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TSH receptor antibodies in breast cancer and benign breast disease: a hospital based study

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ABSTRACT

Background: Associations between breast cancer, benign breast tumours and thyroid disorders are reported in numerous studies. Relationship between thyroperoxidase antibodies (TPOAb), thyroglobulin antibodies (TgAb), and breast cancer have been previously demonstrated. However, no analysis has been performed concerning an association between thyrotropin (TSH) receptor antibodies (TSHRAb) and breast cancer. The aim of the study was to evaluate the presence of TSH Receptor antibodies in women with breast cancer or benign breast tumours, and to analyze a possible relationship between TSH Receptor antibodies, and these two groups of breast diseases with emphasis to laboratory findings.

Methods: Clinical and laboratory details of 87 women hospitalized were prospectively analyzed, using an Post hoc Tukey HSD for normally distributed continuous data, chi-square test for comparison.

Results: TSH Receptor antibody levels in breast cancer was statistically significant. We observed TSHRAb more frequently in patients with breast cancer. We found that TSHRAb is the only variable possessing as a prognostic marker for breast cancer.

Conclusions: The present study indicates that the serum levels of TSH Receptor Antibody are significant higher in patients with Breast cancer. These results have implications not only for the screening of patients but also for the development of new prognostic markers. Further high-quality prospective studies are needed to explore whether TSH Receptor Antibodies are potential prognostic markers for patients with Breast cancer.

Keywords: Breast cancer, Benign breast tumours, TSH receptor antibody, TSH

INTRODUCTION

Breast cancer is the most frequent malignant tumour in women worldwide with about 1 million women being affected.¹ Breast cancer is a hormone dependent malignancy. Thyroid hormone receptors affect both the normal breast cell differentiation and breast cancer cell proliferation, with effects of thyroid hormones similar to those caused by estrogens.^{2,3} Some studies have indicated thyroid autoimmune changes as prognostic factors in breast cancer.⁴ Relationship between thyroid diseases

with breast cancer was demonstrated in several studies.⁵⁻⁸ Some of the studies showed higher incidence of breast cancer in patients with thyroid dysfunction compared to healthy controls.^{5,9-13}

TSH Receptor Antibodies is present in thyroid autoimmune diseases. The ligand for TSH Receptor Antibody (i.e.) TSH Receptor, is also present in breast cancer tissue.¹⁴ Only limited aspects of potential association between TSHRAb and breast cancer have been postulated, whereas the exact mechanism has not

been identified.¹⁵⁻¹⁷ Genetic, environmental and molecular pathways of both female predominant diseases have been described, and integrated analysis of the above entities provides opportunity to identify the potential relevant common etiological mechanism.¹⁸

The potential relationship between TSH Receptor antibodies and breast cancer has not been clearly documented, as the elevated serum levels of TPO Ab and Tg Ab in patients with breast cancer, detected in some studies, have not been confirmed elsewhere. 19-24 Moreover, no conclusive research has been undertaken concerning significance of TSHRAb in patients with breast cancer and benign breast tumours. 25 The aim of this prospective study is to determine the presence of TSH Receptor antibodies in women with breast cancer or benign breast tumours, and to analyse a possible relationship between TSH Receptor antibodies and these two groups of breast diseases with emphasis to laboratory findings.

METHODS

The study was carried out in Saveetha medical college and hospital, Chennai, India. The study included healthy controls (Group 1, n=29), women with benign breast tumours (Group 2, n=29), and women with breast cancer (Group 3, n=29).

All patients were without any known thyroid disease, and studied before any radio or chemotherapy. Breast cancer

patients, women with benign breast tumours and healthy controls gave formal consent for participation in the study. Signed informed consent was obtained from all participants, allowing analysis of all clinical and laboratory data mentioned in this paper.

All patients underwent serological determination of TSH Receptor antibodies based on electro chemiluminescence immune assay. The normal ranges were <1.22 IU/L for TSH receptor antibody. Those women without any breast or thyroid disease were the control group. The clinical and laboratory details of 87 women hospitalized were prospectively analyzed, using a post hoc Tukey HSD for normally distributed continuous data, chi-square test for comperes.

RESULTS

Table 1: Mean age of all three groups.

Group	Control	Benign tumours	Breast
Group	group	Denign tuniours	cancer
Age	45.14±13.58	31.25±8.61	51±14.29

A total number of 87 patients were included in this study. Out of this, 29 women were healthy controls, 29 women with benign breast tumours and 29 women with breast cancers

The age of the patients ranged from 20 years to 92 years (Table 1).

Table 2: Parameters of the study population.

Parameter	Controls mean±SD (group 1)	Benign tumours mean ± SD (group 11)	Breast cancer mean ± SD (group III)	P-value
TSHRAb (<1.22Iu/L)	0.75±0.53	0.59±0.33	0.71±0.49	0.403 (NS)

Table 3: TSH receptor antibody values within study population.

Groups	Control group	Benign tumours	Breast cancer	Total
Normal range	27 (93.1%)	29 (100.0%)	23 (79.3%)	79 (90.8%)
Elevated	2 (6.9%)	0 (0%)	6 (20.7%)	8 (9.2%)
Total	29 (100.0%)	29 (100.0%)	29 (100.0%)	87 (100.0%)

All patients were without any known thyroid disease are studied. TSHR Ab were determined in healthy controls, women with benign breast tumours and breast cancer (Table 2).

Those women without any breast or thyroid disease were the control group. Out of these 29 patients in control group, 2 had elevated TSH Receptor antibody level. Among the 29 patients with benign breast tumours there was no elevation of TSHR Ab (Table 3), which indicated no association of TSHR Ab with benign breast tumours.

Out of 29 patients with breast cancer, 6 had elevated levels of TSH Receptor antibodies, which indicated TSH Receptor antibodies are statistically significant in breast cancer (Table 3), (Figure 1), and association of TSH Receptor antibodies with breast cancer.

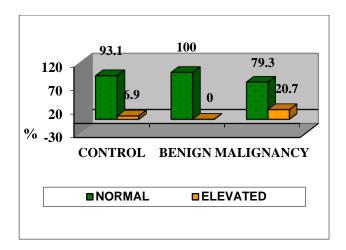


Figure 1: Comparison between TSHR AB and group.

DISCUSSION

TSHR Ab is a positive determinant of breast cancer. The prevalence of TSHR Ab in breast cancer is 20.7%. In the present study, among 29 patients with breast cancer, 6 patients were found positive for TSHR Ab. TSHR Ab levels were significantly higher in our series in patients with breast cancer, comparing to controls and to patients with benign breast tumors.

Mammary gland is derived from iodide- concentrating ectoderm.¹⁸ Breast has absorption capacity of iodide for use as a milk ingredient during lactation.^{6,26} Increased intake of iodine is considered as a protective factor against the occurrence of breast cancer.²⁷ The incidence of breast cancer has been attributed to differences in dietary iodine intake, and an effect of iodine on breast has been postulated (Mittra I, 1976).²⁷ Uptake of iodide in to the breast alveolar and ductular cells happens in the mechanism of active transport via the glycoprotein -Na⁺/I-symporter (NIS).²⁸ The expression of NIS occurs in 80% to 90% breast cancer cases. TSH receptors are present in fatty tissue, which is abundant in mammary gland (Davies tf.1994).²⁹ Additionally, some endocrine stimuli identified in thyroid products exert a simultaneous action on the breast and the various thyroid antibodies which could also interact with receptors on breast tumours. Thyroid antibodies could interact with the receptors on breast tumours. 30 Interaction between TSHR Ab and breast Cancer can occur, common in the adipose tissue.³¹ TSH Receptor expression is common in breast cancer, with higher prevalence in low- grade breast cancer.14

In our study, TSHR Ab levels were significantly higher in breast cancer comparing to benign breast tumours and controls. They are positive determinants of breast cancer. Therefore, we suggest that TSHR Ab can be called a positive predictor for the subsequent development of breast cancer.

However, further research is needed to elucidate the mechanism linking Breast cancer and TSHR Ab. The major limitation of our study was the small sample size. Further studies including a larger group of patients are necessary to confirm the results. (Ditsch et al., 2010; Szychta et al., 2013). ^{2,33}

CONCLUSION

The present study indicates that the serum levels of TSH Receptor Antibody are significant higher in patients with Breast cancer. These results have implications not only for the screening of patients but also for the development of new prognostic markers. Further high-quality prospective studies are needed to explore whether TSH Receptor Antibodies are potential prognostic markers for patients with Breast cancer.

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Institutional Ethics Committee

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