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THE RADIATION EFFECT ON BLOOD CELLS IN CANCER PATIENTS WHO HAVE UNDERGONE EXTERNAL RADIATION THERAPY- ANALYTICAL STUDY

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تأثير الإشعاع على خلايا الدم لدى مرضى السرطان الذين خضعوا للعلاج الإشعاعي الخارجي دراسة تحليلية

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Abstract:
Normal leukocytes count ranges from 4500-11000, Platelets 150,000-400,000/mm3 and Hemoglobin level male: 13.5-17.5 g/dL, female: 12.0-16.0 g/dL. External beam radiation therapy is a treatment using high-energy ionizing radiation is part of cancer treatment methods to control and kill malignant cells at the treatment site. However, normal cells and cancer cells are affected at the same time, the effect depends on the sensitivity of the Cells as well as the value of the dose deposited to the area. This study is aimed at assessing only changes in WBCs, Plts and Hgb level. PATIENTS AND METHODS: Forty-two patients from the University Hospital radiotherapy department in Tripoli, Libya, were included in this study from April to August 2024. The information related to the study was collected from the archive unit of the department after approval to conduct the study. RESULTS: Out of the 42 patients, 26 (61.90%) females and 16(38.1%) males, the median age was 51.4years the age group has diversified (17 to 82) years. According to the treatment sites we classified them into eight groups the most common cancer was breast cancer accounting for 20 (47.6%), 6(14.28%) of cases were head and neck, 4(9.52%) larynx cancers, 4(9.52%) lymphoma cancer, 2(4.76%) lung, 3(7.14%) prostate, 2(4.76%) cervix and 1(2.38%) rectum. We found a statistically significant (P<0.10) reduction in total (WBCs) count, Plts counts and Hgb level when compared the results of Pre RT to Post RT. CONCLUSION: Leukocytes, platelets and hemoglobin level, are the main hematological

indicators that predict the response rate to treatment, severity of the disease. The effectiveness and progress of radiation therapy can be estimated in this way.

Keywords: Effect, radiotherapy, criteria, hematology, cancer patients.

الملخص

يتراوح عدد كريات الدم البيضاء الطبيعي بين 4500 و11000، والصفائح الدموية بين 150,000 و400,000/مم3، ومستوى الهيموغلوبين لدى الذكور: 13.5-17.5 غ/ديسيلتر، والإناث: 12.0-16.0 غ/ديسيلتر. العلاج الإشعاعي الخارجي هو علاج يستخدم إشعاعًا مؤينًا عالي الطاقة، وهو جزء من طرق علاج السرطان للسيطرة على الخلايا الخبيثة في موقع العلاج والقضاء عليها. ومع ذلك، تتأثر الخلايا الطبيعية والسرطانية في الوقت نفسه، ويعتمد التأثير على حساسية الخلايا، بالإضافة إلى قيمة الجرعة المُوَضَّعة على المنطقة. تهدف هذه الدراسة إلى تقييم التغيرات في مستويات كريات الدم البيضاء، والصفائح الدموية، والهيموغلوبين فقط. المرضى والطرق: شملت هذه الدراسة اثنين وأربعين مريضًا من قسم العلاج الإشعاعي بمستشفى جامعة طرابلس، ليبيا، في الفترة من أبريل إلى أغسطس 2024. جُمعت المعلومات المتعلقة بالدراسة من وحدة الأرشيف بالقسم بعد الموافقة على إجرائها. النتائج: من بين 42 مريضًا، كان متوسط أعمارهم 51.4 عامًا، وتراوحت الفئات العمرية بين 17 و82 عامًا. وفقًا لمواقع العلاج، قمنا بتصنيفها إلى ثماني مجموعات، وكان السرطان الأكثر شيوعًا هو سرطان الثدي بنسبة 20 (47.6٪)، و6 (14.28٪) من الحالات كانت في الرأس والرقبة، و4 (9.52٪) سرطانات الحنجرة، و4 (9.52٪) سرطان الغدد الليمفاوية، و2 (4.76٪) الرئة، و3 (7.14٪) البروستاتا، و2 (4.76٪) عنق الرحم و1 (2.38٪) المستقيم. لقد وجدنا انخفاضًا مهمًا إحصائيًا (P <0.10) في إجمالي عدد (خلايا الدم البيضاء)، وعدد الصفائح الدموية ومستوى الهيموجلوبين عند مقارنة نتائج ما قبل العلاج الإشعاعي بنتائج ما بعد العلاج الإشعاعي. الخلاصة: تُعد كريات الدم البيضاء والصفائح الدموية ومستوى الهيموجلوبين المؤشرات الدموية الرئيسية التي تتنبأ بمعدل الاستجابة للعلاج وشدة المرض. ويمكن تقدير فعالية وتقدم العلاج الإشعاعي بهذه الطريقة.

الكلمات الدالة: تأثير، العلاج الإشعاعي ، معايير، أمراض الدم، مرضى السرطان.

Introduction:

Radiotherapy is a therapeutic modality for cancer alongside the surgery and chemotherapy. About 50% of cancer patients receive radiotherapy during the course of their disease[1]. with an estimate that radiation therapy contributes about 40% to curative treatment [2]. Radiation used to destroy cancer cells is called ionizing radiation because it forms ions and deposits energy in the tissue cells through it. The energy deposited can kill cancer cells or cause genetic changes that lead to cancer cell death. High energy radiation can damage the genetic material of cells, such as DNA, and thus prevent the cells' ability to further divide and prolife rate. Radiation can damage both normal and cancer cells, but the main goal of radiotherapy is to maximize the radiation dose to abnormal cancer cells while minimizing exposure to normal cells around cancer cells or in the irradiated area [3]. Exposure to ionizing radiation is known to have lethal effect to blood cells because hematopoietic cells are sensitive to radiation exposure even in low doses. Cervical cancer and radiotherapy may kill blood cells, and the blood components counts will decrease [4]. Blood cells that may be influenced by radiotherapy are hemoglobin, leukocytes, and platelet cells. The decrease of leukocytes is associated with a decrease in body immunity system that plays an important role to fight infections. If the immunity falls, the body will be prone to infections [5]. Thrombocytes have the role in coagulation. The decrease in thrombocytes is called thrombocytopenia. At the thrombocyte level of thrombocytes have the role in coagulation.The decrease in thrombocytes is called thrombocytopenia. At the thrombocyte level of <10.000/µL, spontaneous bleeding increases. At the thrombocyte level of <50.000/µL, surgical procedures are often complicated by bleeding. At

the thrombocyte level of <100.000/µL, chemotherapy and radiotherapy are given more carefully because they
might worsen the thrombocytopenia and higher the risk of bleeding. Things explained above are what makes therapy in cancer in optimal [6]. Erythrocyte cells contain hemoglobin which has an important function of delivering oxygen from the lungs to all tissues in the body [7]. Anemia is a state of decreasing hemoglobin to <12g/dL [8]. And is one of the factors that can case tumor cells to experience hypoxia and is considered as a tumor response to radiotherapy by reducing oxygenation to the tumor and casing the cells to become radio-resistant or the level of ionizing radiation that the organism can withstand [9]. Tumor hypoxia itself can be a contributing factor to radiotherapy unresponsiveness. Also hypoxic tumor can cause a tendency to become more progressive and metastasize [10].

A study on the decrease in the number of erythrocytes, leukocytes and platelets in cervical cancer patients after radiotherapy from Tutut in 2012 proved that there was a decrease in the number of erythrocyte cells, leukocytes and platelets in patients after radiotherapy, the subjects of this study were all cervical cancer patients who received radiation therapy at the Radiotherapy Unit of Dr. Moewardi Hospital period May-October 2011, In this study, external radiotherapy using Cobalt-60 was used [11]. Nisa Azarina in her 2014 study regarding the effects of radiotherapy on Blood Cell production in patients with Cancer Mammae and Ca-Cervix found that platelet and leukocyte cells experienced significant changes after exposure to radiation, while erythrocyte and hemoglobin cells did not show any significant response [12]. Retianingsing in 2017 also observed the study of Standardization of Co-60 Radiotherapy Against Blood Cell quantity in cervical cancer in Sanglah Hospital, Denpasar. The results of this study showed that erythrocytes did not show a decrease, while leukocytes showed a decrease that was not very sharp or very low, Hgb was constant, and neutrophils at the beginning showed an increase which then decreased [13]. This research is different from previous studies, the previous study used a Co-60 radiation source and the radiation technique was not explained, while this study explained the radiation technique used was a 3-Dimensional technique performed using linear accelerator machine to treat all patients which lessens the exposure to normal tissue.

METHODS AND MATERIALS:

The subject of this study is 42 patients with cancer. They were treated with external radiotherapy and completed the treatment sessions using a linear speed device for treatment purposes only, the study was conducted from April 2024 to August 2024. Some patients underwent surgical, chemotherapy treatment and hormonal therapy before radiation therapy. We classified the study sample into eight groups according to the site of treatment (breast cancer, gastrointestinal tract (GIT), prostate, lung cancer, lymphoma, cervix, brain, head and neck).

The blood cell counts was checked before and during radiation therapy by automatic cell counter as a routine. In this study we focused on Lymphocytes, Platelets and hemoglobin counts as vital indicators. This study is an analytical study based on the collection of medical data from the records of the study sample radiotherapy clinic of the University Hospital- Tripoli. The data was entered into MS Excel 2007 version and the results were expressed as mean, and the comparison of mean was done using Student t –test and MedCal software 2024, P <0.1.

RESULTS

WBCs were markedly decreased significantly after the end of the radiotherapy compared to the white blood cells count at the beginning of the radiotherapy sessions. The difference among the periods were statistically significant as shown in (Fig 1).The number of platelets decreased after the end of the course of radiation therapy compared to the same results recorded for the same patients at the beginning of radiation therapy in all groups of the study sample, The statistical

difference between the groups was shown in (Fig 2).The hemoglobin rate decreased slightly at the end of treatment compared to the hemoglobin rate at the beginning of radiation therapy as shown in (Fig 3).

Table 1: The demographic data of the studied group of patients.

Variables	Categories	Frequency %
Gender	Female	26(61.90%)
	Male	16(38.09%)
Age	Minimum	17
	Mean± SEM	51.40±2.69
	Maximum	82

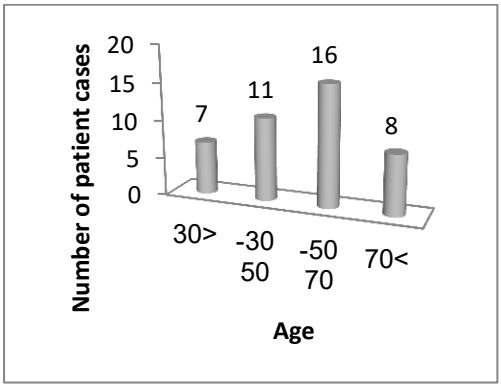
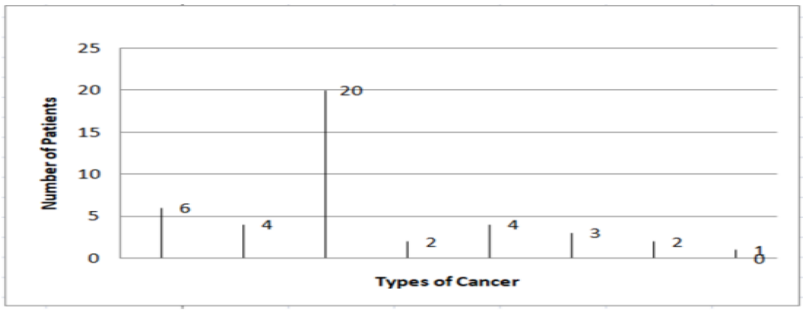


Figure 1. Number of patients according to age

Table 2: The frequency and percentage of the different types of cancer in the studied group of patients who underwent radiotherapy.

Group	Site	n(%)
I	Head and neck,	6(14.28%)
	Larynx	4(9.52%)
II	Breast	20(47.61%)
	Lung	2(4.76%)
	Lymphoma	4(9.52%)
3 III	Prostate	3(7.14%)
	Cervix	2(4.76%)
	Rectum	1(2.38%)



1. Figure. 2 .The frequency of the different types of cancer in the studied group of patients who underwent radiotherapy.

Table 3. Comparison of Haematological Parameters in Study Pre (n=42) and Post n=42) full cycle radiotherapy.

Index	Reading	Mean± SD	*P* = 0.10
WBC	Post RT	5.4721±1.7763	0.597
	Pre RT	5.6974± 2.1049	
PLts	Post RT	232.657±73.059	0.810
	Pre RT	236.893±86.504	
Hgb	Post RT	12.2931±1.4914	0.779
	Pre RT	12.3962±1.8580	

WBC= Leukocytes, RBC= Red blood cell, PLTs= Platelets, Hgb= Hemoglobin, CI= Confidence interval, SD= Standard deviation, SED= Standard deviation Error difference.

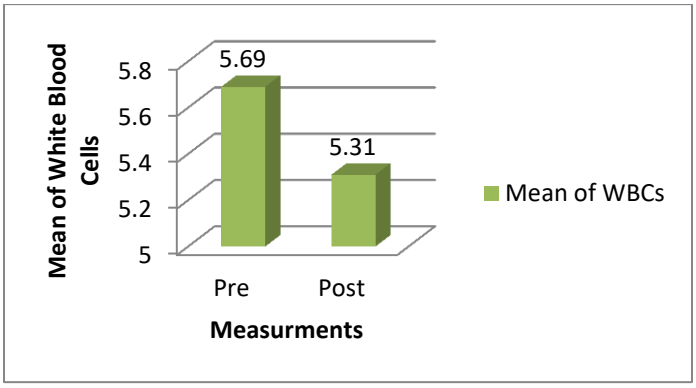


Figure.3. A comparison between White blood cells count *Pre* and *Post* Radiation therapy.

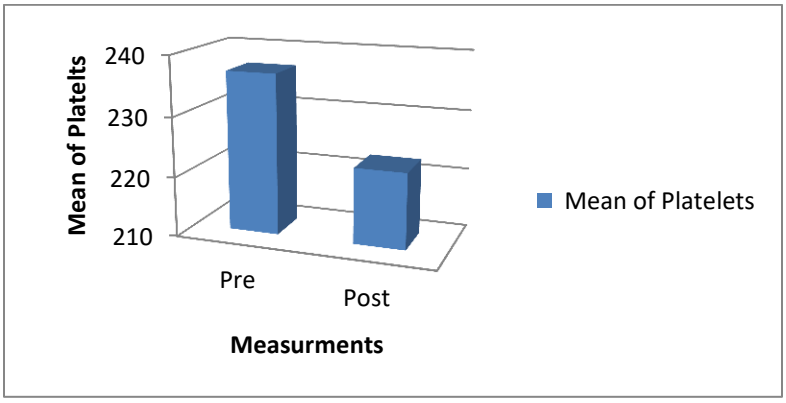


Figure.4. A comparison between Platelets count *Pre* and *Post* Radiation therapy.

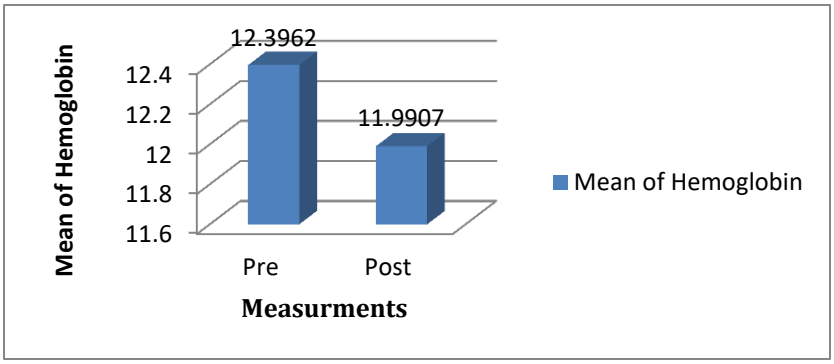


Figure.6. A comparison between Hemoglobin level *Pre* and *Post* Radiation therapy.

5.1. Discussion

Out of the 42 patients who received External radiation therapy at University Hospital-Tripoli Radiotherapy Department outpatient clinic. (Table 1) The demographic data of the studied group of patients Gender and age 26(61.90%) were female, and 16(38.09%) were male, the median age was 51.40±2.69 years. The male to female ratio was 0.615. The study sample was divided into eight main sites according on the anatomical location of the treatment, and the distribution of cases was as follows 6(14.28%) of cases were head and neck, 4(9.52%) Larynx cancers, 20(47.61%) Female Breast cancer, and 2(4.76%) Lung cancer, 4(9.52%) lymphoma cancer, 3(7.14%) Prostate cancer, 2(4.76%) Cervix cancer only 1(2.38%) as shown in (Table 2). The most common cancer in the studied population was breast cancer, 20(47.61%). Head and neck, and Larynx prostate, Lymphoma cancers were the second-most common cancers accounting for 6(14.28%). The results showed a positive results in total WBCs the reduction was statistically significant (*P*= 0.597), Platelets counts (*P* =0.810*)* and Hgb level was (*P*=0.779*)*, the decreased as shown in (Table 3). It is known that there are several factors that affect the rate of vital blood indicators, most likely due to food as a result of complications of radiation therapy, including the patient's unwillingness to eat food, as well as diarrhea, which is a complication of radiation therapy to the abdominal area (gastrointestinal tract) and is accompanied by loss of a large amount of fluid, on the other hand, systemic infections that invade the body when the patient's general immune system is weak[14]. Blood biomarkers are often used in routine tests to diagnose many diseases and to reflect the level of human health status, such as infections, anemia, immune disorders, cancer and many other diseases. The biomarkers of blood components of patients with tumors during external radiation therapy are affected to varying degrees by the controls that were set as an indicator in this study to evaluate the results, where they found that the average values of blood biomarkers were higher than the post-treatment index.

The previous study found that the decrease in vital indicators of blood components in oncology patients in particular is an indicator and a bad warning for the patient’s health in general, because patients who suffer from a severe deficiency in blood vital indicators were in an advanced disease stage and therefore have chances of recovery and survival in a good way. Less than other patients who were diagnosed with tumors early. Also, a decrease in blood parameters may be a sign of aggressive cancer due to its role in tumor development by changing the tumor microenvironment [15]. In general, it can be said that the decrease in vital blood indicators during radiotherapy negatively affects the desired results of the prescribed treatment plan and contributes to increasing the multiplication and spread of cancer cells in the body and reduces the patient’s recovery rates [16-17]. It is useful to monitor the health status of patients during radiotherapy especially monitoring parameters throughout the duration of treatment and after the end of treatment, due to the possibility of predicting the degree of recovery and also predicting the survival rate after treatment, which is usually estimated at 5 years as the results of monitoring blood indicators in radiotherapy treatment patients are documented in each patient's file, especially hemoglobin, platelets and neutrophils lymphocytes [18]. It has been suggested that lymphocytes should also be considered as a prognostic marker that may reflect the immune status of patients during and after treatment [19]. Other than systemic effect, radiotherapy also causes local side effects in the surrounding healthy tissue because oxidation of protein and lipids induced by the free radicals produced by exposure radiotherapy [18]. There are currently 2 scoring system for evaluating the late radiation toxicity, RTOG/EORTC and LENT/SOMA. These scores are specific for each organ tissue. However, there is no evaluation regarding the hematologic value [21, 22]. For acute radiation toxicity, there is only RTOG/EORTC scoring systems. This scoring system has evaluation regarding the hematologic value, where the lower the hematologic evaluation value, the higher the radiation toxicity score [21].

The real effect of radiation on aneurysms in a significant way often occurs in cases of irradiation of a large volume of the body at high doses of 3000 - 4000 cGy [23- 25] , also in cases of tumor treatment in specific places of the body and with advanced technologies that ensure accuracy and limited irradiation reduces the effect of radiation on blood production, which in turn translates into an increase or decrease in blood indices from normal rates.

The results of some studies showed that the average differences in basic blood parameters including leukocyte count, platelet count and hemoglobin rate in patients after completion of treatment showed some differences but did not reach statistically significant levels when compared at the beginning of treatment due to the fact that many patients are given stimulant drugs after external radiation therapy to stimulate and promote blood aneurysms to work normally [26].

In summary Radiotherapy had a significant impact on the body overall physiology, especial blood parameters in patients receiving radiation therapy had a significant decrease at a mean level of all blood parameters (WBCs, Plts and Hgb) during treatment and after treatment. It is known that the human body is an integral biological unit and its interconnection whose components interact to lead to the phenomenon of life. This unit is affected by several factors, including chemical or physical materials, and its effect is generally reflected in all the vital indicators of a person.

This study has some limitations, the main limitation of this study was the lack of careful follow-up and the lack of documentation of the results of the patient's biomarkers after surgery or chemotherapy. The results obtained from this study are consistent with the results of previous studies.

5.2. CONCLUSION

Therefore, from this study we conclude that blood biomarkers have differed in patients between the two periods at the beginning of treatment and at the end of treatment in patients with malignant tumors. We observed a decrease in blood levels, leukocyte deficiency as well as platelet and hemoglobin level in patients when compared with blood levels before the start of treatment and the differences are statistically significant. The data also indicated that some patients have received combination treatments, namely radiation therapy and chemotherapy, and it is known that chemotherapy has an effect on all body systems, which led to uncertainty that the effect is due to radiation therapy as a side effect. Blood tests are an important and integrated part of the treatment plan and the follow -up of cancer patients. It can help assess the degree of response to treatment and the development of various malignant tumors.

5.3.Recommendations

1. We recommend further future studies to determine whether the change is due to tumor progression or regression or just due to the effect of ionizing radiation on body physiology.
2. We recommend using modern radiotherapy devices, and techniques such as 3DRT, IMRT and IGRT which allows the exposure of the tumor area only, which in turn contributes to a significant and effective reduction in complications.
3. We recommend paying attention to documenting the results of the patient’s complete blood test on a regular weekly basis during all stages of the various treatments and paying attention to the patient’s healthy nutrition because it is an essential element that has an important impact on the patient’s health and contributes to strengthening the immune system and increasing recovery rates.

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Author contribution

All authors made a significant contribution to the work reported, whether in the conception, study design, execution, data acquisition, analysis and interpretation, or in all these areas; participated in drafting, revising or critically reviewing the article. Final approval was given for publication; all authors have agreed to the journal to which the article has been submitted and agree to be accountable for all aspects of the work

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The authors report no conflicts of interest in this work.

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