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STUDY ON UTILITY OF ANTIBODY TESTING IN DIFFERENCIATED THYROID CARCINOMA

Pathology

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ABSTRACT

Introduction: In recent years, the incidence of thyroid cancer has been rising. Fine-needle aspiration biopsy (FNAB) is the "gold standard" for evaluating thyroid nodules, but majority of nodules with FNAB results are classified as indeterminate. Thus, the predictors that improve preoperative risk stratification for nodules are still needed. Some clinical parameters have been confirmed to be associated with DTC, such as young (<20) or old (>70) age, male gender, history of ionizing or exposure to radiation of the head and neck as a youth, family history of thyroid cancer, nodule size and type, or rapid growth associated with hoarseness. The aim of the study is to estimate the levels of thyroglobulin antibodies and thyroid peroxidase antibodies in patients with thyroid nodules undergoing thyroid surgery at our tertiary care hospital. **Materials and Methods:** Physical examination, thyroid ultrasonography, and thyroid profiles were performed before surgical procedure. A fasting blood sample were collected for thyroid profile T3, T4, TSH, TgAb and TPOAb and are estimated by chemiluminiscence immuno assay as per the manufacturer's instructions. All the patients had undergone thyroid ultrasound. **Results and Discussion:** In the present study, we included a total of 800 patients presented with thyroid nodule based on inclusion and exclusion criteria. All the patients had undergone physical examination, fasting thyroid profile testing, thyroid ultrasound, FNAB and histopathology post-surgery. Out of the 800 patients 190 were males 510 were females. 164 had solitary nodule and 636 patients had multiple nodules. The mean age was found to be 44.6±10.36 in DTC group and 47.8±13 in benign nodule group. The mean TSH values were found to be 1.6±0.98 in DTC group compared to benign group which was 1.06±0.6 this difference between the two groups was statistically significant. In DTC group, 56 (33.3%) patients had solitary nodule and 112 (66.6%) had multiple nodules. Similarly, in benign nodule group 108 (17.08%) had solitary nodule and 524 (82.9%) had multiple nodules. Thyroglobulin antibodies and thyroid peroxidase antibodies were evaluated in both the groups; it is noted that 47 (27.9%) patients had elevated TgAb (>40 IU/mL) in DTC group and 68 (10.75%) patients had elevated TgAb (>40 IU/mL) in benign nodule group. TPOAb found to be elevated in 23 (13.6%) in DTC group and 28 (4.4%) in benign nodule group. The antibody elevation both TgAb and TPOAb is highly significant in DTC group compared to benign nodule group. Multivariate regression analysis showed that the TSH, TgAb and TPOAb had highly significant in DTC group. **Conclusion:** In this present study, we found elevated levels of TSH, TgAb and TPOAb in DTC group and in benign nodule group, but the elevation was more significant in DTC group. Our data revealed that the presence of elevated TgAb correlated with an increased risk for DTC. High serum TgAb levels may serve as a predictive marker for DTC independent of TSH levels. Our data suggests that elevated TgAb along with other risk factors, such as decreased age, single nodule, and elevated TSH level, may provide useful information for the diagnosis and prognosis of DTC.

KEYWORDS

thyroid carcinoma, fine-needle aspiration biopsy, thyroglobulin antibody, thyroid peroxidase antibody and histopathology.

INTRODUCTION

Thyroid disorders represent most widespread endocrine illnesses, affecting individuals in India and the global population. A thyroid function test is used to diagnose, screen, and monitor patients. Hyperthyroidism is a clinical condition due to excessive circulation of thyroid hormone, they are further classified as primary, secondary and tertiary hyperthyroidism based on the pathogenesis arising from thyroid gland, pituitary and hypothalamus respectively. In contrast, hypothyroidism is due to a deficiency of thyroid hormone, they are further classified as primary, secondary and tertiary hypothyroidism based on the pathogenesis arising from thyroid gland, pituitary and hypothalamus respectively.

Recent epidemiological research found that the prevalence of several autoimmune endocrine illnesses, such as autoimmune thyroid disease (AITD), has been steadily rising [1]. The complex etiology of AITD includes genetic and environmental factors. Graves' disease (GD) and Hashimoto's (HT), which make up majority of cases of AITD, have a high correlation in those over the age of 45 to 50 years. These patients have high levels of autoantibodies against thyroid proteins, namely thyroglobulin, thyroid peroxidase, and thyroid stimulating hormone receptors antibodies (TRAb). Genes such as the truncated short GalTase (TSGT) protein and thyroid stimulating hormone (TSH) receptor, as well as many immune-regulatory genes, were also found in association with AITD [1-3].

In recent years, the incidence of thyroid cancer has been rising. Fine-needle aspiration biopsy (FNAB) is the "gold standard" for evaluating thyroid nodules, but majority of nodules with FNAB results are classified as indeterminate. Thus, the predictors that improve preoperative risk stratification for nodules are still needed. Some clinical parameters have been confirmed to be associated with DTC, such as young (<20) or old (>70) age, male gender, history of ionizing or exposure to radiation of the head and neck as a youth, family history of thyroid cancer, nodule size and type, or rapid growth associated with hoarseness.

In addition, many retrospective studies have linked higher serum TSH level with an increased risk of DTC. Although these potential predictors may play an important role in the preoperative diagnosis of thyroid carcinoma, the need for other prediction factors exists. The relationship between thyroid autoimmunity and DTC has been discussed for many years [4-10].

However, data specifically correlating thyroid autoantibodies and DTC occurrence is limited. A few studies have attempted to define this relationship, but the conclusions are debatable. Due to the controversy, as well as the high prevalence of DTC, we retrospectively evaluated the surgical data obtained from a large number of patients with thyroid nodules to assess the association between thyroid autoantibodies (ATAs) and DTC.

AIM AND OBJECTIVES

The aim of the study is to estimate the levels of thyroglobulin antibodies and thyroid peroxidase antibodies in patients with thyroid nodules undergoing thyroid surgery at our tertiary care hospital.

MATERIALS AND METHODS

Source of data and place of study: The present study was conducted in the Dept. of Pathology in association with Dept. of surgery of our hospital. This was a retrospective study, we collected the data by reviewing the case records of the patients presented with thyroid nodule who had undergone surgical treatment. Inclusion criteria: We included the patients diagnosed with thyroid nodule, who has undergone thyroid profile testing, antibody testing, thyroid ultrasonography, FNAB and histopathology post-surgery. Exclusion criteria: We excluded the those previously exposed to high doses of radiation, whose final pathology revealed the presence of undifferentiated thyroid cancer, history of surgery, whom serum thyroid peroxidase antibody (TPOAb) or thyroglobulin antibody (TgAb) data were unavailable.

Data Collection and Methodology: Physical examination, thyroid

ultrasonography, and thyroid profiles were performed before surgical procedure. A fasting blood sample were collected for thyroid profile T3, T4, TSH, TgAb and TPOAb and are estimated by chemiluminiscence immuno assay as per the manufacturer's instructions. All the patients had undergone thyroid ultrasound.

In this present study, we used 40 IU/mL, 100 IU/mL, and 500 IU/mL for further categorizing elevated TgAb and 50 IU/mL, 100 IU/mL, and 500 IU/mL for elevated TPOAb. Thyroid Ultrasound was carried out to characterize the thyroid nodule size, number, and echo pattern, thyroid nodules were evaluated preoperatively by four trained radiologists via high-resolution ultrasound images. Histopathological Diagnosis. Final histological data were available for all the patients included in the cohort. An experienced pathologist assessed the presence or absence of DTC, including PTC and FTC. For patients with DTC, tumors were staged according to the system established by the American Joint Committee on Cancer with regard to tumour size, status of extra thyroidal invasion, lymph node metastasis, and distant metastasis. Statistical analysis: All continuous data were expressed as mean ± standard deviation (SD). Two continuous numeric variables with a normal distribution were analyzed using an independent Student's - test.

RESULTS

We retrieved the data of 800 patients (3 years) FNAC and Histopathology slides were retrieved and reviewed. All the slides were observed and findings recorded.

Table 1: Shows the demographic, clinical and laboratory findings in the study subjects

	DTC	Benign nodule
Number of study subjects	168	632
Males	42 (25%)	148 (23.41%)
Females	126 (75%)	484 (76.5%)
Mean age in years	44.6±10.36	47.8±13
TSH (mIU/L)	1.6±0.98	1.06±0.6*
Nodule type		
Solitary	56 (33.3%)	108 (17.08%)
Multiple	112 (66.66)	524 (82.91)
TgAb >40 IU/mL	47 (27.9%)	68 (10.75%)
TPOAb >50 IU/mL	23 (13.6%)	28 (4.4%)

Table 2: Shows multivariate regression analysis predicting DTC

	Odds ratio	p value
Age	0.98	HS
Solitary nodule	1.86	HS
TSH	1.26	HS
TgAb >40 IU/mL	2.3	HS
TPOAb>50 IU/mL	1.3	S

DISCUSSION

In the present study, we included a total of 800 patients presented with thyroid nodule based on inclusion and exclusion criteria. All the patients had undergone physical examination, fasting thyroid profile testing, thyroid ultrasound, FNAB and histopathology post-surgery. Out of the 800 patients 190 were males 510 were females. 164 had solitary nodule and 636 patients had multiple nodules. The mean age was found to be 44.6±10.36 in DTC group and 47.8±13 in benign nodule group. The mean TSH values were found to be 1.6±0.98 in DTC group compared to benign group which was 1.06±0.6 this difference between the two groups was statistically significant. In DTC group, 56 (33.3%) patients had solitary nodule and 112 (66.6%) had multiple nodules. Similarly, in benign nodule group 108 (17.08%) had solitary nodule and 524 (82.9%) had multiple nodules. Thyroglobulin antibodies and thyroid peroxidase antibodies were evaluated in both the groups; it is noted that 47 (27.9%) patients had elevated TgAb (>40 IU/mL) in DTC group and 68 (10.75%) patients had elevated TgAb (>40 IU/mL) in benign nodule group. TPOAb found to be elevated in 23 (13.6%) in DTC group and 28 (4.4%) in benign nodule group. The antibody elevation both TgAb and TPOAb is highly significant in DTC group compared to benign nodule group. Multivariate regression analysis showed that the TSH, TgAb and TPOAb had highly significant in DTC group.

Our study demonstrated that the prevalence of DTC was significantly higher in patients with elevated TgAb over 40 IU/mL than those with TgAb under 40 IU/mL. Further analysis revealed that TgAb ≥ 40 IU/mLmight be a predictive marker for DTC independent of other potentially confounding factors such as decreased age, single nodule, and elevated TSH level.

Since Dailey et al. [11] proposed an association between thyroid malignancy and Hashimoto disease, the relationship between these two disorders has long been disputed [12-14]. In one recent prospective study [15], Azizi et al. suggested that the association between Hashimoto disease and thyroid cancer is antibody specific. In agreement with it, we observed that elevated TgAb concentration is associated with high prevalence of DTC. Besides, in our study, a positive correlation between DTC and high serum TPOAb levels was also observed.

The influence of previous thyroid autoimmunity on the outcome of patients with DTC remains controversial. Souza et al. [16] reported that pre-existing thyroid autoimmunity or ATAs exerted a protective effect on the outcome of DTC. Specifically, patients with ATAs and a previous history of thyroid autoimmunity had a fewer metastases and reduced recurrence compared to those without a history of autoimmunity. Recently, a large retrospective survey further supported the beneficial effect of thyroid autoimmunity on DTC [17]. Serum TSH levels have also been associated with DTC. In this study, high TSH levels were related to elevated TgAb and TPOAb. Furthermore, logistic regression analysis revealed that elevated TSH levels might be an independent risk factor for DTC, despite the evaluation based on the overall TSH level.

CONCLUSION

In this present study, we found elevated levels of TSH, TgAb and TPOAb in DTC group and in benign nodule group, but the elevation was more significant in DTC group. Our data revealed that the presence of elevated TgAb correlated with an increased risk for DTC. High serum TgAb levels may serve as a predictive marker for DTC independent of TSH levels. Our data suggests that elevated TgAb along with other risk factors, such as decreased age, single nodule, and elevated TSH level, may provide useful information for the diagnosis and prognosis of DTC.

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