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Original Research Article

Comparative study of hematological parameters along with effect of chemotherapy and radiotherapy in different stages of breast cancer

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ABSTRACT

Background: Breast cancer is one of the most common malignancies found among women in India. Haematological parameters have been shown to predict severity, mortality and treatment follow-up in breast cancer patients. The aim of the study was to compare haematological parameters along with effect of chemotherapy and radiotherapy in different stages of breast cancer patients.
Methods: Total 235 human subjects were taken in the study. Out of which 100 normal ages matched healthy subjects were considered as controls and 135 breast cancer patients subjects as cases which were further divided into their respective stages according to TNM classification.
Results: Estimation of haematological parameters was done by Sysmex Automated Hematology Analyzer Kx-21. The statistical differences between cases and control were determined by using student independent sample t-test.
Conclusions: We found hemoglobin level, polymorphs, lymphocytes, monocytes and RBC count were statistically reduce ($p<0.05$) while other parameters were non-significant as compared to control healthy subjects. We also found deranged haematological parameters in all four stages of breast cancer. The data also indicated that patients which were on combined therapies i.e. radio and chemo have more deranged and decreased levels of haematological parameters as compared to individual therapies.

Keywords: Breast cancer, Haematological parameters, Sysmex automated haematology analyzer

INTRODUCTION

Cancer is a term for diseases in which abnormal cells divide without control and can invade other tissues.[1] Cancer that forms in tissues of breast, usually the ducts (tubes that carry milk) and lobules (glands that produce milk) known as breast cancer. It occurs in both men and women, although male breast cancer is rare.[2] Breast cancer is one of the most common and leading causes of cancer death among women worldwide.[3] More than 1.2 million cases are diagnosed every year, affecting 10-12% of the female population and accounting 500,000 deaths per year worldwide.[4] The incidence of breast cancer in India is 70-90 per 100,000 population and cancer prevalence is established to be around 2.5 million with over 800,000 new cases and 5,50,000 deaths occurring each year. Complete blood count is a prerequisite investigation requested from all cancer patients before surgery, use of chemotherapy and radiotherapy. Poor parameters adversely influence the outcome of cancers. Hematological parameters and markers of the systemic inflammatory response have been correlated with prognosis in several malignancies. The white blood cell count (total and differentials) and packed cell volume

predict disease severity and mortality risk.[5-8] Blood contains a variety of cells in appropriate proportions in normal persons. Any kind of severe disease or abnormality has a direct impact on blood parameters so it is necessary to study the changes in hematological parameters in breast cancer patients, at regular intervals during treatment i.e. chemotherapy and radiotherapy.

A complete blood count (CBC) is a blood test that gives important information about the kinds and numbers of cells in the blood, especially red blood cells, white blood cells and platelets. CBC helps health professional check any symptoms, such as weakness, fatigue, or bruising, patient may have. It also helps in the diagnosis of other opportunistic diseases.[9]

METHODS

The present study has been carried out in the Department of Biochemistry and Department of Radiotherapy, G.R Medical College and J.A. Group of Hospitals, Gwalior. Total 235 human subjects were taken in the study. Out of which 100 normal ages matched healthy subjects were considered as controls and 135 breast cancer patients' subjects as cases which were further divided into their respective stages according to TNM classification. Out of total 135 breast cancer patients there were 40 patients of stage I, 30 patients of stage II, 30 patients of stage III and 35 patients of stage IV.

Inclusion criteria

- Female patients (age >20 years) diagnosed with breast cancer.
- All patients with operable breast lumps and recurrent breast lump in a previously operated case of carcinoma breast.

Exclusion criteria

- Pregnant women
- Patients with benign breast diseases

Before starting analysis, the written consent from all subjects was taken. The study has been approved by institutional ethical committee and was carried out by keeping all norms in mind. The clinical manifestations of disease, personal history of patients were recorded in study proforma. The blood samples collected in heparinized vial were centrifuged at 3000rpm for 15 minutes. Supernatant (plasma) was collected in clean and dry test tube for the estimation of hematological parameters.

Estimation of parameters was done by Sysmex Automated Hematology Analyzer Kx-21. The SysmexKX-21 is an automatic multi-parameter blood cell counter for in vitro diagnostic use in clinical laboratories. The KX-21 processes approximately 60 samples an hour and displays the particle distribution curves of WBC, RBC, and platelets on the LCD screen, along with data of 18 parameters, as the analysis results.

The KX-21 employs three detector blocks and two kinds of reagents for blood analysis. The WBC count is measured by the WBC detector block using the DC detection method. The RBC count and platelets are taken by the RBC detector block, also by using the DC detection method. The HGB detector block measures the hemoglobin concentration using the non-cyanide Hemoglobin method. The analysis result was displayed in the Analysis Result Display Area on the LCD screen. In the Analysis Result Display Area, the analysis result was displayed each time when a new sample was analyzed.

Statistical analysis

The results were expressed as Mean±Standard Deviation. The statistical differences between cases and control were determined by student independent sample t-test. Data analyses were performed with the Statistical Package for the Social Sciences, version 21.0 (SPSS, Chicago, Illinois, USA). The p value less than 0.05 were considered as significant.

RESULTS

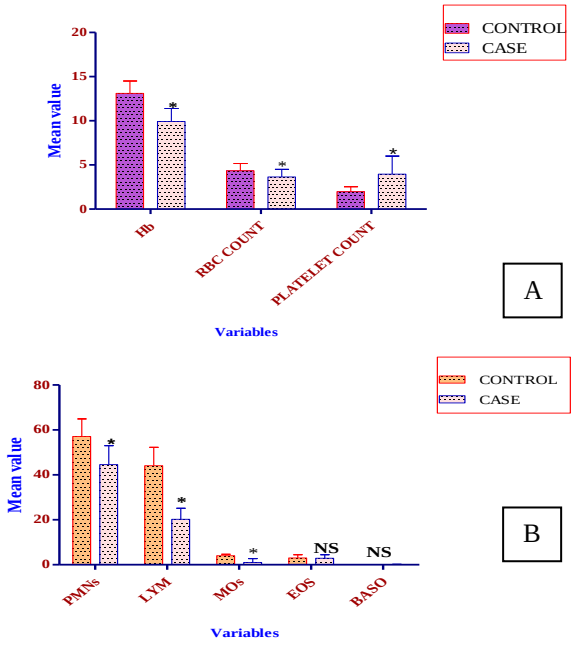
We found significant changes in hematological parameters in control healthy subjects and breast cancer patients (Table 1).

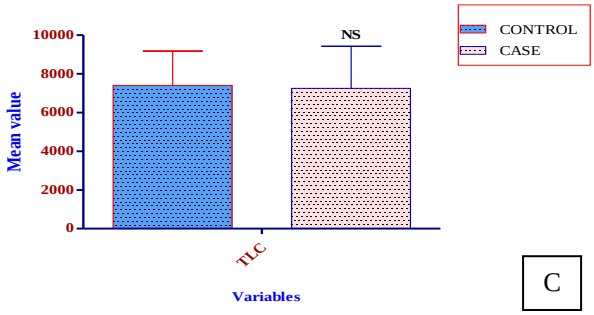
Table 1: Significant changes of hematological parameters in control healthy subjects and breast cancer patients.

Groups		Hb	TLC	PMNs	LYM	MOS	EOS	Baso	RBC Count	Platelet count
Control healthy subjects (N=100)	Mean	13.1	7392	57.13	44.08	4.00	3.02	00	4.35	1.98
	±SD	1.41	1776.88	7.77	8.22	0.69	1.39	00	0.81	0.54
Breast cancer patients (N=135)	Mean	9.92*	7246.52NS	44.57*	20.23*	1.01*	2.91NS	0.04NS	3.64*	2.04NS
	±SD	1.47	2174.93	8.37	4.95	1.67	1.50	0.2	0.86	0.58
	SE	0.18	261.77	1.07	1.21	0.16	0.19	0.01	0.11	0.07

* Significant at 0.05($p<0.05$); NS Non Significant

The data indicated that hemoglobin level, polymorphs, lymphocytes, monocytes and RBC count were statistically reduce ($p<0.05$) while other parameters were non-significant as compared to control healthy subjects. (Figure 1A-C).





*Significant at 0.05($p<0.05$), [NS]Non Significant

Figure 1 (A-C): Significant changes of haematological parameters in healthy control subjects and breast cancer patients.

We also found that hemoglobin level and lymphocyte count gradually decreases with stages while other parameters were also deranged but not specific trend observed (Table 2). Out of 135 breast cancer patients, 40 patients were on chemotherapy, 44 patients were on radiotherapy and 51 were on both i.e. radio-chemotherapy. We found that patients which were on radio-chemotherapy (both) had decreased mean values in all parameters as compared to individual therapies.

Table 2: showing the comparative Mean±SD of hematological parameters in different stages of breast cancer.

	Hb	TLC	PMNs	LYM	EOS	MOs	Baso	RBC count	Platelet count
Stage I	10.94 ±1.27	6746 ±1752	56.02 ±8.26	33.75 ±9.25	2.67 ±1.54	0.92 ±1.57	0.1 ±1.54	3.93 ±0.80	2.08 ±0.53
Stage II	10.42 ±0.77	6840 ±1980	44.70 ±6.36	36.00 ±6.23	2.56 ±1.26	0.81 ±1.22	00 ±00	4.10 ±0.34	1.92 ±0.82
Stage III	9.11 ±0.97	5446 ±1376	53.23 ±8.13	24.50 ±8.40	3.26 ±1.61	1.33 ±1.61	00 ±00	3.66 ±0.73	2.05 ±0.55
Stage IV	8.44 ±0.95	2905.71 ±783.38	44.02 ±9.22	20.91 ±5.77	1.41 ±0.23	0.91 ±1.82	0.01 ±0.16	3.17 ±0.92	2.03 ±0.60

Table 3: Effect of treatment on comparative Mean±SD of hematological parameters in breast cancer patients.

Treatment	Hb	TLC	PMNs	LYM	MOs	EOS	Baso	RBC count	Platelet count
Chemotherapy (N=40)	9.95 ±1.42	4580 ±1100	42.00 ±3.55	20.44 ±3.05	1.05 ±0.11	2.66 ±1.04	00 ±00	3.62 ±0.81	1.22 ±1.05
Radiotherapy (N=44)	9.90 ±0.89	5000 ±600	44.27 ±1.05	21.00 ±4.00	1.25 ±0.89	3.00 ±0.89	0.1 ±0.54	3.35 ±2.05	1.50 ±1.95
Radio-chemotherapy (Both) (N=51)	8.05 ±1.00	3500 ±2100	42.05 ±2.00	16.00 ±2.80	0.99 ±1.00	3.55 ±1.60	00 ±00	3.55 ±1.60	1.00 ±0.85

Radiotherapy receiving patients have low levels of hemoglobin, RBC count and polymorphs. Patients which were on chemotherapy have low levels of hemoglobin, RBC count, polymorphs, lymphocytes and platelet count (Table 3).

DISCUSSION

Complete blood picture is a routine test which is used frequently by clinicians to support the working diagnosis of several diseases, such as anemia's, acute infections,

hemorrhagic states, allergic disorders, cancers, and immune disorders, health screening and pre-operative evaluations. Anemia is frequent in cancer patients and its incidence increases with chemotherapy. The probability of requiring transfusions also increases with chemotherapy. Anemia negatively impacts survival and accentuates fatigue in cancer patients. Cancer promotes inflammatory cytokine production, which suppresses erythropoiesis and erythropoietin (EPO) production.[10]

In Present study, we also found significantly ($p<0.05$)low levels of hemoglobin level and low RBC count in breast cancer patients as compared to normal healthy subjects. RBC of patients affected by breast cancer are more sensitive to the denaturing action, hence the formation of hemin, is significantly shorter than in normal subjects.[11] Kandemir et al investigated the prevalence of anemia (Hb conc. <12 g/dl) in 336 women with early stage breast cancer and its association with other known prognostic factors.[12] Low blood counts are observed as a side effect of chemotherapies during adjuvant chemotherapy process.[13] Absolute lymphocyte count showed a highly decline after chemotherapy processes, which can be considered among the adverse effects of chemotherapy in breast cancer patients.[9] In present study we also found significant ($p<0.05$) decreased levels of lymphocyte count in breast cancer patients. It could be due to increased levels of pro- inflammatory cytokines, such as IL-1, IL-6, TNF-α, and INF-δ that induce iron retention by the reticulo-endothelial system, gastrointestinal tract, and liver, thereby exerting an inhibitory effect on erythroid precursors.[14] Rana Singh AP et al also reported decrease in absolute lymphocyte count with increase in stage of carcinoma.[15] Ufelle SA et al reported significant decrease in all hematological parameters in breast cancer when compared with control.[16] This is in accordance with our study. We also found that hemoglobin level and lymphocyte count gradually decreases with stages while other parameters were also deranged but not specific trend observed. Stage-specific mean values of lymphocytic counts of breast cancer can be employed as a useful guide to assess the progression of disease. Nemoto et al and others observed no change in peripheral lymphocyte count in patients of breast carcinoma.[17-19] Many other scientists also observed changes in different stages of breast cancer.[15,20-22]

In the current study, we found that patients which were on radio-chemotherapy (both) had decreased mean values in all parameters as compared to individual therapies. Normally, blood cells are placed among the most rapidly dividing cells in the body and the most sensitive to chemotherapy and radiotherapy.[23] Furthermore, about 5 % of cancer patients have chemotherapy-induced side effects that are associated with 8.5% of all cancer deaths.[24] About 33% patients of cancer experience infection as a result of chemotherapy, of which 57% are associated with neutropenia.[25] This is in accordance of our data. In chemotherapy and radiotherapy, various drugs and rays are used to kill the neoplastic cells without damaging healthy surrounding tissues Nevertheless, there exist some undesired adverse effects during and after therapy e.g. GIT disturbances, infertility, disturbed homeostasis etc. Chemotherapy induced bone marrow damage results in thrombocytopenia and anemia that threaten the patient's life quality and the overall effectiveness of anticancer treatments.[26] About 10-25% of solid cancer patients (i.e. breast cancer, ovarian) that have been treated with intensive chemotherapy, suffer from incidence of thrombocytopenia.[27,28] During radiotherapy, gamma irradiation induces alterations on RBCs different functional units in membrane such as lipid bilayer, protein and cytoskeleton.[29] Moreover, radiation induces lipid per oxidation of fatty acids.[30] The production of peroxides and cross-linkages in the membrane can disorder the upper region of the bilayer favor the diffusion of water and finally it causes hemolysis of cells.[31]

CONCLUSION

Therefore, from the present study we conclude that breast cancer patients have deranged hematological parameters. We observed anemia, neutropenia, lymphocytopenia and low monocytic count in breast cancer patients. The data also indicated that patients which were on combined therapies i.e. radio and chemo have more deranged and decreased levels of hematological parameters as a side effect of treatment. Hematological investigations are important part and parcel of treatment and follow up of breast cancer patients. It can help in the assessment of disease progression and the behavior of different malignancies.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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