



Research Article

Evaluation of Tissue-Based and Serum-Based Tumor Markers in Breast Cancer Patients at the University of Ilorin Teaching Hospital

*Happiness Chimunya Protus¹, Abdulrazak Nuhu², Mutiu A. Alabi⁶, Kolawole Ayobami Tajudeen Ogunwale², Suleiman Ibrahim Eleha^{1,3}, Abidemi Bunmi Ajayi-Benson¹, Olaleke Oluwasegun Folaranmi⁴, Olusegun Kayode Adepoju⁵, Oladepo Ezekiel Adeshina⁵, Akinola Adekunle Fowotade², Oladipo Evelyn⁷, Seidat Omolabake Hassan⁸, Obateru Peace Adedoyin⁵, Hamza Uthman Akin², and Musa Ahmed²

¹Department of Chemical Pathology and Immunology, University of Ilorin Teaching Hospital, Ilorin, Kwara State, Nigeria

²Department of Medical Laboratory Science, Kwara State University, Malete, Kwara State, Nigeria

³Department of Medical Laboratory Science, University of Offa, Offa, Kwara State, Nigeria

⁴Department of Anatomic Pathology, Kwara State University, Malete, Kwara State, Nigeria, and University of Ilorin Teaching Hospital, Ilorin, Kwara State, Nigeria

⁵University of Ilorin Teaching Hospital, Ilorin, Kwara State, Nigeria

⁶Department of Biochemistry, Kwara State University, Malete, Kwara State, Nigeria

⁷Department of Nursing Services, University of Ilorin Teaching Hospital, Ilorin, Kwara State, Nigeria

⁸Department of Histopathology, University of Ilorin Teaching Hospital, Ilorin, Kwara State, Nigeria

*Corresponding Author's email: happypinky58@yahoo.com; Phone: +2347035494950

ABSTRACT

Tissue-based immunohistochemical markers oestrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) remain the standard for molecular characterisation of breast cancer, but their acquisition is invasive, costly, and often inaccessible in resource-constrained settings. Circulating serum tumour markers offer a less invasive alternative, but their correlation with tissue-based receptor status in Nigerian breast cancer patients remains poorly characterised. This cross-sectional study evaluated and correlated tissue-based (ER, PR, HER2) and serum-based (carcinoembryonic antigen [CEA], cancer antigen 15-3 [CA15-3], and cancer antigen 27-29 [CA27-29]) tumour markers among 30 histologically confirmed breast cancer patients attending the University of Ilorin Teaching Hospital. Serum CEA, CA15-3, and CA27-29 were measured by enzyme-linked immunosorbent assay, and ER, PR, and HER2 status were determined by immunohistochemistry on archived tumour tissues. The ER, PR, and HER2 positivity were observed in 63.3%, 36.7%, and 23.3% of participants, respectively; Luminal A was the most frequent inferred molecular subtype (26.7%), followed by triple-negative disease (23.3%). Median CEA, CA15-3, and CA27-29 concentrations were 2.9 ng/mL, 62.7 U/mL, and 111.0 U/mL, respectively. CEA correlated positively with CA15-3 ($p=0.614$, $p=0.001$) and CA15-3 with CA27-29 ($p=0.561$, $p=0.002$), but none of the three markers differed significantly by ER, PR, or HER2 status (all $p>0.05$), and exploratory ROC analysis showed no statistically significant discrimination of ER status (AUC 0.59–0.73, all $p>0.05$). Serum CEA, CA15-3, and CA27-29 correlate with one another but do not reliably reflect tissue-based receptor status in this cohort, and cannot substitute for immunohistochemistry in receptor classification.

Keywords: Breast cancer; Carcinoembryonic antigen; CA15-3; CA27-29; Her2; Oestrogen Receptor; Progesterone Receptor

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INTRODUCTION

Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer-related death among women worldwide, with an estimated 2.3 million new cases and 670,000 deaths in 2022 (Sung *et al.*, 2021; Ferlay *et al.*, 2026). Although survival has improved substantially in high-income countries with organised screening and early detection, women in resource-constrained settings such as Nigeria continue to present at advanced stages, contributing to disproportionately poor outcomes (World Health Organization, 2024).

Molecular classification of breast cancer relies on immunohistochemical assessment of tissue-based markers ER, PR, and HER2 which guide prognostication and therapeutic decision-making (Igibah *et al.*, 2025). However, obtaining and processing tumour tissue for immunohistochemistry is invasive, costly, and dependent on specialised infrastructure that is often limited in low- and middle-income countries. Serum tumour markers such as CEA, CA15-3, and CA27-29, measurable by enzyme-linked immunosorbent assay, offer a comparatively inexpensive and minimally invasive alternative; although these markers are established tools for monitoring treatment response and detecting recurrence, their relationship to tissue-based receptor status remains inadequately defined, and current evidence does not support their use for diagnosis or screening in isolation (Varzaru *et al.*, 2024).

Despite the substantial burden of breast cancer at the University of Ilorin Teaching Hospital (UITH), a tertiary referral centre for Kwara State and neighbouring North-Central states, there is no local data correlating tissue-based molecular subtypes with circulating tumour marker concentrations. Combining tissue and serum markers could improve diagnostic reach in settings where access to immunohistochemistry is limited, and affordable serum-based testing may help identify patients who would benefit from more detailed molecular work-up (Popoola *et al.*, 2025). This study therefore evaluated and correlated tissue-based (ER, PR, HER2) and serum-based (CEA, CA15-3, CA27-29) tumour markers among breast cancer patients attending UITH, to determine whether this

affordable serum panel reflects the tissue-based receptor profile in this population.

MATERIALS AND METHODS

Study Design and Area

This was a hospital-based, cross-sectional study conducted at the University of Ilorin Teaching Hospital (UITH), Ilorin, Kwara State, Nigeria, a tertiary referral centre for oncology services in Kwara State and neighbouring North-Central states.

Study Participants

Thirty histologically confirmed breast cancer patients aged 18 years and above, recruited from the Oncology, Surgery, and Pathology departments of UITH, were enrolled using a non-probability, purposive consecutive sampling technique; every eligible patient presenting during the study period was recruited until the target sample size was reached. Eligible participants had viable archived formalin-fixed, paraffin-embedded tumour tissue and an accessible peripheral blood sample, and had not yet commenced chemotherapy, radiotherapy, or hormonal therapy. Patients with a history of a concurrent or prior primary cancer, insufficient tumour cellularity or severely haemolysed, lipaemic, or icteric blood samples, missing vital clinical data, pregnancy or lactation, or acute or chronic inflammatory, hepatic, or renal disease were excluded. The sample size was calculated using Hulley's formula for a correlation coefficient, based on an expected correlation of 0.493, a 95% confidence level ($Z\alpha=1.96$), and 80% power ($Z\beta=0.84$), giving a minimum requirement of approximately 30 participants (Hulley *et al.*, 2013).

Ethical Considerations

Ethical approval for this study was obtained from the University of Ilorin Teaching Hospital Health Research Ethics Committee (UITH/CAT/189/21B/819) on 16 July 2026. Written informed consent was obtained from all participants prior to enrolment, and participant confidentiality was maintained throughout using coded identifiers.

Collection of Samples and Laboratory Analysis

Venous blood of 5mL was collected aseptically from each participant by antecubital venipuncture, allowed to clot at room temperature, and centrifuged to obtain serum, which was stored at -20°C until analysis. Serum CEA, CA15-3, and CA27-29 were

measured by sandwich enzyme-linked immunosorbent assay, with absorbance read at 450 nm and concentrations derived from the standard curve; CA15-3 samples were diluted 1:21 in the kit diluent before analysis, as recommended by the assay manufacturer. Archived formalin-fixed, paraffin-embedded tumour tissue blocks were retrieved from the Morbid Anatomy Department with participant consent, and 3–4 µm sections were cut, mounted, and stained with haematoxylin and eosin to confirm histopathological diagnosis. The ER, PR, and HER2 expression were assessed by immunohistochemistry using standard avidin-biotin complex or polymer-based methods, with known positive and negative controls included in each staining batch; stained slides were scored by a pathologist under light microscopy for the intensity and proportion of positively stained cells. Surrogate molecular subtypes were inferred from the combined ER, PR, and HER2 status.

Data Analysis

Data were analysed using IBM SPSS Statistics, version 26.0. Continuous variables were summarised as mean $\pm$ standard deviation and median (range); non-parametric comparisons of serum marker concentrations by ER, PR, and HER2 status were performed using the Mann-Whitney U test. Associations among the serum tumour markers were assessed using Spearman's rank correlation. The discriminatory performance of the serum tumour markers for ER status was evaluated by receiver operating characteristic (ROC) curve analysis, reporting the area under the curve (AUC) with 95% confidence interval, and the sensitivity, specificity, and predictive values at the cut-off maximising the Youden index. Statistical significance was set at $p < 0.05$.

RESULTS

Thirty breast cancer patients were studied. Participants were predominantly aged 40–49 years (43.3%), followed by those aged 50–59 years (30.0%), and most were of Yoruba ethnicity (80.0%). Traders constituted the largest occupational group (36.7%), and secondary education was the most common educational level (50.0%) (Table 1). A positive family history of cancer was reported by 10.0% of participants, while 73.3% reported no family history;

most participants were diagnosed at Stage I (60.0%). Regarding parity, 60.0% had three previous births, and 60.0% of participants had a history of menopause (Table 1).

Table 2 shows the distribution of tissue-based receptor status and the inferred molecular subtypes. The ER positivity was observed in 63.3% of participants and PR positivity in 36.7%; HER2 positivity was observed in 23.3% of participants. Among the inferred surrogate molecular subtypes, Luminal A was the most frequent (26.7%), followed by triple-negative breast cancer (23.3%), Luminal B/HER2-negative (20.0%), Luminal B/HER2-positive (16.7%), HER2-enriched (6.7%), and indeterminate/other subtypes (6.7%).

Serum tumour markers CEA, CA15-3, and CA27-29 showed considerable variability among study participants (Table 3). Median concentrations were 2.9 ng/mL for CEA, 62.7 U/mL for CA15-3, and 111.0 U/mL for CA27-29, with substantially higher mean values relative to the corresponding medians, particularly for CEA (mean 35.1 ng/mL versus median 2.9 ng/mL) indicating a positively skewed distribution of the serum tumour-marker concentrations.

There were no statistically significant differences in CEA, CA15-3, or CA27-29 concentrations between ER-positive and ER-negative participants ($p = 0.061$, 0.461 , and 0.089 , respectively), nor according to PR status or HER2 status (all $p > 0.05$) (Table 4). The CEA and CA27-29 showed numerically higher median concentrations among ER-positive participants, although these differences were not statistically significant.

Table 5 presents the exploratory receiver operating characteristic analysis of the serum tumour markers for discrimination of ER status. CEA showed the highest discriminatory performance (AUC 0.729, 95% CI 0.513–0.945, $p = 0.061$), followed by CA27-29 (AUC 0.711, 95% CI 0.491–0.932, $p = 0.089$); CA15-3 showed comparatively poor discriminatory performance (AUC 0.590, 95% CI 0.353–0.827, $p = 0.461$). The optimal cut-offs by Youden's index were >2.6 ng/mL for CEA (sensitivity 62.5%, specificity 55.6%) and >98.5 U/mL for CA27-29 (sensitivity 66.7%, specificity 55.6%); none of the AUCs reached statistical significance. ROC analysis was not extended to PR or HER2 status because of the small number of positive cases for these markers.

Table 1: Demographic and Clinical Characteristics of Breast Cancer Participants

Characteristic	Frequency (n=30)	Percentage (%)
Age (years)		
30–39	3	10.0
40–49	13	43.3
50–59	9	30.0
60–69	5	16.7
Ethnicity		
Yoruba	24	80.0
Other	6	20.0
Occupation		
Civil servant	8	26.7
Trader	11	36.7
Apprentice	7	23.3
Other	4	13.3
Level of education		
No formal education	3	10.0
Primary education	3	10.0
Secondary education	15	50.0
Tertiary education	9	30.0
Family history of cancer		
Positive	3	10.0
Negative	22	73.3
No idea	5	16.7
Stage at diagnosis		
Stage 0	6	20.0
Stage I	18	60.0
Stage II	5	16.7
Stage III	1	3.3
Parity (previous births)		
1	7	23.3
3	18	60.0
4	5	16.7
Menopausal status		
Postmenopausal	18	60.0
Premenopausal	12	40.0

Table 2: Tissue-Based Receptor Status and Inferred Molecular Subtypes

Variable	Category	Frequency (n=30)	Percentage (%)
ER status	Positive	19	63.3
	Negative	11	36.7
PR status	Positive	11	36.7
	Negative	19	63.3
HER2 status	Positive	7	23.3
	Negative	23	76.6
Inferred molecular subtype	Luminal A (ER+/PR+/HER2-)	8	26.7
	Luminal B (ER+/PR-/HER2-)	6	20.0
	Luminal B (ER+/PR-/HER2+)	5	16.7
	HER2-enriched (ER-/PR-/HER2+)	2	6.7
	Triple-negative (ER-/PR-/HER2-)	7	23.3
	Other/indeterminate	2	6.7

Table 3: Descriptive Statistics of Serum Tumour Markers

Biomarker	n	Mean	Median	SD	Range (Min–Max)
CEA (ng/mL)	30	35.1	2.9	59.6	0.4–203.0
CA15-3 (U/mL)	30	143.5	62.7	161.3	5.8–635.8
CA27-29 (U/mL)	29	195.5	111.0	181.5	11.8–659.0

Table 4: Association of Serum Tumour Marker Concentrations with ER, PR, and HER2 Status

Tissue marker	Status	n	CEA (ng/mL)	CA15-3 (U/mL)	CA27-29 (U/mL)	p (CEA / CA15-3 / CA27-29)
ER	Positive	19	6.8 (1.6–43.8)	63.3 (17.4–231.0)	189.6 (89.7–326.0)	0.061 / 0.461 / 0.089
ER	Negative	11	1.7 (1.1–5.9)	44.5 (21.4–62.7)	98.5 (45.9–234.8)	0.061 / 0.461 / 0.089
PR	Positive	11	2.3 (0.9–43.8)	44.5 (17.4–263.8)	111.0 (32.2–320.3)	0.879 / 0.823 / 0.896
PR	Negative	19	5.9 (1.7–19.1)	48.5 (32.4–129.7)	154.3 (74.9–265.9)	0.879 / 0.823 / 0.896
HER2	Positive	7	1.7 (1.5–1.8)	35.0 (27.0–38.5)	47.0 (34.7–181.1)	0.417 / 0.378 / 0.558
HER2	Negative	23	5.9 (1.8–19.1)	62.7 (21.4–231.0)	189.6 (79.9–265.9)	0.417 / 0.378 / 0.558

Data are presented as median (interquartile range), P-values were determined using the Mann-Whitney U test. CEA correlated positively with CA15-3 ($p=0.614$, $p=0.001$), and CA15-3 correlated positively with CA27-29 ($p=0.561$, $p=0.002$); the correlation between CEA and CA27-29 was weak and not statistically significant ($p=0.265$, $p=0.176$) (Figures 1–3).

Table 5: Exploratory Discriminatory Performance of Serum Tumour Markers for ER Status

Biomarker	AUC	95% CI	p-value	Cut-off (Youden)	Sens (%)	Spec (%)	PPV (%)	NPV (%)
CEA (ng/mL)	0.729	0.513–0.945	0.061	>2.6	62.5	55.6	71.4	45.5
CA27-29 (U/mL)	0.711	0.491–0.932	0.089	>98.5	66.7	55.6	72.7	45.5
CA15-3 (U/mL)	0.590	0.353–0.827	0.461	–	–	–	–	–

AUC = area under the curve; CI = confidence interval; PPV = positive predictive value; NPV = negative predictive value. ROC analysis was not performed for PR and HER2 status because of the small number of positive cases ($n=11$ and $n=7$, respectively), which would render the derived AUC estimates statistically unstable.

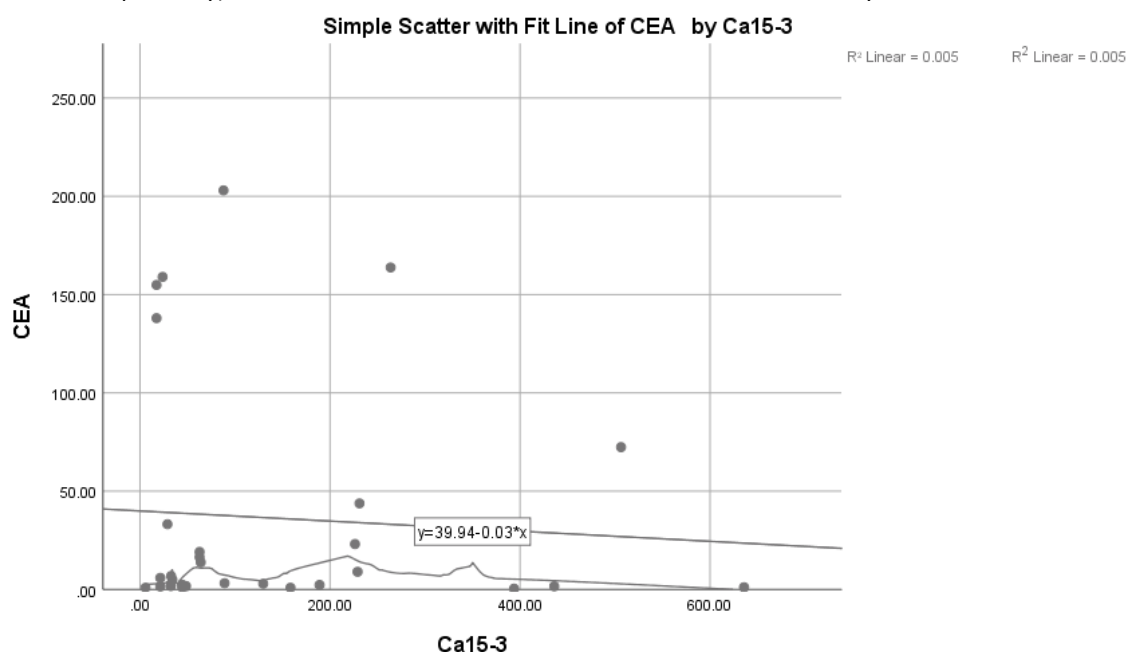


Figure 1: Scatter plot of the relationship between CEA and CA15-3 concentrations among breast cancer participants (Spearman's $\rho=0.614$, $p=0.001$)

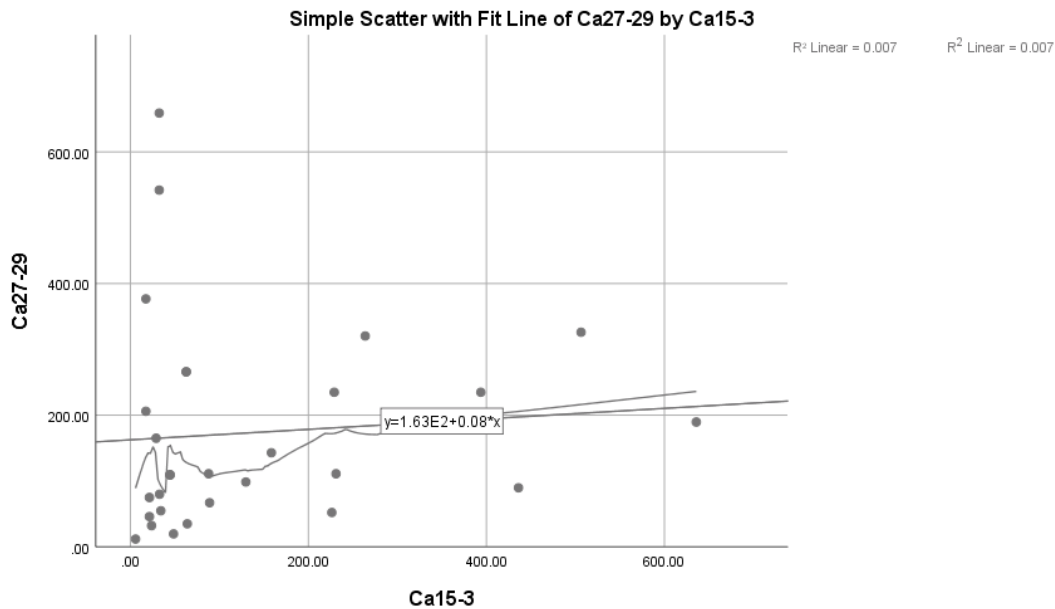


Figure 2: Scatter plot of the relationship between CA27-29 and CA15-3 concentrations among breast cancer participants (Spearman's $\rho=0.561$, $p=0.002$).

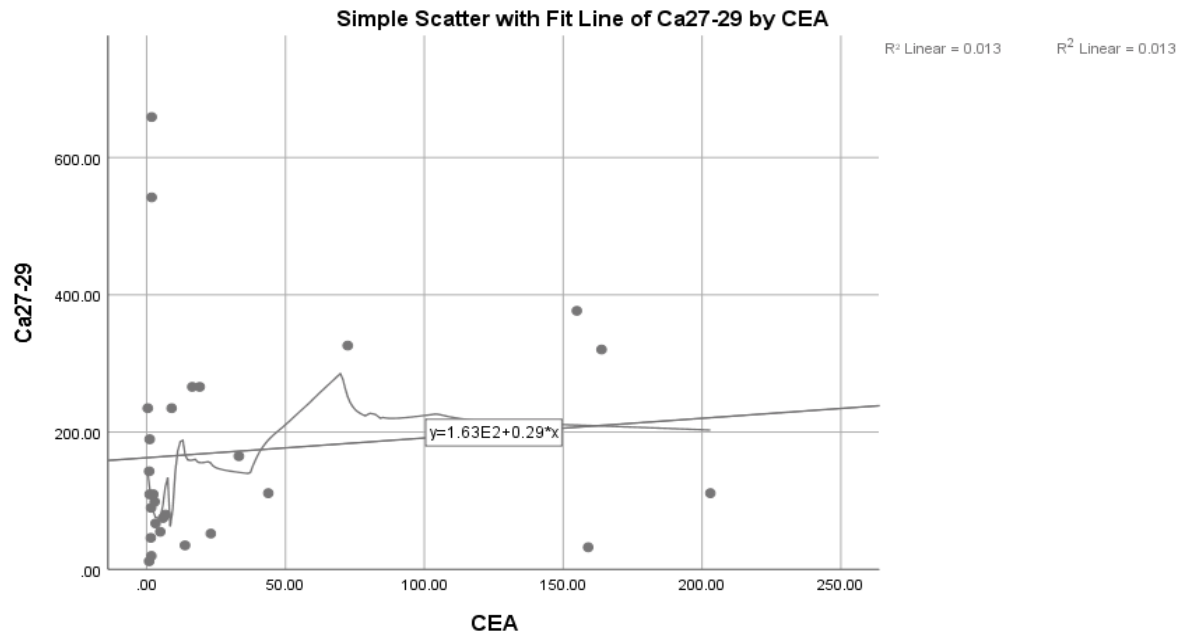


Figure 3: Scatter plot of the relationship between CEA and CA27-29 concentrations among breast cancer participants (Spearman's $\rho=0.265$, $p=0.176$)

DISCUSSION

The predominance of participants in the 40–49 year age group (43.3%), followed by those aged 50–59 years (30.0%), is consistent with the broader Nigerian breast cancer demographic profile, in which studies from tertiary institutions have reported mean ages at presentation of 46–52 years, contrasting with the later, predominantly postmenopausal onset typical of

Western populations (Igibah *et al.*, 2025). The predominance of Yoruba ethnicity (80.0%) in this cohort most plausibly reflects the demographic composition of the hospital's catchment population rather than differential susceptibility across ethnic groups.

The predominance of Stage I disease at diagnosis (60.0%) is a notably favourable finding relative to

many Nigerian cohorts, where advanced-stage presentation has historically predominated (Agodirin *et al.*, 2020); given the cross-sectional, single-institution design of this study, however, this finding should not by itself be taken as evidence of improved population-level early detection, as it may equally reflect selection effects related to institutional referral patterns. The 10.0% prevalence of a positive family history of cancer is somewhat lower than the 15–20% typically cited in the literature (Adedokun *et al.*, 2023), which may reflect under-reporting rather than a genuinely lower prevalence of hereditary disease in this population.

ER positivity (63.3%) in this cohort falls within the range reported globally, though below the 70–80% typically reported in Western populations, while HER2 positivity (23.3%) falls at the higher end of the 15–20% range usually reported (Igibah *et al.*, 2025). Luminal A was the most frequent inferred molecular subtype (26.7%), but the combined proportion of triple-negative (23.3%) and Luminal B (36.7%) subtypes was substantial—consistent with the elevated prevalence of aggressive, hormone receptor-poor phenotypes previously reported in women of African descent, and with implications for prognosis and access to targeted therapy in this setting (Omoruyi *et al.*, 2018; Adeniji *et al.*, 2020).

The serum tumour markers examined here were positively correlated with one another: CEA with CA15-3 ($p=0.614$, $p=0.001$), and CA15-3 with CA27-29 ($p=0.561$, $p=0.002$). The moderate-to-strong correlation between CEA and CA15-3 is consistent with previous reports linking elevated CA15-3 or CEA to poorer disease-free and overall survival in breast cancer (Fu & Li, 2016), and with evidence that combining CA15-3 with other circulating markers can improve diagnostic performance (Modi *et al.*, 2021). The correlation between CA15-3 and CA27-29 is biologically plausible, as both assays detect the same MUC1 mucin glycoprotein using different monoclonal antibodies (Varzaru *et al.*, 2024), while the weaker, non-significant correlation between CEA and CA27-29 ($p=0.265$, $p=0.176$) is consistent with their distinct biological origins and suggests these markers may provide complementary rather than redundant information (Khorrami *et al.*, 2019; Jiang *et al.*, 2021). None of the three serum markers differed significantly by ER, PR, or HER2 status, and the exploratory ROC analysis provided no statistically significant evidence that CEA, CA15-3, or CA27-29 could discriminate ER-positive from ER-negative disease. This finding, together with the wide confidence intervals around the AUC estimates,

indicates that in this cohort circulating concentrations of these markers cannot be assumed to correspond directly with tissue-based receptor phenotype; serum markers may instead reflect tumour burden or systemic disease activity, whereas ER, PR, and HER2 characterise the molecular phenotype of the tumour tissue itself (Lauro *et al.*, 1999; Clinton *et al.*, 2003). These findings do not support the use of CEA, CA15-3, or CA27-29 as substitutes for tissue-based receptor assessment, though they leave open the possibility that circulating markers provide complementary information for disease monitoring.

CONCLUSION

In this cross-sectional study at the University of Ilorin Teaching Hospital, serum CEA, CA15-3, and CA27-29 were significantly correlated with one another but were not significantly associated with tissue-based ER, PR, or HER2 status, and did not discriminate ER-positive from ER-negative disease with statistical significance. These findings do not support the use of these serum markers as substitutes for tissue-based receptor assessment by immunohistochemistry, but suggest that combinations of circulating biomarkers merit further investigation as complementary tools for disease monitoring in Nigerian breast cancer populations.

Author Contributions: Happiness Chimunya Protus conceived the study, collected the clinical and biological samples, and performed the serum biomarker analysis. Abdulrazak Nuhu and Mutiu A. Alabi supervised the study and its design. Kolawole Ayobami Tajudeen Ogunwale and Abidemi Bunmi Ajayi-Benson contributed to laboratory analysis. Suleiman Ibrahim Eleha performed the statistical analysis. Olaleke Oluwasegun Folaranmi performed the histopathological analysis. Akinola Adekunle Fowotade facilitated institutional access for the histopathology component of the study. Olusegun Kayode Adepoju, Oladepo Ezekiel Adeshina, and Oladipo Evelyn contributed to participant recruitment and sample collection. Seidat Omolabake Hassan reviewed and edited the manuscript. All authors read and approved the final manuscript

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