Journal of Cancer Management and Research
2025 Volume 3, Issue 1
DOI: 10.59657/2996-4563.brs.25.019

BioRes Scientia
Value your Research

Research Article

Open Access

Carcinoembryonic Antigen Levels and Some Coagulation Parameters of Breast Cancer Patients Attending University of Calabar Teaching Hospital

Besong Elvis Obi[1], Akpotuzor David Uchendu[1], Shella Obi Besong[2], Anthony Nduka Kokelu[3], Micheal Abimbola Oladosu[4], Moses Adondua Abah[5]*, Daniel Ebubechi Obasi[6], Daniel Oyedemi[7], Chukwuekee Chisom Victoria[8], Chinomso Kosarachi Iwumune[9], Bolade Sunday Agbanigo[10], Ufuoma Blessing Agbanigo[11], Ashimi Abdullahi Aderemi[12], Joseph Oteng [13,14], Ekpenyong Utomobong Sunday[15], Dickson Godspower Ejike[16], Akande Anthony Olalekan[17]

[1]Department of Haematology, Faculty of Medical Laboratory Science, University of Calabar, Nigeria. [2]Department of Nursing Science, Faculty of Allied Health Sciences, University of Maiduguri, Nigeria. [3]Department of Physiology and Integrative Biology, Faculty of Molecular Biosciences, The State University of New Jersey, USA. [4]Department of Biochemistry, Faculty of Basic Medical Sciences, University of Lagos, Lagos, Nigeria. [5]Department of Biochemistry, Faculty of Biosciences, Federal University Wukari, Taraba, Nigeria. [6]Department of Medicine and Surgery, Faculty of Clinical Sciences, University of Ibadan, Oyo, Nigeria. [7]Department of Emergency Medicine, Warrington and Halton NHS Foundation Trust, Chesire, England. [8]Department.of Pharmacy, Faculty of Pharmaceutical Sciences, University of Port Harcourt, Rivers State, Nigeria. [9]Department of Medical Laboratory Sciences, Faculty of Health Sciences, Nnamdi Azikiwe University, Awka, Anambra State, Nigeria. [10]Department of Dental Surgery, Faculty of Dentistry, College of Medicine, University of Ibadan, Oyo State, Nigeria. [11]Department of Medicine and Surgery, Faculty of Clinical science, College of Medicine, University of Ibadan, Oyo State, Nigeria. [12]Department of Chemistry and Biochemistry, Faculty of Science and Mathematics, Georgia southern University Statesboro Georgia. USA. [13]Department of Public Health, Faculty of Epidemiology, University of Port Harcourt.Port harcourt Nigeria. [14]Association of public health in Ghana, Allied health professionals Council Ghana. [15]Department of Internal Medicine, Nephrology Unit, University of Uyo Teaching Hospital, Uyo, Akwa Ibom State, Nigeria. [16]Department of Biochemistry, Faculty of Sciences, University of Port Harcourt, Rivers State, Nigeria. [17]College of Public Health, Division of Environmental Health Sciences, The Ohio State University, 1841 Neil Avenue, Columbus, OH.

**Corresponding author: Moses Adondua Abah.*

Abstract

Breast cancer stands out as the most prevalent cancer among women globally and its prevalence is notably high in Nigeria. The intricate interplay between the tumor and the haemostatic system plays a pivotal role in breast cancer progression. The study aimed at providing information on the carcinoembryonic antigen (CEA) and some haematological parameters of breast cancer patients. With ethical approval and informed consent, 45 breast cancer patients attending the oncology unit of the Surgery Department, University of Calabar Teaching Hospital (UCTH) were enrolled. Forty-five age-matched staff and students of UCTH served as controls. Demographic and clinical data were obtained from patients' case notes and interview. The haematological parameters of patients were analyzed. Statistical analysis was performed using SPSS version 22, and significance was set at $P < 0.05$. The results obtained in this study revealed that majority (71.1%) of the patients had invasive ductile carcinoma while 22% had comorbidities. A significant reduction ($p=0.001$) was observed for haemoglobin (98.53±7.20 and 120.16±7.38 g/L), packed cell volume (0.31±0.02 and 0.37±0.02 L/L), total white cell count (4.76±1.38 and 5.61±1.62 X 10^9/L), neutrophils (2.21±1.03 and 2.97±0.89 X 10^9/L) and thrombin time (19.33 ±3.98 and 21.31 ±2.88 secs) when values for the test was compared to the control. Conversely, there was a significant rise ($p< 0.05$) in CEA (4.94 ±3.19 versus 2.55 ±0.32ng/ml), fibrinogen (3.59 ±0.87 and 3.13 ±0.68 g/L), D-dimer (1.79 ±1.89 versus 0.69 ±0.65 mg/ml) and prothrombin time (13.80 ±1.98 versus 12.64± 0.71 secs) for breast cancer patients versus the controls. Histological subtypes and presence of comorbidities did not influence the studied parameters except for CEA which was significantly raised ($p=0.02$) for those with comorbidities compared to those without (6. 98 ±5.73 ng/ml versus 4.63 ± 1.70 ng/ml). The CEA level was observed to decrease as the treatment course progressed hence it is a useful indicator of response to treatment. Strong negative correlations were noted between thrombin and fibrinogen ($r=-0.732$ $p=0.001$), as well as between haemoglobin and monocyte count ($r=-0.567$ $p=0.00$). Conversely, moderate positive relationships were observed between monocyte count and CEA ($r= 0.314$ $p=0.036$), as well as between monocyte count and fibrinogen levels ($r= 0.314$ $p=0.036$). It can be concluded that there were elevated levels of CEA, D-dimer, fibrinogen, and prothrombin time in breast cancer patients, accompanied by significant reductions in haemoglobin, PCV, total white cell and neutrophil counts. Monocyte count correlated positively with CEA and fibrinogen levels and may be used as a substitute marker for monitoring response to treatment for breast cancer.

Keywords: breast cancer; carcinoembryonic antigen (cea); haematological parameters; biomarker; comorbidities

Introduction

Breast cancer is the most common cancer among women, causing a significant number of deaths worldwide (Ife *et al.*, 2024). It affects both high-income and low-income countries, but the rates are particularly high in Nigeria (WHO, 2022). Nigerian women have a higher prevalence of advanced triple-negative breast cancer compared to women of European descent. Breast cancer also occurs more frequently in premenopausal and younger women in sub-Saharan Africa compared to western nations. The incidence of breast cancer is increasing in low-income countries, and it is estimated that there will be a significant rise in new cases by 2040, mainly in low-income countries (Bellanger *et al.*, 2018). The rise in breast cancer incidence can be attributed to various factors, including obesity, hormone replacement therapy, and increased utilization of early detection methods. However, the exact contributions of these factors are still debated. Research studies on breast cancer in sub-Saharan Africa, including Nigeria, are limited but crucial for identifying environmental and genetic risk factors (Azubuike *et al.*, 2018). Breast cancer awareness and detection efforts have garnered significant attention recently, as indicated by various sources (Akpotuzor *et al.*, 2008; WHO, 2022). Moreover, the medical landscape for this condition appears promising, with a growing number of treatment centers and therapeutic options becoming accessible.

Carcinoembryonic antigen (CEA) and cancer antigen 15-3 (CA15-3) are serum tumor markers used in the diagnosis and monitoring of breast cancer. Elevated levels of CEA are observed in metastatic and recurrent breast cancer and are associated with poor overall survival. However, the clinical usefulness of serial tumor marker measurements for surveillance in asymptomatic women after breast cancer treatment is not supported (Di Gioia *et al.*, 2015). Studies have reported varying incidences of serum CEA positivity, ranging from 36% to 70%. Increased CEA levels are known to correlate with tumor burden, tumor grade, site of metastasis, and are associated with poor overall survival (OS) and progression-free survival (Anoop *et al.*, 2022). The primary application lies in monitoring metastatic disease during treatment, especially utilizing CA15-3. Among the serum tumor markers in breast cancer, CA15-3 and CEA are the ones commonly used (Maccio *et al.*, 2017). Therefore, the estimation of serum CEA can be considered as an additional tool for assessing treatment response, monitoring, and gaining prognostic information. However, due to conflicting results, the clinical utility of these markers remains uncertain (Li *et al.*, 2020).

The host haemostatic system, similar to the tumor microenvironment and immune response, is now acknowledged as a significant factor influencing both the control and advancement of cancer (Inder *et al.*, 2013). Within the context of breast cancer in women, the interplay between the tumor and the haemostatic system is increasingly recognized as a crucial determinant of breast cancer progression. Various components of haemostasis, including platelets, coagulation factors, and fibrinolysis, have the potential to influence numerous processes that are known to drive breast cancer progression. These processes include sustained proliferation, evasion of immune-mediated destruction, prevention of apoptosis, angiogenesis, tumor invasion, and metastasis (Hanahan and Weinberg, 2011), all of which are directly influenced by elements of the haemostatic system. Breast cancer progresses from its early stage to becoming metastatic by a series of events where cancerous cells invade and travel through the bloodstream to distant locations in the body, resulting in the accumulation of tumor cells in non-breast tissues. Recent research suggests that haemostatic elements, such as platelets, coagulation, and fibrinolysis, play a crucial role in facilitating the metastatic potential of breast cancer (Inder *et al.*, 2013). Various steps in the advancement of breast tumors, including cellular transformation, proliferation, tumor cell survival, and angiogenesis, can be influenced by components of the haemostatic system. Consequently, targeting the haemostatic system may offer promising avenues for novel therapeutic approaches in breast cancer treatment, utilizing both existing drugs and those currently in development (Inder *et al.*, 2013).

Cancer is widely accepted as a predisposing factor for thromboembolic events. At the general population level, these events show an incidence rate of 1 to 50 per 1000 people/year, while patients with malignancies generally exhibit a 4 to 10 times greater risk of undergoing coagulopathy such as deep vein thrombosis (Mandoi *et al.*, 2018). It is therefore necessary to study the role coagulation plays in breast cancer condition by assessing some coagulation parameters and casino embryonic antigen of breast cancer patients.

Materials and Method

Study Design

This research is a cross-sectional, case-control study in which qualitative data were obtained using a structured interviewer-administered questionnaire which collated information on subject's demography and socioeconomic characteristics including gender, age, marital status, occupation and education. Information on type, presence of co-morbidity and chemotherapy was obtained from patients' case notes.

Study Site

This study was carried out in the Departments of Surgery and Haematology, University of Calabar Teaching Hospital Calabar, Nigeria. University of Calabar Teaching Hospital is a tertiary health facility located in Calabar, the Cross River State Capital. It serves as a major treatment center for residents in Calabar and a referral center for neighboring states.

Ethical Approval and Informed Consent

Ethical approval was sought and obtained from the Research Ethics Committee of the University of Calabar Teaching Hospital (UCTH/HREC/33/Vol.III/161) and informed consent was obtained from each subject.

Study Population

A total of 90 subjects were enrolled comprising 45 female breast cancer patients drawn from Surgical Oncology Unit UCTH and 45 apparently healthy age-matched individuals drawn from staff of UCTH to serve as control.

Inclusion Criteria

Consenting female adults (18 years and above) with histologically confirmed breast cancer including those that have started treatment one month after surgery and those that have not started treatment but have under gone surgery were recruited as subjects. The control group were apparently healthy females without lump in their breast, consenting, and are not on any medication three months preceding the study.

Exclusion Criteria

Non-consenting female adults, those below the age of 18 years, breast cancer pregnant subjects, breast cancer patients who have been on treatment for more than one year were excluded for the subjects whereas for the control group, non-consenting female adults, those below the age of 18 years, those with breast lump, pregnant women and those on any form of medication were excluded.

Sample Size Calculation

The sample size was determined mathematically using the expression provided below:

Sample size formulae = $N = \frac{z^2 \times p(1-p)}{e^2}$

Z = Z-score = 1.96

E = Margin of Error = 0.05

P = prevalence of breast cancer in Calabar = 21%. (Ebughe, Ugbem, Ushie and Effewongbe, 2019).

$$N = \frac{(1.96)^2 \times 0.21(1-0.21)}{0.05^2}$$

Sample size = 255. This was reduced to I/5 (45) due to cost of reagents.

Sample Collection

Five milliliters (5mls) of blood were drawn from each subject, 2mls was added into EDTA sample bottle to a concentration of 1.5mg/ml for analysis of full blood count (FBC) parameters as well as carcinoembryonic antigen while the remaining 3mls was added into 3.13% tri-sodium citrate in the ratio of 9:1 for the determination of PT, APTT, TT, fibrinogen and D-dimer. The EDTA samples were analyzed within 3 hours of collection. The citrated samples were centrifuged at 3,000 rpm for 10 minutes to obtain platelet poor plasma.

Full blood Count Assay

Full blood count was determined with the use of a Mindray BC 2800, a five-part automated haematology analyzer. The automatic voltage regulator, the uninterrupted power supply unit and the power button on the Mindray BC 2800 analyser was turned on. The 'ready' for analysis was allowed to appear with a temporary wait for the analyser to come to 'ready state'. The sample numbers of the subject were entered into the device. The blood in EDTA was mixed gently, opened and placed under the sample probe. The start switch was put on and the device aspirated the required volume. The EDTA bottle was held against the sample probe until the buzzer sounded twice. At the end of each analysis, the device displayed and printed a hard copy of the report for onward documentation.

Prothrombin Time Test (One-stage technique)

All reagents, controls and samples were brought to room temperature 15 minutes prior to testing. The PT reagent was pre-warmed at 37°C for 5 minutes. 100µl

of PT reagent was transferred to each tube using a micro pipette. 50 µl of samples and controls were added to the tubes prepared in step 3, the stop watch was started while the mixture was mixed in a water bath at (37°C) for 8 seconds, then the time taken for clot formation was recorded. The reference range is given as 10-14 seconds.

Prothrombin time ratio (PTR) = clot time of the test plasma/clot time of the control plasma

INR = PTR (ISI) Example: for a PTR of 2.0 and an ISI of 1.0, INR = 2.0 (1.0) = 2.0

Activated Partial Thromboplastin Time Test

All reagents, controls and samples were brought to room temperature 15 minutes prior to testing. Pipette 50 µl of PTT reagent into each tube. Pipette 50 µl of sample, controls to the tubes prepared. Incubate for 3 minutes at 37°C. Add 25µl of $CaCl_2$ solution to each tube, start the stop watch, mix in a water bath (37°C) for 20 seconds, then record the time taken for clot formation. The reference range is given as 25-35 seconds.

Thrombin Activated Time Test

The working reagent, control and samples were brought to room temperature; 0.150ml of plasma was added into glass test tube and left for 2 minutes at 37 C. The working reagent (0.150ml) was added and the stop watch started immediately. The tube was examined for the presence of clot as soon as it was formed, and the stopwatch was stopped. The time taken for the clot to form is the thrombin time. Result is expressed in seconds or in ratio. The reference range is given as 19-22 seconds.

Determination of Fibrinogen Level

All reagents were allowed to equilibrate to room temperature (15- 30°C). 1:5, 1:10, 1:20, 1:30 and 1:40 dilutions of fibrinogen calibrator were prepared using Owren's Veronal buffer. Duplicate determinations on each dilution of the fibrinogen calibrator were carried out. 0.2 mL of calibrator dilution was incubated for 2 minutes at 37°C. 5 minutes at 37°C was not exceeded. 0.1 mL of Thrombin Reagent (room temperature) was added to immediately initiate the timed reaction. The clotting time was determined. The duplicate times for each calibrator was averaged. The average clotting times obtained versus the respective fibrinogen concentration was plotted

Patients' plasma and controls were diluted in the ratio 1:10 with Owren's Veronal buffer (1 part specimen and 9 parts buffer). 2. Patient and control dilutions were tested in duplicate. 0.2 mL of diluted specimens was pipetted into a specimen cup and incubated for 2 minutes at 37°C. 5 minutes at 37°C. was not exceeded. 0.1 mL of Thrombin Reagent (room temperature) was added to initiate the timed reaction. The clotting time was determined by averaging the readings of the duplicate determinations. The reference range is given as 1.50 - 4.50 g/L.

Determination of D-Dimer Level

D-dimer molecules are generated through the degradation of crosslinked fibrin during fibrinolysis. D-dimer generation requires the activity of three enzymes: thrombin, activated factor XIII (factor XIIIa), and plasmin. The process starts when thrombin generated by the coagulation system converts soluble fibrinogen to fibrin monomers. These monomers then form fibrin polymers through noncovalent interactions based on allosteric changes within the protein as a result of thrombin cleavage of fibrinopeptides from the N-terminal domain. Fibrin is strengthened through interactions with factor XIII, which, after activation by thrombin, cross-links the D domains of adjacent fibrin monomers. Plasmin digestion of the fibrin clot results in the D-dimer molecule. Reference range is given as 0-0.5 mg/ml.

Carcinoembryonic Antigen (CEA) Fluorecare Assay

CEA reagent kit was brought to room temperature. 70ul of plasma was added to 280ul of diluting fluid without air bubbles, mixed and allowed to stand for two 2 minutes. 70ul of the mixture was added to the specimen hole on the test card and allowed to stand for 15 minutes at room temperature. The test card was inserted into the holder of the analyzer and results were read after few seconds as it was displayed on the screen. Results were recorded in ng/ml.

Statistical Analysis

Data on FBC, PT, APTT, fibrinogen, thrombin, D-Dimer and CEA are considered parametric and thus were presented as mean with standard deviation. The analysis was done using student t-test on SPSS package version 22. Statistical significance was set at $P<0.05$.

Results

Demographic Characteristics of Breast Cancer Patients and Control

The demographic characteristics of the studied subjects is shown in Table1 below. The breast cancer patients had a mean age of 47.47±11.70 years with a range of 24.77-70.17 years. The marital status of the

studied subjects revealed 11 (24.4%) and 20 (44.4%) as single for breast cancer patients and control group while 75.6% (34) and 55.6% (25) were married. Among the breast cancer patients, 20% (9) of them had no children while the majority of them had 2 children (22.2%); 15.6% had one child while 13.3% had 3 or 4 children with 6.7% and 8.9% having 5 and 6 children respectively. For the control group, 44.4% (20) had no children, 33.3% of them had 4 children while 22.3% (10 persons) had 3 children.

Table 1: Demographic characteristics of breast cancer patients and control

Variables	Breast cancer patients		Control	
	n=45		n=45	
Age (years)	47.47 ±11.70		45.44 ± 11.80	
Marital status				
Single n (%)	11	24.4	20	44.4
Married n (%)	34	75.6	25	55.6
Number of children				
0	9	20.0	20	44.4
1	7	15.6	----	----
2	10	22.2	----	----
3	6	13.3	10	22.3
4	6	13.3	15	33.3
5	3	6.7	----	----
6	4	8.9	----	----

Tumor Size, Histological Subtypes and Co-morbidity of Breast Cancer Patients

As presented in Table 2, for breast cancer patients, tumor size of 6cm occurred most frequently (26.75%), followed by 7cm (20.0%) and 8cm (17.8%) respectively. The histological sub types involved are invasive ductile carcinoma with the highest occurrence of 71.1%, while the non-invasive ductile carcinoma showed 28.9%. Co-morbidity was present in 10 patients (22.2%) while the remaining 35 persons (77.8%) had no other condition aside breast cancer. Figure 1 shows the types of co-morbidities presented by breast cancer patients. It was observed that co-morbidities included high blood pressure (9%), ulcer (9%), asthma (2%) and HIV (2%). The chemotherapy course cycle among the breast cancer patients were recorded (table 3). About 13.3% (6) as at the time of study were yet to commence treatment but had their surgical tumor removed.

Table 2: Tumour size, histological subtypes and co-morbidity of breast cancer patients

Tumour Size (cm)	Number	% Distribution
3	3	6.7
4	6	13.3
5	3	6.7
6	12	20.7
6.5	1	2.2
7	9	20.0
8	8	17.8
9	1	2.2
10	1	2.2
12	1	2.2
Histological sub types		
Invasive ductile carcinoma	32	71.1
Non-Invasive ductile carcinoma	13	28.9
Co-morbidity		
Absent	35	77.8
Present	10	22.2

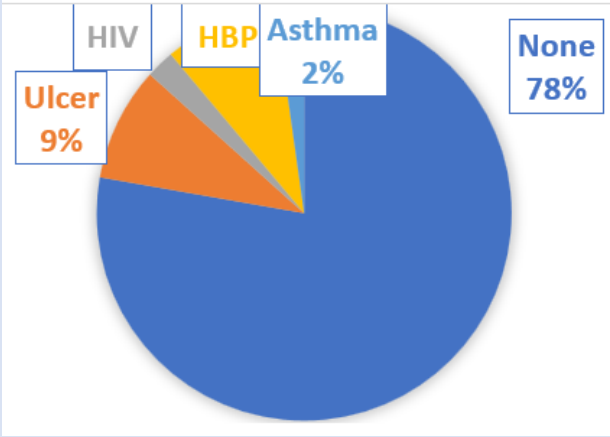

Figure 1: Types of co-morbidities presented by breast cancer patients

Chemotherapy Course of Breast Cancer Patients

Table 3 shows the result for chemotherapy course of breast cancer patients. The treatment cycles for their management were between 1 and 6. Those on the 2nd ,6th and 3rd cycles participated more 28.9% (13), 24.4% (11) and 15.6% (7) in that order, while those on 5th, 4th and 1st cycles had the least in the order 4.4% (2), 6.7% (3) and 6.7% (3).

Table 3: Chemotherapy course of breast cancer patients

Course	Number	% Distribution
Naive	6	13.3
1st	3	6.7
2nd	13	28.9
3rd	7	15.6
4th	3	6.7
5th	2	4.4
6th	11	24.4

Hematological Assessment of Breast Cancer Patients and Control

The studied hematological parameters of breast cancer patients and the control group is shown in Table 4. The packed cell volume (0.31±0.02L/L), hemoglobin concentration (98.53±7.20g/L), total white cell count (4.76±1.38 $x10^9$/L) and neutrophil count (2.21±1.03 $x10^9$/L) were significantly reduced ($p<0.05$) for breast cancer patients when compared with the values for the control (0.37±0.02L/L, 120.16±7.38g/L, 5.61±1.62$x10^9$/L and 2 2.97± 0.89$x10^9$/L.) On the other hand, the lymphocyte, monocyte, eosinophil and platelet count of breast cancer patients (2.45±1.03$x10^9$/L, 0.08 ±.08$x10^9$/L, 0.03± 0.05$x10^9$/L and 216.15± 38.25$x10^9$/L) were observed to be comparable ($p>0.05$) with those of the control group (2 .50±0.68$x10^9$/L, 0.08±0.08$x10^9$/L, 0.04±0.06$x10^9$/L and 231.80± 64.77$x10^9$/L).

Table 4: Some hematological parameters of breast cancer patients and control

Parameters	Breast cancer patients n=45	Control n=45	P-value
PCV (0.33- 0.45 L/L)	0.31±0.02	0.37±0.02	0.001*
HB (115-118 g/L)	98.53±7.20	120.16±7.38	0.001*
TWBC (3.6 - 11.0 X 10^9/L)	4.76±1.38	5.61 ±1.62	0.002*
NEUT (1.8 - 7.5 X 10^9/L)	2.21 ±1.03	2.97 ±0.89	0.001*
LYMPH (1.0 - 4.0 X 10^9/L)	2.45±1.03	2.50 ± 0.68	0.800
MON (0.2 - 0.8 X 10^9/L)	0.08 ±0.08	0.08 ±0.08	0.942
EOS (0.1 - 0.4 X 10^9/L)	0.03 ± 0.05	0.04 ±0.06	0.699
BASO (0.02 - 0.10 X 10^9/L)	0.00 ± 0.00	0.00 ±0.00	--
PLAT (140 - 400 X 10^9/L)	216.15±38.25	231.80±64.77	0.176

Assessment of Carcinoembryonic Antigen Level and Coagulation Parameters of Breast Cancer Patients and Control

As presented in Table 5, carcinoembryonic antigen (CEA) was observed to be significantly higher (P=0.001) for breast cancer patients than for the control (4.94±3.9 ng/ml versus 2.55±0.32 ng/ml). The coagulation parameters revealed significantly raised fibrinogen (3.61±0.87g/L; P=0.005), D-Dimer (1.79±1.89mg/ml; p=0.001) and prothrombin time (13.80±1.98 seconds; p=0.001) when compared with the control values (3.13±0.68g/l, 0.69±0.65mg/ml and 12.64±0.71 seconds). Conversely, the thrombin time was significantly lower (p=0.005) for breast cancer patients versus the control (19.22±3.95 versus 21.31±2.88 seconds). No significant change (P=0.612) was observed for activated partial thromboplastin time of the breast cancer patients and control (34.89+5.75 and 34.36+4.04 seconds).

Table 5: Carcinoembryonic antigen level and coagulation parameters of breast cancer patients and the control

Parameters	Breast cancer patients n=45	Control n=45	P-value
CEA (0 - 2.5 ng/ml)	4.94 ±3.19	2.55 ±0.32	0.001*
FIB (1.50 - 4.50 g/L)	3.59 ±0.87	3.13 ±0.68	0.005*
D-Dimer (0 - 0.5 mg/ml)	1.79 ±1.89	0.69 ±0.65	0.001*
TT (19 - 22 seconds)	19.33 ±3.98	21.31 ±2.88	0.005*
PT (11 - 16 seconds)	13.80 ±1.98	12.64± 0.71	0.001*
APTT (25 -35 seconds)	34.89 ±5.75	34.36 ± 4.04	0.612

Assessment of Hematological Parameters, Carcinoembryonic Antigen Level, and Coagulation Parameters Based on Histology Sub Types and Presence of Co-morbidities of Breast Cancer Patients. Tables 6 and 7 shows that there are no significant differences (P>0.05) in the hematological parameters, CEA level and some coagulation parameters of breast cancer patients based on the histological sub types: invasive ductile carcinoma and non- invasive ductile carcinoma. In Table 8, the age, tumor size and hematological parameters of breast cancer patients were compared based on the presence or absence of co-morbidities. No significant difference was observed (p>0.05). Similarly, there was no difference (p>0.05) in the coagulation parameters based on the presence or absence of co-morbidities as shown in Table 9; however, the CEA level was observed to be significantly higher (P=0.02) for breast cancer patients with co-morbidities when compared to those without co-morbidities (6.98±5.72ng/ml versus 4.36±1.70ng/ml).

Table 6: Hematological parameters based on the histology sub types of breast cancer patients

	IDC n=32	NDIC n=13	P-value
Tumor Size (cm)	6.70 ±1.76	5.39 ± 1.80	0.290
PCV L/L)	0.30±0.017	0.31±0.024	0.525
Hb (g/L)	98.25 ±6.26	99.23± 9.38	0.684
TWBC($X10^9$/l)	4.65±1.31	5.01 ±1.56	0.440
NEUT ($X10^9$/l)	2.21 ±1.07	2.22 ±0.97	0.958
LYMPH ($X10^9$/l)	2.36±1.01	2.69 ± 1.10	0.345
MONO ($X10^9$/l)	0.08 ±0.08	0.09 ±0.09	0.875
EOS ($X10^9$/l)	0.03 ± 0.05	0.043±0.05	0.978
BASO ($X10^9$/l)	0.00 ± 0.00	0.00 ±0.00	------
PLAT ($X10^9$/l)	216.69±41.44	216..08 ±30.47	0.962

Table 7: Carcinoembryonic antigen level and some coagulation parameters of breast cancer patients based on histology sub types

Parameters	IDC n=32	NDIC n=13	P-value
CEA (ng/ml)	5.10 ±3.68	4.5 4 ±1.45	0.596
FIB (g/L)	3.52±0.82	3.80 ±0.98	0.352
D-Dimer (mg/ml)	1.83±1.97	1.68 ±1.75	0.819
TT (seconds)	21.25 ±1.21	19.22 ±3.95	0.189

PT (seconds)	13.50 ±1.22	14.31± 1.3	0.112
APTT (seconds)	34.44 ±5.38	36.00 ± 6.71	0.416

Table 8: Age, tumor size and hematological parameters of breast cancer patients based on the presence of co-morbidities

Parameters	Absent n=35	Present n=10	P-value
Age (years)	46.06 ± 10.93	52.40±13.52	0.132
Tumour Size (cm)	6.07 ±1.93	7.20 ± 1.32	0.900
PCV (L/L)	0.307±0.016	0.301±0.028	0.402
HB (g/L)	99.06 ±6.10	96.70 ± 10.38	0.367
TWBC ($X10^9$/L)	4.64±1.19	5.17 ±1.90	0.285
NEUT ($X10^9$/L)	2.14 ±0.98	2.44 ±1.32	0.431
LYMPH ($X10^9$/L)	2.41±1.02	2.60 ± 1.14	0.616
MONO ($X10^9$/L)	0.76 ±0.08	1.00 ±1.05	0.437
EOS ($X10^9$/L)	0.31 ± 0.05	0.30 ±0.04	0.939
BASO ($X10^9$/L)	0.00 ± 0.00	0.00 ±0.00	~~~~
PLAT ($X10^9$/L)	218.31± 37.89	210.20±40.88	0.560

Table 9: Carcinoembryonic antigen level and some coagulation parameters of breast cancer patients based on the presence of co-morbidities

Parameters	Absent n=35	Present n=10	P-value
CEA (ng/ml)	4.63 ± 1.70	6. 98 ±5.73	0.020*
FIB (g/L)	3.58±0.83	3.69 ±1.04	0.101
D-Dimer (mg/ml)	1.54±1.56	2.65 ±2.68	0.714
TT (seconds)	19.06 ±3.66	19.80 ±5.03	0.606
PT (seconds)	13.54 ±1.38	14.70± 3.30	0.104
APTT (seconds)	35.23 ±5.38	33.70 ± 7.80	0.465

CEA Levels in Different chemotherapy Courses and Correlation Between Hematological Parameters and Coagulation Parameters. The CEA levels in different chemotherapy cycles is presented in Figure 2. A significant reduction was observed from the naive state to the 1st cycle, then followed by steady reduction in the levels of CEA as the chemotherapy cycles progressed. Figures 3-6 shows correlation graphs between some of the studied parameters. Thrombin and fibrinogen showed a strong negative association (r=-0.732; P=0.001) while a moderate positive correlation was observed between CEA levels and monocyte count (r=0.314; P=0.036). Monocyte count was observed to correlate positively with fibrinogen levels (r=0.352; P=0.018) and negatively with hemoglobin concentration (r=0.567; P=0.001).

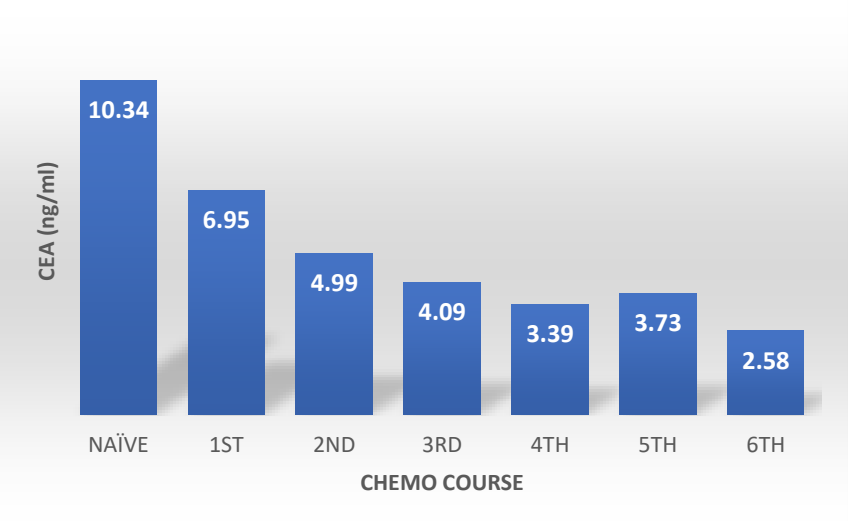

Figure 2: CEA levels in different chemotherapy courses

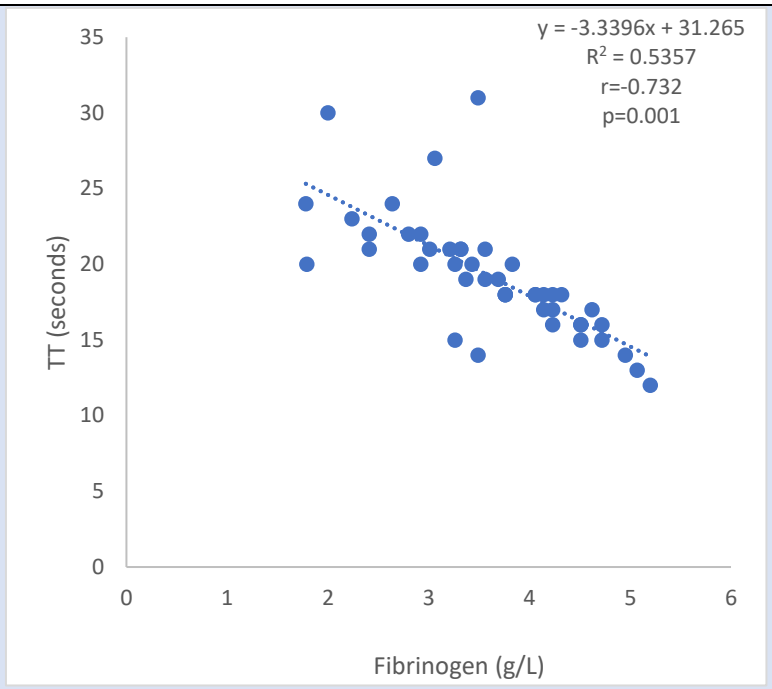

Figure 3: Correlation between thrombin time and fibrinogen level

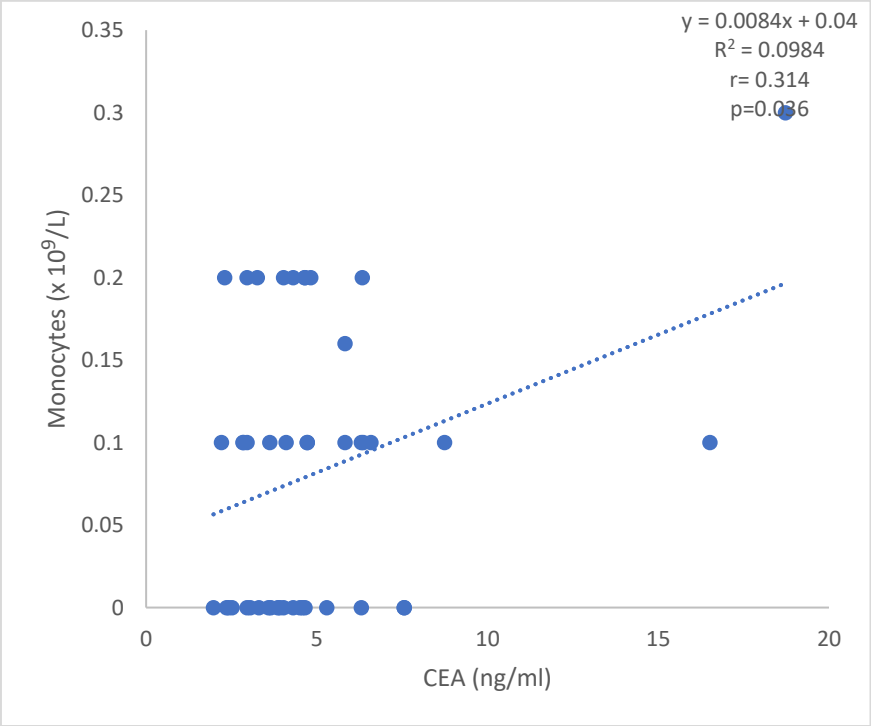

Figure 4: Correlation between monocyte count and CEA levels

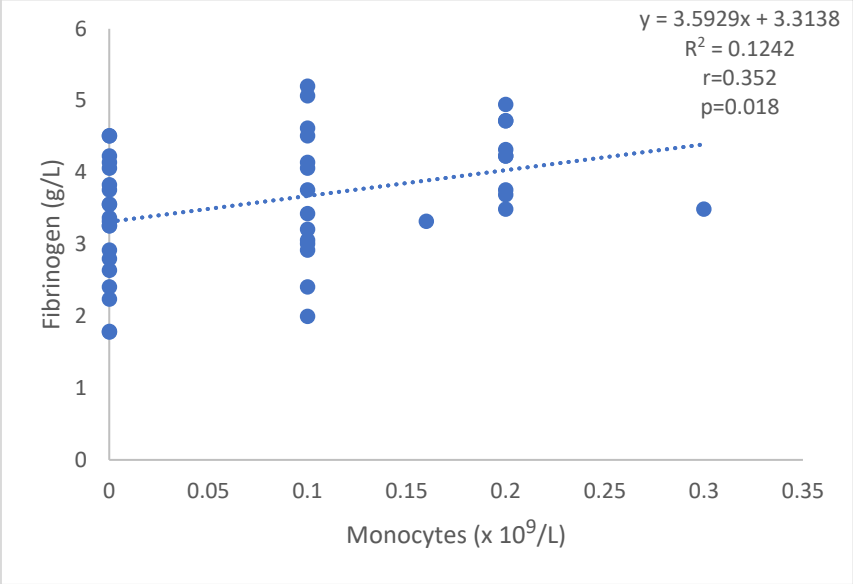

Figure 5: Correlation between monocyte count and fibrinogen levels

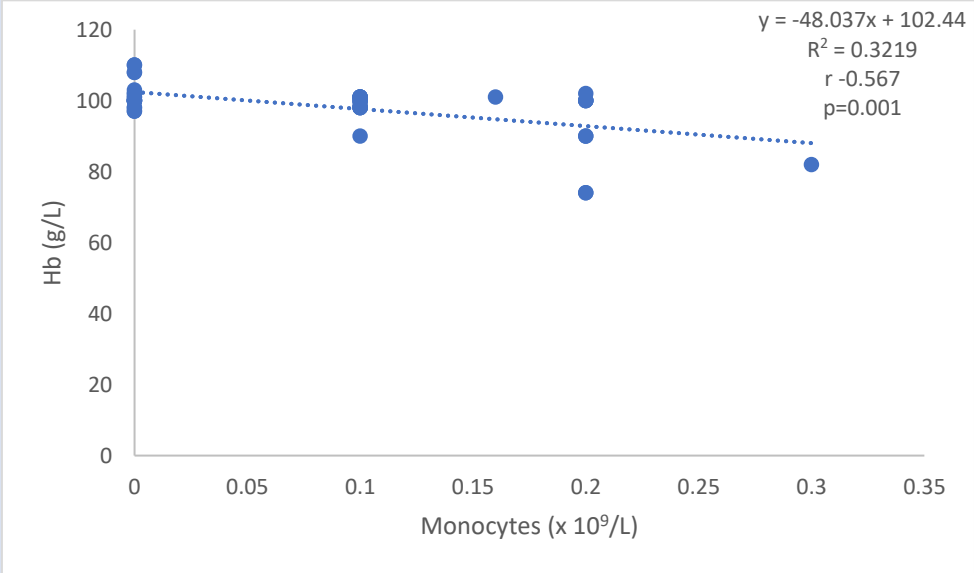

Figure 6: Correlation between hemoglobin concentration and monocyte count

Discussion

Breast cancer is the second most common type of cancer after lung cancer (10.4% of all cancer incidence, both sexes counted) and the fifth most common cause of cancer deaths (Kabel and Baali, 2015). Early detection of breast cancer both primary and recurrent, is of considerable clinical importance, and it can be used to make treatment decisions while tumor burden is low, and when patients are most likely to respond to adjuvant therapy (Shah, Rosso and Nathanson, 2014). The implications of this with regards to maternal health and the attendant impact on family well-being call for better understanding and management of breast cancer. This is particularly of importance in our financially-constrained setting with inadequate health infrastructure and paucity of data (Azubuike *et al.*, 2018). Routinely assessed haematological parameters provide an overview of health status particularly with regards to anaemia, systemic immunological response as well as haemostatic involvement. These parameters can predict severity, mortality, and follow-up treatment in cancer management (Guo *et al.*, 2019). The present study was designed to investigate changes in carcinoembryonic antigen levels and some haematological parameters of breast cancer patients on treatment in Calabar, South-South, Nigeria.

The breast cancer patients had their mean age as 47.47±11.70 with a range of 24.77- 70.17 years thus implying that breast cancer occurs both in the young, middle age and the old. The tumor sizes of 6cm, 7cm and 8cm (26.75, 20.0%, 17.8%) respectively occurred

most frequently. Invasive ductile carcinoma 71.1%, was the highest occurrence of histological sub type of breast cancer seen in the present study while the non-invasive ductile carcinoma was present in 28.9% of breast cancer patients studied. This is expected as it has been established that invasive ductal carcinoma is the most common type of breast cancer (Felson and Parker, 2023). Co-morbidity was present in 22.2% of the breast cancer patients which included ulcer, high blood pressure, HIV and asthma. This has implications in terms of poor survival as breast cancer patients have been reported to suffer poor quality of life and emotional health and increased risk of cardiovascular disease (Arneja and Brooks, 2021), whereas another study suggested that co-morbidities did not significantly increase risk of mortality (Nechuta *et al.,* 2013). Chemotherapy agent used for the breast cancer is 5-flurouracil; the protocol runs for 6 courses at intervals of 4 weeks per course. About 13.3% as at the time of study were yet to commence treatment but had their surgical tumors removed. Those on the 2nd ,6th and 3rd courses participated more 28.9%, 24.4% and 15.6%.

The packed cell volume and haemoglobin concentration were significantly lower for breast cancer patients. This finding is consistent with the report of Erhabor et al. (2018) who coordinated a study among breast cancer patients in Cross- River, South-South and Sokoto North Western Nigeria. The finding of anaemia, is noted among the basic challenges in the management of cancer patients and is perhaps due to possible different underlying mechanisms, such as bone marrow suppression leading to reduced erythropoietic activity, iron sequestration, blood loss from the anatomical site of surgical intervention and general lack of appetite associated with the ill- health (Ibrahim *et al*., 2016). The total white blood cell counts as well as absolute neutrophil count were significantly reduced (p=0.001) among the enrolled breast cancer subjects compared with the control group. The total white blood cell counts and its sub-populations are known to be cellular markers of inflammation; therefore, the lower values recorded have been associated with immunosuppression and drug interruption of normal haemopoiesis in cancer treatment (Steele, 2012). This finding is consistent with that of Erhabor et al. (2018). Carcinoembryonic antigen (CEA) is a glycoprotein that is normally produced during fetal development but is usually not present in significant amounts in the adult body. The carcinoembryonic antigen (CEA) test measures the level of CEA in the blood; an elevated level of CEA can be found in the blood of individuals with various types of cancers, including breast cancer. However, it is important to note that CEA is not specific to breast cancer and can be elevated in other malignancies. In the present study, significantly higher levels of CEA were observed for breast cancer patients than for the control group with a ratio of almost 2 times. The exact reasons for increased CEA levels in breast cancer patients are not fully understood, but several factors may contribute to this phenomenon and these include, tumor production, invasion and tissue destruction. In tumor production, cancer cells, including those in breast tumors, can produce CEA, thus resulting in elevated levels. On the other hand, invasive nature of cancer cells can lead to the destruction of normal tissue; as cancer cells invade surrounding tissues, they may release CEA into the bloodstream, contributing to the elevated level seen (Anoop *et al.,* 2022). The normal range for CEA is 0 to 2.5 nanograms per milliliter of blood (ng/mL). If CEA levels remain elevated during treatment, the treatment may not have been as successful as hoped. Our finding revealed good response to treatment (Figure 2); the CEA level reduced as the chemo-course progressed, achieving near normal levels by the 6th course thus implying that CEA can be used to monitor the therapeutic response in patients undergoing chemotherapy. Furthermore, it was noted that in the interpretation of CEA, values greater than 10 ng/mL suggests extensive disease, while levels greater than 20 ng/mL suggest that, the cancer may be spreading therefore continuous rising level of CEA in breast cancer may indicate that the cancer is either not responding to treatment, or there is recurrence after treatment (Anoop *et al.,* 2022).

The coagulation parameters studied revealed significantly raised fibrinogen levels in breast cancer. Fibrinogen is a protein in the blood that plays a crucial role in blood clotting. It is a positive acute phase reactant and therefore tends to elevate in the face of inflammation such as in a case of breast cancer. The reason for the raised level seen may be attributed to inflammation and tumor growth. Cancer is often associated with chronic inflammation, and breast cancer is no exception. As cancer cells grow and multiply, they can stimulate inflammatory responses in the body. Inflammation, in turn, can trigger the liver to produce more fibrinogen. This is part of the body's natural response to injury or disease. It has also

been reported that cancer cells can activate the blood coagulation system, leading to the formation of blood clots (Wu *et al.,* 2014). This phenomenon known as 'tumor-induced coagulation' or hypercoagulability, is common in cancer patients. Furthermore, fibrinogen is involved in the clotting process, and its production may increase as a result of the body's attempt to manage this state of hypercoagulability. A series of studies have also reported the prognostic and predictive value of coagulation factors especially the change in fibrinogen levels across different cancer types (Ilhan-Mutlu *et al.,* 2020) including breast cancer. In a large retrospective study of 2073 consecutive breast cancer patients, Wen and colleagues reported that an elevated preoperative plasma fibrinogen level was an independent prognostic factor for overall survival in breast cancer patients who underwent surgical treatment (Wen *et al.,* 2015). Again, a retrospective analysis including 520 consecutive breast cancer patients revealed an increased per-treatment plasma fibrinogen level with shorter disease-specific survival (Krenn-Pilko *et al.,* 2015). Monitoring fibrinogen levels in cancer patients should be often, part of the broader assessment of the overall breast cancer health care and response to treatment. Elevated fibrinogen levels may also have implications for the risk of thrombosis (formation of blood clots), which is a concern in cancer patients.

The findings of this study showed reduced thrombin time for breast cancer patients. Thrombin, a serine protease is a pivotal element of the coagulation cascade. It measures the time it takes for fibrinogen to be converted to fibrin by the enzyme thrombin, which is a key step in blood clot formation. Thrombin has been known to expresses pro-inflammatory properties as it binds protease-activated receptors (PARs) found on platelets, leukocytes and endothelial cells thereby regulating cellular activation of haemostasis in an inflammatory condition such as in breast cancer. Thrombin also suppresses clotting by its binding to thrombomodulin which leads to the loss of procoagulant properties (Akpan *et al.,* 2018) and explains the reduction in thrombin levels as well as the higher PT observed. Since thrombin clots fibrinogen, a reduction in thrombin levels will lead to accumulation of fibrinogen. Hence a significant negative correlation exists between thrombin clotting time and fibrinogen levels as shown in Figure 3. In the context of breast cancer patients, a reduced thrombin clotting time indicates a faster clotting process. Several factors may contribute to a shortened thrombin time and these factors include, hypercoagulability in which cancer is known to be associated with a state of hypercoagulability, meaning an increased tendency for blood to clot. Elevated prothrombin time as observed for breast cancer patients indicates a longer clotting time and can be associated with a deficiency in certain clotting factors due to liver dysfunction, malnutrition and loss of weight. Breast cancer and cancer treatments can lead to malnutrition and weight loss. Inadequate nutritional intake can affect the synthesis of clotting factors by the liver, potentially contributing to an elevated prothrombin time. Furthermore, in some cases, breast cancer patients may develop a condition known as disseminated intravascular coagulation (DIC) which is characterized by widespread activation of the clotting system, leading to the consumption of clotting factors. As a result, the prothrombin time may be prolonged due to the depletion of some clotting factors. Again, some cancer treatments, including certain chemotherapy drugs and radiation therapy, can affect the production and function of clotting factors. Chemotherapy, in particular, may cause bone marrow suppression, affecting the synthesis of clotting factors and leading to an elevated prothrombin time.

Breast cancer, like many other types of cancer, can trigger changes in the blood coagulation system. Breast cancer cells can promote a prothrombotic (clot-promoting) environment. Tumor cells may release factors that activate the coagulation cascade, leading to increased thrombin generation and faster clot formation. Furthermore, inflammation is a common feature of cancer, and can influence the coagulation system by enhancing the production of clotting factors and contribute to a shortened thrombin clotting time seen in breast cancer patients. Some cancer treatments, including certain chemotherapy drugs, may affect the coagulation system either by enhancing or impairing the blood clotting process. It is therefore advocated that monitoring clotting parameters, including thrombin clotting time, should be crucial in cancer patients to assess their risk of thrombosis and guide for appropriate interventions (Mirshahi *et al.,* 2015). No significant change was observed between the activated partial thromboplastin time levels of the breast cancer patients and the control group.

D-dimer is a biomarker that indicates the presence of blood clot formation and breakdown in the body. Elevated D-dimer levels as observed for breast cancer

patients are often associated with conditions that involve increased blood coagulation and fibrinolysis (the process of breaking down blood clot) (Bleker *et al.,* 2016). It is a degradation product of fibrin, which is produced when cross-linked fibrin is degraded by plasmin-induced fibrinolytic activity. Several factors may contribute to increased D-dimer levels. Breast cancer cells can activate the coagulation system, leading to the formation of blood clots. At the same time, these clots may be broken down through fibrinolysis. The ongoing cycle of coagulation and fibrinolysis results in the release of D-dimer into the blood stream. On the other hand, breast cancer is often associated with chronic inflammation. Inflammatory processes can contribute to a hypercoagulable state, promoting the formation of blood clots. As these clots break down, D-dimer is released, causing an increase in its level. Advanced stages of breast cancer, especially if the cancer has metastasized to other organs, can lead to an increased risk of thrombosis (Bremnes *et al.,* 2011). The presence of cancer cells in distant organs can trigger systemic changes in the coagulation and fibrinolytic pathways, resulting in elevated D-dimer level. Furthermore, breast cancer patients are at an increased risk of developing venous thromboembolism (VTE), which includes conditions like deep vein thrombosis (DVT) and pulmonary embolism (PE). The presence of these thromboembolic events can result in elevated D-dimer level. Monitoring of D-dimer levels in breast cancer patients can be important for assessing the risk of thromboembolic events and guiding appropriate interventions. However, it is essential to recognize that elevated D-dimer levels are not specific to breast cancer and can be seen in various other conditions, including infections, trauma, surgery, and inflammatory disorders (Bremnes *et al.,* 2011; Bleker *et al.,* 2016).

Findings from the current study revealed no significant change in the studied parameters based on the histology sub types (invasive ductile carcinoma and non- invasive ductile carcinoma). Similarly, the breast cancer patients were grouped based on the presence or absence of comorbidity and all the parameters studied showed no significant differences except for the carcinoembryonic antigen that revealed significantly higher levels for those with presence of comorbidity when compared with those without any other complications. This could be attributed to the impact of the co-infection. However, the most co-infections encountered were ulcer, high blood pressure, HIV and asthma (figure 5). The impact of the chemotherapy course on the studied parameters was also assessed (figure 6). A significant drastic reduction in the CEA level was observed from the naive state to the 1st course, then followed a steady reduction in the levels of CEA as the chemo course progressed. The decline in CEA levels as treatment progressed is thus suggestive of effective therapy in the management of the studied population and also a good marker for monitoring breast cancer treatment.

Analysis of correlations between thrombin versus fibrinogen and haemoglobin versus absolute monocyte count showed strong negative associations (r= -0.732, P=0.001 and r= -0.567, P=0.001). The finding is understandably so because thrombin is a substrate for fibrinogen formation thus lower thrombin time will result in higher fibrinogen concentration level. Monocyte play a role in the inflammatory response, in the tumor micro environment, interaction with cancer cells results in the release of inflammatory mediators and cytokines. These inflammatory signals tend to influence hematopoiesis, potentially impacting on the production of red blood cells and haemoglobin (Richards *et al.,* 2013). On the other hand, moderate, positive correlations were observed between monocyte count and CEA (r=0.314, P=0.036) and monocyte count with fibrinogen (r=0.352, P=0.018) respectively. The relationship between carcinoembryonic antigen (CEA) and monocyte count in breast cancer patients is complex and multifaceted. Monocyte, a type of white blood cell are known to be involved in the immune response. Breast cancer, like many cancers, is associated with chronic inflammation. In the tumor microenvironment, the interaction between cancer cells and immune cells, including monocytes, can influence the production and release of various proteins including the CEA (Klaile *et al.,* 2013). Again, monocytes can differentiate into macrophages, and in the context of cancer, are often referred to as tumor-associated macrophages (TAMs). These TAMs can be found within the tumor microenvironment where they play a role in promoting or inhibiting tumor growth. The presence of TAMs and their interaction with cancer cells can contribute to the release of CEA and other biomolecules. The interplay between cancer cells and immune cells involves the release of various signaling molecules, including cytokines. Cytokines produced by monocyte and other immune cells can influence

the expression of CEA by cancer cells (Grunnet and Sorensen, 2012). These same mechanisms have been reported for fibrinogen including others such as angiogenesis (formation of new blood vessels) and invasion into surrounding tissues which stimulate the release of factors that affect both the immune response and the coagulation system, potentially leading to changes in fibrinogen levels. Furthermore, in the setting of cancer, including breast cancer, there are alterations in the coagulation and fibrinolysis pathways which may contribute to the release of factors that influence the clotting process. These mechanisms are the rationale behind the positive correlations between monocyte count and CEA and fibrinogen levels (Grunnet and Sorensen, 2012; Klaile *et al.*, 2013).

Conclusion

Based on the findings of this study, it can be concluded that, the PCV, Hb concentration, TWBC, absolute neutrophil counts and thrombin time were significantly lower while CEA, fibrinogen levels, D-dimer, and prothrombin time were significantly higher for breast cancer patients when compared with the control. The CEA levels improved with progressive chemotherapy courses hence it is a useful marker for diagnosis and monitoring of treatment for breast cancer. The monocyte count correlated positively with fibrinogen and CEA levels and this implies that there is increased mobilization of monocyte in response to breast cancer. Monocyte count may be useful as a diagnostic and prognostic aid in breast cancer.

Declarations

Acknowledgments

We acknowledge all the authors of this work for their contributions.

Conflicts of Interest

All authors declare that they have no conflict of interest associated with this research work.

Funding

No special funding was received for this research work.

References

1. Akpan PA, Akpotuzzor JO & Osim E.E. (2018). Haemostatic indicies as markers for monitoring pulmonary tuberculosis trearment. Nigerian Journal of Physiological Science. 33:031-035.
2. Akpotuzor JO, Akwiwu EC, Okpokam DC, Keunmoe P. (2011). Analyses of haematological malignancies records from University of Calabar Teaching Hospital Calabar, Nigeria (1983-2008). International Journal of Natural and Applied Sciences. 7(1): 133-136.
3. Anoop TM, Joseph P R, Soman S, Chacko S, Mathew M. (2022). Significance of serum carcinoembryonic antigen in metastatic breast cancer patients: A prospective study. World Journal of Clinical Oncology, 13(6):529-539.
4. Arneja J and Brooks JD. (2021). The impact of chronic morbidities at the time of breast cancer diagnosis on quality of life and emotional health. Plos one. 16(8):256536.
5. Azubuike SA, Muirhead C, Hayes L, McNally L. (2018). Rising global burden of breast cancer: the case of sub-Saharan Africa (with emphasis on Nigeria) and implications for regional development: a review. World Journal of Surgical Oncology, 16:63.
6. Bellanger M, Zeinomar N, Tehranifar P, Terry M. (2018). Are global breast cancer incidence and mortality patterns related to country-specific economic development and prevention strategies?. Journal of Global Oncology, 4:1-16.
7. Bleker S.M, van Es N, Kleinjan A, Büller HR, Kamphuisen PW, Aggarwal A, Beyer Westendorf J, Camporese G, Cosmi B, Gary T, Ghirarduzzi A, Kaasjager K, Lerede T, Marschang P, Meijer K, Otten H-M, Porreca E, Righini M, Verhamme P, Van Wissen S. (2016). Current management strategies and long-term clinical outcomes of upper extremity venous thrombosis. Journal of Thrombosis and Haemostasis, 14(5):973-981.
8. Di Gioia D, Stieber P, Schmidt GP, Nagel D, Heinemann V, Baur-Melnyk A. (2015). Early detection of metastatic disease in asymptomatic breast cancer patients with whole-body imaging and defined tumour marker increase. Breast Journal Cancer, 112:809-818.
9. Erhabor O, Mbata EC, Retsky M, Erhabor T. and Adias T.C. (2018). Some full blood count parameters among women of African descent with breast cancer in Sokoto, North Western Nigeria. Journal of Pregnancy and Reproduction, 2(1):1-6.

10. Grunnet M, Sorensen J.B. (2012). Carcinoembryonic antigen (CEA) as tumor marker in lung cancer. Lung Cancer, 76(2):138-143.
11. Guo W, Lu X, Liu Q, Zhang T, Li P, Qiao W, Deng M. (2019). Prognostic value of neutrophil-to-lymphocyte ratio and platelet-to- lymphocyte ratio for breast cancer patients: An updated meta-analysis of 17079 individuals. Cancer Medicine, 8(9):4135-4148.
12. Hanahan D, Weinberg RA. (2011) Hallmarks of cancer: the next generation. Cell, 15:646-674.
13. Ibrahim U.A, Yusuf A.A, Ahmed S.G. (2016). The Pathophysiologic Basis of Anaemia in Patients with Malignant Diseases. Gulf Journal of Oncology, 1(22):80-89.
14. Ife AV, Abah MA, Moranyo AE, et al. (2024). Effect of Cucumis callosus fruit extract on the liver function of DMBA-induced mammary cancer in female albino wistar rats. Int J Complement Alt Med. 17(6):255-261.
15. Ilhan-Mutlu A, Starlinger P, Perkmann T, Schoppmann SF, Preusser M, Birner P. (2015). Plasma fibrinogen and blood platelet counts are associated with response to neoadjuvant therapy in esophageal cancer. Biomark Medical, 9(4):327-335.
16. Inder Lal, Kim Dittus, Chris E Holmes. (2013). Platelets, coagulation and fibrinolysis in breast cancer progression. Breast Cancer Research, 15(4):207.
17. Kabel AM, Baali FH. (2015). Breast cancer: insights into risk factors, pathogenesis, diagnosis and management. Journal of Cancer Research and Treatment, 3:28-33.
18. Krenn-Pilko S, Langsenlehner U, Thurner E-M, Stojakovic T, Pichler M, Gerger A, Kapp KS, Langsenlehner T. (2014). The elevated preoperative platelet-to-lymphocyte ratio predicts poor prognosis in breast cancer patients. British Journal of Cancer, 110:2524-2530.
19. Li J, Liu L, Feng Z, Wang X, Huang Y, Dai H, Zhang L, Song F, Wang D, Zhang P, Ma B, Li H, Zheng H, Chen K. (2020) Tumor markers CA15-3, CA125, CEA and breast cancer survival by molecular subtype: a cohort study. Breast Cancer journal, 27:621-630.
20. Maccio G, Goussot V, Berriolo-Riedinger A, Riedinger JM. (2017) Clinical value of CEA for detection of distant metastases in newly diagnosed breast cancer: comparison with CA 15-3. Annals of Biology for Clinicians (Paris), 75:431-441.
21. Mirshahi S, Pritchard LL, Pocard M, Mirshahi M and Soria J. (2015). Pathogenesis and Diagnosis of Venous Hypercoagulable States in Cancer. Journal of Hematology & Thromboembolic Diseases, 3:16-19.
22. Richards DM, Hettinger J, Feuerer M. (2013). Monocytes and macrophages in cancer: development and functions. Cancer Microenvironment, 6(2):179-191.
23. Shah R, Rosso K, Nathanson SD. (2014). Pathogenesis, prevention, diagnosis and treatment of breast cancer. World Journal of Clinical Oncology, 5(3):283-298.
24. Wen J, Yang Y, Ye F, Huang X, Li S, Wang Q, Xie X. (2015). The preoperative plasma fibrinogen level is an independent prognostic factor for overall survival of breast cancer patients who underwent surgical treatment. Breast, 24(6):745-750.
25. World Health Organization (2022). Fact sheets on cancer.
26. Wu S.G, He Z.Y, Zhou Z.Y. (2014). Serum levels of CEA and CA15-3 in different molecular subtypes and prognostic value in Chinese breast cancer. Journal of Breast Cancer, 23(1):88-93.

Cite this article: Besong E Obi, Akpotuzor D. Uchendu, Shella O. Besong, Anthony N. Kokelu, Moses A. Abah, et al. (2025). Carcinoembryonic Antigen Levels and Some Coagulation Parameters of Breast Cancer Patients Attending University of Calabar Teaching Hospital. *Journal of Cancer Management and Research*, BioRes Scientia publishers. 3(1):1-15. DOI: 10.59657/2996-4563.brs.25.019

Article History: **Received:** February 15, 2025 | **Accepted:** March 05, 2025 | **Published:** March 14, 2025