Predicting Breast Cancer Risk Using Simple Blood Parameters

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Abstract

Background: The most common cancer in the world is breast cancer. For Iraq, this tumor is the number one cancer in women. In the countries of middle- and low-income economy. the mammography and other expensive and technologically sophisticated diagnostic methods are unattainable because of elevated costs & deficiency in the trained personnel. The cheap, available, and easy complete blood count reflects the response of cellular immunity in a cancer patient. Any alteration in hematological parameters influences the disease progression. Hematological parameters have been correlated with prognosis in several malignancies. The aim of this study the utility of complete blood count in Predicting Breast Cancer Risk.

Patient and methods: A case control study done in breast early detection consultation clinic at cancer management specialized center at Salah Al-Deen Governorate. A convenient sample of patient those visited the clinic during the period 1st Jan. 2020- 30th June 2022 was taken, 50 breast cancer patient were compared with 50 patient with benign breast lesion. Breast ultrasound was taken for both groups then biopsy was taken and send for histopathology depending on the results of histopathology the patient was grouped into the study groups. Final complete blood counts of the patients before pre-biopsy were evaluated in preoperative peripheral blood measurements. These Complete Blood Count parameters were compared between benign and malignant patients.

Results: The mean age of the patient were significantly higher than the control group. The right sided breast lesion was 24 (48%) among cases in comparison to control group 16(32%), the left sided lesion was higher among cases than control group 23(46%) in comparison to 15(30%), while lesion in both breast found among control group higher than the cases 3(6%), 19 (38%), respectively. Most of the diagnosed at stage III 21(42%) followed by stage II 20(40%). The mean HB was non significantly lower among cancer patients (10.78±1.9)than control group (11±0.93).there is no significant difference between cases and controls regarding platelet count (329.92±58.04), (285.53±62.15). The red cell distribution width was significantly higher among cases (13.82±1.64) than controls (12.27±0.88). The Neutrophil cell count is significantly higher among cases (3.71±1.5) than controls (2.6±0.5). The Neutrophil Lymphocyte ratio is significantly higher among cases (2.07±1.29) than controls (1.09±0.31).

Conclusions: Simple Blood Parameters including NLR and anemia are factors that independently correlate with overall survival in breast cancer patients. These factors have the advantage of being derived from simple and inexpensive blood testing.

Keywords: Predicting Breast Cancer Risk by Blood Parameters, Blood Parameters in Predicting Breast Cancer

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Introduction

Breast cancer is the second most common cause of death in women. Because of lifestyle changes, reproductive factors, and elevated life expectancy, there is a sharp increment in the global incidence, this is according to WHO. [1] The breast cancer–related deaths mainly occur in middle- and low-income countries (around 58%), versus (40-60%) survival rates for breast cancer in these countries because of lack of early detection programs leading to diagnoses in late stages, where 80% of these tumors are incurable [2, 3]. In the countries of middle- and low-income economy. the mammography and other expensive and technologically sophisticated diagnostic methods are unattainable because of elevated costs & deficiency in the trained personnel. [4, 5] The other point is that mammograms are mostly used to determine ER-positive breast cancer [6] and are not advised for younger women. Moreover, detection at an earlier stage utilizing conventional methods is not prognostic for all race groups [7]. So, development of affordable, portable, and accurate means of detecting breast cancer risk before the tumors arise is a critical need and this will provide solutions for growing . Development of such technologies has the potential to expedite the solution for the growing women's health problem to health problem to prohibit elevating their death and disability especially in low- and middle-income countries. [8] The common process that to the all risk factors of cancer identified till now. The activated inflammatory process is regarded to be included in invasion, tumor growth, metastasis and angiogenesis. [9] So, some inflammatory markers in the blood count like platelets, neutrophils, lymphocytes, neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), mean platelet volume (MPV) have been studied in different patients with malignant tumors. [10] The aim of this study role of simple blood parameters for predicting breast cancer risk.

Patient and methods:

A case control study done in breast early detection consolation clinic at cancer management specialized center at Salah Al-Deen Governorate. A convenient sample of patient those visited the clinic during the period 1st Jan. 2020- 30th June 2022 was taken, 50 breast cancer patient were compared with 50 patient with benign breast lesion. All patients were informed about the study aims and the procedures will done and written acceptance on enrollment in the study was taken. Breast ultrasound was taken for both groups then biopsy was taken and send for histopathology depending on the results of histopathology the patient was grouped into the study groups. Patients with systemic inflammatory disease, on medicines that could affect platelet functions (i.e. aspirin), and any disease that can affect the blood count parameters were excluded from the study. Final blood counts of the patients before pre-biopsy were evaluated in preoperative peripheral blood measurements. When blood was taken, care was taken not to have other causes of leukocytosis in the patient. blood count parameters, hemoglobin, HCT (hematocrit), neutrophil count lymphocyte count , MCV (average size of oxygen-carrying cells), RDW (red cell distribution width) , PDW (distribution range of platelets), MPV (mean platelet volume), Neutrophil /lymphocyte ratio platelet /lymphocyte ratio NLR, PLR and MPV/platelet ratio was reported for both study groups. These Complete Blood Count parameters were compared between benign and malignant patients. Statistical analysis done using SPSS version 25 data presented using frequency and proportions , mean and standard deviation, Receiver Operator Curve (ROC) used for identification of then cut of points for the parameters, then sensitivity and specificity positive predictive and negative predictive values with test accuracy calculated for each chosen parameter.

Results

The mean age of the patient were significantly higher than the control group (51.8±10.5), (46.3±11.14) respectively this difference was statistically significant. The right sided breast lesion was 24 (48%) among cases in comparison to control group 16(32%), the left sided lesion was higher among cases than control group 23(46%) in comparison to 15(30%), while lesion in both breast found among control group higher than the cases 3(6%), 19(38%), respectively, this relation was statistically significant as shown in table 1.most of the diagnosed at stage III 21(42%) followed by stage II 20(40%).

Table 1 general characteristics of the study groups

	cases		Control		P value
	F	%	F	%	
Age (mean±SD)	51.8	10.5	46.3	11.14	0.012 S
side of lesion					
Right	24	48	16	32	
Left	23	46	15	30	
Both	3	6	19	38	0.0005S
Stage at diagnosis					
I	4	8			
II	20	40			
III	21	42			
IV	5	10			NA

The mean HB was non significantly lower among cancer patients (10.78±1.9)than control group (11±0.93).there is no significant difference between cases and controls regarding platelet count (329.92±58.04), (285.53±62.15). The red cell distribution width was significantly higher among cases (13.82±1.64) than controls (12.27±0.88). The Neutrophil cell count is significantly higher among cases (3.71±1.5) than controls (2.6±0.5). The Neutrophil Lymphocyte ratio is significantly higher among cases (2.07±1.29) than controls (1.09±0.31).

Table 2. The hematological parameters of study groups

Parameters	cases		control		P value
	Mean	Std. Deviation	Mean	Std. Deviation	
HB	10.78	1.90	11.00	0.93	0.6
hematocrit	35.24	5.15	35.20	2.24	0.9
Platelet (u/mm3)	329.92	58.04	285.53	62.15	0.19
PDW	16.16	13.60	13.53	0.64	0.13
RDW	13.82	1.64	12.27	0.88	0.002
MPV	15.01	19.19	10.58	0.46	0.3
Neutrophil	3.71	1.50	2.60	0.5	0.012
lymphocyte	2.22	1.46	2.69	0.62	0.24
NLR	2.07	1.29	1.09	0.31	0.03
PLR	195.25	75.85	110.07	45.30	0.005
MPR	0.05	0.02	0.04	0.00	0.5
RPR	0.05	0.02	0.04	0.01	0.3

PDW: platelets distribution range; RDW :red blood cell distribution

width; MPV: mean platelet volume; NLR : NEU/LYM ratio; PLR : PLT/LYM ratio; MPR :MPV/PLT ratio; RPR : RDW/PLT ratio

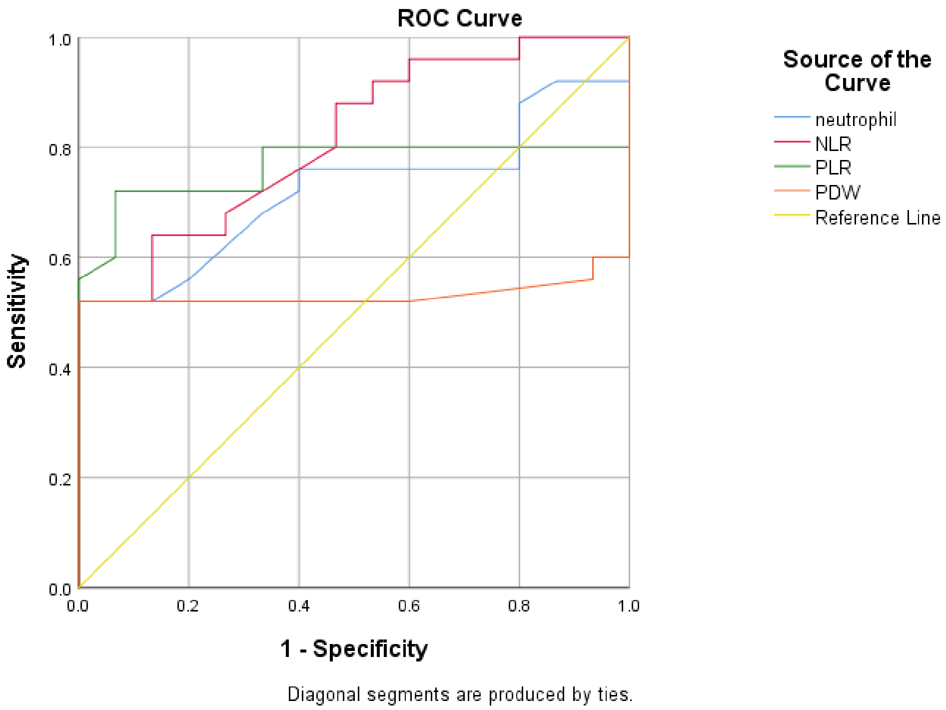

Figure 1. ROC analysis of Neutrophil, NLR, PLR, and PDW

The receiver operator curve was done for the Neutrophil the area under curve was 72.1%, for the cutoff point 3.65 the sensitivity was 52% specificity 100%, false positive was 0%, and false negative 48% the accuracy was 70%. For NLR 81.5% of the data was covered for the cut-of point 1.65 , the sensitivity was 52% specificity 100%, false positive was 0%, and false negative 48% the accuracy was 70%. For PLR 76.4% of the data was covered for the cut-of point 149.7, the sensitivity was 60% specificity93%, false positive was 7%, and false negative 40% the accuracy was 73%. For PDW 53.2% of the data was covered for the cut-of point 14.5, the sensitivity was 52% specificity 100%, false positive was 0%, and false negative 48% the accuracy was 70%.

Table 3. The specificity and diagnostic accuracy of the significant parameters in predicting cancer diagnosis.

Parameter	AUC	Cut- of point	Sensitivity	Specificity	False Positive	False negative	accuracy	PPV	NPV
Neutrophil	72.1%	3.65	52	100	0	48	70	100	55.6
NLR	81.5%	1.65	52	100	0	48	70	100	55.6
PLR	76.40 %	149.7	60	93	7	40	73	94	58.3
PDW	53.20 %	14.5	52	100	0	48	70	100	55.6

Discussion

The mean age of the patient were significantly higher than the control group (51.8±10.5), (46.3±11.14) respectively this difference was statistically significant this goes with Karim SA [11] found that the mean age at diagnosis was 49.42 ± 11.66 years compared to control 46.7 ± 10.2). This is supported by the Al-Hashimi MMY 2021 who found that breast cancer incidence rates increased with age, with the largest increase was observed in females 70+ age group, followed by females aged 60-69. [12] Ahmed Mjali et al found that median age was 45 years, range was (25-70) years. Ahmed Mjali et al found that the median age in our study was 45 years, this younger than median age in other parts of Iraq (49 years), Turkey (51 years) and US (62 years) this may be explained by our small sample size and short follow- up period [14-16].

The current study revealed that the right sided breast lesion was (48%) among cases in comparison to control group (32%), the left sided lesion was higher among cases than control group (46%) in comparison to (30%), while lesion in both breast found among control group higher than the cases (6%), (38%), respectively. This is different from Arkan OJ Al-Isawi 2022 found that the Left (185)/Right (157) = 1.157 and the percent of both sides involvement was 2.6%. [17]

The current study revealed that the most of the diagnosed at stage III (42%) followed by stage II (40%). This is similar to Arkan OJ Al-Isawi 2022 found that the average female-age at time of diagnosis: 47.59 (SD: 13.11),cases with age <50 y: 66.4%,patients in early TNM stage (pT0 & pT1 categories) forming only 4.68%. concerning the types of tumor: infiltrative ductal carcinoma of no special type: 86.26%, medullary type: 7.02% mucinous: 2.05 & invasive lobular: 4.09%, malignant phyllodes: 0.29%, and metaplastic carcinoma:0.29%. Left (185)/Right (157) = 1.157 and the percent of both sides involvement was 2.6%.[17] Ahmed Mjali et al found that the most common presenting stage in our patients was stage III in 40 patients (39.60%) followed by stage II in 32 patients (31.68%), stage IV in 22 patients (21.78%) and stage I in 7 patients (6.93%). [13]

The current study revealed that the mean HB was non significantly lower among cancer patients (10.78±1.9) than control group (11±0.93). Rafael de C Silva 2022 found that the hemoglobin <12 g/dL associated with staging >II ($p < 0.0001$), with the presence of metastasis ($p < 0.0001$), and with negative hormone receptor ($p < 0.05$). also found that anemia is a factor that independently correlate with overall survival in breast cancer patients and has the advantage of being derived from simple and inexpensive blood testing. [18] Another study demonstrated that hemoglobin levels are also useful to predict survival in breast cancer patients. The presence of anemia at diagnosis (Hemoglobin (Hb) <12 g/dL) was associated with reduced local relapse-free survival, lymph node metastasis-free survival, distant metastasis-free survival, relapse-free survival, and overall survival [19].

Rana AP 2015 found that the no significant correlation between anaemia and breast cancer could be identified. In patients with cancer, >60% cases have Hb < 12 gm% along with altered red cell indices; amongst that 4.7% of the cases had Hb < 7 gm%. Anorexia associated with cancers generally can result in nutritional anaemia seen in the cases. [20] On the other hand metastasis to the bone marrow from breast cancer can be associated with suppression of erythropoiesis. Benign group also have shown anaemia (mean Hb < 10 gm%) probably due to lower socioeconomic status and poor nutrition [21-22]. This is similar to results of Seretis C et al 2013study that demonstrated that patients with grade II carcinoma had a significantly higher RDW mean value compared to the patients with grade III carcinoma. Also demonstrated that elevated RDW could be helpful in the differential diagnosis of the nature of a breast tumor -benign or malignant-, being significantly higher in the group of patients with breast cancer. Finally concluded that Red cell distribution width may be a novel biomarker of the activity of breast cancer.[23]

The present study showed that Neutrophil cell count is significantly higher among cases (3.71±1.5) than controls (2.6±0.5). Fujimoto Y et al 2019 found that the low NLR is a significant prognostic factor for RFS of breast cancer patients with ALC-high. The novelty of the present study is that we were able to demonstrate the prognostic usefulness of NLR exclusively in the ALC - high subgroup. This is the first study to demonstrate that the prognostic usefulness of NLR is restricted in the subgroup of ALC-high. Since NLR and ALC are measured in daily clinical practice, these findings may contribute to a better understanding of the mechanisms underlying NLR, and will be useful for identifying patients with high recurrence risk more accurately who need additional treatments. [24]

The present study showed that the Neutrophil /Lymphocyte ratio (NLR) is significantly higher among cases (2.07±1.29) than controls (1.09±0.31). Rafael de C Silva 2022 found that the NLR>4 showed association with staging>II ($p<0.05$), with the presence of metastasis ($p < 0.0001$), and with negative hormone receptor ($p < 0.0001$). also found that NLR is a factor that independently correlate with overall survival in breast cancer patients and has the advantage of being derived from simple and inexpensive blood testing. [18] Corbeau, I in 2020 found that NLR appears to be a prognostic factor for disease free survival and overall survival in patients with early BC receiving adjuvant chemotherapy. [25] The current study revealed that there is no significant difference between cases and controls regarding platelet count (329.92±58.04), (285.53±62.15).This is higher than study done by Rana AP 2015 found that the mean platelet count of cases (291.51 ± 103.38) was also higher than that of benign group (222.82 ± 57.62). [20] Liu S et al 2020 found that the platelets were prognostic factors for many tumors, and high platelets were associated with poor prognosis. Platelets have important predictive value for the prognosis of breast cancer patients with ipsilateral supraclavicular lymph node (ISLN) metastasis.[26] Preoperative thrombocytosis has been identified as an adverse prognostic indicator in some malignancies [27, 28]. Shimada H et al 2004 found that a high platelet count was found to be associated with tumor progression and poor survival in esophageal carcinoma cases. [29] Platelet lymphocyte ratio (PLR) has a prognostic value analogous to NLR: higher values are associated with shorter survival in patients with breast cancer [30].

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