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Research Article

The association between lipid profile and breast cancer in Sudanese women

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Abstract: Breast cancer is the most commonly diagnosed cancer in women worldwide, and is the second leading cause of cancer deaths. Female breast cancer is by far the leading cancer in the Sudan. It accounts for 16.5% of all cancers (30.24% of all female cancers in 2009). Sudan is experiencing rapidly increasing cancer incidences that carry many challenges that are distinctive of developing countries. These include a high incidence of advanced, complicated stage of the disease at presentation, and a high frequency of cancer that is related to a number of risk factors that are required for stabilization. The aim of this study was to find out the association between lipid profile and breast cancer among Sudanese women. This is a retrospective case control study was conducted at Radiation and Isotope Center- Khartoum (Sudan), during the period from January to April 2011. In these study 50 patients (newly diagnosed with breast cancer) their age varied from20 to 80 years with mean age of 48.3 years. There were 50 healthy controls with age group of 20 to 80 years with mean age of 48.6years. Serum Lipid profile was done in these patient's fasting blood samples. Cholesterol, HDL-cholesterol and Triglycerides were measured manual using Spinreact reagent and LDL cholesterol was calculated using Friedewald formula. Serum cholesterol and LDL cholesterol were significantly elevated in patients with breast cancer when compared with controls ($p<0.0001$ and $p<0.0001$respectively).Whereas the levels of HDL cholesterol and triglycerides did not show any significant changes between the patients and the controls. ($p= 0.0637$and 0.05548 respectively). This study concludes that, there is a significant association between elevation of serum total cholesterol and LDL-cholesterol and risk of breast cancer in Sudanese women. A cohort study is highly recommended to document this relationship.
Keywords: Breast cancer, lipid profile, Sudan.

INTRODUCTION

Breast cancer is the most commonly diagnosed cancer in women worldwide, and is the second leading cause of cancer deaths [1]. It is responsible for the death of millions of women worldwide every year. Malignancy of the breast is one of the commonest causes of death in women aged between 40 -44 year [2]. Each year, another 10 million cases occur. As the second most common cause of all deaths, the global mortality from cancer is profound. The cancer problem confronting developing countries is potentially one of crisis proportions. By 2020, nearly 70% of deaths in the looming cancer pandemic will be in economically disadvantaged countries, reflecting survival rates in these regions that are often less than half those of more developed countries[3].

Breast cancer accounts for 0.2% of all cancer cases in men. The aetiology of the disease is unknown, although both low radiation and oncogenic viruses may play a role. A variety of interrelated genetic, hormonal, environmental, sociobiological and physiological factors exert an influence on the development of this disease [4,5].

Breast cancer incidence, mortality and survival vary widely among women of different racial or ethnic background[6].

There is a high mortality and poor survival rate among Africans both in the diaspora and on the mother continent. This has been attributed at least partially to low utilization of breast cancer screening measures to detect tumors at a more treatable stage [7].

Diet may be a factor in the variation of the incidence of breast cancer among women from different racial or ethnic communities [8]. There has been much debate regarding the correlation between the intake of total and saturated fat and the risk of breast cancer [9].

Epidemiological studies have provided evidence on the postulated association between fat intake and breast cancer risk. Ecological studies have also shown that there is strong positive association between estimated per capita fat intake and breast cancer rates internationally and that there is a positive correlation between increase in fat consumption and increase in breast cancer rates over time in a number of countries [9].

Breast cancer in Sudan:

Female breast cancer is by far the leading cancer in the Sudan. It accounts for 16.5% of all cancers (30.24% of all female cancers in 2009). A vast majority of these cancers were from Khartoum, with 41.7% in 2009 followed by El.Gazera state with 10.4% in that year, as reported by the Radio & Isotope Center Khartoum (RICK) [10] . This is the prime center that has prompted these services in Sudan.

In 2009 about 948 patients of breast cancer were presented to the center, with a majority of patients aged 35 to 54 year [10].

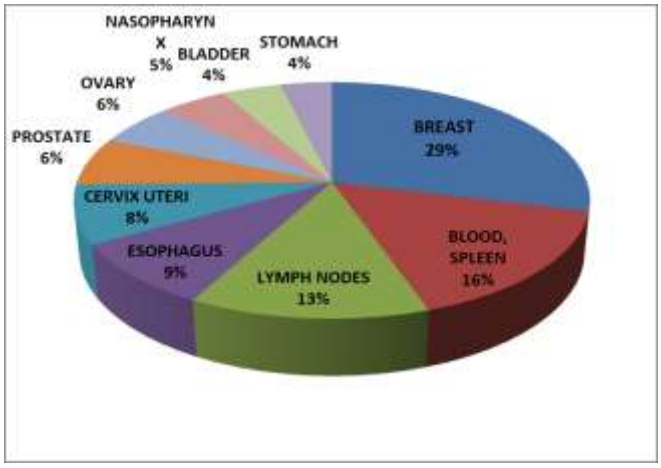

Fig-1: Percentages of common types of cancer registered in RICK 2009.

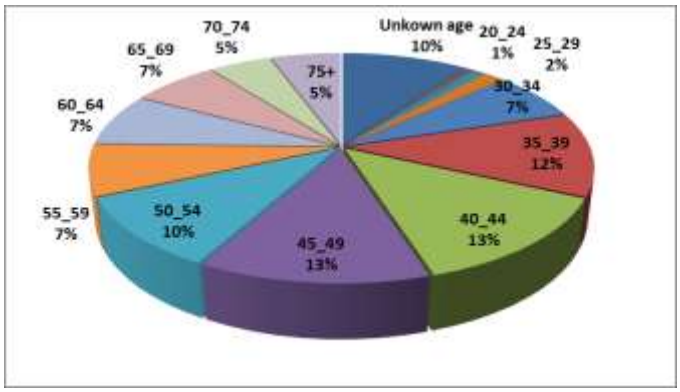

Fig- 2: Breast cancer by age groups registered in RICK in 2009.

Sudan is experiencing a rapidly increasing cancer incidence that carries many challenges that are distinctive of developing countries. These include a high incidence of advanced, complicated stage of the disease at presentation, and a high frequency of cancer that is related to a number of risk factors that are required for stabilization [11].

Awareness and screening programs:

Breast cancer awareness and cancer screening helps detect breast cancer at an early stage, and this would improve the outcome. One of the main problems concerning breast cancer relates to the lack of patients awareness about the disease [12].

In most countries, October is recognized as National Breast Cancer Awareness Month (NBCAM). The primary purpose is to promote screening mammography as the most effective way to save lives by detecting breast cancer at early stages [13].

A clinical or self-breast involves feeling the breast for lumps or other abnormalities. Research evidence does not support the effectiveness of either

type of breast exam, because by the time a lump is large enough to be found it is likely to have been growing for several years and will soon be large enough to be found without an exam[14].

Mammographic screening for breast cancer uses x-rays to examine the breast for any uncharacteristic masses or lumps. The Cochrane collaboration in 2009 concluded that mammograms reduce mortality from breast cancer by 15 percent but also result in unnecessary surgery and anxiety, resulting in their view that it is not clear whether mammography screening does more good or harm [15].

In women at high risk, mammography screening is recommended at an earlier age and additional testing may include genetic screening that tests for the BRCA genes and / or magnetic resonance imaging. Molecular breast imaging is currently under study and may also be an alternative [16].

Risk Factors of breast cancer:

The primary risk factors for breast cancer are sex, age, lack of childbearing or breastfeeding, higher hormone levels, race and economic [17]. The World Cancer Research Fund that high body weight and low physical activity increase the risk of a disease [18].

Smoking tobacco also increases the risk of breast cancer with the greater the amount smoking and the earlier in life smoking begins the higher the risk [19].

Genetic factors usually increase the risk slightly or moderately; the exception is women and men who are carriers of BRCA mutations. These people have a very high lifetime risk for breast and ovarian cancer, depending on the portion of the proteins where the mutation occurs [20].

Additional risk factors include a high-fat diet [21], alcohol intake [22], obesity, and environmental factors such as radiation, endocrine disruptors and shift work. Although the radiation from mammography is a low dose, the cumulative effect can cause cancer [23]. Those with a normal body mass index at age 20 who gained weight as they aged had nearly double the risk of developing breast cancer after menopause in comparison to women who maintained their weight [24].

The association between lipid profile and breast cancer risk in women has been confirmed in different studies in different countries and nations. A study was done in Ghana by William & Kwame between May 2002 and March 2003 on patients with breast cancer and healthy controls with similar age range (25 – 80 years) to carry out a comparative study to investigate the effect of lipid profile and obesity on the risk of a women developing breast cancer [25]. In this study patients and controls were assessed for lipid profile, and BMI (Body Mass Index) .there was a significant increase in BMI, total cholesterol, triglyceride and LDL cholesterol in the breast cancer patients compared to the controls. This study confirms the association between dyslipidemia, BMI and increased breast cancer risk in Ghanaian women [25].

In USA, another study by Tanya *et al* in 1997, examine the relationship between plasma lipid and lipoproteins level, and breast cancer risk in African-American women [26]. The study population comprised 163 African-American women (58 patients and 105 controls) with mean age of 57.2 years. Patients and controls were assessed for lipid profile. There were no statistically significant differences observed in total cholesterol and HDL between patients and controls. But women with breast cancer had significantly higher triglyceride levels compared to the controls[26]. Serum total cholesterol level is not associated with the risk of breast cancer in postmenopausal Korean women by Mina and Yun-Mi song. About 170 postmenopausal Korean women categorized into four groups quartiles of cholesterol levels, were followed up for occurrence of breast cancer from 1993 to 2003. Relative risk was assessed by Cox proportional hazard analysis. A Positive association between cholesterol level and breast cancer risk was found with 31% greater age-adjusted risk of breast cancer in highest cholesterol group, than that in the lowest cholesterol group. The strength of association was reduced slightly but persisted after the adjustment for reproductive and behavioral covariates. However the association further attenuated and the positive trend was no longer significant when BMI was additionally adjusted [27]. Stratified analysis by BMI showed that the risk of breast cancer increased with increasing cholesterol level only in normal BMI group. But the interaction term was not significant [27]. In 2007 Shun *et al* find that Taiwanese women with higher VLDL-cholesterol and lower apoA-I considered as highly risk to develop breast cancer. A total of 150 breast cancer patients before treatment and 71 controls were assessed for lipid profile [28]. The breast cancer patients had significantly lower apoA-I and higher values of VLDL-cholesterol than controls. The findings of the study demonstrate that, higher VLDL-cholesterol and lower apoA-I values were significantly associated with breast cancer [28].

A study was done in Libya in 7th October hospital, Benghazi by El Saiety *et al* [29] , during 2009 and 2010 to identify whether there is an association between alterations in lipid profile and breast cancer risk in a local Libyan subjects. The study showed a significant alteration in serum lipid profile in breast cancer patients in the local Libyan population. There were 40 patients (25 cases are premenopausal and 15 are post-menopausal) with various stages of breast cancer and 21 healthy controls have been conducted in the study. Serum Lipid profile was done in these patients. In the case of premenopausal woman there was

significant rise of total cholesterol and HDL cholesterol whereas triglycerides and LDL cholesterol had not shown any significance. In the postmenopausal group there is significant elevation of serum triglycerides, total cholesterol and HDL cholesterol but LDL cholesterol had not shown any significant difference. There is a striking difference in triglyceride levels in postmenopausal woman from premenopausal woman [29].

MATERIAL AND METHOD

Study population:

This study was carried out at Radiation & Isotope Center-Khartoum (RICK) Sudan.in the period between January 2011 and April 2011.The participation of the respondents was voluntary and informed consent was obtained from each of them. One hundred females were selected for this study of whom 50 were breast cancer patients (ascertained as cases) depending on clinical and histological evidences and 50 were apparently healthy individuals (ascertained as controls).

Patients:

The eligibility criteria for the female patients were the following:

- Newly diagnosed histologically confirmed breast cancer patients.
- Breast cancer patient undergoing treatment with radiotherapy, chemotherapy or hormonal therapy was excluded. Patient on any drugs that may interfere with lipid metabolism and Patients with thyroid diseases were also were excluded.
- It is important to note that all patients with breast cancer who participated in the study were measured and interviewed after surgery and prior to any chemotherapy, radiation therapy, or hormonal treatment regimens.

Control:

Apparently Healthy individuals (well trained for self-examination program). Not taking oral contraceptives or any form of hormonal medication. Without previous history of malignant conditions, particularly breast cancer.

Survey instruments:

A research associate interviewed each eligible individual at the Howard University Cancer Center to obtain demographic, family, and medical history, cigarette and alcohol consumption patterns, and socioeconomic status, based on education and occupation.

Samples collection and preparation:

Participants were asked to fast for overnight. And under a septic condition 2.5 ml venous blood was collected in a plain container, using disposable syringes from the anticubital vein, after cleaning the skin with 70% alcohol. The blood was allowed to clot and serum was separated by centrifugation at 3200 rpm for three minutes and stored at (-80 C) until assayed.

Anthropometric measurements:

The body mass index (BMI) is expressed as kg/m2, where kg is the weight (kilograms) and m the height (meters).

The measurement of weight and height for this index was obtained with subjects in light indoor clothing without shoes.

Biochemical assays:

Serum biochemistry was performed with spectrophotometric method using Genway spectrophotometer and Spinreact assay kits. Assay were carried out as described by the manufacture. Parameters that were determined include: total cholesterol, Triglyceride, and HDL-cholesterol .LDL-cholesterol was determined using Friedewald formula, when the level of triglycerides less than 400mg/dl. All lipids were measured in the medical laboratory of Khartoum university, standardized laboratory, by enzymatic methods.

Statistical analysis:

Descriptive statistics, including means and frequency distributions, were used to describe breast cancer patients and controls and SPSS version 13 was used for analysis of data.

RESULTS

T. Cholesterol:

The mean of T. Cholesterol concentrations for patients and control was 212.86 mg/dl and 148.88 mg/dl respectively. (Table-1). There is significant difference in T. Cholesterol concentrations between patient and control ($p>0.05$). (Table 2)

LDL -cholesterol:

The mean of LDL-cholesterol concentrations for patients and control was 146.25mg/dl and 90.66mg/dl respectively. (Table 1)There is a significant difference in LDL-cholesterol concentrations between patient and control ($p>0.05$). (Table 2)

HDL cholesterol:

The mean of HDL-cholesterol concentrations for patients and control was 39.07mg/dl and 35.36 mg/d respectively. (Table 1). There is no significant difference in HDL between patient and control ($p>0.05$). (Table 2)

Triglycerides:

The mean of triglycerides concentrations for patients and control was 146.25 mg/dl and 90.66 mg/dl respectively. (Table 1). There is no significant difference in T.G between patient and control ($p>0.05$). (Table 2)

BMI:

The mean of BMI for patients and control was 25.02 mg/dl and 28.68 mg/dl respectively. (See table 1) There is a significant difference in BMI between patient and control (p>0.05). (Table 2)

Table-1: mean of age, T. Cholesterol, T.G, HDL, LDL and BMI for patients and control

	breast cancer patients	Control
Age in years	48.30	48.60
T. Cholesterol(mg/dl)	212.86	148.88
T.G (mg/dl)	136.08	115.18
HDL (mg/dl)	39.07	35.36
LDL(mg/dl)	146.25	90.66
BMI	25.02	28.68

Table-2: Results of ANOVA

		Sum of Squares	df	Mean Square	F	Sig.
Age in years	Between	2.25	1	2.25	.01	.90
	Within	14856.5	9	151.59		
	Tota	14858.7	9			
T. Cholesterol (mg/dl)	Between	102336.	1	102336.01	30.46	.00
	Within	329233.	9	3359.52		
	Tota	431569.	9			
T.G (mg/dl)	Between	10920.2	1	10920.25	3.64	.05
	Within	293577.	9	2995.68		
	Tota	304497.	9			
HDL (mg/dl)	Between	344.10	1	344.10	1.30	.25
	Within	25909.5	9	264.38		
	Tota	26253.6	9			
LDL(mg/dl)	Between	77256.2	1	77256.20	24.30	.00
	Within	311549.	9	3179.07		
	Tota	388805.	9			
Body mas index	Between	334.89	1	334.89	12.65	.00
	Within	2593.86	9	26.46		
	Tota	2928.75	9			

Table-3: Test of Homogeneity of Variances, the odds ratio has been adjusted for age

	Levene Statistic	df1	df2	Sig.	Odd ratio	95% CI
Age in years	.389	1	98	.534		
T. Cholesterol(mg/dl)	14.766	1	98	.000	62.4	
T.G (mg/dl)	.092	1	98	.763		
HDL (mg/dl)	2.955	1	98	.089		
LDL(mg/dl)	11.525	1	98	.001	8.6	
Body mas index	.734	1	98	.394		

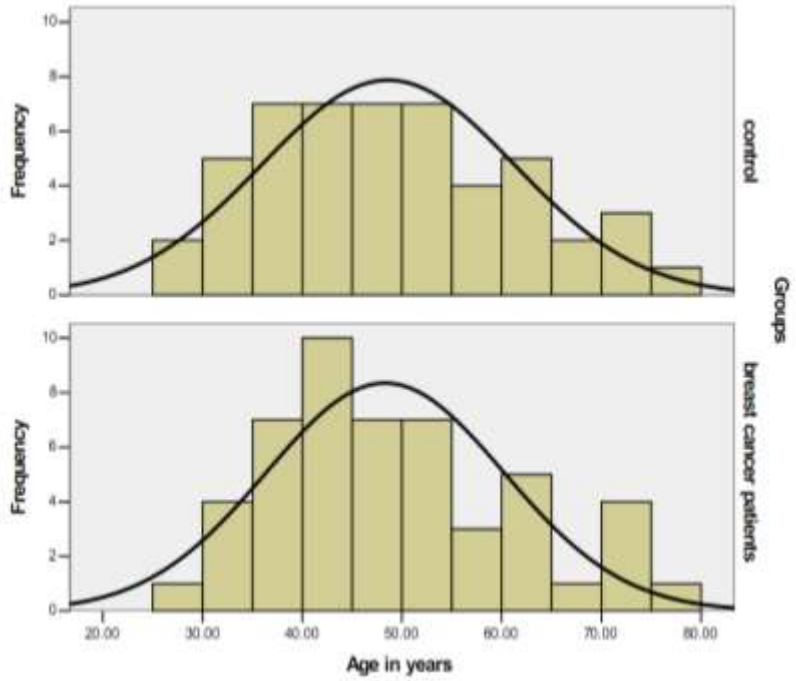

Fig. 3: The histogram of age in years for patients and controls.

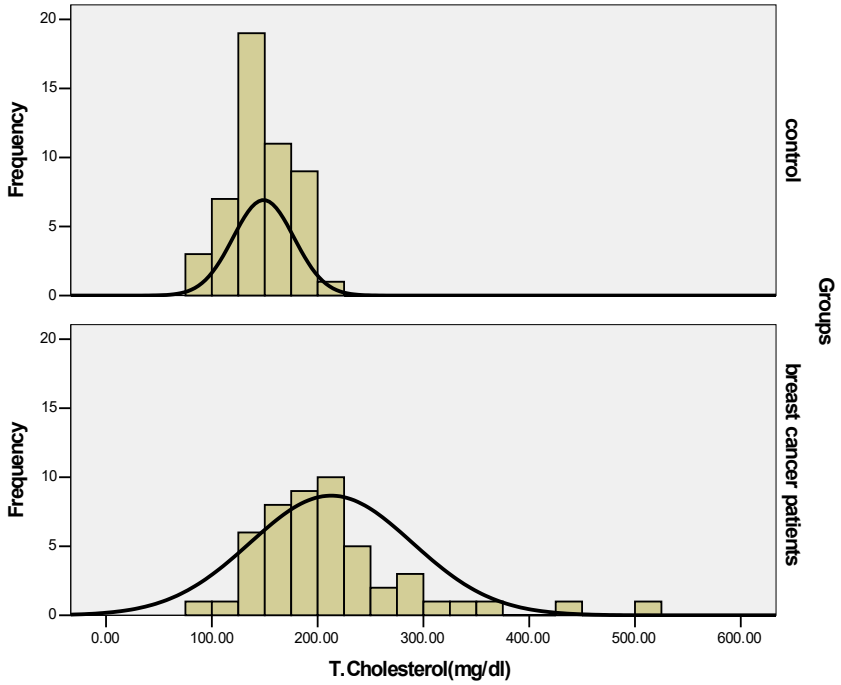

Fig. 4: The histogram of total cholesterol in patients and controls.

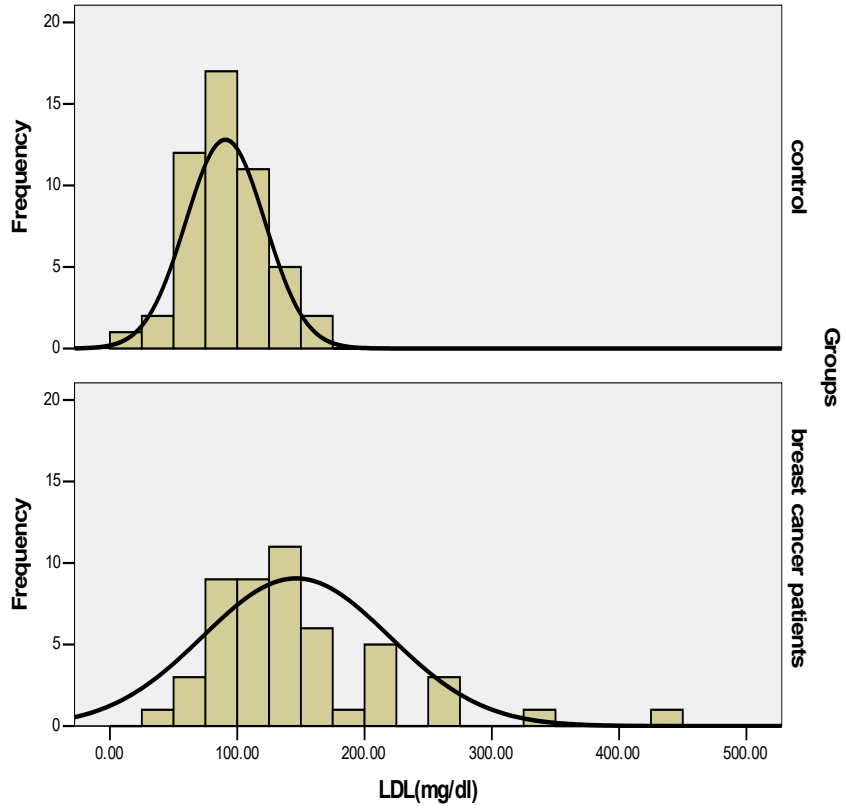

Fig. 5: The histogram of LDL-cholesterol in patients and controls.

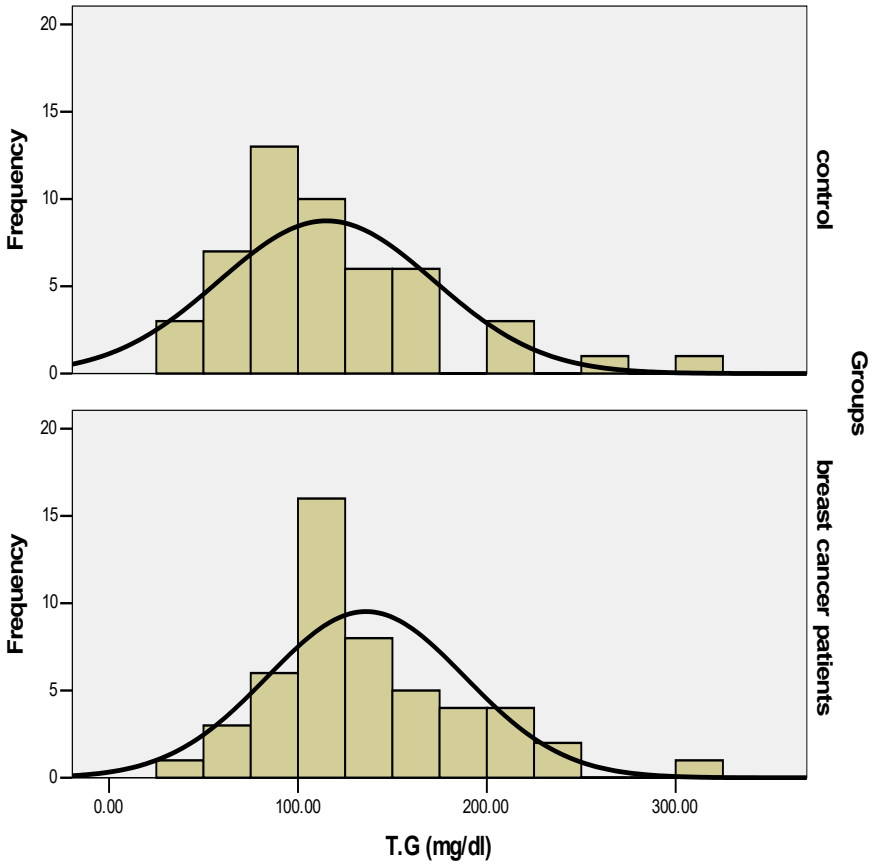

Fig. 6: The histogram of T.G in patients and controls.

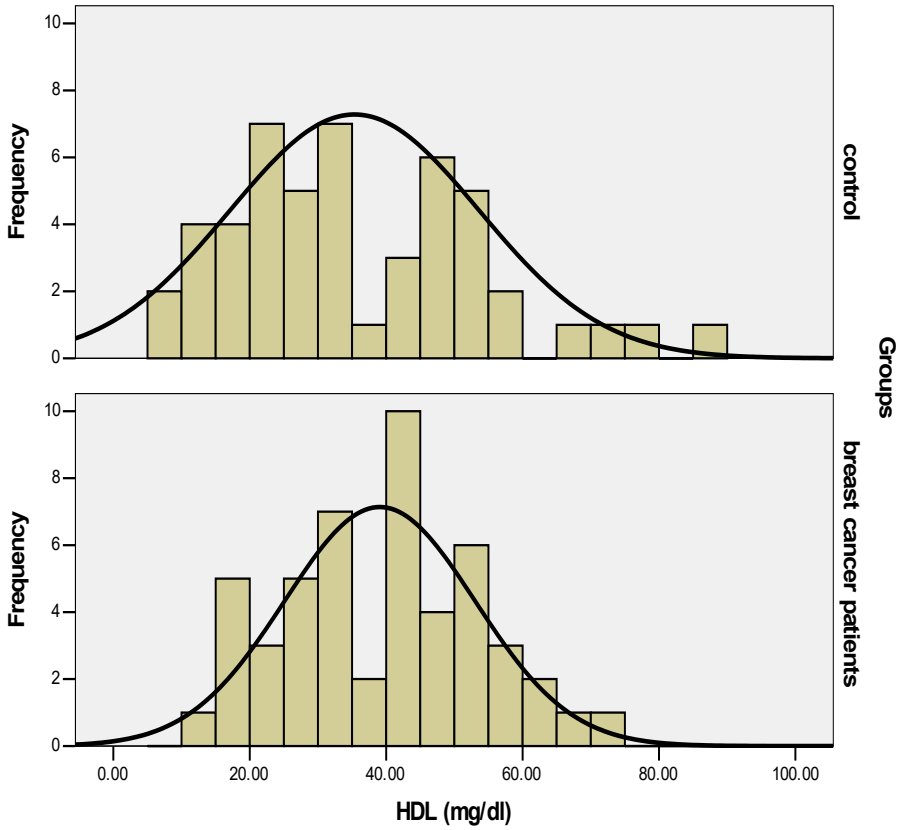

Fig. 7: The histogram of HDL –cholesterol in patients and controls.

DISCUSSION

Breast cancer is one of the commonest causes of cancer mortality in females ; it is responsible for the death of millions of women worldwide every year, is so widespread that it has become a genuine problem for public health. Sudan is experiencing rapidly increasing cancer incidences that carry many challenges that are distinctive of developing countries.

In this study the mean age at diagnosis of breast cancer patients selected at random was 48.30 years (table 1), and the number of the patients was increased with age and reached its maximum higher in age group 40-45 year (figure 3); this is in agreement with the medical records of RICK [10] which reported that the majority of the Sudanese women with breast cancer were found to be within the age group 40-50 years. This situation is rather unfortunate since this is age when women are found to be most active as mothers, wives, etc.

Our study revealed that high levels of total cholesterol was associated with increased breast cancer risk (odd ratio =62.4), after adjustment for age, which agree with the finding of William & Kwame [25] in Ghanaian women and El saiety *et al* [29] in Libyan women, and disagrees with Tanya *et al* [26] in Taiwanese women and Mina & Yan-Mi song [27] in Korean women. This may be due to relatively similar lifestyles and socio-cultural environments of Ghanaian, Libyan and Sudanese women (Africans), which they differs from Asian populations. The significant association between the high levels of T. Cholesterol and breast cancer risk may be attributed to differences in fat metabolism among breast cancer patients and controls.

Our study also find that high levels of LDL was associated with increased breast cancer risk (odd ratio=8.6) which agree with previous study done by William & Kwame [25], and disagree with studies by Tanya *et al*[26] , Mina & Yan-Mi song [27], Shun *et al* [28] and El saiety *et al* [29] .

The elevated serum LDL which is marked susceptible to oxidation this may cause oxidative stress leading to cellular and molecular damage there by resulting in cell proliferation and malignant conversion.

Concerning triglyceride the present study finds that there was no association with breast cancer risk, and these agree with finding of El saiety *et al*[29], and disagree with William & Kwame[25], Tanya *et al*[26], and Shun *et al* [28].

The variations in results of the present study and previous studies mentioned may be due to environmental, behavioral and genetic differences.

CONCLUSION

This study concludes that, there is a significant association between elevation of serum total cholesterol and LDL-cholesterol and risk of breast cancer in Sudanese women. A cohort study is highly recommended to document this relationship.

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