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Article *in* Indian Journal of Public Health Research and Development · July 2019

DOI: 10.5958/0976-5506.2019.01583.3

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Antioxidants and Antibodies in Structural Thyroid Diseases

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ABSTRACT

Thyroid nodules are a very frequent finding, and their prevalence steadily increases with age. Routinely clinical factors such as age, gender, and radiation history are meaningful for predicting thyroid nodules. There are few studies exploring the association of serum indexes of thyroid hormones or autoantibodies with the risk of thyroid nodules. Hence present study was undertaken with following objectives. To measure the serum markers of FT3, FT4,TSH, anti TPO antibody, anti-thyroglobulin antibody and role of Vitamin E and vitamin C antioxidants in relation with thyroid serum markers in various thyroid diseases. Correlation of these serum markers with cytological diagnosis was done. Serum analysis of thyroid hormones, autoantibodies level and FNAC was done with patients having thyroid swelling.

It was noted in present study that prevalence of positive serum autoantibodies displays geographical heterogeneity, unrelated to goitre prevalence. Autoantibodies levels are raised in autoimmune thyroid diseases and in few variants of thyroid malignancy. And it was also observed anti-Oxidants (vitamin e and vitamin c) levels were variable in thyroid disorders. To conclude autoantibodies are markedly raised in thyroiditis condition and the incidence of autoimmune thyroiditis is increasing in iodine sufficient as well as iodine deficient geographical areas. In present study it was also observed that autoantibodies levels were raised in papillary carcinoma thyroid indicating role of anti-TPO and anti-TG in etiopathogenesis. Antioxidants levels were variable and low in most of thyroid diseases suggesting its role in etiopathogenesis.

Keywords: *auto-antibodies, antioxidants, goitre, papillary carcinoma*

Introduction

Thyroid diseases are among the commonest endocrine disorders worldwide. India too, is no exception. According to a projection from various studies on thyroid disease, it has been estimated that about 42 million people in India suffer from thyroid diseases. Routinely clinical factors such as age, gender, and radiation history are meaningful for predicting thyroid nodules. There are few studies exploring the association of serum indexes of thyroid hormones or autoantibodies with the risk of thyroid nodules. Although thyroid hormones and autoantibodies are reported to be dependently associated with thyroid function and thyroid diseases, little attention has been paid to whether thyroid hormones and autoantibodies are associated with thyroid nodules[2]. Thyroid nodule, as an entity, is one of the most common diseases originating from the endocrine system. Thyroid nodules may be single, multiple, solid, or cystic and may or may not be functional.[3] Most thyroid nodules are benign tumours and 5% are reported as malignant.[4,5] Autoimmune thyroiditis (AT) is a common disorder of the thyroid gland. It is usually diagnosed when thyroid autoantibodies (TPOAbs/TGAbs) are detected in patients with hypothyroidism or goiter.[6]

Autoimmune diseases (AID) appear when the host immune system turns against its own antigens leading to dysfunction or destruction of tissues and organs. AID may develop in mechanisms involving immune deregulation, genetic predisposition and due to influence of environmental factors.[7] Thyroid autoimmune

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diseases like GD and Hashimoto thyroiditis (HT) affect the thyroid gland and are called autoimmune thyroid diseases (AITD).[8]

Oxidative reactions occur in all tissues and organs, thyroid gland being one, in which oxidative processes are indispensable for thyroid hormone synthesis. Both hyper- and hypothyroidism have been proven to promote cellular oxidative stress by influencing the intensity of oxygen reactions and have been shown to affect concentrations of the vitamins involved in scavenging of free radicals (usually decreasing their concentrations, although study results differ) i.e. vitamins A, C and E.[9]

Therefore, this study was undertaken to determine whether there is an association between thyroid nodules, thyroid hormones levels and thyroid autoantibodies and correlation of these markers with cytological diagnosis. Also an attempt to understand the role of Vitamin E and vitamin C antioxidants in relation in various thyroid diseases was made.

Methodology

This was prospective study carried out in 2016 at out tertiary care hospital. The study group includes patients with thyroid swelling referred to Department of Pathology for FNAC. Patients with thyroid swelling with thyroid hormone therapy or antithyroid drugs were excluded.

Early morning fasting 5ml of venous blood sample was collected in plane vaccutainer and the collected serum sample was run through Vidas biochemical analyzer based on the principal chemiluminescent immunoassay. Serum markers estimation included Free thyroxine(T4), Free tri-iodothyronine (T3), Thyroid stimulating hormone (TSH), Anti thyroglobulin antibody (AntiTG ab), Anti thyroperoxidase (anti TPO), Vitamin C and E levels (HPLC method).

Descriptive statistics as well as 95% confidence interval for a single proportion and a mean was calculated.

Results

In this one year cross sectional study total 54cases with thyroid swelling referred to cytology section were included and all cases we had serum biomarker level estimation. In present study females outnumbered males with 43 females (79%) and 11 males (21%), youngest being 12yrs and oldest age 72yrs.(TABLE I: AGE DISTRIBUTION)

Table I: Age distribution

Sex/age	10-20	21-30	31-40	41-50	51-60	61-70	>70	Total
Female	5	14	10	5	6	2	1	43
Male	1	2	3	3	1	1	-	11

The commonest thyroid disease was colloid goiter followed by thyroiditis. Lymphocytic thyroiditis was common followed by granulomatous thyroiditis and other variants. Papillary carcinoma was commonest malignant lesion affecting females in 3rd and 4th decade.(Table II)

Table II: Various thyroid diseases with sex distribution of disease

Thyroid lesion	Females	Males	Total
Goitre (colloid/nodular/toxic)	13	3	16
Lymphocytic thyroiditis	14	1	15
Granulomatous thyroiditis	2	2	4
Graves disease	7	0	7
Follicular neoplasm			
Follicular adenoma	1	2	3
Follicular carcinoma	0	2	2
Papillary carcinoma	6	0	6
Medullary carcinoma	0	1	1
Total	43	11	54

Thyroid function test (free T3, free T4 and TSH) and autoantibodies level ie anti-TPO and anti-TG levels were measured and mean calculated with SD and observed that most of thyroid disorders were in euthyroid state and auto-antibodies level were raised in autoimmune thyroiditis and few cases of papillary carcinoma. (Table III).

Table III: Thyroid function test and auto-antibodies level in thyroid diseases

Thyroid lesion	Total	TSH 0.4-4.0 muIU/ml	FT3 3.5-7.8 pmol/L	FT4 9 – 25 pmol/L	Anti TG <20 IU/ml	Anti TPO < 35 IU/ml
Goitre (colloid/nodular/toxic)	16	1.62+/-0.76	3.02+/-042	1.22+/-0.24	16.63+/-3.42	35.2+/-3.23
Lymphocytic thyroiditis	15	20.66+/-4.05	1.42+/-0.37	.53+/-0.16	43.25+/-7.46	63.26+/-5.96
Granulomatous thyroiditis	4	2.22+/-0.43	6.24+/-1.56	19.45+/-6.5	26+/-3.50	35.2+/-2.50
Graves disease	7	0.02+/-0.01	13.3+/-3.69	30+/-4.79	34.85+/-6.76	42.28+/-5.92
Follicular neopalsm;						
Follicular adenoma	3	0.83+/-0.16	4+/-1.73	11.3+/-1.67	12.6+/-3.77	25+/-0
Follicular carcinoma	2	2+/-0	3.9+/-0.1	20+/-0	12+/-1.41	17.5+/-2.42
Papillary carcinoma	6	2.1 +/- 0.54	4.65+/-1.16	13.8+/-4.16	30.5+/-14.53	33.3+/-17.93
Medullary carcinoma	1	0.9	4	13	20	39

Also anti-oxidants levels i.e. Vitamin C and Vitamin E were measured and observed that the levels were affected in thyroid abnormality with markedly reduced level in malignancy followed by thyroiditis and then goiter. (Table IV)

Table IV: vitamin C & vitamin E measurements in various thyroid diseases

Thyroid lesion	Total	Vitamin C level 0.2–2.0 mg/dl	Vitamin E level 5–20 µg/ml
Goitre (colloid/nodular/toxic)	16	1+/-0.56	9+/-1.5
Lymphocytic thyroiditis	15	0.1+/-0.01	1.75+/-0.5
Granulomatous thyroiditis	4	0.45+/-0.5	4.5+/-1.2
Graves disease	7	0.5+/-0.06	1.62+/-0.04
Follicular neopalsm;			
Follicular adenoma	3	0.2+/-0.01	4.6+/-1.3
Follicular carcinoma	2	0.2+/-0.01	3+/-1.2
Papillary carcinoma	6	0.7+/- 0.04	2.18+/-0.56
Medullary carcinoma	1	0.4	2

Discussion

Thyroid nodule is one of the most common diseases originating from the endocrine system.. Thyroid swelling may or may not be associated with functional derangement. The thyroid epithelial cells, induced by random mutations or rearrangements, will grow from a normal state to an abnormal state. This induction of growth exacerbates cellular mutagenesis that generates the nodules. [10,11] Most thyroid nodules are benign tumours and 5% are reported as malignant.[4,5] Various studies like Weimin Xu et al, J Paweł et al, showed female preponderance over males in acquiring thyroid disease, which was also noticed in our study.[3,6]

Most of autoimmune thyroid diseases are accompanied by the presence of anti-thyroid peroxidase (TPO), anti-thyroglobulin (Tg), and anti-thyroid-stimulating hormone receptor (TSHR) antibodies. However autoantibodies association with thyroid malignancy is also noted in few papillary carcinoma of thyroid. Antibodies against thyroid antigens such as carbonic anhydrase, megalin, T3 and T4, sodium iodide symporter (NIS), and pendrin have also been detected, although rarely.[12,13]

Prevalence of the thyroid autoantibody positivity is relatively high worldwide. It is well-known that

in iodine-sufficient areas there is a higher rate of AT prevalence than in iodine-deficient ones.[14] Iodine intake is probably one of the most important factors that affects thyroid autoimmunity and the incidence of AT.[15]

TPOAb and TGAb are two important thyroid autoantibodies which are commonly found in patients with thyroid diseases. [16] As shown in some previous studies, TPOAb is correlated with the severity of lymphocytic infiltration and could induce antibody-dependent cell-mediated cytotoxicity. [17,18] Boelaert K. et al.[19] reported that TPOAb was dependently associated with thyroid diseases, but little attention has been paid to whether measuring other thyroid autoantibodies, in addition to TSH, could help predict thyroid nodules in human populations.[3]

Our results showed raised antiTPO and antiTG in lymphocytic thyroiditis and papillary carcinoma which were similar to the findings of M. Parham et al. [20] in Iran. They indicated that the different prevalence of thyroid autoantibodies might explain the wide range of the reported prevalence of thyroid nodules. In addition, Eun Sook Kim et al.[21] reported that TGAb was associated with an increased risk of thyroid cancer in thyroid nodules. Similarly, other studies[22,23] also showed an analogous association with malignancy by considering positive thyroid autoantibodies as a whole, including TPOAb and TGAb.[3]

Oxidative reactions occur in all tissues and organs, thyroid gland being one, in which oxidative processes are indispensable for thyroid hormone synthesis. Both hyper- and hypothyroidism have been proven to promote cellular oxidative stress by influencing the intensity of oxygen reactions and have been shown to affect concentrations of the vitamins involved in scavenging of free radicals (usually decreasing their concentrations, although study results differ) i.e. vitamins A, C and E[9]. A study done by Salwa H. N. Al-Rubae'i and Abass K. Al-Musawi observed that there are marked variations in vitamin A, E and C in both hypothyroidism as well as hyperthyroidism.[24]

Vitamin A is a potent antioxidant and acts as a scavenger of free radicals either independently or as a part of large enzyme system. Vitamin A deficiency (VAD) has multiple effects on thyroid function in animals.[25] Hyperthyroidism is a hyper metabolic state accompanied by an increase in the total consumption of oxygen, fostering formation of reactive oxygen species and other free radicals, or the occurrence of oxidative stress. [26]

Lowered Vitamin E level is presumably due to its use in preventing free radical damage that seems more extensive in thyroid dysfunction patients.[27] Mano et al found in their study patients with various thyroid disorders that they presented elevated Vitamin E levels in their thyroid tissue.[24] Researchers concluded that Vitamin E acts as a scavenger in thyroid follicular cell dysfunction. Additional studies have demonstrated that active oxygen radicals inhibit the activity of an enzyme responsible for the conversion of T4 to the active hormone T3 and that sufficient Vitamin E levels may mitigate that effect.[28] Present study also detects low vitamin E levels in thyroid disorders.

Vitamin C is considered the most powerful natural antioxidant[29] which is capable of ''scavenging" reactive oxygen species by reducing free radicals to more stable species.[30] Present study were in good agreement with those obtained by Mohan et al.[31] and Alicigüzel et al.[32] as these studies described low levels of Vitamin C in hyperthyroidism and increase oxidative stress at the same time, it also indicate that antioxidant vitamin become oxidized and it is eventually consumed in exerting its antioxidant action.

Conclusion

Present study concludes that autoantibodies levels were raised in thyroiditis and papillary carcinoma thyroid indicating role of anti-TPO and anti-TG in etiopathogenesis. vitamin C and E levels in various thyroid diseases were variable.

Ethical Clearance: Taken from Institutional Ethical Committee (IEC)

Source of Funding: Self

Conflict of Interest: Nil

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