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Original Research Article

Hematological Changes Associated with Radiation Sensitivity Risk in Iraqi Breast Cancer Patients

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Abstract: ***Background:*** Breast cancer (BC) is a leading cause of morbidity and mortality in women worldwide, some experience significant adverse effects, potentially due to factors such as age, lifestyle, oxidative stress, and genetic variations. Radiation-induced damage affects DNA, leading to cell death and bone marrow suppression, which impacts blood cell production. ***Patients and Methods:*** 75 breast cancer under radiotherapy (aged 35-75), comprising 60 BC women and 15 healthy controls, recruited from Wasit City and Babylon City between October 2023 and January 2024. Blood samples were collected for haematological study, at various stages of radiotherapy: before the first dose (BFD), after the first dose (AFD), after half the dose (AHD), and after the last dose (ALD). ***Results:*** Significant reductions in white blood cell (WBC) and monocyte counts were observed, especially in the ALD group, compared to healthy controls. Lymphocyte levels also decreased, with a significant difference at AFD and ALD stages. Haemoglobin (HGB), showed reductions over the course of treatment, with the most significant changes occurring in the ALD group. The study confirms that radiation affects blood cell counts, particularly WBCs, Monocyte, Lymphocyte, HGB, impacting immune function and treatment response. ***Conclusion:*** Radiation therapy in BC patients leads to significant changes in blood cell counts, which may contribute to immune suppression and delayed healing. Monitoring blood cell levels is crucial to manage these effects and adjust treatment as needed to improve patient outcomes.

Keywords: Radiotherapy, Breast Cancer, WBC, Monocyte, Lymphocyte.

INTRODUCTION

The most frequent cancer and the sixth most common cause of cancer death for women worldwide is breast cancer. 2.3 million women were expected to have received a breast cancer diagnosis in 2020, accounting for 11.7% of all cancer cases and 6.9% of all female cancer deaths. There were significant regional differences in breast cancer incidence rates [1]. Approximately 20% of breast cancers worldwide are thought to be brought on by modifiable risk factors such being overweight or obese, drinking alcohol, and not exercising, which suggests that promoting healthier lifestyle choices could lessen the burden of the illness [2].

About 50% of patients with malignant breast tumors receive radiation therapy, which is an effective cancer treatment. While most patients appear to tolerate the treatment, some experience serious side effects. Numerous factors, including age, lifestyle, oxidative stress, inflammatory reactions, genetic susceptibility, and variations in genes involved in the response to radiation-induced DNA damage, may contribute to this diversity in response [3].

High-energy radiation known as ionizing radiation (IR) can break covalent bonds by releasing electrons from atoms and molecules to create ions [4]. IR causes DNA breaks, especially DSBs, which have a direct impact on DNA structure. Secondary consequences include the production of reactive oxygen species (ROS), which oxidize proteins and lipids and cause various DNA damage, such as single strand breaks (SSB) and the formation of abasic sites. All of these alterations work together to cause mitotic failure and cell death [5]. The production of blood cells in the bone

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marrow can occasionally be slowed down by radiation [6]. Low blood cell counts may delay your next round of treatment or lead your doctor to reduce medication dosage or prescribe a new medication [7]. Regular blood tests are essential to monitor blood cell levels during and after radiotherapy [8]. The aim of this study was to investigate the hematological changes in women with breast cancer undergoing radiation therapy.

MATERIAL AND METHODS

A case–study was conducted on 60 patients and 15 healthy women as a control group, who were treated at Wasit, and Babylon Oncology center who were suffering from breast cancer. All patients were treated with 3D conformal radiotherapy (X-ray) as part of radiotherapy planning. Patients were treated with a total dose of centigrade (cGy), using a radiotherapy device between16 October 2023 and 20 January 2024. The inclusion criteria were only for breast cancer patients from Wasit and Babylon cities of different ages who attended oncology centers for radiotherapy.

For all patients, hematologic tests were performed before the start, after First dose, after half dose, and at the end of radiation treatment. The parameters were measured by a haematological analyser (Sysmex-XN-350, compact 5-part differential analyzer, Germany).

Statistical analysis

All data were statistically analyzed by IBM SPSS 28 (SPSS Inc., Chicago, IL). Frequencies and percentages with the use of the chi-square test reported nominal data. Calculate the effect size by Partial Eta2 (η2), which is expressed as η2 = 0.01 indicates a small effect, η2 = 0.06 indicates a medium effect, η2 = 0.14 indicates a large effect.

Ethical considerations

The study was conducted in accordance with the ethical principles that derive their origin from the Declaration of Helsinki. The study was approved by the Ethical Committee of the College of Biotechnology, Department of Medical Biotechnology, Al Qasim Green University.

RESULTS

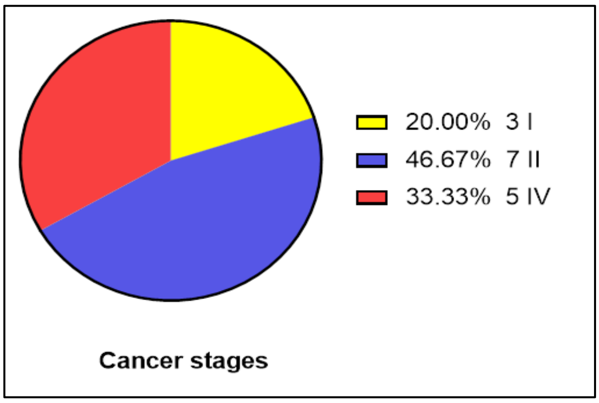

Figure 1: Distribution of patients according to cancer stage

Most women that diagnosed with BC in present study were in stage II of disease 7 (46.67%) followed by stage III 5 (33.33%) and only 3 patients were stage one (20.00%) as shown in figure (4.2). This indicates that most patients were detected at an intermediate stage, which is important since, although not as good as Stage I, Stage II still gives a respectable prognosis with prompt treatment. It is especially troubling that around one-third of patients received a Stage III diagnosis since it entails more extensive therapy and worse survival rates.

The results of present study showed that the majority of patients 11 (73.33%) undergoing surgery and chemotherapy and 2 (13.33%) had surgery only. In addition, 1 (6.67%) received endocrine therapy and another one received chemotherapy alone.

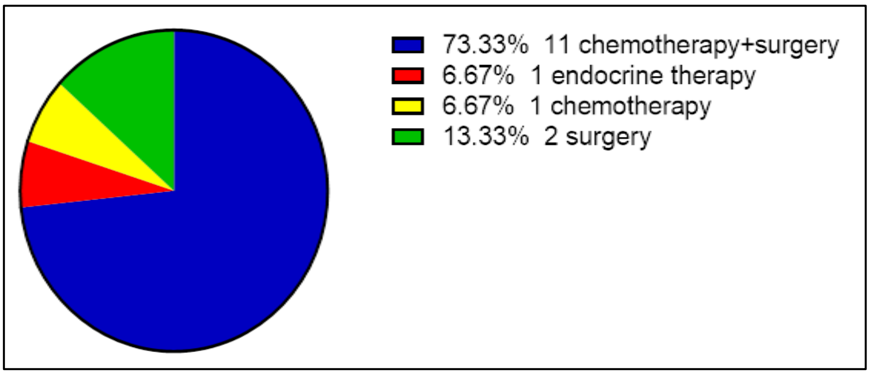

Figure 2: Distribution of patients according to type of medication

The results in Table 1 illustrates the impact of varying doses of radiotherapy on blood counts, specifically white blood cells (WBC), monocytes, and hemoglobin (HGB) levels. The results show there is a significant decline in all measured parameters the treatment progresses from before the first dose (BFD) to after the last dose (ALD). Notably, WBC, Monocyte and hemoglobin levels, decrease from the BFD group to the

ALD group, indicating a marked decrease in immune function. The p-values indicate statistically significant differences across the groups ($p < 0.001$ for WBC and monocyte counts, $p = 0.008$ for HGB), while the partial eta squared values suggest a medium to large effect size, particularly for WBC and monocyte counts. These findings highlight the detrimental effects of radiotherapy on blood parameters, emphasizing the need for monitoring and potential intervention to manage these side effects during treatment.

Table 1: Relationship between the doses of radiotherapy and blood counts (BFD before first dose, AFD after first dose, AHD after half dose, ALD after last dose)

Group	**WBC (10^3/ul)**	**Monocyte (10^3/ul)**	**Lymphocyte (10^3/ul)**
Healthy	8.05±1.76 a	0.60±0.17 a	32.41±8.75 a
BFD	8.03±3.06 a	0.51±0.23 a	25.55±7.68 b
AFD	5.31±1.84 b	0.42±0.11 b	30.18±14.46 ab
AHD	4.11±1.28 c	0.38±0.15 b	33.01±19.22 b
ALD	3.02±1.37 d	0.24±0.08 c	30.12±14.63 b
p-value	**0.0001**	**0.0001**	**0.010**
Partial Eta^2 (effect size)	**0.513**	**0.438**	**0.216**

Table (2) presents the frequency distribution of red blood cells (RBC), hemoglobin (HGB), and platelet larger cell ratio (P-LCR) across different study groups following radiotherapy treatment. The control group demonstrates the highest values for RBC (4.71 ± 0.33), HGB (12.24 ± 1.23), and P-LCR (26.00 ± 9.16). In contrast, there is a notable decline in these parameters as the treatment progresses; specifically, the RBC count decreases significantly from 4.50 ± 0.47 in the BFD group to 3.70 ± 0.79 in the ALD group. HGB levels also show a decrease from 11.45 ± 1.36 (BFD) to 10.65 ± 1.86 (ALD). Although the P-LCR shows some fluctuations, it remains lower in the treated groups compared to the control. The p-values indicate significant differences across groups ($p < 0.001$ for RBC and P-LCR, $p = 0.008$ for HGB), with partial eta squared values reflecting medium effect sizes for RBC and P-LCR, suggesting considerable impacts of radiotherapy on these blood parameters. These results underline the adverse effects of radiotherapy on blood cell production and overall hematologic health.

Table 2: Frequency distribution of red blood cell (RBC), Hemoglobin (HGB), Platelet Larger Cell ratio (P-LCR), Count according to Different Study Groups, (BFD before first dose, AFD after first dose, AHD after half dose, ALD after last dose

Groups	**RBC (10^6/ul)**	**HGB (g/dL)**	**P-LCR %**
Control	4.71±0.33 a	12.24±1.23 a	26.00±9.16 a
BFD	4.50±0.47 a	11.45±1.36 bc	17.92±4.66 b
AFD	3.92±0.83 bc	10.95±2.08 bc	19.6±11.34 b
AHD	4.04±0.45 b	11.61±1.29 b	18.13±7.97 b
ALD	3.70±0.79 c	10.65±1.86 c	17.59±6.12 b
p-value	**0.0001**	**0.008**	**0.006**
Partial Eta2 (effect size)	**0.459**	**0.225**	**0.241**

DISCUSSION

Breast cancer, a malignancy that primarily affects breast tissue, can be treated effectively with radiotherapy, which uses high-energy radiation to target and destroy cancer cells. This treatment is often employed after surgery to eradicate any remaining cancerous cells and reduce the risk of recurrence, though it can also be used preoperatively to shrink tumors. Family history was identified as one of the primary risk factors for BC, women who had a family member diagnosed before the age of 50 were more likely to have the disease than those whose family members were diagnosed at a later age [9].

Surgery, chemotherapy, radiotherapy, endocrine therapy, targeted therapy, and immunotherapy are among the treatments for BC, and the treatment plans necessitate the collaboration of several subspecialties. Chemotherapy-based preoperative systemic therapy can lower the breast tumor volume, allowing for breast conservation and reducing the requirement for axillary lymph node dissection (ALND), which is the standard of care for non-metastatic BC [10].

The results in Table 1 agreement with other result that show, lymphocytes are highly sensitive to ionizing radiation, even low doses can induce apoptosis (programmed cell death), leading to a reduction in circulating lymphocytes [11]. Also, agreement with [12], that shown high percentage of patients develop adverse effects in normal tissue following RT. Also, agreement with Lumniczky *et al*., [12], that shown, Lymphocytes migrate to inflamed and damaged tissues, including irradiated areas. Once there, they can be damaged or destroyed, further reducing circulating levels. Lymphocytes are very sensitive to radiation compared to other types of blood cells; this may be making them vulnerable to direct destruction when exposed to RT. Even low doses of radiation can quickly reduce the number of these cells.

The results in Table 2 are consistent with Wersal, *et al*., [13] that found significantly decreases in erythrocytes, hemoglobin, platelets and leucocytes. Also, agreement with Mahmood, *et al*., [14], that showed a reduction RBC and other cells after RT. Kosmachevskaya *et al*., [15], that explain, radiation can directly damage RBC membranes, leading to hemolysis. The indirect interaction of IR maybe leads to hydrolysis of water molecules resulting in hydrogen and a hydroxyl free radical molecule. And result of this study may be to the Systemic inflammation triggered by radiation exposure. Radiation maybe causes oxidative stress and damage to RBCs, leading to their premature destruction (hemolysis).

Mahmood *et al*., [14] that showed significantly reduced in HGB in blood stream under RT. HGB reduced maybe to Tissue inflammation and increased cell damage.

Radiation therapy may lead to an overall decrease in the platelet count (thrombocytopenia), affecting the percentage of large platelets, As the number of plates produced decreases, the percentage of large plates may be lower, Radiation may increase the rate of platelet breakdown in the spleen or blood, leading to a decrease in the proportion of large platelets before their maturation process is complete [16].

CONCLUSIONS

These findings confirm that radiation therapy adversely affects blood cell counts, impacting immune function and potentially compromising treatment responses. Consequently, regular monitoring of blood cell levels is essential for managing these side effects, enabling timely adjustments in treatment to enhance patient outcomes and mitigate immune suppression and delayed healing.

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