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Evaluation of the relationship between endocrine organ masses; the thyroid and breasts

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Abstract

Aim: The aim of this study is to investigate the co-occurrence of thyroid masses (TM) and breast masses (BM) and to examine related demographic features.

Materials and Methods: The study included female patients; who were followed up in the general surgery outpatient clinic in the years between 2015 and 2020 because of thyroid nodules and underwent breast ultrasonography concurrently. Participants were divided into two groups as group-1 with the co-occurrence of thyroid and breast masses and group-2 with a TM but having no BM. The two groups were compared for age, body mass index (BMi), the number of children, the length of breastfeeding, TM size, TSH levels, vitamin D levels, and smoking status.

Results: The study included 267 patients with thyroid nodules. Of the patients; 70.03% had comorbid BM but 29.96% had no BM. No statistically significant differences were found in age, smoking status, BMi, TSH levels, vitamin D levels, and thyroid nodule size between the two groups ($p > 0.05$). The number of births was fewer and the duration of breastfeeding was shorter in the group of patients having BM concomitantly ($p < 0.001$). There was not a correlation between the size of TM and the size of BM (p: 0.839, r: 0.012).

Conclusion: in our study, it was found that most of the patients with thyroid nodules also had a mass in their breasts and this finding was associated with the duration of breastfeeding, the number of births, and the vitamin D level.

introduction

Thyroid masses (TM) are quite common in the population and approximately 90% of them are benign while 10% are malignant [1]. Epidemiological data show that having a thyroid nodule is five times more in women compared to men [2, 3]. The incidence of thyroid nodules has been found to increase with female gender, iodine deficiency, radiation exposure, and ageing [4]. Furthermore, it has been argued that primarily the thyroid-stimulating hormone (TSH) in the serum is responsible for the development of thyroid nodules and that the following factors including obesity, insulin resistance, and metabolic syndrome may be involved, too (5). in parallel to the advances in imaging methods, TM is becoming more prevalent today than before. Ultrasonography is the most common imaging method for the detection and follow-up of TM [4].

Breast masses (BM) are common in the population. BM are mostly benign [6]. However, it has been reported that women with benign BM have a higher risk of developing breast cancer compared to their otherwise healthy counterparts [7, 8]. Because breast cancer is the most common type of malignancy in women, it receives further attention. Today, the most widely used diagnostic tool for detecting BM is ultrasonography [6].

Both the breast and the thyroid are endocrine organs. Lesions originating from these organs are generally common in women and their frequency varies by the geographical region and depends on the sensitivity of imaging devices used for diagnosis [9]. Studies in the literature have shown that there is an interplay between breast and thyroid diseases [10, 11]. it has been shown that the interplay occurs between both benign and malignant diseases of both organs [9]. Most of the studies in the literature have focused on the quality and the type of the relationship between thyroid diseases and the malignant lesions of the breast [10]. The aim of this study is to investigate the association between TM and BM and examine associated demographic features.

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Materials and Methods

The study included 267 female patients; who presented to the general surgery outpatient clinic with TM and, at the same time, underwent breast examination and breast ultrasonography in the years between 2015 and 2020. The study was conducted in compliance with the Declaration of Helsinki, after the ethics committee approval dated 27/08/2020 and numbered 2020/41.

All female patients included in the study were examined by a general surgeon in the general surgery clinic. The diagnosis of TM was made by thyroid ultrasonography after taking the anamnesis from and performing a physical examination for each patient. The diagnosis of BM was made by breast ultrasonography after the assessment of the patients by taking anamnesis and performing a physical examination. Participants were divided into two groups as group-1 with the co-occurrence of thyroid and breast masses and group-2 with a TM but having no BM. Pregnant women, individuals younger than 18 years old and individuals, who underwent mammoplasty, mastectomy, or neck surgery were excluded from the study.

Face to face interviews were conducted with patients meeting the study criteria to inquire about the age, height, body weight, comorbidities, and the smoking and alcohol use status. information about the number of pregnancies, the number of births, and the number of months of breastfeeding were recorded. A detailed physical examination of both the breasts and the neck was performed in the general surgery outpatient clinic. TSH and vitamin D levels were evaluated in each patient.

The data were analyzed with iBM SPSS V23. Conformity to normal distribution was evaluated with the Kolmogorov-Smirnov test. Mann-Whitney U test was used to compare the quantitative data that were not normally distributed according to the paired groups. in the comparison of categorical data according to groups, Pearson Chi-square test was employed. Spearman's rho correlation coefficient was used to examine the correlation between non-normally distributed thyroid and breast size. Analysis results were presented as mean ± standard deviation and median (minimum-maximum) for quantitative data, and frequency (percentage) for categorical data. The significance level was taken as $p < 0.050$.

Considering the weak correlation between breast and thyroid size (r=0.25), according to 95% confidence $(1 - \alpha)$, 95% test power (1-β), and two-way hypothesis, the minimum number of samples to be included in the study was determined as 202. The study was completed on 267 cases in total, and the power of the test was found to be 98.6% according to the post hoc power analysis result.

Results

A difference was found between the median values of the number of children according to the groups ($p < 0.001$). While the median of group 1 was 2.0, the median of group 2 was found as 3.0. The median values of breastfeeding duration differ according to the groups ($p < 0.001$). While the median of group 1 was 10.0, the median of group 2 was determined as 18.0. There was no difference between the distributions of other parameters according to the groups ($p > 0.050$) (Table 1). No statistically significant relationship was found between thyroid size and breast size (r=0.012; p=0.839)

Discussion

Of the 267 patients included in the study, a mass in the breast was detected to be concomitant with the thyroid mass in 70.03% but no BM was detected in 29.96%. it was determined that age, BMi, size of the mass in the thyroid, and TSH and vitamin D levels did not have a statistically significant effect on the development of BM. However, it was found that the number of births was higher and the duration of breastfeeding was longer in the patients not having a mass in the breast. A correlation of the mass size was not found between the two endocrine organs.

Li et al conducted a study on a cohort of 6,371 Chinese women and randomly performed concomitant ultrasound examinations of the thyroid and the breast. They detected concomitant masses in these two endocrine organs at a rate of approximately 7% [12]. in another population screening study, a mass in the breast was detected in some of the patients with a mass in the thyroid. That study reported that the likelihood of developing a malignant disease of the breast was high in women; who were diagnosed with malignant thyroid diseases at a young age [13]. in another study, the likelihood of developing malignant breast disease was found to be considerably high in patients with benign thyroid disease. it is recommended that patients with TM should be evaluated for malignant breast disease [14]. Our study results are consistent with the literature in this aspect.

it has been reported that patients with breast cancer are more likely to develop thyroid cancer compared to otherwise healthy individuals [15]. in studies; where estrogen was used alone or in combination, it has been found that serum TSH levels, which were considered to be primarily responsible for nodule formation in the thyroid, were found to have contributed to the development of BM by acting on the genes responsible for mass formation in the breast [16]. in another laboratory study, it has been determined that triiodothyronine (T3) contributes to the formation of BM by enhancing the proliferative effects of 17beta-estradiol (E2) found in the breast tissue [17]. Furthermore, estrogen receptors (ER) are detected at high proportions in TM in a clinical study. Therefore, it was argued that estrogen can be involved in the formation and growth of TM (18). in the literature, in vitro experimental studies report that the availability of ER at high proportions in the thyroid tissue increased the proliferation rate of thyroid cells by 50-150%. This has been suggested as the reason for the higher occurrence of TM in women [19].

in a clinical study on 2473 women, it was found that lower numbers of birth and shorter breastfeeding duration were associated with an increased risk of BM and that a longer length of breastfeeding and higher numbers of birth decreased the occurrence of breast cancer [20]. A study from Japan included women; who did not give birth and women; who gave birth and were breastfeeding. That study found that giving birth and breastfeeding were protective against the development of TM [21]. A study on

Table 1. Comparison results by groups

	Group 1		Group 2		p
	Mean ± sd	Median (min. -max.)	Mean ± sd	Median (min. -max.)	
Age	45.4 ± 10.3	46.0 (18.0 - 75.0)	47.6 ± 10.6	48.0 (21.0 - 72.0)	0.197*
BMi	26.3 ± 3.4	25.8 (17.7 - 37.5)	26.5 ± 3.5	26.5 (19.5 - 34.6)	0.439*
Number of children	2.5 ± 1.1	2.0 (0.0 - 9.0)	3.2 ± 1.1	3.0 (0.0 - 6.0)	< 0.001*
Breastfeeding duration	10.2 ± 4.7	10.0 (0.0 - 30.0)	17.0 ± 6.6	18.0 (0.0 - 24.0)	< 0.001*
Right thyroid	9.9 ± 8.7	8.0 (0.0 - 40.0)	10.7 ± 9.2	7.5 (0.0 - 50.0)	0.647*
Left thyroid	8.8 ± 9.7	6.0 (0.0 - 40.0)	9.0 ± 8.9	7.0 (0.0 - 45.0)	0.579*
TSH	2.3 ± 2.4	1.7 (0.0 - 20.1)	2.8 ± 4.7	1.5 (0.0 - 37.0)	0.807*
Vit D	16.8 ± 11.0	14.1 (3.3 - 78.0)	19.5 ± 12.7	15.7 (3.4 - 73.5)	0.106*
Smoking	40 (21.4%)		12 (15.0%)		0.227**

*Mann-Whitney U test, **Pearson chi-square test, frequency (percentage), BMi body mass index, TSH, thyroid-stimulating hormone

African and American women found a negative correlation between breastfeeding duration and the development of breast cancer in both white and black women (22). in a clinical study conducted on 816 Korean women, the protective effect of long-term breastfeeding against thyroid diseases was proven based on the negative correlation of long-term breastfeeding with TSH levels and the occurrence of hypothyroidism [23]. it has been argued in that study that this finding has occurred because thyroid cells were exposed to high estrogen levels when women did not breastfeed or the length of breastfeeding was short [24].

Studies have found that; in women with low vitamin D levels, the incidence of breast cancer is high but the incidence of benign masses in the breast is also high particularly in young adult women [25]. it has been found that adequate levels of vitamin D prevent the development of benign and malignant masses in the breast by inhibiting the proliferation and transformation of breast tissue cells [26]. in their study, Laney et al found that; compared to the healthy population, vitamin D levels were low in individuals having benign or malignant nodules in the thyroid [27]. in laboratory studies and animal experiments, it was found that vitamin D reduced the formation of thyroid masses by inhibiting the proliferation and the invasive nature of thyroid cells [28]. in our study, vitamin D levels were found to be low in all patient groups. We interpreted that the vitamin D levels in all groups were lower than the normal range values because all groups consisted of individuals with thyroid or breast masses.

The limitation of our study is its retrospective design. The strength of our study is that it reveals the relationship between TM and BM in women and establishes the involvement of TSH and vitamin D levels, breastfeeding, and the number of births in such a relationship.

Conclusion

In our study, we found out that most of the patients with thyroid nodules also have a mass in their breasts. Therefore, we are of the opinion that it would be appropriate to examine both the thyroid and breasts for the presence of a mass in a patient presenting with a lump in any of these two organs.

References

1. Papini E, Guglielmi R, Bianchini A, et al. Risk of Malignancy in Nonpalpable Thyroid Nodules: Predictive Value of Ultrasound and Color-Doppler Features. J Clin Endocrinol Metab 2002;87(5):1941–6.
2. Tunbridge WMG, Evered DC, Hall R, et al. The Spectrum of Thyroid Disease in a Community: The Whickham Survey. Clin Endocrinol (Oxf) 1977;7(6):481–93.
3. isik A, Firat D, Yilmaz i, et al. A survey of current approaches to thyroid nodules and thyroid operations. int J Surg. 2018;54:100-4.
4. Dean DS, Gharib H. Epidemiology of thyroid nodules. Vol. 22, Best Practice and Research: Clinical Endocrinology and Metabolism 2008: 901–11.
5. Yildirim Simsir i, Cetinkalp S, Kabalak T. Review of Factors Contributing to Nodular Goiter and Thyroid Carcinoma. Med Princ Pract 2020; 29(1):1–5.
6. Guray M, Sahin AA. Benign Breast Diseases: Classification, Diagnosis, and Management. Oncologist 2006;11(5):435–49.
7. isik A, Soran A, Grasi A, Barry N, Sezgin E. Lymphedema after Sentinel Lymph Node Biopsy: Who is at Risk? Lymphat Res Biol. 2021;10.
8. Palli D, Turco MR Del, Simoncini R, et al. Benign breast disease and breast cancer: A case-control study in a cohort in italy. int J Cancer 1991; 47(5): 703–6.
9. Sindoni A, Fama F, Rosano A, et al. Thyroid nodules coexisting with either cystic or solid breast nodules: A new clue for this association between nodules coming from ultrasonography. Gland Surg 2017; 6(6):630–7.
10. Adamopoulos DA, Kapolla N, Michalakis A, et al. Thyroid disease in patients with benign and malignant mastopathy. Cancer. 1986;57(1):125–8.
11. Bolf EL, Sprague BL, Carr FE. A Linkage Between Thyroid and Breast Cancer: A Common Etiology? Cancer Epidemiol Biomarkers Prev 2019; 28(4):643–9.
12. Li H, Wang Z, Liu J-S, et al. Association Between Breast and Thyroid Lesions: A Cross-Sectional Study Based on Ultrasonography Screening in China. Thyroid 2020; 30(8): 1150–8.
13. Vassilopoulou-Sellin R, Palmer L, Taylor S, Cooksley CS. incidence of breast carcinoma in women with thyroid carcinoma. Cancer 1999; 85(3):696–705.
14. Muller i, Pinchera A, Fiore E, et al. High prevalence of breast cancer in patients with benign thyroid diseases. J Endocrinol invest. 2011;34(5):349-52.
15. Nielsen SM, White MG, Hong S, et al. The Breast-Thyroid Cancer Link: A Systematic Review and Meta-analysis. AACR 2016; 25(2): 231–8.
16. Silva JM, Domínguez G, Gonzílez-Sancho JM, et al. Expression of thyroid hormone receptor/erbA genes is altered in human breast cancer. Oncogene 2002; 21(27): 4307–16.
17. Hall LC, Salazar EP, Kane SR, et al. Effects of thyroid hormones on human breast cancer cell proliferation. J Steroid Biochem Mol Biol 2008; 109(1–2):57–66.
18. Yane K, Kitahori Y, Konishi N, et al. Expression of the estrogen receptor in human thyroid neoplasms. Cancer Lett 1994; 84(1): 59–66.
19. Rajoria S, Suriano R, Shanmugam A, et al. Metastatic phenotype is regulated by estrogen in thyroid cells. Thyroid 2010; 20(1): 33–41.
20. Shinde SS, Forman MR, Kuerer HM, et al. Higher parity and shorter breastfeeding duration. Cancer 2010;116(21):4933–43.

21. Pham TM, Fujino Y, Mikami H, et al. Reproductive and menstrual factors and thyroid cancer among Japanese women: The Japan collaborative cohort study. J Women's Heal 2009 ;18(3):331–5.
22. Mayberry RM, Stoddard-wright C. Breast cancer risk factors among black women and white women: Similarities and differences. Am J Epidemiol 1992;136(12):1445–56.
23. Kim SW, Lee JH, Shon HS, et al. Association of breastfeeding with thyroid function and autoimmunity in postmenopausal women. Endocrine 2021; 71(1):130–8.
24. Xhaard C, Rubino C, Cléro E, et al. Menstrual and Reproductive Factors in the Risk of Differentiated Thyroid Carcinoma in Young Women in France: A Population-Based Case-Control Study. Am J Epidemiol 2014; 180(10):1007–17.
25. Schnitt, Stuart J. Pathology of benign breast disorders. Breast diseases 2000:90.
26. Boeke CE, Tamimi RM, Berkey CS, et al. Adolescent dietary vitamin D and sun exposure in relation to benign breast disease. Cancer Causes Control 2015; 26(8): 1181–7.
27. Goldner W, Laney N, Meza J, et al. The prevalence of vitamin D deficiency is similar between thyroid nodule and thyroid cancer patients. int J Endocrinol 2010:2010.
28. Feldman D, Krishnan A V, Swami S, et al. The role of vitamin D in reducing cancer risk and progression. Nature Reviews Cancer 2014; 14: 342–57.