Short Research Article

Full Blood Count and Cancer Antigen 15.3 Levels of Breast Cancer Subjects in Umuahia, Abia State, Nigeria.

ABSTRACT

Full blood count which is measurable indices of blood gives the total number and morphology of all the cellular component of the blood and is an important tool in disease diagnosis and monitoring of treatment. Cancer antigen 15.3 (CA 15.3) levels are mostly recommended for patients with metastatic breast cancer that are undergoing treatment therapy to monitor their tumor and check if the tumor is responding to the treatment therapy. It could also be used to survey disease recurrence after treatment of metastatic breast cancer.

Aim: The aim of this study is to evaluate full blood count and cancer antigen 15.3 levels of breast cancer subjects in Umuahia, Abia State, Nigeria.

Study Design: A case-control study design was used in this study.

Place and Duration of study: Study was carried between May 2023 to October 2023 at the surgery department of federal medical center umuahia, Abia state,

Materials and Methods: A total of 120 subjects aged between 14 to 75 years were enrolled in this study. Of this 120 subjects, 60 were clinically diagnosed breast cancer patients while 60 were apparently healthy subjects. The breast cancer (BRCA) subjects were classified into stage I to IV of which 5 subjects (8.33%) were in Stage I, 14 subjects (23.33%) were in Stage II, 23 subjects (38.33%) were in Stage III and 18 subjects (30%) were in Stage IV. The haematological parameters were carried out using the five-part Mindray BC-5180 Haematology autoanalyzer manufactured by the Chinese Mindray company. The determination of the CA15.3 levels was done using enzyme linked immunosorbent assay (ELISA) technique. Data were analyzed using Graph Pad Prism version 8.2 and descriptive statistics was used for mean and standard deviation while Inferential statistics was used for students t-test, ANOVA and correlation. Statistical significance was set at 95% confidence interval ($p \leq 0.05$).

Results: There was statistically significant increase in WBC (9.3 ± 4.5 $x10^9$/L versus 6.8 ± 1.7$x10^9$ /L) (p=0.0001), monocyte (7.4 ± 1.8 % versus 3.3 ± 1.1 %) (<0.0001) and mean platelet volume (9.0 ± 1.2 fl versus 8.1 ± 0.7 fl) (<0.0001) in breast cancer patients when compared with control subjects. There was however statistically significant decrease in eosinophils (1.5 ± 1.6% versus 2.1 ± 1.9%)(p=0.0413), basophils (0.1 ± 0.2 versus 0.5 ± 0.4)(p=<0.0001), RBC (3.5 ± 0.7 $x10^{12}$/l versus 4.9 ± 0.6 $x10^{12}$/l)(p=<0.0001), PCV (27.2 ± 6.4 % versus 35.9 ± 3.0 %)(p= <0.0001), PDW (13.5 ± 0.8 versus 17.0 ± 1.7)(p=<0.0001), HB (8.8 ± 2.1g/dl versus 11.9 ± 1.1g/dl)(p=<0.0001), MPV (9.0 ± 1.2fl versus 8.1 ± 0.7 fl)(p=<0.0001) and LMR (4.4 ± 2.5 versus 7.7 ± 6.1)(p= 0.0002) in breast cancer patients when compared with control subjects . Other haematological parameters like neutrophils, lymphocytes, MCV, MCH, MCHC and platelets did not show any statistical significant difference. There was statistically significant increase in cancer antigen 15.3 levelsin breast cancer patients when compared with control subjects (23.2 ± 8.0 U/ml versus 9.3 ± 5.4 U/ml) (p=<0.0001).

Conclusion: This study has established that cancer antigen 15.3 levels, does not really show the severity of breast cancer in a subject. Although high levels of cancer antigen levels were seen in the diseased individuals, but one would expect that in patients with advanced stages, very high levels of CA15-3 will be observed, but it was not so, in this study. Also this study established that, chemotherapy sessions are important for quick recovery as it was seen in this study, the subjects were not consistent with their sessions, which led to poor prognosis for most of them.

1. INTRODUCTION

Cancer cells share similar DNA and RNA to the cells of the organism in which they originate, which is why they might not be recognized by the immune system as foreign, especially if the immune system is weakened (Mieszkowski, 2004).DNA mutations from which could be from radiations, tissue inflammations caused by viruses, bacteria and fungi; produce mutations that cause cancer (Mieszkowski, 2004). People of advanced age are also at high risk of breast cancer (Ershler, 2005). It is called breast cancer because of the organ from which it originated (Khuwaja and Abu-Rezq, 2004). Cancer could also be referred to as an “Entropic Disease” because the cells keep dividing, refusing to die off (Miezkowski, 2004).

Worldwide, breast cancer is the second most common cancer and it is also very common among women (Ferley *et al.,* 2015). In the United States 1 in 8 women have a life time risk of this disease (DeSantis *et al.,* 2017). The incidence rate of breast cancer is higher in developed countries and it varies with race and ethnicity (DeSantis *et al.,* 2013). It varies from 27 per 100,000 in Middle Africa and East Asia to 92 per 100,000 in Northern America (Ferley *et al*., 2013).

The fact that breast cancer presents at late stages usually with unfavorable prognosis in most developing countries especially Nigeria (Gukas*et al*, 2005; Gakwaya*et al.,* 2008), is due to lack of awareness of the disease and risk factors and also the fact that screening methods are unavailable (Adebamowo*et al*., 2008).

Methods :

2.0 STUDY DESIGN

A case-control study design was used in this study. Samples were gotten from patients actively suffering from breast cancer and the control samples were gotten from apparently healthy subjects.

2.1 STUDY AREA

This study was carried out in Federal Medical Center Umuahia. Umuahia being the capital city of Abia state and one of the thirty-six states of Nigeria. It is located between latitude 4˚49.30'N - 6˚02'N and between long 7˚08'E - 8° 04'E in the southeastern part of Nigeria (Igbokwe and Nwankwo, 2011). Abia state has a population of about 3.7 million inhabitants and it is predominantly inhabited by Igbos. It is a state located in the southeastern geopolitical zone of Nigeria, bordered to the Northeast by Enugu and Ebonyi, Northwest by Anambara state, West by Imo state, South East by AkwaIbom, South by Rivers State and East by Cross River.

2.2 SAMPLE COLLECTION

5ml of blood samples was collected using a standard venipuncture technique aseptically and 3mls was dispensed into an ethylene diamine tetracetic acid (EDTA) bottle while the other 2mls was put in a plain bottle so that the serum will be extracted. The serum for the Cancer Antigen levels were separated the same day the sample was collected and frozen till when they were analyzed. The cancer antigen levels were done in batches, making sure that no sample stayed up to 1 week in storage. While the full blood count levels were done the same day the samples were collected.

2.3 SAMPLE ANALYSIS

The haematological parameters were carried out using five-part Mindray BC-5180 haematology analyzer manufactured by the Chinese Mindray company. And the principle of the test is based on the Coulter principle which developed by Wallace H. Coulter in the late 1940s states that particles pulled through an orifice, concurrent with an electric current, produce a change in impedance proportional to the volume of the particle traversing the orifice. The pulse in impedance originates from the displacement of electrolyte caused by the particle. But a five parthaematology analyzer uses both Coulter's principle and flow cytometry to carry out its function.

The determination of the CA15.3 levels was done with an Enzyme linked immunosorbent assay (ELISA) machine. ELISA machine works on the principle that specific antibodies bind the target antigen and detect the presence and quantity of antigens binding. The plates/wells used for the testing are coated with antibodies with high affinity, specific to the antigen to be tested. This assay makes use of ELISA procedure and it provides useful

measurements of antigen-antibody concentration. The determination of the CA15.3 levels was done with an Enzyme linked immunosorbent assay (ELISA) using Cancer Antigen 15-3 kit, Lot number EIA-56K712, Expiry date 2024-09-27.

2.4 STATISTICAL ANALYSIS

Data were analyzed using Graph Pad Prism version 8.2 and descriptive statistics was used for mean and standard deviation while Inferential statistics was used for students t-test, ANOVA and correlation. Statistical significance was set at 95% confidence interval ($p \leq 0.05$).

3.0 RESULTS

There was statistically significant increase in WBC (9.3 ± 4.5 $x10^9$/L versus 6.8 ± 1.7$x10^9$ /L) (*P*=.0001), monocyte (7.4 ± 1.8 % versus 3.3 ± 1.1 %) (<0.0001), mean platelet volume (9.0 ± 1.2 fl versus 8.1 ± 0.7 fl) (<0.0001) and Cancer antigen 15-3 levels (23.2 ± 8.0) versus (9.3 ± 5.4) (<0.0001) in breast cancer patients when compared with control subjects. There was however statistically significant decrease in eosinophils (1.5 ± 1.6% versus 2.1 ± 1.9%)(*P*=.0413), basophils (0.1 ± 0.2 versus 0.5 ± 0.4)(*P*<0.0001), RBC (3.5 ± 0.7 $x10^{12}$/l versus 4.9 ± 0.6 $x10^{12}$/l)(p=<0.0001), PCV (27.2 ± 6.4 % versus 35.9 ± 3.0 %)(*P*= <.0001), PDW (13.5 ± 0.8 versus 17.0 ± 1.7)(*P*=<0.0001), HB (8.8 ± 2.1g/dl versus 11.9 ± 1.1g/dl)(*P*=<.0001), and LMR (4.4 ± 2.5 versus 7.7 ± 6.1)(*P*= 0.0002) in breast cancer patients when compared with control subjects . Other haematological parameters like neutrophils, lymphocytes, MCV, MCH, MCHC and platelets did not show any statistical significant difference as shown in Table 2.

There was statistically significant linear increase in neutrophils from stage I to stage IV(46.4 ± 5.6% to 54.0 ± 13.0 % to 59.5 ± 9.5% to 68.3 ± 10.3%)(f=8.075)(*P*=.0001); the reverse was observed in lymphocytes, there was statistically significant linear decrease from (47.6 ± 6.1% to 35.2 ± 13.0% to 30.6 ± 9.7 to 22.4 ± 9.6 %)(f=9.168)(*P*=<.0001). Statistically significant linear increase was observed in monocytes at stage I, II, III (4.9 ± 0.9% to 7.3 ± 1.2 to 7.9% to 7.9 ± 1.3%), and then a sudden slight decrease observed at stage IV (7.5 ± 2.3%)(f=4.416)(*P*=.0074) of breast cancer. Statistically significant linear decrease in stages I, II and III was observed in RBC counts (4.7 ± 0.2$x10^{12}$/l to 3.5 ± 0.5$x10^{12}$/l to 3.2 ± 0.7$x10^{12}$/l)(f=6.546)(*P*=.0007), haemoglobin concentration (11.6 ± 1.0 % to 8.8 ± 1.6 % to 8.1 ± 2.1 %)(f=4.670)(p=0.0056) and PCV (36.2 ± 3.1% to 26.7 ± 4.9% to 24.9 ± 6.4%)(f=5.533)(0.0021) however, at stage IV – the RBC count (3.6 ± 0.7$x10^{12}$/l)(f=6.546)(*P*=.0007), haemoglobin concentration (9.1 ± 1.9 %)(f=4.670)(*P*=.0056) and PCV (28.1 ± 5.9 %)(f=5.533)(0.0021) became slightly higher than observed in stage I, II and III of breast cancer. Mean platelet volume from a value of (10.0 ± 2.5 fl)(f=7.161)(*P*=.0004) in stage I, recorded a decrease at stage II (7.8 ± 0.8 fl)(f=7.161)(*P*=.0004), followed by steady statistically significant increase at stage III (9.3 ± 1.0 fl)(f=7.161)(*P*=.0004) and IV (9.4 ± 1.2 fl)(f=7.161)(*P*=.0004). Lymphocyte to monocyte ratio recorded a steady statistically significant decrease in values from stage I of breast cancer to stage IV (10.0 ± 2.5 to 4.9 ± 2.0 to 3.7 ± 1.7 to 3.3 ± 1.6)(f=18.15)(*P*=.0001). Other parameters like WBC, eosinophils, basophils, MCV, MCHC, MCH, Platelets and Cancer Antigen 15.3 recorded no statistical significance details are shown in Table 3.

As shown in Table 3, cancer antigen levels do not give an exact picture of the severity of breast cancer in a subject because at stage IV CA 15.3 levels were (25.5 ± 9.1) when compared to stage I where the levels were (20.4 ± 11.6) and stage II where the levels were (23.9 ± 6.5) and then stage III experienced lower levels at (21.7 ± 7.0). one would expect that at more advanced stages of the disease, really high levels of cancer antigen 15.3 will be experienced. And from this study, the values were insignificant at 0.3993.

There was statistically a linear significant increase in neutrophils (54.1± 9.2% to 54.7± 14.1% to 61.6 ± 11.6% to 66.4 ± 10.2%)(f=4.409)(0.0075) from the 6th chemotherapy session. Lymphocyte indicated statistically significant decrease (35.8 ± 10.4% to 35.9 ± 14.1% to 29.6 ± 10.5 % to 23.6 ± 9.5%)(f=4.343)(*P*=.0080) in patients receiving chemotherapy above eight sessions. Mean cell haemoglobin concentration of cancer patients indicated statistically significant decrease (32.4 ± 0.6g/dl to 33.3± 0.8g/dl to 32.8 ± 1.0g/dl to 32.2 ± 1.3g/dl)(f=3.133)(*P*=.0326) only after more than eight sessions of chemotherapy. Mean platelet volume showed linear statistically significant increase (8.1 ± 1.2fl to 8.9 ± 1.1fl to 9.1 ± 1.0fl to 9.5 ± 1.0fl(f=4.295)(*P*=.0085) that peaked from the ninth session of chemotherapy. Lymphocyte to monocyte ratio indicated statistically declining values (5.5 ± 2.3 to 5.7 ± 3.6 to 3.5 ± 1.5 to 3.2 ± 1.4)(f=4.514)(p=0.0066), while CA-15.3 showed fluctuating values with sharp significant decrease (25.0 ± 7.5U/ml to 18.7 ± 6.1U/ml to 21.8 ± 8.1U/ml to 26.2 ± 8.4U/ml)(2.914)(.0422) at the third to fifth session of chemotherapy. Other parameters like WBC, eosinophils, monocytes, basophils, RBC, HB, PCV, MCH, MCV, platelets and PDW indicated no statistically significant difference. As shown in table 4.

Table 1: Demographic Characteristics of Study participants

Parameter	Frequency	Percentage (%)
Total No.	120	100.00
BRCA Subjects	60	50
Control Subjects	60	50
Age Range(BRCA subjects in years)		
14-23	4	6.67
24-33	10	16.67
34-43	26	43.33
44-53	12	20
54-63	4	6.67
64-73	2	3.33
74-83	2	3.33
STAGE (BRCA)		
I	5	8.33
II	14	23.33
III	23	38.33
IV	18	30

Key: BRCA- Breast Cancer

Table 2: Comparison of Mean($\bar{x}$) ± Standard Deviation of Full Blood Count levels and Cancer Antigen 15.3 in Breast Cancer Subjects and Control Subjects

Parameters (Units)	BRCA ($\bar{x}$ ± SD)	Control ($\bar{x}$ ± SD)	p-value	Remark
	N = 60	N = 60		
WBC (x10^9/l)	9.3 ± 4.5	6.8 ± 1.7	0.0001	S
Neutrophils (%)	59.7 ± 12.2	63.3 ± 8.1	0.0613	NS
Lymphocytes (%)	30.6 ± 12.3	31.5 ± 7.7	0.6364	NS
Eosinophils (%)	1.5 ± 1.6	2.1 ± 1.9	0.0413	S
Monocytes (%)	7.4 ± 1.8	3.3 ± 1.1	<0.0001	S
Basophils (%)	0.1 ± 0.2	0.5 ± 0.4	<0.0001	S
RBC (x10^{12}/l)	3.5 ± 0.7	4.9 ± 0.6	<0.0001	S
HB (g/dl)	8.8 ± 2.1	11.9 ± 1.1	<0.0001	S
PCV (%)	27.2 ± 6.4	35.9 ± 3.0	<0.0001	S
MCV (fl)	75.9 ± 6.9	73.4 ± 9.0	0.0907	NS
MCH (pg)	25.0 ± 2.5	24.7 ± 3.6	0.6230	NS
MCHC (g/dl)	32.6 ± 1.1	33.2 ± 2.0	0.0726	NS
Platelets (x10^9/l)	277.4 ± 65.8	290.0 ± 63.6	0.2932	NS
PDW (fl)	13.5 ± 0.8	17.0 ± 1.7	<0.0001	S
MPV (fl)	9.0 ± 1.2	8.1 ± 0.7	<0.0001	S
LMR	4.4 ± 2.5	7.7 ± 6.1	0.0002	S
CA 15.3 (U/ml)	23.2 ± 8.0	9.3 ± 5.4	<0.0001	S

Key: BRCA = Breast Cancer; $\bar{x}$ = Mean; SD = Standard Deviation; S = Significant; NS = Non-Significant; LMR = Lymphocyte to Monocyte Ratio; RBC = Red Blood Cell Count; HB = Haemoglobin Concentration; PCV = Packed Cell Volume; MCV = Mean Cell Volume; MCH = Mean Cell Haemoglobin; MCHC = Mean Cell Haemoglobin Concentration; PDW = Platelet Distribution Width; MPV = Mean Platelet Volume; CA 15.3 = Cancer Antigen 15.3.

Table 3: Comparison of Mean($\bar{x}$) ± Standard Deviation of Haematological Parameters and Cancer Antigen 15.3 in Breast Cancer Subjects based on Stages of the Disease

Parameters (Units)	Stage I (a); n = 5 $\bar{x}$ ± SD	Stage II (b); n = 14 $\bar{x}$ ± SD	Stage III (c); n = 23 $\bar{x}$ ± SD	Stage IV (d); n = 18 $\bar{x}$ ± SD	F-value	p-value	TMC
WBC ($x10^9$/l)	6.7 ± 2.8	8.1 ± 4.1	8.6 ± 3.6	11.6 ± 5.4	2.757	0.0508^{NS}	
Neutrophils (%)	46.4 ± 5.6	54.0 ± 13.0	59.5 ± 9.5	68.3 ± 10.3	8.075	0.0001^{S}	a-d $^{0.0007}$
							b-d $^{0.0018}$
							c-d $^{0.0469}$
Lymphocytes (%)	47.6 ± 6.1	35.2 ± 13.0	30.6 ± 9.7	22.4 ± 9.6	9.168	$<0.0001^{S}$	a-c $^{0.0085}$
							a-d $^{<0.0001}$
							b-d $^{0.0052}$
Eosinophils (%)	0.11 ± 0.11	0.14 ± 0.13	0.13 ± 0.19	0.20 ± 0.19	0.625	0.6015^{NS}	
Monocytes (%)	4.9 ± 0.9	7.3 ± 1.2	7.9 ± 1.3	7.5 ± 2.3	4.416	0.0074^{S}	a-b $^{0.0406}$
							a-c $^{0.0035}$
							a-d $^{0.0161}$
Basophils (%)	0.02 ± 0.04	0.19 ± 0.13	0.17 ± 041	0.06 ± 0.09	1.163	0.3320^{NS}	
RBC ($x10^{12}$/l)	4.7 ± 0.2	3.5 ± 0.5	3.2 ± 0.7	3.6 ± 0.7	6.546	0.0007^{S}	a-b $^{0.0061}$
							a-c $^{0.0003}$
							a-d $^{0.0083}$
HB (g/dl)	11.6 ± 1.0	8.8 ± 1.6	8.1 ± 2.1	9.1 ± 1.9	4.670	0.0056^{S}	a-b $^{0.0341}$
							a-c $^{0.0029}$
PCV (%)	36.2 ± 3.1	26.7 ± 4.9	24.9 ± 6.4	28.1 ± 5.9	5.533	0.0021^{S}	a-b $^{0.0125}$
							a-c $^{0.0011}$
							a-d $^{0.0375}$

MCV (fl)	76.6 ± 6.1	75.1 ± 6.7	74.9 ± 7.1	77.6 ± 6.1	0.585	0.6270^{NS}	
MCH (pg)	26.3 ± 3.9	24.8 ± 2.3	24.7 ± 2.8	25.2 ± 1.9	0.589	0.6243^{NS}	
MCHC (g/dl)	32.6 ± 0.5	32.9 ± 0.7	32.7 ± 1.1	32.5 ± 1.4	0.389	0.7611^{NS}	
Platelets ($x10^9$/l)	318.4 ± 48	261.2 ± 79	286.4 ± 58	268.4 ± 64	1.212	0.3138^{NS}	
PDW (fl)	13.1 ± 1.2	13.1 ± 0.8	13.8 ± 0.8	13.5 ± 0.9	2.219	0.0959^{NS}	
MPV (fl)	8.9 ± 1.4	7.8 ± 0.8	9.3 ± 1.0	9.4 ± 1.2	7.161	0.0004^{S}	b-c $^{0.0009}$
LMR	10.0 ± 2.5	4.9 ± 2.0	3.7 ± 1.7	3.3 ± 1.6	18.15	$<0.0001^{S}$	b-d $^{0.0005}$ a-b $^{<0.0001}$ a-c $^{<0.0001}$ a-d $^{<0.0001}$
CA 15.3(U/ml)	20.4 ± 11.6	23.9 ± 6.5	21.7 ± 7.0	25.5 ± 9.1	1.001	0.3993^{NS}	

Key: BRCA = Breast Cancer; $\bar{x}$ = Mean; SD = Standard Deviation; S = Significant; NS = Non-Significant; LMR = Lymphocyte to Monocyte Ratio; RBC = Red Blood Cell Count; HB = Haemoglobin Concentration; PCV = Packed Cell Volume; MCV = Mean Cell Volume; MCH = Mean Cell Haemoglobin; MCHC = Mean Cell Haemoglobin Concentration; PDW = Platelet Distribution Width; MPV = Mean Platelet Volume; CA 15.3 = Cancer Antigen 15.3; TMC = Tukey Multiple Comparison Test.

Table 4: Comparison of Mean ($\bar{x}$) ± Standard Deviation (using ANOVA) of Haematological Parameters and Cancer Antigen 15.3 in Breast Cancer Subjects based on Chemotherapy Dose

Parameters (Units)	0-2 Doses (a); n = 14	3-5 Doses (b); n = 14	6-8 Doses (c); n = 13	>8 Doses (d); n = 19	F-value	p-value	TMC
	$\bar{x}$ ± SD	$\bar{x}$ ± SD	$\bar{x}$ ± SD	$\bar{x}$ ± SD			
WBC ($x10^9$/l)	6.7 ± 2.0	10.4 ± 4.6	9.1 ± 4.7	10.5 ± 5.1	2.371	0.0801^{NS}	
Neutrophils (%)	54.1 ± 9.2	54.7 ± 14.1	61.6 ± 11.6	66.4 ± 10.2	4.409	0.0075^{S}	a-d $^{0.0160}$ b-d $^{0.0238}$
Lymphocytes (%)	35.8 ± 10.4	35.9 ± 14.1	29.6 ± 10.5	23.6 ± 9.5	4.343	0.0080^{S}	a-d $^{0.0196}$

							b-d $^{0.0181}$
Eosinophils (%)	1.8 ± 1.7	1.2 ± 1.9	1.0 ± 0.8	1.8 ± 1.6	0.849	0.4727^{NS}	
Monocytes (%)	6.8 ± 1.4	7.1 ± 1.8	7.6 ± 1.8	7.9 ± 2.0	0.967	0.4147^{NS}	
Basophils (%)	0.2 ± 0.1	0.2 ± 0.5	0.1 ± 0.1	0.1 ± 0.1	1.361	0.2640^{NS}	
RBC (x10^{12}/l)	3.8 ± 0.8	3.4 ± 0.7	3.6 ± 0.6	3.3 ± 0.7	1.086	0.3625^{NS}	
HB (g/dl)	9.3 ± 2.1	8.8 ± 2.1	9.1 ± 1.7	8.4 ± 2.2	0.640	0.5925^{NS}	
PCV (%)	28.7 ± 6.7	26.8 ± 6.7	27.8 ± 5.0	26.0 ± 6.9	0.519	0.6707^{NS}	
MCV (fl)	75.1 ± 7.8	76.8 ± 6.0	75.3 ± 5.9	76.1 ± 7.9	0.158	0.9241^{NS}	
MCH (pg)	24.4 ± 2.5	25.9 ± 2.8	25.3 ± 2.1	24.6 ± 2.5	1.037	0.3831^{NS}	
MCHC (g/dl)	32.4 ± 0.6	33.3 ± 0.8	32.8 ± 1.0	32.2 ± 1.3	3.133	0.0326^{S}	b-d $^{0.0264}$
Platelets (x10^{9}/l)	298.6 ± 70	269.7 ± 73	264.1 ± 55	277.9 ± 63	0.722	0.5427^{NS}	
PDW (fl)	13.3 ± 0.9	13.2 ± 1.0	13.6 ± 0.9	13.7 ± 0.6	1.080	0.3651^{NS}	
MPV (fl)	8.1 ± 1.2	8.9 ± 1.1	9.1 ± 1.0	9.5 ± 1.0	4.295	0.0085^{S}	a-d $^{0.0040}$
LMR	5.5 ± 2.3	5.7 ± 3.6	3.5 ± 1.5	3.2 ± 1.4	4.514	0.0066^{S}	a-d $^{0.0392}$
							b-d $^{0.0223}$
CA 15.3(U/ml)	25.0 ± 7.5	18.7 ± 6.1	21.8 ± 8.1	26.2 ± 8.4	2.914	0.0422^{S}	b-d $^{0.0390}$

Key: BRCA = Breast Cancer; $\bar{x}$ = Mean; SD = Standard Deviation; S = Significant; NS = Non-Significant; LMR = Lymphocyte to Monocyte Ratio; RBC = Red Blood Cell Count; HB = Haemoglobin Concentration; PCV = Packed Cell Volume; MCV = Mean Cell Volume; MCH = Mean Cell Haemoglobin; MCHC = Mean Cell Haemoglobin Concentration; PDW = Platelet Distribution Width; MPV = Mean Platelet Volume; CA 15.3 = Cancer Antigen 15.3; TMC = Tukey Multiple Comparison Test.

4.0 DISCUSSION

This study was carried out to evaluate the haematological parameters and CA 15-3 antigen levels of breast cancer patients in Federal Medical Center Umuahia, Nigeria. Women suffer this disease mostly and it is the leading cause of cancer related deaths in the world. A total of 120 subjects were enrolled in this study. They were aged between 14 to 75 years, of these 120 subjects, 60 were clinically diagnosed breast cancer patients while 60 were apparently healthy subjects. The age range of BRCA subjects were between 14 to 83, the stage of BRCA were from stage I to IV, their age at menarche ranged between 9-17 years of age. When comparing the mean standard deviation of haematological parameters and CA 15.3 levels of breast cancer patients and control subjects, there was statistically significant increase in WBC, monocyte, mean platelet volume and CA-15.3 in

Breast Cancer Patients when compared to controls also, significant statistical decrease was observed in neutrophils, eosinophil, basophil, RBC, haemoglobin concentration, packed cell volume, platelet distribution width and lymphocyte to monocyte ratio of Breast Cancer Patients, when compared with control subjects without breast cancer this also agrees with a study conducted by Akinbami*et al.* (2013) due to the fact that during inflammatory responses, the cells involved in systemic inflammation tend to increase in number to respond to the inflammatory process which a study by Dimitrios *et al.* (2016) agreed with. Other parameters recorded no statistical significant difference. When comparing their haematological and CA 15.3 parameters based on the stage of their disease, there was a statistically significant linear increase in neutrophils from stage I to stage IV; the reverse was observed in lymphocytes, statistically significant linear decrease. There was a statistically significant linear increase was observed in monocytes at stage I, II, III, and then a sudden slight decrease observed at stage IV of breast cancer. A statistically significant linear decrease was observed in RBC counts, haemoglobin concentration and PCV at stage I, II, III, and IV, however, at stage IV, the RBC count, haemoglobin concentration and PCV became slightly higher than observed in stage II and III of breast cancer. Mean platelet volume recorded a decrease at stage II, followed by steady statistically significant increase at stage III and IV. As the stage of the disease goes up, the levels of neutrophils increase thereby indicating poor prognosis. Lymphocyte to monocyte ratio recorded a steady statistically significant decrease in values from stage I of breast cancer to stage IV. Low lymphocytes levels reflect poor disease responses due to the fact that the lymphocytes which should be involved in immunological responses are not doing so which could lead to low survival outcomes for patients which also agreed with a study by Yang *et al.* (2020). Other parameters recorded no statistical significant difference. There was a linear statistical significant increase in percentage neutrophils from the 6^{th} chemotherapy session. Percentage lymphocyte indicated statistically significant decrease in patients receiving chemotherapy above eight sessions. Mean cell haemoglobin concentration of cancer patients indicated statistically significant decrease only after more than eight sessions of chemotherapy. Mean platelet volume showed linear statistically significant increase that peaked from the ninth session of chemotherapy. Lymphocyte to monocyte ratio indicated statistically declining values, while CA-15.3 showed fluctuating values with sharp significant decrease at the third to fifth session of chemotherapy. High levels of neutrophils in breast cancer indicate poor prognosis due to the fact that neutrophils facilitate tumor proliferation by suppressing the immune system. CD8+ T lymphocyte which attacks tumor cells is suppressed by nitric oxide synthase released by neutrophils under stimulation by transforming growth factor beta. There was increase in neutrophils from the sixth chemotherapy session in patients in this study due to the fact that the patients here are either not responding to the chemotherapy regimen or are not consistent to their chemo sessions and also most of the patients in this study were in advanced stages of the disease and neutrophil counts tend to get higher in advanced stages. A study by Salako *et al.* (2021) did not agree with this because they observed neutropenia in their subjects following chemo doses. Other parameters indicated no statistically significant difference.

4.1 Conclusion

Increase in neutrophil levels in this study from stage I-IV indicate poor prognosis or a poor disease survival for the subjects in this study. Monocytes have the ability to sense the presence of tumor, so an increase in their levels from stage I-III in this study indicate poor prognosis for the subjects here. Decrease in Red blood cell levels from stage I-III could be probably because as subjects undergo chemotherapy, health cells are destroyed in the process. Stage I &II experienced decrease in Mean platelet volume while Stage III &IV experienced an increase in MPV because platelets count tends to increase during infections. Decrease in Lymphocyte Monocyte ratio indicate poor prognosis for the subjects in this study. Subjects in this study, showed significant increase in neutrophil levels from 6th chemotherapy session probably because more of the subjects in this study were in their advanced stages and most likely weren't consistent with their chemotherapy sessions. Lymphocyte levels too experienced declining levels from the 8th chemotherapy session due to the fact that the patients in this study were not responding to the treatment therapy. Mean cell Haemoglobin levels showed declining values due to the fact that during chemo, healthy cells are destroyed along side the diseased ones. Mean platelet volume showed high levels that peaked from the 9th session due to the fact that most subjects in this study were in their advanced stages. Lymphocyte monocyte levels, showed declining values due to the fact that subjects here might not have been taking their chemo sessions as at when due. But as from the 3rd to the 5th chemo session, Cancer Antigen 15-3 levels showed declining values, which is a good sign. This study has established that cancer antigen 15.3 levels, does not really show the severity of breast cancer in a subject. Although high levels of cancer antigen levels were seen in the diseased individuals, but one would expect that in patients with advanced stages, very high levels of CA15-3 will be observed, but it was not so, in this study. Also this study established that, chemo sessions are important for quick recovery as it was seen in this study, the subjects were not consistent with their sessions, which led to poor prognosis for most of them.

4.2 Recommendations

It is therefore recommended that:

1. Regular routine breast checks should be engaged in to enable the detection of breast cancer on time, to avoid detecting it at late stages.
2. Patients having breast cancer should take their chemotherapy sessions seriously to avoid poor prognosis of the disease.

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