

Blood Cell Count Ratios In Post-Operative Breast Cancer Patients On Chemotherapy

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ABSTRACT

Introduction: Neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio are thought to be better in predicting systemic inflammation and thrombotic tendencies. These risks are inherent in the treatment options such as surgery and chemotherapy which are relatively available to breast cancer patients in Nigeria. This study therefore considered the assessment of these blood cell count ratios among breast cancer patients who had undergone surgical removal of the tumour as well as those on a post-operative six-course chemotherapy.

Methods: This study was conducted at University of Calabar Teaching Hospital in Calabar, Cross River State of Nigeria. The blood cell counts were carried out by automation. Statistical analysis of data was done using SPSS 22.0. A p-value of ≤ 0.05 was considered to infer a statistically significant difference.

Results: This study recorded significant decreases in the haematocrit level, haemoglobin concentration, total white blood count as well as the absolute neutrophil and lymphocyte counts of the breast cancer patients compared to control subjects. There was also a significant increase for platelet-to-lymphocyte ratio among breast cancer patients compared to control subjects. The progression of the chemotherapy courses resulted in an initial decline of both neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios up till the third course, after which upward surges were observed.

Conclusion: Apart from anaemia and relative leucopenia, the enrolled breast cancer patients were generally observed to be at risk of thrombosis. Risks of systemic inflammation and thrombosis appear to be higher immediately after surgery and from the fourth course of chemotherapy to the sixth.

Key words: Breast cancer, chemotherapy, thrombosis, inflammation

Introduction

Epidemiology of cancer in resource-poor settings as we have in Nigeria is fraught with the challenges of underreporting and late-stage presentation arising from lack of awareness and poor health infrastructure^{1,2}. Available data across the globe has shown that breast cancer is among the leading contributors to cancer-associated morbidity and mortality particularly among women³⁻⁵. Already health challenges with female preponderance have been reported locally ranging from relatively short-term medical cases of anaemia and malaria to conditions requiring long-term medical attention such as HIV infection and diabetes⁶⁻⁸. These reports collectively highlight the need for more intentional health interventions in support of maternal health. While the foregoing may be applicable to conditions with long-term survival rates with proper management, cancer management remains precarious with varying disease progression and survival rates. Thus, breast cancer which is predominantly seen in women, although it affects a lower proportion of males, constitutes a significant area of interest in maternal healthcare as cancer-related mortality exceeds the combined mortality from HIV infection, tuberculosis and malaria¹.

Currently, medical management for breast cancer in Nigeria depends on certain factors such as disease staging, availability of treatment and of course patient's preference among other factors but generally includes in an increasing order such options as radiotherapy, surgery and chemotherapy⁹. Apart from the contributions of laboratory analyses to disease diagnosis, laboratory tests are important in the monitoring of treatment. Estimation of blood cell counts are commonly utilized for this purpose to essentially aid review anaemia, inflammation and the risk of bleeding. In this

regard, direct assessment of blood cell counts report for the level of haematocrit, concentration of haemoglobin, total and absolute differential white cell count as well as platelet count were traditionally considered to be enough. In recent times though, deriving ratios from some of the full blood count components is gaining popularity for better management of disease conditions. Notably, neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio have been reported to be important morbidity indicators compared to the individual parameters^{10,11}. They are thought to be better in predicting systemic inflammation and thrombotic tendencies. Such information would be helpful for better management of breast cancer patients as both surgery and chemotherapy carry some risk of adversely affecting blood vessels and promoting thrombosis. This study therefore considered the assessment of these blood cell count ratios among female breast cancer patients who had undergone surgical removal of the tumour as well as those on a post-operative six-course chemotherapy.

Materials and methods

This study was conducted among thirty-five post-operative breast cancer patients who were accessing healthcare at the University of Calabar Teaching Hospital in Calabar, Cross River State of Nigeria. They were all females aged between 30-50 years. An equal number of age-matched apparently healthy non-pregnant women who were not on any form of medication as at the time of the study served as controls. This study employed purposive sampling technique in enrolling the post-operative breast cancer patients at different courses of chemotherapy. There were 7 categories comprising pre-chemotherapy, first course through to the sixth course. An equal

Table 1. Blood cell parameters of Breast Cancer Patients and Control subjects

Parameters	Breast cancer Patients n= 35	Controls n = 35	p-Value
HCT (l/l)	0.31 ± 0.02	0.37 ± 0.02	0.001
Hb (g/l)	98.74 ± 6.34	120.71 ± 6.65	0.001
WBC (x 10 ⁹ /l)	4.61 ± 1.26	5.94 ± 1.50	0.001
NEUT (x 10 ⁹ /l)	2.18 ± 1.01	2.89 ± 1.01	0.004
LYMPH (x 10 ⁹ /l)	2.34 ± 1.00	2.95 ± 0.86	0.008
MONO (x 10 ⁹ /l)	0.07 ± 0.01	0.07 ± 0.01	0.896
EOSINO (x 10 ⁹ /l)	0.02 ± 0.01	0.02 ± 0.01	0.996
PLT (x 10 ⁹ /l)	210.80 ± 38.29	219.14 ± 56.23	0.471
NLR	1.19 ± 0.92	1.03 ± 0.38	0.340
PLR	112.75 ± 78.99	78.69 ± 26.62	0.018

Values are expressed as mean ± standard deviation,

HCT = Haematocrit, Hb = Haemoglobin concentration, WBC = White Blood Cell Count, NEUT = Absolute Neutrophil count, LYMPH = Absolute Lymphocyte count, MONO = Absolute Monocyte count, EOSINO = Absolute Eosinophil count, PLT = Platelet count, NLR = Neutrophil-to-Lymphocyte Ratio, PLR = Platelet-to-Lymphocyte Ratio

Figure 1. Impact of treatment progression on neutrophil-to-lymphocyte ratio among Breast Cancer Patients

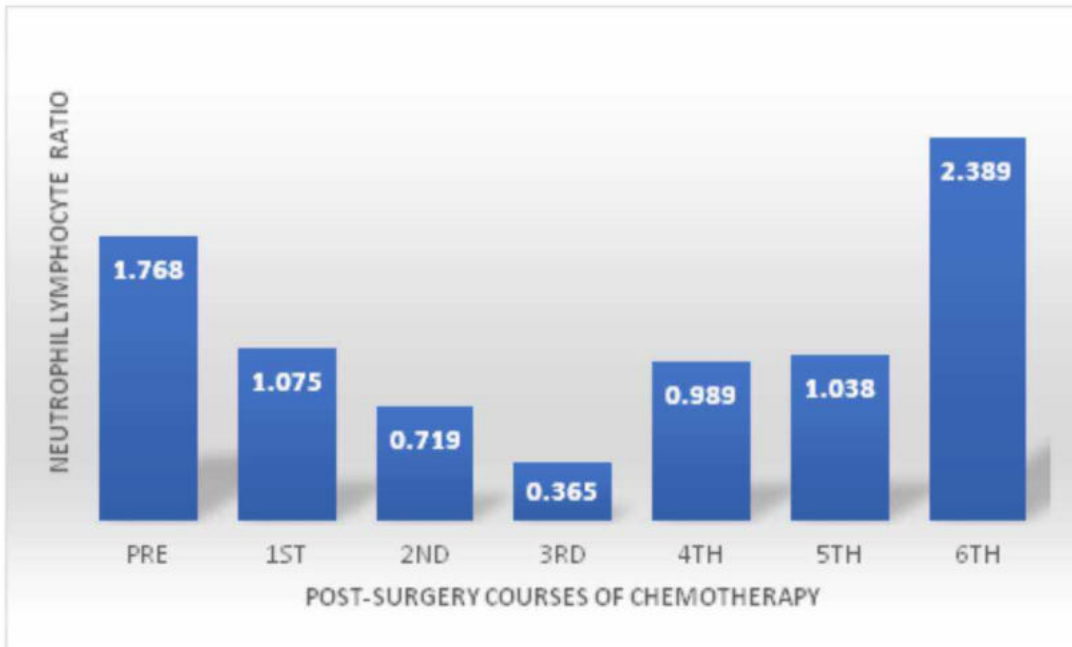
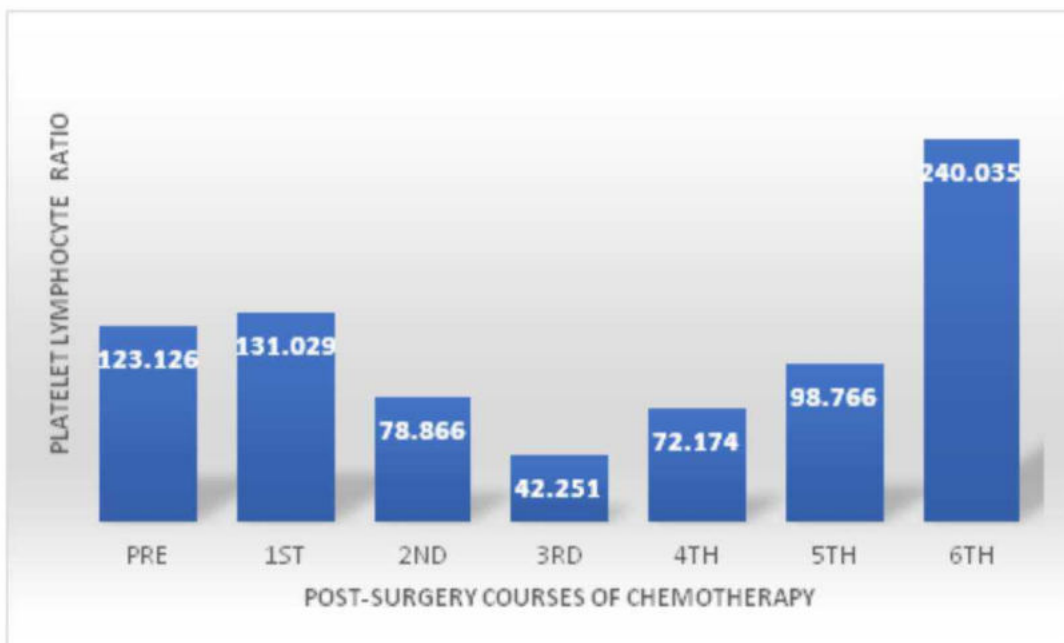


Figure 2. Impact of treatment progression on platelet-to-lymphocyte ratio among Breast Cancer Patients



number of 5 participants were enrolled for each of the 7 categories. Ethical approval was duly sought and obtained from The Ethics and Health Research Committee of University of Calabar Teaching Hospital. Informed consent was obtained from each study participant.

The blood cell counts were carried out by automation using SMART-1 Hematology Analyzer from Kinghawk Technology Co., Ltd, China. This analyser was controlled and calibrated according to manufacturer's instructions to ensure its fitness for use. A structured questionnaire was administered by three trained interviewers to obtain biodata and socio-demographic characteristics. Statistical analysis of data (Student t-test) was done using SPSS 22.0. Results are presented as mean and standard deviation. A p-value of ≤ 0.05 was considered to infer a statistically significant difference.

Results

The study participants comprised 70 non-pregnant women between the ages of 30 and 50 years. Half of this number (35) were post-operative breast cancer patients at different courses of chemotherapy, while the remaining 35 control subjects were apparently healthy and not on medication as the time of the study.

There were significant decreases in the haematocrit level, haemoglobin concentration, total white blood count as well as the absolute neutrophil and lymphocyte counts of the breast cancer patients compared to control subjects. Additionally, a significant increase was observed for platelet-to-lymphocyte ratio among breast cancer patients compared to control subjects (Table 1).

The progression of the chemotherapy courses showed some observable effect on both the neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio. In both instances, an

initial decline of the mean ratio was observed up till the third course, after which the study recorded upward changes (Figures 1 and 2).

Discussion

The present study compared haematocrit, haemoglobin concentration, total white blood cell count, absolute differential white blood cell counts, platelet count, neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio between post-operative breast cancer patients on chemotherapy and control subjects. The findings of this study are part of the initial observations in an ongoing follow up study among breast cancer patients in our locality. Significant decreases were recorded for haematocrit level and haemoglobin concentration among the breast cancer patients compared to control subjects. In fact, the recorded mean values reflected anaemic status for these subjects. Tumour-associated anaemia arises from diverse mechanisms related to both the presence of the tumour and attempts at treatment^{12,13}. In the case of the former, excessive nutritional demand for blood supply to the growing tumour, marrow infiltration and immune-mediated down-regulation of erythropoietic signals from the tumour play important roles in the occurrence of anaemia. In addition, the adverse effect of cancer drugs on cell populations account more for anaemia in cancer during chemotherapy. Anaemia thus, remains one of the challenges in the management of cancer.

Concerning the adverse impact of chemotherapy on blood cell populations, reduction in general leucocyte population and some sub-populations were seen in this study. Cancer-related leucocyte depletion heightens the risk of infection for affected subjects and often necessitates prophylactic interventions for proper management of patients¹⁴. It was

interesting to observe that although no significant changes occurred for platelet count between both groups, a significant increase was observed for platelet-to-lymphocyte ratio among breast cancer patients compared to control subjects. Platelet-to-lymphocyte ratio has been noted to reflect the risk of thrombosis than direct assessment of platelet counts alone and is in fact associated with poor prognosis in breast cancer^{15,16}. This finding, thus, suggests an existing thrombotic risk that would otherwise go unnoticed among the patients

This research investigation also assessed changes in neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios among breast cancer patients at varying stages of post-operative chemotherapy. Starting from post-operative pre-chemotherapy group through six courses of the drug administration, this study enrolled 5 participants for each of the 7 groups culminating into a 35-member study population. The progression of the chemotherapy courses showed some observable effect on both the neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio. In both instances, an initial decline of the mean ratio was observed up till the third course, after which the study recorded upward changes. The interventions of surgery and chemotherapy both increase the risk of thrombosis through

their adverse changes to vascular membrane^{17,18}.

Inflammatory processes can arise in thrombosis due to the endothelial injuries and thrombogenesis, while systemic inflammation also modifies the coagulation process and promotes thrombogenesis. Apparently, the occurrence of one instigates the involvement of the other in a continuous vicious cycle barring timely and proper intervention¹⁹⁻²¹. The present study observed these risks to be high immediately after surgery and from the fourth course of chemotherapy to the sixth. This finding reveals possible critical periods for close monitoring and management of thrombosis in caring of breast cancer patients.

In conclusion, the present study observed anaemia and lower values of total white cell count, absolute neutrophil and lymphocyte counts among the enrolled breast cancer patients. The subjects were also observed to be at risk of thrombosis as seen in the significant increase of platelet-to-lymphocyte ratio. Risks of systemic inflammation and thrombosis appear to be high immediately after surgery and from the fourth course of chemotherapy to the sixth.

Conflict of Interest: Authors declare no conflict of interest.

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