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A Tertiary Medical College Hospital based Observational study to evaluate the correlation between antithyroid peroxidase antibody levels in patients with invasive breast cancer

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ABSTRACT: Background: Very few studies have assessed prevalence of anti-thyroid peroxidase antibodies in women with breast cancer. In this study, we aimed to assess the prevalence of anti-thyroid peroxidase antibodies in women with breast cancer.
Methods: Tertiary hospital based cross - sectional study carried out at Saveetha Medical College, Chennai, during the period of August 2018 to July 2020. Seventy-five women in surgical oncology ward/OPD were included in the study. Subjects included in the study were between age 35 to 80 years, provided they fulfilled inclusion and exclusion criteria. History was noted, serum anti-thyroid peroxidase antibodies test was done. Results were noted and analyzed.
Results: Out of 75 subjects, 21.3% of women with breast cancer were having elevated anti-thyroid peroxidase antibodies.
Conclusions: Prevalence of anti-thyroid peroxidase antibodies is high among women with breast cancer. These results have implications both for screening of patients for thyroid disorders and also for development of new prognostic markers. Therefore, routine screening is preferable among women with breast cancer.
Keywords: Breast cancer, Anti-TPO antibodies, Chemiluminescence immunoassay

1. INTRODUCTION

Breast cancer is the most common cancer in females. Breast cancers arise from the interlobular connective tissue in the breast and can be broadly classified into invasive or *in situ* cancers. *In situ* breast cancers histologically do not invade the basement membrane. Out of the 1.3 million cases of invasive breast cancer that are diagnosed annually, 450,000 women succumb to the disease**.**[1] With early screening, neoadjuvant therapy and community education, the mortality associated with breast cancer has declined since 1990.[2]

Thyroid peroxidase (TPO) is an enzyme that primarily exerts its action in the thyroid follicular cells; it oxidizes iodide ions to iodine and adds tyrosine residues to thyroglobulin to form T3 and T4.[3] Anti-TPO autoantibodies produced against the thyroid tissue is involved in the pathogenesis of autoimmune thyroid conditions (Hashimotos thyroiditis, Graves disease). These antibodies are detected in the blood and elevated levels signify the presence of an autoimmune thyroid disease.[4] Breast and thyroid tissue originate embryologically from same type of cells.[5] Smyth et al demonstrated an association of thyroid disease with breast cancer.[6]

Contrasting studies have postulated that the development of an autoimmune thyroid disease is independent of the estrogen and progesterone receptor status in breast cancer.[7]

This study was done to measure anti-TPO antibody levels in patients with breast cancer, and to understand the role of anti-TPO antibody and breast cancer.

2. METHODS

The study was conducted in the Department of Surgical Oncology at Saveetha Medical College, Chennai. The study period is between August 2018 to July 2020. The study subjects were females, aged between 35 years and 80 years. Seventy five female patients were selected for this study.

INCLUSION CRITERIA

- Women between 35 – 80 years of age
- Histopathological proven biopsy of invasive ductal breast cancer
- Patients with early breast cancer, locally advanced breast cancer and metastatic breast cancer

EXCLUSION CRITERIA

- Women less than 35 years and more than 80 years of age
- Pre-existing thyroid pathology
- Patient on thyroid supplementation or anti0thyroid medication
- Prior chemotherapy or radiotherapy to the breast
- Prior breast conservation surgery
- Patients with in situ breast lesions

A core needle biopsy using a 14G needle was done prior to the withdrawal of venous blood samples. After obtaining written consent from the patient and under aseptic precautions, a core needle biopsy was done under local anaesthesia (10 ml of 2% plain lidocaine). Tissue obtained was sent for histopathological assessment to confirm the diagnosis of an invasive ductal breast carcinoma.

Following the histopathology report, using a 5 ml sterile syringe, 2 ml of venous blood was collected from the anterior cubital vein of the patient. The sample was sent to the microbiology lab and was analysed via chemiluminescence immune assay for anti-thyroid peroxidase antibodies. The normal range in our hospital is <9 IU/L for anti-thyroid peroxidase antibodies. This cut-off value is considered for the purposes of this study.

3. RESULTS

All statistical analysis was performed using statistical package for social science for Microsoft windows. The data were not normally distributed and therefore non-parametric tests were performed. Descriptive statistics were presented as numbers and percentages.

The data were expressed as mean and SD. Independent sample test, Mann-Whitney test and chi-square test was used. A two-sided P value <0.05 was considered statistically significant. Out of these 75 subjects, 21.3% of women with breast cancer were having elevated levels of anti – thyroid peroxidase antibodies. 4% women lying in the age group of 35- 50 years and 17.3% women in the age group of 51-80 years were having elevated levels of anti – thyroid peroxidase antibodies with mean serum anti-TPO antibodies levels of 3.62 ± 2.89 mIU/ml and 6.46 ± 15.19 mIU/ml respectively. These observations are tabulated in Table 1.

Table 1: Observed data.

Age group	**Percentage of women with breast cancer with elevated Anti-TPO antibody levels**	**Serum Anti-TPO antibody levels in < 9 IU/ml (mean±SD)**
35-50	4%	3.62±2.89
51-80	17.3%	6.46±15.19

4. DISCUSSION

The relationship between autoimmune thyroid disease and breast cancer is unclear. Studies investigating the relationship have resulted in conflicting results. It has been proposed that the presence of thyroid abnormalities may influence breast cancer progression.[8] The correlation between breast cancer and raised anti-TPO antibodies have been mentioned in various studies. Some studies have attributed the iodine concentrating ability of thyroid follicular and breast epithelial cells via sodium iodide symporter expression. Another study demonstrated the existence of TSH receptors in the breast tissue and their interaction of thyroid autoantibodies with receptors present on neoplastic breast tissues. [9,10]

Muller et al suggested that higher levels of TPO can serve as prognostic factor in patients with breast cancer. It has been observed that the breast tumor cells and thyroid tissue share common properties of expressing TPO and the sodium iodide symporter gene. [11]

In areas where endemic goitre is common, some studies have hypothesised that there might be an endocrine stimuli could interact with receptors on breast tumors as well as thyroid tissue.[12] These findings may contribute to the identification of common genetic and environmental factors underlying this disease association. The feeding areas for our hospital in our study is not endemic to goitre and this relationship could not be made out.

Autoimmune thyroid disorders are predominantly associated with the presence of thyroid autoantibodies directed to TPO and thyroglobulin.[13,14] Our results indicate an increased prevalence of anti-TPO antibodies in patients with breast cancer. It has been demonstrated that there was an overall increased prevalence of both thyroid disorders and TPO Ab in patients with breast carcinoma. In the present study, screening could detect 21% of breast cancer patients were positive for anti-TPO antibodies.

Grani et al revealed that the presence of anti-TPO antibodies was associated with a reduced incidence of distant metastases in breast cancer patients.[15] These findings suggest the usefulness of screening for thyroid disease in any patient with breast cancer.

Our study highlights that there is a correlation between anti-TPO antibodies and breast cancer. Additionally, the percentage of post menopausal women with raised anti-TPO antibodies is more than the group of premenopausal women with breast cancer. Obesity is one of the risk factors in the development of breast cancer among post-menopausal women. Adipose tissue is responsible for the production of hormones and cytokines that helps in regulating the thyroid hormones.[16]

5. CONCLUSION

Prevalence of anti-thyroid peroxidase antibodies is high among women with breast cancer. These results have implications both for screening of patients for thyroid disorders and also for development of new prognostic markers. Therefore, routine screening of anti-thyroid peroxidase antibodies is preferable among women with breast cancer**.** More robust data in terms of numbers to correlate age wise distribution and BMI scale between breast cancer patients and normal population may provide conclusive evidence in this regard.

6. REFERENCES

[1] Garcia M, Jemal A, Ward EM, et al. Global Cancer Facts & Figures 2007. American Cancer Society. 2007
[2] Jemal A, Siegel R, Xu J, et al. Cancer statistics, 2010. CA Cancer J Clin. 60:277–300.
[3] Ruf J, Carayon P (Jan 2006). "Structural and functional aspects of thyroid peroxidase". *Archives of Biochemistry and Biophysics*. 445(2): 269–77.
[4] Rapoport B McLachlan SM 2001Thyroid autoimmunity. *J Clin Invest* 108:1253–1259
[5] Sabitha Kandi, Pragna Rao 2012 Anti-thyroid peroxidase antibodies: Its effect on thyroid gland and breast tissue Annals of tropical medicine and public health. Vol 5, Issue 1,page 1-2
[6] Smyth PPA, Smith DF, McDermott EWM, Murray MJ, Geraghty JG, O'Higgins NJ. A direct relationship between thyroid enlargement and breast carcinoma. J Clin Endocrinol Metab 1996;81:937–41
[7] G. Grani, P. Dicorato, M. Dainelli, I. Coletta, A. Calvanese, M. Del Sordo, A. De Cesare, F.M. Di Matteo, V. D'Andrea,A. Fumarola et al. Thyroid diseases in women with breast cancer. *Clin Ter 2012; 163 (6):e401-404*

[8] Yasemin Kemal, Guzin Demirag, Kubilay Ekiz, Idris Yucel. Antithyroid peroxidase antibody positivity is associated with lower incidence of metastasis in breast cancer March 2015, Pages: 629-632

[9] Gogas J, Kouskos E, Tseleni-Balafouta S, Markopoulos C, Revenas K, Gogas G, et al. Autoimmune thyroid disease in women with breast carcinoma. Eur J Surg Oncol. 2001 Nov;27(7):626-30.

[10] Jiskra J, Barkmanova J, Limanova Z, Lánská V, Smutek D, Potlukova E, et al. Thyroid autoimmunity occurs more frequently in women with breast cancer compared to women with colorectal cancer and controls but it has no impact on relapse-free and overall survival. Oncol Rep. 2007 Dec;18(6):1603-11.

[11] I. Muller, C. Giani, L Zhang, F.A. Grennan-Jones, E.Fiore, V. Belardi, V. Rosellini Does Thyroid Peroxidase Provide An Antigenic Link Between Thyroid Autoimmunity And Breast Cancer? IJC -Vol 134, Issue 7, September 2013

[12] G.S.R.Kedari, G.S.R.Hareesh 2012 Relationship between levels of thyroid hormones and thyroid antibodies in breast cancer IJCRR - Vol 04 Issue 11, June, Pages: 64-69

[13] Czarnocka B. Thyroperoxidase, thyroglobulin, Na(+)/I(-) symporter, pendrin in thyroid autoimmunity. Front Biosci (Landmark Ed). 2011;16:783–802.

[14] McLachlan SM, Rapoport B. Thyroid peroxidase as an autoantigen. Thyroid. 2007;17(10):939–48.

[15] Farahati J, Roggenbuck D, Gilman E, Schütte M, Jagminaite E, Seyed Zakavi R, et al. Anti-thyroid peroxidase antibodies are associated with the absence of distant metastases in patients with newly diagnosed breast cancer. Clin Chem Lab Med. 2012;50(4):709–14.

[16] Ortega-Olvera, C., Ulloa-Aguirre, A., Ángeles-Llerenas, A. *et al.* Thyroid hormones and breast cancer association according to menopausal status and body mass index. *Breast Cancer Res* 20**,** 94 (2018).