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Studying the Relationship Between Hypothyroidism and Breast Cancer

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Abstract

Objectives: Breast cancer is one of the most common diseases in women and hypothyroidism is an important risk factor for developing this cancer. Therefore, the present study aimed to investigate the relationship between hypothyroidism and breast cancer development in women. In addition, the effect of age and weight on hypothyroidism was studied in patients with breast cancer.

Materials and Methods: A total of 200 women who referred to Shams, Amir-al-Momenin, and Noor-Nejat hospitals of Tabriz located in East Azarbijan were selected during a 4-month period in order to participate in this case study. The participants included 100 women with a definite diagnosis of breast cancer vs. 100 healthy women. The levels of thyroid hormones (T3, T4, & TSH) were analyzed and the correlation between these levels and the incidence of breast cancer was determined.

Results: Based on the findings, no significant difference was observed between both groups regarding the age, weight, and levels of thyroid hormones ($P > 0.05$). Further, the results revealed that the correlation between the age and weight of the studied women and the level of hormones was negligible. However, in patients with breast cancer, there was a significant relationship between T3 serum level and age ($P = 0.005$).

Conclusions: Generally, no significant relationship was found between the development of breast cancer and hypothyroidism in the patients with breast cancer.

Keywords: Hypothyroidism, Breast cancer, T3, T4, TSH

Introduction

Thyroid disorders along with breast cancer are considered among the most widespread diseases in women. Furthermore, endogenous and exogenous sex hormones contribute to the etiology of breast cancer (1,2). High levels of thyroid hormones have estrogen-like effects in the in vitro (3) which increase the proliferation of cancer cells in the breast (4) and stimulate angiogenesis (5). Different researchers reported that hypothyroidism promotes the incidence risk of breast cancer (6) and some others highlighted hyperthyroidism (7), goiter (8), and autoimmune thyroid diseases (2) as the risk factors of this type of cancer. Recent research findings found that an increased risk of breast cancer in women with hyperthyroidism and its slight reduction in developing hypothyroidism indicates the relationship between thyroid function and the risk of breast cancer development (9). Several studies emphasized that there is a positive correlation between T3 levels and mortality rates of breast cancer (10).

Hypothyroidism is the second most widely diagnosed disease among endocrine disorders after diabetes, involving a major part of national plans for preventing major noninvasive diseases such as heart diseases, cancers, and diabetes. Moreover, hypothyroidism develops when the thyroid gland is unable to produce enough hormone required by the body, causing cardiovascular, bone, neuropsychiatric complications, and other hypothyroid outcomes in the patients (11).

The results of various empirical studies suggested that thyroid hormones can stimulate cell proliferation in the breast tissue (4), and thyroid receptors are present in the malignant and normal breast cells (12). Additionally, thyroid hormones improve estradiol-mediated effects in the cell proliferation (4) and imitate the impacts of estradiol, and therefore promote the growth and stimulation in expressing progesterone receptors (13). As a result, thyroid function and hormonal levels can synergistically be associated with tumor growth. In addition, the results of some studies indicated that the amount of free T4 (14), T3 total (15), free T4, and TSH (6), or TSH alone (16) are related to the incidence of breast cancer.

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Accordingly, this study sought to examine the relationship between hypothyroidism and the incidence of breast cancer. Further, it attempted to explore the effect of age and weight on hypothyroidism in patients with breast cancer. Thyroid tests included determining the TSH, T3, and T4 levels, as well as, measuring the age and weight of the patients before the surgery in the women who referred to Shams, Amir-al-Momenin, and Noor-Nejat hospitals of Tabriz located in North West of Iran.

Materials and Methods

The population of the study included all the patients who referred to the cancer diagnostic center of Noor-Nejat, Amir-Al-Momenin, and Shams hospitals in Tabriz during 4 months out of which 100 cases were diagnosed with breast cancer. Therefore, their blood samples were collected before tumor resection surgery. Furthermore, the blood samples of 100 healthy women were collected as the control group (using Cochran formula). Before administering any treatment, the range of the patients' thyroid hormones was measured by chemiluminescence technics (Abbott instrument) including chemotherapy or hormone therapy. Then, the relationship between hypothyroidism and breast cancer was evaluated considering the age and weight of the patients.

The inclusion criterion was women developing breast cancer and the exclusion criteria encompassed pregnancy, abnormal serum lipid levels, goiter, diabetes, ischemic heart disease, a history of treatment with corticosteroid, estrogen, tamoxifen, and raloxifene, as well as a history of active liver disease, chronic and advanced kidney disease, pituitary disease, or total thyroidectomy. Moreover, to observe the ethical considerations, patients' names were kept confidential and no cost was received for the test. Additionally, written consents were taken from the studied women for conducting these tests.

The data were normalized by the Kolmogorov-Smirnov test and statistically evaluated using the SPSS software, version 21. In addition, to study the difference between these 2 groups, independent *t*-test and the Mann-Whitney U test were applied for normal and abnormal data, respectively. Finally, the correlation between age and weight and serum levels of hormones was assessed using the Pearson correlation test.

Results

The age ranges of the studied patients and the control group were 24-83 and 27-84 years and their weight criteria varied from 61-86 and 60-89 kg, respectively. The results demonstrated that there was no significant difference in terms of age and weight between the 2 groups ($P > 0.05$). As regards the hormonal measurement test, the results indicated that T3 and T4 hormones were normally distributed while the TSH hormone was not normally distributed. Further, no statistically significant difference was found between the 2 studied groups evaluating the T3 and T4 hormones by Student's *t* test ($P > 0.05$). Furthermore, studying the TSH difference between the 2 groups using the Mann-Whitney U test represented no statistically significant difference ($P > 0.05$). Table 1 demonstrates the mean ± standard deviation of different parameters in both groups. Finally, based on the results of correlation analysis, a significant indirect relationship was found between age and T3 hormone only in the control group ($P = 0.005$), while the correlation between age and weight and thyroid hormones was not significant ($P > 0.05$). The results of this section are provided in Table 2.

Discussion

The mammary gland is derived from iodide-producing ectoderm (17). Breast functions similar to the thyroid gland and can absorb iodide and add it to the milk during the lactation. Additionally, dysfunction of thyroid hormones leads to iodine uptake abnormality and its deficiency and autoimmune diseases and thus cancer development (18). Accordingly, increased iodine consumption is considered a protective factor against the incidence of breast cancer (19). Based on the reports, low levels of iodine were observed in the breast cancer tissues compared to the normal breast tissues or benign mammary tumors (20,21). In this study, levels of thyroid hormones were compared between the breast cancer and control groups according to which no abnormality was found in the thyroid gland examination in any of the studied groups. The results represented no significant difference between the age, weight, and level of the T3, T4, and TSH hormones in both groups ($P > 0.05$). The correlation between age and weight and the level of the studied hormones was negligible while there was a significant relationship between T3 serum levels and the age in the case group ($P = 0.005$).

Various studies were conducted regarding the relationship between the levels of thyroid hormones and breast cancer. For example, Szychta et al evaluated the TSH, FT4, and FT3 levels between women with breast cancer and benign breast tumors and control group and found no significant difference in this respect (7). In

Table 1. The Results of Comparing the Mean ± Standard Deviation of Different Parameters in Both Groups Under Investigation

Groups	Age (y)	Weight (kg)	Hormone Value		
			T3 (ng/dL)	T4 (µg/dL)	TSH µIU/mL)
Case	53.63 ± 11.85	76.44 ± 5.96	0.20 ± µ1.10	8.02 ± 1.28	2.67 ± 2.49
Control	52.28 ± 11.74	76.24 ± 7.96	1.06 ± 0.18	8.15 ± 1.19	2.65 ± 2.06
P value	0.219	0.712	0.116	0.523	0.678

Table 2. The Results of Studying Pearson Correlation Coefficient Between the Age and Weight and the Studied Hormones in Both Groups

Groups	Variable	Age (y)			Weight (kg)		
		T3	T4	TSH	T3	T4	TSH
Case	Pearson correlation	-0.280	0.007	0.036	0.012	-0.026	0.124
	P value	0.005	0.943	0.722	0.906	0.798	0.218
Control	Pearson correlation	-0.021	-0.012	0.123	-0.091	0.060	-0.081
	P value	0.839	0.909	0.224	0.367	0.556	0.423

addition, Brandt et al indicated that high levels of FT4 and low levels of thyroid peroxidase antibodies (TPO-Ab) were associated with an increased risk of breast cancer (2). Further, Lemaire et al found a high level of T3 in patients with breast cancer. However, Rasmusson et al reported that T3 level was associated with no stages of a tumor development (22). In another study, the T3 level was decreased in several patients with breast cancer, especially in the metastatic (advanced) cases (23). Furthermore, Tosovic et al demonstrated that T3 level was directly correlated with the risk of breast cancer in postmenopausal women. However, the lack of association between T3 and the breast cancer was highlighted by a number of studies (14).

Although several researchers have linked high level of TSH with advanced breast cancer (23), some others reported that there was no relationship between TSH level and the tumor stage (22). For instance, Hellevik et al (16) found no such an association between the TSH and breast cancer; such result was also obtained by Tosovic et al (14, 15).

Conversely, Chaker et al studied 316 patients and 312 healthy women and found that hypothyroidism increases the risk of breast cancer development (24). Another study on 551 patients randomly diagnosed with breast cancer emphasized that there was a significant and positive relationship between the promotion of T3 level and the development of breast cancer (25). Additionally, Dinda et al examined 676 patients with breast cancer and 680 healthy women and observed that high levels of FT4 and low levels of TPO-Ab increased the risk of developing breast cancer. Moreover, T3 levels were found to have a significant relationship with the tumor size and increased the severity of invasion (2). Similarly, by studying patients with breast cancer (n = 65), Carcinoma *in situ* (n = 13), malignant tumors (n = 27), and 38 healthy people, Ditsch et al observed that T3 and T4 levels were significantly different in the patients with breast cancer, that is, T3 and T4 levels were higher in the patients with breast cancer (26). Tosovic et al reported that the FT4 levels were associated with a higher risk regarding the onset of breast cancer. In addition, they found that the risk of breast cancer development increased in overweight women (14). Further, Turken et al in their study on 150 unhealthy and 100 healthy individuals found a positive relationship between high levels of T4 and the higher risk of breast cancer incidence (27). In another study, a negative association was observed between T4 level and breast cancer . Furthermore, examining 766 patients with breast cancer, Brandt et al demonstrated that survival rates in patients with breast cancer were directly correlated with FT4 level (25).

In the majority of the above-mentioned studies, there was a positive relationship between breast cancer and thyroid diseases including autoimmune or non-autoimmune while, no such relationship was found in the present study. Moreover, some other studies approved the findings of the current study. In previous studies, the relationship between weight and age of patients with breast cancer thyroid disease was not addressed while in the present study the correlation coefficient between T4 serum levels and TSH levels was found ≤zero in both groups (the patients with breast cancer vs. healthy women), indicating the lack of correlation between the variables and the age of healthy and unhealthy individuals. However, T3 serum level was slightly correlated with the age of the patients in the group with breast cancer.

Conclusions

Generally speaking, the results of the current study on 100 patients with breast cancer and 100 healthy individuals revealed that there was no significant relationship between breast cancer and serum levels of thyroid hormones (i.e., T3, T4, & TSH) in patients with breast cancer and hypothyroidism.

Conflict of Interests

Authors have no conflict of interests.

Ethical Issues

The study was approved by Islamic Azad University (No. IR.IAU.TABRIZ.REC.1396.78).

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References

1. Henderson BE, Ross R, Bernstein L. Estrogens as a cause of human cancer:the Richard and Hinda Rosenthal Foundation award lecture. Cancer Res. 1988;48:246-53.
2. Brandt J, Borgquist S, Manjer J. Prospectively measured thyroid hormones and thyroid peroxidase antibodies in relation to risk of different breast cancer subgroups: a Malmo Diet and Cancer Study. Cancer Causes Control.

2015;26:1093-104. doi:10.1007/s10552-015-0602-8
3. Dinda S, Sanchez A, Moudgil V. Estrogen-like effects of thyroid hormone on the regulation of tumor suppressor proteins, p53 and retinoblastoma, in breast cancer cells. Oncogene. 2002;21:761-8. doi:10.1038/sj.onc.1205136
4. Hall LC, Salazar EP, Kane SR, Liu N. Effects of thyroid hormones on human breast cancer cell proliferation. J Steroid Biochem Mol Biol. 2008;109:57-66. doi:10.1016/j.jsbmb.2007.12.008
5. Davis PJ, Leonard JL, Davis FB. Mechanisms of nongenomic actions of thyroid hormone. Front Neuroendocrinol. 2008;29:211-8. doi:10.1016/j.yfrne.2007.09.003
6. Kuijpens JL, Nyklictek I, Louwman MW, Weetman TA, Pop VJ, Coebergh JW. Hypothyroidism might be related to breast cancer in post-menopausal women. Thyroid. 2005;15:1253-9. doi:10.1089/thy.2005.15.1253
7. Szychta P, Szychta W, Gesing A, Lewinski A, Karbownik-Lewinska M. TSH receptor antibodies have predictive value for breast cancer - retrospective analysis. Thyroid Res. 2013;6:8. doi:10.1186/1756-6614-6-8
8. Smyth PP, Smith DF, McDermott EW, Murray MJ, Geraghty JG, O'Higgins NJ. A direct relationship between thyroid enlargement and breast cancer. J Clin Endocrinol Metab. 1996;81:937-41. doi:10.1210/jcem.81.3.8772554
9. Søgaard M, Farkas DK, Ehrenstein V, Jørgensen JOL, Dekkers OM, Sørensen HT. Hypothyroidism and hyperthyroidism and breast cancer risk:a nationwide cohort study. Eur J Endocrinol. 2016;174:409-14.
10. Tosovic A, Bondeson A-G, Bondeson L, Ericsson U-B, Manjer J. Triiodothyronine levels in relation to mortality from breast cancer and all causes:a population-based prospective cohort study. Eur J Endocrinol. 2013;168:483-90.
11. Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J, et al. Cancer incidence and mortality patterns in Europe:estimates for 40 countries in 2012. Eur J Cancer. 2013;49:1374-403. doi:10.1016/j.ejca.2012.12.027.
12. Conde I, Paniagua R, Zamora J, et al. Influence of thyroid hormone receptors on breast cancer cell proliferation. Ann Oncol. 2006;17:60-4. doi:10.1093/annonc/mdj040
13. Nogueira CR, Brentani MM. Triiodothyronine mimics the effects of estrogen in breast cancer cell lines. J Steroid Biochem Mol Biol. 1996;59:271-9.
14. Tosovic A, Becker C, Bondeson AG, et al. Prospectively measured thyroid hormones and thyroid peroxidase antibodies in relation to breast cancer risk. Int J Cancer. 2012;131:2126-33. doi:10.1002/ijc.27470
15. Tosovic A, Bondeson AG, Bondeson L, Ericsson UB, Malm J, Manjer J. Prospectively measured triiodothyronine levels are positively associated with breast cancer risk in postmenopausal women. Breast Cancer Res. 2010;12:R33. doi:10.1186/bcr2587
16. Hellevik AI, Asvold BO, Bjoro T, Romundstad PR, Nilsen TI, Vatten LJ. Thyroid function and cancer risk:a prospective population study. Cancer Epidemiol Biomarkers Prev. 2009;18:570-4. doi:10.1158/1055-9965.EPI-08-0911
17. Venturi S. Is there a role for iodine in breast diseases? The Breast. 2001;10:379-82.
18. Zygmunt A, Adamczewski Z, Wojciechowska-Durczynska K, et al. Evaluation of efficacy of iodine prophylaxis in Poland based on the examination of schoolchildren living in Opoczno Town (Lodz Voivodship). Thyroid Res. 2012;5:23. doi:10.1186/1756-6614-5-23
19. Mittra I, Perrin J, Kumaoka S. Thyroid and other autoantibodies in British and Japanese women: an epidemiological study of breast cancer. Br Med J. 1976;1:257-9.
20. Kilbane MT, Ajjan RA, Weetman AP, et al. Tissue iodine content and serum-mediated 125I uptake-blocking activity in breast cancer. J Clin Endocrinol Metab. 2000;85:1245-50. doi:10.1210/jcem.85.3.6442
21. Lemaire M, Baugnet-Mahieu L. Thyroid function in women with breast cancer. Eur J Cancer Clin Oncol. 1986;22:301-7.
22. Rasmusson B, Feldt-Rasmussen U, Hegedus L, Perrild H, Bech K, Hoier-Madsen M. Thyroid function in patients with breast cancer. Eur J Cancer Clin Oncol. 1987;23:553-6.
23. Rose DP, Davis TE. Plasma triiodothyronine concentrations in breast cancer. Cancer. 1979;43:1434-8.
24. Chaker L, Visser TJ. Thyroid function: thyroid dysfunction and breast cancer risk - an unfinished story. Nat Rev Endocrinol. 2016;12:313-4.
25. Brandt J, Borgquist S, Almquist M, Manjer J. Thyroid function and survival following breast cancer. Br J Surg. 2016;103:1649-57. doi:10.1002/bjs.10284
26. Ditsch N, Liebhardt S, Von Koch F, et al. Thyroid function in breast cancer patients. Anticancer Res. 2010;30:1713-7.
27. Turken O, NarIn Y, DemIrbas S, et al. Breast cancer in association with thyroid disorders. Breast Cancer Res 2003;5:R110-3. doi:10.1186/bcr609