Evaluate the Alterations in Hematological Parameters among Breast Cancer Patients at the Sabratha National Cancer Institute in Western Libya

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Abstract: Background: *Breast cancer is a type of cancer that develops in the tissues of the breast, most commonly the ducts and lobules. It is the most common female malignancy, the second most common cause of cancer-related mortality worldwide for women, and its incidence is on the rise in Libya. In patients with breast cancer, hematological indicators can forecast follow-up care, mortality, and severity.* ***Objectives:*** *The current study aims to assess the alterations in hematological parameters among patients with breast cancer at the Sabratha National Cancer Institute.* ***Materials and Methods:*** *The present study was conducted on 100 breast cancer patients, attending the National Cancer Institute of Sabratha for breast examination to detect cancerous or pre-cancerous conditions of the breast or other medical conditions from the 1st August 2018 to the 31st January 2021, were enrolled in this prospective study. Also, 100 healthy individuals without any chronic disease were recruited for the control group. Their ages ranged from 19 to 80 years old. Blood samples were collected by vein puncture, 3 ml of venous blood withdrawn from each participant in the study by using disposable syringes under an aseptic technique; they were then transferred to a sterile EDTA tube, for complete blood count. Complete blood count was determined using an automated hematology analyzer Sysmex (KX 21) machine in the Centre laboratory of the National Cancer Institute of Sabratha. The data were analyzed using Statistical Package for Social Sciences (SPSS 26) software.* ***Results:*** *The results showed a significant (P<0.01) decrease in RBCs counts, hemoglobin concentrations, hematocrit values, MCV, MCH, MCHC, lymphocytes %, and blood platelets count in breast cancer patients when compared with healthy women. On the other hand, WBCs count and neutrophils % were significantly (P<0.01) increased in breast cancer patients compared with the healthy women.* ***Conclusion:*** *It can be concluded that hematological parameters among patients with breast cancer showed a significant change compared with healthy women. The easiest and most important examination tool for diagnosing disease is a complete blood count. Additional hematological research is required to validate these findings. Additionally, patients with breast cancer should have their hematological markers regularly monitored.*

Keywords: Breast Cancer, Hematological parameters alterations, Sabratha National Cancer Institute, Western Libya.

1. Introduction:

Breast cancer is a type of cancer that develops in the tissues of the breast, most commonly the ducts and lobules. It can affect both men and women (Kufe *et al.*, 2003, Ali, 2014). Globally, women are more frequently diagnosed with breast cancer. It is responsible for 25% of all malignancies in women. This malignancy has a high death rate and is invasive (Divsalar *et al.,* 2021). Breast cancer affects one million women annually, according to Hunter, 2000. Over the previous 40 years, there has been a steady increase in the incidence rate of breast cancer. It is the second most common cause of cancer-related mortality worldwide for women between the ages of 20 and 59 (Jemal *et al.*, 2003, Ali, 2014). Breast cancer is the most common female malignancy, and its incidence is on the rise in Libya (Amshahar and Ashur,2020).

The new detection of cancer is increasing in economically developing countries as a result of population aging and growth, as well as the increasing adoption of cancer-related lifestyle choices, including smoking, physical inactivity, and high-fat diets (Jemal *et al.,* 2011).

Many risk factors increase the incidence of breast cancer, including sex; Women are more susceptible to breast cancer than men, as is obesity. Excess weight may increase the possibility of disease, lack of exercise and drinking alcohol, hormone replacement therapy during menopause, exposure to ionizing radiation, early puberty for girls, having children at a late age or not having children, advanced age and family history of the disease (Rosenthal , 2001).

A complete blood count is a standard test that doctors often order to diagnose a range of illnesses, including anemia, acute infections, hemorrhage, cancer, allergic malignancies, immunological disorders, screening for health issues, and preoperative evaluations. It offers vital details regarding many cell types, particularly those of the RBCs, WBCs, and blood platelets (Ali, 2014, Wang *et al.,* 2018, Divsalar *et al.,* 2021). Divsalar *et al.,* 2021 reported that complete blood count in patients with breast cancer are deranged compared with the controls. Therefore, before beginning any treatment, hematological parameters should be tested for in patients with breast cancer as they have a prognostic value (Chen *et al.,* 2020, Khan *et al.,* 2020, Divsalar *et al.,* 2021). In patients with breast cancer, hematological indicators can forecast follow-up care, mortality, and severity (Divsalar *et al.,* 2021).

2. Objectives:

The current study aims to assess the alterations in hematological parameters among patients with breast cancer at the Sabratha National Cancer Institute.

3. Materials and Methods

3.1. Study design and population

From 1 st August, 2018, to 31st January, 2021, 100 patients with breast cancer who visited the National Cancer Institute of Sabratha for a breast examination to check for cancerous or precancerous conditions in the breast or other medical conditions were enrolled in this prospective study. The Sabratha National Cancer Institute's Research and Ethical Committee gave its approval for this study. For the control group, 100 healthy individuals free of any chronic illnesses were also enlisted. The mean ages of patients and healthy individuals were 47±12 and 46±12.51, respectively and the ages ranges between 19 and 80 years. Each research participant had a vein puncture to obtain 3 ml of venous blood, which was then aseptically extracted using disposable syringes and transferred to a sterile EDTA tube for a complete blood count.

3.2. Determination of Hematological Parameters

An automated hematology analyzer Sysmex (KX 21) machine in the National Cancer Institute of Sabratha's Center laboratory was used to measure the red blood cells count, hemoglobin concentration, hematocrit value, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, white blood cell count, differential count of leucocytes, and blood platelet count.

3.3. Statistical analysis

The data were analyzed using Statistical Package for Social Sciences (SPSS 26) software. To evaluate if the distribution of continuous variables was normally distributed, the Kolmogorov-Smirnov test was employed. The student's t-test was used to determine the statistical significance of the differences between the groups. The results were expressed as mean ± standard deviation and considered statistically significant when *p<0.05*.

4. Results:

4.1. **Red blood cells count and its indices in healthy women and breast cancer patients**

The data in Table (1) and Figure (1) show a significant (*P<0.01*) decrease in RBCs counts (3.40 ± 0.04) x10^6 cell/µl in the breast cancer patients as compared with the healthy women (4.35 ± 0.11) x10^6 cell/µl.

A significant (*P<0.01*) decrease in hemoglobin concentrations was found (10.62 ± 0.13) g/dl, in the breast cancer patients when compared with the healthy women (13.81 ± 0.12) g/dl (Table 1 & Figure 2). Hematocrit values were significantly (*P<0.01*) decreased (30.71 ± 0.61) in the breast cancer patients when compared to the healthy women (41.93 ± 0.96) (Table 1 & Figure 3).

The results in the same table show a significant (*P<0.01*) decrease in MCV $(85.02 \pm 0.15 \ \mu^3)$, MCH $(27.14 \pm 0.41 \ pg)$, and MCHC $(33.83 \pm 0.32 \ g/dl)$ in the breast cancer patients when compared to the healthy women $(89.62 \pm 0.62 \ \mu^3)$, $(29.94 \pm 0.32 pg)$, and $(33.83 \pm 0.32 \ g/dl)$, respectively (Table 1 & Figures 4-6).

Table. 1: Red blood cells count and its indices in healthy women and breast cancer patients

Groups Parameters	Healthy Women Mean ± SD	Breast Cancer Patients Mean ± SD
Red Blood cells count (x10^6 cell/µl)	**4.35 ± 0.11**	**3.40 ± 0.04**[**]
Hemoglobin concentration (Hb, g/dl)	**13.81 ± 0.12**	**10.62 ± 0.13**[**]
Hematocrit value (Hct, %)	**41.93 ± 0.96**	**30.71 ± 0.61**[**]
Mean Corpuscular Volume (MCV, µ3)	**89.62 ± 0.62**	**85.02 ± 0.15**[**]
Mean Corpuscular Hemoglobin (MCH, Pg)	**29.82 ± 0.21**	**27.14 ± 0.41**[**]

Mean Corpuscular Hemoglobin Concentration (MCHC, g/dl)	33.83 ± 0.32	31.42 ± 0.16[**]	[**]:

Significant at *P<0.01* compared with the healthy women.
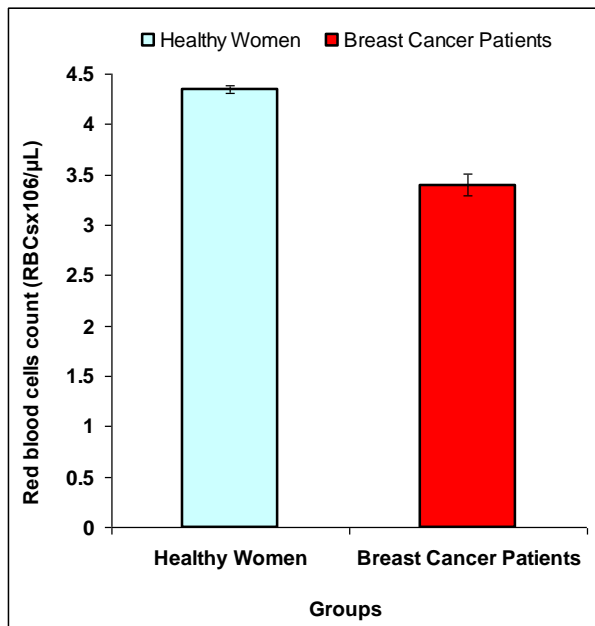

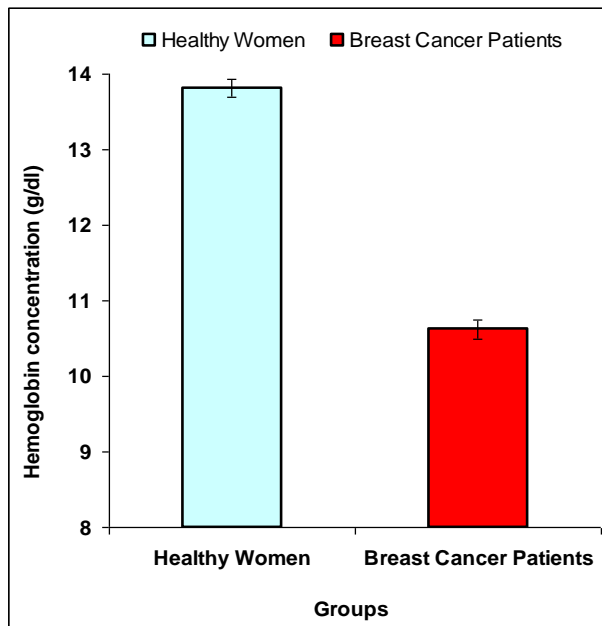Figure.1: Red Blood cells count in healthy women and breast cancer patients

Figure.2: Hemoglobin concentration in healthy women and breast cancer patients.
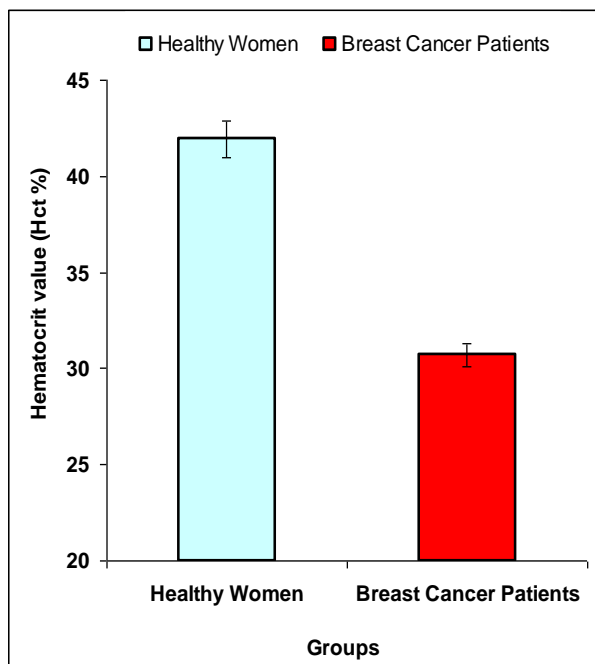

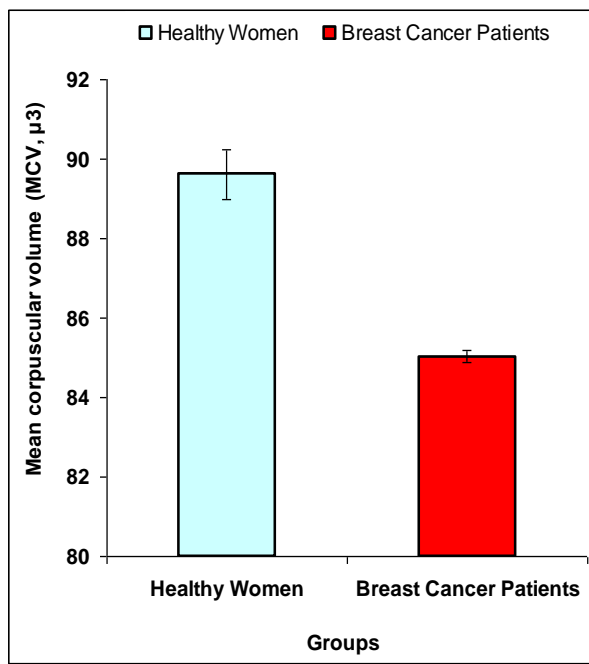Figure.3: Hematocrit value in healthy women and breast cancer patients.

Figure.4: Mean corpuscular volume in healthy women and breast cancer patients.
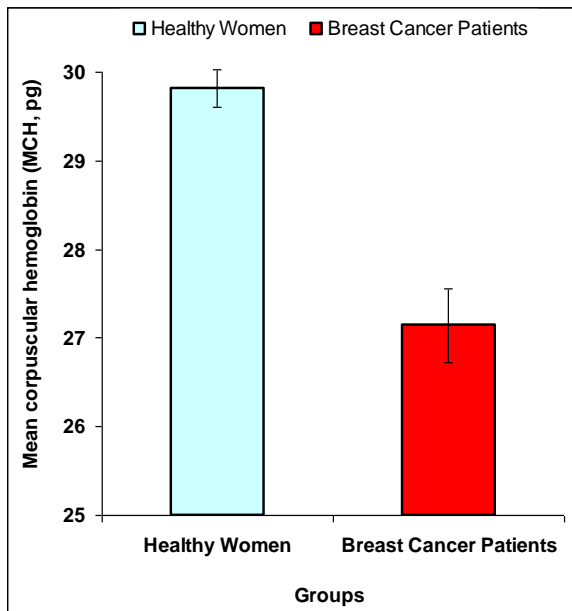
Figure.5: Mean corpuscular hemoglobin in healthy women and breast cancer patients.
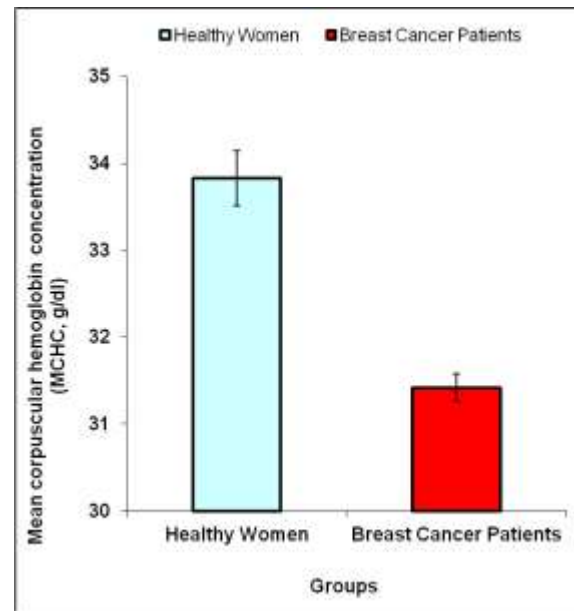

Figure.6: Mean corpuscular hemoglobin concentration in healthy women and breast cancer patients.

4.2. White blood count, differential count, and platelets count in the healthy women and breast cancer patients

WBCs count exhibited a significant ($P<0.01$) increase in breast cancer patients when compared with the healthy women (Table 2 & Figure 7).

The data recorded in table (2) and figure (8, &10) indicated a significant ($P<0.01$) increase in neutrophils % (61. 85± 0.53) and mixed % (10.13 ± 0.13) in breast cancer patients as compared with the healthy women (58.19 ± 0.84), and (6.18 ± 0.12), prospectively.

On the other hand, lymphocytes % and blood platelets count were significantly ($P<0.01$) decreased [(28.02 ± 0.24) and (25 0± 9.1)) x10^3 cell/µl in breast cancer patients as compared to the healthy women (35.63 ± 0.91) and (280 ± 8.3) x10^3 cell/µl), respectively (Table. 2& Figure. 9& 11).

Table. 2: White blood count, neutrophils %, lymphocytes %, mixed %, and platelets count in the healthy women and breast cancer patients

Parameters	Groups Healthy Women Mean ± SD	Breast Cancer Patients Mean ± SD	** :
WBCs Count (x10^3)	5.39 ± 0.22	7.86 ± 0.14**	
Neutrophils %	58.19 ± 0.84	61.85 ± 0.53**	
Lymphocytes %	35.63 ± 0.91	28.02 ± 0.24**	
Mixed %	6.18 ± 0.12	10.13 ± 0.13**	
Platelets Count (x10^3)	280 ± 8.3	250 ± 9.1**	

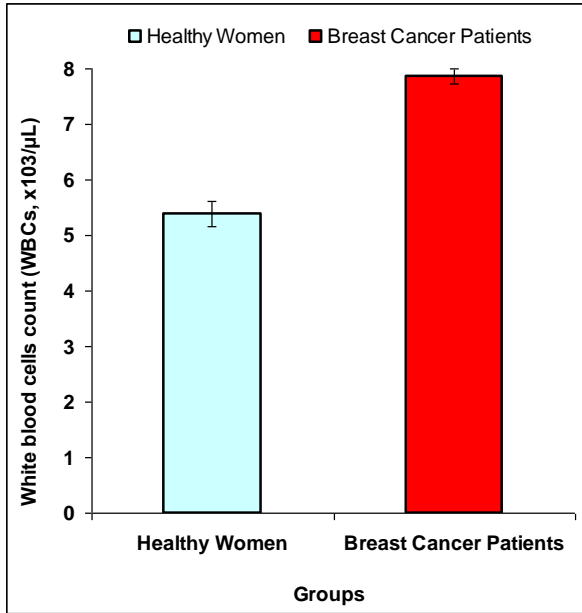**Significant at *P<0.01* compared with the healthy women.**

Figure.7: White blood cells count in healthy women and breast cancer patients.
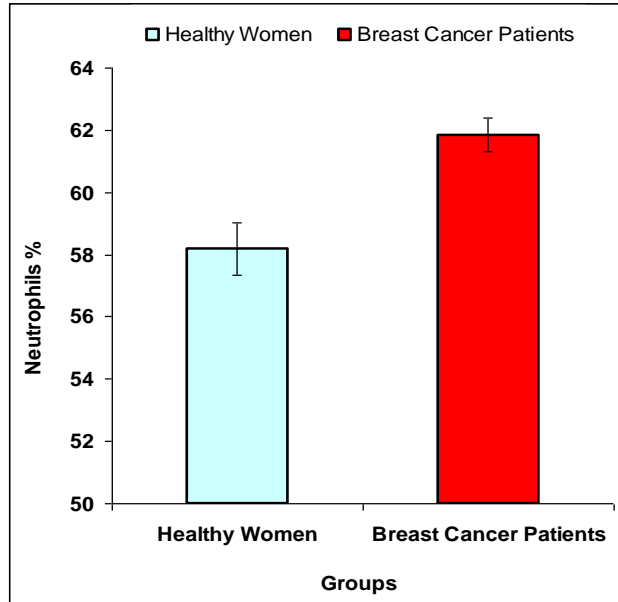

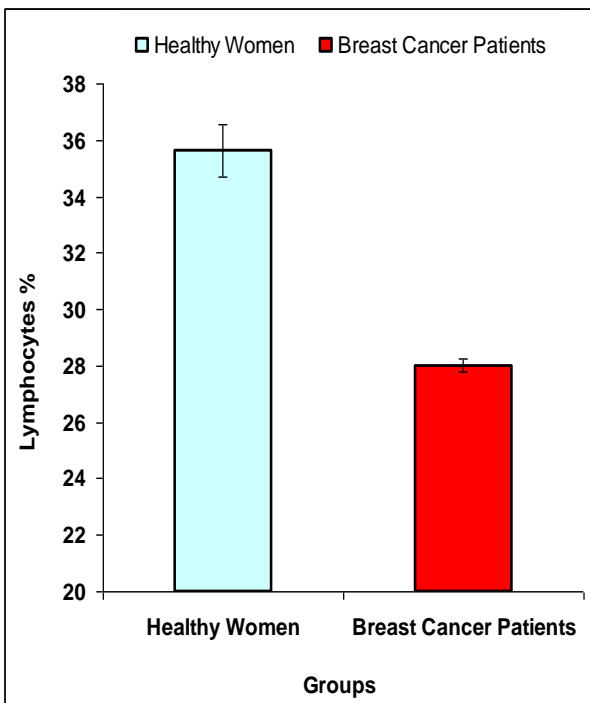**Figure.8:** Neutrophils % in healthy women and breast cancer patients.

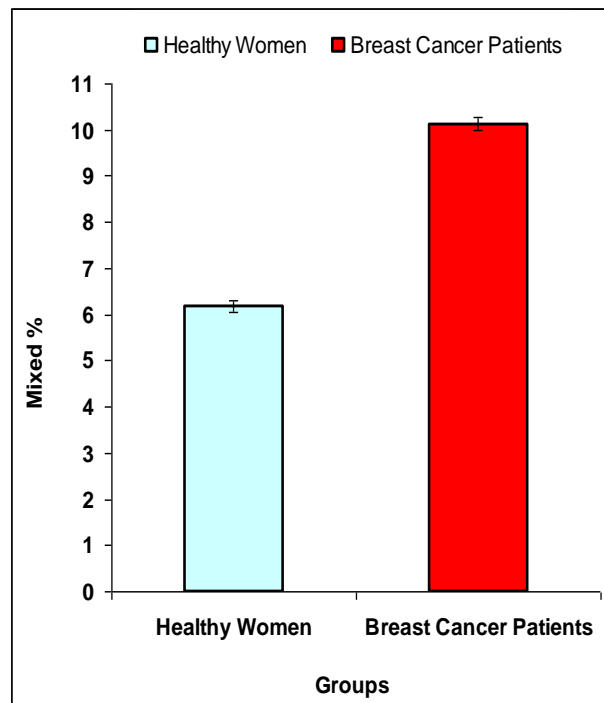**Figure.9:** Lymphocytes % in healthy women and breast cancer patients.

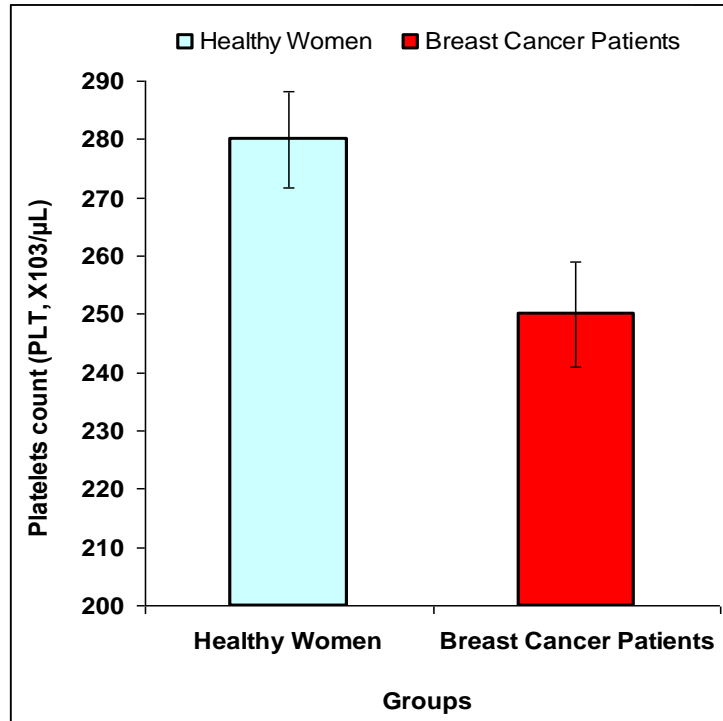**Figure. 10:** Mixed % in healthy women and breast cancer patients.

Figure.11: Platelets count in healthy women and breast cancer patients.

5. Discussion

The current study has investigated the alterations in hematological parameters among 100 patients with breast cancer at the Sabratha National Cancer Institute in western Libya compared with healthy women

The hematological parameters have prognosis value in patients with breast cancer (Chen *et al.,* 2020, Divsalar *et al.,* 2021), so, it is an essential test for patients with breast cancer before using any treatment (Khan *et al.,* 2020, Divsalar *et al.,* 2021).

The results of the current study are showed a significant ($P<0.01$) decrease in RBCs counts, hemoglobin concentrations, hematocrit values, MCV, MCH, and MCHC in breast cancer patients when compared with the healthy women. These results are in concordant with the study of Divsalar *et al.,* 2021 who found that a significant decrease in RBCs count, hemoglobin concentration, hematocrit value, mean corpuscular volume, and mean corpuscular hemoglobin in patients with breast cancer compared with the controls. Also, Gascon and Barret-Lee, 2006 and Akinbami *et al.,* 2013 were recorded that the mean MCV, MCH, and MCHC of breast cancer patients were lower than the controls. Also, Ali, 2014 reported that RBCs count and Hct were decreased in breast cancer patients compared with the controls. In ddition, Ufelle *et al.,*2012 recorded that a significant decrease in hematocrit value in breast cancer patients compared with the controls.

These hematological parameters may have decreased due to metastasis to the bone marrow from breast cancer can be associated with suppression of erythropoiesis. Infection in fungating malignancies may be associated with red blood cell hemolysis (Akinbami *et al.,* 2013), elevated levels of pro-inflammatory cytokines, such as IL-1, IL-6, TNF-α, and INF-δ, which cause the liver, gastrointestinal tract, and reticulo-endothelial system to retain iron, inhibiting erythroid precursors in the process (Moraes *et al.,* 2000, Ali, 2014), and the effect of the breast cancer on erythropoiesis (Akinbami *et al.,* 2013). The current study found that, in comparison to healthy women, patients with breast cancer had a considerably lower ($p<0.01$) red cell count and hematocrit level. The mean age of these patients was 47.9±12.6 years. Could this be as a result of the parameters' tendency to decline beyond the fifth decade (Castro *et al.,* 1987, Ulrich and Simon, 2010, Ali, 2014) or the existence of cancer, which is linked to both bone marrow suppression and immunosuppression (Ali, 2014).
The platelet count is an indicator of systemic inflammation that is brought on by tumor growth (Klinger and Jelkmann, 2002, Alexandrakis *et al.,* 2003).

The results of the current study are showed a significant ($P<0.01$) decrease in blood platelets count in breast cancer patients when compared with the healthy women. These results are in agreement with the previous studies (Beresford *et al.,*2006, Ufelle *et al.,*2012,

Ali, 2014). Bone marrow metastasis may be associated with defective thrombopoiesis causing malignancy induced thrombocytopenia (Akinbami *et al.,* 2013).

On the other hand, Akinbami *et al.,* 2013 mentioned that the mean of blood platelet count of breast cancer patients was higher than the controls. Proinflammatory cytokines like IL-1 and IL-6 cause the development of megakaryocytes and thrombocytosis (Klinger and Jelkmann, 2002, Alexandrakis *et al.,* 2003).

Khan *et al.,* 2017claimed that the hematological parameters, in particular lymphocytes and neutrophils, are important tools for stage diagnosis and breast cancer monitoring.

The results of the current study are showed a significant (P<0.01) decrease in lymphocytes % in breast cancer patients when compared with the healthy women. A similar results obtained by Ali, 2014, Etim *et al.,* 2018, and Shilpa *et al.,* 2020 who recorded that the mean of lymphocyte % was significantly decreased in breast cancer patients compared to the controls. Olufemi *et al.,* 2013 found that a non significant decrease in lymphocytes % in females with breast cancer compared with the controls. Tumor growth factor B, interleukin-10, reactive oxygen species, and other immunosuppressive substances generated by the tumor or its microenvironment reduced the generation of lymphocytes (Whiteside 2006).

The present study showed a significant (*P<0.01*) increase in WBCs count and neutrophils % in breast cancer patients compared with the healthy women. A similar finding has been reported by Akinbami *et al.,* 2013 who found that the mean WBC counts, and neutrophil percentages of breast cancer patients were higher than the controls. Infection in fungating malignancies may be associated with leucocytosis (Akinbami *et al.,* 2013). Neutrophilia was independent risk predictors for breast cancer (Okuturlar *et al.,* 2015). Certain chemokines secreted by tumour cells, such as angiotensin II or granulocyte-colony stimulating factor, stimulate the bone marrow to produce more neutrophils (McAllister and Weinberg 2014). Also, Divsalar *et al.,* 2021 recorded that a significant increase in WBCs count in breast cancer patients compared with the controls. The fact that neutrophilia was linked to neoplasms of all kinds may be the cause of this. 50% of neutrophils, which are typically observed to border the walls of vessels and are not typically seen in blood counts, demarginate. This can be caused by a lymphovascular invasion that results in tumor cells demarginating the vascular spaces (either lymphatics or small capillaries). The primary process of tumor immunity is the destruction of cancer cells by CD8+ cytotoxic T-lymphocytes. The lymphocytes known as natural killer cells have the ability to eliminate cancer cells without the need for prior sensitization. To avoid immunization, many cancers, however, downregulate the expression of class 1 major histocompatibility complex components. As a result, the lymphocyte count could be high or low (Akinbami *et al.,* 2013).

6.   Conclusion:

It can be concluded that hematological parameters among patients with breast cancer showed a significant changed compared with the healthy women. The easiest and most important examination tool for diagnosing disease is a complete blood count. Additional hematological research is required to validate these findings. Additionally, patients with breast cancer should have their hematological markers regularly monitored.

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