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An Evaluation of Inflammatory and Nutritional Status of Breast Cancer Outpatients in a Tertiary Hospital in Nigeria

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ABSTRACT

Aim: To assess the relationship between nutritional status and inflammatory markers of breast cancer patients, and to identify predictors of malnutrition in these patients.

Methods: This is a cross-sectional study of 45 patients with breast cancer assessed between January and June 2018. Nutritional status was evaluated by objective and subjective methods. The inflammatory markers and inflammation-based scores evaluated were C-reactive protein (CRP), albumin, erythrocyte sedimentation rate (ESR), Glasgow Prognostic Score (GPS), CRP/albumin ratio, and Albumin/CRP ratio.

Results: A total of 45 patients were evaluated. Majority of the patients have high levels of both CRP and ESR (73.3% and 86.7% respectively). More than 70% of the patients were well nourished. There was no significant association between CRP ($P = 0.067$), ESR ($P = 0.094$) and SGA (Subjective Global Assessment) categories. Albumin ($P < 0.001$), Albumin/CRP ratio ($P = 0.002$), CRP/albumin ratio ($P = < 0.001$), and GPS ($P < 0.001$) were significantly associated with SGA categories. On multivariate analysis, albumin ($P < 0.001$), Albumin/CRP ratio ($P = 0.004$), CRP/albumin ratio ($P = 0.009$), GPS ($P = 0.01$), and ECOG ($P = 0.009$) were the only markers independently related to malnutrition.

Conclusion: The inflammation-based scores were significantly associated with malnutrition and can be used as biochemical nutritional assessment tools in cancer patients.

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Background

Breast cancer is a major cause of morbidity and mortality worldwide, accounting for over 600,000 deaths in women in 2018 making it the leading cause of deaths attributable to cancer among women (1). While early screening, diagnosis and treatment have improved the outcomes in the western countries, mortality and morbidity still remain a major challenge in low and middle-income countries. Thus identification of prognostic markers is an important objective for both researchers and clinicians.

Inflammation has been shown to play a major role in cancer development, progression and outcome (2–4), and has been termed the seventh hallmark of cancer (5). Chronic low-grade inflammation mediated by such cytokines like interleukin-1 (IL-1), interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α) and interferon (IFN- γ) have been found to correlate with the progression of some types of malignancies (6). Their prolonged secretion have been implicated in the

development of anorexia and cachexia with increased lipolysis, muscle proteolysis and increased synthesis of acute-phase reactants especially C-reactive protein (CRP) (7). This vicious cascade if not interrupted causes malnutrition and invariably cachexia. Many studies have shown the relationship between inflammatory markers and nutritional status (8–10), and nutritional assessment tools have been designed to quickly recognize early malnutrition. Malnutrition is a universal condition in cancer patients, and it is known to increase morbidity, decrease quality of life, increase chemotherapy toxicity as well as reduce their efficacy, and affect survival (11, 12). Early identification of malnutrition risk through nutritional screening has been shown to be an interventional method in reducing morbidity and mortality associated with malnutrition in cancer patients. Nutritional assessment tools were thus developed to aid in screening for malnutrition. Nutritional assessment tools can be either subjective or objective-oriented. Both have been assessed and validated (13, 14). The Subjective Global

Assessment (SGA) and the Scored Patient-Generated Subjective Global Assessment (PG-SGA) are the only subjective malnutrition screening tools that are recommended by the ASPEN Board of Directors for a routine clinical use (15). The Glasgow Prognostic Score which combines two inflammatory markers, CRP and albumin serve as a prognostic factor that identifies who is likely to develop cachexia with reduced response to treatment and predicts survival (16). The CRP/albumin ratio and the Albumin/CRP ratio are other commonly employed measures that have predictive value in the nutritional status of cancer patients.

Despite the validation of these assessment tools in cancer patients, the tools have not been used for the nutritional assessment of cancer patients in Nigeria. This study, therefore, aims to correlate the inflammatory markers with the clinicopathologic status of breast cancer patients as well as evaluate the association between the nutritional and the inflammatory status in patients with breast cancer.

Methods

This was a cross-sectional study that was done at the University of Ilorin Teaching hospital from January 2018 to June 2018. There were 45 female breast cancer patients enrolled in the study. They consisted of 30 PATIENTS on chemotherapy and 15 that were treatment naïve. This division was done to elucidate the differences in nutritional status and inflammation of patients on chemotherapy (chemotherapy have been noted to have a negative impact on nutritional status) and the treatment naïve. All patients provided written consent to participate in the study, and an assurance of confidentiality of information collected was given. Eligibility for this study included histologically diagnosed breast cancer, and age equal to or greater than 18 years. The criteria for exclusion included: 1) pregnancy, 2) patients on anticoagulant or antiplatelet therapy, 3) patients on growth factors, 4) diagnosed of any other cancer, 5) with an Eastern Cooperative Oncology Group (ECOG) performance status higher than 3, 6) and hospitalized or bedridden. Clinicopathologic details such as age, marital status, education, disease stage, tumor size (longest diameter measured with a caliper in centimeters), lymph node status (present or absent) etc were obtained too.

The Subjective Global Assessment (SGA) questionnaire designed by the Canadian Malnutrition Task ForceTM was administered to all the patients to determine their nutritional status. Anthropometric

variables including body weight and height were measured using a bathroom weighing scale and a stadiometer respectively. The body mass index (BMI) was calculated as weight divided by height squared (kg/m^2). The results of the SGA were classified as A (well-nourished), B (mildly/moderately malnourished), and C (severely malnourished) (16). The WHO cutoff ranges were used for BMI classification; $<18.5 \text{ kg}/\text{m}^2$ as underweight, $18.5\text{--}24.9 \text{ kg}/\text{m}^2$ as normal, $25\text{--}29.9 \text{ kg}/\text{m}^2$ as overweight, and $>30 \text{ kg}/\text{m}^2$ as obese (17).

For the evaluation of the inflammatory markers, plasma CRP, albumin and estimated sedimentation rate (ESR) were used, while the Glasgow Prognostic Score, CRP/albumin ratio, Albumin/CRP ratio were derived. At the time of the administration of the questionnaire, CRP, albumin and ESR were requested from the laboratory and later retrieved. CRP $< 10 \text{ mg}/\text{l}$, albumin $> 35 \text{ g}/\text{l}$, ESR $< 20 \text{ mmh}$ were taken as normal values. For classification of GPS, albumin and CRP values were scored based on the combination of the results. patients with both an elevated C-reactive protein ($>10 \text{ mg}/\text{l}$) and hypoalbuminaemia ($<35 \text{ g}/\text{l}$) were allocated a score of 2. Patients in whom only one of these biochemical abnormalities was present were allocated a score of 1. Patients in whom neither of these abnormalities was present were allocated a score of 0 (18). The CRP/albumin ratio stratified patients as having no risk (<0.4), low risk (0.4 to 1.2), moderate risk (1.2 to 2.0) or high risk (>2) (10). The Albumin/CRP ratio classified patients as well-nourished (ASG A) with values = 1.25 , mildly malnourished (ASG B) = $0.10\text{--}1.25$, while malnourished ones (ASG C) display values = 0.10 (19).

For statistical analysis, patients classified as group B and C under the SGA were considered as under-nourished, while patients classified as group A were considered as well-nourished. The descriptive data were given in percentage. The Pearson chi-square test was used for comparisons of proportions between groups, the analytic assessment and the differences were considered to be statistically significant when the P -value obtained was <0.05 . A Spearman correlation analysis was done to evaluate the correlation between the inflammatory markers and some clinicopathologic features. The R-values were obtained to observe the strength and direction of the correlation. Risk factors associated with malnourishment using the SGA were analyzed by binary logistic regression. We calculated the odds ratio (OR) with the respective 95% confidence intervals. The criterion for inclusion of a variable in the multivariate model was a P -value < 0.05 .

Table 1. Clinicopathologic characteristics of the patients.

Variables	Catchments		P*
	Chemo n (%)	T.N n (%)	
Age groups (Years)			0.860
<35	3 (10.0)	1 (6.7)	
35–50	16 (53.3)	10 (66.7)	
51–65	6 (20.0)	2 (13.3)	
≥66	5 (16.7)	2 (13.3)	
Level of education			0.802
None	6 (20.0)	4 (26.7)	
Primary	5 (16.7)	1 (6.7)	
Secondary	7 (23.3)	4 (26.7)	
Tertiary	12 (40.0)	6 (40.0)	
Marital status			0.107
Married	25 (83.3)	10 (66.7)	
Single	0 (0.0)	2 (13.3)	
Divorced	2 (6.7)	0 (0.0)	
Widowed	3 (10.0)	3 (20.0)	
Occupation			0.826
White-collar	11 (36.7)	5 (33.3)	
Others	19 (63.3)	10 (66.7)	
BMI			0.209
Underweight	0 (0.0)	1 (6.7)	
Normal	13 (43.3)	4 (26.7)	
Overweight	11 (36.7)	4 (26.7)	
Obese	6 (20.0)	6 (40.0)	
ECOG			0.286
0	16 (53.3)	12 (80.0)	
1	3 (10.0)	0 (0.0)	
2	9 (30.0)	2 (13.3)	
3	2 (6.7)	1 (6.7)	
Stage			0.025
1	2 (6.7)	0 (0.0)	
2	3 (10.0)	7 (46.7)	
3	18 (60.0)	4 (26.7)	
4	7 (23.3)	4 (26.7)	
Lymph node involvement			0.612
Present	24 (80.0)	11 (73.3)	
Absent	6 (20.0)	4 (26.7)	
Tumor size (cm)			0.832
<10	17 (56.7)	8 (53.3)	
>10	13 (43.3)	7 (46.7)	
CRP (mg/L)			0.153
<10	6 (20.0)	6 (40.0)	
>10	24 (80.0)	9 (60.0)	
Albumin (g/L)			0.277
<35	13 (43.3)	4 (26.7)	
>35	17 (56.7)	11 (73.3)	
ESR (mm/hr)			0.999
<20	4 (13.3)	2 (13.3)	
>20	26 (86.7)	13 (86.7)	
SGA			0.200
A	19 (63.3)	13 (86.7)	
B	9 (30.0)	1 (6.7)	
C	2 (6.7)	1 (6.7)	

Chemo – Chemotherapy; T.N – Treatment Naïve; BMI – Body mass index; ECOG – Eastern Cooperative Oncology Group; ESR – Erythrocyte sedimentation rate; CRP – C-reactive protein; SGA – Subjective Global Assessment.

*Pearson's Chi-square test.

in the univariate analysis. Statistical analysis was performed using SPSS version 23.0.

Results

This was a cross-sectional study that included 45 breast cancer patients. Of the 45 patients, 60% of them had a BMI >25 kg/m², and 73.3% had

advanced-stage disease (stages III and IV). Almost two-thirds of them were into other occupations than white-collar jobs (64.4%). Most of the breast cancer patients had a good performance status (ECOG 0, 62.2%), and none of the variables between those on chemotherapy, and the treatment naïve patients were statistically significant except for the tumor stage ($P=0.025$). The clinicopathologic variables are presented in Table 1.

According to the evaluation of the nutritional status, more than 70% of the patients were well nourished (71.1%), with a little over a quarter of them at the risk of malnutrition (28.9%) (SGA subgroup B and C). These results are seen in Table 1.

There was a high prevalence of systemic inflammation in the patients as represented by high levels of both CRP and ESR (73.3% and 86.7% respectively). The other inflammatory markers i.e., GPS and CRP/Albumin ratio showed some abnormal alterations in the results (GPS 1 and 2, 73.4%; CRP/Albumin ratio > 1.2, 24.5%). Results are in Table 1.

A statistically significant correlation was observed between ECOG and all the inflammatory markers (CRP, $r=0.407$, $P=0.005$; ESR, $r=0.344$, $P=0.021$; GPS, $r=0.413$, $P=0.005$; CRP/Albumin ratio, $r=0.388$, $P=0.008$), however both albumin and Albumin/CRP ratio showed statistically significant negative correlation (Albumin, $r=-0.323$, $P=0.030$; Albumin/CRP, $r=-0.392$, $P=0.008$). CRP ($r=0.491$, $P=0.001$), GPS ($r=0.520$, $P=0.001$), CRP/Albumin ratio ($r=0.488$, $P=0.001$), Albumin/CRP ratio ($r=-0.489$, $P=0.001$) were the only markers that had statistical significant correlation with tumor stage. GPS was the only inflammatory marker that had statistical significant correlation with tumor size ($r=0.328$, $P=0.028$). These results are seen in Table 4.

The SGA was found to have statistically significant correlation with GPS ($r=0.542$, $P<0.001$), CRP/Albumin ($r=0.582$, $P<0.001$), and Albumin/CRP ($r=-0.580$, $P<0.001$) showing an association between inflammatory markers and nutritional status. The SGA also had a statistically significant correlation with ECOG ($r=0.335$, $P=0.025$), but had no significant correlation with BMI ($r=-0.272$, $P=0.071$). These results are seen in Figure 1.

A Pearson correlation showed that SGA was significantly associated with the inflammatory markers albumin ($P<0.001$), GPS ($P<0.001$), CRP/Albumin ($P<0.001$), Albumin/CRP ($P<0.001$), but was not statistically significant with CRP ($P=0.067$), and ESR ($P=0.094$). These results are seen in Table 5.

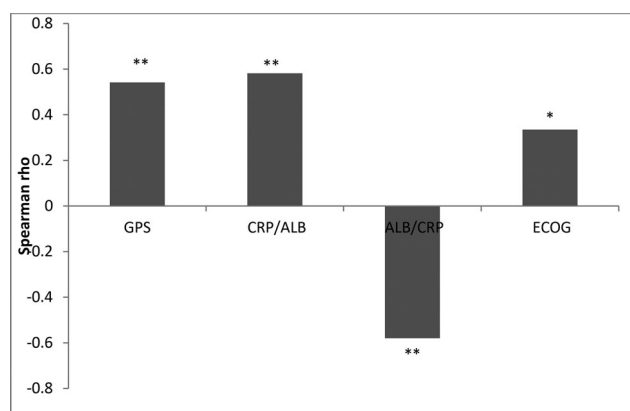


Figure 1. Correlation of SGA with inflammation-based scores and performance status. ** $P < 0.001$ compared with SGA. * $P = 0.025$ compared with SGA.

In the multivariate analysis, factors were independently evaluated with nutritional status, SGA. Albumin ($P = <0.001$), GPS ($P = 0.01$), CRP/Albumin ($P = 0.009$), Albumin/CRP (0.004) were independent predictors of nutritional status. These results are seen in [Table 7](#).

Discussion

This is a pioneering study in which we were able to show the relationship between inflammatory markers and nutritional status in breast cancer patients in Nigeria. Our results thus showed that inflammatory markers can be used in the assessment of malnutrition.

Several studies have shown that inflammation can facilitate the growth, invasion, and metastasis of cancer cells through inflammatory mediators such as CRP, IL-6, and transcription factor NF- κ B, including circulating and infiltrating immune cells derived from the systemic immune reaction to tumor cells or their secretions (20–23). This systemic inflammation often leads to cachexia and malnutrition, which can increase morbidity and mortality. Cancer cachexia is a multifactorial syndrome driven by a complex combination that includes decreased food intake and impaired metabolism with modified catabolism and inflammation (24). This syndrome is common in advanced cancer cases and is a major cause of death (25). The incidence of malnutrition in cancer patients have been reported to be as high as 80%, and to be associated with a reduced response to treatment and quality of life (26, 27). While 85% of gastric/pancreatic cancer patients reported weight loss in a study by DeWys, 70% of breast cancer patients reported no weight loss (28). According to the global subjective assessment (SGA), 28.9% of the breast cancer patients in this

study were malnourished or at risk of malnutrition (categories B and C) ([Table 2](#)). 11 of the categories B and C patients were on chemotherapy (24.4%), and the remainder were not. A similar result was reported by Vergara et al. in breast cancer patients where 67.5% were well nourished (SGA-A), and the remainder were not (29). These results are seen in [Table 1](#).

Majority of the patients that were malnourished or at risk of malnutrition had advanced cancer (stages III and IV). This shows that cachexia is more prevalent in patients that have an advanced disease which is associated with poor quality of life, and prognosis (30), moreover malnutrition has been muted to promote tumor growth and metastasis as well as alter the immune system and the tumor cell microenvironment (18, 31).

Few studies have evaluated systemic inflammation in breast cancer patients, and to the best of our knowledge, no study has been done on the association between nutritional status and inflammation in breast cancer patients in Nigeria. Our study showed that most of the patients had altered levels of inflammatory markers with their clinicopathologic features, especially those with advanced stage, and lymph node involvement (These results are seen in [Table 3](#)). CRP, a short pentraxin, present in plasma only in pentameric form, is the most widely accepted index of systemic inflammation (32). It has a predictive role in survivors of several cancers (33). Studies carried out by Allin and Nordestgaard showed that elevated CRP levels at the time of diagnosis of breast cancer were associated with reduced survival (34). ESR, another inflammatory marker in this study, has also been shown in other studies to predict survival in cancer patients (35, 36). In this study, CRP showed significant association with tumor stage and lymph node status only ([Table 3](#)), and a Spearman correlation showed it was significantly positively correlated with tumor stage, lymph node status and ECOG (These results are seen in [Table 4](#)). However, it had no association with SGA. ESR also showed a significant association with tumor stage, and GPS, and was positively correlated with ECOG, however it had no association with SGA. This may be as a result of their high variability, or the small sample size. In a study done by Read et al., patients with advanced colorectal cancer were initially found to have a positive correlation between SGA and CRP ($r = 0.430$; $P = 0.003$). However, when two outliers were excluded, the association did not remain significant ($r = 0.278$, $P = 0.065$) (37). In a recent large scale cohort study, both CRP and ESR were seen to have some predictive value in

Table 2. SGA Global assessment categories.

Categories	SGA-A	SGA-B	SGA-C
Nutrient intake	No decrease in food/ nutrient intake	Definite decrease in food/ nutrient intake	Severe decrease in food/ nutrient intake
Weight	<5% weight loss	5–10% weight loss without stabilization/gain	>10% weight loss which is ongoing
Nutrient impact symptoms	No/minimal symptoms affecting food intake	Mild/some symptoms affecting food intake	Significant symptoms affecting food/nutrient intake
Functional capacity	No deficit in function	Moderate functional deficit or recent deterioration	Severe function deficit or recent severe deterioration
Physical exam	No deficit in fat or muscle mass	Mild/moderate loss in fat and/or muscle mass	Obvious signs of fats and/or muscle loss

cancer diagnosis, but due to their poor sensitivity for cancer, they were not useful as 'rule out' tests (38). Cachexia has been reported to exist without overt systemic inflammation (32).

Albumin is an important serum protein that is generally taken as an indicator for nutritional status. In addition, it is speculated to enhance immunity, weaken the cell growth rate and DNA replication as well as acts as antioxidants against some carcinogens (39–41). Thus hypoalbuminaemia which is usually a reflection of systemic inflammation (42) is associated with a worse prognosis in cancer patients (43). In this study, 37.8% (17) of patients had hypoalbuminaemia with 13 of them on chemotherapy. Albumin had a significant association with tumor size, and a Spearman correlation showed it was significantly negatively correlated with ECOG. As a measure of the nutritional status, it had a significant association with SGA (<0.001), and even in the multivariate analysis, it was a predictor of nutritional status. But due to the influence of non-nutritional factors, albumin is not seen as a perfect nutritional marker (44).

Recently, inflammation-based scores such as the Glasgow Prognostic Score (GPS), the CRP/Albumin ratio have been shown to have prognostic value in cancer management (45, 46), and also reflect the nutritional status (10, 24, 47). Wu et al. showed that the Albumin/CRP ratio was a useful parameter in predicting overall survival and disease-free survival in hepatocellular carcinoma patients (48). In this study, the Spearman correlation analysis showed that GPS, CRP/Albumin ratio was significantly positively correlated with ECOG, tumor stage and lymph node status, while Albumin/CRP ratio was significantly negatively correlated with the same clinicopathologic parameters (These results are seen in Table 4). When SGA was assessed with the inflammation scores, there was a significant association between SGA and all the inflammation score parameters; this was also reported with albumin, demonstrating that malnourished patients (SGA-B, C) were at a high risk of developing 'laboratory' cachexia and its associated complications

(These results are seen in Table 5). Fruchtenicht et al. (49) in Brazil also showed a significant relationship between SGA and CRP/Albumin ratio, Albumin/CRP ratio and albumin in gastrointestinal tumor patients, but not with GPS. However, Quyen et al. (50) showed a significant correlation between GPS and SGA among oesophageal cancer patients, just like we did.

With regards to inflammation-based scores, the GPS stands out (37, 45, 51). In a study with 165 cancer patients, Elahi et al. reported that there was a linear reduction of the survival time with a high GPS score, both in patients with colorectal tumors and in gastric cancer patients (52). Murri et al. also demonstrated that GPS has a predictive value among metastatic breast cancer patients (53). Also, Silva et al. demonstrated the clinical utility of modified GPS in a palliative care setting, stratifying them into nutritional states i.e., No cachexia, Undernourished, Pre cachexia, and Refractory cachexia, and they were significantly associated with SGA (24). The Albumin/CRP ratio was also shown to be significantly associated with GPS as well as SGA and could serve as an auxiliary method to identify high-risk individuals of malnutrition (19). The Albumin/CRP ratio was also reported to be a prognostic risk factor for mortality in gastrointestinal and lung cancer patients (54). These findings on GPS are in agreement with our results which shows GPS has a significant association with disease stage, lymph node status, and ESR. These results are seen in Table 6.

While the position of the GPS has been established, the CRP/Albumin ratio appears to be gaining more attention. Ranzani et al. (55) first proposed the concept of CRP/Albumin ratio and demonstrated its value for mortality of septic patients. The CRP/Albumin ratio has been shown to be an independent prognostic factor in patients with various cancers (56–58). In a meta-analysis done by Wu et al., the CRP/Albumin ratio was correlated with certain phenotypes of tumor aggressiveness, such as poor histological grade, clinical stage, advanced tumor depth, positive lymph node metastasis, and positive distant metastasis (59). Being

Table 3. Clinicopathologic features of cancer patients according to risk values of inflammatory markers.

	Albumin			CRP			ESR		
	<35	>35	<i>P</i> *	<10	>10	<i>P</i> *	<20	>20	<i>P</i> *
Age			0.931			0.786			0.313
<35	2 (11.8)	2 (7.1)		1 (8.3)	3 (9.1)		1 (16.7)	3 (7.7)	
35–50	9 (52.9)	17(60.7)		8 (66.7)	18 (54.5)		5 (83.3)	21(53.8)	
51–65	3 (17.6)	5 (17.9)		1 (8.3)	7 (21.2)		0 (0.0)	8 (20.5)	
>65	3 (17.6)	4 (14.3)		2 (16.7)	5 (15.2)		0 (0.0)	7 (17.9)	
BMI			0.053			0.868			0.645
<18.5	1 (5.9)	0 (0.0)		0 (0.0)	1 (3.0)		0 (0.0)	1 (2.6)	
18.5–24.99	10 (58.8)	7 (25.0)		4 (33.3)	13(39.4)		1 (16.7)	7 (41.0)	
25–29.99	3 (17.6)	12(42.9)		4 (33.3)	11 (33.3)		3 (50.0)	12 (30.8)	
>30	3 (17.6)	9 (32.1)		4 (33.3)	8 (24.2)		2 (33.3)	10 (25.6)	
Stage			0.052			0.006			0.001
1	0 (0.0)	2 (7.1)		2 (16.7)	0 (0.0)		2 (33.3)	0 (0.0)	
2	1 (5.9)	9 (32.1)		5 (41.7)	5 (15.2)		2 (33.3)	8 (20.5)	
3	9 (52.9)	13 (46.4)		5 (41.7)	17(51.5)		2 (33.3)	20 (51.3)	
4	7 (41.2)	4 (14.3)		0 (0.0)	11 (33.3)		0 (0.0)	11 (28.2)	
Tumor size			0.033			0.113			0.141
<10	6 (35.3)	19 (67.9)		9 (75.0)	16 (48.5)		5 (83.8)	20 (51.3)	
>10	11 (64.7)	7 (32.1)		3 (25.0)	17 (51.5)		1 (16.2)	19 (48.7)	
Lymph node status			0.189			0.007			0.079
Absent	2 (11.8)	8 (28.9)		6 (50.0)	4 (12.1)		3 (50.0)	7 (17.9)	
Present	15 (88.2)	20 (71.4)		6 (50.0)	29 (87.9)		3 (50.0)	32 (82.1)	
ECOG			0.052			0.059			0.240
0	7 (41.2)	21 (75.0)		11 (91.7)	17 (51.5)		6 (100)	22 (56.4)	
1	1 (5.9)	2 (7.1)		1 (8.3)	2 (6.1)		0 (0.0)	3 (7.7)	
2	8 (47.1)	3 (10.7)		0 (0.0)	11 (33.3)		0 (0.0)	11 (28.2)	
3	1 (5.9)	2 (7.1)		0 (0.0)	3 (9.1)		0 (0.0)	3 (7.7)	

BMI – Body mass index; ECOG – Eastern Cooperative Oncology Group; ESR – Erythrocyte sedimentation rate; CRP – C-reactive protein.

*Pearson's Chi-square test.

Table 4. Spearman correlation between inflammatory markers and clinicopathologic features of breast cancer patients.

Factors	CRP		ALBUMIN		ESR	
	<i>r</i>	<i>P</i> -value	<i>r</i>	<i>P</i> -value	<i>r</i>	<i>P</i> -value
AGE	0.117	0.444	0.173	0.257	−0.047	0.758
BMI	0.279	0.063	0.258	0.087	−0.106	0.490
ECOG	0.407	0.005**	−0.323	0.030*	0.344	0.021*
Tumor stage	0.491	0.001**	−0.290	0.053	0.209	0.169
Lymph node status	0.305	0.042*	−0.204	0.179	0.146	0.338
tumor size	0.264	0.080	−0.244	0.107	0.150	0.326
Factors	GPS		CRP/ALB		ALB/CRP	
	<i>r</i>	<i>P</i> -value	<i>r</i>	<i>P</i> -value	<i>r</i>	<i>P</i> -value
AGE	−0.127	0.404	−0.145	0.341	0.139	0.361
BMI	−0.274	0.069	−0.278	0.064	0.272	0.071
ECOG	0.413	0.005**	0.388	0.008**	−0.392	0.008**
tumor stage	0.520	<0.001**	0.488	0.001**	−0.489	0.001**
Lymph node status	0.333	0.025*	0.307	0.040*	−0.303	0.043*
tumor size	0.328	0.028*	0.271	0.072	−0.274	0.069

BMI – Body mass index; ECOG – Eastern Cooperative Oncology Group; ESR – Erythrocyte sedimentation rate; CRP – C-reactive protein.

**Correlation is significant at 0.01.

*Correlation is significant at 0.05.

another index of albumin, a known nutritional marker, the CRP/Albumin ratio is expected to be associated with malnutrition. The CRP/Albumin ratio in our study was significantly associated with SGA, and there was also a strong significant positive correlation with SGA. Similar findings were also reported by other researchers (10, 49). In the logistic regression analysis, assessing factors independently associated with malnutrition, the three inflammation-based scores, Albumin/CRP ratio ($P = 0.004$), GPS ($P = 0.01$), CRP/Albumin ratio ($P = 0.009$) were

independent predictors of malnutrition (These results are seen in Table 7).

Although BMI is commonly used in the evaluation of nutritional status including cancer patients, our results show that BMI cannot be relied on as a marker of malnutrition, because it is not an appropriate tool to differentiate body components (60). In this present study, the results for BMI was not associated with SGA or GPS and was not significantly correlated with any of the inflammatory markers. However, some researchers have pointed out a close link between obesity and low-grade inflammation as well as association with breast cancer (61, 62). Adipose tissues of the breast are known to be associated with elevated levels of proinflammatory mediators, enhanced expression of aromatase, increased estrogen receptor- α (ER- α)-dependent gene expression, altered adipokine levels and increased circulating estrogen, all which are believed to play a role in breast cancer development (63). The role of inflammation in cancer development is not clearly established and in the Malmo Diet and Cancer Cohort study which aimed to examine if low-grade inflammation is related to postmenopausal breast cancer risk, and if obesity modifies this association, low- grade inflammation was not seen to increase breast cancer risk and obesity did not modify the associations between inflammation biomarkers and breast cancer (64).

Table 5. Association of SGA with clinicopathologic variables.

Variables	SGA		χ^2	P*
	A n(%)	B/C n(%)		
Age groups (Years)			6.887	0.076
<35	2 (50.0)	2 (50.0)		
35–50	19 (73.1)	7 (26.9)		
51–65	8 (100)	0 (0.0)		
BMI			5.160	0.160
Underweight	0 (0.0)	1 (100)		
Normal	10 (58.8)	7 (41.2)		
Overweight	12 (80.0)	3 (20.0)		
Obese	10 (83.3)	2 (16.7)		
ECOG			9.371	0.025
0	23 (82.1)	5 (17.9)		
1	3 (100)	0 (0.0)		
2	4 (36.4)	7 (63.6)		
3	2 (66.7)	1 (33.3)		
Stage			1.809	0.613
1	2 (100)	0 (0.0)		
2	8 (80.0)	2 (20.0)		
3	14 (63.6)	8 (36.4)		
4	8 (73.7)	3 (27.3)		
Lymph node involvement			0.495	0.482
Present	24 (68.6)	11(31.4)		
Absent	8 (80.0)	2 (20.0)		
Tumor size (cm)			0.654	0.419
<10	19(76.0)	6 (24.0)		
>10	13(65.0)	7 (35.0)		
CRP (mg/L)			3.366	0.067
<10	11(91.7)	1 (8.3)		
>10	21 (63.6)	12 (36.4)		
Albumin (g/L)			17.061	<0.001
<35	6 (35.3)	11(64.7)		
>35	26 (92.9)	2 (7.1)		
ESR (mm/hr)			2.813	0.094
<20	6 (100)	0 (0.0)		
>20	26 (66.7)	13 (33.3)		
CRP/Albumin			19.028	<0.001
<0.4	21 (95.5)	1 (4.5)		
0.4–1.19	8 (66.7)	4 (33.3)		
1.2–2.0	3 (42.9)	4 (57.1)		
>2.0	0 (0.0)	4 (100)		
Albumin/CRP			9.486	0.002
>1.25	27 (84.4)	5 (15.6)		
0.11–1.24	5 (38.5)	8 (61.5)		
GPS			17.076	<0.001
0	11 (91.7)	1 (8.3)		
1	16 (93.8)	1 (6.3)		
2	6 (35.3)	11 (64.7)		

BMI – Body mass index; ECOG – Eastern Cooperative Oncology Group; ESR – Erythrocyte sedimentation rate; CRP – C-reactive protein; SGA – Subjective Global Assessment.

*Pearson's Chi-square test.

McMillan (18) in one of his works was of the opinion that the use of prognostic scores based on systemic inflammation will allow the identification of patients with cachexia or those in the risk of developing such condition, who are more likely to have a poorer response to treatment and shorter survival. Finally, from this pioneering work in Nigeria, we found there is a high prevalence of systemic inflammation in Nigerian breast cancer patients as was also observed by Ofunre et al. (65) in Benin, however, ECOG, albumin and the inflammation-based scores are considered as independent predictors of malnutrition based on this study.

Table 6. Association of variables with GPS.

	GPS			P - value
	0 n (%)	1 n (%)	2 n (%)	
Age (YEARS)				0.941
<35	1 (25.0)	1 (25.0)	2 (50.0)	
36–50	8 (30.8)	9 (34.6)	9 (34.6)	
51–65	1 (12.5)	4 (50.0)	3 (37.5)	
>65	2 (28.6)	2 (28.6)	3 (42.8)	
BMI (Kg/m ²)				0.193
<18.5	0 (0.0)	0 (0.0)	1 (100.0)	
18.6–24.99	4 (23.5)	3 (17.6)	10 (58.8)	
25.0–29.99	4 (26.7)	8 (53.3)	3 (20.0)	
>30	4 (33.3)	5 (41.7)	3 (25.0)	
ECOG				0.080
0	11 (39.3)	10 (35.7)	7 (25.0)	
1	1 (33.3)	1 (33.3)	1 (33.3)	
2	0 (0.0)	3 (27.3)	8 (72.7)	
3	0 (0.0)	2 (66.7)	1 (33.3)	
Stage				0.023
1	2 (100.0)	0 (35.7)	0 (0.0)	
2	5 (50.0)	4 (40.0)	1 (10.0)	
3	5 (22.7)	8 (36.4)	9 (40.9)	
4	0 (0.0)	4 (36.4)	7 (63.6)	
Lymph node status				0.026
Present	6 (17.1)	14 (40.0)	15 (42.9)	
Absent	6 (60.0)	2 (20.0)	2 (20.0)	
Tumor size (cm)				0.083
<10	9 (36.0)	10 (40.0)	6 (24.0)	
>10	3 (15.0)	6 (30.0)	11 (55.0)	
ESR (mm/h)				0.034
<20	4 (66.7)	2 (33.3)	0 (0.0)	
>20	8 (20.5)	14 (35.9)	17 (43.6)	

BMI – Body mass index; ECOG – Eastern Cooperative Oncology Group; ESR – Erythrocyte sedimentation rate; CRP – C-reactive protein.

*Pearson's Chi-square test.

Table 7. Multivariate analyses of associations between inflammatory markers and SGA.

Variables	B	S.E	Wald	P-value	OR (95%CI)
Albumin	−3.171	0.892	12.632	<0.001	0.042 (0.007 – 0.241)
CRP/Albumin	3.332	1.277	6.808	0.009	28.00 (2.291–342.15)
Albumin/CRP	2.156	0.750	8.274	0.004	8.64 (1.988–37. 554)
GPS	3.004	1.161	6.692	0.01	20.167 (2.071–196.375)
ECOG	2.086	0.798	6.836	0.009	8.05 (1.686–38.442)

This work has some limitations which include being a single center, cross-sectional study. A multi-centre, prospective research will be needed to confirm the predictive value of these inflammatory markers. The sample size which is small is likely to increase bias. While CRP and albumin are considered as reliable immunonutritional markers that can easily be assessed in the clinical laboratories, they have low specificity for cancer-induced inflammation. It is hoped that this study will spur more research into the nutritional status of Nigerian cancer patients.

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Data Availability Statement

The data that support the findings of this study are available from the corresponding author, (O.I), upon reasonable request.

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