# Association of Breast Cancer and Dyslipidemia in Nepali Women

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**Citation**

Karki OB, Timilsina B, Ghimire P, Pokharel D. Association of Breast Cancer and Dyslipidemia in Nepali Women. *Kathmandu Univ Med J.* 2025;90(2):229-33.

## ABSTRACT

**Background**

Breast cancer, which is a multi-factorial disease is one of the primary causes of cancer-related mortality in women. The association of serum lipids with breast cancer is being debated.

**Objective**

To examine any possible association between fasting lipid profile and breast cancer in Nepali women.

**Method**

A case-control study was conducted among 36 breast cancer patients, 40 patients with benign breast lump and 38 apparently healthy control women from February 2022 to December 2024. Ethical clearance was obtained from institutional review committee (MEMG/IRC/500/GA) prior to study. A convenient sampling technique was used. Data entry and analysis were done using SPSS version 20. Chi-square tests and analysis of variance (ANOVA) were used for statistical comparisons of categorical and continuous data respectively. P-value of <0.05 was considered statistically significant.

**Result**

Of the 114 participants included in this study, 36 were malignant breast cancer patients, 40 were benign breast lump patients and 38 controls with the mean ages of 52.75 ± 10.39, 48.45 ± 12.78 and 45.80 ± 10.14 years respectively. The prevalence of dyslipidemia was 75%, 25% and 26.31%, among malignant breast cancer patients, benign breast lump patients and control group respectively with the mean value of triglyceride (160.01 ± 78.34, 111.75 ± 60.40 and 97.99 ± 31.34) respectively and the difference was statistically significantly ($p < 0.001$). In addition, the mean serum concentrations of total cholesterol were significantly different between the three groups (1588.36 ± 39.95, 132.09 ± 39.95 and 138.31 ± 45.34, p=0.020).

**Conclusion**

The overall prevalence of dyslipidemia was high in breast cancer patients in comparison to patients with benign breast lump or normal controls.

## KEY WORDS

*Breast neoplasms, Dyslipidemias, Lipids*

## INTRODUCTION

Breast cancer accounted for 11.7% (2261419) of new cancer cases and 6.9% (684996) of cancer deaths in 2020, and incident cases are expected to increase by more than 47% by 2040.[1] In Nepal, in the year 2020, there were 1973 new cases and 1049 deaths due to breast.[2] In addition to established risks factors like, age, genetic influence and, use of contraceptives, lack or short duration of breastfeeding, several other environmental factors play a crucial role in the mechanism of breast cncer.[3,4] Various studies have suggested that increased dietary fat consumption and dyslipidemia can be correlated with increased risk of breast cancer and breast cancer of poor prognosis.[5] Excessive intake of lipids promotes cancer development by inducing an inflammatory response, increment in cell proliferation, reduction in cancer cell apoptosis, promotion of reactive oxygen species and angiogenesis.[3,6] It also increases the expression of β-scavenger receptor (CD36), a member of cell surface fatty acid receptors. Clinically, inhibition of CD36 has been found to reduce the metastasis of human melanoma and breast cancer.[7]

In different experimental mouse models, the role of cholesterol and its transporters in breast cancer development has been demonstrated.[7] The cholesterol metabolite 27-hydroxycholesterol was found to induce proliferation of estrogen receptor-positive breast cancer cells and facilitate metastasis.[8,9] Activation of different inflammatory pathways by oxidation of lipoproteins and glycation of different lipoproteins may have a role in inhibiting apoptosis and augmenting proliferation and migration of cancer cell.[10,11] Unfortunately, various studies on the influence of dyslipidemia on breast cancer risk are divergent and inconclusive, and no consensus has yet been made.

The aim of this study is to study association of lipid profile between the patients diagnosed with breast cancer, benign breast lumps and normal controls.

## METHODS

The present study is a case-control study, conducted in department of general surgery at Manipal Teaching hospital from February 2022 to December 2024.

Sample size was determined using the following formula.[12]

$$n = \frac{(z_\alpha + z_\beta)^2 x\ (\sigma_1^2 + \sigma_2^2)}{(\mu_1 - \mu_2)^2}$$

Here, n = estimated sample size, μ1 = mean of the quantitative variable in women with breast cancer, μ2 =mean of the same quantitative variable in women without breast cancer, σ1 = standard deviation of the respective quantitative variable in women with breast cancer, σ2 = standard deviation of the respective quantitative variable in women without breast cancer, Zα = Z value of the standard normal deviate at a given level of significance, and Zβ = Z value of standard normal deviate at a given power. Taking the corresponding values from a previous study by Owiredu et al. (μ1 = 202.00, μ2 = 174.50, σ1 = 53.60 and σ2 = 40.50) and taking a 95% level of significance (Zα = 1.96) and 50% power (Zβ = 0.50), the sample size for each group was 36.[13]

First, a total of 36 women with breast cancer were chosen as cases. Then they were individually matched to two control subjects (1. women but had benign breast disease only and did not develop breast cancer, and 2. Women who had no breast disease and were apparently healthy) according to age. Minimum of 36 participants were recruited in each group. But later there were 40 patients with benign breast lump and 38 apparently healthy control women. Therefore, a total of 114 participants were considered for inclusion.

Females of any age, histologically proven of having breast carcinoma by F.N.A.C. or biopsy and those who agreed to sign written consent to participate in the study.

Patients with cancer of any other origin apart from carcinoma breast: patients with post-mastectomy or post chemotherapy status for carcinoma breast, patients receiving any drug which alters lipid profile, patients on oral contraceptives, pregnant females, patients taking corticosteroids or suffering from hepatic disorders/severe malnutrition were excluded.

The presence of a breast mass was confirmed on physical examination by the surgeon or by ultrasound of breast or mammographic study. Biopsy proven {fine needle aspiration cytology (FNAC)/ tru-cut biopsy/excision biopsy} confirmed cases were enrolled as “malignant breast cancer patients ” and biopsy-negative breast mass patients were included as the “benign breast disease groups”. Women who attended the clinic for suspected breast lesions but were negative for breast cancer or benign breast lump both clinically and by mammography/ultrasound of the breast and axilla were included as controls.

A detailed relevant clinical history including personal family and obstretic and menstrual history was taken and complete physical examination done. In case of patients with breast cancer staging of tumor and histopathological diagnosis was also recorded.

Venous blood samples (5 ml) was collected from the selected patients after overnight fasting and analysed for lipid profile parameters. Fasting lipid profile comprising of total cholesterol (TC), triglyceride (TG), low density lipoprotein (LDL) and high-density lipoprotein (HDL), very low-density lipoprotein (VLDL) was recorded. Dyslipidemia was defined according to the guidelines, where hypercholesterolemia was marked as TC > 200 mg/dL or hypertriglyceridemia was marked as TG > 150 mg/dL.[14] The LDL and VLDL values were categorized as high when it exceeds 100 mg/dl and 140 mg/dl respectively, and HDL was considered low if it was below 40 mg/dl. Subjects were classified as dyslipidemic

when any one of the components of the lipid profile except HDL is beyond the upper limit and in cases where the HDL level is below the lower limit.

All collected data were recorded in proforma. The researchers were fully aware of the privacy and anonymity of the participants and followed the guidelines of the Declaration of Helsinki throughout the study. The study protocol was approved by the Institutional Review Board (MEMG/IRC/500/GA) Manipal College of Medical Sciences, Pokhara. Written informed consent was obtained from the participants before inclusion.

Statistical analysis was done using SPSS version 21 statistical software (SPSS Inc, Chicago, IL). Frequencies and percentages were computed for qualitative variables and variables compared by Chi-square test. One-way ANOVA was used to compare serum lipid levels between controls, benign breast lump, and malignant breast cancer participants. A p-value of < 0.05 was considered statistically significant.

## RESULTS

A total of 114 participants were included in this study. Of them, 36 (31.57%) were malignant breast cancer patients 40 (35.08 %) were benign breast lump patients and 38 (33.33%) controls. The mean ages of malignant breast cancer patients, benign breast lump and controls were 52.75 ± 10.39 48.45 ± 12.78 and 45.80 ± 10.14 years respectively. The age distribution of study subjects is as in figure 1.

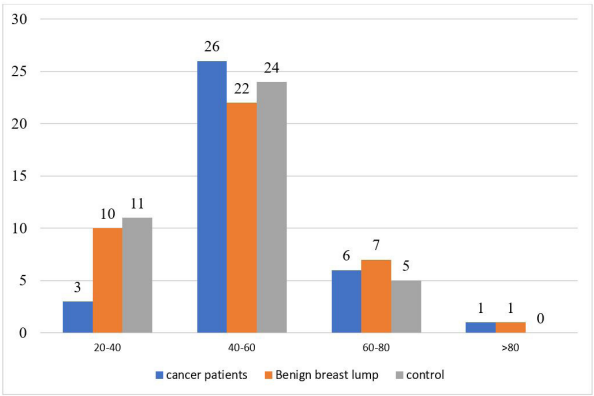


**Figure 1. Age distribution of study subjects (n=114).**

Among carcinoma breast patients, right side breast was affected in 19 (52.8%) patients and left side in 17 (47.2%) of cancer patients. Among benign breast lump, 25 (62.5%) were fibroadenoma and the remaining were phyllodes tumor, lipoma and benign breast lesions. Histopathology of malignant breast cancer, 21 (58.338%) ductal carcinoma 10 (27.7%) and the remaining were lobular carcinoma, adenocarcinoma and medullary carcinoma. The 94% presented with lump in the breast while 6% with history of nipple discharge. The duration of symptoms varied from seven days to three years.

The mean value of TG among malignant breast cancer patients, benign breast lump patients and control group were (160.01 ± 78.34, 111.75 ± 60.40 and 97.99 ± 31.34, p < 0.001) respectively and the difference was significantly. In addition, the mean serum concentrations of TC were significantly different between the three groups (1588.36 ± 39.95, 132.09 ± 39.95 and 138.31 ± 45.34, p = 0.020) malignant breast cancer patients, benign breast lump patients and control group respectively (Table 1).

**Table 1. One way ANOVA Test for Serum Lipid Level Between Breast Cancer, Benign Breast Lump and Apparently Healthy Controls.**

| Lipid components | Breast Cancer Mean±SD | Benign breast lump Mean±SD | Control Mean±SD | p-value |
|---|---|---|---|---|
| Serum TG (mg/dl) | 160.01±78.34 | 111.75±60.40 | 97.99±31.34 | 0.000 |
| Serum TC (mg/dl) | 158.36±39.95 | 132.09±39.95 | 138.63±45.34 | 0.020 |
| Serum HDL-c (mg/dl) | 47.02±14.76 | 46.10±12.18 | 47.41±11.00 | 0.897 |
| Serum LDL-c (mg/dl) | 90.89±21.06 | 76.28±35.78 | 75.11±32.62 | 0.05 |
| Serum VLDL-c (mg/dl) | 69.50±37.58 | 73.45±27.98 | 69.71±23.26 | 0.213 |

The overall prevalence of dyslipidemia in our study was 42.10%. Dyslipidemia was present among 75%, 25% and 26.31% of malignant breast cancer patients, benign breast lump patients and control group respectively (Table 2).

The prevalence of high TG levels was statistically significant among controls, benign breast lump and malignant breast cancer were 10.52%, 17.5% and 47.2% respectively (Table 2).

**Table 2. Prevalence of dyslipidemia and components abnormality among controls, patients with benign breast lump and malignant breast tumour patients.**

| Components of lipid level | | Breast cancer group (n) | Benign breast lump Group(n) | Control group (n) | p-value |
|---|---|---|---|---|---|
| TG (mg/dl) | < 150 | 19 | 33 | 34 | 0.001 |
| | ≥ 150 | 17 (47.2%) | 7 (17.5%) | 4(10.52%) | |
| TC (mg/dl) | < 200 | 28 | 36 | 32 | 0.345 |
| | ≥ 200 | 8 | 4 | 6 | |
| HDL-c (mg/dl) | ≥ 40 | 26 | 33 | 35 | 0.080 |
| | < 40 | 10 | 7 | 3 | |
| LDL-c (mg/dl) | < 100 | 22 | 34 | 33 | 0.012 |
| | ≥ 100 | 14(38.88%) | 6 (15%) | 5(13.15%) | |
| VLDL-c (mg/dl) | < 150 | 32 | 37 | 37 | 0.357 |
| | ≥ 150 | 4 | 3 | 1 | |
| Dyslipidemia | | 27 (75%) | 10(25%) | 10(26.3%) | |

## DISCUSSIONS

In the present study, the mean age of the patients with malignant breast cancer was 52.75 ± 10.39 years which is close to the values in other studies.[15,16] Asian countries have the peak age of breast cancer ranging from 40 to 50 years old, whereas in western countries, the peak age ranges from 60 to 70 years old.[17] Majority of the patients with malignant breast cancer were in Stage II (52%) and stage III (24%) in our series with 11% of cases were in Stage I and 13% from stage IV. Among all the participants studied in this study 70% were pre-menopausal and the rest 30% were post-menopausal, which is similar to other studies.[16]

The etiology of breast cancer is multifactorial. Factors like early menarche, late menopause, obesity, sedentary lifestyle, an older age during the first pregnancy and oncogenic factors related to hormones, genetics, are the risk to raise the prevalence of this disease. The greatest proven risk factor for breast cancer is obesity.[18] Lately numerous reports have shown an association of lipids and lipoproteins with breast cancer patients, with contradicting results.[19] The physiological mechanisms involved in this process are not only diverse but also very complex. Lipids are needed by tumor cells for lipid signaling, membrane production and inflammatory activation. When compared to healthy mammary epithelial cells, cell lines from breast cancer showed abnormal lipid metabolism in preclinical research.[20] The present investigation revealed significantly higher levels of TG, TC, LDL in patients with breast cancer patients as compared with the controls. The overall prevalence of dyslipidemia in our study was 42.10%. Dyslipidemia was present in 75%, 25% and 26.31% of patients with malignant breast cancer benign breast lump and control group respectively which is lower than the overall prevalence of dyslipidemia found in the study done in Ethopia by Kumaie et al. was 75.27; 91.3% in malignant breast cancer, 83.82% benign breast lump and 64.83% controls.[21] The levels of TC (p-value = 0.020) and TG (p-value = 0.000) were significantly (p-value < 0.05) elevated in carcinoma breast group compared to benign breast lump and normal control group, while other lipid levels such as HDL-C (p-value = 0.897) and VLDL - C (p-value = 0.213) were not significantly different between these groups. The findings by Kumaie et al. from Ethiopia had lower (p-value=0.008) mean serum levels of HDL-c observed among women with malignant breast cancer (38.26 ± 7.44) as compared to benign breast lump (44.69 ± 14.48) and controls (47.61 ± 9.12), (p=0.004).[21] But the difference in HDL-c among the different groups was not significant in our study. The results of our study are also comparable to study by Yalagachin G where the levels of TC (p-value = 0.009) and TG (p-value = 0.000) were significantly (p-value < 0.05) elevated in carcinoma breast group compared to normal control group, while other lipid levels such as HDL-C (p-value = 0.920) and LDL - C (p-value = 0.920) were not significantly different between these groups.[2] A concordant finding was reported in Ghana by Owiredu et al.[22] Another study in India by Prabhakar et al. reported a dyslipidemia prevalence of 21.3% among benign breast disease patients.[23] The study showed elevated serum triglyceride levels while other parameters such as TC, HDL, LDL were within normal limits in women with benign breast diseases.[23]

Laamiri et al. suggested that Tumor cells' lipid metabolism is not the same as that of normal cells, and that elevated serum TC levels may be a major factor in carcinogenesis.[24,25] Elevated cholesterol levels that are promoting the development of mammary tissue carcinogenesis may be an attempt to provide the high demand for the formation of plasma membranes and other chemicals containing cholesterol in newly formed cells derived from rapidly proliferating breast cancer cells.[26] Elevated blood TG levels in breast cancer patients in our study can be attributed to the cancer cells' activation of adipocytes to lipolyze their stored triglyceride.[27] In a case-control study by Pikul et al. which compared lipid profiles of carcinoma breast patients (N = 249) with that of normal controls (N = 154) found that TC level in breast cancer group was not significantly higher however TG, LDL levels in breast cancer group were significantly higher than normal control group.[28] On contrary, studies conducted in Morocco showed no statistically significant difference in mean serum TC level between malignant breast tumor and control groups.[29]

It is a single centre study. Randomisation was not done during sampling and investigator blinding was not applied during the study are the limitation of the study.

## CONCLUSION

The prevalence of dyslipidemia was high among breast cancer patients than patients with benign breast lumps or normal control population. There was significantly high mean serum total cholesterol and triglyceride level on malignant breast cancer than benign breast lump and controls. This study may be useful in the future research to elucidate the relationship between altered lipid profile and carcinogenesis of the breast.

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