ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at:www.ijmacr.com

Volume – 6, Issue – 1, Janaury - 2023, Page No. : 250 - 257

Anti-TPO levels in Papillary thyroid carcinoma in comparison with Colloid goiter- A descriptive, comparative study

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How to citation this article: Dr. Shreya shah,Dr. Reeta Kataruka,Dr. Chandrashekhar P. Bhale, "Anti-TPO levels in Papillary thyroid carcinoma in comparison with Colloid goiter- A descriptive, comparative study", IJMACR-January - 2023, Volume – 6, Issue - 1, P. No. 250 – 257.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Introduction: To investigate the levels of anti-TPO in Papillary thyroid carcinoma in comparison with Colloid goiter.

Materials and Methods: This is a comparative descriptive study from July 2021- December 2021 was conducted in department of Pathology at MGM Medical College and Hospital, Aurangabad over a period of six months. Anti TPO levels were observed in all the thyroid nodule cases pre-operatively and were confirmed by Histo pathological reports.

Observations and Results: The clinical data of 20 patients with pathologically confirmed thyroid nodule who underwent surgical treatment were enrolled in this study. The enrolled patients were divided into benign nodule and papillary thyroid carcinoma group according to their Histo pathological result. Out of 20 cases 90 % were women and 10 % were men. The mean age for cases and control were 42+20 and 36 +10 respectively. Mean anti TPO levels in colloid goiter was 1.7 + 1.4 and mean anti TPO levels in papillary thyroid carcinoma is 36 +20. However, no differences with respect to other variables were observed between cases and controls. Eight papillary thyroid carcinoma and twelve colloid goiter cases were studied. One case had Hashimoto's with papillary thyroid carcinoma and one had Hashimoto's thyroid with colloid goiter. This nullifies the effect of anti-TPO in Hashimoto's.

Conclusion

1. Colloid goiter and Papillary thyroid carcinoma are seen more commonly infemales than males.
2. Papillary hyperplasia with colloid goiter also shows normal anti TPO levels.
3. Anti TPO level is normal in all colloid goiter cases.
4. Anti TPO levels increases in all papillary thyroid carcinoma.

Keywords: Anti-TPO, Colloid goiter, Hashimoto's, Papillary thyroid

Introduction

Thyroid malignancy is the most common endocrine malignancy in clinical practice.Although itsprevalence is still rare butit isgrowing rapidly in the last years, with approximately 14.3new cases per 100,000 per year[1].Most frequent Histo morphologicaltype observed is papillary thyroid carcinoma (PTC), whichrepresents 84% of thyroid malignancies[2]. Despite extensive researchon itspathogenesis, it is still remains largely unclear especially for its association with thyroid autoimmunity. Association between papillary thyroid carcinoma (PTC) and thyroid auto immunity with resultant intrathyroidal lymphocyte infiltration and anti-Thyroid peroxidase (TPO) antibodies is long been documented. First paper reporting the possible association was published more than 60 years ago[1]. Numerous papers thereafter followed these to investigate their association.

Thyroid peroxidase (TPO) is the critical thyroid enzyme for iodination and coupling of tyrosine residues in thyroglobulin to synthesize thyroid hormone[3]. Anti-TPO antibodies are found in 90–95% of autoimmune thyroid diseases (AITD) patients and 10– 15% of non-AITD patients[4]. Anti-TPO antibodies in euthyroid individuals have no blocking TPO activity or interference with the blocking activity of anti-TPO anti-bodies from AITD patients[5]. In contrast, anti-TPO antibodies from AITD patients can damage thyrocytes and inhibit enzymatic activity[6]. Thyroglobulin (Tg) is a large glycoprotein containing three molecules of T4 and only 0.3 molecules of T3. Antibodies against Tg can be induced by significant destruction of the thyroid gland[7]. Anti-TPO antibodies are more common than anti-Tg antibodies and more indicative of thyroid disease[8].

Antithyroid antibodies are considered a sensitive marker of autoimmune thyroid diseases[9]. However, these anti-bodies can be detected in 5% to 27% of the general population[10]. Hashimoto thyroiditis (HT) is one of the most common autoimmune diseases, with an estimated frequency of 5–10 % with females affected more than males[11].

HT is characterized by T-lymphocyte infiltration of the thyroid gland, destruction of thyroid follicles, and their replacement by fibrotic tissue. The presence of anti-thyroid autoantibodies [against thyroid peroxidase (anti-TPO) or against thyroglobulin (anti-Tg)] and the typical thyroid ultrasound morphology (nonhomogeneous and hypoechoic ultrasound pattern of thyroid tissue, with increased vascularization) are the diagnostic markers of HT.

The link between chronic inflammation and development of malignant tumors has been already proven in a number of human tumours, e.g., colorectal cancer and inflammatory bowel disease, hepatocellular carcinoma and chronic B and C hepatitis, cervical cancer, and HPV infection[12]. The possible relationship between HT and differentiated thyroid cancer has been first described by Dailey et al. in 1955 who observed frequent inflammatory cell infiltration surrounding thyroid cancer in thyroid histological samples[13]. Since that time, many papers with inconsistent results have been published. Some authors consider pre-existing HT or the presence of antithyroid antibodies as a risk factor for developing TC[14,15,16,17,18], whereas others do not[19,20]. With this perspective present case control study was undertaken to investigate the levels of anti-TPO in Papillary thyroid carcinoma in comparison with Colloid goiter to assess their possible role

Material and Method

Present comparative descriptive study was conducted over a period of six months between July 2021 to December 2021 in department of Pathology at MGM Medical College and Hospital, Aurangabad. Ethical clearance was taken prior to performing present study from institutional ethics committee. Total 20 newly diagnosed patients presenting with nodular goiter were included in the present study. Patients who were already undertreatment and managed conservatively were excluded from the study. Detailed clinical history was taken in all subjects. Medical history of levothyroxine therapy also enquired irrespective of what the primary goal of levothyroxine therapy was (sub situation of hypothyroidism or suppression therapy). After careful history taking, 4 ml of blood was collected in a plain vial after overnight fasting. Serum was separated and FT4, TSH&Anti-TPO antibody was estimated by micro plate enzyme linked immunosorbent assay using the kit of Accubind. All subjects were asked to report again after obtaining the histopathological report. Based on these reports they were classified into 2 groups as colloid goiter (Controls) and papillary carcinoma (Cases)

Operational definition

Patients with TPO-Ab levels > 9 IU/mL were considered TPO-Ab-positive[21]

Statistical significance

All the data were tabulated and analysed using Microsoft Excel, 2019. Data are expressed as mean ± SD, frequency and percentage N (%). 'Unpaired t-test' were used for comparing the two groups, $\chi 2$-test was used to evaluate correlation between two variables. Statistical significance was assumed if P value less than 0.05

Result

In Table 1 showing distribution of clinical history, mean ± SD for cases found as 42 ± 20.45 and for controls as 36 ± 10.8. Amongst total 20 cases 2 (10 %) were males and 18 (90 %) were females.InTable 2 showing distribution of Anti TPO Antibody, Anti TPO antibody was found elevated in 8 (40 %) subjects. Amongst these 7 (35 %) subjects were of Papillary carcinoma (PTC) and 1 (5 %) of colloid goiter. Mean ± SD for Papillary carcinoma cases found as 36 ± 20 and for colloid goiter as 1.7 ± 1.4 Statistically significant difference found for Anti TPO antibody positivity (P=<0.0001). Sensitivity, Specificity, PPV and NPV for Anti TPO antibody test was (100 %), (100 %), (100 %) and (100 %) respectively

Table 1: Distribution of clinical history

Sn.	Variable	Cases 12 (%)	Controls 8 (%)	Total 20(100%)
1	Age (Mean ± SD)	42 ± 20.45	36 ± 10.8	20(100%)
2	Gender			
	Male N (%)	1(5%)	1 (5 %)	2 (10 %)
	FemaleN (%)	11(55%)	7(35 %)	18 (90 %)

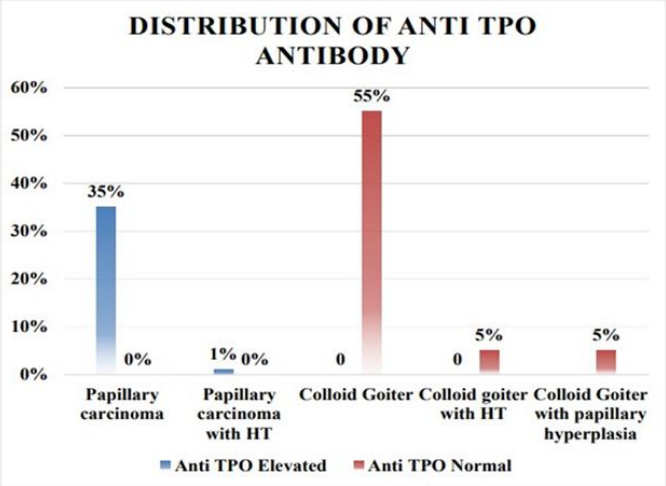
Table 2: Distribution of Anti TPO Antibody

Sn.	Histopathology	Anti TPO Ab		Total N (%)	Mean ± SD (IU/ml)	Unpaired t Test
		Elevated N (%)	Normal N (%)			
1	Papillary carcinoma (PTC)	8 (40%)	0 (0%)	8 (40%)	36±20	t: -6.002 P<0.0001
2	Colloid goiter (CG)	0 (0 %)	12 (60 %)	12 (60 %)	1.7 ± 1.4	
Total N (%)		8 (40 %)	12 (60 %)	20 (100 %)	-	
Sensitivity: 100 %, Specificity: 100 %, PPV: 100 %, NPV: 100 %						

Table 3: Distribution of Anti TPO Antibody

Sr No.	Histopathology	Anti TPO Ab		Total N (%)	Mean ± SD (IU/ml)	Unpaired t Test
		Elevated N (%)	Normal N (%)			
1	Papillary carcinoma (PTC) Papillary Carcinoma (PTC) with HT	7 (35 %) 1 (5%)	0 (0 %)	8 (40 %)	36 ± 20	t: -6.002 P<0.0001
2	Colloid goiter (CG) Colloid goiter (CG) with HT Colloid goitre with papillary hyperplasia	0 (0 %)	10 (55 %) 1 (5%) 1 (5%)	12 (60 %)	1.7 ± 1.4	
Total N (%)		8 (40 %)	12 (60 %)	20 (100 %)	-	

Graph 1: Distribution of Anti TPO Antibody



Discussion

Present study included total 20 newly diagnosed patients presenting with nodular goiter. Detailed clinical history was taken in all subjects and Serum FT4, TSH & Anti-TPO antibody was estimated by micro plate enzyme linked immunosorbent assay using the kit of Accubind.

All subjects were asked to report again after obtaining their histopathological report. Based on these reports they were classified into 2 groups as colloid goiter and papillary carcinoma.

Anti TPO antibody titre was assessed in both groups and correlated to find any significance. Results obtained consisted of, Anti TPO antibody was found elevated in 8 (40 %) subjects. Amongst these 7 (35 %) subjects were of Papillary carcinoma (PTC) and 1 (5 %) of colloid goiter with HT. Mean ± SD for Papillary carcinoma cases found as 208.5 ± 76.49 and for colloid goiter as 10.85 ± 10.23. Statistically significant correlation found for Anti TPO antibody positivity (P=0.0003). Sensitivity, Specificity, PPV and NPV for Anti TPO antibody test was (87.50 %), (91.67 %), (87.50 %) and (91.67 %) respectively.

In similar study byJan Krátkýet al (2018)[22]theycompared the presence of HT and thyroid function in patients with TC andbenign nodules. Following a thyroid nodule fine needle aspiration biopsy, they looked at 2571 patients. A total of 182 controls who were sex and age matched and 91 patients with primary TC were included. Positive anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin (anti-Tg) antibodies were linked to TC (anti-TPO 44% in TC vs. 27% in controls, anti-TG 35% in TC group vs. 21% in controls, P = 0 018, and median 1.88 mIU/l vs. 1.21 mIU/l vs. 1.21 mIU/l); Positive anti-TPO was found to be an independent risk factor (OR 2.21, P = 0 018) using multiple logistic regression, whereas spontaneously suppressed TSH 0 5 mIU/l was found to be a protective factor (OR 0.3, P = 0 01) against TC. They concluded that, nodules in subjects withpositive antithyroid antibodies could be considered to have a higher risk of malignancy. However, based on our results, it is notpossible to declare that TC is triggered by HT.Yuji Nagayama et al (2018)[23]summarized relevant papers published between 2012 and2018. Numerous papers showed significant rise in the prevalence of thyroid autoimmunity (positive intrathyroidal lymphocyte infiltration and/or anti-thyroglobulin/thyroid peroxidase antibodies) in patients with thyroid cancers compared to those with benign nodules. Difference in thyroid autoimmunity rates between PTC patients and those with other forms of thyroid malignancies seems to indicate the strong correlation between the two diseases.Thyroid autoimmunity is probably brought on by antigens that are present in both healthy and malignant thyroid tissues. Ahmed Rabiee et al (2021)[24]performed a retrospective work of 112 cases managed with total thyroidectomy with positive antithyroid peroxidase anti-bodies (TPO-Ab). Before surgery, everyone was thyroidally healthy. Prior to surgery as well as six and twelve months thereafter thyroid antibody levels were evaluated. Histopathology indicated lymphocytic thyroiditis

(30.4%), colloid nodules (22.3%), and Hashimoto thyroiditis (47.3%). Prior to surgery all patients had TPO-Ab positivity. After surgery, TPO-Ab did not significantly change (p = 0.817 and p=0.560, respectively). Additionally, there was no difference in TPO-Ab levels across the three histological diagnoses (p = 0.086 and p = 0.673, respectively). They Concludedthat Anti thyroid antibodies are not valuable markers for diagnosis or prognosis of benign thyroid diseases subjected to total thyroidectomy. We do not recommend their use beyond supporting evidence of the possibility of the autoimmune nature of the illness if other criteria are confirmed. Bera Swati et al (2013)[25]evaluatedAnti-TPO antibody level in 86 patients, along with 25 healthy controls to detect its change in various forms of thyroid nodules particularly in thyroid malignancy when compared with healthy controls. The study found that there was an increase in Anti-TPO antibody levels in benign and toxic forms of multi nodular goitre and papillary carcinoma, but not in follicular adenoma or follicular carcinoma.

TPO is expressed on the surface of thyroid cells, both healthy and cancerous. Anti-TPO antibodies can therefore detect TPO produced on the surface of cancer cells[26]. TPO is a key autoantigen in autoimmune thyroid disorders like Graves' disease and Hashimoto's thyroiditis. The results of our current investigation show that Papillary thyroid cancer have higher levels of Anti-TPO Ab. However, colloid goiter showed no discernible variation in the level of the same measure. The research of the immunological factors that contribute to the development of papillary cancer may prove to be fruitful.

Conclusion

From present study findings we can conclude that

1. Colloid goiter and Papillary thyroid carcinoma are seen more commonly in females than males.
2. Papillary hyperplasia with colloid goiter also shows normal anti TPO levels.
3. Anti TPO level is normal in all colloid goiter cases.
4. Anti TPO levels increases in all papillary thyroid carcinoma

Abbreviations

PTC: Papillary Thyroid Carcinoma

HT: Hashimotos Thyroiditis

Anti-tpo:anti-thyroid peroxidase

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