ACUTE-PHASE INFLAMMATORY MARKERS VARY WITH CLINICO-PATHOLOGICAL CHARACTERISTICS IN BREAST CANCER PATIENTS INDEPENDENT OF VITAMIN D STATUS

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ABSTRACT

Background: **Inflammation plays a central role in the induction and development of breast cancer (BC) but its activity could be altered by vitamin D, an anti-inflammatory hormone. Currently, information on the relationship between serum vitamin D levels and inflammation across different clinico-pathological subtypes of BC is limited. This study was therefore conducted to determine the serum levels of selected acute-phase proteins and vitamin D in BC patients with varying clinico-pathological characteristics.**

Methods: **Eighty eight histologically confirmed BC patients were stratified using the Tumour Node Metastasis (TNM) staging and clinical imaging into Early Stage (ES) and Late Stage (LS), With Metastasis (WM) and Without Metastasis (WoM), and Well Differentiated (WD) and Poorly Differentiated (PD). Serum levels of albumin, C-reactive protein-(CRP) and 25-hydroxyvitamin D (VitD) were determined using standard methods. Thereafter, CRP-Albumin ratio (CAR) was calculated, as appropriate.**

Results: **Fifty-four (61.3%) and 34 (38.7%) patients were in ES and LS of BC, respectively. The median CRP level and CAR were insignificantly higher in LS compared with ES. Thirty-four (38.6%) and 54 (61.4%) patients were WM and WoM, respectively. The median CRP level and CAR were significantly higher in WM compared with WoM. Sixty-seven (76.1%) and 21 (23.9%) had PD and WD cancer, respectively. The median CRP level and CAR were insignificantly higher in PD compared with WD. However, serum VitD level was similar in all the groups.**

Conclusion: **Irrespective of the serum vitamin D level, breast cancer patients exhibited an acute phase profile that varies with clinico-pathological characteristics.**

Keywords: Albumin, Breast cancer stage, C-reactive protein, Metastasis, Tumour differentiation

INTRODUCTION

Breast cancer (BC) is the most common adult malignancy and the most common cancer among women.[1,2] It is a global public health challenge as it accounts for nearly one in eight cancer diagnoses worldwide and contributing to approximately one in six cancer deaths in women.[3] By 2050, the global incident cases of BC are forecast to reach 3·56 million, with 1·37 million deaths among females.[4] Unfortunately, the disease burden is disproportionately high in low-income countries, with these countries accounting for nearly 56.8% of cancer of the breast cases globally, and Sub-Saharan Africa having the highest mortality-rates.[5,6]

Despite major advances in diagnostic and therapeutic care that have improved survival, mortality is still high particularly in majority of low- and middle-income countries.[7] This trend may be linked to various factors including the variability in tumour behaviour, which poses challenges to the implementation of personalised treatment strategies.[7,8]

Inflammation plays an important role in driving tumorigenesis and growth of most cancers. It is involved in several phases of tumoural growth through intrinsic genetic alterations and extrinsic signalling pathways.[9] Reports have shown that inflammatory cell-rich and mediator-rich tumour microenvironments actively drive tumour development, enhance metastatic potential, and modulate treatment outcome.[10,11] Some inflammatory biomarkers have been found to vary significantly in cancer patients.[12] Expectedly,

inflammatory markers such as C-reactive protein (CRP) and CRP-albumin ratio (CAR), have been found to be altered in individuals with different types of cancer.[12] Alteration in these inflammatory markers have been reported to have prognostic properties in patients with breast cancer.[13] The alteration has also been used in predicting the prognosis of patients with different subtypes of breast cancer. Chen *et al.*[14] reported that preoperative values of CAR are an independent indicator for luminal breast cancers with HER2-negativity. Therefore, understanding the pattern of alteration in acute phase proteins in various clinicopathological subgroups of breast cancer could provide new insights to guide the formulation of targeted therapy.

The interrelationship between inflammation and nutrition is well established even, in BC patients. Changes in its serum levels are closely associated with inflammation, metabolic dysregulation and disease severity thereby, limiting its role as a sole indicator of nutritional status.[15] Xiang *et al.*[16] reported that reduced serum albumin concentration is predictive of poor prognosis in metastatic breast cancer patients. Breast cancer patients with low serum albumin levels have also been shown to have significantly shorter recurrence-free survival and overall survival.[17] Similarly, CAR has been reported to be a good predictor of prognosis in cancer patients.[18] The report of Liu *et al.*[19] indicated that preoperative CAR had a significant association with survival and prognosis in patients who had luminal B subtype BC.

Vitamin D is a pleiotropic hormone involved in calcium and phosphorus homeostasis and with profound antimicrobial and immunomodulatory properties.[20, 21] It enhances both the innate and adaptive immune responses by promoting anti- inflammatory signalling pathways.[21-23] Several immune cells, including neutrophils, monocytes, macrophages, B-cells and T-cells, express vitamin D receptor (VDR) through which vitamin D modulates their activities, directly or indirectly.[24]

Epidemiological data have linked high levels of circulating vitamin D with decreased risk of cancer of the breast, suggesting higher likelihood of BC incidence in individuals with vitamin D deficiency (VDD).[25-27] This association is believed to be due to the cancer chemo-preventive properties of vitamin D via its ability to regulate important biological pathways involved in cancer biology including cell proliferation, apoptosis, differentiation, autophagy, and epithelial-mesenchymal transition.[28, 29] Currently, there is insufficient information on whether circulating vitamin D levels vary based on specific tumour characteristics in BC patients.

Breast cancer is categorized into molecular subtypes characterized by a distinct genetic composition, progression pattern, drug responsiveness, specific molecular therapeutic targets, and varying treatment outcomes.[30] While molecular profiling is gaining prominence, conventional clinicopathological factors including the age, tumour histology and grade, tumour-size, and hormone-receptor-status continue to play significance role in risk assessment and guiding treatment strategies. While these factors have proven useful in stratifying BC, studies continue to highlight their limitations in delivering reliable risk classification necessary for personalised treatment planning.[30] Therefore, the need for the identification of affordable and reliable predictors of cancer classification remains clinically and economically significant, especially in resource-limited settings such as Nigeria. Currently, there is a dearth of information on the pattern of differential inflammatory profile of C-reactive protein, albumin, CAR and serum vitamin D alteration among Nigerians with different breast cancer characteristics. We hypothesised that these biomarkers differ according to tumour characteristics and may provide affordable adjunctive markers for breast cancer classification and risk stratification in resource-limited settings such as Nigeria.

MATERIALS AND METHODS

Study site/location/setting

This study was conducted at the Department of Immunology, College of Medicine, University of Ibadan.

Study design

This is a cross-sectional study.

Study population

A total of 88 patients with BC were enrolled in this study. They were enrolled from the Department of Radiation Oncology, University College Hospital, Ibadan. All the patients were histologically confirmed.

Diagnosis of breast cancer

Breast cancer diagnosis was confirmed through histopathological examination. Briefly, breast tissue was obtained by ultrasound-guided core needle biopsy. Typically, multiple cores (3 – 5) tissue samples were collected to ensure adequate tissue for pathological evaluation. The biopsy specimens were fixed in 10% neutral buffered formalin within one hour of collection (to preserve cellular morphology), processed, embedded in paraffin wax, sectioned, and

stained with haematoxylin and eosin (H&E). The stained sections were examined microscopically by a Consultant Histopathologist for assessment of tissue architecture, cellular morphology, and evidence of malignancy. The presence of atypical epithelial cells with histopathological features consistent with carcinoma was considered diagnostic of breast cancer.

Inclusion criteria

Breast cancer patients who were 25 years or above with no history of stroke, metabolic disorders, cardiovascular diseases, or autoimmune conditions, and who voluntarily consented to take part in the study were enrolled.

Exclusion criteria

Patients who were younger than 25 years, those with history of alcohol or tobacco use, and those with prior diagnoses of cerebrovascular conditions, metabolic, cardiovascular or autoimmune diseases were excluded from the study. Also, patients living with HIV, those with recent anti-inflammatory or psychotropic medications use or on vitamin D supplementation and those who declined consent were excluded from the study.

Sample size determination and sampling technique

This exploratory study adopted a convenience sampling approach. All eligible patients who consented and met the inclusion criteria during the study period were consecutively enrolled in the study.

Ethical considerations

The research protocol was reviewed and approved by the University of Ibadan/University College Hospital (UI/UCH) Joint Ethics Review Committee (Approval Number: UI/EC/21/0065). Additionally, written informed consent was obtained from the participants before their enrolment in the study.

Data collection

Data on clinical history

Information on clinical history of each participant was obtained using a short-structured questionnaire and clinical case file review.

Measurement of anthropometric indices and blood pressure

Body weight, height, body mass index (BMI), waist circumference (WC), hip circumference (HC) and blood pressure (BP) were determined using standard methods as described by Charles-Davies *et al.*[31]

Blood sample collection

Venous blood (10 ml) was collected from each study participant into plain sample bottles. The samples were allowed to retract and centrifuged at 3000 rpm for 10 minutes. The serum samples obtained were stored at -20°C until the time of laboratory analysis.

Laboratory analysis

The serum concentration of C-reactive protein (CRP) was measured using a sandwich enzyme-linked immunosorbent assay (ELISA) following the manufacturer's guidelines (Thermo Fisher Scientific Inc., USA). The serum albumin concentration was measured using the bromocresol green (BCG) colorimetric method, in accordance with the manufacturer's guidelines (DIALAB, Austria). The serum vitamin D was determined using a competitive ELISA following the manufacturer's guidelines (Calbiotech, Inc., USA).

Calculation of CRP-albumin ratio (CAR)

The CRP-albumin ratio (CAR) was calculated as the ratio of the serum level of CRP (mg/L) to the serum level of albumin (g/L). Albumin concentrations originally measured in g/dL were converted to g/L prior to CAR calculation i.e., CAR = CRP (mg/L)/ Albumin (g/L).[32]

Breast cancer staging

Staging of the breast cancer was performed according to the 8th edition of the American Joint Committee on Cancer (AJCC) TNM Staging System.[33] The staging system incorporates both the anatomical stage, based on primary tumour size (T), regional lymph node involvement (N), and distant metastasis (M), and the prognostic stage, which integrates the TNM classification with histological grade and tumour biomarker status, including oestrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) status. For the purpose of this study, patients were categorised into early-stage and late-stage BC groups to facilitate subgroup analysis. Early-stage breast cancer comprised Stage 0 (ductal carcinoma in situ), Stages I and II, and selected operable Stage IIIA tumours, whereas late-stage breast cancer comprised locally advanced disease (Stages IIIB–IIIC) and metastatic disease (Stage IV).

Patients were further classified as non-metastatic or metastatic according to the presence or absence of distant metastases on staging investigations. Histopathological grading was based on routine pathological examination, with well-differentiated tumours characterised by close resemblance to normal breast tissue and generally favourable biological behaviour, whereas poorly differentiated tumours exhibited marked cytological atypia, high mitotic activity, and more aggressive clinical behaviour. Histopathological confirmation of BC was established

by identifying characteristic malignant features, including loss of normal ductal or lobular architecture, nuclear pleomorphism, increased nuclear-to-cytoplasmic ratio, increased mitotic activity, stromal invasion, single-file cellular arrangement where applicable, and loss of E-cadherin expression in invasive lobular carcinoma.

Data analysis

Data analysis was performed using SPSS software, version 25.0. The distribution of the variables was ascertained using Shapiro-Wilk test. The Shapiro-Wilk statistic and p-value for vitamin D, albumin, CRP and CAR were 0.836, 0.000; 0.970, 0.037; 0.885, 0.000; and 0.944, 0.001, respectively indicating that the variables did not assume Gaussian distribution. Therefore, Mann-Whitney U test was used to compare differences in the median levels of the parameters. Correlation between variables was assessed using the Spearman's rho correlation. Results are expressed as mean ± standard deviation or median (interquartile range), as appropriate. P-value less than 0.05 was considered statistically significant.

RESULTS

The characteristics of the study participants are shown in Table 1. The participants were largely of middle-age as they were between the ages of 25 years and 84 years with the average age of 51.6 ± 12.9 years. Although majority of the patients were normotensive, most of them were overweight and had central obesity as reflected by the average BMI and WC.

Considering the BC stage, 1 (1.1%), 53 (60.2%), 26 (29.6%), and 8 (9.1%) patients were in stages 1, 2, 3, and 4, respectively. Therefore, the participants were grouped into 2 categories as early stage (stages 1 and 2) and late stage (stages 3 and 4). As shown in Table 2, there was slight elevation in the median CRP level and CAR in patients with late stage BC compared with those with early stage BC. The mean levels of vitamin D and albumin were similar between the two groups. Thirty four (38.6%) of the patients had metastasis, while 54 (61.4%) had no metastasis. As shown in Table 3, the median CRP level and CAR were significantly higher in BC patients with metastasis compared with those without metastasis. However, the mean levels of vitamin D and albumin were similar between the two groups.

Considering the differentiation of cancer, 67 (76.1%) of the patients had poorly differentiated BC, while 21 (23.9%) had well differentiated BC. As shown in Table 4, the median levels of CRP and CAR were insignificantly higher in patients with poorly differentiated breast cancer compared with those with

Table 1: Characteristics of the study participants

	Mean ± Standard Deviation	Minimum	Maximum
Age (years)	51.6 ± 12.9	25	84
Body weight (kg)	67.7 ± 15.0	39.0	109.0
Height (m)	1.65 ± 0.09	1.40	1.88
BMI (kg/m^2)	25.1 ± 5.2	15	39
WC (cm)	91.8 ± 23.6	32	133
HC (cm)	107.4 ± 25.3	45	156
SBP (mmHg)	130.9 ± 20.5	90	190
DBP (mmHg)	79.3 ± 14.0	40	108
Pulse rate (b/s)	80.9 ± 15.6	52	120

BMI = Body mass index, WC = Waist circumference, HC = Hip circumference, SBP = Systolic blood pressure, DBP = Diastolic blood pressure

Table 2: Serum levels of CRP, albumin and vitamin D in patients with early and late stages of breast cancer

Parameter	Early stage (n = 54)	Late stage (n = 34)	Z-value	*P*-value
Vitamin D (ng/ml)	37.89 (29.39 – 56.36)	41.40 (31.88 – 57.13)	-0.746	0.456
CRP (mg/L)	3.36 (1.32 – 7.48)	6.21 (1.50 – 7.72)	-0.1045	0.296
Albumin (g/dL)	3.74 (3.33 – 4.41)	3.86 (3.44 – 4.43)	-0.574	0.566
CAR	0.10 (0.04 – 0.17)	0.14 (0.04 – 0.21)	-1.148	0.251

CRP = C-reactive protein, CAR = CRP-albumin ratio

Table 3: Serum levels of CRP, albumin and vitamin D in patients with metastatic and non-metastatic breast cancer

Parameter	Without metastasis (n = 54)	With Metastasis (n = 34)	Z-value	*P*-value
Vitamin D (ng/ml)	38.56 (29.42 – 56.72)	41.40 30.90 – 56.31)	-0.206	0.837
CRP (mg/L)	3.11 (1.14 – 6.71)	6.57 (3.32 – 8.02)	-3.102	0.002*
Albumin (g/dL)	3.66 (3.33 – 4.37)	3.99 (3.47 – 4.48)	-1.345	0.178
CAR	0.08 (0.03 – 0.16)	0.16 (0.09 – 0.23)	-2.879	0.004*

**Significant at P<0.05, CRP = C-reactive protein, CAR = CRP-albumin ratio*

well differentiated breast cancer. However, the mean levels of vitamin D and albumin were similar between the two groups (Table 4).

Seven (8.0%) of the patients had invasive lobular breast cancer, while 81 (92.0%) had invasive ductal breast cancer. As shown in Table 5, the median levels of CRP and CAR were slightly lower in patients with invasive lobular BC compared with those with invasive ductal BC.

As shown in Table 6, the serum albumin level had a significant negative correlation with CAR. In contrast,

Table 4: Serum levels of CRP, albumin and vitamin D in patients with poorly differentiated and well differentiated breast cancer

Parameter	Poorly differentiated (n = 67)	Well differentiated (n = 21)	Z-value	*P*-value
Vitamin D (ng/ml)	42.51 (31.34 – 56.76)	34.03 (28.78 – 45.32)	-1.640	0.101
CRP (mg/L)	5.44 (1.51 – 7.59)	2.26 (1.40 – 7.28)	-0.641	0.521
Albumin (g/dL)	3.85 (3.45 – 4.40)	3.61 (3.28 – 4.40)	-0.798	0.425
CAR	0.13 (0.03 – 0.20)	0.06 (0.04 – 0.18)	-0.524	0.600

CRP = C-reactive protein, CAR = CRP-albumin ratio

Table 5: Serum levels of CRP, albumin and vitamin D in patients with invasive ductal and invasive lobular breast cancer

Parameter	Invasive ductal (n = 81)	Invasive lobular (n = 7)	Z-value	*P*-value
Vitamin D (ng/ml)	38.67 (29.61 – 56.60)	47.46 (30.24 – 61.30)	-0.332	0.740
CRP (mg/L)	5.09 (1.51 – 7.54)	1.48 (0.73 – 5.81)	-1.098	0.272
Albumin (g/dL)	3.83 (3.43 – 4.42)	3.61 (2.99 – 4.10)	-0.821	0.411
CAR	0.13 (0.04 – 0.19)	0.05 (0.02 – 0.16)	-0.969	0.333

CRP = C-reactive protein, CAR = CRP-albumin ratio

Table 6: Correlation between the serum levels of vitamin D, albumin, C-reactive protein and CAR in patients with breast cancer

	Vitamin D		CAR		Albumin		CRP	
	r - value	*P*- value	r – value	*P*- value	r - value	*P*- value	r – value	*P*- value
Vitamin D	-	-	-0.040	0.713	0.048	0.594	-0.028	0.795
CAR	-0.040	0.713	-	-	-0.255	0.016*	0.941	0.000*
Albumin	0.048	0.594	-0.255	0.016*	-	-	0.018	0.871
CRP	-0.028	0.795	0.941	0.000*	0.018	0.871	-	-

**Significant at P<0.05, CRP = C-reactive protein, CAR = CRP-albumin ratio*

serum CRP level had a significant positive correlation with CAR.

DISCUSSION

The intricate interplay between inflammation and tumour development is well established. [9-11] CRP is a biomarker of systemic inflammation which is often elevated in advanced cancer.[34] Although statistically insignificant, the observed slight elevation in CRP levels and CAR in patients with late-stage BC compared with those with early-stage BC reflects an enhanced systemic inflammatory response. This could be attributed to large tumour burden, necrosis of tumour cells and increased cytokine production as the disease progresses. This observation, which supports the report of Hong *et al.*[35], aligns with disease severity, tumour progression and systemic inflammatory response.

Breast cancer metastasis is a multifaceted process that involves the interplay of anatomical, cellular and genetic factors.[36] Metastatic tumours are known to create an immunosuppressive microenvironment through mechanisms such as the recruitment of regulatory T-cells and myeloid-derived suppressor cells, which inhibit the proliferation and function of immune cells.[37] The observed significant elevation in CRP levels and CAR in patients with metastasis compared with patients without metastasis suggests that there is a direct link between systemic inflammation and BC progression. This observation corroborates the reports of Allin *et al.*[38] and Han *et al.*[39] which showed that elevated CRP levels are associated with poor prognosis in patients with breast cancer. Also, the report of Barik *et al.*[40] showed that patients with metastasis had significantly higher CAR compared to those without metastasis and that elevated CAR is associated with advanced tumour stage, lymph node involvement, and poor differentiation, all of which often coexist with metastatic disease. Furthermore, elevated CAR has been shown to predict unfavourable distant metastasis-free survival in patients with nasopharyngeal cancer.[41] Mechanistically, the observed elevation in CRP level and CAR in patients with metastasis is underpinned by complex interactions between the tumour and the host immune system occasioned by higher tumour burden, poor nutritional status and plethora of inflammatory responses in various organs where the tumour cells metastasized to. Metastatic tumours promote inflammation through the secretion of cytokines such as IL-6, TNF-α, and VEGF, which enhance neutrophil activation and platelet aggregation while suppressing lymphocyte function.[42] These processes not only aid tumour progression and metastasis but also impair optimal immune response. Observation from this study connotes that metastatic tumours induce a stronger inflammatory response than localised tumours as increases in tumour burden have been shown to intensify inflammatory signalling leading to higher CRP levels and consequently higher CAR.[43]

Breast cancer with poorly differentiated morphology is associated with tumour aggression and poor prognosis.[44] The observed insignificant elevation of CRP level and CAR in poorly differentiated breast cancer patients compared with patients with well-differentiated breast cancer is consistent with the report of Allin *et al.*[38] which showed that elevated CRP levels were associated with poorer outcomes across tumour grades, including moderately and poorly differentiated tumours. The observed elevation in CRP levels and CAR in poorly differentiated breast cancer patients may reflect enhanced tumour-associated inflammation accompanying aggressive tumour biology. Poorly differentiated tumours are often characterised by increased proliferative activity, tissue destruction, and cytokine production, which can stimulate hepatic synthesis of acute-phase proteins such as CRP. These observations clearly reflect that there are distinct immunological and inflammatory profiles based on tumour differentiation status.

Important immunological and molecular differences exist between invasive lobular carcinoma (ILC) and invasive ductal carcinoma (IDC).[45] The observed slightly lower levels of CRP and CAR in ILC compared with IDC may reflect underlying biological and immunological differences between the two histological subtypes. Invasive ductal carcinoma is generally associated with greater tumour heterogeneity, higher proliferative activity, and a more pronounced

inflammatory tumour microenvironment, which may contribute to increased systemic inflammatory responses and elevated acute-phase proteins such as CRP. On the other hand, ILC exhibits distinct tumour biology characterised by unique genomic and stromal features, lower proliferative activity, and altered immune-related signatures compared with IDC.[45, 46]

Vitamin D is known for its anti-inflammatory and anti-tumorigenic properties.[47, 48] In the present study, serum vitamin D levels were comparable across BC patients with different clinicopathological characteristics. This observation may suggest that vitamin D status may not be strongly influenced by tumour stage, metastatic status, or histological differentiation in this cohort. It could therefore be conceptualised that hypovitaminosis D in BC represents a more generalized systemic alteration rather than a marker of specific tumour aggressiveness or progression. Previous studies investigating the relationship between vitamin D and clinicopathological parameters in breast cancer have yielded inconsistent findings, with some reporting associations with tumour progression and others demonstrating no significant relationship.[49] This inconsistency could be attributable to the multifactorial determinants of vitamin D status including dietary intake, sunlight exposure, body composition, lifestyle factors, and genetic variability in vitamin D metabolism, which may obscure tumour-specific effects.[49]

Expectedly, a significant positive correlation was observed between serum CRP and CAR. This observation is consistent with the well-established role of CRP as an acute-phase protein and a key inflammatory marker. CRP is synthesized by the liver in response to pro-inflammatory cytokines such as IL-6 and TNF-á, which are often elevated in breast cancer patients.[39] Higher CRP levels indicate increased systemic inflammation, which is a hallmark of cancer progression and metastasis. An elevated CAR in breast cancer patients reflects a dual state of increased inflammation (elevated CRP) and reduced nutritional status (reduced albumin), making it a more robust prognostic indicator compared to CRP or albumin alone.[13] The positive correlation observed in this study supports the clinical utility of CAR as an integrative biomarker for monitoring systemic inflammation and predicting outcomes in breast cancer patients.

Hypoalbuminaemia is frequently associated with cancer progression, systemic inflammatory burden and poor clinical outcomes.[50] The significant negative correlation between serum albumin and CAR observed in this study aligns with previous findings in patients with cancer. Since CAR is calculated as the ratio of CRP to albumin, lower albumin levels directly contribute to an elevated CAR. Decreased serum albumin levels in breast cancer patients may be attributed to cancer-induced cachexia, chronic inflammation, or impaired protein synthesis due to tumour burden. Cancer-associated inflammation and cachexia have been shown to be frequently accompanied by hypoalbuminaemia which reflects both systemic inflammatory activation and metabolic dysregulation during tumour progression.[51] The observed inverse relationship underscores the potential of CAR as a comprehensive marker of nutritional status and systemic inflammation in BC patients.

Limitation

This study has a number of limitations. First, the use of convenience sampling without an a priori sample calculation and the relatively small sample size may affect the generalisability of the findings and the statistical power to detect modest differences and associations. Second, the cross-sectional design precludes inference of causal or temporal relationships between biomarkers and various clinico-pathological characteristics of breast cancer. Therefore, larger longitudinal studies are suggested to further elucidate the role of vitamin D and its interplay with acute phase proteins in breast cancer biology, progression, and clinical outcomes.

CONCLUSION

Breast cancer patients exhibited an acute phase profile that varies with clinicopathological characteristics. However, the serum vitamin D level appears not to be affected by varying clinicopathological characteristics of the patients. Exploration of the interplay between tumour biology, systemic inflammation and nutritional status in different patient cohorts may provide insights for personalized treatment strategies in breast cancer patients.

Conflict of interest

The authors have no competing interest to declare.

Contribution of authors

GOA and MAJ designed the study, MAJ collected the samples, MAJ and SKR did the laboratory analysis and data analysis, SKR wrote the initial draft of the manuscript, GOA, MAJ and SKR revised and approved the final draft, GOA supervised the entire research.

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REFERENCES

1. **Xu H,** Xu B. Breast cancer: Epidemiology, risk factors and screening. Chin J Cancer Res. 2023; 35 (6):565-583.
2. **Pino-Rosón C,** Ávila-Arroyo S, Parra-Blázquez D, *et al.* Breast cancer incidence and survival by subtype, stage at diagnosis and socioeconomic deprivation among young women in the community of madrid, spain. Int J Cancer. 2026; 158(10):2549-2559.
3. **Arnold M,** Morgan E, Rumgay H, *et al.* Current and future burden of breast cancer: Global statistics for 2020 and 2040. Breast. 2022; 66:15-23.
4. GBD 2023 Breast Cancer Collaborators. Global, regional, and national burden of breast cancer among females, 1990-2023, with forecasts to 2050: A systematic analysis for the global burden of disease study 2023. Lancet Oncol. 2026;27(3):302-326.
5. **Cumber SN,** Nchanji KN, Tsoka-Gwegweni JM. Breast cancer among women in sub-saharan africa: Prevalence and a situational analysis. Southern African Journal of Gynaecological Oncology. 2017;9(2):35–37.
6. **Igbokwe KK.** Comparative examination of breast cancer burden in sub-saharan africa, 1990-2019: Estimates from global burden of disease 2019 study. BMJ Open. 2024;14(3):e082492.
7. **Anderson BO,** Ilbawi AM, El Saghir NS. Breast cancer in low and middle income countries (lmics): A shifting tide in global health. Breast J. 2015;21(1):111-118.
8. **Zhang X,** Xie J, Yang Z, *et al.* Tumour heterogeneity and personalized treatment screening based on single-cell transcriptomics. Comput Struct Biotechnol J. 2025;27:307-320.
9. **Berger E,** Delpierre C, Hosnijeh F, *et al.* Association between low-grade inflammation and breast cancer and b-cell myeloma and non-hodgkin lymphoma: Findings from two prospective cohorts. Sci Rep. 2018;8(1):10805.
10. **Ethier JL,** Desautels D, Templeton A, *et al.* Prognostic role of neutrophil-to-lymphocyte ratio in breast cancer: A systematic review and meta-analysis. Breast Cancer Res. 2017;19(1):2.
11. **Pêczek P,** Gajda M, Rutkowski K, *et al.* Cancer-associated inflammation: Pathophysiology and clinical significance. J Cancer Res Clin Oncol. 2023;149(6):2657-2672.
12. **Janciauskiene S,** Wrenger S, Günzel S, *et al.* Potential roles of acute phase proteins in cancer: Why do cancer cells produce or take up exogenous acute phase protein alpha1-antitrypsin? Front Oncol. 2021;11:622076.
13. **Hutajulu SH,** Astari YK, Ucche M, *et al.* Prognostic significance of c-reactive protein (crp) and albumin-based biomarker in patients with breast cancer receiving chemotherapy. PeerJ. 2025;13:e19319.
14. **Chen F,** Chen D, Jin L, *et al.* Prognostic significance of neutrophil-to-lymphocyte ratio and c-reactive protein/albumin ratio in luminal breast cancers with her2-negativity. Front Oncol. 2022; 12:845935.
15. **Li Y,** Chen L, Yang X, *et al.* Dynamic association of serum albumin changes with inflammation, nutritional status and clinical outcomes: A secondary analysis of a large prospective observational cohort study. Eur J Med Res. 2025; 30(1):679.
16. **Xiang M,** Zhang H, Tian J, *et al.* Low serum albumin levels and high neutrophil counts are predictive of a poorer prognosis in patients with metastatic breast cancer. Oncol Lett. 2022;24(6): 432.
17. **Fujii T,** Tokuda S, Nakazawa Y, Kurozumi S, Obayashi S, Yajima R, *et al.* Implications of low serum albumin as a prognostic factor of long-term outcomes in patients with breast cancer. In Vivo. 2020;34(4):2033-2036.
18. **Xu HJ,** Ma Y, Deng F, *et al.* The prognostic value of c-reactive protein/albumin ratio in human malignancies: An updated meta-analysis. Onco Targets Ther. 2017;10:3059-3070.
19. **Liu X,** Guo X, Zhang Z. Preoperative serum hypersensitive-c-reactive-protein (hs-crp) to albumin ratio predicts survival in patients with luminal b subtype breast cancer. Onco Targets Ther. 2021;14:4137-4148.
20. **Amrein K,** Venkatesh B. Vitamin d and the critically ill patient. Curr Opin Clin Nutr Metab Care. 2012;15(2):188-193.
21. **Geiger C,** McNally JD, Christopher KB, Amrein K. Vitamin d in the critically ill - update 2024. Curr Opin Clin Nutr Metab Care. 2024.
22. **Onifade A,** Rahamon S, Arinola O. Plasma levels of vitamin d and c-reactive protein in adult nigerians with covid-19. African Journal of Biomedical Research. 2024;27(2).

23. **Wei R,** Christakos S. Mechanisms underlying the regulation of innate and adaptive immunity by vitamin d. Nutrients. 2015;7(10):8251-8260.
24. **Martens PJ,** Gysemans C, Verstuyf A, Mathieu AC. Vitamin D's effect on immune function. Nutrients. 2020;12(5).
25. **Atoum M,** Alzoughool F. Vitamin d and breast cancer: Latest evidence and future steps. Breast Cancer (Auckl). 2017;11:1178223417749816.
26. **Welsh J.** Vitamin D and breast cancer: Past and present. J Steroid Biochem Mol Biol. 2018;177:15-20.
27. **Torres A,** Cameselle C, Otero P, Simal-Gandara J. The impact of vitamin D and its dietary supplementation in breast cancer prevention: An integrative review. Nutrients. 2024;16(5):573.
28. **Vanhevel J,** Verlinden L, Doms S, *et al.* The role of vitamin d in breast cancer risk and progression. Endocr Relat Cancer. 2022;29(2):R33-r55.
29. **Vanhevel J,** Verlinden L, Loopmans S, *et al.* The combination of the cdk4/6 inhibitor, palbociclib, with the vitamin d(3) analog, inecalcitol, has potent in vitro and in vivo anticancer effects in hormone-sensitive breast cancer, but has a more limited effect in triple-negative breast cancer. Front Endocrinol (Lausanne). 2022;13:886238.
30. **Masood S.** Breast cancer subtypes: Morphologic and biologic characterization. Womens Health (Lond). 2016;12(1):103-119.
31. **Charles-Davies M,** Arinola O, Fasanmade A, *et al.* Indices of metabolic syndrome in 534 apparently healthy nigerian traders. Journal of US-China Medical Science. 2012;9(2):91-100.
32. **Dai M,** Wu W. Prognostic role of c-reactive protein to albumin ratio in cancer patients treated with immune checkpoint inhibitors: A meta-analysis. Front Oncol. 2023;13:1148786.
33. **Zhu H,** Doðan BE. American joint committee on cancer's staging system for breast cancer, eighth edition: Summary for clinicians. European journal of breast health. 2021;17(3):234-238.
34. **Hart PC,** Rajab IM, Alebraheem M, Potempa LA. C-reactive protein and cancer-diagnostic and therapeutic insights. Front Immunol. 2020;11: 595835.
35. **Hong T,** Liu A, Cai D, *et al.* Preoperative serum c-reactive protein levels and early breast cancer by bmi and menopausal status. Cancer Invest. 2013;31(4):279-285.
36. **Nathanson SD,** Detmar M, Padera TP, *et al.* Mechanisms of breast cancer metastasis. Clin Exp Metastasis. 2022;39(1):117-137.
37. **Lindau D,** Gielen P, Kroesen M, *et al.* The immunosuppressive tumour network: Myeloid-derived suppressor cells, regulatory t cells and natural killer t cells. Immunology. 2013;138(2):105-115.
38. **Allin KH,** Nordestgaard BG, Flyger H, Bojesen SE. Elevated pre-treatment levels of plasma c-reactive protein are associated with poor prognosis after breast cancer: A cohort study. Breast Cancer Res. 2011;13(3):R55.
39. **Han Y,** Mao F, Wu Y, *et al.* Prognostic role of c-reactive protein in breast cancer: A systematic review and meta-analysis. Int J Biol Markers. 2011; 26(4):209-215.
40. **Barik A,** Rashmi A, Singh V, Kumar Upadhyay A. C-reactive protein/albumin ratio and clinicopathological features in ovarian cancer: A prospective study. Cureus. 2024;16(12):e76542.
41. **Wang Y,** Yang L, Xia L, Chen Y. High c-reactive protein/albumin ratio predicts unfavorable distant metastasis-free survival in nasopharyngeal carcinoma: A propensity score-matched analysis. Cancer Manag Res. 2018;10:371-381.
42. **Hanahan D,** Weinberg RA. Hallmarks of cancer: The next generation. Cell. 2011;144(5):646-674.
43. **Kanno H,** Hisaka T, Akiba J, *et al.* C-reactive protein/albumin ratio and glasgow prognostic score are associated with prognosis and infiltration of foxp3+ or cd3+ lymphocytes in colorectal liver metastasis. BMC Cancer. 2022;22(1):839.
44. **Zhu JW,** Charkhchi P, Adekunte S, Akbari MR. What is known about breast cancer in young women? Cancers (Basel). 2023;15(6):1917.
45. **Du T,** Zhu L, Levine KM, *et al.* Invasive lobular and ductal breast carcinoma differ in immune response, protein translation efficiency and metabolism. Sci Rep. 2018;8(1):7205.
46. **Barroso-Sousa R,** Metzger-Filho O. Differences between invasive lobular and invasive ductal carcinoma of the breast: Results and therapeutic implications. Ther Adv Med Oncol. 2016;8(4):261-266.
47. **El-Sharkawy A,** Malki A. Vitamin d signaling in inflammation and cancer: Molecular mechanisms and therapeutic implications. Molecules. 2020;25(14).
48. **Fenercioglu AK.** The anti-inflammatory roles of vitamin d for improving human health. Curr Issues Mol Biol. 2024;46(12):13514-13525.
49. **Hossain S,** Beydoun MA, Beydoun HA, *et al.* Vitamin D and breast cancer: A systematic review and meta-analysis of observational studies. Clin Nutr ESPEN. 2019;30:170-184.
50. **Soeters PB,** Wolfe RR, Shenkin A. Hypoalbuminemia: Pathogenesis and clinical significance. JPEN J Parenter Enteral Nutr. 2019;43(2):181-193.
51. **Baracos VE,** Martin L, Korc M, *et al.* Cancer-associated cachexia. Nat Rev Dis Primers. 2018; 4:17105.