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Association of Total Cholesterol and Estrogen Receptor in Patients with Breast Cancer

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[1]Conception & Study Design, Data Collection & Processing, Critical Review.
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ABSTRACT

Objective: To determine the association of total cholesterol and Tumour Estrogen receptor in patient with breast cancer at tertiary care Hospital.

Material and Methods: This cross-sectional study was conducted at the Department of Biochemistry and Diagnostic and Research Centre, Liaquat University of Medical & Health Sciences Jamshoro from February 2021 to August 2021. All the female patients with biopsy proven diagnosis of breast cancer and those patients with no prior history of any other comorbidities were included. 5 ml venous blood sample fasting was collected from the cuboidal vein of each patient as was sent to diagnostic laboratory for analysis of total Cholesterol (TC), serum estrogen level, tumour estrogen receptor. All the data was recorded on study Performa. All the data was entered into the SPSS 20.0 version.

Results: A total of 56 patients were studied; their mean age was 46.51±8.29 years and mean duration of breast cancer was 6.10±4.34 months. Majority of the patients 44.6% were obese and 26.8% were overweight, while normal weight patients were 26.8%. However, one patient was underweight. Mean total cholesterol was 110.72±40.18 mg/dl. Mean serum estrogen was 29.49±46.35 and mean tumour receptors were 1.50±0.50. Tumour estrogen receptors was positive in 50.0% of the cases. Although statistically insignificant (p = 0.440), the average total cholesterol in patients with positive tumour oestrogen was high.

Conclusion: Obesity was commonly seen in patients with breast cancer, according to the findings of this study. Obesity has an impact on the development and recurrence of breast cancer. Obesity, inflammation, and the tumour microenvironment all work together to promote tumor development in patients.

Keywords: Breast cancer, total cholesterol, Tumour Estrogen receptor.

INTRODUCTION

Breast cancer is the most frequently diagnosed malignancy in females and is a 2nd leading cause of death from cancer at present.[1] Fortunately, developments in early diagnosis and the emergence of successful target therapeutics had a substantial positive influence on total BC patient safety, but BC's lifetime risk tends to increase, emphasizing the need to recognize the environmental and genetic influences that predispose females to this disease. A report in 1909 that observed the presence of (fatty nature) crystals in tumour parts prepared without the fixation of alcohol was one of the first findings linking cholesterol and cancer.[2] It is unclear how serum lipid concentrations relate to the risk of breast cancer,

however, given that cholesterol is a precursor to sex-steroid hormones, increased cholesterol levels may raise the breast cancer risk.[3,4] According to a number of epidemiological studies, significantly increased cholesterol concentrations have been linked to a decreased overall or site-specific incidence of cancer and death since the 1980s.[5] The increase TG, LDL-C and VLDL-C and decrease HDL-C value increase the risk of the coronary heart disease, and breast cancer risks included having a high body fat percentage and a high serum lipid profile.[6,7] Certain studies have linked changes in plasma lipid and lipoprotein concentrations to malignant growth of breast tissue in women. Recent studies have reignited interest in the potential contribution of endogenous and dietary lipids to the development and prognosis of malignancy.[8] *Estrogen receptors* (ERs) are one of the most successful tumour markers in breast cancer, The estrogen receptor has a role in cellular growth, proliferation, and differentiation, the most significant biological measure of therapeutic response in malignancy is the estrogen receptor. It belongs to the nuclear steroid receptor family and regulates transcription through the activation of the hormone 17-p estradiol estrogen (E2).[9] The majority of estrogen's activities, as is widely known, result from its binding to the intracellular estrogen receptor (ESR), which controls gene expression. In humans, two distinct genes that encode distinct intracellular isoforms of ESR exist. The estrogen receptor alpha (ER alpha) protein is highly expressed in the liver, adipose cells, mammary, and cardiovascular system and is encoded by the first identified ESR1 gene, which is placed on chromosome.[6] It has been shown that activated ER alpha controls the expression of various other genes involved in the metabolism of lipoprotein in the liver, increasing the levels of serum HDL, TG, and cholesterol while decreasing the levels of LDL, total cholesterol, and lipoprotein.[10,11]

There are few findings which suggest/shows the association of total cholesterol and tumor estrogen receptor. Collect the more significance gap the association between breast cancer, this study has been conducted to evaluate the association of total cholesterol, serum estrogen level and tumor estrogen receptor. This may be the helpful in diagnosis and better treatment of breast cancer.

MATERIALS AND METHODS

This descriptive cross-sectional study was conducted at the Department of Biochemistry and Diagnostic and Research Centre, Liaquat University of Medical & Health Sciences, Jamshoro, from February 2021 to August 2021. The study was conducted after approval of the synopsis by ethical committee. All the female patients with biopsy proven diagnosis of breast cancer and patients with no prior history any other comorbidities were included. All women receiving radiotherapy, chemotherapy, or hormonal therapy, as well as any medications that may interfere with lipid metabolism, were excluded. Written consents were taken from all the patients or their relatives. Detail history clinical examination including parity and BMI was taken. 5 ml intravenous blood sample was collected from each patient and was analyzed in the diagnostic laboratory for total cholesterol (TC), serum estrogen level, tumour estrogen receptor. The "esterase technique" was used to assess blood cholesterol levels. The procedure was carried out using the Roche Hitachi (Chemistry Analyzer) Cobas System (Roche, USA).

All the information regarding lipid biomarkers of the patient, including total Cholesterol (TC), serum estrogen level, tumour estrogen receptor and body mass index (BMI) was noted, and the duration of breast cancer was assessed. Self- structured study proforma was used to collect the data and SPSS version 26 was used for the analysis.

RESULTS

A total of 56 patients were studied; their mean age was 46.51±8.29 years. Mean duration of breast cancer was 6.10±4.34 months. Out of all 8.9% patients were nulliparous, 33.9% patients had parity 1-3, 39.3% had parity 4-6 and in 17.9% patients' parity was >6.

Only two patients had a positive family history. The majority of the patients were obese (44.6%), overweight (26.8%), and normal weight (26.8%). However, one patient was underweight. The mean TC was 110.72±40.18, mean HDL and LDL were 40.25±11.26 and 109.79±40.03, respectively, while mean serum estrogen was 29.49±46.35. (Table **I**)

Tumour estrogen receptors were positive in 50.0% of the cases, while in remaining 50% it was negative. (Table **II**)

Table I: Descriptive Statistics of Age and Breast Cancer Duration (n=56)		
Variables	Statistics	
Age (mean±SD)	46.51±8.29 years	
Duration breast cancer	6.10 ± 4.34 months	
Parity	Nulliparous	05(08.9%)
	1-3	19(33.9%)
	4-6	22(39.3%)
	>6	10(17.9%)
Family history	Positive	02(3.6%)
	Negative	54(96.4%)
Obesity	Under weight	01(01.8%)
	Normal weight	15(26.8%)
	Over weight	15(26.8%)
	Obese	25(44.6%)
Total cholesterol	110.72±40.18 mg/dl	
HDL	40.25±11.62 mg/dl	
LDL	109.79±40.03 mg/dl	
Serum estrogen	29.49±46.35	

Table II: Positive Frequency of Tumor Estrogen Receptors (n=56)		
Tumor estrogen receptor	**N**	**Percent**
Positive	28	50.0%
Negative	28	50.0%
Total	56	100.0%

Table III: Mean of TC, HDL and LDL According to Tumor Estrogen Receptors (n=56)					
Lipid Profile	**Tumor estrogen receptor**	**N. of patients**	**Mean±SD**	**SEM**	**P-value**
Total cholesterol	Positive	28	114.92±46.19	8.73	0.440
	Negative	28	106.54±33.44	6.32	
High density lipoprotein (HDL)	Positive	28	39.80±09.60	2.22	0.751
	Negative	28	40.71±11.75	1.78	
Low density lipoprotein (LDL)	Positive	28	117.02±44.63	8.43	0.183
	Negative	28	102.81±34.36	6.38	

Mean TC was high 114.92±46.19 in patients with positive tumour estrogen receptor and 106.54±33.44 was in those having tumour receptor negative, while findings were statistically insignificant. However average of HDL, LDL and BMI were also statistically insignificant as per tumour estrogen positive, p-values were quite insignificant as shown in table **III**.

DISCUSSION

Breast cancer is second leading factor of cancer-linked mortality in females. Stronger diagnostic tools and more potent treatments have been made possible by advancements in our understanding of the illness, enabling early identification and improved performance. Numerous studies have linked environmental and lifestyle variables to the development and the disease progression. Due to their possible link to breast cancer and accessibility of management, overweight and cholesterol stand out.[12] In this study, the mean age of the patients was 46.51±8.29 years, and the mean duration of breast cancer was 6.10±4.34 months. Similarly, Lin C et al[13] reported that mean age of patients of breast cancer was 49.4 ± 9.52 years. On the other hand, Lofterød T et al[14] reported that the mean age of patients at diagnosis was 57.9 years. In another case control study, Llanos AA et al[15] reported that the mean ages at enrollment of cases and controls were 57.6 and 52.4 years, respectively. However, Li X et al[16] also mentioned mean age of breast cancer group 49.93 ± 10.44 years.

The mean total cholesterol in this study was 114.92±46.19 in patients with positive tumour oestrogen and 106.54±33.44 in those with negative tumour receptor. On other hand Jung SM et al[17] reported that average of total cholesterol 193.3 mg/dL in cases of breast cancer. The permeability and structural stability of cellular membrane are both maintained by cholesterol that is crucial structural element of the membranes. Due to its role in the synthesis of lipid in the plasma membrane, whereby it

brings receptor proteins in intimate interaction with 2nd messenger molecules in massive concentrations, cholesterol is also connected to cellular signaling pathways.[18] However in an old study of Hoyer and Engholm et al[19] found no apparent relationship between the serum TC concentrations of breast cancer patients and controls. Ni H et al[20] conducted meta-analysis and suggested that serum levels of TG but not TC and LDL-C may be inversely associated with breast cancer risk.

In this study most of the patients 39.3% had parity 4-6, 33.9% patients had parity 1-3, followed by 8.9% patients were nulliparous and in 17.9% patient's parity was >6. On other hand Badar F et al[21] reported that among the 3,777 in whom the parity was noted, on an average, females had 4 children (1 - 15). In another study Bano R et al[20] observed that, whenever parity rises, breast cancer risk falls. The more the protection, the more full-term pregnancies there are, results showed that cases had a lower likelihood of breastfeeding. In this study the family history of breast cancer, only two patients had family history positive. Though Badar F et al[21] reported that the family history of breast cancer was positive in 16.9% of the cases. These finding were higher as compared to this study, but several risk factors proven to enhance a person's probability of developing breast cancer, like as dietary variables, overweight, usage of contraceptive pills, family history and old age are still unknown as to what specifically causes breast cancer.[21]

In this study, tumour estrogen receptors were positive in 50.0% of the cases, while in the remaining 50% these were found negative. Pervaiz F et al.[22] conducted a study on 345 patients, and 149 (43%) were found to have positive hormone receptor status. In this study according to descriptive statistics of cholesterol, serum estrogen and tumour estrogen receptors, mean total cholesterol was 110.72±40.18. Mean serum estrogen was 29.49±46.35 and mean tumour receptors was 1.50±0.50. Despite the fact that several studies have failed to uncover links between lipoproteins and breast cancer, certain major clinical trials have found a direct link with LDL cholesterol levels and risk of breast cancer, as well as an inverse relation between HDL cholesterol and breast cancer risk, However, our findings show that there is a 50% positive association between LDL and HDL cholesterol and a 50% negative correlation between LDL and HDL cholesterol and breast cancer risk, Similarly, Flote VG et al[23] discovered that the quantity of cholesterol, free cholesterol, phospholipids, and apolipoprotein A1 in HDL and HDL subfractions was linked with progesterone receptor expression in a small exploratory hypothesis. They also discovered that there was no relation between lipoproteins and ER expression, but that there was an inverse relationship between HDL1 index and that very low-density lipoprotein (VLDL) was positively related with nodal metastasis.

CONCLUSION

The average cholesterol was high in patients having positive tumour estrogen receptors compared to those having negative tumour estrogen receptors, while this average was statistically insignificant. It's still controversial whether total blood cholesterol has a role in the development of breast cancer. A number of studies show that high cholesterol levels before to diagnosis protect against the development of cancer, prompting some doctors to urge drug treatment to lower cholesterol levels. This was a single-center study with a small sample size. Breast cancer has a complex etiology. As a result, isolated cholesterol levels may not be the deciding factor in carcinogenesis. Because the number of studies was so small, the findings of our analysis should be considered with caution. In the future, more large-scale prospective clinical large-scale trials should be conducted.

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