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Research Article

Relationship Analysis of Risk Factors in Carcinoma Breast with Particular Relevance to Lipid Profile and Obesity

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ABSTRACT
Background: Breast cancer is the second most common cancer in the world. One of the reasons for increasing prevalence of carcinoma breast and that too in younger women has been attributed to lifestyle changes like smoking, alcohol, obesity, sedentary work, lack of physical activity etc. All these factors also have a strong association with lipid metabolism.
Materials and Methods: This study was a descriptive study, here a total of 50 female patients with carcinoma breast and recurrent cases of carcinoma breast were studied. Which was conducted at Department of General Surgery at Rajarajeswari Medical College and Hospital, Bangalore from October 2017 to October 2019.
Results: The mean duration of lump was found to be 4.35 months.
The mean age of menarche in pre-menopause was found to be 13.96 years and postmenopause 13.61 yrs.
Most common stage in post menopause was found to be 3A and pre menopause 2B.
The mean TC in pre-menopause was found to be 179.04 and post-menopause 188.3.
The mean TG in pre-menopause was found to be 151 and post-menopause 146.61.
The mean LDL in pre-menopause was found to be 118.22 and post-menopause 120.57.
The mean HDL in pre-menopause was found to be 39.61 and post-menopause 41.74.
The mean HDL in pre-menopause was found to be statistically significant with p value 0.049*
Conclusion: We conclude that decreased HDL-cholesterol among pre-menopausal women may act as a marker of increased breast carcinoma risk.

Keywords: Carcinoma Breast, Lipid Profile, Obesity.

INTRODUCTION

Breast cancer is the second most common cancer in the world only second to lung cancer and the most frequent cancer among women with an estimated incidence of 1.67 million in 2012 (25% of all cancers)[1]. Incidence rates vary nearly four-fold across the world, with rates ranging from a lowest of 27 per 100,000 women in Middle Africa and Eastern Asia to a highest of 92 per 100,000 women in Northern America.[1] Breast cancer is the fifth most common cause of cancer-related deaths (522,000 deaths annually)[1]. It is the most frequent cause of cancer death in women in less developed regions (14.3% of total cancer deaths), whereas it is the second most common cause of cancer death in more developed regions (15.4% of total cancer deaths) after lung cancer.[1] The mortality rates ranging from the lowest of 6 per 100,000 women in Eastern Asia to the highest of 20 per 100,000 women in Western Africa.[1] In India, the incidence of breast cancer is significantly lower than in western countries. Still breast cancer has ranked number one cancer among Indian females with an age-adjusted rate as high as 25.8 per 100,000 women and mortality 12.7 per 100,000 women.[2] The incidence of breast cancer in India varies from as low as 5 per 100,000 female population per year in rural

areas to 30 per 100,000 female population per year in urban areas.[3] Breast cancer has been described as an alarming health problem in India[4]. A survey carried out by the Indian Council of Medical Research (ICMR) in the metropolitan cities viz. Delhi, Mumbai, Bangalore, and Chennai; from 1982 to 2005; has shown that the incidences of breast cancer have doubled. Over the years, the incidences of breast cancer in India have steadily increased and as many as 100,000 new patients are being detected every year.[5] A 12% increase has been registered by cancer registries from 1985 to 2001, which represented a 57% rise of the cancer burden in India.[5,6] These variations in the distribution of carcinoma breast among different geographies are mainly due to variations in diet and lifestyle across the regions. Benign breast diseases gaining more importance in recent times owing to increased awareness about breast cancer. Majority of lesions occur in the breast are benign.[7] Worldwide, benign pathological condition accounts for approximately 90% of presentations related to breast. Furthermore, fibro-adenoma, fibrocystic disease and breast abscesses accounting for most of these lesions[8]. Some of the benign breast diseases are important risk factors for the development of breast cancer. The disorder of lipid metabolism is pathologically linked to hyperlipidaemia, lipid storage disease, obesity, and other related diseases. Intriguingly, recent studies have revealed that hyperlipidaemias play an important role in carcinogenesis by varieties of mechanisms such as abnormal expression of various genes, proteins, and dysregulation of cytokines and signalling pathways, oxidative damage due to lipid peroxidation to name a few. Malignant transformation and accelerated cancer cell proliferation is in high demand for energy, which induces alterations in lipid metabolism to allow the survival of cancer cells.[9] Based on a clinic-pathological study of breast cancer, researchers have found that plasma levels of Total Cholesterol (TC),Triglycerides (TG),High Density Lipoprotein Cholesterol (HDL-C), and Low Density Lipoprotein Cholesterol (LDL-C) of breast cancer patients were significantly higher than that of the control group. In addition, TC and TG levels of patients with metastasis were significantly higher than that of patients without lymphatic metastasis.[10] Meanwhile, LDL-C and very low- density lipoprotein (VLDL-C) is in favour of breast cancer progression and metastasis through protein kinase B (AKT)-induced epithelial-mesenchymal transition (EMT) and cancer angiogenesis.[11] Furthermore, lipid-lowering drugs and anti-lipid peroxidation treatment are assuming importance in prevention and treatment of variety of cancers. Hence elucidation of association between lipid metabolism and cancer in particular breast cancer is of paramount importance.

MATERIALS AND METHODS

Design

This study was a descriptive study, here a total of 50 female patients with carcinoma breast and recurrent cases of carcinoma breast were studied. Which was conducted at Department of General Surgery at Rajarajeswari Medical College and Hospital, Bangalore from October 2017 to October 2019. All the subjects satisfying inclusion and not falling in the purview of exclusion criteria were enrolled in the study. They were informed about the study and the importance of their participation in the same. Informed consent was taken.

Participants

A total of 50 female patients with carcinoma breast and recurrent cases of carcinoma breast were studied. Patients were selected with the following inclusion and exclusion criteria. Inclusion criteria comprises of all patients proven of having carcinoma breast and recurrent cases of carcinoma breast. While male patients having carcinoma breast were excluded.

Study Procedure

All the subjects satisfying inclusion and not falling in the purview of exclusion criteria were enrolled in the study. They were informed about the study and the importance of their participation in the same. Informed consent was taken. Comprehensive history was noted. Relevant examination was done, including that of breast, axilla. Height and weight of subjects were recorded. Lipid profiles of all study subjects were estimated with early morning fasting (minimum of 8 hours) venous blood sample at the same centralised laboratory, Rajarajeswari Medical College and Hospital, Bangalore.

Data Analysis

The Statistical software namely SPSS 22.0, and R environment ver.3.2.2 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc. Descriptive and inferential statistical analysis has been carried out in the present

study. Results on continuous measurements are presented on Mean +/- SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Leven`s test for homogeneity of variance has been performed to assess the homogeneity of variance. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis. Fisher Exact test used when cell samples are very small.

RESULTS

Table 1: Lipid Profile

Lipids	No. of patients (n=50)	Percentage	Mean ± SD
Total Cholesterol (mg/dl)			
<200	39	78.0	182.08±31.31
200-280	10	20.0	
>280	1	2.0	
TGL (mg/dl)			
<150	26	52.0	145.98±52.42
150-500	24	48.0	
>500	0	0.0	
HDL (mg/dl)			
<35	4	8.0	40.10±4.50
35-60	46	92.0	
>60	0	0.0	
LDL (mg/dl)			
<70	0	0.0	118.60±18.57
• 70-190	50	100.0	
• >190	0	0.0	

LIPID PROFILE	Reference range
TC	150 – 220mg/dl
TG	40 – 140 mg/dl
HDL	42 – 88 mg/dl
LDL	< 135 mg/dl

Of total 50 patients, 78% women had total cholesterol < 200mg/dl with mean of 182, 52% had triglycerides of <150 with mean 145.98, 92% had HDL in the range of 35-60 years with mean of 40 and 100% patients had LDL 70 – 190mg/dl with mean of 118.6mg/dl.

Table 2: BMI (kg/m2) distribution in relation to Menopausal history:

BMI (kg/m²)	Total	Menopausal History	
		Pre Menopause	Post Menopause
<18.5	3(6.5%)	3(13%)	0(0%)
18.5-25	25(54.3%)	10(43.5%)	15(65.2%)
25-30	15(32.6%)	8(34.8%)	7(30.4%)
>30	3(6.5%)	2(8.7%)	1(4.3%)
Total	46(100%)	23(100%)	23(100%)

43.5% premenopausal women were in the BMI range of 18.5 – 25 and 65.2% postmenopausal women were in the BMI range of 18.5 – 25.

Table 3: Association of lipid parameters in relation to Menopausal history:

Lipids	Total	Menopausal History		P value
		Pre Menopause	Post Menopause	
Total Cholesterol (mg/dl)	183.67±30.79	179.04±39.74	188.30±17.76	0.313
TGL (mg/dl)	148.8±49.88	151.00±58.70	146.61±40.41	0.769
HDL (mg/dl)	40.67±3.69	39.61±3.61	41.74±3.53	**0.049***
LDL (mg/dl)	119.39±18.17	118.22±22.96	120.57±12.04	0.666

Decreased levels of HDL in post - menopausal women is significantly related to the incidence of carcinoma breast.

Table 4: Comparison of clinical variables according to Menopausal history of patients:

variables	Total	Menopausal History		P value
		Pre Menopause	Post Menopause	
Duration lump months	4.65±6.20	5.43±7.37	3.89±4.88	0.412
Age of menarche	13.78±1.07	13.96±1.22	13.61±0.89	0.277
BMI (kg/m^2)	24.18±3.12	24.15±3.56	24.21±2.67	0.949
Tumor Size	6.07±2.03	5.87±2.28	6.26±1.76	0.519

Mean duration of lump is more in pre-menopausal than in post- menopausal, mean tumor size is more in postmenopausal than in premenopausal whereas mean age of menarche and BMI is similar in both pre and post- menopausal which is not statistically significant.

Table 5: Association of clinical features distribution in relation to Menopausal history

variables	Total (n=46)	Menopausal History		P value
		Pre Menopause (n=23)	Post Menopause (n=23)	
Tumor Size				
• 0	1(2.2%)	1(4.3%)	0(0%)	0.875
• 1-5	16(34.8%)	8(34.8%)	8(34.8%)	
• 6-10	28(60.9%)	13(56.5%)	15(65.2%)	
• 11-15	1(2.2%)	1(4.3%)	0(0%)	
Multiple lumps				
• No	46(100%)	23(100%)	23(100%)	1.000
• Yes	0(0%)	0(0%)	0(0%)	
Bilateral				
• No	46(100%)	23(100%)	23(100%)	1.000
• Yes	0(0%)	0(0%)	0(0%)	
Hyperlipidaemia				
• No	39(84.8%)	19(82.6%)	20(87%)	1.000
• Yes	7(15.2%)	4(17.4%)	3(13%)	

Table 6: Stage of tumor distribution in relation to Menopausal history:

Stage of tumor	Total	Menopausal History	
		Pre Menopause	Post Menopause
1	0(0.0%)	0(0.0%)	0(0.0%)
2A	7(15.2%)	4(17.4%)	3(13%)
2B	11(23.9%)	8(34.8%)	3(13%)

3A	19(41.3%)	7(30.4%)	12(52.2%)
3B	6(13%)	2(8.7%)	4(17.4%)
3C	1(2.2%)	1(4.3%)	0(0%)
4	2(4.3%)	1(4.3%)	1(4.3%)
Total	46(100%)	23(100%)	23(100%)

P=0.329, Not Significant, Fisher Exact Test

34.8% premenopausal women has stage 2B and 52.2% postmenopausal women had stage 3A disease, but not statistically significant.

DISCUSSION

As it has been described in earlier, there is an association between altered lipid metabolism and the genesis of carcinoma breast. The physiological mechanisms involved in this process are not only diverse but also very complex. While many studies have elucidated that carcinoma breast patients will have deranged lipid levels compared to normal individuals, there are lacunae in the evidence to prove the causative role of lipid metabolism in carcinogenesis of the breast. Our study intended to find out the relation of the altered lipid profile in carcinoma breast patients in comparison to normal controls and benign breast diseases.

Analysing the results of our study, we found that there was no statistically significant correlation between baseline characteristics such as age (p- value=0.277), BMI (p-value=0.949) smoking, duration of symptoms (p- value = 0.949) and the carcinoma breast.

Mean Age at Presentation

In current study mean age was found to be 50.66 years which is similar to the study by his et al in 2014 with mean age of 49.5 years. The study by owiredu et al in 2009 and rohariya et al in 2017 had nearer mean age of 48.21 and 48.54 years respectively.

Age at Menarche

Early age at menarche has been consistently associated with an increased risk of breast cancer. In this study we found 34% of patients had their menarche at 13 yrs and 34% at 14 years which was similar to study by Rohariya et al[12], Norsa'adah B et al[13],

Peela JR et al[14]. It is reported that women who experience menarche at an early age (before age 12) have a 20% increase in risk compared to women who experience menarche at or after 14 years of age

Family History

Previous studies that have evaluated the significance of family history of Breast cancer risk but have reported variable results. A pooled analysis of existing prospective cohort studies found no interaction for effects of family history on breast cancer. Women with a positive family history of breast cancer should be especially alert to the importance of maintaining a lean body mass as an important way to lower breast cancer risk after menopause. We found only one patient with positive family history constituting 2%. Which was similar to study by Ghosh et al in 2014.[15]

Stage of Cancer

In our study 40% were in stage 2, 56% in stage 3 and 4% in stage 4. This reflects the late presentation of cases in Indian population due to lack of awareness. It is similar to study by Saxena et al[16] in 2005 which showed stage 3 to be more (35.2% 3B, 27.1% of 3A) followed by stage 2 (16.3%) and 7.9% had stage 4 diseases.

BMI

In our study 54% patients had BMI in the range of 18.5 – 25 with mean BMI of 24.39 kg/m^2 which was not significant with incidence of carcinoma breast. It was similar to a study by Melvin et al in 2012[17] with 67% patients having BMI in the range of 18.5 – 24.99.

Lipid Profile:

- In our study triglycerides are mildly elevated in both pre and post - menopausal women but there is no significant correlation with incidence of carcinoma breast statistically.
- However, decreased HDL levels found in pre- menopausal woman correlates with increased incidence of carcinoma breast. It is statistically significant with p value of 0.049. This is similar to a study by Anna et al in 2008 which suggested low HDL-cholesterol among pre - menopausal may be a marker of increased breast cancer risk.

Other studies by rohariya et al, owiredu et al shows no relation between HDL and carcinoma breast. They show elevated total cholesterol levels acting as a risk factor in carcinoma breast.

Parity

A case-control carried out in Mumbai, India indicated that single women compared to married women had 4–5-fold higher risk for development of breast cancer in the age group of 40–54 years and 55 and above.[18] but in our study, most of the patients with carcinoma breast had parity of 2 and only one patient was nulliparous. This was similar to study by Kotsopoulos et al[19], Iqbal et al[20] and Fortner et al[21].

Breast Feeding

Breastfeeding is hypothesized to reduce the risk of Breast Cancer primarily through two mechanisms, differentiation of breast tissue and reduction of the lifetime number of ovulatory cycles, but previous reviews of the association between breastfeeding and breast cancer have not consistently found that breastfeeding reduces the risk of breast cancer. [99] In our study 96% of women with carcinoma breast fed their children and only 1 of them did not breast feed. It is similar to a study by Fortner et al where majority of the women breast fed.

Age at menopause

In our study 23 patients with carcinoma breast have attained menopause with 16 attaining menopause between 45 – 55 years. Post – menopausal women had mean BMI of 24.21, mean duration of 3.89 months and stage 3A.

CONCLUSION

Continuing increased incidence of breast cancer has added urgency to investigations of control and preventive measures. It is important to incorporate primary and secondary preventive measures of breast cancer as number of affected individuals is rising and the age of onset is shifting towards younger age groups. Present study is a descriptive study including 50 patients with carcinoma breast. Findings of our study confirm that decreased HDL is associated with incidence of carcinoma breast in premenopausal women. There was no significant correlation with BMI, smoking, TC, TG, LDL and carcinoma breast. We conclude that decreased HDL – cholesterol among premenopausal women may act as a marker of increased breast carcinoma risk.

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Author Contributions

Conceptualization: all authors. Data collection: all authors. Data analysis: all authors. First draft of the manuscript: all authors. Approved this manuscript for submission: all authors.

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Conflicts of Interest

There are no conflicts of interest.

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