Low Total White Blood Cell Count and High HDL- cholesterol in breast cancer patients undergoing chemotherapy at Cape Coast Teaching Hospital; A longitudinal single center study.

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8 Abstract

9 Background: People with primary invasive breast cancer receive both local (Surgery and radiation therapy) and systemic treatment (chemotherapy and hormonal therapy). However, there are substantial short- and long-term side effects from chemotherapy and several studies have been conducted to that effect which indicate that chemotherapy has adverse effects on organs and cell lines among breast cancer patients

- 14 Aim: To assess the effects of chemotherapy on clinical, haematological and biochemical profile
- 15 of breast cancer patients undergoing chemotherapy.
- 16 Method: A longitudinal study conducted in the female surgical ward of the Cape Coast Teaching
- 17 Hospital (CCTH). 51 patients diagnosed with breast cancer and scheduled to start chemotherapy
- 18 were recruited for the study using randomized sampling technique. Their clinical (blood pressure,
- 19 demographic (age, marital status, employment status) and anthropometric (body mass index)
- 20 data were recorded. Biochemistry (lipids, uric acid and creatinine) and hematological profile
- (hemoglobin, white blood cell and platelet) for day 1, day 21 and day 42 of their cycles weremonitored.
- 22 monitored.
- **Result:** Majority of the participants were within 46-60 years, married, overweight and had informal form of occupation. Throughout the cycles, systolic blood pressure significantly decreased till after the third cycle (p-value 0.026), diastolic blood pressure significantly decreased after second cycle but increased slightly after the third cycle (p=0.029). Hemoglobin though insignificant, decreased after second cycle but increased sharply after the third cycle (p=0.281). White blood cells (WBC) significantly decreased throughout cycles (p-value 0.008),
- High Density Lipoprotein (HDL) and Uric acid increased throughout cycles- p-values 0.014 and
 0.852 respectively and creatinine was maintained throughout cycles (p-value 1.000).
- Conclusion: Throughout cycles, chemotherapy had significant adverse effect on the clinical profile (systolic and diastolic blood pressure), White blood cells (WBC) and High-Density Lipoprotein (HDL) in patients undergoing treatment.
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Keywords: Chemotherapy, Advanced breast cancer, Invasive ductal carcinoma (No Special
 Type, NST), Invasive ductal carcinoma (Not Otherwise Specified, NOS).

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43 Introduction

Breast cancer is cancer that develops from breast tissue and like other cancers, occurs because of an interaction between an environmental (external) factor and a genetically susceptible host.⁽¹⁾ Signs of breast cancer may include a lump in the breast, a change in breast shape, dimpling of the skin, fluid coming from the nipple, or a red scaly patch of skin.⁽²⁾ Risk factors for developing breast cancer include: female sex, obesity, lack of physical exercise, drinking alcohol, hormone replacement therapy during menopause, ionizing radiation, early age at first menstruation, having children late or not at all, and older age.⁽³⁾

World Health Organization reports have shown that the incidence of breast cancer is second only to the incidence of cervical cancer and 1.4 million patients diagnosed annually with breast cancer worldwide.⁽⁴⁾ With regards to Ghana, Ghana has no population-based cancer registry however there were 1,469 breast cancer patients identified through medical records during 2009 to 2014 and also noted that it is expected to increase as Ghana's population ages and a Western lifestyle is adopted.⁽⁴⁾

57 People with primary invasive breast cancer receive both local (Surgery and radiation therapy) 58 and systemic treatment (chemotherapy and hormonal therapy). However, the National 59 Comprehensive Cancer Center Network, and other groups recommend adjuvant chemotherapy 60 for women with invasive breast tumors greater than 1 cm in diameter, irrespective of whether 61 axillary lymph nodes are involved.⁽⁵⁻⁷⁾

There are substantial short- and long-term side effects from chemotherapy and several studies have been conducted to that effect. Studies by (8-12) have covered short- and long-term side effects of chemotherapy on organs and cell lines among breast cancer patients. However, there is scanty data on the effects of chemotherapy on haematological and biochemical profile among breast cancer patients in our part of the world. Hence the reason for this study, to assess the effects of chemotherapy on clinical, haematological and biochemical profile of breast cancerpatients undergoing chemotherapy.

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70 Methodology

71 Study design/Study Site

72 This longitudinal single center study was conducted at the Female Surgical Ward and Laboratory

vunit of the Cape Coast Teaching Hospital from April 2016 to February 2017. The hospital serves

as the main referral facility for the Central region and the South western parts of the country.

75 Study Population/Inclusion and Exclusion criteria

51 participants were recruited using randomized sampling technique. Breast cancer patients
undergoing chemotherapy were recruited as subjects. Patients undergoing surgery and radiation
were excluded.

79 Ethical Consent

Ethical approval was granted by the Institutional Review Board of the University of Cape Coast (IRB/UCC), and the hospital. Informed consent was obtained from the participants before conducting the study.

83 Anthropometric Data

Their anthropometric data before the first dose and after the completion of every cycle of chemotherapy were taken

86 Blood Pressure measurement

We retrieved the recorded blood pressure (systolic and diastolic blood pressure) from theirfolders.

89 Blood Sample

Four (4) ml of venous blood was taken from the patients into the labeled SST (Serum Separator
gel Tube) tube, allowed to stand for 20 minutes then centrifuged to separate the serum from the
whole blood. Serum obtained from the centrifuged sample was analyzed for lipid profile (LDL,
HDL, TC and TG), uric acid and creatinine levels, using automated ELITECH Auto analyzer.
Blood samples for analysis were taken before the first dose and after the completion of every
cycle of chemotherapy.

96 Statistical analysis

97 Data was entered into Microsoft Excel and Statistical Package for Social Sciences (SPSS) 16.0 98 for windows version was used for statistical analysis. Continuous variables like age were 99 reported using mean and standard deviation. Bivariate analysis was reported using t-test and 100 multivariate analysis was done using ANOVA and the significance level was set at 0.05.

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102 **Results**

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Table 1 describes the general characteristics of breast cancer patients. Of the 51 participants, majority of were within the age range of 46-60years (43.1%), married (51.0%), had informal form of employment (74.5%), had invasive ductal carcinoma (NOS) (60.8%) and were overweight (45.1%)

9 Table 1: General char	Table 1: General characteristics of study participants				
Parameter	Frequency (N)	Percentage (%)			
Age groups					
≤45	19	37.3			
46-60	22	43.1			
≥60	10	19.6			
Marital Status					
Single	3	5.9			
Married	26	51.0			

Divorced	10	19.6
Widowed	10	23.5
Type of employment	12	23.5
Formal	5	9.8
Informal	38	74.5
Unemployed	8	15.7
Diagnosis		
Advanced breast cancer	6	11.8
Invasive ductal carcinoma (NST)	14	27.5
Invasive ductal carcinoma (NOS)	31	60.8
BMI Classification		
Underweight	1	2.0
Normal weight	10	19.6
Overweight	23	45.1
Obese	16	31.4

110 BMI: Body Mass Index, NST: No Special Type, NOS: Not Otherwise Specified.

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113 Demographic characteristics of participants with the various classes of breast cancer are shown 114 in Table 2. Demographic distribution of the participants showed that patients with advanced 115 breast cancer (ABC), invasive ductal carcinoma (NST), and invasive ductal carcinoma (NOS) 116 were mainly within 46-60, \leq 45, and \geq 61 years respectively. Majority were married with a few 117 being single. Most had informal form of occupation and were overweight as well.

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121 <u>Table 2: Demographic characteristics of participants with the various classes of carcinoma</u>. Parameter Advanced Invasive ductal Invasive ductal P-value Breast carcinoma (NST) carcinoma (NOS) Cancer (n=14) (n=31) (n=6)

	(n=6)			
Age				0.375
≤45	2(33.3)	8(57.1)	9(29.0)	
46-60	3(50.0)	3(21.4)	9(29.0)	
≥61	1(16.7)	3(24.4)	6(31.4)	
Marital Status				0.773
Single	0(0.0)	1(7.1)	2(6.5)	
Married	4(66.7)	9(57.1)	14(45.2)	
Divorced	0(0.0)	2(14.3)	8(25.8)	
Widowed	2(33.3)	3(21.4)	7(22.6)	

Occupation				0.748
Formal	1(16.7)	2(14.3)	2(6.5)	
Informal	4(66.7)	11(78.6)	23(74.2)	
Unemployed	1(16.7)	1(7.1)	6(19.4)	
BMI kg/m ²	29.85±6.61	31.32±8.85	28.55 ± 5.85	0.458
BMI Classification				0.814
Underweight	0(0.0)	0(0.0)	1(3.2)	
Normal weight	0(0.0)	3(23.1)	7(22.6)	
Overweight	4(66.7)	5(38.5)	14(45.2)	
Obese	2(33.3)	5(38.5)	9(29.0)	
RMI. Rody Mass Ind	lov			

- **BMI: Body Mass Index**

Table 3 demonstrates the baseline hematological and biochemical characteristics of the participants. Most of the study participants showed insignificant mean values of hematological parameters (Hb, PLT and WBC) before first dose. Uric acid (p value=0.044) and creatinine (p value=0.0.17) recorded significant mean values before first dose with majority within normal range except for uric acid where patients with advanced breast cancer (ABC) had equally (50%) high and normal uric acid levels. The lipid profile of the participants before first dose was mainly normal except for patients with invasive ductal carcinoma (NOS) who had insignificant high levels of LDL (62.1%).

Table 3: Hematological and biochemical characteristics of participants before 1st dose

Parameter	Advanced Breast Cancer (n=6)	t Invasive ductal carcinoma (NST) (n=14)	Invasive ducta carcinoma (NOS) (n=31)	l P-value
HB g/dl	11.28±1.75	11.88±1.27	11.90±1.41	0.778
HB Ranges				0.543
Low	1(25.0)	6(42.9)	6(26.1)	
Normal	3(75.0)	8(57.1)	17(73.9)	
High	0(0.0)	0(0.0)	0(0.0)	
WBC 10 ⁹ /l	6.08±1.85	5.97±1.90	5.35±2.45	0.659
WBC Ranges				0.709
Low	1(25.0)	4(28.6)	10(43.5)	
Normal	3(75.0)	10(71.4)	12(52.2)	
High	0(0.0)	0(0.0)	1(4.3)	
Platelets 10 ³ /ul	271.50±39.62	279.21±88.35	316.57±184.62	0.710
Platelets Ranges				0.860
Low	0(0.0)	1(7.1)	2(8.7)	
Normal	4(100.0)	12(85.7)	18(78.3)	
High	0(0.0)	1(7.1)	3(13.0)	
Creatinine umol/l	48.63±33.72	75.30±11.75	80.56±20.71	0.0.17
Creatinine Ranges				
Low	1(25.0)	0(0.0)	1(4.3)	
Normal	3(75.0)	13(92.9)	17(73.9)	
High	0(0.0)	1(7.1)	5(21.7)	
Uric acid umol/l	393.53±176.55	273.84±42.79	310.49±79.02	0.044
Uric acid Ranges				0.043
Low	0(0.00)	0(0.0)	1(4.5)	
Normal	2(50.0)	14(100.0)	19(86.4)	
High	2(50.0)	0(0.0)	2(9.1)	
Cholesterol	4.26±0.75	5.11±1.20	5.83±1.49	0.055
Cholesterol Range				0.142
Norm(<5.2mmol/l)	4(80.0)	5(62.5)	11(37.9)	
High(>5.2mmol/l)	1(20.0)	3(37.5)	18(62.1)	
HDLÌ	0.79±0.49	1.29±0.43	1.21±0.42	0.112
HDL Ranges				0.523
>0.91mmol/l (N)	3(60.0)	7(85.7)	21(72.4)	
<0.91mmol/l (L)	2(40.0)	1(12.5)	8(27.6)	
LDL	2.79±0.81	3.13±0.96	3.89±1.51	0.146
LDL Ranges				0.142
<3.4mmol/l (N)	4(80.0)	5(62.5)	11(37.9)	
>3.4mmol/l (H)	1(20.0)	3(37.5)	18(62.1)	
VLDL	0.66±0.11	0.70±0.54	1.18±1.60	0.902
VLDL Ranges				0.113
Low (<0.10mmol/l)	0(0.0)	0(0.0)	0(0.0)	
Normal (0.10-1.70)	5(100.0)	7(87.5)	29(100.0)	
High (>1.70mmol/l)	0(0.0)	1(12.5)	0(0.0)	
Triglyceride	1.46±0.24	1.53±1.18	1.60±0.55	0.902
Triglyceride Ranges				0.119
Low (<0.45mmol/l)	0(0.0)	0(0.0)	0(0.0)	
Normal (0.45-1.71)	5(100.0)	7(87.5)	18(62.1)	
High (>1.71mmol/l)	0(0.0)	1(12.5)	11(37.9)	

151 Table 4 shows hematological and biochemical characteristics of participants after 2nd dose. After

the second dose, all the hematological and biochemical parameters of participants remained normal except for invasive ductal carcinoma (NST) patients who had 60% low Hb and WBC (P value). Creatinine and uric acid of all participants recorded significant mean values in the patients with NOS (p=0.029) and NST p =0.018) respectively. Majority of the participants had high levels of cholesterol, HDL >0.91mmol/l, and LDL >3.4mmol/l but normal levels of VLDL and Triglyceride (p=0.733 and p=0.736 respectively).

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162 Table 4: Hematological and biochemical characteristics of participants after 2nd dose

Parameter	Advanced Breast	Invasive ductal	Non-Invasive ductal	P-value
	Cancer (n=6)	carcinoma (NST)	carcinoma (NOS)	
HB g/dl	12.50±1.80	11.57±1.21	11.78±1.19	0.533
HB Ranges				0.278
Low	1(33.3)	6(60.0)	6(30.0)	
Normal	2(66.7)	4(40.0)	14(70.0)	
High	0(0.0)	0(0.0)	0(0.0)	
WBC 10 ⁹ /l	3.83±1.75	4.86±1.85	4.50±2.05	0.720
WBC Ranges				0.637
Low	1(33.3)	6(60.0)	9(45.0)	
Normal	2(66.7)	4(40.0)	11(55.0)	
High	0(0.0)	0(0.0)	0(0.0)	
Platelets 10 ³ /ul	281.00±37.72	301.10±147.74	262.40±115.17	0.718
Platelets Ranges				0.823
Low	0(0.0)	1(10.0)	3(15.8)	
Normal	3(100.0)	7(70.0)	14(73.7)	
High	0(0.0)	2(20.0)	0(0.0)	
Creatinine umol/l	54.13±48.20	66.45±11.50	80.41±73.79	0.029
Creatinine Ranges				0.007
Low	1(33.3)	0(0.0)	0(0.0)	
Normal	1(33.3)	10(100.0)	18(90.0)	
High	1(33.3)	0(0.0)	2(10.0)	
Uric acid umol/l	417.37±173.56	275.20±49.46	310.35±60.41	0.018
Uric acid Ranges				0.246
Low	0(0.0)	0(0.0)	0(0.0)	
Normal	2(66.7)	10(100.0)	17(85.0)	
High	1(33.3)	0(0.0)	3(15.0)	
Cholesterol	5.35±1.02	6.39±0.33	5.92±1.17	0.769
Cholesterol Range				0.478
Norm(<5.2mmol/l)	1(33.3)	0(0.0)	7(43.8)	
High(>5.2mmol/l)	2(66.7)	2(100.0)	9(56.3)	
HDL	1.30±0.15	1.66±0.34	1.48±0.46	0.657
HDL Ranges				0.849
>0.91mmol/l (N)	3(100.0)	2(100.0)	15(93.8)	

<0.91mmol/l (L)	0(0.0)	0(0.0)	1(6.3)	
LDL	3.41±0.61	3.97±0.52	1.50±0.78	0.910
LDL Ranges				0.281
<3.4mmol/l (N)	1(33.3)	0(0.0)	9(43.8)	
>3.4mmol/l (H)	2(66.7)	2(100.0)	7(43.8)	
VLDL	0.64 ± 0.29	0.76 ± 0.14	0.80±0.35	0.733
VLDL Ranges				-
Low (<0.10mmol/l)	0(0.0)	0(0.0)	0(0.0)	
Normal (0.10-1.70)	3(100.0)	2(100.0)	16(100.0)	
High (>1.70mmol/l)	0(0.0)	0(0.0)	0(0.0)	
Triglyceride	1.42 ± 0.65	1.68 ± 0.32	1.77±0.76	0.736
Friglyceride Ranges				0.924
Low (<0.45mmol/l)	0(0.0)	0(0.0)	0(0.0)	
Normal (0.45-1.71)	2(66.7)	1(50.0)	9(56.3)	
High (>1.71mmol/l)	1(33.3)	1(50.0)	7(43.8)	

Hematological and biochemical characteristics of participants after 3rd dose is demonstrated in table 5. After the 3rd cycle, most of the participants recorded insignificant normal hematological and biochemical parameters except uric acid which showed significant mean value, p-value 0.045. Though manifested insignificant, majority of the participants had low WBC, normal PLT levels, and equal normal and low Hb levels. Regarding biochemical parameters most patients had normal creatinine and uric acid, high cholesterol and HDL, low LDL, normal VLDL and Triglyceride.

184 Table 5: Hematological and biochemical characteristics of participants after 3rd dose

Parameter	Advanced Breast Cancer	Invasive ductal carcinoma (NST)	Invasive ductal carcinoma (NOS)	P-value
HB g/dl	12.20±1.25	12.06±0.90	16.82±23.15	0.859
HB Ranges				0.876
Low	1(33.3)	2(40.0)	10(52.6)	0.070
Normal	2(66.7)	3(60.0)	8(42.1)	
High	0(0.0)	0(0.0)	1(5.3)	
WBC 10 ⁹ /I	3.89 ± 1.27	3.81±0.88	4.33±1.92	0.805
WBC Ranges	5.09-1.27	5.01±0.00	4.33±1.92	0.305
Low	1(33.3)	3(60.0)	11(57.9)	0.711
Normal	2(66.7)	2(40.0)	8(42.1)	
	2(00.7) 0(0.0)	2(40.0) 0(0.0)	8(42.1) 0(0.0)	
High Distalata 10 ³ /1				0.910
Platelets 10 ³ /ul	310.33±41.06	263.60±128.07	267.79±114.42	0.819
Platelets Ranges		1(20.0)	2(15.0)	0.800
Low	0(0.0)	1(20.0)	3(15.8)	
Normal	3(100.0)	3(60.0)	14(73.7)	
High	0(0.0)	1(20.0)	2(10.5)	
Creatinine umol/l	78.33±8.80	75.58±8.08	75.17±18.67	0.955
Creatinine Ranges				0.841
Low	0(0.0)	0(0.0)	2(10.5)	
Normal	3(100.0)	5(100.0)	16(84.2)	
High	0(0.0)	0(0.0)	1(5.3)	
Uric acid umol/l	312.33±35.73	247.66±42.50	336.38±73.01	0.045
Uric acid Ranges				0.137
Low	0(0.0)	0(0.0)	0(0.0)	
Normal	3(100.0)	5(100.0)	12(63.7)	
High	0(0.0)	0(0.0)	7(36.8)	
Cholesterol	4.63±1.01	6.71±0.00	6.69±1.55	0.278
Cholesterol Range	1.05±1.01	0.7120.00	0.0921.55	0.468
Norm(<5.2mmol/l)	1(50.0)	0(0.0)	1(14.3)	0.400
High(>5.2mmol/l)	1(50.0)	1(100.0)	6(85.7)	
HDL	1.32 ± 0.47	. ,		0.807
	1.32±0.47	1.74±0.00	1.54 ± 0.56	0.807
HDL Ranges	2(100.0)	1(100.0)	(05.7)	0.788
>0.91mmol/l (N)	2(100.0)	1(100.0)	6(85.7)	
<0.91mmol/l (L)	0(0.0)	0(0.0)	1(14.3)	0.260
	2.62±0.21	0.44 ± 0.00	4.25±1.47	0.368
LDL Ranges				0.208
<3.4mmol/l (N)	2(100.0)	0(0.0)	3(42.9)	
>3.4mmol/l (H)	0(0.0)	0(0.0)	4(57.1)	
VLDL	0.68±0.21	0.62 ± 0.00	0.89±30	0.529
VLDL Ranges				-
Low (<0.10mmol/l)	0(0.0)	0(0.0)	0(0.0)	
Normal (0.10-1.70)	2(100.0)	1(100.0)	7(100.0)	
High (>1.70mmol/l)	0(0.0)	0(0.0)	0(0.0)	
Triglyceride	1.50±0.47	1.36±0.0	1.96±0.66	0.533
Triglyceride Ranges				0.565
Low (<0.45mmol/l)	0(0.0)	0(0.0)	0(0.0)	
Normal (0.45-1.71)	1(50.0)	1(100.0)	3(42.9)	
High (>1.71mmol/l)	1(50.0)	0(0.0)	4(57.1)	

186	Table 6 shows the clinical, hematological and biochemical demographics of participants
187	throughout the cycles of chemotherapy. SBP and DBP significantly reduced by 2 nd cycle and
188	increased again slightly after 3 rd cycle (p=0.026 and p=0.029 respectively). WBC reduced
189	significantly throughout the cycles (p=0.008), and HDL increased significantly throughout the
190	cycles (p=0.014). The comparative mean values of the rest of the parameters throughout the
191	cycles were insignificant although Hb decreased by the 2 nd cycle and increased after 3 rd cycle
192	(p=0.281), Uric acid increased throughout the cycle (p=0.852), creatinine was maintained
193	throughout cycles (p=1.000). Cholesterol, LDL, VLDL and Triglyceride increased throughout
194	the cycle of chemotherapy.

Table 6: Clinical, hematological and Biochemical demographics of participants throughout the cycles. 198

98	the cycles.				
	Parameter	Before 1 st dose	After 2 nd dose	After 3 rd dose	P-value
	Blood pressure (mmHg)				
	SBP	133.5 ± 20.14	124.5 ± 14.55	123.3 ± 15.26	0.026
	DBP	82.54 ± 11.27	76.64 ± 8.96	77.19 ± 10.35	0.029
	Hb (g/dl)	11.84 ± 1.37	11.78 ± 1.23	15.44 ± 10.39	0.281
	WBC (x 109/L)	5.63 ± 2.20	4.55 ± 1.93	4.18 ± 1.69	0.008
	PLT (x 103/uL)	299.4 ± 147.6	275.8 ± 120.1	271.7 ± 109.1	0.622
	Uric acid (µmol/l/L)	306.1 ± 86.64	309.4 ± 78.71	317.3 ± 72.58	0.852
	Creatinine (µmol/L)	75.65 ± 21.28	75.61 ± 14.72	75.60 ± 16.07	1.000
	Cholesterol	5.51±1.45	5.88 ± 1.55	6.27±1.57	0.293
	HDL	1.17±0.45	1.47 ± 0.42	1.52 ± 0.49	0.014
	LDL	3.62 ± 0.22	3.63±0.29	3.93±0.44	0.801
	VLDL	0.71±0.31	0.78 ± 0.32	0.82 ± 0.28	0.662
	Triglyceride	1.57 ± 0.68	1.72±0.71	1.81 ± 0.61	0.521
99	SBP: Systolic Blood Press	sure, DBP: Diastoli	c Blood Pressure.		
n					

Table 7 Compares the various clinical, hematological, and biochemical parameters among the stages of the cycles, Comparing the various parameters, SBP significantly decreased after 2nd dose to after 3rd does, DBP decreased significantly from 1st dose to after 2nd dose, WBC decreased significantly throughout all the stages of the cycle and HDL increased from the 1st dose to after 2nd dose significantly. Comparison of the rest of the parameters recorded insignificant values.

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218 Table 7: Anova comparison of parameters throughout the cycles

Parameter	Before 1 st dose	After 2 nd dose	After 3 rd dose	P *	Ρα
BP		$- \circ$			
	133.49	124.45	123.26	0.050	0.035
Systolic (mmHg) Diastolic (mmHg)	82.54	76.54	77.19	0.030 0.031	0.035
HB (g/dl)	82.34 11.84	11.78	15.44	0.999	0.071
WBC $(10^{9}/l)$	5.63	4.55	4.18	0.040	0.257
PLT $(10^{3}/\mu l)$	299.41	275.82	271.74	0.653	0.596
Uric Acid (µmol/l)	306.07	309.43	317.28	0.977	0.798
Creatinine (µmol/l)	75.65	73.79	75.60	0.887	1.000
Cholesterol	5.51	5.88	6.28	0.545	0.251
HDL	1.173	1.471	1.520	0.027	0.054
LDL	3.616	3.629	3.934	0.991	0.738
VLDL	0.714	0.780	0.823	0.638	0.505
Triglyceride	1.571	1.717	1.809	0.636	0.508

219 One-way Anova Multiple comparison of parameters using initial measurement (Before 1st)

220 as a baseline for comparison with the other measurements. P^* indicates before 1^{st} dose 221 verse after 2^{nd} dose whiles P^{α} indicates before 1^{st} dose verse after 3^{rd} dose.

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228 Discussion

Chemotherapy is the anti-cancer treatment of choice for hundreds of thousands of cancer patients diagnosed each year,⁽¹³⁾ of which Cyclophosphamide, Adriamycin and 5-Fluorouracil (CAF) is one of the most effective anti-neoplastic therapies in use today. This drug combination is prescribed to millions of women worldwide for the adjuvant or palliative treatment of breast cancer.⁽¹⁴⁾ However chemotherapy, CAF regimen is known to have adverse effect on the hematological and biochemical profile thus results in neutropenia, thrombocytopenia, anemia, hyperuricaemia, dyslipidemia.⁽⁹⁾

Our study in the same vein reinforces documented findings on the adverse effect of chemotherapy. Throughout cycles, we recorded systolic blood pressure decreasing till after the third cycle, diastolic blood pressure decreased after second cycle but increased slightly after the third cycle. Hemoglobin though insignificant, decreased after second cycle but increased sharply after the third cycle. White blood cells (WBC) decreased throughout cycles, HDL and uric acid increased throughout cycles and creatinine remained unchanged throughout cycles.

Systolic and diastolic blood pressure recorded significant p values indicating low risk of effect 242 on the cardiovascular system. This is in line with a multi-centered study by Henderson et al 243 among breast cancer patients which recorded that the incidence of cardiotoxicity during 244 chemotherapy was not significant.⁽⁹⁾ However, our findings is in contrast to a meta-analysis 245 study by Ann et al (2001) which stated cardiac dysfunction as a long term effect of cancer 246 247 chemotherapy. The duration of the study accounts for the difference in findings. Our study lasted for approximately six months (up to the third cycle) whiles that of Ann et al, covered data of 248 breast cancer patients over years.⁽¹⁰⁾ Henderson et al (2003) in his multi-centered study among 249 250 breast cancer patients indicated anemia to increase in frequency with each doxorubicin dose

administration though hemoglobin levels normalized per our findings and none was diagnosed of anemia. This difference is as a result of the drugs administered. Doxorubicin was administered in both studies however in our studies, haematinics were administered in addition to curb the likelihood of anemia among the patients.⁽⁹⁾ The WBC level observed to decrease by the third cycle chemotherapy in our study affirms earlier longitudinal studies by Crawford, Leanna and Henderson conducted among lymphoma and breast cancer patients respectively.^(8, 9, 15)

Lipid abnormalities have been reported among Ghanaian breast cancer patients (16) and our 257 study support this finding. All lipid parameters increased throughout cycles however with only 258 HDL being significant. It corresponds with a case-control and longitudinal study by Moorman et 259 al in North Carolina, Australia and Muthusamy et al in India respectively which recorded normal 260 lipid levels and increased HDL levels at 3 and 6 months of chemotherapy respectively.^(11, 17) 261 Again hyperuricaemia causing renal dysfunction results from high cell turn over (tumour lysis 262 syndrome) thus implies in cancer treatment-there is high cell turnover-resulting in 263 hyperuricaemia.⁽¹⁸⁾ Increasing uric acid levels throughout cycles in our study asserts this. 264 Nevertheless, creatinine levels normalised throughout cycles, owing to the limited duration of the 265 study. 266

Overall our study confirms old age and overweight as factors associated with breast cancer. It avows most studies which most recruited patients were within 40-60yrs and overweight.^(9, 11, 12, 19) The limitation of this study was the short duration of the study, however the corresponded well with other previous studies thus further studies prolonging the study duration needs to be conducted to build on these findings.

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274 Conclusion

Chemotherapy has significant adverse effect on the clinical profile (systolic and diastolic blood pressure), white blood cells (WBC) and High-Density Lipoprotein (HDL) in breast cancer patients undergoing treatment. Prolonged observation will prompt health practitioners on the possible complications likely to results from mentioned parameters and thus help increase prophylactic measures for any complications.

280 281 282 283 284 285 **Declarations** 286 **Consent for Publication** 287 Author's approval for publication of research findings including participant's details was sought 288 before being added for publication. 289 Conflict of Interest: There are no conflicts of interests. 290 291 292 293 References NCI. National Cancer Institutes; SEER Stat Fact Sheets 2011 [Available from: 294 1. http://seer.cancer.gov/statfacts/html/breast.html. 295 2. Saunders C, & Jassal, S. . Breast cancer 2009. 296 WHO. World Cancer Report 2014.; 2014. Report No.: 92-832-0429-8. 297 3. Thomas AS, Kidwell, K. M., Oppong, J. K., Adjei, E. K., Osei-Bonsu, E., Boahene, A., 298 4. Jiggae, E., Gyan, K., & Merajver, S. D. Breast Cancer in Ghana: Demonstrating the Need for 299 Population-Based Cancer Registries in Low- and Middle-Income Countries. American Society of

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