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The association between fibrocystic breast and thyroid autoimmunity

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ABSTRACT

Aims: The relationship between thyroid disorders and breast diseases including breast cancer and benign breast disease, has been a topic of interest and controversy. Our study aimed to investigate the potential association between autoimmune thyroid disease (ATD) and fibrocystic breast disease (FBD)

Methods: This retrospective study investigated the relationship between ATD an FBD. A total of 242 female patients aged 18 years or older were recruited for the study. Data were collected from medical records and patient interviews. The related parameters were recorded for each participant.

Results: This study included two hundred forty-two age-matched (29.78±4.55) and body mass index (BMI)-matched (24±2.38) women. A Mann-Whitney test did not find a statistically significant association between the case and control in terms of free thyroxine (FT4) (p value >0.05). There was a statistically significant difference between groups in terms of thyroid-stimulating hormone (TSH) (p value <0.001), antithyroid peroxidase (anti-TPO) (p value <0.001), and anti-thyroglobulin (anti-TG) (p value<0.001). A chi-square test did not find a statistically significant association between thyroid autoantibody and fibrocystic breast test results (p value > 0.05).

Conclusion: While our study did not find a significant association between these two conditions, other studies have reported varying results. Hormonal alterations, autoimmune factors, and genetic predispositions are among the potential mechanisms that could explain the associations observed in some studies.

Keywords: Autoimmune thyroid disease, thyroid disorders, fibrocystic breast, thyroid autoimmunity, risk factors

INTRODUCTION

Fibrocystic breast disease (FBD) affects up to 50% of women at some point during their lives.[1] It is characterized by the presence of lumps, cysts, and fibrous tissue in the breast.[2] Although there is no association between FBD and a higher breast cancer risk, it can cause discomfort, pain, and anxiety in affected women.[3] The cause of FBD is not yet known, but hormonal factors, genetic predisposition, and environmental exposures are believed to play a role in its development.[4]

Autoimmune thyroid diseases (ATDs), such as Hashimoto's thyroiditis and Graves' disease, are among the most prevalent autoimmune disorders, affecting up to 10% of the population.[5] The thyroid gland plays a critical role in regulating metabolism and other physiological processes, and its dysfunction can lead to a wide range of symptoms and complications. Recent studies have suggested a possible link between FBD and thyroid hormones.[6]

One of the possible mechanisms linking FBD and thyroid autoimmunity is estrogen's role in these conditions. Estrogen is a hormone involved in breast development and function, as well as in thyroid hormone synthesis and metabolism.[7] Estrogen dominance, a condition characterized by an imbalance between estrogen and progesterone levels, has been implicated in the development of FBD.[8] Moreover, estrogen has been shown to modulate the immune system, and its excess may contribute to the development of autoimmune diseases, including ATDs.[9] Therefore, it is possible that the effects of estrogen on breast tissue and the thyroid gland may be interrelated and that disturbances in estrogen balance may contribute to the co-occurrence of FBD and thyroid autoimmunity.

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Another possible association between FBD and thyroid autoimmunity is inflammation. Inflammation is a complex biological response to harmful stimuli, and it plays a role in FBD and ATDs pathogenesis.[10] Chronic inflammation of the breast tissue can lead to fibrosis and the formation of cysts, while inflammation of the thyroid gland can result in autoimmune damage and dysfunction.[11] It has been suggested that inflammation may be a common pathway linking various breast and thyroid disorders and that reducing inflammation may benefit both conditions.[12] Therefore, investigating the role of inflammation in FBD and thyroid autoimmunity might be useful for identifying novel strategies for prevention and treatment.

In this study, we investigated whether FBD and ATD tend to occur together. By examining a range of clinical and demographic parameters, we aimed to shed light on the pathophysiology of these conditions and their interplay. By contributing to a more detailed understanding of the complex association between breast health and thyroid function, our study may help to improve the quality of life and health outcomes of women with these conditions.

METHODS

The study was carried out with the permission of BezmiAlem Vakıf University Hospital Ethics Committee (Date: 03.04.2023 Decision No: 2023/49). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This retrospective study was conducted between February 2019 and February 2023 at Bezmialem University Hospital Gynecology and Obstetrics Department. A total of 242 female patients aged 18 years or older were included in the study. The inclusion criteria were: (1) the presence of FBD as confirmed by breast sonography; and (2) availability of thyroid function test results, free thyroxine (FT4), including thyroid-stimulating hormone (TSH), anti-thyroglobulin (anti-TG), and antithyroid peroxidase (anti-TPO) antibodies. Patients with a history of thyroid, breast cancer, or other severe medical conditions were excluded from the study.

The researchers collected data from the medical records of the subjects. The following parameters were recorded for each participant: age, body mass index (BMI), TSH, FT4, anti-TPO antibodies, and anti-TG antibodies. Breast sonography was performed to confirm the presence of FBD, and the severity of FBD was graded via the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) criteria.

Statistical Analysis

The researchers described the study subjects' demographic and clinical characteristics with a series of descriptive statistics. The means ± standard deviations (SD) were presented for all continuous variables, and categorical variables were reported as frequencies and percentages. The association between laboratory values and ATD was analyzed using the Mann-Whitney U test. A Chi-square test was used to examine the association between thyroid autoantibody and fibrocystic breast. All statistical analyses were performed using SPSS 28.0, and a value of less than 0.05 was considered statistically significant.

RESULTS

This study included two hundred forty-two age-matched (29.78±4.55) and BMI-matched (24±2.38) women. The majority of study participants weren't smoker. Table 1 shown descriptive statistics of study parameters.

Table 1. Descriptive statistics of study parameters in women (n=242).

Study parameters	median (range) mean ± SD
Maternal characteristics	
Age	29(20-39)29.78±4.55
BMI	24(18.9-29.6)24±2.38
Laboratory values	
TSH	2(1-2.5)1.8±0.34
FT4	1.2(0.9-1.8)1.18±0.14
ANTI-TPO	10(1.1-144)29.85±28.84
ANTI-TG	2.1(1-126.1)18.99±23.17

SD, standard deviation; BMI, body mass index; TSH, thyroid-stimulating hormone; FT4, Free thyroxine; ANTI-TPO, Antithyroid peroxidase; ANTI-TG anti-thyroglobulin

Table 2 compared case and control groups on the study parameters.

Table 2. Comparison of case and control groups

Study parameters	Thyroid autoantibody positive Case(n=112) M±SD	Thyroid autoantibody negative Control(n=130) M±SD	p value
Laboratory values			
TSH	1.79±0.29	1.69±0.37	<0.001
FT4	1.29±0.12	1.28±0.18	0.198
Anti-TPO	49.79±16.85	4.99±1.89	<0.001
Anti-TG	38.15±18.42	1.4±0.39	<0.001

M, Mean; N, number of subjects; TSH, thyroid-stimulating hormone; FT4, Free thyroxine; Anti-TPO, Antithyroid peroxidase; Anti-TG anti-thyroglobulin.

As stated in Table 2, a Mann-Whitney test showed no significant difference between the case and control regarding FT4 (p value>0.05). The groups showed significantly different TSH values (p value<0.001). The case group was statistically higher than the control (M=1.79; SD=0.29 vs. M=1.69; SD=37). The level of Anti-TPO differed between the groups significantly

(p value<0.001). Also, the groups showed significantly different Anti-TG values (p value<0.001).

Table 3 shown the relationship between thyroid autoantibody and fibrocystic breast.

Table 3. The relationship between thyroid autoantibody and fibrocystic breast

	Positive fibrocystic breast n(%)	Negative fibrocystic breast n(%)	p value
Thyroid autoantibody			0.962
positive	77 (53.8)	53 (53.5)	
negative	66 (46.2)	46 (46.5)	

*A Chi-square test.

As stated in Table 3, a chi-square test showed no significant relationship between thyroid autoantibody and fibrocystic breast (p value > 0.05).

DISCUSSION

Some studies found association between thyroid and breast diseases, but the reasons are not yet well understood.[13] There are controversial results about the relationship between thyroid diseases and breast cancer. Some studies have reported a correlation between breast cancer and thyroid diseases, while others have concluded that there is no such relationship between the two.[14] Some studies suggest that females who suffer from hypothyroidism are more prone to develop breast cancer, but the relationship between the two conditions remains unclear.[15] Our study adds to the existing literature by investigating the association between fibrocystic breast and thyroid autoimmunity, but further research is required better to understand the association between thyroid and breast pathologies.

While several studies have reported an increased thyroid disorders prevalence in patients with breast cancer,[14,16] our study did not find a significant association between fibrocystic breast changes and thyroid autoimmunity. However, other research has suggested that thyroid dysfunction might be related to benign breast disease.[16] A study shows that 14.9% of female patients with benign breast disease were diagnosed with hypothyroidism. In addition to breast disease, the thyroid profile can be helpful in diagnosing these female patients.[14] Another study found a significant increase in breast cancer risk for patients who were positive for thyroid autoimmunity, but it was not the case for other types of thyroid diseases, such as thyroid cancer.[17]

Several mechanisms may underlie the association between thyroid and breast disorders, which are still not fully understood, but there are several factors that have been suggested as contributing to it, including genetic predisposition, environmental factors, hormonal signaling, and immune system dysfunction.[13,15] Hormonal factors may be associated with breast and thyroid diseases, as both organs are hormone-responsive and share similar hormonal pathways. For example, estrogen and progesterone receptors are present in both breast and thyroid tissues, and thyroid hormones modulate the estrogen receptors' expression in breast cancer cells.[18] Additionally, some studies have suggested that hypothyroidism might be related to breast cancer in postmenopausal women.[15] Autoimmunity and functional immune system alterations have also been proposed as predisposing factors for the association between thyroid and breast disorders.[13]

Several studies have worked on the association between thyroid and breast disorders, with varying results. One retrospective observational study found that people with Anti-TPO were significantly more likely to have breast cancer.[19] Another study reported the presence of thyroid diseases, both autoimmune and not autoimmune, in patients with breast cancer.[20] A prospective observational study found that thyroid dysfunction was associated with benign breast disease.[21] A literature review concluded that survivors of breast cancer may be at a higher risk of thyroid pathologies, including thyroid malignancy.[22] A meta-analysis found that the levels of Anti-TG, Anti-TPO, and FT3 were found to be higher in breast cancer patients.[23] These studies suggest a potential relationship between breast and thyroid diseases, although the specific mechanisms and factors involved are not yet fully understood.

A study on Korean women showed that breastfeeding had been found to be associated with a lower risk of cervical, thyroid, and breast cancer.24 Furthermore, different thyroid diseases have been found in a number of breast cancer cases, and hypothyroidism has been suggested to be associated with breast cancer in women of postmenopausal age. These results suggest a potential association between thyroid function and breast cancer risk, although further research is needed to understand better the mechanisms underlying this association. The relationship between breast feeding and cancer risk may vary across populations and be influenced by several factors such as age, parity, and hormonal status. Therefore, it is necessary to determine whether these findings can be generalized to other populations and to identify other modifiable factors that may reduce cancer risks.

Despite the potential relationship between thyroid and breast disorders, in line with our findings, some studies did not find a significant association between fibrocystic breast disease and thyroid autoimmunity. For example,

a study on patients with benign breast disease found that only 14.9% had hypothyroidism, and there was no established relation between thyroid hormone status and benign breast disorders.[25] A study has shown that the levels of anti-TPO antibodies are elevated in subjects with breast cancer, but there is no difference in the rate of autoimmune thyroiditis between healthy individuals and breast cancer patients.[26,27] These results suggest that the association between breast disease and thyroid disorders may be complex and multifactorial, and more research is needed to understand the underlying mechanisms better. Other factors like environmental exposures, genetic predisposition, and lifestyle may also modulate the risk of breast disease and thyroid disorders. Therefore, it is important to continue investigating the potential links between breast disease and thyroid disorders to identify modifiable factors that can reduce cancer risks and improve overall health outcomes in women.

Our study from patient data did not show a significant association between FBD and thyroid autoimmunity. Although some studies have suggested a relationship between thyroid autoimmunity and breast cancer, the correlation between FBD and thyroid autoimmunity remains inconclusive. Our study has some limitations, including the use of patient data, which may not represent the general population. Also, the design of the study was cross-sectional, which limits our ability to establish causality or determine the temporal relationship between the two conditions. Furthermore, the study did not account for potential confounding factors, such as age, hormonal status, and environmental exposures, which may influence the relationship between FBD and thyroid autoimmunity.

Our study adds to the existing literature on the topic and highlights the need for further research to understand the potential link between these conditions better. Future studies should use more rigorous study designs, larger sample sizes, and more comprehensive assessments of thyroid function and breast health to elucidate better the relationship between FBD and thyroid autoimmunity.

CONCLUSION

The relationship between FBD and ATD remains a topic of ongoing debate and investigation. While our cross-sectional study did not find a significant association between these two conditions, other studies have reported varying results, with some suggesting a link between thyroid and breast disorders.14-18 Hormonal alterations, autoimmune factors, and genetic predispositions are among the potential mechanisms that could explain the associations observed in some studies. Given the complexity of the relationship between breast and thyroid diseases, further research is needed to understand better the underlying mechanisms and potential links between these conditions. This knowledge could help inform clinical management and treatment strategies for patients with breast and thyroid disorders. In the meantime, it may be beneficial for physicians to consider screening for thyroid disease in patients with breast disease.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of BezmiAlem University Hospital Ethics Committee (Date: 03.04.2023 Decision No: 2023/49).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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