

## Study of Some Biochemical and Blood Parameters as Screening Markers for Breast Cancer Patients before Adjuvant Therapy in Thi Qar Government-Southern Iraq

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### Abstract

Breast cancer is the most common malignancy disease in women. The study includes Eighty-three cases were divided according age into women (patients and healthy ) average age more than forty five( Age > 45 year) Fifty - five confirmed subject of breast cancer patients (n = 42), healthy as control group (n=18) and women (patients and healthy) average age less than forty five Age (< 45 year) twenty three distributed to(2) groups too .The first group confirmed (n=13)cases of breast cancer patients and second group (n=10)as control group. They were evaluated for blood parameters and some biochemical parameters that are associated with breast cancer occurring in Thi-Qar Government .Iraq. study has revealed that significant decreasing ( $p < 0.001$ ) observed in HB , PCV, RBC and WBC levels and a significant increasing ( $P < 0.05$ ) Platelets , ESR and Monocyte retrospectively in cancer patients comparison to normal control subjects and significant correlation ( $P < 0.05$ ) between Neutrophil and Lymphocyte , rates of NLR and PLR were significantly higher in breast cancer patients compared to control group at Age > 45 year .While the results showed for women mean Age (< 45 year). The mean haemoglobin (Hb) , packed cell volume( PCV) and Red blood cells (RBC) levels in the patient group were a significantly and lower than the control group at ( $p > 0.05$ ). There was high significant differences in WBCs , neutrophils, lymphocytes, monocytes also significant difference ESR ( $p > 0.01$ ) compared with healthy female .The values of NLR and PLR were showed significantly but no high in the patients compare with healthy group. In this study biochemical Parameters(lipid profile ) ,were showed a significant decreasing at ( $p > 0.01$ ) for ;lipid profile parameters (Cholesterol, T.G, HDL and LDL) compared with biochemical Parameters measurement values of female control mean Age > 45 year , while results showed that significant increasing at ( $p > 0.05$ )in some lipid profiles in breast cancer patients compared with healthy control group in women Age (<45 year).

**Keywords:** Breast cancer, Lipid profile, Blood Parameters.

### Introduction

BC is abnormal growth of cells and ducts lining the breast branches. The growth of these cells is random and uncontrollable and has the ability to spread to tissues, cells and other organs of the body. Both men and women can have breast cancer. Studies have shown that breast cancer is rare in men. BC is the most common cancer in women worldwide; nearly 1.7 million new cases were diagnosed in 2012, making it the second most common type of cancer.

According to the World Health Organization (WHO), recurrent cancer of breast among women accounts for about 23% of all female

cancers in countries with high health care, more than 40% of all breast cancer cases are found in poor countries [1]. 1, 6 while in the Republic of Iraq, breast cancer accounts for about a quarter of all registered cancer cases among the Iraqi population. This is the leading cause of death among Iraqi women [2]. One of the most commonly used methods for detecting risks in breast cancer are diagnosis, tumor markers and organization of population screening and prognosis.

It can also predict response to treatment, monitoring and treatment [2].Adjuvant therapy is any treatment given after breast

surgery. This may include chemotherapy, hormonal therapy, targeted drug therapy, radiation therapy, or a combination of treatments [6]. Hematological parameter the routine blood test especially lymphocytic count has the potential to serve as a marker for reflecting cancer during disease progression. Therefore, this present study included analysis of hematological parameters can be used as an adjuvant tool to distinguish individuals with BC patients from healthy individuals [3].

Any alteration in blood parameters influences the disease progression [7, 4]. The full blood count predicts multiple diseases in the body, including cancer or coronary artery disease, and anemia predicts higher mortality rates for cancer patients with other diseases such as heart failure.

Blood counts are important for cancer patients and may be considered as important signs of cancer diagnosis. In study worked on gastric cancer patients was results showed an effect the prognostic importance of monocytes, lymphocytes, other plasma cells, platelet / lymphocyte ratio, and neutrophil / lymphocytes and mean platelet volume [5], in other study phenomenon was observed in patients with advanced cancer of the colon. were this patients much worse 5 years related to cancer Survival for patients with peripheral monoclonal counting > 300 / mm<sup>3</sup> of patients Number <300 / mm<sup>3</sup> ,platelets involved in promoting the spread and growth of malignancy, while (W.B.C) blood cells are mediators in this response [13 ,14,15,16].

White blood cells predict cancer or coronary artery disease, and anemia is risk factor expected to increase the death of cancer patients with heart failure. Blood counts are important for cancer patients and may be important signs of cancer diagnosis, including Hemoglobin, Red blood cells, White blood cells, Platelets count. Neutrophil. Lymphocytes, thrombocytopenia and lymphocytes some studies have confirmed that these blood parameters are possible signs of predicting the development or recurrence of the cancer disease or generally remaining in several forms of disease [17, 20].

Biochemical parameters play important role in diagnosis and remarked some diseases, Increase or decrease some biochemical parameters such as lipid profile are

considered a risk factor in cancer patients and are taken as an indicator of cancer. Several signs of the tumor are common in studies involving alpha-phyto protein, fetal antigen, human chorionic gonadotropin, cholesterol concentrations, high density lipoprotein (HDL), low density lipoprotein (LDL), specific prostate antigen and relatively lesser makers such as de-ethrogenase, alkaline phosphatase, etc [21].

Some late studies showed have indicated that high concentrations and levels of and triglycerides (TG) , Total cholesterol has a significant role in causing carcinogenicity of cells, and increased levels of low-density lipoprotein cholesterol, which is more prone to oxidation may lead to higher lipid peroxide in BC disease [22].

The current study aimed to assess and investigate whether some blood parameters Hemoglobin, Red blood cells, Platelets count. Neutrophil. Lymphocytes, thrombocytopenia and lymphocytes, and some changes in white blood cell and platelet average platelet size, neutrophil count, neutrophil percentage, lymphocyte count, lymphocyte percentage, neutrophil to lymphocyte ratio (NLR), platelet count, and platelet to lymphocyte ratio (PLR) and some biochemical parameters such as (Cholesterol, T.G, HDL and LDL) are useful markers for distinguishing between breast cancer patients and healthy individuals and newly diagnosed breast cancer.

## Material Methods

### Patients and Sample Collection

The present study was started with eighty-three cases patients and healthy female ranging in age from 29 to 66 years at unit tumors of cancer in habboubi hospital- Thi Qar Government .Iraq ,were divided according age into women (patients and healthy ) average age more than forty five( **Age > 45 year**) fifty-five confirmed cases of newly diagnosed breast cancer patients(**n=42**)as first group and healthy(**n=18**) as control group and women (patients and healthy ) average age less than forty five **Age (< 45 year)** twenty three divided into (2) groups.

The, first group confirmed (**n=13**) subject of breast newly diagnosed cancer patients and second group (**n=10**) as control group.

Sample collection and ethics statement, study carried out between November 2017 and May 2017.

Blood samples were collected from the vein during the fasting period in the morning, with minimal stagnation in the evacuated tubes. After at least 30 minutes, but within two hours,. After at least 30 min, but within two hours, for full blood count analysis, done on the same day of collection than the remain in tubes were centrifuged at 20 °C for 12 min , then stored frozen, in vials at(-80) °C before use in successive measurements.

### Complete Blood Count (CBC)

Determination Complete blood count (CBC) by a Coulter LH 750 auto analyzer (Beckman Coulter, CA, USA).Including hemoglobin concentration (HB), packed cell volume (PCV), red blood cell concentration(RBC), mean cell volume, mean corpuscular hemoglobin concentration, white blood cells(WBC) and platelet parameters and regarding neutrophil count ,white blood cell count, neutrophil percentage, lymphocyte percentage, lymphocyte count, neutrophil to lymphocyte ratio( NLR ), platelet count,, and platelet to lymphocyte ratio (PLR )was retrospectively

### Biochemical Parameters Measurements

Measurement of total cholesterol conc. by enzymatic colorimetric CHOD-PAP method [23].

Estimation of serum HDL-C conc. By enzymatic colorimetric [24]

Estimation of serum triglyceride conc. by enzymatic colorimetric GPO-PAP method [25].

Calculation of serum LDL- concentration using Fried wald's formula [26].

### Statistical Analysis

Data were analyzed using Special Package for Social Science (SPSS) version 16.0. The descriptive data were given as means  $\pm$  SD. Least Significant Difference (LSD) the accepted level of significances were ( $P < 0.05$ ), ( $P < 0.01$ ).

### Results

The study population included 83 female patients are diagnosed newly breast cancer and healthy individuals were enrolled into this retrospective study.60 cases of breast disease healthy women were (**Age > 45 year**). Calculated mean BMI for breast cancer **Patient** and healthy women (control group) were show and analyzed age and BMI at (Table 1).

**Table 1: Characteristics (Age > 45 year - BMI) distribution of the Patient and Control Groups**

Number of cases	Age (mean $\pm$ SD) year	BMI (mean $\pm$ SD)Kg/m <sup>2</sup>
Breast cancer patients(n=42)	55.6 $\pm$ 7.40	27.97 $\pm$ 3.87
Control(n=18)	51.23 $\pm$ 14.00	25.503 $\pm$ 3.22

23 cases of breast cancer disease and healthy women were (Age < 45 year).

Calculated mean BMI for cases were show and analyzed age and BMI at (Table 2).

**Table 2: Characteristics (<45 year - BMI) distribution of the Patient and Control Groups**

Number of cases	Age (mean $\pm$ SD) year	BMI (mean $\pm$ SD)Kg/m <sup>2</sup>
Breast cancer patients(n=13)	42.22 $\pm$ 3.59	21.34 $\pm$ 4.41
Control(n=10)	39.75 $\pm$ 5.15	23.88 $\pm$ 5.62

The laboratory blood parameters of Breast Cancer patients and control group are shown in Table (3).The mean values of HB , PCV, RBC and WBC were significantly lower in BC patients compared to the control group (Age > 45 year). the cases HB =8.49, PCV= 29.41,RBC= 3.96 and WBC= 5.95 retrospectively, decreases significantly( $P < 0.05$ ) compared to the control group as shown in table (3),while increases significantly for

Platelets=357.94 , ESR= 18.49 and Monocyte=23.45 compared to the control group .Also significant correlation( $P < 0.05$ ) between Neutrophil and Lymphocyte of the patients and healthy groups were noted on analysis of variance. The rate of (N.L.R) and (P.L.R) were high significantly in B C patients than in the control group, (2.80 and 123.3 vs 1.63 and 108.50, respectively,  $p=0.01$ ), at Age> 45 year (Table 3).

**Table3: Relation of blood parameters between Patient and Control Groups group Age (> 45 year)**

Blood parameters	Grup1 B.C(n=42)	Grou2 Control (n=18 )
HB (mean ± SD)	* 8.49± 1.24	12.8 ± 1.06
PCV (mean ± SD)	*29.41± 3.14	36.41 ± 2.59
RBC (mean ± SD)	*3.96± 0.77	4.73± 0.60
Platelets (mean ± SD)	*357.94± 68.91	223.4± 34.12
ESR (mean ± SD)	*18.49± 0.88	7.41± 0.80
WBC (mean ± SD)	*5.95± 1.38	6.75± 0.82
Neutrophil (mean ± SD)	*5.97± 0.84	4.56± 0.85
Lymphocyte (mean ± SD)	2.93± 0.64	2.36 2.61
Monocyte (mean ± SD)	**23.45± 4.44	7.89± 1.10
NLR	**2.80± 3.39	1.63± 1.12
PLR	**123.3±	108.50

B.C: Breast Cancer, HB: hemoglobin, PCV packed cell volume, WBCs: White blood cell count, CBC: complete blood count, ESR: erythrocyte sedimentation rate, NLR: neutrophil-lymphocyte ratio, PLP: platelet-lymphocyte ratio, n = number of patients or healthy women in each group, P<0.05, P\*\*< 0.01

Also when analyzers of results relation of blood parameters between Patient and Control Groups group Age (< 45 year), by statically found The mean haemoglobin (Hb), packed cell volume( PCV) and Red blood cells (RBC) the concentrations of these blood parameters in the patients group were significantly lower than the control group 9.77±2.66g/ dl, 23.44±4.89 and 4.60±1.36 vs. 13.2±3.86/dl, 37.32±5.34 and 5.11±1.00,

respectively, (p>0.05). There was high significant differences in WBCs, lymphocytes, neutrophils, monocytes also significant difference ESR (p>0.01) compared with healthy female. The values of NLR and PLR were showed significantly but no high in breast cancer patients compare in the healthy group, and all results showed in Table (4).

**Table4: Relation of blood parameters between Patient and Control Groups group Age (< 45 year)**

Blood Parameters	Grup1 B.C(n=13)	Group2 Control (n= 10 )
HB (mean ± SD)	*9.77± 2.66	13.2 ± 3.86
PCV (mean ± SD)	*23.44± 4.89	37.32± 5.34
RBC (mean ± SD)	*4.60± 1.36	5.11± 1.00
Platelets (mean ± SD)	**265.62± 45.51	219.67± 22.14
ESR (mean ± SD)	**19.28± 2.00	8.50± 1.96
WBCs (mean ± SD)	**6.88± 2.94	5.87± 0.59
Neutrophil (mean ± SD)	**7.74± 2.40	3.96± 2.11
Lymphocyte (mean ± SD)	**4.04± 1.93	2.73± 2.95
Monocyte (mean ± SD)	**14.42± 4.76	6.67± 3.00
NLR	*1.67± 1.79	1.46± 3.00
PLR	**102.20± 13.04	83.77± 17.50

B.C: Breast Cancer, HB: hemoglobin, PCV packed cell volume, WBCs: White blood cell count, CBC: complete blood count, ESR: erythrocyte sedimentation rate, NLR: neutrophil-lymphocyte ratio, PLP: platelet-lymphocyte ratio, n = number of patients or healthy women in each group, P<0.05, P\*\*< 0.01

The Table (5) showed astatically analyzed results for biochemical Parameters that studies in this piper were showed a statistically significant decreasing at (p>0.01)

for parameters (Cholesterol, T.G, HDL and LDL) compared with biochemical Parameters measurement values of female control that age over than 45 years.



Table 5: Serum lipid profiles in BC patients and control groups Age (&gt;45 year)

Biochemical Parameters	Group1 B.C(n=43)	Group2 Control (n= 18 )
Cholesterol (mean $\pm$ SD)	**223.71 $\pm$ 4.34	147.29 $\pm$ 5.90
T.G (mean $\pm$ SD)	**194.31 $\pm$ 8.20	92.93 $\pm$ 3.01
HDL (mean $\pm$ SD)	**54.89 $\pm$ 6.00	43.05 $\pm$ 3.89
LDL (mean $\pm$ SD)	**111.74 $\pm$ 4.40	82.62 $\pm$ 4.04

B.C: Breast Cancer, T.G: Triglyceride, HDL: high density lipoprotein, LDL: low density lipoprotein, P\* $<$ 0.05, P\*\* $<$  0.01

While results the present study showed that significant increasing at (p>0.05) in some lipid profiles in breast cancer patients compared with healthy control group in women Age (<45 year) were cholesterol in mg/dL , T.G mg/dL ,HDL mg/dL were 193.71 $\pm$ 9.10, 164.49 $\pm$ 7.32 and 50.01 $\pm$ 5.99 in

cases and 145.92 $\pm$ 2.10, 123.60 $\pm$ 7.34 and 38.52 $\pm$ 1.08 in healthy group respectively. While LDL showed significant decreasing at (p>0.05) in B.C group 87.24 $\pm$ 8.90 compared with control group 102.00 $\pm$ 5.5 and this results in Table (6).

Table 6: Lipid Profiles in BC Patients and Control Groups Age (&lt; 45year)

Biochemical Parameters	Group1 B.C(n=12)	Group2 Control (n= 10 )
Cholesterol (mean $\pm$ SD)	*193.71 $\pm$ 9.10	145.92 $\pm$ 2.10
T.G (mean $\pm$ SD)	*164.49 $\pm$ 7.32	123.60 $\pm$ 7.34
HDL (mean $\pm$ SD)	*50.01 $\pm$ 5.99	38.52 $\pm$ 1.08
LDL (mean $\pm$ SD)	*87.24 $\pm$ 8.90	102.00 $\pm$ 5.5

B.C: Breast Cancer, T.G: Triglyceride, HDL: high density lipoprotein, LDL: low density lipoprotein, P\* $<$ 0.05, P\*\* $<$  0.01

## Discussion

A total of 71% of the patients presented None of the 55 patients was younger than 20 years, however, 76.36% of them were between more than 45 years, while 23.63% presented between 21-45 years .This is similar to many studies around the world, where breast cancer affects older women (45-65) years greater than of young women less 40 years [27, 28]. Breast cancer is one from more common cancer diseases in women and ranks as the second cause of deaths cancer in the world [29]. Therefore, early detection of breast cancer and control of metastasis of cancer cells very important part of breast cancer prevention and treatment.

This study showed that women are diagnosed with breast cancer has a significant decrease in some blood cells such as haemoglobin (Hb), packed cell volume (PCV) and Red blood cells (RBC). Decreased hemoglobin, erythrocytes, and packed cell volume can be associated anemia associated with cancer, in general, including breast cancer.

Bone marrow transduction can be linked to breast cancer by suppressing red blood cells. Infection may be associated with different malignancies with hemolysis in red blood cells (anemia) and blood cells [30]. In study 2006 among the cancer patients to determine the prevalence of anemia the all red cell indices of cases were also lower than the healthy (control) while the mean RDW which is the coefficient of variation of red blood cells

anisocytosis of cancer patients was higher than the healthy group [31].

And a significant increase in other some blood parameters such as Platelets , ESR and Monocyte. Also a significant increase WBCs, Neutrophil and Lymphocyte percentages of subjects were much higher as compare with the control. This can because that all types neoplasms were associated with neutrophilia.

Demargination of 50% of neutrophils occur which are normally found to marginate the walls of vessels and are not normally represented in blood count. There may be a lymph vascular invasion leading to demargination of tumor cells occupying the vascular spaces (either lymphatic or small capillaries).Eliminates cancerous cells that occupy the blood vessels (either lymphocytes or small capillaries).

The main mechanism of action of tumor immunity is killing cancer cells CD8+ cytotoxic T-lymphocyte [32]. Several clinical studies in the world have confirmed that interactions between WBCs and platelets on the one hand and tumor cells on the other side may cause measurable changes in blood pictures. In addition, studies have revealed possible diagnostic values for the indicator of blood test parameters for breast cancer [33, 36]. (NLR) is the most studied parameter in B C, in particular, in a study by Ozyalvacli et al [37].

Noted that neutrophils for lymphocyte levels significantly increased in patients with breast cancer compared with patients with benign proliferative, breast disease. This agree with current study, several studies reported NPL : neutrophil-to-lymphocyte ratio and, PLP: platelet-lymphocyte ratio, they have the highest mortality rates of 5 years of patients compared with low in this parameters [38,39].

The study by Yao and colleagues [40] showed that the percentage of platelets to lymphocytes did not have a strong effect at different times in patients with breast cancer, also that the average platelet in breast cancer patients was higher than in patients with benign breast tumors [41]. Cancer causes myeloid suppression and anemia because a significant decrease in the blood content of red blood cells (RBC) and hemoglobin in this study [42, 43], blood parameters were also studied accordingly. The most important mechanisms proposed by mitochondrial dysfunction in changes in nucleotide pools is the adoption of mitochondria for a key enzyme in de novo pyrimidine biosynthesis, dihydro orotate dehydrogenase [44].

In current study there is a significant and significant increase difference in some biochemical parameters cholesterol, TG, LDL and decrease level of HDL-C in breast cancer patients groups and healthy women. These results are consistent with earlier studies [45].

The current study indicates that high levels of total serum cholesterol, TAG, LDL-C, low serum level and HDL-C are associated with breast cancer the main of studies suggest that high levels of TG and cholesterol have an important role in the development of cancer (carcinogenesis) and high concentrations of LDL is more prone to oxidation may lead to elevation lipid peroxidation in BC patients.

Recent studies reveal that the decreased concentration of HDL might cause the discorded of metabolites [46]. In a study carry out in Norway, it was reported that decrease high density lipoprotein cholesterol levels (H.D.L) was related to breast cancer

risk and important component of the metabolic syndrome[46],in other study reveal that the decreased level of -HDL-C might cause the reactive oxygen metabolites to remain unopposed [47].The present study confirmed the age and BMI plays a big role in decrease of some blood parameters such as as hemoglobin (Hb), packed cell volume (PCV) and Red blood cells (RBC) and increase other blood parameters such as Platelets, ESR and Monocyte and a significant increase WBCs, Neutrophil and Lymphocyte percentages of cases were higher than the control at breast cancer patients Age (mean  $\pm$  SD) 55.6  $\pm$ 7.40 rang (48,49)years and BMI (mean  $\pm$  SD)Kg/m<sup>2</sup> 27.97  $\pm$  3.87 compared with some parameters at young women breast cancer patients Age (mean  $\pm$  SD) 42.22  $\pm$ 3.59 less 40 years and BMI (mean  $\pm$  SD)Kg/m<sup>2</sup> 21.34 $\pm$ 4.41.

These results are consistent with many studies on breast cancer patients In a study by Sellers (50) obese post-menopausal women With a family history of the disease of breast cancer was found to have a chance of greater disease ,developing breast cancer than obese women without a family history, some studies could suggest that obesity with rise of age for women have a strong association between obesity and breast cancer in a number of clinical and epidemiological effects related to obesity, such as timing of weight gain and body fat distribution, may affect the relationship between obesity and breast cancer, [51, 52]. These inverse relationships between weight gain and the risk of breast cancer are mostly present.

## Conclusions

Hematological parameters: Increase levels of Platelets, Monocyte, Lymphocyte,WBCs, Neutrophil, Lymphocyte Neutrophil to-lymphocyte ratio (NLR) and Platelets to-lymphocyte ratio (PLR) and decrease levels haemoglobin (Hb) , packed cell volume ( PCV) and Red blood cells (RBC), have diagnostic power and can discriminate patients with breast cancer from patients without cancer, adding increase in levels some biochemical parameters such as cholesterol, TG, HDL and decrease level of LDL in patients become Screening Markers the gold standard in breast cancer screening and thereby increase the early detection of cancer.

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