Lipid Profile in breast cancer patients

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Abstract: *Breast cancer is the second commonest malignancy affecting half a million women worldwide each year. Malignancy of the breast is one of the commonest causes of death in women aged between 40-45 years. Dyslipidaemia can affect cell integrity in patients of breast cancer. The aim of this study was to carry out a comparative study to investigate the effect of lipid profile, oestradiol (EST) and obesity on the risk of a woman developing breast cancer. A hospital-based randomized case control study was done among 100 consented women with histological diagnosed breast cancer and 100 control normal healthy women from same age group and demographic data. Their fasting blood samples were analyzed for serum total cholesterol, high-density lipoprotein (HDL), triglycerides and low-density lipoprotein (LDL).*

Significant decreased levels of total cholesterol (p = 0.043) and HDL cholesterol levels (p = 0.036) were observed in breast cancer patients compared to control group. The study has been come up with altered pattern of lipid profile in breast cancer. The reason for hypo-cholesterolaemia may be due to its increased utilization by neoplastic cells for new membrane biogenesis. There was a significant increase in Body Mass Index (BMI) (p = 0.011), triglyceride (p = 0.026) and low density lipoprotein (LDL cholesterol) (p = 0.001) of the breast cancer patients compared to the controls. With the exception of EST that decreased, the lipid profile generally (TG) increased with age in both subjects and controls with the subjects having a much higher value than the control taken in the study. There was also a significant positive correlation between BMI and TC (r2 = 0.022; p = 0.002) and also between BMI and LDL-cholesterol (r2 = 0.031; p = 0.0003). Apart from the LDL-cholesterol that were increased significantly only in the later-age phase in comparison to the controls, BMI, TC and TG were increased in both pre-menopausal and post menopausal phases with HDL-cholesterol remaining decreased or unchanged. This study confirms the association between lipid profile, BMI and increased breast cancer risk.

Keywords: Breast Cancer, BMI, LDL, HDL

1. Introduction

Carcinoma of the breast is the second commonest malignancy affecting half a million women worldwide each year. It is one of the major causes of death among women between 40 and 44 years age group that has become a genuine public health problem. Breast is the most common site of cancer in women. The incidence of breast cancer increases with age, being uncommon below the age of 32 years; however its behaviour varies from slow to rapid progressive disease despite available treatment. Epidemiological studies have revealed that 1 in 50 women in India can develop breast cancer in their lifetime. Risk factors for breast cancer are age, early menarche, Iate menopause, delayed pregnancy, obesity, history of ovarian cancer and hormone replacement therapy. The etiology of the disease is unknown although radiation exposure and oncogenic viruses may play a role. Genetic, environmental, hormonal, socio-biological and dietary factors may also contribute to initiate breast cancer[2]. The etiology of lipid changes associated with breast cancer is multifactorial and relationship of lipid changes to breast cancer is still a subject of controversy. Lipids are major cell membrane components essential for cell growth and division of normal and malignant cell. Mammary tissue is rich in lipids. Some studies have found that malignant proliferation of breast tissue in women is associated with changes in plasma lipid and lipoprotein levels. Recent reports have focused renewed attention on possible role of dietary and endogenous lipids in etiology and prognosis of cancer. Cholesterol, an important factor in etiology of coronary heart disease has recently become focus of attention in the etiology of cancer also[4]. A number of epidemiological studies have shown the increased risk of death from cancer with hypo-cholesterolaemia, although several studies proposed the low levels of cholesterol is a predisposing factor for carcinogenesis[5]. So the present study was planned to investigate the alteration in the lipid profiles of patients with carcinoma of breast in comparison with age matched control women. There is a high mortality and poor survival in breast cancer because of partial to low utilization of breast cancer screening measures to detect tumours at a more treatable stage. Breast cancer primarily affects women with occasional incidence in men and female to male ratio of breast cancer prevalence is reported to be 100:1. Despite the identification of high risk factors, only 35% of breast cancer can explained by known or suspected risk factors, including modifiable behaviours involving diet, overweight, and exercise and alcohol use.

There has been much debate regarding the correlation between the intake of total and saturated fat and the risk of breast cancer. Epidemiological studies have provided evidence on the postulated association between fat intake and breast cancer risk. Migrants from low-to-high-risk countries demonstrate substantial increase in breast cancer risk and corresponding increases in fat consumption. Alteration of oestrogen levels due to changes in gut bacteria by increased fat consumption or obesity with underlying hormonal changes may lead to breast cancer. Obesity is associated with decreased production of sex hormone-binding globulin, resulting in significant increase in the biological active unbound form of oestradiol , which promotes tumour growth in obese women. Increased levels of circulating lipids and lipoproteins have also been associated with breast cancer risk, though published results have been inconsistent.

The aim of this study, therefore, is to find out the effect of lipids and obesity on breast cancer risk . Most of the patients in our study were of high body weight due to varied reasons.

2. MATERIAL AND METHOD-

[1] Serum Lipid Profile was estimated by the following method-

MATERIALS USED -: (CHEMICALS) –

The following chemicals and biochemicals were purchased and utilized.

1. Chema Diagnostica Qualigens fine chemicals A devision of Glaxo India Ltd.

2. Span diagnostic limited, Surat, India.

(A) Cholesterol Estimation Kit (one step method of Wybenga and Plleggi) (Catalog No. – 25924)

(B) HDL Estimation Kit (One step method of Wybenga and Plleggi) (Catalog No.–25924)

(c) Triglyceride Estimation Kit (Enzymatic colorimetric method GPO–PAP liquid stable single regent) (Catalog No. 77034 (6×250 ml)).

OPTICAL MEASUREMENTS -

Linearity-

All routine colorimetric estimations were performed on Spectro-colorimeter 103 and Spectro-photometer 106, and Colorimeter 114, (5-filters) (Systronics, India).

BLOOD COLLECTION - Venous blood samples were collected into Vacationer plain tubes after an overnight fast from the patients. The blood was allowed to clot, centrifuged at 5000 rpm for 20 min within 25 min of sample collection and serum was collected and stored at -80 oC until assayed. Measurement of body weight was done scientifically to the nearest 0.5 kg. The height was measured with a wall-mounted ruler & was done to the nearest 0.5 cm. BMI was calculated by dividing weight (kg) by height squared (m2).

ISOLATION OF SERUM-

The blood samples obtained were stored at room temperature and then centrifuged at $4°$ to $8°$C for 6 to 8 min at 3500 rpm to remove serum from the blood.

ESTIMATION OF TOTAL CHOLESTEROL (mg/100 ml)-

Cholesterol in the blood sample was determined by the one step procedure of Wybenga and Plleggi (Catalog no-25924). This procedure is based on the oxidation of Cholesterol to Cholesterol Oxidase (CHO). This is again oxidized to Cholest 4-en 3-one and Hydrogen Peroxide. Hydrogen peroxide formed reacts with 4-amino antipyrine and 4-chlorophenol in the presence of peroxide (POD) to produce pink colored quinonemine dye. The intensity of the color produced is proportional to the cholesterol concentration in the sample. Briefly the assay comprises of the following reactions-

CE

Cholesterol Esterase-------------> Cholesterol + Fatty Acid

CHOD

Cholesterol +O2----------------> Choleste-4-en-3 one+ H_2O_2

POD

H_2O_2+ 4-AAP + 4- Chlorophenol------->Quinoneimine + H_2O

(Coloured Dye)

Protocol- Reagent 1 - Cholesterol reagent.

Reagent 2 - Standard Cholesterol.

Serum, 0.25 ml and cholesterol reagent 5.00 ml were mixed in a test tube thoroughly and then kept in boiling water bath for 90 seconds. The tube was subsequently cooled to room temperature under running tap water. The optical density (O.D) of the test sample was read using a Spectrophotometer at 560 nm. Standard cholesterol solution was prepared by using 0.25 ml of standard cholesterol solution and was mixed with 5.0 ml of cholesterol reagent and carried through the same steps as applied to serum samples.A blank solution was prepared by using 5.00 ml cholesterol reagent in test tube and carrying the subsequent steps as above. Absorbances of the cholesterol standard and serum samples were then read at 560 nm against the blank. All the reagents of the kit are stable at 2-8°C. As the reagent 1–Cholesterol reagent is corrosive, so mouth pipetting was avoided.

This assay was linear up to 600-mg/100 ml cholesterol value.

ESTIMATION OF HIGH DENSITY LIPOPROTEIN (HDL) mg/100 ml-

HDL in the blood/serum samples was determined by the procedure of Gorden et al (1977). The procedure is based on the principle of production of Hydrogen Peroxide, which finally gives blue color. The optical Density of the developed color is measured at 600 nm, which is proportional to the HDL in the test sample.For the estimation of HDL mg (%) the diagnostic Kit of Span Diagnostics Ltd was used (Catalog No. 25924) based on the one step method of Wybenga and Plleggi. The principle behind the process is that Anti-human β Lipo-protein Ig in reagent A binds to lipoproteins (LDL, VLDL and Chylomicrons) other than HDL. This immuno-complex blocks cholesterol other than HDL. When reagent B is added, only HDL Cholesterol reacts with enzymatic chain (CHE-CO).Hydrogen Peroxide produced by enzymatic reaction yields a blue color complex upon oxidative condensation with F-DAOS and 4-APP in presence of peroxidase, whose absorbance is read at 600 nm, proportional to HDL Cholesterol concentration in the sample.

PROTOCOL-For the estimation, 0.3 ml of fresh/stored serum was used. Firstly, the serum test samples were mixed with 0.3 ml precipitating reagent (Polyethylene Glycol 16%, Additives and Stabilizers). This is used to precipitate Lipo-proteins-LDL and VLDL. Both are mixed well and then kept at room temperature for about 10 minuets. After this, the solution was centrifuged at 2000 rpm for 15 minutes. From this 0.2 ml clear supernatant was taken and 5.0 ml Cholesterol Reagent was added to it. The contents were mixed well and then the tube was kept immediately in the boiling water bath for 90 seconds and cooled immediately to room temperature under running tap water. The optical density was read on a spectrophotometer at 600 nm. The same procedure was applied for preparing standard solution. The developed color was stable at least 10 minutes. It was kept away from strong light sources.

Linearity - This assay was linear up to 400 mg/100 ml levels.

ESTIMATION OF TRIGLYCERIDE (TG) mg/100 ml- Triglycerides in the blood/serum samples were determined by the procedure of Bucolo David (1973). The procedure is based on the principal of production of red colored dye, Quinoneimine, which absorbs sharply at 510 nm. Briefly the assay comprises to the following reactions-

Lipase (serum/microbial)
1) Triglyceride---------------------->Glycerol + Fatty Acids

Glycerol Kinase
2) Glycerol +ATP-------------->Glycerol 3- phosphate + ADP

Glycerol Phosphate Oxidase
3) Glycerol-3-phosphate+O_2---->Dihydroxy acetone phosphate+ H_2O_2

Peroxidase
4) H_2O_2+4-AAP+4-chlorophenol------------->Quinoneimine+H_2O
(Colored Dye)

For the estimation of Triglyceride (mg/100 ml) the diagnostic kit of Chema diagnostics Ltd Glaxo–was used which was azide free (catalog No. 77034) (6× 250 ml) was used. Triglycerides in the samples are hydrolyzed by microbial lipases to glycerol and free fatty acids (FFA). Glycerol is phosphorylated by Adenosine 5-triphosphate (ATP) to glycerol -3-phosphate (G-3-P) in a reaction catalyzed by glycerol-kinase (GK).G-3-P is oxidized to dihydroxy-acetone phosphate (DAP) in a reaction catalyzed by the enzyme glycerol phosphate oxidase (GOP).In this reaction hydrogen peroxide (H_2O_2) is produced in equimolar concentration by the level of triglyceride present in the sample.H_2O_2 reacts with 4-Amino-antipyrine (4-AAP) and 4-chlorophenol, in a reaction catalyzed by peroxidase (POD).The result of this oxidative coupling is Quinoneimine, a red colored dye. The absorbance of this dye in solution is proportional to the concentration of triglycerides in the sample.

The reagents of the kit were supplied already in liquid, ready to use form. The kit for in vitro diagnosis was used.

PROTOCOL- Serum, 0.02 ml was mixed with 2 ml reagent. Both were mixed well and incubate at 37° C for 5-8 min. The optical density was read at 510 nm in spectrophotometer. The same procedure was carried out for preparing standard solution. The absorbance of test and standard solutions were read at 510 nm against blank reagent.

This assay was linear at least to 1000 mg/100 ml Triglyceride value.

CALCULATIONS-The following formula was used to determine the mg/100 ml value of the following-

(A) TOTAL CHOLESTEROL-

(Normal level -130-250 mg/100 ml in adults)

$$\text{Serum Cholesterol (mg/100 ml)} = \frac{\text{Optical density of Test (Ax)}}{\text{Optical density of Standard (As)}} \times 200$$

(B) HIGH DENSITY LIPO-PROTEIN (HDL)-

(Normal level - 35-75-mg/100 ml for adult female)

$$\text{HDL (mg/100 ml)} = \frac{\text{Optical density of Test}}{\text{Optical density of standard}} \times 50$$

(C) ESTIMATION OF TRIGLYCERIDE (TG)-

(Normal level = 10-190 mg /100 ml for adult woman)

$$\text{TG (mg/100 ml)} = \frac{\text{Optical density of test}}{\text{Optical density of standard}} \times 200$$

(D) CALCULATION OF LOW-DENSITY LIPOPROTEIN (LDL mg /100 ML)

For this the **fw** formula was adopted =

(Normal Range = 30-60 mg/100 ml)

(A) Triglyceride mg/100 ml = **x**

(B) X + HDL mg/100 ml = **y**

(C) Total cholesterol –**y** = **LDL** (mg /100 ml)

ESTIMATION OF TOTAL OESTRADIOL-The serum samples were collected the and given to the collection centre of Rainbaxy Lab , Bilaspur, The results were collected thereafter , 82% of the Serum Oestradiol samples analysis cost was bear by the subjects themselves.

STATISTICAL METHODS USED IN THE ANALYSIS OF DATA- For statistical analysis of data the package SPSS-STAT was used. Mean, Standard Deviation, Degree of Correlation-all are calculated by using this package, butt Value –Level Of Significance was manually calculated on the basis of two sample means by using the formula-

$$S = \frac{(m_1)^2 + (m_2)^2}{\sqrt{n_1 + n_2 - 2}}$$

$$t = \frac{(m_1)^2 - (m_2)^2}{S} \times \frac{\sqrt{n_1 \times n_2}}{n_1 + n_2}$$

The data were compiled in MS excel worksheet and subsequently analysed in SPSS software, version 10.0. Frequency, mean, standard deviation were calculated and data were analyzed by applying Student's unpaired 't' test. P- Value <0.05 was considered to be statistically significant.

STUDY AREA - Bilaspur city and nearby area , Chattisgarh.

PARTICIPANTS- The following two groups of participants were selected for the present study –

A.CONTROL GROUPS- Human female volunteers of 50 with age (32-60 years) were picked up to serve as participants. The total numbers of controls was 100 females. None of the participant had any family history of any cardiac problems. None of the women studied reported ever received any hormonal treatment. The mean age of the control group was 34 years; their average weight was 52 kgs. They belonged to different economic status, from higher income group (monthly income more than 20,000/- month) to lower income group (2000/- month) and they were of different religions, their dietary habits very much varied.

B.EXPERIMENTAL GROUPS-This group comprised of 50 breast cancer patient women (time after diagnosis–2 to 6 years). They belonged to the age group of 32 to 60$^+$years. Their average age was 46 years. They were contacted mainly from Dr -------The average body weight was 56 Kgs. The experimental group also belonged to women of different economic status, (from higher to lower income group), different religions, with different dietary habits.

3. Observations-

The findings about demographic characteristics have been shown in Table 1. Cases showed a younger age at menarche, older age at menopause and low parity as compared to controls.

Family history of breast cancer in first degree relatives was positive in 13 patients (26%) and tobacco consumption in 12 (24%) cases. Anthropometric measurement BMI was found in normal range in the control group, but in higher side in case - group. Table 2 shows the mean values with SD and range for total cholesterol, triglycerides, HDL and LDL cholesterol for control and case groups. Analysis of the data showed that among various lipid parameters serum total cholesterol (p-0.043) and HDL cholesterol (p = 0.036) levels significantly decreased (p<0.05) whereas serum triglycerides levels increased significantly (p = 0.06) in breast cancer patients as compared to control group. LDL levels in cases were found at higher side of normal range.

The breast cancer patients have significantly higher BMI similar to overweight individuals with decreased levels of total cholesterol, increased levels of triglycerides and low density lipoprotein as compared to the control group (Table 1). Fifty five percent of the breast cancer patients had their serum total cholesterol lesser or equal to the lower limit of the reference range (200 mg/dl) whilst 20% of the controls had their level significantly lower or equal to the extreme lower limit of the reference range. With advanced age (Table 2), there was higher lipid profile as reflected by increase trend in TG and LDL-cholesterol in the breast cancer patients up to age of 60 years and in the control group of 60 years of age. It has been found in this study, that the breast cancer patients have higher values in lipid parameters except Total Cholesterol and HDL-cholesterol than the control group at corresponding age group. There is minimal change in the level of HDL-cholesterol as age increased for both breast cancer patients and the control (Table II). Even though, oestradiol level decreases as the age progresses in both the breast cancer patients and the control group, however breast cancer patients have lower level than the control at the corresponding age . BMI shows little variation with age in both the breast cancer patients and the control group. However, breast cancer patients have slightly higher BMI than their corresponding control at the various age groups.

Table 1 – Demographic Characteristics of the Study Population		
Parameters	Control (n = 50)	Cases (n = 50)
Age in years [range (mean +SD)]	40 – 70 (44.5+8.1)	40 – 70 (48.2 + 9.3)
Family history of breast cancer (No. of cases)	1	13
Basal metabolic rate in kg/m2 [mean + SD(range)]	23.2 + 4.8 (19.1 - 27.8)	29.8 + 3.5 (18.5 - 25.3)
Age at menarche in years [mean + SD(range)]	13.2 + 1.4 (11.3 - 15)	11.8 + 0.7* (11 - 12.7)
Age at menopause in years [means + SD(range)	41.6 + 3.7 (39 – 44)	45.3 + 4.3 (41 – 49)
Parity (range)	2.6 (1 - 5)	1.2* (0 - 3)

Tobacco consumption	(No of cases)	7	12

*p<0.05 when compared to control

Table 2 – Biochemical Parameters of Whole Study Population					
Control/ cases	Total Cholesterol (mg%)	Triglycerides (mg%)	HDL (mg%)	LDL (mg%)	EST (mg/dl)
Control :					
Mean	162.6	110.0	46.2	126.9	36.80
+ SD	18.4	19	7.2	32.2	39.30
Range	151 – 234	80 – 150	36 – 58	60 – 180	38.23-39.43
Cases :					
Mean	132.3*	166.8*	28.5*	162.2	32.30
+ SD	6.9	8.1	2.5	21.3	35.50
Range	102 – 148	152 – 231	22 – 32	70 – 190	35.50-37.30

*p<0.05 when compared to control

LONGITUDINAL CHANGES IN LIPID PROFILE OF CASES

	3 Months	p	12 months	p	18 Months	p	24 months	p
Change from Base Line	Mean+ SE		Mean+ SE		Mean+ SE		Mean+ SE	
Cholesterol Change	- 9.1+ 6.2	NS	−28.9 ± 4.8	<0.0001	−19.0 ± 7.3	0.010	−29.3 ± 6.3	<0.0001
HDL Change	- 3.2+ 6.2	NS	−2.7 ± 2.2	<0.0001	−5.3 ± 2.5	0.040	−3.0 ± 2.7	NS
LDL Change	+ 5.1+ 4.2	NS	−7.7 ± 5.4	NS	−7.5 ± 6.8	NS	−2.3 ± 5.1	NS
Triglyceride Change	+ 22.3.+16.2	NS	+13.4 ± 9.2	NS	−9.9 ± 16.3	NS	+22.0 ± 10.4	0.040

4. Discussion-

In this study, 100 women including 50 breast cancer patients and 50 controls were assessed to find out the lipid profiles. We observed hypocholesterolaemia with decreased HDL cholesterol and increased triglycerides in breast cancer patients. Cholesterol and triglycerides, important lipid constituents of cell carry vital physiological functions like maintenance of the structural and functional integrity of all biological membranes. In some malignant diseases, blood cholesterol undergoes early and significant changes. Low levels of cholesterol in the proliferating tissue and in blood compartment could be due to carcinogenesis. Direct lipid lowering effect of tumor cells or some secondary malfunction of the lipid metabolism may contribute to hypocholesterolaemia. The present finding confirms the results of De Alvarez and Goodell who studied lipoproteins in patients with gynecological cancers. Barclay et al also showed decreased lipoprotein levels in breast cancer patients. Schatzkin et al and Chyou et al have observed an inverse trend between cholesterol and cancer. Raste and Naik and Patel et al also observed low levels of total cholesterol, HDL and increased triglycerides in breast cancer patients. The results are strengthened by the present study. Cholesterol is an important constituent of lipoprotein fractions like LDL, HDL and VLDL. The pathogenesis of the decreased cholesterol and

HDL is not known exactly. It could be due to decreased synthesis or increased catabolism. What leads to hypocholesterolaemia is exactly not known. Cholesterol synthesis by liver could be inhibited by tumour metabolites. It can be presumed it either due to carcinogenesis or predisposing factors. Low HDL cholesterol is an additional predictor of cancer and it may be mediated by utilization of cholesterol for membrane synthesis. Significant increase in triglycerides is in contrast to Alexpoulos et al who reported no statistical significance, but it is in accordance with Owiredu et al. Decreased levels of cholesterol and HDL, cholesterol and increased level of triglycerides may be especially useful in early detection of cancer. The inverse association between cholesterol, HDL cholesterol and breast cancer may reflect a physiological response to early stage or cancer. Rose and Shipley reported 66% higher mortality rate due to cancer in patients with low cholesterol than in high cholesterol levels. So it may be a useful indicator for initial changes occurring in neoplastic cells. Hazards of decreased cholesterol levels remain still unclear. The precise reason for malignancy associated hypo-cholesterolemia remains obscure.It has also been hypothesized that the adult weight gain or increased BMI is a strong predictor of breast cancer risk. Several other case-control and prospective studies have also reported that elevated total serum cholesterol is associated with increased breast cancer risk. The higher BMI in the breast cancer patients as

compared to the control and the significantly raised BMI level in the breast cancer patients during the pre- and post-menopausal period, indicates a strong association between increased BMI and breast cancer risk. This observation is in agreement with the findings of previous studies. The significantly increased level of TC in the breast cancer patients compared to the controls and its significant positive correlation with BMI in these patients indicates that, there is an association between TC, BMI and breast cancer risk. This study has also demonstrated a 16% increase in total serum cholesterol levels of the premenopausal patients compared to the control group which is in agreement with a 15% increase in total serum cholesterol levels for premenopausal patients reported by other studies by . This study also demonstrated a significant difference between total serum cholesterol levels of cancer cases and the controls.

However a major link has been established between cell growth and cholesterol biosynthesis. If cholesterol synthesis is inhibited and no exogenous cholesterol is available, cell growth will be blocked . Cholesterol inhibition, either by decreasing cholesterol availability (lowering of plasma cholesterol) or by decreasing intracellular cholesterol synthesis could inhibit tumor cell growth and possibly prevent carcinogenesis . It has been reported in this study that the serum triglyceride in postmenopausal cancer patients were higher than the control. The percentage increase of triglyceride levels (22%) in this study is consistent with an earlier report of 22% [10], but much lower than the percentage increase of triglyceride levels (31%) reported some were else [10]. On the other hand, there was no significant change in serum triglyceride levels between the premenopausal patients and controls. Though elevated serum triglyceride levels in premenopausal breast cancer patients have been reported [20]. No significant difference was observed in HDL-cholesterol levels between the breast cancer patients and controls in this study; however LDLcholesterol levels increased between the patients and the controls. . The elevated serum LDL-cholesterol,which is more susceptible to oxidation, may result in high lipid peroxidation in breast cancer patients. This may be cause of oxidative stress leading to cellular and molecular damage thereby resulting in cell proliferation and malignant conversions. Several studies have investigated the role of diet especially dietary fat, in the etiology of breast carcinoma, but its significance has remained controversial [21,22]. Although, the relationship between diet and serum lipid levels is complex, diets containing a large amount of saturated fats may lead to higher lipid levels, particularly cholesterol [14]. Elevated lipid levels precede the development of obesity and breast cancer and thus, may have an etiological or predictive significance [21].Obesity is not only associated with decreased production of sex hormone binding globulin [7] which results in a significant increase in biologically active unbound form of oestradiol, but also results in the increased production of oestrone, which is produced by aromatization of androstenedione in peripheral adipose tissue. It therefore leads to an overall increase in the active levels of circulating oestrone and oestradiol which may promote the growth and metastatic potential of breast tumor in larger women. In this study, no significant change was observed in oestradiol levels between the premenopausal cases and the controls. During the postmenopausal phase however, this study demonstrated a significant increase in the level of oestradiol compared to the controls. There was a 50% increase in oestradiol which is much higher than the 30% reported else were [23], earlier data with

regard to total oestrogens also suggest increased levels of oestrogen in breast cancer patients [24,25]. It has been hypothesized that the risk of breast cancer is essentially determined by the intensity and duration of exposure of breast epithelium to oestrogen [26]. Oestrogen, like all other steroid hormones is able to cross cell membranes and bind in a specific manner to their receptors to form a specific hormone-receptor complexes. These complexes bind to specific DNA sites in oestrogen dependent tissues called Hormone Responsive Elements and cause increased transcription of various genes.The end result is increased cell growth,proliferation and protein synthesis and enzyme synthesis [27], with concurrent carcinogenesis. The findings of this study confirm the detrimental effect of increased BMI or obesity on breast cancer risk. Obesity leads to overall increase in the active levels of circulating oestrone and oestradiol, which may promote the growth and metastatic potential of breast 30tumors in obese women. The results also indicate an increased risk of breast cancer with dis-lipidemia especially during the postmenopausal stage.

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