University of Thi-Qar Journal of Science (UTJsci)
E-ISSN: 2709-0256, P-ISSN: 1991-8690, Vol. 11, No. 2, Dec. 2024

Investigation of Doxorubicin Efficiency in Some Hematological Parameters in Women with Breast Cancer in Iraq

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Received: 2024-09-20, Revised:2024-10-12, Accepted: 2024-11-04, Published: 2024-12-31

***Abstract*— Breast cancer is a prevalent disease among females worldwide. Low levels of doxorubicin are used as a standard treatment, predicting severity, mortality, and treatment compliance. This study aims to explore differences in hematological profiles and effects of doxorubicin in breast cancer patients. A descriptive cross-sectional study in Thi-Qar province compared the hematological parameter of the forty Female Breast Cancer patients. Patients' data were then grouped according to four categories: chemotherapy sessions. It will take 8 months of chemotherapy and will involve one session every 21 days. The results showed that the patients had an average white blood cell count of 5.85, lower than the control group's 8.8, and a mean hemoglobin of 10.99. The patient group had a mean platelet count of 321.7, higher than the control group's 251.4, indicating a statistically significant difference at a significance level of $\alpha \leqslant 0.05$. Doxorubicin continues to be used in the management of breast cancer; nonetheless, its utilization is limited because of toxicity, including cardiotoxicity and myelosuppression. As it is with tradition in advanced breast cancer, the vast majority of the submitted patients experienced some form of hematological alteration, which includes anemia, leucopenia, and thrombocytosis. Hematologic studies are thus very relevant in breast cancer management, its progression, and also in detection of some sequential malignancies related to breast cancer.**

***Keywords*— Doxorubicin, Breast cancer, Hematological parameters, Chemotherapy.**

I. INTRODUCTION

Cancer is the unrestricted growth of a minute percentage of the individual's cells that is out of billions of cells; it spreads to other organs. Tumours, most often cancerous, can develop in any organ or any part of the body. The body goes through the process of cell division, and as such, new cells are formed, replacing the damaged or dead cells. When this controlled mechanism is interrupted, damaged or abnormal cells are capable of growing and dividing unusually leading to the formation of tumors. There are two types of tumors: Benign and malignant [1]. Cancer is one of the major killers globally [2], and the only disease that comes close to it in deaths recorded is cardiovascular disease [3]. Lifestyle changes have been shown to be responsible for 90-95% of all the cancers known today; these include smoking, obesity, and lack of physical exercise. Inheritance is another factor that plays a role, which comprises 5-10 percent [4]. Breast cancer is one of must prevalent diseases in the female population globally [5] and is responsible for 25% of all female cancers [6]. It affects 12. 8% among women and has a rather high mortality. It is the number one killer of women and is likely to increase to 45% of the developed countries by the year 2025 [7-9]. In Iraq, it is the first cancer in the ranking diagnosed in women [10]. Another target indication of chemotherapy is for most kinds of decreasing the size and load of tumors and preventing cancer for recurring after an operation. Nevertheless, services development of these drugs is associated with drug resistance as well as toxic side effects, which may help cancer to progress and metastasize [1] [11]. Doxorubicin (DOX), also known as Adriamycin, is an anticancer drug used to treat pediatric and adult cancers that include solid tumors, leukemia, lymphoma, and breast cancer. However, effective management is discouraged by toxicity aspects, which include hematologic toxicity, gastrointestinal intolerance, extravasation, and alopecia [2, 12-14]. DOX is known to act on DNA molecules and dismantle the functions of topoisomerase II enzyme, altering the chromatin of cancer cells to cause death. It also creates free radicals and thus enables radical attack through the process of oxidative stress. It is an essential hematological test to identify various diseases, for instance, anemia, infections, bleeding, allergic malignancies and cancer, immune disorders, total body health screening, and pre-operative examination. It offers outline information about cell types that Include red blood cells (RBC), White blood cells (WBC), and Platelets (PLT) [1,2]. Complete blood count (CBC) is cost-effective and accurate in assessing diseases, and its usefulness is quite evident in patients diagnosed with breast cancer [3] . Assessment of the hematologic variables is essential in treatment management [4]. This research aims to evaluate changes in hematological profiles of women cancer patients receiving DOX, to hematological changes.

https://doi.org/10.32792/utq/utjsci/v11i2.1304

II. Materials and Methods

a) Patients

Some hematological parameters were also measured in a cross- sectional study both on old and young female breast cancer patients attending private hospitals and daily clinics in Thi-Qar province compared to healthy individuals as control subjects. Forty female breast cancer patients and 40 healthy women were enrolled between October, 2023 and April, 2024 Chemotherapy treatment sessions were used to segment patients into four groups: The complete blood count questionnaire along with the session questionnaire list, and 1st treatment, 2nd treatment, 3rd treatment, and 4th treatment for each session on complete blood count questionnaire list was used to gather data concerning the ages, weights, number of doses as well as the question to the chronic illness patients were provided.

b) Hematological Parameters

A total of 2 ml of blood from each patient and a control sample were collected into an EDTA tube for CBC testing and analysis on the same collection day Total white blood cell count was determined by a complete blood picture. Complete Blood Picture Device: Fully automated hematology analyzer- China 2013. It is estimated that the majority of the breast cancer patients diagnosed at different stages will need to undergo use of chemotherapy Doxorubicin, 60 mg/m^2 is diluted with 100 ml of normal saline and is given via intravenous drip for about ten to fifteen minutes. The patients normally receive chemotherapy for about eight months where one session is given every 21 days.

C) Statistical Analysis

A statistical analysis of this study was done using SPSS version 24. A T-test at probability level $p \leqslant 0.05$ was used to compare blood parameters between patients and the healthy group, with $p \leqslant 0.05$ mean significant differences. A comparison of blood parameters between the two study groups according to dose was done using the ANOVAtest with the least significant difference (LSD).

III. Results

The current study included 80 females, 40 patients with breast cancer, and 40 healthy as a control group. The mean age of patients and control group was 48.50 ± 13.08 and 41.95 ± 15.87, respectively. From the table 1 that was constructed, it was evident that the patients' average white blood cell count was 5. 85, which was below 8.16 that was recorded for control group, the (t) test result outcome comes out equal to 4. 43. Accordingly, it can be concluded that there is a statistically significant difference between the patient and control groups at a significance level of ($p \leqslant 0.05$). Mean hemoglobin of the patients was 10. 99 whereas the control group scored an average of 13.58, the mean value of the t-test was obtained as 7.50, this is an indication of a statistically significant difference of the results with the accepted level of significance being ($\leqslant 0.05$). The patient group presented with a mean platelet count of 321. 70, which was considerably higher as compared to control group having an average score of 251.43, in accordance with the t-test equal 3. 11, thus signifying that the two groups have a statistically significant differences at the set level of significance of ($p \leqslant 0.05$).

Table 1: Hematological parameters of female breast cancer patients (treated with DOX) and control

Parameters	Mean ± Std. Deviation		t	P-value
	Control	Patients		
WBC 4-10×103/µl	8.16 * ± 2.06	5.85 ± 2.58	4.43	0.00 *
Hb 12-17gm/dl	13.58 * ± 1.34	10.99 ± 1.72	7.50	0.00
Platelets 150-400×103/µl	251.43 ± 28.06	321.70 * ± 140.02	3.11	0.003

*** P value ≤ 0.05 was considered statistically significant.**

As indicated in the Table 2, we compared the mean ± Std. deviation of the given hematological parameters in breast cancer patients and controls. Mean WBCs in various groups were analyzed and found to have different variations ($P \leq 0.05$) in breast cancer groups, namely 8. 06 ±1. 29; 6. 36 ± 2. 29; 5. 53 ± 3. 14; 6. 34 ± 1. 52 respectively to the control group (8. 16 ± 2. 06 2^{nd}, 3^{rd}, and 4^{th} dose groups demonstrate significant reduction compared with the control group. Mean depressed hemoglobin value was observed in breast cancer groups (12. 22 ±1. 95; 11. 35 ±2. 04; 10. 58 ±1. 00; 10. 80±1. 21) as compared to control group (13. 58 ± 1. 34) with significant ($P<0.01$). The 1^{st} (276.54± 117.05), 3^{rd} (288.78 ± 89.78) and 4 th (322.75± 113.3) treated groups and control group (280.00 ±68.11) showed no significant difference between them in platelet count. A significant reduction level of $P<0.05$ in 2^{nd} group (251.43 ± 28.06) in platelet count compared with 4^{th} (322.75± 113.33).

Table 2: Comparative analysis of blood parameters among various groups

Dose	WBCs	Hb	platelets
Control	8.16 ± 2.06 a	13.58 ± 1.34 a	280.00 ±68.11 ab
Dose 1	8. 06 ±1.29 a	12.22 ±1.95 b	276.54± 117.05 ab
Dose 2	6.36 ±1.29 b	11.35 ±2.04 c	251.43 ± 28.06 b
Dose 3	5.53 ± 3.14 b	10.58 ±1.00 d	288.78 ± 89.78 ab
Dose 4	6.34 ± 1.52 b	10.80 ± 1.21 d	322.75± 113.33 a
LSD	0.88	0.61	42.4

Similar letters in the same row indicate non-significance at the p< 0.005

In Table 3, the current study showed that the relationship between white blood cells and a number of dose was inverse and without significant differences (r= -0.211). Regarding hemoglobin, the relationship was inverse with dose number (r= -0.052) and direct with white blood cells (r= 0.164) with non-significant references at $p \leq 0.05$. As for

platelets, their relationship was inverse with dose number and hemoglobin (r= - 0.307 and r= - 0.114) with non-significant differences, but the relationship between platelets and white blood cells was direct with significant differences (r= 0.599).

Table 3: Correlation between number of doses and WBCs, Hb, and platelets counts.

Correlations					
		No. of doses	**WBC**	**Hemoglobin**	**Platelets**
Number of doses	**Pearson Correlation**	**1**			
	Significant P- value				
WBCs	**Pearson Correlation**	**-0.211**	**1**		
	Significant P- value	**0.190**			
Hemoglobin	**Pearson Correlation**	**-0.052**	**0.164**	**1**	
	Significant P- value	**0.748**	**0.313**		
Platelets	**Pearson Correlation**	**-0.307**	**0.599***	**-0.114**	**1**
	Significant P- value	**0.054**	**0.000**	**0.484**	
***. Correlation is significant at the 0.01 level.**					

IV. Discussion

Complete blood counts (CBCs) are used to aid in the practical diagnosis of many diseases, such as anemia, acute infections, bleeding conditions, allergic disorders, malignancies, and immune disorders, as well as preoperative evaluations and health screening. According to data in Table 1, breast cancer patients showed low levels of hemoglobin, leukopenia, and thrombocytosis. This may be because chronic low-grade inflammation leads to increased levels of pro-inflammatory cytokines such as IL-1, IL-6, TNF-α, and INF-δ, which causes iron retention by the reticuloendothelial system, gastrointestinal tract, and liver, thus inhibiting red blood cell and white blood cell precursors and leading to anemia and, this study corresponds with the report of [3-6]. While there were significant changes in PLT count between breast cancer patients and the control group ($p > 0.003$), This may be caused by infections, which on their own would maintain platelets or due to the use of certain medications that would otherwise maintain platelets. There is a correlation between instance and grade of systemic inflammation and thrombocytosis and significant cytokine roles in thrombogenesis, including interleukin 6. L6 is considered to be prothrombotic by activating thrombopoietin with the help of a human monocyte cell line [7, 8]. In cancer patients, it has also been observed that interleukin-6 has thrombogenic activity as it has a thrombocytosis effect [9].

Table (2) showed that there was a significant reduction in WBCs count in the 2^{nd}, 3^{rd}, 4^{th} dose groups as compared to the control group; other researchers have also observed the same [10]. The research of [10] depicted that the WBC in breast carcinoma patients is significantly low as matched to control. This confirmed with the findings of the study conducted by reported by [11], who observed that the absolute leukocyte count was 5-6 ×10/l. CIA that it results from malignant invasion of normal tissues resulting in blood loss, bone marrow infiltration with erythropoiesis, and iron deficiency following inflammation. Low hemoglobin has its impact and consequences of reduced oxygen availability in tumor microenvironment. Rheological disorders, for instance, chronic anemia might be implicated in low PCV. Hemorrhagic anemia may also develop, and this leads to iron deficiency , hence deficiency of hemoglobin [6]. The mean serum level of hemoglobin fell ($P< 0.01$) in breast cancer groups 1^{st}, 2^{nd} , 3^{rd} , and 4^{th} respectively , when compared to the control group (13.58 ± 1.34)Such low values of Hb have implications on both the side effects and oxygen delivery to the tumour site. This may be attributed to chronic anemia since a lowercase PCV is quite revealing of a possible anemic state. It may be hemorrhagic anemia and can cause deficiency of iron also [12, 13]. This could be because of infections that keep platelets or some drugs that would keep platelets this is similar to a study [14] that shows that doxorubicin/paclitaxel treatment increases the peripheral blood platelets significantly, similar to the previous study, where platelet sparing effect of paclitaxel was observed in patients treated with paclitaxel and carboplatin other than what might happen when combined with other toxic [9, 15, 16]. As for Table No. 3, the relationship between the blood parameters was insignificant except for the only significant relationship at the 0.01 level between the platelets and WBC count [16].

V. Conclusion

Although doxorubicin continues to be used for the treatment of breast cancer, its application is associated with marked adverse effects such as myelosuppression and cardiotoxicity. Thus, it can be summarized from the present study that breast cancer patients have altered, abnormal hematological picture. These patients often had abnormal levels of hematological parameters, building including such alterations as anemia, leucopenia, and thrombocytosis. Hematological studies play a significant role in the assessment of disease progression and the categorization of various tumors.

Conflict of interest

Authors declare that they have no conflict of interest.

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