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RELATIONSHIP BETWEEN LEVELS OF THYROID HORMONES AND THYROID ANTIBODIES IN BREAST CANCER

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ABSTRACT

Objective: Breast cancer is a common malignancy in women in both western countries and in India and is still one of the leading causes of death in women. The relationship between breast cancer and thyroid diseases is controversial. The aim of the present study is to evaluate the incidence of auto immune and non auto immune thyroid diseases in breast cancer patients

Methods: The role of thyroid hormones status in breast cancer patients was estimated by measuring serum free Triiodothyronine, serum free Tetraiodothyronine, serum Thyroid Stimulating hormone levels and the role of antibodies by measuring anti thyroid peroxidase (anti-TPO) antibodies, anti thyroglobulin antibodies(anti-Tg) in blood. For this, 100 cases of breast cancer patients were included. The findings were compared with 75 age matched healthy females.

Results: A significant increase in the levels of Thyroid Stimulating Hormone and anti-Thyroid peroxidase antibodies were observed in the cases as compared to controls. There were no significant differences in the levels of free Triiodothyronine(FT3), free Tetraiodothyronine(FT4), and anti thyroglobulin antibodies(anti-Tg). **Conclusion:** Our results indicate increased incidence of auto immune and non auto immune thyroid diseases in breast cancer patients when compared to controls.

Keywords: Autoimmune Thyroid diseases, Non auto immune thyroid diseases, anti TPO antibodies, anti Tg antibodies.

INTRODUCTION

Breast cancer is a hormone dependent neoplasm. It is the most common malignancy in women in western countries and accounts for 18.4% of all cancers in female patients.(1).Qualitative changes in the lifestyle of women in developed countries that can influence risk factors for breast cancer, such as age at menarche, menopause, or first pregnancy, may partially explain this phenomenon.(2).The fact that both breast

cancer and thyroid disease predominantly affect females and that both have a postmenopausal peak incidence has inevitably resulted in a search for an association between the two diseases.(3,4). Conflicting results regarding the clinical correlation between breast cancer and thyroid diseases have been reported in the literature. Many studies showed that thyroid diseases are common among women with breast cancer(5),whereas other reports did not

confirm such an association of breast cancer with thyroid diseases(6,7).Almost every form of thyroid disease, including nodular hyperplasia(8),hyperthyroidism(3) and thyroid cancer(9,10), has been identified in association with breast cancer. These findings have led to the investigation of the relationship between breast cancer and autoimmune thyroid diseases.(AITDS).The aim of the present study was to determine the prevalence of thyroid diseases in patients with breast cancer as compared with that in the general female population and further investigate the possible relationship between thyroid disorders and breast cancer risk to create awareness in female population.

MATERIALS AND METHODS

The present study was conducted in the department of surgery and department of biochemistry , S.V. Medical college, Tirupati. The study included 100 patients with breast cancer and 75 age matched controls. All the subjects belonged to age group of 35-75 years and had no history of previous thyroid diseases. Out of cases, a total of 80 patients had invasive ductal carcinoma,10 had invasive lobular carcinoma and 10 had

mixed(invasive ductal and lobular) carcinoma. Four weeks after surgical procedure , clinical, ultrasonographic evaluation were done for all the patients and biochemical parameters were studied in all the subjects before starting chemotherapy, hormone therapy or radiotherapy. Informed consent was obtained from all the cases and controls regarding the study and the parameters which were estimated. Fasting blood samples were collected by venipuncture technique and for separation of serum, the blood is centrifuged at 3000rpm for 5 min. The separated serum is used to estimate serum TSH,FT3,FT4,TPO antibodies and anti TG abs. Serum TSH,FT3 & FT4 were estimated by ELISA method(11,12). Estimation of thyroid auto antibodies by using RIA for thyroid peroxidase antibodies(TPO-Abs)) and quantitative indirect enzyme immunoassay based on the sandwich method(antithyroglobulin immunoradiometric assay kit) for thyroglobulin antibodies(TG-Abs) which are also called as microsomal antibodies were done. All the results were expressed as mean \pm SD and statistical comparison was done.

RESULTS

Table 1: Comparison of levels of thyroid hormone status in controls and cases

	Patients (n=100)	Controls (n=75)	P value
FT3(pmol/l)	3.78 \pm 0.53	3.72 \pm 0.57	Not Significant
FT4(pmol/l)	9.34 \pm 0.26	9.27 \pm 0.28	Not Significant
TSH(μ IU/ml)	4.31 \pm 0.52	3.58 \pm 0.49	<0.001 (Highly Significant)

Table 2: Comparison of levels of thyroid antibodies in cases and controls

	Patients (n=100)	Controls (n=75)	P value
TPO antibodies(IU/ml)	106.21 \pm 21.33	22.47 \pm 5.14	<0.001 (Highly Significant)
Thyroglobulin antibodies(IU/ml)	28.92 \pm 7.52	28.75 \pm 7.50	Not Significant

Evaluation of thyroid function was based on serum thyroid hormones. The mean values for serum thyroid hormones were 3.78 ± 0.53 (pmol/l) for FT3, 9.34 ± 0.26 for FT4 and 4.31 ± 0.52 for TSH in breast cancer patients. The mean values in the control group were 3.72 ± 0.57 (pmol/l) for FT3, 9.27 ± 0.28 (pmol/l) for FT4 and 3.58 ± 0.49 for TSH. The differences between breast cancer patients and the control group in mean serum free T3, free T4 were not statistically significant whereas TSH is statistically significant. The mean values for serum thyroid auto antibodies were 106.21 ± 21.33 for anti TPO antibodies and 28.92 ± 7.52 for anti Thyroglobulin antibodies in breast cancer patients, and 22.47 ± 5.14 and 28.75 ± 7.50 , respectively in the control group. Thus, the mean value for serum anti-TPO antibodies was higher in breast cancer patients than in the control group, whereas the difference between the groups in mean values for serum antithyroglobulin antibodies was not statistically significant.

DISCUSSION

The present study found a high prevalence of autoimmune thyroiditis, confirmed mainly by antibody positivity, in breast cancer patients. The coincidence of thyroid disease and breast cancer has long been a subject of debate. Although associations with hyperthyroidism, hypothyroidism, thyroiditis and nontoxic goiter have been reported in the literature, no convincing evidence exists of a casual role for overt thyroid disease in breast cancer. Geographical variations in the incidence of breast cancer have been attributed to differences in dietary iodine intake, and an effect of iodine on the breast has been postulated.(13). The possible interactions between thyroid gland and breast

tissue are based on the common property of the mammary and thyroid epithelial cell to concentrate iodine by a membrane active transport mechanism(14) as well as on the presence of TSH receptors in fatty tissue, which is abundant in mammary gland.(15) Increased incidence of breast cancer has been reported in areas of endemic goiter but no change in incidence occurred when the goiter rate decreased after iodine prophylaxis. Nonetheless, an association of breast cancer with nontoxic goiter continues to be reported in areas of low iodine intake.(16). Reports on the association of breast cancer with decreased dietary iodine intake have suggested that such deficiencies may result in subclinical hypothyroidism predisposing to breast disease. The presence of an iodine pump in both thyroid and breast (17) have led to studies on a possible direct effect of iodine on the breast.(18). Studies in humans(19) have shown that treatment with elemental iodine results in the resolution of fibrocystic breast disease and breast pain. In the thyroid, I⁻ is required for thyroid hormonogenesis whereas in the breast I⁻ is needed in breast milk as a source of neonatal nutrition. Both organs require a method of oxidizing I⁻ to I₂(organification) in order to produce iodoproteins(20,21). This involves the presence of H₂O₂ as an oxidizing agent catalyzed by TPO in the thyroid and by lactoperoxidases in the breast. Apart from the requirement for iodide as a nutrient in breast milk, there is no known role for iodine in the normal or diseased breast. However, a breast requirement for I₂ rather than I⁻ has been suggested.(22). It has been postulated that formation of iodolipids such as iodolactones or iodoaldehydes represents a form of thyroidal auto regulation(23), which may be the mode of

action of iodide inhibition of thyroid function in the Wolff-Chaikoff effect.(24-26). Additionally ,some endocrine stimuli identified in thyroid products that exert a simultaneous action on the breast and the various thyroid antibodies, which could also interact with various receptors on breast tumors, have been postulated to be responsible for the coincidence of mammary and thyroid gland disorders.(10,27). The presence of circulating TPO antibodies in asymptomatic individuals has been implicated as conferring an increased risk for future hypothyroidism(28), there is no agreement on the significance of its association with breast cancer.(29). A fivefold excess in breast cancer has been reported in Japanese patients with AITD(30). However, no significant association between breast cancer and Hashimoto's thyroiditis was reported in a study from the Mayo Clinic in the USA(31). Thus, like other reported associations, the relationship between AITD, iodine intake and breast cancer is far from clear. Equally, there is little agreement on the significance of any published association between a range of thyroid disorders and breast cancer.(3,4).

It has been proposed that the presence of thyroid abnormalities may influence breast cancer progression.(32). A recent report suggested a better prognosis for breast cancer among patients with increased levels of TPO(32). It has been proposed that the immune response might be directed both by tumor and by thyroid tissue(33), or that the tumor and thyroid share common properties, as they both express TPO and the sodium iodide symporter gene.(34,35), Although high TPO level has been shown to be very important factor in antibody-dependent cell cytotoxicity in the thyroid, and there may be a possible association between autoimmune thyroiditis and the immune system, there is

no agreement on the significance of its association with breast cancer.

Despite the many different studies and approaches to the problem outlined above, there is still no definitive answer as to the significance of the association between thyroid status and breast cancer. Although available evidence strongly indicates that thyroid hypo function contributes to breast cancer progression, the possibility that thyroid autoimmunity might be associated with improved prognosis deserves further investigation. The possibility of genetic pre-disposition to both conditions also needs to be explored.

CONCLUSION

In this paper, we have studied thyroid autoantibody levels and thyroid function tests in breast cancer patients and controls. There was a significant difference between the groups in terms of TPO Abs levels and TSH levels. However no difference was demonstrated for other variables, such as Tg Abs FT3 and FT4. These results indicate a significant association between breast cancer and autoimmune and non autoimmune thyroid disorders. However, more research on this subject is required to confirm this association.

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