Evaluation of Lipid Profile and Thyroid Hormones in Breast Cancer Women

Hadeel Ali Shamkhi Al-Husseinawi[1*], Anwar Shati Mohammed[2], Azhar Abdul adheem Kamil[3]
[1,2,3] Ministry of Health, Thi-Qar Health Directorate, Laboratory Department

Email: hadeabas6584@gmail.com

Abstract. Background: Breast cancer is the foremost cause of cancer-related mortality among women globally and the second most prevalent cause of cancer death among women in the United States Aim of the Study: The study aimed to determine the association between lipid and thyroid dysregulation with breast cancer. Material and Method: A total of hundred individuals were participate in this case-control study (50 women had a breast cancer, and 50 women without disease as a control group). The study was done at Al-habobi Teaching Hospital during the period from February to June 2024. The parameters were evaluated by using Cobas 111 for biochemical tests and Cobas 411 for hormones. The Results: The study showed all level of lipid profile increased significantly in cancer patients than control group, with except the level of HDL decreased significantly in breast cancer patient. With regard thyroid hormones the study noted only the T4 decreased significantly in breast cancer patient than control group, while the other hormones not effected by disease. Conclusion: The present study concluded that lipid levels are significantly affected in women with breast cancer, while thyroid hormones are not affected by the disease

Highlights:

1. Breast cancer is a leading cause of global female mortality.
2. Assess lipid and thyroid dysregulation association with breast cancer.
3. Lipid levels significantly altered; thyroid hormones mostly unaffected in breast cancer.

Keywords: Breast Cancer, Lipid Profile, Thyroid Hormones

Introduction

Worldwide, lung cancer is the second most common type of cancer in both men and women, whereas breast cancer ranks first among women. One quarter of all malignancies in 2012 were breast cancers, with more than 1.67 million cases recorded [1]. The fact that low- and middle-income countries (LMICs) account for around 60% of breast cancer deaths and 50% of new cases challenges the idea that this illness is exclusively a disease of impoverished nations. According to the International Agency for Research on Cancer (GLOBOCAN 2012) [2], the incidence of breast cancer varies substantially around the world, from a low of 27 per 100,000 women in South Africa to approximately 92 per 100,000 women in North America. Cancer in general is on the rise,

but cervical cancer in particular is becoming more common in low- and middle-income nations [3].

White adipocytes primarily function in mature adipose tissues, which are mostly responsible for maintaining the body's metabolic equilibrium. Triacylglycerol (TAG) is the end product of lipid metabolism here; free fatty acids (FFA) are released as needed [4]. Adipocytes secrete hormones that play an active role in endocrine signalling to other tissues, in addition to their role in energy utilisation. Proliferation of cells, adipokines, and cytokines [5]. Breast cancer patients may have an increased risk and be easier to diagnose if their serum blood lipids change. Extensive research has shown that changes in plasma lipids and cholesterol, which can be caused by obesity or malnutrition, are risk factors for malignant neoplasms, including breast cancer. The link between cholesterol and cancer risk has been the subject of several epidemiological studies, with mixed findings [6].

Recent experimental research has indicated that elevated plasma cholesterol may promote tumorigenesis in breast cancer. leading to increased breast cancer proliferation. for instance, the generation of hypercholesterolaemia in murine models [7]. It is frequently linked to diminished high-density lipoprotein (HDL-C) cholesterol levels, which in certain studies have been correlated with breast cancer risk [8].

Numerous research indicate that thyroid hormones may facilitate cancer progression, whereas clinical data suggests that hypothyroidism positively influences the trajectory of breast cancer. Thyroid hormones regulate growth, cell differentiation, and metabolism in mammals. High-affinity binding sites for T3, identified in nuclei isolated from human tumours, including breast cancer, indicate that thyroid hormones may influence breast cancer development at the cellular level. T3 has demonstrated a carcinogenic impact in specific human cell lines by enhancing the expression of the epithelial growth factor receptor (EGF-r) gene. In breast cells, the oestrogen response element (ERE) necessary for gene transcription and cellular proliferation can also be activated by T3 [11]. Likewise, thyroxine (T4). Oestradiol may activate the MAPK pathway, hence facilitating cell growth. Moreover, thyroid stimulating hormone (TSH) has been observed to exert a comparable impact on breast cells. TSH receptors have recently been identified in breast cancer tissue using RT-PCR analysis [12].

Methods

Sample Collection and Parameters Evaluation

A total of hundred individuals were participate in this case-control study (50 women had a breast cancer, and 50 women without disease as a control group). The study was done at Al-habobi Teaching Hospital during the period from February to June 2024. The parameters were evaluated by using Cobas 111 for biochemical tests and Cobas 411 for hormones.

Statistical Analysis

The data of the current study were statistically analysis by using SPSS version 26, based in using independent sample t test at p. value <0.05.

Result and Discussion

Concentration of Lipid Profile in Breast Cancer Women and Control Group

The current study was showed a significant difference between all lipid profile parameters in breast cancer women compared with control group, was showed the level of cholesterol, triglycerides, LDL, and VLDL increased significantly in patients than control group, while the level of HDL decrease significantly in breast cancer women than control group at p. value <0.05, as in Table 1.

Table 1: Concentration of Lipid Profile

Lipid Profile	Breast Cancer Patients No. 50	Control Group No. 50	p. value
	Mean ± S. D		
Cholesterol mg/dl	201.37±25.88	190.42±10.9	0.011
Tryglyceride mg/dl	232.63±86.65	185.36±65.14	0.001
HDL	49.61±9.65	54.31±7.31	0.011
LDL	201.37±25.88	110.61±9.2	0.001
VLDL	39.98±10.45	31.80±8.98	<0.001

Concentration of Thyroid Hormones in Breast Cancer Women and Control Group

The current results were detected a non-significant difference in the levels of both T3 and TSH between breast cancer women compared with control group, while the

level of T4 decrease significantly in breast cancer women compared with control group at p. value <0.05, as in in Table 2.

Table 2 Thyroid function tests in studied groups

Thyroid Hormones	Breast Cancer Patients No. 50	Control Group No. 50	p. value
	Mean ± S. D		
T$_3$ ng/dL	87 ± 32.55	93 ± 25.6	0.611
T$_4$ ug/dL	4.9 ± 1.57	5.6 ± 1.39	0.036
TSH µIU/mL	3.09 ± 1.92	2.91 ± 1.57	0.607

Discussion

Evaluation of Lipid Profile in Breast Cancer Patients and Control Group

Lipids are biomolecules and key constituents of membranes. They significantly contribute to several biological processes, including cellular growth and division, as well as the formation of both normal and malignant tissues [13]. In certain malignancies, blood cholesterol exhibits significant early alterations. Numerous investigations have demonstrated an inverse correlation between blood lipid profiles and various tumors [14]. Conversely, elevated total cholesterol levels have been proposed to significantly contribute to cancer development. This study aimed to determine the effect of breast cancer on plasma lipids by comparing healthy women (control group) to those with the disease and measuring total cholesterol, triacylglycerol, LDL-C, HDL-C, and VLDL-C.

Cancer risk has been linked to lipids and lipoproteins. Because cholesterol plays such a crucial part in the production of steroid hormones, which are known to increase the risk of breast cancer, the study found that women who had the disease also had higher total cholesterol levels [15]. The findings of this study align with Al-Swelmien [16], which demonstrated a notable elevation in total cholesterol levels in breast cancer patients and a correlation between total cholesterol and breast cancer risk. A recent analysis indicates that the development of breast cancer is correlated with elevated cholesterol levels in comparison to other tumors [17].

The findings of the present investigation diverged from those reported by Li et al. [18]. They indicated that despite the reduction in blood triglyceride levels, this decline was a risk factor for individuals with breast cancer. Prior research has indicated that blood triglyceride levels are not associated with breast cancer risk [19]. The correlation

between elevated triglyceride levels and reduced globulin-bound sex hormones results in heightened free oestradiol and an increased risk of breast cancer enlargement.

A statistically significant difference in HDL-C levels was seen between the case and control groups, indicating that raised blood HDL-C may serve as a biochemical marker for increased breast cancer risk [20]. These findings corroborate the research conducted by Al-swelmien [16]. The elevation in HDL-C levels seen in this investigation corroborates the findings of Loosen et al. [21], who reported an increase in HDL cholesterol and an associated risk of breast cancer.

Because of its major role in oxidation, a rise in LDL-C concentration is considered a cancer risk factor [22]. Increased lipid peroxidation occurs during oxidative stress, and LDL-C is a major contributor to oxidation. According to Xu et al. [23], a rise in LDL-C lipid peroxidation products occurs when there are elevated amounts of reactive oxygen species and/or when circulating plasma antioxidants are unable to effectively eliminate free radicals.

The results of this study were similar to those reported by Shah et al. [24], who found that plasma levels of VLDL were significantly higher in breast cancer patients than in the control group and patients with benign breast carcinoma. A recent study indicated that VLDL in vitro increased breast cancer cell viability, raised the levels of mesenchymal markers Slug, Vimentin, and β-Catenin, and promoted breast cancer cell migration and invasion. Additionally, VLDL increased the secretion of angiogenic factors in breast cancer cells and stimulated angiogenic activity [25].

Evaluation of Thyroid Hormones in Breast Cancer Patients and Control Group

The relationship between thyroid disorders and breast cancer risk is unclear. Thyroid hormones promote gene expression through their interaction with thyroid hormone receptors. The non-genomic effects of thyroid hormone have been demonstrated. Epidemiological studies have yielded inconsistent findings; some suggest a correlation between hypothyroidism or hyperthyroidism and breast cancer risk, whereas others indicate no association [26, 27].

Thyroid hormones are associated with growth, development, metabolism, and the physiological functions of nearly all mammalian tissues, including breast tissue [28]. Triiodothyronine (T3) exhibits proliferative effects across various cancer types. T3 has

the potential to stimulate tumour growth and plays a significant role in the formation and progression of breast cancer cell lines [29].

Thyroid dysfunction was detected in 3% of the breast cancer patients in our study, but reports from previous research varied from 7% to 39% [30]. Possible causes for this variation include dietary, racial, and regional considerations. Possible ethnic, regional, and health-related factors contributing to this difference [31]. Despite in vitro evidence that thyroid hormones affect breast epithelial growth, epidemiological studies have failed to find a correlation between thyroid problems and an increased risk of breast cancer [32]. Another study found a link between hyperthyroidism and the risk of breast cancer in 17 cases and 19 controls; however, the sample size was too small to draw firm conclusions, thus this result needs more research [33].

References

[1] Z. Momenimovahed and H. Salehiniya, "Epidemiological Characteristics of and Risk Factors for Breast Cancer in the World," Breast Cancer: Targets and Therapy, vol. 11, pp. 151–164, Apr. 2019.

[2] D. Adeloye et al., "Estimating the Incidence of Breast Cancer in Africa: A Systematic Review and Meta-Analysis," Journal of Global Health, vol. 8, no. 1, Jun. 2018.

[3] A. D. Shrestha, D. Neupane, P. Vedsted, and P. Kallestrup, "Cervical Cancer Prevalence, Incidence and Mortality in Low- and Middle-Income Countries: A Systematic Review," Asian Pacific Journal of Cancer Prevention: APJCP, vol. 19, no. 2, pp. 319–324, 2018.

[4] M. Reyes-Farias et al., "White Adipose Tissue Dysfunction in Obesity and Aging," Biochemical Pharmacology, vol. 192, p. 114723, Oct. 2021.

[5] S. Parrettini, M. Cavallo, F. Gaggia, R. Calafiore, and G. Luca, "Adipokines: A Rainbow of Proteins With Metabolic and Endocrine Functions," Protein and Peptide Letters, vol. 27, no. 12, pp. 1204–1230, Dec. 2020.

[6] A. González-Ortiz et al., "Impact of Cholesterol-Pathways on Breast Cancer Development: A Metabolic Landscape," Journal of Cancer, vol. 12, no. 14, pp. 4307–4316, 2021.

[7] C. B. Hassen et al., "Is Cholesterol a Risk Factor for Breast Cancer Incidence and Outcome?" The Journal of Steroid Biochemistry and Molecular Biology, vol. 232, p. 106346, Sep. 2023.

[8] B. R. Gauthier et al., "Thyroid Hormones in Diabetes, Cancer, and Aging," Aging Cell, vol. 19, no. 11, p. e13260, Nov. 2020.

[9] I. Ross, D. B. Omengan, G. N. Huang, and A. Y. Payumo, "Thyroid Hormone-Dependent Regulation of Metabolism and Heart Regeneration," Journal of Endocrinology, vol. 252, no. 3, pp. R71–R82, Mar. 2022.

[10] B. Ren and Y. Zhu, "A New Perspective on Thyroid Hormones: Crosstalk With Reproductive Hormones in Females," International Journal of Molecular Sciences, vol. 23, no. 5, p. 2708, Feb. 2022.

[11] I. Tawfik et al., "Breast Cancer Cells Utilize T3 to Trigger Proliferation Through Cellular Ca2+ Modulation," Cell Communication and Signaling, vol. 22, no. 1, p. 533, Nov. 2024.

[12] D. Pei, "How Do Biomolecules Cross the Cell Membrane?" Accounts of Chemical Research, vol. 55, no. 3, pp. 309–318, Jan. 2022.

[13] K. E. Johnson et al., "The Relationship Between Circulating Lipids and Breast Cancer Risk: A Mendelian Randomization Study," PLoS Medicine, vol. 17, no. 9, p. e1003302, Sep. 2020.

[14] R. Vona, E. Iessi, and P. Matarrese, "Role of Cholesterol and Lipid Rafts in Cancer Signaling: A Promising Therapeutic Opportunity?" Frontiers in Cell and Developmental Biology, vol. 9, p. 622908, Mar. 2021.

[15] A. Al-Swelmien, "Serum Lipid Profile in Breast Cancer Patients," Rawal Medical Journal, vol. 39, no. 3, pp. 254–256, Jul. 2014.

[16] F. Ghahremanfard et al., "The Valuable Role of Measuring Serum Lipid Profile in Cancer Progression," Oman Medical Journal, vol. 30, no. 5, pp. 353–359, Sep. 2015.

[17] X. Li et al., "The Effect of Preoperative Serum Triglycerides and High-Density Lipoprotein-Cholesterol Levels on the Prognosis of Breast Cancer," The Breast, vol. 32, pp. 1–6, Apr. 2017.

[18] L. J. Vatten and O. P. Foss, "Total Serum Cholesterol and Triglycerides and Risk of Breast Cancer: A Prospective Study of 24,329 Norwegian Women," Cancer Research, vol. 50, no. 8, pp. 2341–2346, Apr. 1990.

[19] K. Fan, T. Sun, and F. Yin, "LDL-C/HDL-C Ratio: A Strong Metabolic Risk Factor of Invasive Breast Cancer," [journal name missing], [year missing].

[20] S. H. Loosen et al., "Low Blood Levels of High-Density Lipoprotein (HDL) Cholesterol Are Positively Associated With Cancer," Journal of Cancer Research and Clinical Oncology, vol. 148, no. 11, pp. 3039–3046, Nov. 2022.

[21] K. K. Patel and K. Kashfi, "Lipoproteins and Cancer: The Role of HDL-C, LDL-C, and Cholesterol-Lowering Drugs," Biochemical Pharmacology, vol. 196, p. 114654, Feb. 2022.

[22] L. Xu et al., "Association Between Circulating Oxidized OxLDL/LDL-C Ratio and the Severity of Coronary Atherosclerosis," Diabetes Research and Clinical Practice, vol. 191, p. 110040, Sep. 2022.

[23] F. D. Shah et al., "Significance of Alterations in Plasma Lipid Profile Levels in Breast Cancer," Integrative Cancer Therapies, vol. 7, no. 1, pp. 33–41, Mar. 2008.

[24] Z. U. Din et al., "Crosstalk Between Lipid Metabolism and EMT: Emerging Mechanisms and Cancer Therapy," Molecular and Cellular Biochemistry, vol. [missing], Apr. 2024.

[25] E. Baldini et al., "Thyroid Diseases and Breast Cancer," Journal of Personalized Medicine, vol. 12, no. 2, p. 156, Feb. 2022.

[26] M. Ghalibaf, "The Association Between Breast Cancer and Thyroid Function: From Birth to Death," Multidisciplinary Cancer Investigation, vol. 5, no. 2, pp. 1–8, Feb. 2021.

[27] L. E. Zyla et al., "Effects of Thyroxine on Apoptosis and Proliferation of Mammary Tumors," Molecular and Cellular Endocrinology, vol. 538, p. 111454, Dec. 2021.

[28] J. Jin et al., "Thyroid Hormone Changes Correlate to Combined Breast Cancer With Primary Thyroid Cancer," Breast Cancer: Targets and Therapy, vol. [missing], Dec. 2024.

[29] C. M. Kitahara et al., "Thyroid Dysfunction and Cancer Incidence: A Systematic Review and Meta-Analysis," Endocrine-Related Cancer, vol. 27, no. 4, pp. 245–259, Apr. 2020.

[30] C. H. Weng et al., "Breast Cancer Risk in Postmenopausal Women With Medical History of Thyroid Disorder in the Women's Health Initiative," Thyroid, vol. 30, no. 4, pp. 519–531, Apr. 2020.

[31] C.-H. Weng, E. R. Okawa, M. B. Roberts, S. K. Park, C. B. Umbricht, J. E. Manson, and C. B. Eaton, "Breast Cancer Risk in Postmenopausal Women With Medical History of Thyroid Disorder in the Women's Health Initiative," Thyroid, vol. 30, no. 4, pp. 519–530, Apr. 2020, doi: 10.1089/thy.2019.0328.

[32] L. Bach, K. Kostev, L. Schiffmann, and M. Kalder, "Association Between Thyroid Gland Diseases and Breast Cancer: A Case–Control Study," Breast Cancer Research and Treatment, vol. 182, no. 1, pp. 207–213, Jul. 2020, doi: 10.1007/s10549-020-05689-7.

[33] B. Wang, Z. Lu, Y. Huang, R. Li, and T. Lin, "Does Hypothyroidism Increase the Risk of Breast Cancer: Evidence From a Meta-Analysis," BMC Cancer, vol. 20, pp. 1–9, Dec. 2020, doi: 10.1186/s12885-020-07582-5.