Original Article

Full blood count pattern of pre-chemotherapy breast cancer patients in Lagos, Nigeria

Akinsegun Akinbami (MD, MSc, MPH) [*1]
Abiodun Popoola (MD) [2]
Adewumi Adediran (MD) [3]
Adedoyin Dosunmu (MD) [1]
Olajumoke Oshinaike (MD) [4]
Philip Adebola (MD) [4]
Sarah Ajibola (MD, MSc) [5]

1- Department of Hematology and Blood Transfusion, Lagos State College of Medicine, Ikeja, Lagos, Nigeria.
2- Department of Oncology, Lagos State University College of Medicine, Ikeja, Lagos, Nigeria.
3- Department of Hematology and Blood Transfusion, Faculty of Clinical Sciences, College of Medicine, University of Lagos, Idiaraba, Nigeria.
4- Department of Medicine, Lagos State University, College of Medicine, Ikeja, Lagos, Nigeria.
5- Department of Hematology and Blood Transfusion, Lagos University Teaching Hospital, Idiaraba, Nigeria.

*** Correspondence:** Akinsegun Akinbami, Department of Hematology and Blood Transfusion, Lagos State University College of Medicine, Ikeja, Lagos, Nigeria.

E-mail: ajoke_clinic@yahoo.co.uk
Tel: 00234 802 306 4925

Received: 3 July 2012
Revised: 20 Nov 2012
Accepted: 2 Dec 2012

Abstract

Background: Full blood count has been shown to predict disease severity and mortality risk in cancer patients. This study aimed to highlight the degree of derangements of full blood count parameters and provide mean values in pre-chemotherapy breast cancer patients compared with apparently normal control subjects.

Methods: This was an unmatched case-control study among breast cancer patients attending Oncology clinic of Lagos State University Teaching Hospital, Ikeja and the nurses of the institution as control. A total of 4.5 mls of blood was collected from each participant into EDTA bottle for full blood count analysis, done on the same day of collection.

Results: A total of 100 histologically diagnosed, consenting, pre-chemotherapy patients of the clinic (cases) and 50 nurses of the institution as controls were studied. Anemia was found in 58%, 43% and 20% of cases compared with 38%, 36% and 2% of controls using PCV< 36%, 30-36% and 30%, respectively. The mean MCV, MCH, MCHC (82.62±7.48 fl, 26.01±2.78 pg, 30.73±4.06 g/l respectively) of cases were lower than the controls (85.36±5.74 fl, 27.24±1.90 pg, 31.81±0.8 g/l, respectively and RDW of cases (15.61±3.53) was higher than the control (14.24±0.75). The mean WBC counts, neutrophil and lymphocyte percentages of cases (6.96±7.22, 54.75±13.1% and 38.19±12.70%, respectively) were higher than the controls (5.47±1.57, 44.39±8.78% and 8.82±15.97%, respectively). The mean platelet count of cases 291.51±103.38 was also higher than the controls (222.82±57.62).

Conclusion: Breast cancer patients presented with deranged full blood count pattern, consequent to the disease compared with the controls.

Keywords: Full blood count, Pre-chemotherapy, Breast cancer

Caspian J Intern Med 2013; 4(1): 574-579

Full blood count is a prerequisite investigation requested from all cancer patients before surgery, use of chemotherapy and/or radiotherapy. Poor parameters adversely influence the outcome of cancers. Hematological parameters and markers of the systemic inflammatory response have been correlated with prognosis in several malignancies. The white blood cell count (total and differentials) and packed cell volume predict disease severity and mortality risk (1-4). For example, elevated WBC counts predict a worse prognosis in patients with cancer or coronary artery disease and anemia predicts increased risk of death of cancer patients with heart failure (5-8).

Furthermore, these two tests provide direct management guidance in common circumstances, for example, bleeding and infection. Patients with an absolute granulocyte count of 6000/mm^3 or more were observed to have a shorter survival than the patients with less than 6000/mm^3. A similar phenomenon was observed independently in patients with advanced carcinoma of the colon (9, 10). A significantly worse 5-year cancer-related survival for patients with peripheral blood monocyte count>300/mm^3 than for patients with a count<300/mm^3 was observed in Japan (11).

The prognostic significance of neutrophils, lymphocyte, platelet, mean platelet volume, platelet-lymphocyte ratio and neutrophils-lymphocyte ratio in patients with locally and advanced gastric cancer were assessed in Turkey and found to influence overall survival (12). The higher the lymphocyte count, the better the overall survival, the lower the platelet-lymphocyte ratio, the better the overall survival. The lymphocytes in the peripheral blood of patients with breast cancer were studied (13).

Peripheral blood lymphocyte counts were found to be significantly lower in the short-survivors when compared with the long survivors. Lymphocyte count may be a host factor that influences survival in breast cancer. An analysis was made of the correlation existing between curability by conventional treatment of the 589 cases of the different types of cancer with reasonable possibilities of cure, and the total number of leukocytes in peripheral blood (14). A positive significant correlation was found between cancer curability and the total number of peripheral lymphocytes, a negative correlation was found between the total number of peripheral neutrophils (segmented and nonsegmented) and cancer curability.

No correlation was found between curability of cancer and monocytes, eosinophils, or basophils. These findings indicate that the immunologic activity of peripheral lymphocytes may be a favorable factor in the cure of cancer by conventional treatment. The prognostic significance of peripheral lymphocyte counts in breast cancer patients was assessed retrospectively, evaluating 5–year survival rates in relation to pretreatment lymphocyte counts in 453 patients with breast carcinoma (15). It concluded that lymphocyte counts may serve as prognostic indicators in patients with breast cancer. Low lymphocyte counts may be related to the presence of suppressor substances.

An increased pre-operative platelet count has been identified as an adverse prognostic indicator in bronchial cancer, gastric and gynecological malignancies (16-19). A high platelet count is associated with tumor progression and poor survival in patients with esophageal carcinoma (20). It is therefore important to study full blood count in breast cancer patients in order to determine their diagnostic and prognostic values. Routine peripheral blood counts may be useful prognostic factor for evaluating the accuracy of risk stratification in patients with cancers. Chemotherapy and/or radiotherapy could singly or synergistically affect the picture hence the need to study the pattern in pre-chemotherapy, newly diagnosed cancer patients. The objective of the study was to highlight the degree of derangements of full blood count parameters in prechemotherapy breast cancer patients when compared with apparently normal controls.

Methods

This was an unmatched case-control study carried out between June 2010 to October 2011 among the breast cancer patients (cases) attending Oncology clinic of Lagos State University Teaching Hospital, Ikeja and nurses of the institution as controls. Ethical approval was obtained from the Institution's Ethics and Research Committee. There were three groups of patients: group one, breast cancer patients staged prior to surgery and sent for chemotherapy, group two consisted of those sent for chemotherapy before surgery to make the tumor operable by reducing the tumor size, while group three were those who had inoperable tumor and placed on chemotherapy alone.

The latter two groups were staged at the Oncology clinic. A semi structured, self-administered questionnaire was given to all the participating patients and controls to obtain demographic data. The patients were staged clinically according to the tumor, node, and metastasis (TNM) classification. Stage I-Tumor $\leq$2 cm in greatest dimension; no nodal involvement and no metastasis. Stage II-Ranges from non-evident tumor to tumor >5 cm in greatest dimension with either no nodal involvement or metastases in movable ipsilateral axillary lymph node(s) but no distant metastases.

Stage III-Tumor size ranges from either not evident to tumor of any size with direct extension to (a) chest wall or (b) skin; no evidence of regional lymph node metastases or metastases in ipsilateral infraclavicular lymph node(s) with or without axillary lymph node involvement,or in clinically apparent ipsilateral internal mammary lymph node(s) and in the presence of clinically evident lymph node metastasis in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement. No distant metastasis.

Stage IV-Involvement of distant metastases regardless of tumor or nodal status. All patients with a breast mass were carefully examined and the mass measured. The presence or absence of any signs of local advancement (inflammation, peau d'orange, ulceration, satellite nodules, direct chest wall involvement, mobile or fixed axillary nodes, and

supraclavicular lymph node) was noted and recorded. Abdomen and spine were also examined for evidence of spread. In early operable breast cancer (T1-2, N0-1), minimal staging investigations were done, which included a chest x-ray, full blood count, abdominal ultrasound and liver function tests. In more advanced but operable disease (T3, N1-2), these patients had investigations which included a chest x-ray, abdominal ultrasound, bone scan, full blood count, and liver function tests. However, patients presenting with symptoms of bone involvement had bone scan done and those with CNS involvement had a CT scan of the brain.

Collection of samples: A total of 4.5 mls of blood was collected from each participant into EDTA bottle for full blood count analysis, done on the same day of collection. Samples were collected only from consenting breast cancer patients being prepared for chemotherapy and volunteer nurses of the institution as controls.

Procedure: Full blood count was done by Sysmex KN-21N (manufactured by Sysmex corporation Kobe, Japan) a three-part auto analyzer able to run 19 parameters per sample including hemoglobin concentration, packed cell volume, red blood cell concentration, mean corpuscular hemoglobin, mean cell volume, mean corpuscular hemoglobin concentration, white blood cells and platelet parameters.

Well mixed blood sample was aspirated, by letting the equipment sampling probe into the blood sample and then pressing the start button. Approximately 20 ul of blood was aspirated by the auto analyzer. The result of analysis was displayed after about 30 secs.A printout copy of result was released on the thermal printing paper.

Statistical Analysis: The results of 100 histologically diagnosed, consenting, pre-chemotherapy patients of the clinic and 50 age-matched control nurses of the institution were analyzed. Referred patients already on chemotherapy before presentation at the clinic were excluded from the study. Data were analyzed using SPSS version 16.0. The descriptive data were given as means±SD. The Pearson chi-square test and analysis of variance were used for the analytic assessment and the differences were considered to be statistically significant when the p-value obtained was <0.05.

Results

A total of 150 subjects were studied, consisting of 100 histologically diagnosed breast cancer patients (cases) and 50 normal controls. Other characteristics of the patients and control are shown in table 1. In the case and control group 98 and 49 cases were females, respectively.

Table 1. Demographic Parameters

	Cases	Control
Sex		
Females	98	49
Males	2	1
Age		
(Mean±SD) (year)	50.38±12.19	33.33±11.14
21-30	2%	50%
31-40	22%	20%
41-50	32%	20%
51-60	25%	10%
>61	19%	0

A total of 20% (20 of 100) of the cases had PCV <30% at presentation, while 80% (80 of 100) had PCV >30%. Only 1 of 50 (2%) of controls had PCV less than 30% while majority 49 of 50 (98%) had PCV greater than 30%. Using PCV >36% as the cut-off, 58% of cases were anemic, while 42% had normal PCV. Comparatively, 38% of controls were anemic while 62% had normal PCV. 43% (43 of 100) of cases had a PCV range between 30.0-35.99% while 1 had PCV less than 20%.18 of 50 (36%) of controls had PCV between 30.0-35.99% none had PCV less than 20%. The minimum PCV for cases and controls were 19% and 27.3%, maximum of 44.5% and 43.7% and a mean of 34.33±4.65 and 36.58±3.21%, respectively (table 2).

Table 2. Haematologic Parameters

	Cases	Control
PCV		
<20%	1%	0%
<30%	20%	2%
31-35.99%	43%	36%
<36%	58%	38%
MCV (Mean±SD)	82.67±7.48	85.37±5.74
MCH (Mean±SD)	26.01±2.78	27.24±1.90
MCHC (Mean±SD)	30.73±4.06	31.81±0.87
RDW (Mean±SD)	15.61±3.53	14.24±0.75
WBC Total (Mean±SD)	6.96±7.22	5.47±1.57
Neutrophil% (Mean±SD)	54.75±13.1	44.39±8.78
Lymphocyte% (Mean±SD)	38.19±12.72	8.82±15.97
Platelets (Mean±SD)	291.51±103.38	228.82±57.62

Table 3. Haematologic Parameters of Cases According to Staging

Parameters	Stage II	Stage III	Stage IV
Age (Mean±SD)	53.89±12.74	50.42±12.26	46.04±10.64
Haemoglobin (Mean±SD)	11.62±1.20	10.56±1.46	10.75±2.06
Minimum Haemoglobin	9.2	8	6.4
Maximum Haemoglobin	14	12.7	14
Mean PCV (Mean±SD)	35.07±4.01	34.57±3.90	32.73±6.25
Minimum PCV	23.1	24.0	20.0
Maximum PCV	44.5	44.0	41.9
MCV (Mean±SD)	85.05±7.77	80.59±7.85	82.78±6.37
MCH (Mean±SD)	26.56±2.51	25.31±3.22	26.35±2.39
MCHC (Mean±SD)	31.22±0.51	30.81±2.30	30.10±6.84
RDW (Mean±SD)	14.13±1.60	15.80±2.93	16.70±5.02
WBC Total (Mean±SD)	8339.31±11839.65	6377.59±4860.91	15,900±6900
Neutrophil% (Mean±SD)	51.07±15.68	55.61±11.27	57.21±13.25
Lymphocyte% (Mean±SD)	40.64±14.32	37.39±11.73	36.33±12.64
Platelets (Mean±SD)	287.15±120.25	288.05±87.46	310.0±115.57

The PCV was found not to be significantly associated with staging (p=0.23). Analysis of variance did not also show a significant correlation between PCV of the patients and the staging. The mean MCV, MCH, MCHC and RDW of cases were 82.62±7.48 fl, 26.01±2.78 g/l, 30.73±4.06 g/l and 15.61±3.53, respectively. The mean MCV, MCH, MCHC, and RDW of controls were 85.36±5.74, 27.24±1.90, 31.81±0.87 and 14.24±0.75, respectively (table 2). While the mean WBC counts, neutrophil and lymphocyte percentages of cases were 6.96 ±7.22, 54.75±13.1% and 38.19±12.70% respectively. The mean platelet count was 291.51±103.38.The mean WBC, neutrophil and lymphocyte percentage of controls were 5.47±1.57, 44.39±8.78 and 8.82±15.97 respectively. The mean platelet count was 222.82±57.62 (table 2). The full blood count parameters of cases in the context of each stage are presented in table 3. The mean PCV declines with rise in stage while the mean platelet increases with rise in stage. The mean WBC total in stage IV almost doubles stage II value.

Discussion

Breast cancer predominantly affects the female gender as evidenced by this and many other studies. This study reported 98% female prevalence and only 2% of males. It is estimated that one percent of breast cancer develop in males (21). Similar studies in Nigeria reported higher prevalence among males. Oluwole et al reported 3.9% prevalence of breast cancer amongst male population in Nigeria. Adjusted for age and stage, the prognosis for breast cancer in males is similar to the females (22, 23).

A total of 71% of the patients presented to the clinic in advanced stages III and IV and none presented in stage I. A previous study in Nigeria by Ihekwaba reported 73.8% of breast cancers patients presented in stage III. This highlights the need to create more public enlightenment on breast diseases in Nigeria (24). None of the 100 patients was younger than 20 years, however, 79% of them were between 31-60 years, only 2% presented between 21-30 years and 19% were older than 61 years. The mean age of presentation was 50.38±12.19 years. Ihekwaba also reported that 70% of breast cancers in Nigeria were seen between 26-50 years with a peak age range of 36-45 years. This brings to the fore, the commonest age of presentation in Nigeria (24).

This study reported anemia in 58%, 43% and 20% of cases compared with 38%, 36% and 2% of controls using PCV<36%, 30-35.9% and 30%, respectively. This could be compared with 31.3% (using PCV<36%) prechemotherapy obtained by Kirshner among the breast cancer patients in stage II and III (25). This is similar to 32% (using PCV<36%) prechemotherapy reported in 2006 among the cancer patients in a study to determine the prevalence of

anemia The red cell indices (mean MCV, MCH, MCHC) of cases were also lower than the controls while the mean RDW which is the coefficient of variation of red blood cells anisocytosis of cases was higher than the controls (26).

A higher percentage of anemia reported in this study compared with the lower Caucasian values in the cited references and the control group in this study could reflect the disparity in the PCV of the general population in Blacks and Caucasians probably due to lower socioeconomic status and poor nutrition of the former and the effect of cancer of the breast on erythropoiesis on the cases compared with the control group.

The lower PCV of cases could be due to anemia of chronic disorders. The anemia could be hemorrhagic and associated with iron deficiency if the cancer is ulcerating as evidenced by lower MCV, MCH, MCHC and higher RDW compared with the controls. Anorexia associated with cancers generally can also be associated with nutritional anemia seen in the cases. 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 (anemia) and leucocytosis.

The mean WBC counts, neutrophil and lymphocyte percentages of cases were higher than the controls. This can be due to the fact that neoplasms of all types 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 lymphovascular invasion leading to demargination of tumor cells occupying the vascular spaces (either lymphatics or small capillaries). The principal mechanism of tumor immunity is killing of tumor cells by CD8+ cytotoxic T-lymphocyte. The natural killer cells are lymphocytes that are capable of destroying tumor cells without prior sensitization. However, many tumors down-regulate expression of class 1 major histocompatibility complex (MHC) molecules as a way of evading immunity. Lymphocyte count may therefore be elevated or depressed.

The mean platelet count of cases (291.51±103.38) was also higher than that of control (222.82±57.62). Reactive thrombocytosis may be seen in cancer patients as a result of cancer–induced anemia. A negative feedback effect on erythropoietin production in cases as a result of the anemia could be responsible for the thrombocytosis. Erythropoietin has a structural homology with thrombopoetin, although the latter is considerably larger than the former but roughly half of thrombopoetin has identity with or similarity to erythropoietin at the N-terminal region (27). It is therefore, well recognized that thrombocytosis is associated with anemia of chronic disease and several types of anemia. Bone marrow metastasis may be associated with defective thrombopoiesis causing malignancy induced thrombocytopenia. Thrombocytosis and thrombocytopenia may therefore be associated with malignancy depending on the circumstances. In summary, breast cancer patients presented with deranged full blood count pattern consequent to the disease compared with the controls. Hence, full blood count overall mean values and stage-specific mean values and reference ranges of breast cancer patients provided in this study will be a useful guide to an oncologist.

Acknowledgments

We are grateful to all the nurses of Lagos State University Teaching Hospital who participated in this study.

Authors' contributions:
AA-Designed and conceptualized the study.
PA-Reviewed literature
AA-Review manuscript before submission
OO-Analyzed the data
DA- Review manuscript before submission
AP- Review manuscript before submission
Funding: This research was self-funded
Conflict of Interest: No conflict of interest declared

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