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Evaluation Of Glycosylated Hemoglobin and Lipid Profile, In Breast Cancer Subjects Attending Oncology Clinic in Federal Teaching Hospital Owerri

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Abstract

Breast cancer is a major global health concern with substantial implications for mortality and morbidity particularly in low and middle-income countries. A cross sectional and case control study aimed at evaluating the levels of glycosylated haemoglobin and lipid profile, in breast cancer subjects attending oncology clinic in Federal Teaching Hospital Owerri was carried out. A total of 60 subjects comprising of 30 confirmed breast cancer patients and 30 apparently healthy participants who served as the control were recruited for the study. The study focused on female subjects aged from 18-70 years. Anthropometric data were collected including height, weight and body mass index were calculated. Fluorescent immunosorbent assay technique was used to determine glycosylated haemoglobin. Enzymatic end point technique was used to determine the lipid profile. Data were analyzed with student t-test ad Pearson correlation using the software statistical package for social sciences version 23. Tests with a probability value of $p< 0.05$ were considered statistically significant and the results were expressed as mean $\pm$ standard deviation. Results showed that Height (1.57 $\pm$ 0.05m), Weight (52.20 $\pm$ 4.98kg), and BMI (21.30 $\pm$ 2.15kg/m^2) were significantly lower ($p = 0.0001, 0.0001, 0.0012$) respectively in breast cancer subjects when compared with control (1.68 $\pm$ 0.06m, 67.07 $\pm$ 5.97kg, and 23.78 $\pm$ 2.49kg/m^2) respectively. There were also significant higher ($p = 0.00001$) levels of glycosylated haemoglobin (5.94$\pm$0.50%), Total cholesterol (232.40$\pm$16.16mg/dl), Triglyceride (158.47$\pm$5.48mg/l), and LDL-C (172.18$\pm$ 19.06mg/dl) in breast cancer subjects when compared with control subjects (4.85$\pm$0.48%, 136.37$\pm$24.12mg/dl, 66.47$\pm$28.99mg/dl,and 67.20 $\pm$ 19.35mg/dl respectively. However, there was a significant ($p = 0.00001$) lower levels of HDL-C (30.24$\pm$ 3.48mg/dl) in breast cancer subjects when compared with the control subjects (54.53$\pm$17.40mg/dl). The observed metabolic disturbances in breast cancer patients may be attributed to tumor-induced oxidative stress, insulin resistance, increased biosynthetic demands of proliferating cells and the hosts inflammatory markers in the pathophysiology of breast cancer and underscore their potential utility as adjunctive tools for diagnosis, prognosis and therapeutic monitoring.

Keywords: *glycosylated hemoglobin, lipid profile, breast cancer, owerri.*

INTRODUCTION

The most common disease to be diagnosed and the primary cause of cancer-related death for women worldwide is breast cancer. There are several molecular subtypes of this diverse disease, and each one has its own distinct biological behaviour, prognosis, and response to treatment. The prevalence of breast cancer has been rising in Nigeria, and due to a lack of knowledge, restricted access to screening, and socioeconomic obstacles, late presentation is still a significant problem. [1] One kind of cancer that develops in the breast's cells is called breast cancer. It is among the most prevalent cancers in the world that affect women, yet it can also strike men in rare instances. Breast cancer has a long history; as early as 1600, evidence of the disease was discovered in papyri from ancient Egypt [2].

The papyrus details eight instances of breast tumours or ulcers and suggests cauterisation as a cure. Breast cancer was frequently seen as a deadly condition during the Middle Ages, and early surgical treatments had little effectiveness. Women who received a breast cancer diagnosis experienced severe social rejection and stigma. Significant progress was made in the diagnosis and treatment of breast cancer during the 20th century. In the early 1900s, the concept of radical mastectomy, a surgical surgery including the removal of the breast, underlying chest muscles, and lymph nodes, was introduced by surgeon William Halsted. This method became the standard treatment for breast cancer for many years. During the 1970s and 1980s, research and clinical trials led to the development of less invasive surgical methods, such as lumpectomy and modified radical mastectomy, for the treatment of breast cancer. Radiation therapy and chemotherapy have also grown in importance in the treatment of breast cancer [3]. The knowledge and treatment of breast cancer have advanced significantly since the late 20th century. Treatment for breast cancer has been transformed by developments in targeted medicines, molecular biology, and genetics. Genetic testing and individualised treatment strategies have been made possible by the identification of the BRCA1 and BRCA2 genes, which are linked to hereditary breast cancer. In the battle against breast cancer, the significance of early diagnosis through mammography screening and breast self-examinations has been underlined [4].

The aberrant proliferation of cells in the breast tissue is the hallmark of breast cancer, a major global public health concern. It is the most prevalent cancer in women worldwide, and its effects on morbidity, mortality, and quality of life are significant. Comprehending the history and incidence of breast cancer is crucial for directing health regulations, the distribution of resources, early detection initiatives, and patient care tactics in the area. Due to a number of factors, including socioeconomic disparities, cultural attitudes, restricted access to healthcare facilities, and a lack of knowledge about breast cancer risk factors and symptoms, breast cancer is one of the main causes of cancer-related morbidity and mortality among women worldwide [5]. Understanding the epidemiology and demographic features of breast cancer subjects in the area through thorough background investigations is crucial for effectively addressing the burden of breast cancer. Important details including the incidence, prevalence, age distribution, stage at diagnosis, and survival rates of breast cancer patients in the area have been brought to light by epidemiology research on the disease [6]. According to this research, the incidence of breast cancer is rising worldwide, and many instances are discovered at an advanced stage, which results in worse prognoses and greater death rates. Developing effective prevention and control methods that are suited to the unique needs of the population requires an understanding of the epidemiology of breast cancer [7]. Age, gender, educational attainment, marital status, and socioeconomic status are among the sociodemographic traits of breast cancer patients that have been revealed by demographic research. The need for focused initiatives to lower care obstacles and enhance outcomes for all breast cancer patients in the area is highlighted by these studies, which have found differences in access to healthcare services and cancer treatment among various population groups [8]. Genetic predisposition, reproductive factors, lifestyle choices, environmental exposures, and concomitant illnesses have been the main subjects of research on risk factors for breast cancer in Imo State. In addition to other risk factors like early menarche age, late first full-term pregnancy age, obesity, physical inactivity, and exposure to environmental toxins, studies have indicated that genetic mutations, including BRCA1 and BRCA2, contribute to a subset of cases of breast cancer [9]. In order to lower the incidence and effect of breast cancer, targeted prevention and early detection initiatives can be informed by an understanding of these risk factors.

A thorough assessment of numerous biomarkers and indicators is necessary for the diagnosis and treatment of this illness in order to comprehend its aetiology and course. Particularly, it is crucial to assess the lipid profile, inflammatory marker, haematological parameters, and glycosylated haemoglobin in breast cancer patients in Imo State [10]. Glycosylated haemoglobin, or HBA1c, is frequently used to track long-term glycaemic control in diabetics. It represents average blood glucose levels over time. The relationship between diabetes, glucose management, and breast cancer may be better understood in light of studies that have indicated a possible association between higher HBA1c levels and an increased risk of breast cancer as well as worse outcomes in breast cancer patients. [11] The lipid profile, which includes triglycerides, total cholesterol, LDL cholesterol, and HDL cholesterol, is essential for metabolism and cardiovascular health. Increased risk and progression of breast cancer have been linked to changes in lipid levels. Understanding the metabolic changes linked to breast cancer and how they affect treatment results can be gained by looking into the lipid profile of patients in the Imo state. [12] Understanding the intricate interactions between metabolic variables in the pathophysiology of breast cancer requires a thorough assessment of the lipid profile and glycosylated haemoglobin in breast cancer patients. This study could result in the creation of innovative diagnostic and treatment approaches to enhance the control of breast cancer in this area. In Nigeria and around the world, breast cancer is a major health concern that has a substantial impact on morbidity, mortality, and quality of life. A complex interaction of genetic, environmental, societal, and healthcare system factors contributes to the high burden of breast cancer in the region, as seen by the incidence of the disease in Nigeria. A major health concern in Nigeria is breast cancer, which has a high death rate and few alternatives for early identification and treatment. Cultural stigmas associated with the illness, a lack of infrastructure and resources, and restricted access to healthcare services all contribute to the issue. Furthermore, many cases of breast cancer are diagnosed at advanced stages when treatment options are limited due to a lack of knowledge and education

about the disease and the need of early detection. These elements play a part in Nigeria's high breast cancer death rate, underscoring the pressing need for greater knowledge, instruction, and access to high-quality medical care for women there [13].

Biomarkers including lipid profiles and glycosylated haemoglobin are essential for comprehending these difficulties. There is, however, no data on how this biomarker can be successfully incorporated into standard clinical procedures to track the course of the disease and the effectiveness of treatment in patients with breast cancer. The continuous need to enhance the health and well-being of people with breast cancer serves as justification for this study. Assessing lipid profiles and glycosylated haemoglobin presents a special chance to close the gap between underlying biological mechanisms and clinical symptoms. Healthcare professionals can create focused strategies to treat lingering issues in patients with breast cancer by detecting markers of persisting glucose and cholesterol dysregulations. [14]

Prior research has emphasised the significance of lipid profiles and glycosylated haemoglobin in assessing the immune system and the course of breast cancer. Data on this biomarker in the Nigerian population is, however, scarce, especially when it comes to breast cancer patients at medical facilities like the Federal Teaching Hospital in Owerri. Filling in these gaps will help the global effort to successfully manage breast cancer outcomes by offering important information about the survival status of Nigerians with the disease and aiding in the optimisation of therapy approaches. By offering evidence-based suggestions for tracking and improving breast cancer treatments, the study's conclusions may improve the clinical management of the disease. The project will also help achieve the larger public health objectives of lowering healthcare costs, improving patient outcomes, and reducing comorbidities connected to non-breast cancer. This research is especially pertinent for guiding measures to establish equitable and sustainable healthcare solutions, given the high incidence of breast cancer outcomes in settings with low resources and the global inequities in access to breast cancer subjects.

MATERIALS AND METHODS

Study Area

The study was carried out at the oncology clinic of Federal Teaching Hospital Owerri, Imo State, Nigeria. This is a tertiary referral center providing adequate medical care to individuals with breast cancer at their oncology clinic. Owerri is the capital of Imo State set in South Eastern Nigeria. It consists of three local government which includes Owerri North, Owerri West and Owerri municipal with Federal Teaching Hospital lying in Owerri Municipal.

Ethical Consideration

The ethical approval to use their patients and facilities to carry out this study was obtained from Federal Teaching Hospital, Owerri. Also informed and written consent were obtained from prospective study participants who are eligible for the study.

Study Population

The study population consisted of breast cancer subjects confirmed through biopsy who were currently attending the oncology clinic in Federal Teaching Hospital, Owerri.

A total of sixty (60) subjects were recruited for the study, thirty (30) confirmed breast cancer patients who have been undergoing care for not less than 3 months, and thirty (30) apparently healthy participants who were served as control were recruited for this study. The control subjects were selected among staff and intern medical laboratory scientist of the Federal teaching hospital, Owerri. The study focused on mainly female subjects aged from 18years to 70years.

Selection Criteria

Inclusion Criteria

The study included:

i. Female subjects between age range of 18 to 70 years to ensure that they are full female adults and also not too old.
ii. Subjects with confirmed breast cancer that had attended the oncology clinic for not less than three (3) months.
iii. Subjects who gave consent to participate in the study.
iv. Apparently healthy individuals without breast cancer were served as control subjects.

Exclusion Criteria

The study excluded;

i. Subjects below the age of 18 years and above the age of 70 years.
ii. Subjects without breast cancer except the control group.
iii. Subjects who did not willingly give their consent to participate in the study.

iv. Subjects who have severe and known medical conditions like diabetes, cardiovascular diseases etc. that may interfere with study parameters.
v. Pregnant and Lactating mothers to avoid changes in the study parameters as a result of the pregnancy or lactation.
vi. Individuals who had previous history of cancer other than breast cancer to avoid confounding factors in the study results.
vii. Individuals with substance abuse disorders or severe mental health issues.

Anthropometric Assessment

Height and weight of the subjects were measured in order to calculate the body mass index of each participant.

Body Mass Index (BMI)

This was calculated as follows:

Weight (Kg) divided by square of height in meter squared

$$BMI = \frac{\text{Weight (Kg)}}{\text{Height}^2\ (m^2)}$$

Sample Collection

Blood samples (7mls) were collected aseptically using a 10mls sterile syringe and needle by a trained phlebotomist after an overnight fast of 8-12hours. Two (2mls) of the sample were dispensed into an ethylene diamine tetracetic acid (EDTA) container for the determination of glycosylated hemoglobin. The remaining blood samples were dispensed into a clean plain container and labeled. The samples in the plain containers were allowed to clot after which were centrifuged at 3,000rpm for 5 minutes to be separated and obtained the serum. The serum samples were extracted using Pasteur pipette into the appropriate containers and stored at -20ºC prior to use. The serum samples were used for lipid profile and C-reactive protein.

Laboratory Procedure

All reagents and kits for the work were commercially purchased and the manufacturer's standard operating procedures (SOPs) were strictly adhered to.

DETERMINATION OF GLYCOSYLATED HAEMOGLOBIN (HBA1c)

This was determined using Fluorescence Immunosorbent assay

Principle

The Fine care HbA1c Rapid Quantitative Test was based on fluorescence immunoassay technology, specifically the sandwich immunodetection method. The sample was added to the detection buffer and was mixed well. The sample mixture was added into the sample well of the test cartridge, the fluorescence-labeled detector antibody on the membrane was bonded, to the antigen in the sample and formed immune complexes. As the sample mixture migrated on the nitrocellulose membrane of the test strip by capillary action, the complexes of the detector antibody and antigen were captured to the other antibody that has been immobilized on the membrane. Thus, the more antigen in the sample, the more complexes were accumulated on the membrane. Signal intensity of detector HbA1c antibodies reflected the amount of antigens and Fine care FIA meters showed HbA1c concentrations in the blood samples.

DETERMINATION OF TOTAL CHOLESTEROL

This was determined using Enzymatic End point method as modified by Randox (USA) catalogue number (630910)

Principle

The cholesterol was determined after enzymatic hydrolysis and oxidation. The indicator quinoneimine was formed from hydrogen peroxide and 4-aminoantipyrine in the presence of phenol and peroxidase. A pink colored complex was formed which was measured spectrophotometrically at 500nm wavelength.

DETERMINATION OF TRIGLYCERIDE

This was determined using Enzymatic End point method as modified by Randox (UK) catalogue number (830910).

Principle

Determination of triglycerides after enzymatic splitting with lipoprotein lipase. Indicator is quinoneimine which is generated from 4-aminoantipyrine and 4-chlorophenol by hydrogen peroxide under the catalytic action of peroxidase.

DETERMINATION OF HIGH DENSITY LIPOPROTEIN CHOLESTEROL

This was determined using Enzymatic End point method as modified by Randox Kit (USA) catalogue number (567843)

Principle

During the first phase, LDL, VLDL particles and Chylomicrons generate free cholesterol, which through an enzymatic reaction which produced hydrogen peroxide. The generated peroxide is consumed by a peroxidase reaction with N,N-bis-(4-sulphobutyl)-m-toluidine-disodium (DSBmT) which yielded a colorless product. During the second phase, specific detergent solubilizes HDL-cholesterol. In conjunction with Cholesterol oxidase (CO) and Cholesterol esterase action, Peroxidase (PO) + 4-Aminoantiprine (4-AAP) develop a colored reaction which is proportional to HDL-cholesterol concentration. The absorbance is measured at 565nm wavelength.

DETERMINATION OF LOW DENSITY LIPOPROTEIN CHOLESTEROL

This was determined using Enzymatic End point method as modified by Randox Kit (USA) catalogue number (864321)

The Low density lipoprotein was gotten through calculation from the results gotten from the Total cholesterol, Triglyceride and High-density lipoprotein.

The calculations include:

Calculation

$$LDL = TC - \left(\frac{TG}{5.5}\right) - HDL$$

Statistical Analysis

All data generated in this study were subjected to statistical analysis using statistical package for social science (Spss, Version 23). Student t-test was used to analyze difference between two groups Pearson Correlation coefficient was used to determine the correlation between C-reactive protein and other studied parameters and also the correlation between body mass index and the levels of the studied parameters. The level of significance was set at $P < 0.05$ and all values less than 0.05 were considered statistically significant. Values were expressed as mean ± standard deviation while the results were presented in tables.

RESULTS

Table 1: Mean ± standard deviation values of anthropometric characteristics of breast cancer subjects versus control subjects.

Parameters (units)	Breast cancer subjects (n= 30)	Control (n= 30)	T-value	P-value
Age (years)	49.03 ± 7.66	46.67 ± 9.33	1.07	0.287
Height (m)	1.57 ± 0.05	1.68 ± 0.06	8.40	0.0001
Weight (kg)	52.20 ± 4.98	67.07 ± 5.97	10.48	0.0001
BMI (kg/m^2)	21.30 ± 2.49	23.78 ± 2.49	4.13	0.0012

Key **BMI** = Body Mass Index

$P < 0.05$ = Statistically Significant

$P > 0.05$ = Not Statistically Significant

Table 1 shows mean ± standard deviation values of anthropometric characteristics of breast cancer subjects versus control subjects.

The mean ± standard deviation (SD) values of Age (49.03 ± 7.66years) of breast cancer subjects showed no statistical significant difference ($P = 0.287$) when compared to the mean ± standard deviation (46.67 ± 9.33years) age value of the control group.

However, the mean ± standard deviation values of Height (1.57 ± 0.05m), Weight (52.20 ± 4.98kg), and BMI (21.30 ± 2.49kg/m^2 were lower which were statistically significant ($P = 0.0001$, $P = 0.0001$, $P = 0.0012$) respectively in breast

cancer subjects compared with the mean ± standard values (1.68 ± 0.06m, 67.07 ± 5.97kg, 23.78 ± 2.49kg/m^2) respectively of that of the control group.

Table 2: Mean ± standard deviation values of glycosylated haemoglobin, total cholesterol, triglyceride, HDL- cholesterol, and LDL- cholesterol in breast cancer subjects versus control.

Parameters (units)	Breast cancer subjects (n=30)	Control (n= 30)	T-value	P-value
HBA1c (%)	5.94 ± 0.50	4.85 ± 0.48	8.67	0.00001
TC (mg/dl)	232.40 ± 16.16	136.37 ± 24.12	18.12	0.00001
TG (mg/dl)	158.47 ± 5.48	66.47 ± 28.99	17.08	0.00001
HDL- C (mg/dl)	30.24 ± 3.48	54.53 ± 17.40	7.50	0.00001
LDL- C (mg/dl)	171.18 + 19.06	67.20 + 19.35	20.97	0.00001

Key: HBA1c = Glycosylated haemoglobin, **TC** = Total cholesterol, **TG** = Triglycerides, **HDL-C** = High density lipoprotein – cholesterol, **LDL- C** = Low density lipoprotein – cholesterol,

$P < 0.05$ = Statistically Significant

$P > 0.05$ = Not Statistically Significant

Table 2 shows the mean ± standard deviation values of glycosylated haemoglobin, Total cholesterol, Triglyceride, HDL-cholesterol, and LDL-cholesterol in the breast cancer subjects in breast cancer subjects versus control subjects.

The mean ± standard deviation values of HBA1c (5.94 ± 0.50%), Total cholesterol (232.40 ± 16.16mg/dl), triglyceride (158.47 ± 5.48mg/dl), and LDL-cholesterol (171.18 ± 19.06mg/dl) were higher which were statistically significant (P = 0.00001 in all) in breast cancer subjects compared to the mean ± standard deviation values (4.85 ± 0.48%, 136.37 ± 24.12mg/dl, 66.47 ± 28.99mg/dl, 67.20 ± 19.35mg/dl,) respectively 0f the control group.

However, the mean ± standard deviation value (30.24 ± 3.48mg/dl) of HDL-cholesterol was lower which was statistically significant (P = 0.00001) in breast cancer subjects compared to the control group (54.53 ± 17.40).

DISCUSSION

This study assessed the lipid profile and glycosylated haemoglobin (HbA1c) in order to look at the biochemical changes in patients with breast cancer. Significant variations in these indicators between breast cancer patients and healthy people were found in the research, pointing to underlying metabolic disorders linked to the advancement of breast cancer [15]. According to the current study, breast cancer patients had noticeably higher HbA1c values than healthy controls. This confirms earlier findings that hyperglycemia and cancer risk are related. Long-term glucose levels are reflected in glycosylated haemoglobin, which has been linked to insulin resistance, a disorder that encourages tumour growth by increasing the uptake and utilisation of glucose by cancerous cells [16, 17]. It has been shown that, regardless of diabetes status, a higher HbA1c is substantially linked to a higher risk of postmenopausal breast cancer [18]. Chronic hyperglycemia may intensify inflammatory and oxidative stress responses, which are known to have a role in the development of cancer [19, 20].

According to this study, patients with breast cancer had dyslipidaemia, which is characterised by increased levels of triglycerides, total cholesterol, low-density lipoprotein, and lower levels of high-density lipoprotein. It is believed that enhanced lipogenesis and altered lipid metabolism in tumour cells cause the well-documented lipid abnormalities seen in cancer patients [21]. The elevated levels may be explained by the fact that cancer cells need cholesterol for signal transduction and membrane biogenesis. Furthermore, low levels of HDL impair the body's capacity to combat inflammation and oxidative stress, which accelerates the growth of tumours [22, 23]. The results are further supported by a significant link between hyperlipidaemia and an increased risk of breast cancer.

CONCLUSION

This study found that, in comparison to healthy people, breast cancer patients who visited the oncology clinic had notable changes in their lipid profile and glycosylated haemoglobin (HbA1c). Patients with breast cancer had higher HbA1c levels, which suggested underlying problems with glucose metabolism and potential insulin resistance. With elevated total cholesterol, triglycerides, low density lipoprotein, and decreased high density lipoprotein, the lipid profile revealed substantial dyslipidaemia, indicating accelerated lipid turnover and changed metabolic demands linked to tumour growth.

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