Original Research

High atherogenic index of plasma and cardiovascular risk factors among Ghanaian breast cancer patients

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Impact statement

Breast cancer prognosis is negatively impacted by comorbidities, especially in global regions where patients present to clinics with advanced cancer stages. This study reports preliminary findings on atherogenic index of plasma (AIP) and cardiovascular risk factors in Ghanaian breast cancer patients. AIP and cardiovascular risk factors were identified to be high in the breast cancer patients and therefore should be of prime interest to warrant further studies. Ultimately, understanding the contribution of AIP and cardiovascular risk factors in breast cancer will impact positively on clinical management of patients with breast cancer.

Abstract

Comorbidities impact negatively on breast cancer prognosis, especially in developing countries where cases are usually presented to clinics at advanced stages. This study aimed to determine the atherogenic index of plasma (AIP) and cardiovascular risk factors among Ghanaian women diagnosed with breast cancer. A total of 52 breast cancer patients were age-matched with 52 healthy controls. Sociodemographics of participants were obtained using a well-structured questionnaire. Pathological data of patients were obtained from medical records, and all clinical and anthropometric measurements were done using standard instruments. Lipid profile was determined from serum using enzymatic assays, and cardiovascular risk factors were calculated from estimated lipid parameters. Blood pressure, AIP, total cholesterol (T. chol), triglyceride (TG), and low-density lipoprotein cholesterol (LDL-c) were significantly elevated ($P < 0.05$) in the breast cancer patients compared to the controls, but the reverse was observed for high-density lipoprotein cholesterol (HDL-c) ($P < 0.01$). Obesity (odds ratio [OR] = 2.51, $P = 0.015$), hypertension (OR = 4.04, $P < 0.001$), AIP (OR = 10.44, $P < 0.001$), and dyslipidemia ($P < 0.01$) were significantly associated with breast cancer. AIP correlated positively with age ($r = 0.244$, $P < 0.05$), body mass index ($r = 0.225$, $P < 0.05$), blood pressure ($P < 0.01$), T. chol ($r = 0.418$, $P < 0.01$), and TG ($r = 0.880$, $P < 0.01$), but inversely correlated with HDL-c ($r = -0.460$, $P < 0.01$). A greater proportion (88%) of the patients presented with advanced breast cancer. AIP and cardiovascular risk factors were high in the breast cancer patients. Considering that AIP and cardiovascular disease risk factors are of interest in breast cancer patients, further studies are needed to understand the effect of AIP and cardiovascular risk factors on breast cancer outcomes.

Keywords: Breast cancer, dyslipidemia, hypertension, obesity, cardiovascular risk, atherogenic index of plasma

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Introduction

Breast cancer (BC) is the most common cancer among women and is in the leading cause of cancer-related mortality in females worldwide.[1] About 2.1 million patients were diagnosed with BC in 2018, contributing approximately 11.6% of the global cancer burden and 15% of cancer-related deaths in women. Incidence of BC varies in populations and prognosis is generally poor in the developing countries.[2,3] Annual estimates of BC in Africa show a growing incidence of the cancer,[4] and the increasing trend has the potential to worsen the current challenges of the sub-Saharan Africa regions including poverty and the fight against maternal mortality.[5] Edmund *et al.* reported malignancy prevalence of 32.7% among Ghanaian women

from whom breast biopsies were taken and suggested that a significant number of patients present with late stage BC to health facilities in the West African country.[6] In developed countries, promotion of BC screening has resulted in early detection of the disease and shifted the stage of diagnosis from advanced to early, with an overall improved survival of patients.[7]

The etiology of BC is not clearly defined; however, several risk factors including aging, gender, hormonal imbalance, gene mutations, unhealthy lifestyle, and obesity have been associated with the disease.[8] In the USA, it was reported that about 99.3% and 71.2% of BC-related deaths occurred in women at ages 40–50 years (premenopausal ages) and above 60 years (postmenopausal ages), respectively.[8] The risk of developing BC is reported to be almost 100 times greater in women than in men, and generally BC in premenopausal women is associated with poor prognosis compared with women at early adulthood and postmenopausal ages.[9,10] In Ghana, however, an increasing BC incidence has been reported in women, and a shift from the premenopausal ages to early adulthood has been observed.[11]

Extensive studies have implicated hormonal imbalance and expression of hormone receptors including human epidermal growth factor receptor 2 (HER2), prolactin (PRLR), progesterone (PR), and estrogen (ER) in BC progression, while genetic mutations such as BRCA 1/2 have been associated with BC development. The genetic variability has been explored as a molecular target for application of genomic medicine.[12] Several studies have associated lifestyle induction of inflammatory responses with increased risk of BC.[13–15] A strong correlation between physical activity and survival of BC patients has been established, with exercise being considered as a possible adjuvant therapy for cancer patients.[16,17]

Obesity is a public health challenge in developed countries and is implicated in life-threatening conditions including cardiovascular disease, diabetes, and cancers.[18] Prevalence of obesity and dyslipidemia have been shown to be high among BC patients,[19] and an increased body mass index (BMI) has also been reported in postmenopausal women diagnosed with BC.[20] Obesity was also found to increase risk of treatment related complications in BC patients and local recurrence of the cancer.[21] Accumulation of macronutrients in adipocytes stimulates the production and release of inflammatory mediators including tumor necrosis factor α and interleukins leading to pro-inflammatory and oxidative stress which are implicated in non-communicable diseases such as BC.[22]

Dyslipidemia, indicated by increased atherogenic index of plasma (AIP), is a cardiovascular disease predictor. AIP is associated with increase body weight and cardiovascular risk factors[23,24] and have been reported in BC patients.[25,26] However, the association of AIP with BC is inconsistent and warrant further investigation. This study is therefore aimed to determine the prevalence of AIP and cardiovascular risk factors in Ghanaian women diagnosed with BC.

Materials and methods

Study design and study population

This study was a hospital-based cross-sectional study conducted at the Chemotherapy Suite, Department of Surgery, Korle Bu Teaching Hospital (KBTH) from January to July 2014. KBTH is a national referral hospital with many specialist clinics and located in Accra, Ghana. The Ethical and Protocol Review Committee of the School of Biomedical and Allied Health Sciences, University of Ghana approved the study with Certificate Number: SAHS-ET./10359973/AA/46A/2013–2014. A total of 104 participants, made up of 52 BC female patients who were undergoing chemotherapy and age-matched 52 healthy controls, were included in the study. Patients recruited for the study were those diagnosed with BC based on histopathology and receiving chemotherapy. All patients received intravenous (IV) cyclophosphamide 500 mg/BSA, IV adriamycin 50 mg/BSA, and IV 5-fluorouracil 500 mg/BSA. The chemotherapeutic drugs were administered at three weekly intervals for six cycles.

Patients diagnosed with other types of cancers, chronic liver disease, diabetes, kidney disease, cigarette smoking, excessive alcohol consumption, and/or pregnant women were excluded from the study. The controls were recruited from women groups after receiving health talks on BC. A written consent was obtained from the participants after the study objectives had been explained.

Data collection

Sociodemographic data, which included age, education and occupation, were collected using a well-structured questionnaire. Blood pressures were measured using a mercury sphygmomanometer after a patient had rested for at least 15 min, and BMI was calculated from weight and height of participants in light clothing. Drugs that were used for chemotherapy, duration of treatment, and tumor stages were retrieved from the medical records of the patients after obtaining permission from hospital authority.

Venous blood sample (5 mL) was collected from each participant into a gel separator tube after an overnight fast and allowed to clot. The clotted blood was centrifuged at 5000 rpm for 5 min, and serum obtained was transferred into 1.5 mL microtubes and stored at -80 °C till ready for use. The serum was thawed on ice and total cholesterol (T. chol), triglyceride (TG), and high-density lipoprotein cholesterol (HDL-c) levels were determined using HUMAN's clinical chemistry reagents (HUMAN Diagnostics, Wiesbaden, Germany) and chemistry analyzer Mindray BS-120, (Mindray, Shenzhen, China) following the manufacturer's protocol. Low-density lipoprotein cholesterol (LDL-c), atherogenic index (T. chol/HDL-c) and AIP were calculated.

Data analysis

Statistical Package for the Social Sciences (SPSS) version 20.0 was used to analyze the data. Continuous variables

were presented as mean ± SD and compared with student t-test. Difference in categorical parameters between the two groups was determined using Chi-square (χ^2) test and odds ratio (OR) for association. Pearson's correlation coefficient (r) was used to establish relationship between the biochemical and cardiovascular risk (CVR) variables in the BC patients. Multivariate analysis was performed to establish interdependency of variables. P-value < 0.05 was considered statistically significant.

Results

The sociodemographics, clinical and pathological data of the study population are shown in Table 1. The difference between mean ages of the patients and controls was not statistically significant ($P > 0.05$). Both systolic blood pressure (SBP) and diastolic blood pressure (DBP) as well as the mean BMI were significantly raised in the patients as compared to the controls ($P < 0.01$). There were more skilled laborers (11.5%) within the patient group than the controls (1.9%) ($P < 0.01$), and the percentage of traders among the control group was significantly greater than the patients ($P < 0.01$). Greater proportion (67.3%) of the patients presented with stage IV of BC at the clinic, and the advancement of the disease may have resulted in the increase in percentage of patients receiving chemotherapy.

Comparison of circulatory lipids and cardiovascular risks indices are shown in Table 2. There was a significant increase in T. chol, TG, LDL-c, and AIP in the patients than the control group ($P < 0.05$). However, high-density lipoprotein cholesterol (HDL-c) was significantly reduced in the patients than the controls ($P < 0.01$), while difference in cardiovascular risk index between the study populations was not statistically significant ($P > 0.05$).

Tumor stage-stratified analysis of clinical and biochemical parameters of the patients has been presented in Table 3.

Table 1. Sociodemographic, clinical and pathological characteristics of the study participants.

	Breast cancer patients (*N*=52)	**Control group (*N*=52)**		
Variable	Mean ± SD	Mean ± SD	95% CI	*P*-value
Age (years)	47.17 ± 8.97	43.96 ± 10.88	−0.67 to 7.09	0.104
SBP (mmHg)	133.92 ± 21.19	119.79 ± 19.12	6.28 to 21.98	0.001*
DBP (mmHg)	83.10 ± 13.81	76.52 ± 9.42	2.00 to 11.15	0.005*
BMI (kg/m^2)	27.82 ± 4.85	25.61 ± 3.50	0.56 to 3.85	0.009*
Occupation	*n* (%)	*n* (%)	χ^2	
Professionals†	4 (7.7)	2 (3.9)	0.84	NS
Skilled laborers†	6 (11.5)	1 (1.9)	6.69	<0.01
Unskilled laborers	8 (15.4)	7 (13.5)	0.00	NS
Traders	26 (50.0)	36 (69.2)	6.72	<0.01
Unemployed	8 (15.4)	6 (11.5)	0.20	NS
Tumor stage				
T1 < 2 cm	0 (0.0)			
2 cm < T2 ≤ 5 cm	6 (11.5)			
T3 > 5 cm	11 (21.2)			
T4	35 (67.3)			
Treatment				
Adjuvant chemotherapy	30 (57.7)			
Neoadjuvant chemotherapy	22 (42.3)			

All the participants were female. Categorical and continuous data were compared using Chi square (χ^2) and student t-test, respectively. *N*: size of populations; *n*: subgroup; SBP: systolic blood pressure; DBP: diastolic blood pressure; NS: not significant; BMI: body mass index; tumor stage (T): size of the tumor in centimeters; NS: not significance.

*P-values < 0.05 were considered statistically significant.

†Fisher exact test was used to compare proportions less than 5.

Table 2. Lipid profile and cardiovascular risks indices of study population.

Variables	**Breast cancer patients (*N* = 52) Mean ± SD**	**Control group (*N* = 52) Mean ± SD**	**95% CI**	***P*-value**
T. chol (mmol/L)	4.77 ± 1.13	4.29 ± 0.83	0.10 to 0.87	0.015*
TG (mmol/L)	1.50 ± 0.38	0.84 ± 0.26	0.41 to 0.91	<0.001*
HDL-c (mmol/L)	0.94 ± 0.23	1.11 ± 0.30	−0.27 to −0.06	0.002*
LDL-c (mmol/L)	3.44 ± 1.32	2.80 ± 0.87	0.21 to 1.08	0.004*
CVD Risk	4.48 ± 1.33	4.73 ± 1.19	−0.71 to 0.21	0.306
AIP	0.15 ± 0.27	−0.15 ± 0.21	0.21 to 0.41	<0.001*

N: represents the size of populations; T. chol: total cholesterol; TG: triglycerides; HDL-c: high-density lipoprotein cholesterol; LDL-c: low-density lipoprotein cholesterol [(TC-HDL-c)-TG/2.2]; CVD Risk; atherogenic index (T. chol/HDL-c); AIP: atherogenic index of plasma [log (TG/HDL-c).

*P-value < 0.05 was considered statistically significant.

Table 3. Tumor stage-stratified analysis of clinical and biochemical parameters of breast cancer patients.

Parameters	Breast cancer tumor stages (T)			*P*-value
	Stage 2 (T2)	Stage 3 (T3)	Stage 4 (T4)	
BMI (Kg/m^2)	25.53 ± 4.71	29.82 ± 4.97	27.58 ± 4.75	0.1956
SBP (mmHg)	122.50 ± 10.9	140.91 ± 18.14	134.97 ± 21.92	0.2077
DBP (mmHg)	77.50 ± 4.18	86.27 ± 11.82	84.34 ± 14.29	0.5464
T. chol (mmol/l)	5.08 ± 0.84	5.15 ± 1.39	4.60 ± 1.07	0.2928
TG (mmo/l)	1.35 ± 0.47	1.59 ± 0.90	1.49 ± 0.80	0.8584
HDL-c (mmo/l)	1.00 ± 0.25	0.85 ± 0.24	0.96 ± 0.23	0.3294
LDL-c (mmol/l)	3.00 ± 0.93	3.23 ± 1.42	3.58 ± 1.36	0.8297
CVD Risk	4.13 ± 0.37	4.17 ± 0.38	4.63 ± 1.58	0.4890
AIP	0.12 ± 0.21	0.22 ± 0.33	0.14 ± 0.26	0.6601

P-value < 0.05 was considered statistically significant. BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; T. chol: total cholesterol; TG: triglycerides; HDL-c: high-density lipoprotein cholesterol; LDL-c: low-density lipoprotein cholesterol [(TC-HDL-c)-TG/2.2]; CVD Risk: atherogenic index (T. chol/HDL-c); AIP: atherogenic index of plasma [log (TG/HDL-c).

Table 4. Multiple regression analysis of clinical and CVD risk factors on AIP.

Model	Unstandardized coefficients		Standardized coefficients	t	Sig.	95% confidence interval for B	
	B	Std. error	Beta			Lower bound	Upper bound
(Constant)	.124	.098		1.267	.212	−.074	.322
BMI	−.001	.002	−.009	−.247	.806	−.005	.004
SBP	.000	.001	.036	.561	.578	−.001	.002
DBP	.000	.001	−.010	−.159	.874	−.003	.002
T.chol	.023	.010	.098	2.291	.027*	.003	.044
TG	.278	.015	.801	18.253	.000*	.247	.309
HDL	−.459	.040	−.400	−11.339	.000*	−.541	−.377
LDL	.002	.008	.010	.271	.787	−.014	.018
CVD_Risk	−.024	.008	−.116	−3.006	.004*	−.040	−.008

BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; T. chol: total cholesterol; TG: triglycerides; HDL-c: high-density lipoprotein cholesterol; LDL-c: low-density lipoprotein cholesterol [(T.chol-HDL-c)-TG/2.2]; CVD Risk; atherogenic index (T. chol/HDL-c); AIP: atherogenic index of plasma [log (TG/HDL-c).
**P*-value < 0.05 was considered statistically significant.

Table 5. Association of CVD risk factors with breast cancer.

CVD risk factors	Breast cancer patients (*N* = 52) *n* (%)	Control group (*N* = 52) *n* (%)	OR (95% CI)	*P*-value
Overweight	22 (42.3)	16 (30.8)	1.61 (0.90–2.88)	0.142
Obesity	15 (28.8)	7(13.5)	2.51 (1.23–5.10)	0.015*
Hypertension	15 (28.8)	5 (9.6)	4.04 (1.86–8.81)	<0.001*
Hypercholesterolemia	20 (38.5)	7 (11.5)	4.69 (2.27–9.68)	<0.001*
Hypertriglyceridemia	18 (34.6)	2 (2.8)	17.41 (5.13–58.99)	<0.001*
Decreased HDL-c	25 (48.1)	12 (23.1)	3.09 (1.68–5.68)	<0.001*
Increased LDL-c	13 (25.0)	4 (7.7)	3.83 (1.63–8.99)	0.002*
High AIP	21 (40.4)	3 (5.8)	10.44 (4.17–26.13)	<0.001

N: sample size; *n* (%) = frequency of CVD risk factors; hypertension: blood pressure >140/90 mmHg; overweight: 26 ≤ BMI < 30 Kg/m^2; obesity: BMI >30 Kg/m^2; hypercholesterolemia: cholesterol level >5.2 mmol/L; decreased-HDL-c: high-density lipoprotein cholesterol level <1.0 mmol/L; increased-LDL-c: low-density lipoprotein cholesterol level >4.12 mmol/L; hypertriglyceridemia: serum triglyceride level >1.8 mmol/L; AIP: atherogenic index of plasma [log (TG/HDL-c)]; high AIP > 0.24. OR = odds ratio.
**P*-value < 0.05 was considered statistically significant.

Stratification of the clinical and biochemical parameters did not show any statistically significant difference. T. chol and TG showed a positive relationship with AIP; however, HDL-c level, and cardiovascular disease (CVD) risk were negatively related ($P < 0.05$) as shown in Table 4. A unit rise in T. chol and TG levels in serum were found to increase AIP in patients by a factor of 0.023 ($P < 0.05$) and 0.278 ($P < 0.001$), respectively. However, a unit increase in HDL-c level and CVD risk showed a corresponding and significant reduction of AIP by a factor of 0.459 ($P < 0.0001$) and 0.024 ($P = 0.004$), respectively. Other clinical factors such as BMI, SBP, and DBP showed no significant effect on AIP ($P > 0.05$).

Association of CVD risk factors with BC is shown in Table 5. The risk of developing BC is associated with obesity (OR = 2.51, 95% confidence interval [CI] = 1.23–5.101, $P < 0.015$). Hypertension (OR = 4.04, 95% CI = 1.86–8.81,

$P < 0.001$), hypercholesterolemia (OR = 4.69, 95% CI = 2.27 – 9.68, $P < 0.001$), and hypertriglyceridemia (OR = 17.41, 95% CI = 5.13–58.99, $P < 0.001$) were significantly associated with BC. BC patients were highly at risk of developing cardiovascular disease than apparently healthy control group (OR = 10.44, 95% CI = 4.17–26.13, $P < 0.001$) based on the high AIP. As expected, majority of the patients had decreased HDL-c (OR = 3.09, 95% CI = 1.68–5.68, $P < 0.001$) and increased LDL-c (OR = 3.83, 95% CI = 1.63–8.99, $P = 0.002$) than the controls. Logistic regression analysis showed no significant relationship between the clinical and biochemical parameters and AIP ($P > 0.05$), except for T. chol which negatively correlated with AIP ($P < 0.05$) (Table 6).

Age correlated strongly and positively with SBP ($P < 0.01$), T. chol ($P < 0.01$), LDL-c ($P < 0.05$), and AIP ($P < 0.05$) (Table 7); however, age was strongly but inverse correlated with HDL-c ($P < 0.05$). BMI positively correlated with SBP ($P < 0.01$), DBP ($P < 0.05$), T. chol ($P < 0.05$), and AIP ($P < 0.05$). SBP correlated with T. Chol ($P < 0.01$), TG ($P < 0.01$), and AIP ($P < 0.01$), and DBP correlated with TG ($P < 0.01$) and AIP ($P < 0.01$). AIP was strongly and positively correlated with T. chol ($P < 0.01$) and TG ($P < 0.01$) and inversely correlated with HDL-c ($P < 0.01$).

Discussion

Comorbid chronic diseases increase the burden of BC in patients, and these comorbidities are usually detected either at the time of cancer diagnoses or during treatment. Comorbid conditions restrict choice of definitive treatment plan for BC management, and the restriction usually results in poor cancer outcomes including increased risk of prolonged hospitalization and poor quality of life.[27] Common comorbidities reported in BC patients included hypertension, chronic obstructive pulmonary disease, rheumatologic disease, and diabetes mellitus, and all these conditions were reported in about 75% of patients.[28] Dyslipidemia and obesity have also been associated with BC; however, the altered serum lipids and obesity were attributed to late effects of the cancer treatment.[29]

In this study, high AIP correlates with cardiovascular risk factors among Ghanaian women diagnosed with BC, and this observation comes from the altered serum lipids, elevated blood pressures, and high BMI. The serum lipids, T. chol, TG, and LDL-c levels were high in BC patients, while HDL-c level was low in the patients compared to control group. A study from Thailand with women who had early stage breast malignancy showed elevated levels

Table 6. Logistic analysis of cardiovascular risk factors and breast cancer.

Risk factors	Estimate	Standard error	95% CI	*P*-value
BMI	−0.003	0.072	−0.143 to 0.137	0.967
SBP	0.010	0.030	−0.049 to 0.068	0.750
DBP	0.039	0.043	−0.045 to 0.123	0.358
T. chol	−0.903	0.407	−1.702 to (−0.105)	0.026*
TG	1.126	1.665	−2.138 to 4.389	0.499
HDL-c	0.296	2.876	−5.342 to 5.934	0.918
LDL-c	0.135	0.270	−0.394 to 0.664	0.617
CVD Risk	0.834	0.629	−0.398 to 2.066	0.184
AIP	−1.117	5.488	−11.874 to 9.640	0.839

BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; T. chol: total cholesterol; TG: triglycerides; HDL-c: high-density lipoprotein cholesterol; LDL-c: low-density lipoprotein cholesterol [(T. chol-HDL-c)-TG/2.2]; CVD risk; atherogenic index (T. chol/HDL-c); AIP: atherogenic index of plasma [log (TG/HDL-c).
*P-value < 0.05 was considered statistically significant.

Table 7. Pearson's correlation between clinical and cardiovascular risk factors among study participants.

	Age	BMI	SBP	DBP	T.chol	TG	HDL-c	LDL-c	CVR	AIP
Age	1	.110	.325*	.092	.401*	.143	−.248†	.221†	−.186	.244†
BMI	.110	1	.285*	.220†	.230†	.188	−.170	.106	0.009	.225†
SBP	.325**	.285**	1	.727*	.260*	.294*	−.158	.115	−.021	.358*
DBP	.092	.220†	.727*	1	.160	.306*	−.029	−.085	−.052	.880*
T. chol	.401**	.230†	.260*	.160	1	.490*	−.009	.322*	.175	.418*
TG	.143	.188	.294*	.306*	.490*	1	−.029	−.085	−.052	.880*
HDL-c	−.248†	−.170	−.158	−.029	−.009	−.029	1	−.245†	.076	−.460*
LDL-c	.221†	.106	.115	−.085	.322*	−.085	−.245†	1	.237†	.060
CVR	−.186	.009	−.021	−.052	.175	.052	.076	.237†	1	−.051
AIP	.244†	.225†	.358*	.880*	.418*	.880*	−.460*	.060	−.051	1

BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; T. chol: total cholesterol; TG: triglycerides; HDL-c: high-density lipoprotein cholesterol; LDL-c: low-density lipoprotein cholesterol [(TC-HDL-c)-TG/2.2]; CVR: atherogenic index (TC/HDL-c); AIP: atherogenic index of plasma.
*Correlation is significant at 0.01 level (2 tailed).
†Correlation is significant at 0.05 level (2 tailed).

of TG and LDL-c, with unchanged levels of T. chol and HDL-c compared with healthy controls.[30] AIP correlated positively with BMI, SBP and DBP, T. chol, and TG, and inversely with HDL-c, and TG and HDL-c were found to be the main contributing factors of increased AIP.

In a similar study conducted in premenopausal and postmenopausal women with BC, T. chol, TG, and LDL-c levels in the cancer patients were elevated compared to the controls. However, there was no significant difference in the elevation of the lipids between the pre- and postmenopausal women.[31] AIP also positively correlated with age in this study, and the result supports an earlier study in which the correlation was done in HIV patients.[32] Other studies on heart diseases have however shown an inverse relationship between AIP and age, and the discrepancy was partly attributed to the disease condition.[23,33] Association between AIP and metabolic syndrome has also been established, in which the index was shown to increase with body weight and other cardiovascular risk factors.[23,24]

Hypercholesterolemia is associated with BC in Ghanaian women. This conclusion comes from the high cholesterol levels in BC patients. Current study supports earlier findings that associated elevated T. chol with BC,[34,35] and patients diagnosed with lymph node metastasis were found to show significantly elevated T. chol when compared with those without lymph node involvement.[34] Contrary, T. chol level was strongly and negatively correlated with BC. The observation confirmed a study that associated cholesterol levels with a reduced risk of BC.[36] The role of T. Chol in BC etiology is not clear; however, progression of the disease was linked to accumulation of cholesterol metabolite, 27-hydroxycholestrol through activation of ER-receptor pathway.[26] The 27-hydroxycholesterol is generated by cytochrome P450 sterol hydroxylase (CYP27A1), and the metabolite is a ligand for ER and liver X receptors.[34] It has been demonstrated that conversion of cholesterol to 27-hydroxycholesterol is required for ER receptor positive-mediated cancer growth, while cancer metastasis is dependent on the liver X receptor.[34] In a study, serum level of 27-hydroxycholesterol was significantly elevated in BC patients with decreased concentration of oxysterol 7α-hydroxylase (CPY7B1), an enzyme required for 27-hydroxycholesterol metabolism.[37]

Obesity and hypertension were greater risk factors of CVD in BC patients on chemotherapy. Greater proportion of the patients were obese and hypertensive. The current results are consistent with previous studies which associated cardiovascular risk factors with BC in patients on chemotherapy.[19,38,39] High caloric intake, physical inactivity, or genetic factors may contribute to the lipid overload reported in the patients.[40] A study has established a link between hypertension and BC, and chemotherapy exposure has been implicated in both onset and severity of hypertension in cancer patients.[41] Another study proposed mechanisms that may connect hypertension to BC, and these include induction of chronic inflammation mediated by adipose tissue, and regulation of cell turnover through blocking and modification of apoptosis.[42]

Reduction in HDL-c level in BC patients is more critical than increasing TG and T. chol levels in increasing AIP in the patients. This claim comes from the contribution of HDL-c in increasing AIP compared to the positive effect of TG levels on AIP. The observation supports the physiological functions of HDL-c and the consequences of accumulated circulatory TG. HDL-c is reported to show antiatherogenic effects, and the functions of the lipid were linked to anti-inflammatory, anti-apoptotic and antithrombotic processes in endothelial cells.[43] Indeed, the role of HDL-c in the removal of fats and cholesterol from cells within the artery wall atheroma, and the transportation of lipids to the liver for excretion or re-utilization has been linked to acute coronary syndrome.[44] Elevated TG and T. chol levels, on the other hand, have been associated with increased risk of cardiovascular disease,[45] and the increase in risk may be attributed to lipids deposition and arterial obstruction to blood flow.

Greater percentage of the patients from this study presented to the health facility with an advanced BC, in keeping with a previous report.[37] Misconception regarding mastectomy, cultural beliefs, and seeking medical care from traditional healers are some of the reasons that have been suggested as the underlying causes of delayed presentation and late diagnosis of BC cases in health facilities in developing countries.[2]

Although an obvious limitation of this study is the relatively small sample sizes that were used and its possible effect on interpretation of the results, we are of the view that the trends presented in this study highlight the risk factors of CVD as comorbidities in Ghanaian BC patients. Also, future studies should consider physical activity and waist circumference of participants in interpreting AIP, since these factors have been shown to contribute to the index of serum lipids abnormalities.

Conclusion

Women diagnosed with BC showed high AIP which correlated with cardiovascular risk factors. Elevated levels of T. chol, TG, and LDL-c, and decreased level of HDL-c were found in the BC patients. Majority of the patients from this study reported to the health facility with an advanced-stage BC. We however acknowledge that our investigation is preliminary, and there is therefore the need for a larger sample size for validation and to fully understand the effect of AIP and cardiovascular risk factors on BC progression.

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