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Lipid Profile in Patients of Breast Carcinoma

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Abstract: ***Background: There are multiple risk factors for occurrence of breast carcinoma among women. However, the cause and effect relationships between cholesterol and increased cancer risk remain unclear. This has been addressed in multiple retrospective clinical studies although these have yielded equivocal results, with many finding no relationship, some indicating a protective effect, while others implicating cholesterol as a significant risk factor. This descriptive study was aimed to study the relationship between prevalence of dyslipidemia among patients with breast carcinoma. Conclusion: We observed that there is a higher instance of breast cancer patients with post-menopausal status to have high total cholesterol, however our study did not reveal any association of post – menopausal women with elevated Triglycerides, LDL or lower HDL levels.***

Keywords: Breast, Cancer, Dyslipidemia, Cholesterol, Menopausal

1. Introduction

Breast is anatomically a modified sweat gland. Main function being secretion of milk to feed the new born. There are continuous hormonal changes in the organ. From puberty to death the female breast is subjected to constant dynamic changes related to menarche, menstrual changes, pregnancy, lactation and menopause. These rapid changes predispose the breast tissue to many physiological changes.
Breast cancer is the most common female cancer worldwide [1]. Global burden of breast cancer will increase to over 2 million new cases/year by 2030. The incidence of breast cancer is rising in India (22.9%) and is now the second most commonly diagnosed cancer in women after cervical cancer. The age-standardized mortality rate for breast cancer in India was found to be 11.1/100,000 where globally it was 12.5/100,000 according to International Agency for Research on Cancer report in 2008 [2]. 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.

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.The etiology of the disease is unknown although risk factors are gender, age, genetic factors, family history, dense breast tissue, menstrual periods, breast radiation early in life, pregnancy at late ages, use of birth control pills, hormone therapy, not breastfeeding, alcohol, obesity, lack of exercise, and induced abortion[3].

The risk is greater if a woman attains menarche before twelve years of age. Menopause after fifty-five years of age has an increased risk of ovarian, breast, and uterine cancers. Genetic, environmental, hormonal, socio-biological and dietary factors may also contribute to initiate breast cancer. 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 [4-11].

There is a high mortality and poor survival in breast cancer because of partial to low utilization of breast cancer screening measures to detect tumors 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 be explained by known or suspected risk factors, including modifiable behaviors involving diet, overweight, and exercise and alcohol use [12].

Surgical management is a fundamental treatment of breast cancer and in the majority of cases is the first mode of therapeutic intervention. Complications from breast surgical procedures could be costly and may delay subsequent adjuvant therapies. Complications such as Post-Operative Wound Infection, Hematoma, Seroma, Lymphedema and/or Mastectomy Skin Flap Necrosis may arise [13-15].

The aim of the study was to study the prevalence of lipid profile along with the clinical profile of patients with breast carcinoma, which will add to the existing pool of data. This information will help formulate better screening procedures thereby reducing the morbidity and mortality associated with carcinoma of the breast.

2. Material and Methods

This hospital based prospective descriptive study was carried out at a Tertiary Care Teaching Hospital in Pune from November 2017 to November 2019. 70 cases of breast carcinoma were included in the study period. The study group comprised of female patients,with age more than 18 years, reporting to Surgical OPD with inclusion criteria of all cases of histologically proven breast carcinoma by F.N.A.C. or Biopsy.

The exclusion criteria were as follows:
Any female who is

- Pregnant.
- Previous history of Carcinoma Breast, on treatment.
- On Hormone Replacement Therapy.
- On drugs altering lipid metabolism.

2.1 Methodology

- The study was commenced after obtaining written informed consent from the patients for the study.This data was obtained from patient's hospital documents, personal interview/questionnaire, with special emphasis on age, BMI, Menstrual status (age at Menarche/Menopause), Clinical presentation (signs & symptoms), duration of symptoms & Parity.
- Diagnosis of carcinoma breast was established on the basis of clinical features, and tissue histopathology.
- Routine and special investigations were carried out in each patient to judge her general status and evidence of distance metastasis.

2.2 Data Collection and Analysis

- The initial data was collected in the approved proforma.
- After collecting the data, it was tabulated in Microsoft Excel Worksheet for comparison and analysis.

2.3 Statistical Analysis

- The statistical significance of inter-group difference of geometric means of continuous variables is tested using independent sample t test or unpaired t test (for two groups) and using analysis of variance (ANOVA – Linearity trend statistics) (for more than two groups). The underlying normality assumption was tested before subjecting the study variables to the 't' test and ANOVA.
- p value < 0.05 was considered statistically significant.
- The entire data is statistically analyzed using Statistical Package for Social Sciences (SPSS ver 21.0, IBM Corporation, USA) for MS Windows.

3. Results

Total 70 female patients were studied with diagnosis of Carcinoma Breast (Table 1). Our study found that nearly 62.86% of the patients had elevated total cholesterol, with 8.57% having elevated levels ofLow Density Lipoproteins (LDL) and 7.14% having low levels of High Density Lipoproteins (HDL) and 62.86% having elevated triglycerides. The cut off ranges for dyslipidemia were considered as >199mg/dl for elevated cholesterol, >149 for triglycerides, <40mg/dl for low HDL and >129mg/dl for elevated LDL-Cholesterol. The mean cholesterol levels in the study participants were 216.9 mg/dl, triglycerides were 159.8 mg/dl, LDL cholesterol was 100.7 mg/dl and HDLcholesterol was 46.8 mg/dl (Table 2).

Table 1: Demographic Data of the Patients

Parameters	*No. of Patients (n=70)*	*Percentage*	
Age			
≦35	10	14.29%	
36-45	12	17.14%	
46-55	20	28.57%	
56-65	22	31.43%	
≧65	6	8.57%	
Age of Menarche			
12 y	5	7.14%	
13 y	10	14.29%	
14 y	37	52.86%	
15 y	12	17.14%	
16 y	6	8.57%	
Age at first child			
17-20	12	17.14%	
21-23	38	54.29%	
24-27	13	18.57%	
No children	7	10.00%	
Parity			
P0	7	10.00%	
P1	4	5.71%	
P2	40	57.14%	
P3	15	21.43%	
P4	4	5.71%	
BMI			
Underweight	0	0.00%	
Normal weight	35	50.00%	
Over-weight	30	42.86%	
Obese	5	7.14%	
Menopausal Status			
Pre-menopausal	28	40%	
Post-menopausal	42	60%	p=0.01796
Quadrant of cancer involvement			
Upper outer	36	51.43%	
Upper inner	13	18.57%	
Lower outer	12	17.14%	
Lower inner	7	10.00%	
Central	2	2.86%	
Staging			
IA	1	1.43%	
IIA	24	34.29%	
IIB	21	30.00%	
IIIA	15	21.43%	
IIIB	6	8.57%	
IIIC	3	4.29%	
Symptoms			
Lump	66	94.29%	
Pain	33	47.14%	
Ulcer	16	22.86%	
Nipple Retraction	13	18.57%	
Discharge	4	5.71%	
Duration (in months)			
<1	4	5.71%	
1 to 3	16	22.86%	
3 to 6	25	35.71%	
6 to 12	19	27.14%	
>12	6	8.57%	

Table 2: Lipid Profile of the Patients

Parameters	*No. of Patients (n=70)*	*Percentage*	
Elevated Total Cholesterol (≥199 mg/dl)	44	62.86%	
Elevated Triglycerides (≥150mg/dl)	44	62.86%	
Elevated LDL (≥130mg/dl)	6	8.57%	
Decreased HDL (<40 mg/dl)	5	7.14%	
	Mean	***Standard Deviation***	
Total Cholesterol	216.9	36.1	
Triglycerides	159.8	24.6	

LDL – Cholesterol	100.7	19.0	
HDL – Cholesterol	46.8	5.2	
Total Cholesterol	***Normal***	***Abnormal***	
Pre-menopausal	15	13	
Post-menopausal	11	31	p=0.021
Triglycerides	***Normal***	***Abnormal***	
Premenopausal	13	15	
Post-menopausal	13	29	p=0.189
Low HDL	***Normal***	***Abnormal***	
Premenopausal	27	1	
Post-menopausal	38	4	p=0.3434
High LDL	***Normal***	***Abnormal***	
Premenopausal	27	1	
Post-menopausal	37	5	p=0.222

4. Discussion

Our study noted a significant association between elevated cholesterol in relation to the menopausal status (Figure 1). Breast cancer patients with post-menopausal status have a higher instance of having hypercholesterolemia when compared to pre-menopausal patients. However, the current study did not find a significant association between elevated LDL, reduced HDL and triglycerides in pre- and post-menopausal women.

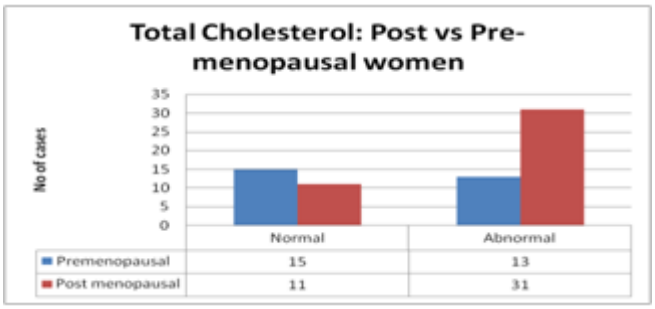

Figure 1: Total Cholesterol levels in Post vs Premenopausal Women

One of the first observations linking cholesterol and cancer was made in 1909 in a study which noted the presence of crystals of a "fatty nature" in tumor sections prepared without alcohol fixation [16]. However, over a hundred years later the cause and effect relationships between cholesterol and increased cancer risk remain unclear. This issue has been addressed in a large number of retrospective clinical studies although these have yielded equivocal results, with many finding no relationship, some indicating a protective effect, while others implicating cholesterol as a significant risk factor [17].

Some of these discrepancies may relate to the differences in the impact of cholesterol on different subtypes of cancer; a possibility that needs to be explored further. Among the most interesting results are those from a recent cohort study in which it was demonstrated that patients with established breast cancer had higher LDL-cholesterol and Very Low Density Lipoproteins (VLDL) -cholesterol, although no association with HDL or total cholesterol and breast cancer was evident [18].

It was also demonstrated, in another study, that when adjusted for obesity, dietary consumption of cholesterol was strongly associated with increased breast cancer risk in postmenopausal but not in premenopausal women [19]. These observations have been corroborated by other epidemiological studies and a large prospective study that suggest a link between dietary cholesterol consumption and breast cancer risk [20-21].

Statins are a class of drugs that inhibit HMG-CoA reductase (HMGCR), the rate-limiting enzyme in cholesterol biosynthesis, and thus lower the de novo synthesis of cholesterol. These drugs are widely used in the treatment of hypercholesterolemia and although their impact on breast cancer incidence has been investigated, no clear relationships have emerged [22].

One hypothesis is that dyslipidemia results in increased cholesterol content in cell membranes thus impacting membrane fluidity and subsequent signaling. Additionally, studies demonstrate that the metabolite, 27-hydroxycholesterol (27HC), can function as an estrogen, increasing the proliferation of estrogen receptor (ER) positive breast cancer cells. This was unexpected as 27HC and other oxysterols activate the Liver X Receptors (LXR) resulting in the reduction of intracellular cholesterol. Resolution of this paradox will require a dissection of the molecular mechanisms by which ER and LXR converge in breast cancer cells. Regardless, the observation that 27HC influences breast cancer provides rationale for strategies that target cholesterol metabolism [23].

A study of more than 1 million patients in the United Kingdom has demonstrated an association between high blood cholesterol and breast cancer. The study was conducted over the course of 14 years. Using a statistical model to analyze the association between the groups, investigators found that having high cholesterol increased the risk of developing breast cancer by 1.64 times [24].

Schairer C et al. [25] conducted a case-control study within the linked Surveillance, Epidemiology, and End Results (SEER) – Medicare data. Cases were women with invasive breast cancer aged 66 + years (N = 30,004) identified by SEER registries (years 2007-2011). Controls were women (N = 198,969) identified from a 5% random sample of Medicare recipients alive and breast cancer free in year of selection. Risk reductions with dyslipidemia were slightly greater when untreated than treated and did not vary much by time between dyslipidemia and breast cancer diagnosis. Whether treated or untreated, dyslipidemia was associated with greater reductions in risk for later stage than earlier stage breast cancer.

Following are the limitations of this study:

1) The study sample was less to extrapolate to regional and national level trends.
2) Genetic testing was not done.
3) Family history and risk factors like alcohol, environmental carcinogens, oral contraceptives were not covered.
4) Management of dyslipidemia was not considered and also its effect on breast cancer upon treatment was not included in the study.

5) This was an observational study with no control group for comparison.

5. Conclusion

Although we observed that there is higher instance of breast cancer patients with post-menopausal status to have high total cholesterol, our study did not reveal any association of post – menopausal women with elevated Triglycerides, LDL or lower HDL levels. Further studies may be done which may include a control group of patients without breast cancer. Also, patients who are on treatment for dyslipidemia may be studied prospectively for occurrence of breast carcinoma.

6. Conflicts of Interest

The authors declare no conflicts of interest

7. Disclosures and Funding

None

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