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Original Research

Assessment of D-Dimer levels in carcinoma of breast patients

Mukesh Kumar Jamwal[1], Suneet Katoch[2], Sanjay Kumar[3]

[1]MBBS, MS (General Surgery), Civil hospital Thural, District Kangra, Himachal Pradesh
[2]MBBS, MS (General Surgery), MGMSC, Khaneri, Rampur, Himachal Pradesh
[3]MBBS, MS (General surgery), MGMSC, Khaneri, Rampur, Himachal Pradesh

ABSTRACT:
Background: Breast carcinoma cases in India accounts for more than 1 in 10 new cancer diagnoses each year. D-dimer (or D dimer) is a fibrin degradation product (or FDP), a small protein fragment present in the blood after a blood clot is degraded by fibrinolysis. Hence; the present study was conducted with the aim of assessing D-Dimer levels in breast carcinoma patients. **Materials & methods:** A total of 30 breast carcinoma patients were enrolled. Complete demographic and clinical details of all the subjects were obtained. Radiographic and clinical examination of all the subjects was carried out. Metastatic profile was assessed. Lymph node status was analysed. Blood samples were obtained and serum D-Dimer levels were analysed. All the results were recorded and analysed by SPSS software. Student t test and chi-square test was used for evaluation of level of significance. **Results:** Mean D Dimer levels were found to be 2.45 μg/mL. In the patients with and without lymph node involvement, mean D-Dimer levels were found to be 2.83 μg/mL and 1.27 μg/mL respectively. Significant results were obtained while comparing the mean D-Dimer levels among the patients with and without lymph node involvement. **Conclusion:** Increased D-Dimer levels are an important prognostic marker of clinical stage, lymphovascular invasion, lymph node involvement, and tumor metastasis.
Key words: Breast carcinoma, D-Dimer

INTRODUCTION

Breast carcinoma cases in India accounts for more than 1 in 10 new cancer diagnoses each year. It is the second most common cause of death from cancer among women in the world. Anatomically, the breast has milk-producing glands in front the chest wall. They lie on the pectoralis major muscle, and there are ligaments support the breast and attach it to the chest wall. Fifteen to 20 lobes circularly arranged to form the breast. The fat that covers the lobes determines the breast size and shape. Each lobe is formed by lobules that contain the glands that are responsible for milk production in response to hormone stimulation.[1-3]
Cancer cells are very similar to cells of the organism from which they originated and have similar (but not identical) DNA and RNA. This is the reason why they are not very often detected by the immune system, in particular, if it is weakened. Mammography is a widely used screening approach in the detecting of breast cancer and proved to help reduce the mortality effectively. Other screening methods, such as Magnetic Resonance Imaging (MRI), which is more sensitive than mammography, have also been implemented and studied during the last decade. There're numerous risk factors such as sex, aging, estrogen, family history, gene mutations and unhealthy lifestyle, which can increase the possibility of developing breast cancer.[4-6]
D-dimer (or D dimer) is a fibrin degradation product (or FDP), a small protein fragment present in the blood after a blood clot is degraded by fibrinolysis. It is so named because it contains two D fragments of the fibrin protein joined by a cross-link. D-dimers are not normally present in human blood plasma, except when the coagulation system has been activated, for

instance because of the presence of thrombosis or disseminated intravascular coagulation.[5-7] Hence; the present study was conducted with the aim of assessing D-Dimer levels in breast carcinoma patients.

MATERIALS & METHODS

The present study was conducted with the aim of assessing D-Dimer levels in breast carcinoma patients. A total of 30 breast carcinoma patients were enrolled. Complete demographic and clinical details of all the subjects were obtained. Radiographic and clinical examination of all the subjects was carried out. Metastatic profile was assessed. Lymph node status was analysed. Blood samples were obtained and serum D-Dimer levels were analysed. All the results were recorded and analysed by SPSS software. Student t test and chi-square test was used for evaluation of level of significance.

RESULTS

Mean age of the patients was 49.25 years. No lymph node involvement occurred in 18 percent of the patients while upto three lymph node involvements occurred in 30 percent of the patients. Four to nine lymph nodes involvement occurred in 22 percent of the patients while ten or more lymph node involvement occurred in 30 percent of the patients. Mean D Dimer levels were found to be 2.45 μg/mL. In the patients with and without lymph node involvement, mean D-Dimer levels were found to be 2.83 μg/mL and 1.27 μg/mL respectively. Significant results were obtained while comparing the mean D-Dimer levels among the patients with and without lymph node involvement.

Table 1: Age-wise distribution of patients

Age group (years)	Number of patients	Percentage
Less than 30	2	4
30 to 40	7	14
41 to 50	16	32
51 to 60	17	34
More than 60	8	16
Total	50	100
Mean	49.25	

Table 2: Distribution of patients according to number of lymph node involvement

Number of lymph nodes	Number of patients	Percentage
Zero	9	18
One to three	15	30
Four to nine	11	22
Ten or more	15	30
Total	50	100

Table 3: Distribution of patients according to D-Dimer levels

D-Dimer levels (μg/mL)	Number of patients	Percentage
≤0.25	2	4
0.26 to 1	8	16
1.01 to 2	14	28
2.01 to 3	6	12
3.01 to 4	15	30
More than 4	5	10
Total	50	100
Mean ± SD	2.45	

Table 4: D-Dimer levels according to presence or absence of lymph node involvement

Lymph node involvement	Mean D-Dimer levels	SD
Present	2.83	1.36
Absent	1.27	0.89
t-statics	-4.26	
p- value	0.000 (Significant)	

DISCUSSION

The development of distant metastases is the primary cause of death in breast cancer patients. Although clinical and experimental trials have demonstrated the relationship between cancer and hemostasis but the exact mechanism is not fully understood. Thus, systemic activation of coagulation and hemostatic system in all cancer patients without thromboembolism has been still under investigation. Advanced breast cancer is either locally advanced or metastatic spread. There is correlation between cancer and hypercoagulation, global hemostasis is more frequently activated in patients with cancer. This systemic activation has been included in (angiogenesis, progression, metastatic spread) of tumor cells. The D-dimer assay depends on the binding of a monoclonal antibody to a particular epitope on the D-dimer fragment. D-Dimer is detected by various laboratory methods, mostly used is based on a different monoclonal antibody against D-dimer.[6-10] Hence; the present study was conducted with the aim of assessing D-Dimer levels in breast carcinoma patients.

Mean age of the patients was 49.25 years. No lymph node involvement occurred in 18 percent of the patients while upto three lymph node involvements occurred in 30 percent of the patients. Four to nine lymph nodes involvement occurred in 22 percent of the patients while ten or more lymph node involvement occurred in 30 percent of the patients. Mean D Dimer levels were found to be 2.45 μg/mL. Khangarot et al in their study fifty patients with diagnosed cancer breast who were treated in surgery department were evaluated for D Dimer and factor VIII levels. D-dimer and Factor VIII levels were measured three times i.e. at the time of commencement of treatment then after three cycles of Chemotherapy (CAF Regimen) and finally after six weeks of surgery. Significantly higher levels of D Dimer and factor VIII were observed in tumors with significant lymphovascular and adipose tissue invasion in comparison to localized tumors. The reduction in D-dimer and Factor VIII values after Surgery was significant for both D-dimer (p value 0.000) and Factor VIII (p value 0.000). The reduction in D-dimer after 3 cycles of chemotherapy was

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significant for D-dimer (575.51 ± 572.47 ng/ml vs. 422.45 ± 363.58 ng/ml; p value 0.046) but not significant for Factor VIII (307.83 ± 184.47 ng/ml vs. 288.78 ± 163.02 ng/ml; p value 0.151). D-dimer and factor VIII may be used as yardstick for systemic adjuvant therapy in node negative < 1 cm breast cancer. D-dimer may prove to be a safe, convenient and easily available biomarker which 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.[10] Shaker et al established whether plasma levels of d-dimer, used clinically are associated with established prognostic markers in early breast cancer. Plasma d-dimer was measured using automated ELISA in 58 patients undergoing surgery for early breast cancer. Plasma d-dimer was correlated with lymphovascular invasion (LVI), ER and PR status, tumour size, tumour grade and lymph node (LN) status. D-dimer correlated with tumour size. Although plasma d-dimer levels did not correlate with hormone receptor status (independent t-test), a raised d-dimer (>400ng/ml) was associated with PR negativity using Chi squared test. This possible relationship with PR negativity warrants further investigation. D-dimer is a potential biomarker for tumour size, LVI and lymph node positivity in early breast cancer.[11]

In the present study, in the patients with and without lymph node involvement, mean D-Dimer levels were found to be 2.83 μg/mL and 1.27 μg/mL respectively. Significant results were obtained while comparing the mean D-Dimer levels among the patients with and without lymph node involvement. Ay C et al assessed the prognostic value of D-dimer levels for overall survival and mortality risk in 1178 cancer patients. D-dimer levels were measured with a quantitative D-dimer latex agglutination assay. The main solid tumors were malignancies of the lung (n=182), breast (n=157), lower gastrointestinal tract (n=133), pancreas (n=74), stomach (n=50), kidney (n=37), prostate (n=133), and brain (n=148); 201 of the patients had hematologic malignancies; 63 had other tumors. During a median follow-up of 731 days, 460 (39.0%) patients died. The overall survival probabilities for patients with D-dimer levels categorized into four groups based on the 1st, 2nd and 3rd quartiles of the D-dimer distribution in the total study population were 88%, 82%, 66% and 53% after 1 year, and 78%, 66%, 50% and 30% after 2 years, respectively (P<0.001). The univariate hazard ratio of D-dimer (per double increase) for mortality was 1.5 (95% confidence interval: 1.4–1.6, P<0.001) and

remained increased in multivariable analysis including tumor subgroups, age, sex and venous thromboembolism. High D-dimer levels were associated with poor overall survival and increased mortality risk in cancer patients.[12]

CONCLUSION
Increased D-Dimer levels are an important prognostic marker of clinical stage, lymphovascular invasion, lymph node involvement, and tumor metastasis.

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