and 3 (6%) in stage IV disease. While 11 (22%) patients had D-Dimer levels 500-1000 ·g/ml with 6 (12%) in stage III, 5 (10%) in stage IV and none in stage II disease. 8 (16%) patients had D-Dimers level 1000-2000 ·g/ml, with 1 (2%) in stage III, 7 (14%) in stage IV and none in stage II disease. (Table-3)

Table-1: Comparison of FDPs and D-Dimers in patients with Breast Carcinoma and Controls.

Parameter	Level	Healthy Controls	Patients with Breast Cancer
FDPs			
	<5 mg/ml	25	7 (14%)
	5-40 mg/ml	–	15 (30%)
	>5 mg/ml	–	28 (56%)
D-Dimers			
	<250 hg/ml	25	1 (2%)
	250-500 hg/ml	–	29 (58%)
	500-2000 hg/ml	–	20 (40%)

Table-2: FDPs in different stages of breast carcinoma.

FDPs (μg/ml	**Stage**			**Total**
	I	**II**	**III**	
>5	3 (6%)	4 (8%)	–	7 (14%)
5-40	8 (16%)	7 (14%)	–	15 (30%)
>40	–	13 (26%)	15 (30%)	28 (56%)
Total	11 (22%)	24 (48%)	15 (30%)	50 (100%)

Table-3: D-dimers in different stages of breast carcinoma.

D-Dimers(ηg/ml)	**Stage**			**Total**
	II	**III**	**IV**	
<250	1 (2%)	–	–	1 (2%)
250 – 500	9 (18%)	18 (36%)	3 (6%)	30 (60%)
500 – 1000	–	6 (12%)	5 (10%)	11 (22%)
1000 – 2000	–	1 (2%)	7 (14%)	8 (16%)
Total	10 (20%)	25 (50%)	15 (30%)	50 (100%)

DISCUSSION

In the laboratory, evidence of intravascular coagulation is readily obtained. The resultant DIC may be compensated or decompensated. The D-Dimer and FDP tests are useful for the rapid diagnosis of DIC.[11].It was observed in this study that FDPs and D-dimers are significantly raised in patients having breast cancer, especilly those with distant metastasis. These findings are in agreement to those found in some previous studies as reported by Gordon,[11] Francis,[12] and Falanga & Rickles.[1]

CONCLUSION

The levels of Fibrinogen Degradation Products and D-Dimers are elevated in breast carcinoma, especially in those with distant metastasis.

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