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Research article

# Hematological study of cancer patients with radio-chemotherapy

Muhammad Iqbal[1], Muhammad Younis[2, 3], Neelma Shoukat[3], Sana Shaikh[3], Nida Akram[2], Raza Abbas[4], Khawar Ali Shahzad[5], Kanwal Mazhar[6], Fawad ur Rehman[7]*

[1]Liaquat University of Medical and Health Sciences, Jamshoro, 76090, Sindh, Pakistan
[2]The key laboratory of development genes and human disease, Institute of Life Sciences, Southeast University, Sipailou 2, Nanjing, 210096, China
[3]Institute of Biochemistry, University of Sindh, Jamshoro, Sindh, Pakistan
[4]School of biological and Environmental Engineering, Nanjing University of Science and Technology, China
[5]Institute of Molecular Biology and Biotechnology, The University of Lahore, Lahore, Pakistan
[6]Key Laboratory of Environmental Medicine and Engineering of Ministry of Education, Department of Nutrition and Food Hygiene, School of Public Health, Southeast University, Nanjing, 210009, China
[7]State key lab of Bioelectronics, School of Biological Science and Medical Engineering, Southeast University, Sipailou 2, Nanjing 210096, China

**Abstract**
Cancer is a complex disease with multiple triggers and high mortality rate all over the world. Currently Chemotherapy, radiotherapy and invasive surgeries are in vogue for cancer therapeutics. There are certain delicate parts where the invasive surgeries are a great deal of risk; therefore we only need to rely on chemo and radiotherapy either separately or combined. These therapies in return highly compromise the patient's life quality as adverse effects. Therefore, the current study was conducted to evaluate the radio and chemotherapy effects on the various blood cells correlated properties i.e. anemia, thrombocytopenia and leucopenia etc. Our results suggest that radiation and chemotherapy cause decrease in thrombocytes and leukocytes count in cancer treated patients. Total 80 samples were measured by hematological analyzer and found a significant decrease in the hematological parameters (thrombocytes, total leukocyte count, cell volume, and hemoglobin) mean values in cancer treated patients when compared to the healthy individuals. It was concluded that radio-chemotherapy have some serious adverse effects on the health and normal physiology of cancer patients.
**Key words:** Cancer, radio-chemotherapy, blood parameters, adverse effects.

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***Corresponding author** FawadurRehman **Email** dawarvet@hotmail.com
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## Introduction

Cancer is still one of the leading causes of death and equally prevalent all over the world. Only early diagnosed tumor with none to less metastasis can be treated either by radiotherapy, surgery or chemotherapy. In chemotherapy, various drugs are used to kill the neoplastic cells without damaging healthy surrounding tissues e.g. *Doxarubicin*, *Bevacizumab*, *Sorafenib*etc.[1, 2]. Nevertheless, there exist some undesired adverse effects during and after therapy e.g. GIT disturbances, infertility, disturbed homeostasis etc. [3, 4].

Thrombocytopenia is a term used to indicate a remarkable reduction or drop in platelet counts [5]. Chemotherapy induced bone marrow damage results in thrombocytopenia and anemia that threaten the patient's life quality and the overall effectiveness of anticancer treatments [6]. About 10-25% of solid cancer patients (i.e. breast cancer, ovarian) that have been treated with intensive chemotherapy, suffer from incidence of thrombocytopenia [7, 8].

During radiotherapy, gamma irradiation induces alterations on RBCs different functional units in membrane such as lipid bilayer, protein and cytoskeleton [9]. Moreover, radiation induces lipid peroxidation of fatty acids [10]. 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 [11].

Leukopenia in cytotoxic chemotherapy is positively associated with survival in several types of neoplastic diseases [12-14]. Cancer patients have antitumor induced sepsis that is associated with 8.5 % mortality [15]. Granulocyte macrophage colony stimulating factor (GM-CSF) is commonly used to reverse leukopenia [16, 17]. Stem Cell Factor (SCF) can prevent chemotherapy induced apoptosis of immature erythroblasts and megakaryocytes, which are exquisitely susceptible to cytotoxic agents [14, 15] and promote recovery after cytotoxic damage [18]. Additional to thrombopoietin, which is an essential growth factor responsible for platelet production, several hematopoietic growth factors such as interleukin (IL) -3, IL-6, IL-11, SCF and stromal cell derived factor-1, have been shown to influence megakaryocytes formation at various developmental stages [19–21]. Here, we conducted a study to find out the adverse effects of radiotherapy and chemotherapy on the blood cells (especially thrombocytes).

## Material and Methods

Total eighty samples were collected i.e. forty from cancer patients and forty from healthy individuals. Cancer patient were selected from Nuclear Institute of Medicine and Radiotherapy (NIMRA), Jamshoro, Sindh. The age group for all samples ranged between 25-50 years.

### Blood Sampling

Two ml of blood was collected via intravenous 22 gauge standard needle syringe. Then the blood was stored in EDTA containing tubes for further processing. All the sampling was done after the consent of the patients and healthy volunteers.
Hematology analyzer (Medononic 620) was used for the platelets (PLT) and white blood cells (WBCs) count. The hematological analyzer was capable of measuring up to twenty blood parameters at a time.

### WBC and PLT concentration detection

Detection was accomplished using the electronic impedance principle and occurs in the orifice of the transducer. The blood was diluted to 1:400 (WBC) and 1:40000 (PLT) through a precise shear system. Two separate measuring chamber and transducer were used for PLT and WBC analysis. To exclude any possibility of cross contamination between the lyzer and the PLT dilution, the PLT and WBC parameters were measured on a precise aliquot of the sample. The amount of samples measured was determined by the volume of a precise glass column that was called a metering tube.

### Mean cell volume (MCV) of RBCs

The MCV parameter was derived from the RBC's distribution curve. As distribution curve has a maximum volume range of 250 fl, the maximum channels also contain clumps of cells that were larger than the volume. Therefore, this channel was excluded from the MCV calculation. The MCV was calculated from the volume position of the discriminating to 249 fl. In general, RBC count that were lower than 0.60 (displayed value) did not give a MCV/HCT value due to lower statistical significance.

### Mean cell hemoglobin (MCH)

The MCH is a calculated value and is defined as HGB/RBC giving the mean HGB concentration in each red cell.

### Mean cell hemoglobin concentration (MCHC)

The MCHC is a calculated value and it is defined as HGB/HCT (hematocrit).The MCHC was calculated from three measured parameters after the excellent instrument stability check.

MCHC =HGB / HCT-HGB / (MCV × RBC).

### Data Analysis

The data were analyzed by using statistical software program SPSS version 18 (SPSS Inc., Chicago, IL).

## Results and Discussion

The results showed that the platelet counts were decreased by 52 % in the cancer treated patients as compared to healthy individuals (Fig. 1). These results obviously demonstrate the thrombocytopenia in the cancer patients when exposed to the radio and chemo therapy. The neoplastic maladies that involve the bone marrow directly, such as leukemia, lymphoma, or multiple myeloma, can also cause a decrease in the production of platelets [22].

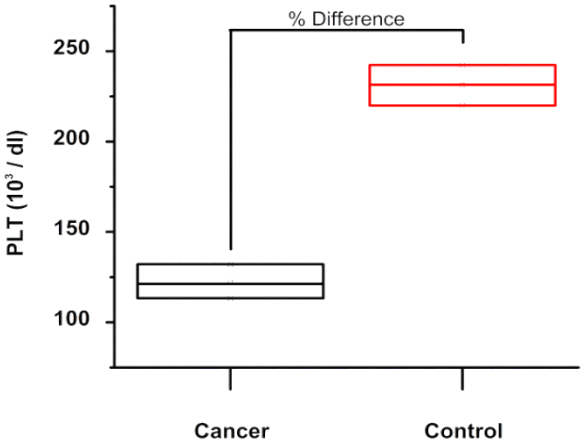


**Fig. 1** Platelets count differences among cancer treated patients and healthy individuals.
PLT =platelet count; % difference = platelets difference in percentage between cancer treated (radio-chemotherapy) i.e. 50 % and healthy individuals (n = 80).

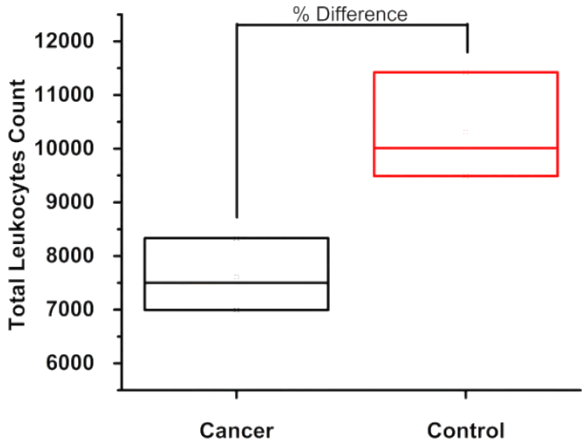


**Fig. 2** Total leukocyte count (TLC) comparison between treated cancer patients and healthy individuals.
% difference = total leukocyte count difference in percentage between cancer treated (radio-chemotherapy) and healthy individuals (n = 80).

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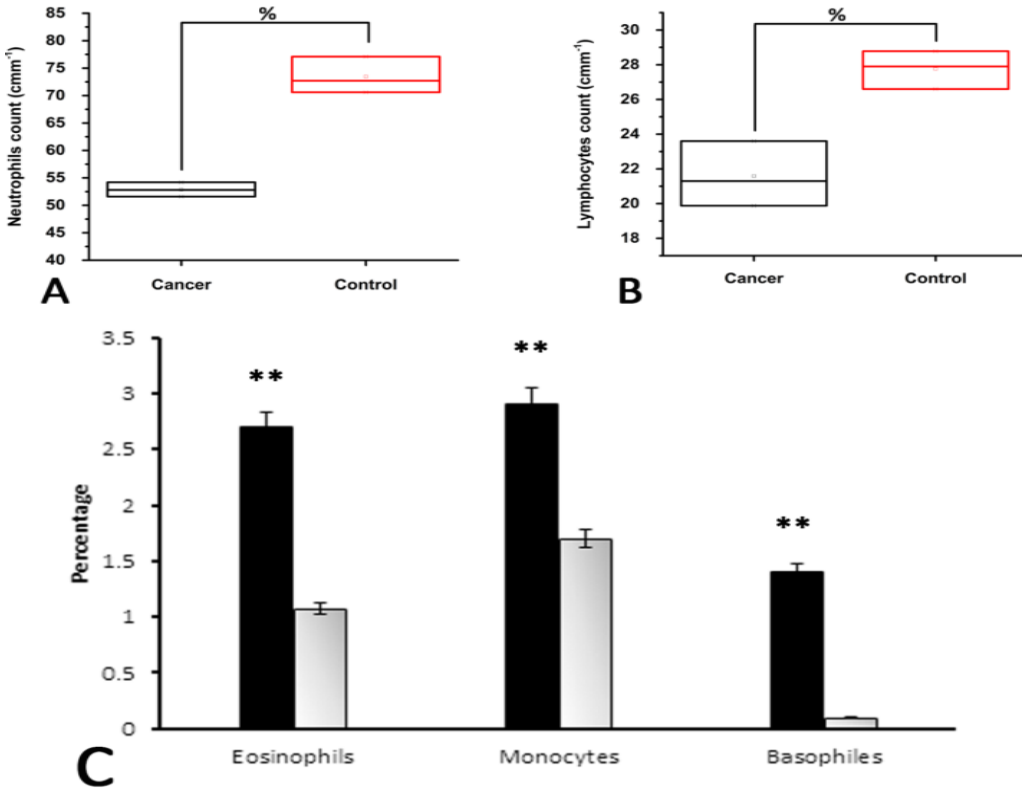


**Fig. 3** White blood cell type comparison between cancers treated patients (radio-chemotherapy) with healthy individuals as control. Figure **A** and **B** show the % difference between cancer treated (radio-chemotherapy) and healthy individuals. In **C** black bars show healthy individuals and white gradient bars represent cancer treated patients (n = 80). ** = represent the significance at $p < 0.01$.

Generally platelets play a key role in clot formation during bleeding in order to save blood loss [23]. Therefore, a reduction in platelet count may primarily lead to incidence of bleeding that may range from mild to severe. Severe bleeding in the presence of thrombocytopenia or when coupled with other clotting disorders can lead to serious morbidity or death. Thrombocytopenia is a general problem experienced by cancer patients, which usually is a result of the use of conventional chemotherapy, and is a dose limiting factor for chemotherapy administration. Even though, occurrence of thrombocytopenia among acute leukemia patients is higher than its incidence among other types of cancer [24-27].

Similarly, the total leukocyte count (TLC) in the control group and cancer patients was also performed. Mean value of TLC for control and cancer patients was 9490±127.4 (SD) and 8332.5±164.9 (SD), demonstrating 12% decrease in the treated patients (Fig. 2). The total neutrophils, lymphocytes, eosinophils, monocytes and basophils mean values observed in cancer treated patients were 52.8±6.3 (SD) $cmm^{-1}$, 23.6±1.7 (SD) $cmm^{-1}$, 2.7±0.3 (SD), 20.9±0.3 (SD) $cmm^{-1}$, 1.4±0.5 (SD) percent, respect-ively, while the mean values in healthy individuals were 23.6±1.7 (SD) $cmm^{-1}$, 2.7±0.3 (SD), 2. (SD), 1.4±0.5 (SD) percent, respectively, while the mean 70.6±6.6 (SD) $cmm^{-1}$, 26.6±1.3 (SD) $cmm^{-1}$, individuals were 70.6±6.6 (SD) $cmm^{-1}$, 26.6±1.3 (SD) $cmm^{-1}$, 1.07±0.4 (SD), 1.7±0.4 (SD), 0.1±00 (SD) percent, respectively (Fig. 3). These results demonstrate 26% decline in the neutrophils count and 11 % decrease in lymphocyte numbers, whereas the eosinophils, monocytes and basophils count were increased by almost 50% in cancer patients when compared with healthy individuals. It also shows that the anticancer therapy damages neutrophils in cancer patients, these cancers and cancer treatments may cause a condition neutropenia [28]. Our results are in corroboration with the earlier findings of Blayney et al. [29]. Some earlier studies on head and neck, gastric, pulmonary and breast cancer therapies also reported a decline in the natural killer cell counts when compared to the healthy individuals [30].

These findings indicate the significant difference in normal and cancer patient's hematology. Certain chemotherapies significantly lower the WBCs count in the subject patients. It is well known that blood and bone marrow neoplasms i.e. leukemia,

lymphoma, or multiple myeloma will decrease the WBCs count in cancer patients [31, 32]. However, the neoplastic diseases which do not directly involve the immune regulatory and circulatory system, upon exposure to the radio and chemotherapy can lead to blood disorders and decreases the total leukocyte count and immune compromise in the patients [33].

The MCV, MCH and MCHC values in cancer patients after various radio and chemotherapies were clearly decreased in cancer patients when compared to healthy individuals (Fig.4). In our earlier studies, we also demonstrated that chemotherapy and radiotherapy may cause decrease in RBCs count and hemoglobin levels of cancer patients [34]. The erythroblasts and megakaryocytes survival, production, and differentiation are coordinated by combinations of cytokines and mediators present within specific bone marrow niches [35].

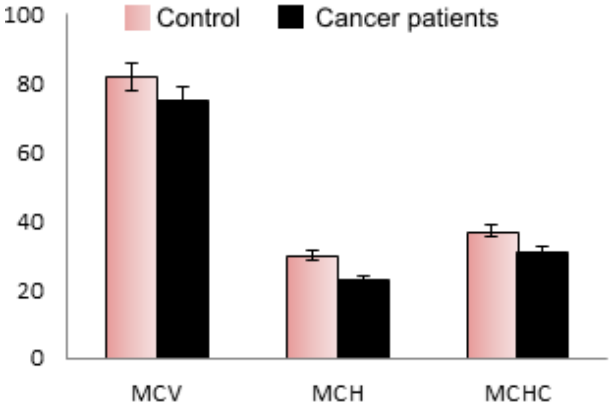


**Fig. 4** Difference between mean cell volume (MCV), mean cell hemoglobin (MCH) and mean cell hemoglobin concentration (MCHC) of control and cancer patients.

Normally, blood cells are placed among the most rapidly dividing cells in the body and the most sensitive to chemotherapy and radiotherapy [36]. Furthermore, above 5 % of cancer patients have chemotherapy-induced side effects that are associated with 8.5 % of all cancer deaths [15]. The hematopoietic growth factors such as erythropoietin and colony stimulating factors are commonly used to promote hematopoietic improvement following chemotherapy; however, those cannot prevent the occurrence of drug induced myelo-suppression of hematopoietic cells [9].

In the present study, we uncovered previously unidentified side effects of chemotherapy and radiotherapy on hematological parameters; because of that cancer patients have a risk of hematological disorders such as anemia, thrombocytopenia, and leucopenia. Specifically, our work demonstrates that chemotherapy-induced thrombocytopenia and leukopenia affect patient's quality of life.

## Conclusions

In short, this study investigated the adverse effects of chemotherapy and radiotherapy either combined or separately when used for neoplastic disease treatment. These therapies affected the blood cells homeostasis, and decreased the thrombocytes and leukocytes count along with other vital hematology parameters as an adverse effect. The role of radio and chemotherapy cannot be overlooked in cancer therapeutics, as these are the only available therapies in vogue following invasive surgeries. However further studies with more safe procedure are needed to overcome their adverse effects for cancer therapies.

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