IJPSR (2023), Volume 14, Issue 5 (Review Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 06 August 2022; received in revised form, 11 October 2022; accepted 17 November 2022; published 01 May 2023

DIFFERENT TREATMENT APPROACHES USED IN AUTOIMMUNE THYROID DISEASE: A COMPREHENSIVE REVIEW

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Keywords:

AITD- Autoimmune Thyroid Disease, HT- Hashimoto's Thyroiditis, GD- Grave's Disease. TPO- Thyroid Peroxidase, TG- Thyroglobulin, Ab- antibody, Radioactive Iodine

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ABSTRACT: Autoimmune thyroid disease triggers because of T cells attack in the immune system (in the thyroid gland). AITD mainly comprises of two types- 'Hashimoto's thyroiditis' (hypothyroidism) & 'Grave's Disease' (thyrotoxicosis). India has '42 million' people groups experiencing thyroid disease, likewise it has perceived that in contrast with men 80% women affect more from immune system thyroid disease. The attentiveness of Autoimmune hyperthyroidism accounts from 3·0 to 7·5%, hypothyroidism accounts for 0·9%. Genetic Susceptibility, Sex Steroids, Stress, Pregnancy, Radiation Exposure, 'Thyroid Peroxidase Antibodies (TPO), 'Thyroglobulin Antibodies' (TG), B & T- Cell Responses exist as prime reasons of AITD. 'Cytokine interferon-gamma' also show dynamic part in origin of HD disease. Radionuclide scan, physical inspection, fine needle aspiration, lymphocytic infiltrate, TPO, and TG detection (by RIA) are significant diagnosis parameters for 'AITD'. Levothyroxin treatment intended for HT and antithyroid drugs are meant for GD. Observing of regular dosing is precarious for both therapies. The side effects of hormonal therapy could be avoided by using the herbal approach (*Bacopa monnieri, Melissa officinalis, Withania somnifera, Emblica officinalis)* to improve thyroid dysfunction. There is also possibilities for novelclinical investigation of the plants to verify their effectiveness in thyroid dysfunction further.

INTRODUCTION:

Thyroid Hormone: After bound to high-affinity thyroid receptors, 'Triiodothyronine' (T3) naturally controls'gene expression' with recognizing specific response in T3-target genes. In reaction to hormones, it prevents or activates transcription [1]. Thyroid hormone (T3) is pivotal for endochondral and intramembranous growth of bones. This hormone significantly does linear development and Bone mass maintenance. Deficiency of T3 hormone in Childs, causes growth deficiency and impaired skeletal development [2, 3].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.14(5).2173-82

This article can be accessed online on www.ijpsr.com

DOI link: http://doi.org/10.13040/IJPSR.0975-8232.14(5).2173-82

Excess quantity of T3 boosts the formation of bone and enhances growth. In adult thyrotoxicosis, amended bone remodeling triggered by a difference between resorption and bone formation, effects in remaining bone damage and improved risk for osteoporotic fracture [4].

Autoimmune Thyroid Disease: Autoimmune diseases arise when the immune system is negatively activated in the body, and continues attacking healthy cells. About 80% of women are affected more by 'autoimmune diseases' than men. The particular cause is unknown, but some recent research shows that variation in certain genes in women could make this huge difference [5]. TH development leads to scarring and destruction of the thyroid gland. It is manifested by a decrease of plasma-free triiodothyronine (T3) and thyroxine (T4), elevated plasma levels of thyroid-stimulating hormone (TSH) and by the presence of antibodies

to thyroid peroxidase (Ab-TPO) and thyroglobulin (Ab-Tg) [6]. The pathology of the disease involves the formation of antithyroid antibodies that attack the thyroid tissue, causing progressive fibrosis [7].

Autoimmune thyroid disease, is a well-known class in 'autoimmune diseases'. It also has high occurrence in women than men.

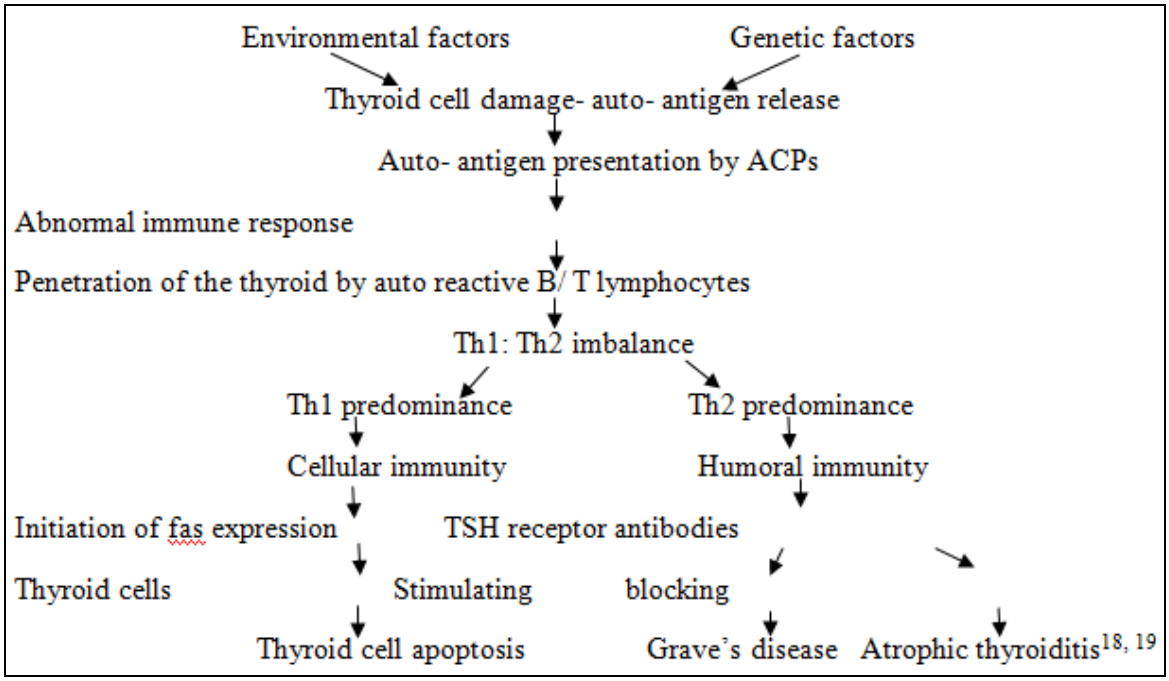
Leading Types: Hashimoto's autoimmune thyroiditis is a form of primary myxedema. 'Cytotoxic T cell' surface molecule undoubtedly has important part in AIT. Consumption of high iodine and Smoking both causes increased incidences of AIT [8, 9]. It has been called by several names including lymphocytic thyroiditis, autoimmune thyroiditis, chronic thyroiditis and lymph adenoid goiter [10]. Graves' disease autoimmune thyroiditis. GD is characterized by hyperthyroidism and the presence of thyroid-stimulating hormone receptor antibodies (TRAb) in serum, while HT is characterized by hypothyroidism and the presence of thyroid peroxidase antibodies (TPOAb) or thyroglobulin antibodies (TgAb) in serum [11, 12, 13]. Rarer autoimmune thyroiditis is mute and postpartum thyroiditis and iatrogenic thyroiditis. Immunological processes triggered by Thyroperoxidase (TPO) antibody, showing antibody status.

Increased 'TPO' and 'thyroglobulin antibodies' occurs with increasing age. But the existence of TPO antibodies is higher than 'TG antibodies 'in every age group. Significantly Hypothyroidism is accompanied by TPO antibodies, not TG antibodies. Hypothyroidism individuals were found negative for anti-TG antibodies [14].

TH has a significant part in skeletal improvement, it manages bone mass and additionally directs linear development. Short height, growth disturbances, epiphyseal dysgenesis, and lower bone age are portrayed in Childhood hypothyroidism. Advanced bone age, augmented growth, cranial sutures, growth plate& premature closure (in severe cases) are portrayed in Child thyrotoxicosis [15]. Atrophic thyroiditis refers to the end-stage of destructive autoimmune thyroiditis [16].

Brief Account of Autoimmunity: 46 years prior, the original evidence of autoimmunity of thyroid were first discovered in a rabbits immunized with thyroglobulin, after that description of antibodies & thyroglobulin in Hashimoto's thyroiditis patient's serum have distinguished. Also, the anus mirabilis and the abnormal thyroid stimulator cause Graves' disease. The affiliation of environmental, genetic, and endogenous factors is needed in the right concentration to initiate autoimmunity for the thyroid [17].

Pathogenesis of AITD:



A hypothesis came that the disbalance between helper and suppressor T-lymphocytes is occurred by decreased suppressor T-lymphocyte function which cause autoimmune thyroid disease's probable pathogenetic mechanism [20].

Prevalence of AITD: In worldwide, the prevalence of 'AITD' in women is 2- 4%, in men is 1%. With growing age its rate always increases. The frequent rate is approximately 0.8/100 in 'autoimmune hypothyroidism,' and 95% of them are women [21]. The prevalence of hypothyroidism, among adult females ranges from 3.0 to 7·5%. It is more regularly in aged females. It is additionally discovered that after 60 a higher TSH in 11.6% of 683 women present and unevenly half of the women holds confirmation of thyroid autoimmunity.

Hypothyroidism is more predominant in Iceland (high iodine intake areas), having 18% in elderly women. The frequency of hyperthyroidism in the ordinary female population has range from 0·9%. It is assessed that 79% of the reasons to develop AITD can be credited to genetics, hormonal and environmental risk factors that are involved [22].

SIGNS & SYMPTOMS:

Hyperthyroidism: Signs-Fine hair, Muscle weakness, thin skin, Low cholesterol, Tachycardia, Glucose intolerance, Tremor, widened pulse pressure, reflexes Stare, rapid deep tendon, Lid lag.

Symptoms: Weight Loss, Menstrual irregularities, Fatigue, Increased Sweating, Heat intolerance, Nervousness, Hyper defecation, Restlessness [23].

Hypothyroidism:

Signs: Depression, Slow reflex, Constipation, Cold, Hair Loss, skin Lethargy, intolerance, Weight gain, Easy fatigue.

Symptoms: Bradycardia, Relaxation, Myxedema, High cholesterol, Dry course, deep hoarse voice, Growth retardation [24].

Triggering Aspects for Grave's disease:

Genetic Susceptibility: There are particular epidemiologic confirmations demonstrating hereditary of Grave's hyperthyroidism and chronic autoimmune thyroiditis. The diseases associate in families and females are inclined for this disease [25].

Stress: Suppression in immunity could prompted by stress, perhaps mediated by movement of cortisol on the immunity cells. Improved immunologic hyperactivity can connected with Suppression of stress. This response could impulsivein 'autoimmune thyroid disease' with genetically prone subjects [26].

Infection: Treatment with Hepatitis C infection by therapy of interferons is well-known factor [27].

Smoking: Risk feature for Grave's hyperthyroidism and moreover a stronger risk feature for Grave's ophthalmopathy.

Sex Steroids: Adequate quantities of estrogen improve the immunological reactivity regarding self-antigens; this has proven with many evidences.

Drugs: In prone individuals, drugs like amiodarone, iodine, iodine having drugs take part in reoccurrence or origination of 'Grave's disease'. They could release thyroid antigens from immune system with directly destruct thyroid cells [28].

Pregnancy: Hyperthyroidism connect with moderate fertility. So, there are few chances to occur Grave's disease throughout pregnancy time. Moreover, immune system suppresses (both B –cell and T-cell functions are lessened) in pregnancy, so disease's complications improve as pregnancy progresses.

But the progress of 'postpartum thyroid disease' may associated by immunosuppression. The presence of fetal cells in 'maternal tissues' (fetal microchimerism) might play role in postpartum autoimmune thyroiditis development [29].

Triggering aspects for Hashimoto's Thyroiditis-

Genetic Susceptibility: Hashimoto's Thyroiditis have family clustering, sometimes alone either with Graves' disease. [30] The sibling reappearance risk is approximately >20.

The identified AITD susceptibility genes include immune-modulating genes, such as the major histocompatibility complex (MHC), cytotoxic T lymphocyte antigen-4 (CTLA-4), CD40 molecule and protein tyrosine phosphatase-22 (PTPN22) and thyroid-specific genes, including TSH receptor (TSHR) and thyroglobulin (TG) [31].

Epidemiological evidence of genetic susceptibility to AITDs is provided by familial clustering of the disease (20–30% of cases show a positive family history of AITDs) [32].

Stress: Numerous stresses interrelated to Hashimoto's thyroiditis. The mechanisms consist of immune suppression initiation by nonantigen-specific mechanism, because of the properties of cortisol or corticotropin-releasing hormone on immune cells, followed by immune hyperactivity prominent to 'autoimmune thyroid disease'.

Sex Steroids and Pregnancy: Women are prone for Hashimoto's thyroiditis in comparison to men, it shows sex steroids character. Other than that, older women are more susceptible to Hashimoto's thyroiditis than younger women. Both B & T cells have diminished functions throughout pregnancy, as the appropriate elevation in CD4+, CD25+, and regulatory T cells.

This immunosuppression has contributed in the postpartum thyroiditis' development. In later years, the conventional Hashimoto's disease progress in nearly 20% patients with having postpartum thyroiditis [33].

Iodine Intake: Prevalence of Hashimoto's disease (Hypothyroidism) starts with slight iodine insufficiency, while higher incidence inter-connected with extreme intake of iodine.

Radiation Exposure: children's exposure in the fate of tragic Chernobyl nuclear has established thyroid auto- antibodies of higher frequency. Many evidences are there, which recommend that, risk for elevation in thyroid dysfunction increases positive thyroid antibodies. In comparison to female subjects without radiation exposure, radiation exposed females have 'autoimmune thyroid disease' (anti-TPO antibodies level> 200IU/mL and hypo echogenicity on ultrasound). People with< 5year exposure to ionization radiation are at high risk [34].

Fetal Micro Chimerism: 'Autoimmune thyroid disease 'individuals have maternal thyroid glands identifying fetal cells' existence. With the relation of thyroid gland these cells may introduce host versus graft reactions and have critical role in the introduction of 'Hashimoto's thyroiditis.

Autoantibodies: TPO Ab's detectable level typically shows the progress of ahigher TSH and consequently show risk feature for hypothyroidism.

Thyroid Peroxidase (TPO) Antibodies: The crucial thyroid enzyme 'Thyroid peroxidase' (TPO) anti- bodies catalyze fabrication of 'thyroid hormone' (coupling and iodination reaction). Patients of 'Grave's disease' and 'autoimmune hypothyroidism', 90% of 'Anti-TPO autoantibodies' are found. In 'autoimmune hypothyroidism', 'thyroglobulin (TG) antibodies 'gathered with predominant antibodies. Anti-TPO antibodies are primarily fromIgG4 subclasses IgG class1and in excess.

Thyroglobulin (TG) Antibodies: When thyroid cells are stimulated by TSH, TG is hydrolyzed and endocytosed in lysosome then released into T3 and T4. The particular location is unclearfor T-and B-cell epitopes. Less than 60% patients found with lymphocytic thyroiditis & thyroglobulin autoantibodies and 30% patients found with Grave's disease.

Thyroid Stimulating Hormone Receptor (TSH-R) Antibodies: 'Atrophic thyroiditis' & 'Grave's disease' instigated by prime autoantigen 'Thyroid stimulating hormone receptor (TSH-R)', Situated on thyroid follicular cell's basal surface. In Grave's disease, thyroid cells get stimulated by complexing of thyroid stimulating antibodies (TSAbs) to receptors, producing an extreme number of thyroid hormones that causes hyperthyroidism. In 'atrophic thyroiditis', inhibited thyroid cell stimulation occured by some antibody that binds to the TSH and receptors.

Classes of TRAb:

- Thyroid stimulating autoantibodies' (TSAb) cause Grave's hyperthyroidism
- 'Thyroid stimulation-blocking antibodies' (TBAb) block receptor complex with TSH

Mechanism of Thyroid Cell Injury: In AITD several antibodies & cell-facilitated mechanisms are accountable for thyroid injury. Compared to normal counterparts, the expressions of CD 95 Lin (death receptor) and CD 95 (death receptor) ligands are higher in thyroid tissues in 'Hashimoto's

thyroiditis'. Here highly increased manifestation in Grave's disease of– 'modulators of apoptosis' (Bcl-2, cFLIP and Bcl-XL). Role of inhibitory apoptosis mechanism supports by this. Although, there is major expression of CD95 /Fasand its ligand in all cases, but Thyrocytes go through apoptosis individual in Hashimoto's thyroiditis. By enhancing caspases expression, the 'cytokine interferon-gamma' likely to have important role in pathology of TH1 disease (Hashimoto's thyroiditis), although FAS facilitated apoptosis alert the cells.

B- Cell Responses: Individual's with 'Hashimoto's thyroiditis' and 'primary myxedema', antibodies like 'TG' and 'TPO'present in higher concentration. In 'Grave's disease', these antibodies are frequent but not common. In 'postpartum thyroiditis', 'TPO antibody' is more recurrent than TG antibodies. For entering in antigen and become pathogenic, 'TPO antibodies' required cell-mediated injuries.

T-Cell Responses: Within thyroid lymphocytic infiltrate, mostly'CD4+' cellsoccurin the 'CD4+' and 'CD8+'. Lymphocyte produces interferon gamma, Cytokines including IL-2, IL-4, IL-6, IL-10, IL-12, IL- 13 and IL-15. These might be varying in concentration depends on patients. Metabolic character of thyroid cells injured by complement attack are originated by alternate or classical pathways. This damage shows secrete Prostaglandins, oxygen metabolites, IL- 6, IL- 1. They all are accountable for enhancing autoimmunity [35].

Other antibodies Na+ / I- symporter- NIS is first verified cultured dog thyroid cells, itis a chief thyroid autoantigen. Antibodies which disturb iodide uptake mediated by NIS; presents 15% in sera of Hashimoto's, 1/3rd in sera of 'Grave's disease'. 'AITD' patients contains 10 to 25 % antibodies for thyroid hormones. Although, some patients also have tubulin, cytoskeletal proteins and some autoantibodies (non-specific) against DNA [21].

Diagnosis of Autoimmune Thyroid Disease: Measurement of circulating antibodies for 'TPO' and 'TG' can detect AITD. Around 98% of patients detect positive for both antibodies. For detecting autoimmune hypothyroidism in comparison to TG Ab, 'TPO Ab' is more sensitive and precise. In a long-lasting 'Hashimoto's thyroiditis' diagnosis, an increased level of TSH with 'TPO antibodies' is the best precise standard [22, 36]. Autoimmune Thyroid Disease & Neoplasms- 1/3rd of patients with thyroid cancer have also established thyroid antibodies and Thyroiditis. For initiation of non-Hodgkin's thyroid lymphoma, Hashimoto's disease (pre-existing) is a key risk factor. Several studies also show that 'breast cancer' could originate from enhanced regularity of autoimmune thyroiditis [21]. Autoimmune Thyroid Disease in kidney disease- Thyroid dysfunction shows major variations in tubular and glomerular functions and also in electrolyte & water homeostasis. From a clinical practice observation point, it is noticeable that both diseases are followed by remarkable changes in water and electrolyte metabolism, besides cardiovascular function.

Concentration of Different Thyroid Hormones [37, 38, 39]:

Thyroid Hormones	Abbreviations	Concentration
'Serum Thyrox' level	'T4'	4.6-12 ug/dl
'Serum Triiodothyronine' level	'T3'	~80-180 ng/dl
'Serum thyroglobulin' level	'Tg'	~0-30 ng/m
'Thyroglobulin antibody level	(TgAb)	> 20 IU/mL.
'Thyroid peroxidase antibody' level	(TPOAb)	> 35 IU/mL.
Free 'Thyroxine' level	(FT4)	0.7-1.9 ng/dl
'TRH stimulation test Peak' level	(TSH)	9-30 IU/ml in 20-30 min
Free 'Thyroxine index' level	(FT4I)	~4-11
'Thyroid hormone binding' ratio	(THBR)	Up to 0.9-1.1
Serum 'thyrotropin' level	(TSH)	~0.5-6 uU/ml
Free 'T3 Index' level	(FT3I)	<80-180
'Radioactive iodine' uptake level	(RAIU)	~10-30%
'Thyroxine-binding globulin' level	(TBG)	~12-20 ug/dl T4 +1.8 µgm

Important test Method for Thyroid Hormone Detection: 'Chemiluminescence' method is used for the identification of 'Thyroid Autoantibodies' (Thyroid Peroxidase & Thyroglobulin Ab), T3, T4,

TSH & FT3, FT4, TSH3G UL and‘ RIA’ is used for detection of TSH Receptors Ab [40].

Study Data of Autoimmune Thyroidism: In UK, genetic preference analysis was organized for autoimmune thyroid disorders. For ‘Grave’s disease’, patients group comprises 2791 Caucasian (white) volunteers (2717 female/ 474 male) & for ‘Hashimoto’s thyroiditis’495 Caucasian (white) volunteers with (427 females/ 68 males) have chosen, from the diverse ‘specialist referral center and thyroid clinics in Bournemouth, Birmingham, Cardiff, Cambridge, Leeds, Exeter, New castle, United Kingdom (UK) and Sheffield they all were recruited.

The presence of biochemical hyperthyroidism indicates some signs of ‘Grave’s disease’-

- ✓ Radionuclide scan illustrates distributed uptake/ Ultrasound scan diffuse goiter.
- ✓ Grave’s opthalmopathy (NOSPESC score $\geq$2)
- ✓ TSH receptor’s positive autoantibodies, positive antibodies for TG and TPO.
- ✓ On physical inspection, diffuse goiter shows.
- ✓ After thyroid, histology lymphocytic infiltration confirmed [41].

Presence of biochemical hypothyroidism demonstrate some signs of ‘Hashimoto’s disease’-

- ✓ Positive TG and TPO antibody.
- ✓ On physical inspection diffuse goiter present.
- ✓ In fine needle aspirate lymphocytic infiltrate present.

In ‘grave’s disease’, there are 9.77% cases of further autoimmune disorders and in ‘Hashimoto’s thyroiditisand 14.3% cases of further immune disorders. In ‘Grave’s disease’ 3.15% of patients (more possibilities in male) have rheumatoid arthritis, 4.25% of patients acquire rheumatoid arthritis associated with ‘Hashimoto’s disease’. Therefore, this is most common simultaneous autoimmune disorder in both cases. In ‘Grave’s’ and ‘Hashimoto’s thyroiditis’ here are threats of almost all autoimmune diseases as like type1 diabetes, Addison’s disease, systemic lupus erythematous, pernicious anemia, vertigo, celiac disease and multiple sclerosis, probably marked increasing %. There was the virtual assembling of parental hypothyroidism with ‘Grave’s disease’ and ‘Hashimoto’s thyroiditis’ [42].

Autoimmune Thyroiditis Prevalence in India: In India, thyroid is very frequent, affecting ~42 million people and increasing considerably. In India, study shows thyroid diseases affecting commonly are-Hyperthyroidism, Hypothyroidism, Goiter & Iodine insufficiency disorder, Thyroid cancer and Hashimoto’s Thyroiditis. A population-built study revealed that % of adult volunteers affected subject with ‘anti-thyroid peroxidase antibodies’ are 16.7%, and for ‘anti-thyroglobulin antibodies’ 12.1%. The occurrence of ‘anti-TPO’ and ‘anti-TG antibodies’ would be 9.5%, 8.5%, if patients with irregular thyroid function were omitted.

In India, for Hashimoto’s thyroiditis’s revolutionary study, 6283 schoolgirls were selected. Between them, they found Goiter in 1810 school girls. ‘Juvenile autoimmune thyroiditis’ constitutes in 58 schoolgirls (7.5%), in between 764 fine needle aspirate cytology definite girls. Subclinical hypothyroidism (15%) and evident hypothyroidism (6.5%) were also indicated from a confirmed instance of fine needle aspiration cytology [43]. It has been noticed that iodine supplementation in deficient areas increases the lymphocytic infiltration of thyroid gland by three-fold, along with an increase in serum level of antithyroid antibodies [44].

Treatment of Diseases: To improve clinical practice and healthcare in children and adolescents with genetic syndromes, pediatricians and pediatric endocrinologists should be aware of the importance of the accurate screening and monitoring of thyroid function and autoimmunity [45]. A proper diagnosis and early management is essential for controlling symptomatology and ensuring less systemic compromise that may lead to cardiovascular, neurological, gastrointestinal, and endocrinological damage [46].

Allopathic Treatment:

Hashimoto’s Thyroiditis:

Synthetic hormones: ‘Thyroid hormone’ deficiency would accelerate ‘Hashimoto's disease, it needed ‘thyroid hormone’ replacement therapy.

Normally this replacement occurred by regular oral intake of thyroid' hormone (synthetic) levothyroxine (Synthroid, Levoxyl, thyronome *etc*). This hormone is naturally formed by thyroid gland. As per'American Thyroid Association', this treatment may give rise to little weight reduction causing fat loss and muscle protein, (>10% of body weight) [47, 48]. This medication helps restore sufficient concentration of hormones and all the hypothyroidism symptoms get reversed. Although levothyroxine medication is commonly for a lifetime, dosage amount always wary according to 'TSH' level in blood (every 12 months) with proper monitoring and guidance of doctor every year [15, 49].

Grave's Disease:

Anti-thyroid Medicines: These drugs prevent thyroid gland by synthesizing more hormones. Ex-Propylthiouracil and Methimazole (Tapazole).

Radioactive Iodine: Above 60 years of hypothyroidism, its oral consumption is beneficial. Thyroid gland absorbs radioactivated iodine, got shrinked.

Surgery: Sometimes, Thyroidectomy is suggested for the treatment of 'Grave's disease'.

Beta Blockers: Suggested for anxiety, sweating, increased heart rates in 'Grave's disease [50].

Observation of the Dosage: In 'Hashimoto's thyroiditis', TSH in the blood is always checked monthly after treatment starts, for initially regulating the correct dosage of externally provided thyroid hormone. Doctors start treating with the initial dosage of medication and thereby steadily rise the dosage (Skipping of the dose will cause returning of symptoms). Excess amounts of 'thyroid hormone 'can regulate worse osteoporosis (bone loss) and also induce arrhythmias. Increasing hormone substitution permits the heart to control the increased metabolism. Satisfactorily if used in the appropriate dose, Levothyroxine drug certainly has not any side effects, also it is inexpensive [51, 52]. In 'Grave's disease,' ophthalmopathy is needed as additional medications like steroids, unusual eye droplets to decrease symptoms [53].

Ayurvedic Treatment: In Ayurveda, the balanced state of Agni (enzymatic activity), dhatu (metal), tridoshas (bodily humours) and mala (impurity) are the baseso that body can achieve samavastha (homeostasis) [53, 54]. Herbal plant extracts and some formulations are used to balance bodily humours and tridoshas [54].

Herbal Formulations:

1. Tab. Thycet 1 bd
2. Tab.punarnavamandur 1 bd
3. Tab kanchnarguggul 1 bd
4. Tab. Chandraprabhavati 1 bd
5. Tab. Bramhivati 1 bd Cap.optilife 1 bd
6. Hanspatyadi Kashay 3 – 4 tsp bd
7. Ashwagandharishta– 3 -4 tsp with water.
8. Varunadi Kashay 3 – 4 tsp bd [55]

Herbs:

Hashimoto's Thyroiditis:

1. *Bacopa monnieri* (Scrophulariaceae), commonly known as 'Brahmi' whole plant raised both T3 & T4, reduce oxidative stress, and improve memory and concentration (200 mg/kg) [54, 56, 57].
2. *Cucumis melo* (Cucurbitaceae) 'Musk melon' fruit peel raised thyroid hormone levels [54].
3. *Withania somnifera* (Solanaceae) 'Ashwagandha' rootlowered cortisol, raise thyroid hormones levels, and lower oxidative stress [54, 56, 57].
4. *Commiphora mukul* (Burseraceae), thyroid stimulatory function [56, 57].
5. *Mangifera indica* (Anacardiaceae), Showed thyroid stimulatory and anti-peroxidase roles [56, 57].
6. *Bauhinia purpurea* L. (Caesalpiniaceae), thyroid hormone regulating act [56].
7. *Costus pictus* D. Don, a Rhizomatous extract, has been explored for anti-hypothyroid efficacy and could significantly restore the normal level of thyroid hormones [57].
8. *Fucus vesiculosus* var. *divaricatus* (Fucaceae) marine alga rich in iodine [56, 57].

Grave's disease:

1. *Melissa officinalis L.* (Lamiaceae), lemon balm is effective in blocking the binding of TSH to the receptor by acting on the hormone and the receptor itself. It also inhibits cyclic AMP production stimulated by TSH receptor antibodies [56, 57].

2. *In autoimmune diseases, Leonurus cardiaca L. (Lamiaceae)* is important to reduce inflammation, making motherwort a good choice in treating hyperthyroidism. In addition to reducing inflammation, the enzyme 5-deiodanase is inhibited [56, 57].

3. *Convolvulus pluricaulis* (Convolvulaceae) acts strongly on some of the liver enzymes and helps improve hyperthyroidism symptoms [56, 57].

4. *Rauvolfia serpentina* L. (Apocynaceae) root extract administered to T4-induced hyperthyroid mice significantly decreased both the serum T3 and T4 concentrations [56, 57].

5. *Emblica officinalis* Gaertn. (Phyllanthaceae) fruit extract decreased both serum T3, T4 concentrations. The decrease in T3 was by inhibiting peripheral conversion of T4 to T3 in extra-thyroid tissues [56, 57].

6. *Moringa oleifera* auct. non-Lam Family: Moringaceae [57] *M. oleifera* leaf extract treatment of female rats decreased serum T3 concentration and increased in serum T4 concentration. This observation suggests the inhibitory activity of the plant extract in the peripheral conversion of T4 to T3 [56].

7. *Ocimum sanctum L.* (Lamiaceae) the leaf extract of O. sanctum administered to male mice for significantly inhibited only T4 concentration [56].

CONCLUSION: This review focused on types, symptoms, prevalence, affecting factors, and cure of AITDs. We saw the incidence of AITDs increasing readily year by year.

It is desirable for the treatment that they get identified early. The symptoms shown in patients suffering' Grave's disease' and 'Hashimoto's disease' are identically general but not really easy to discriminate from other 'Autoimmune diseases and simple 'Thyroid disease'. So, the awareness for 'Autoimmune diseases' must spread around. This has also realized that probably increased 'TPO' levels (thyroid peroxidase), TG (Thyroglobulin) and T& B cells are a key source of 'AITD' followed by interaction of genetic or environmental factors. We also perceived that the imbalance between helper and suppressor T-lymphocytes instigated by decreased suppressor T-lymphocyte function could leadsto 'Autoimmune Thyroid Diseases'. In allopathic approach consistent oral intake of thyroid's hormone (levothyroxine) for Hashimoto's Thyroiditis & Propylthiouracil, Methimazole Radioactive iodine and Surgery for Grave's Disease is used. The herbal approach to thyroid dysfunction is necessary to avoid the side effects of hormonal therapy. Some herbs like *Bacopa monnieri*, *Withania somnifera*, *Cucumis melo*, *Melissa officinalis*, *Rauvolfia serpentine*, *Emblica officinalis* are efficacious in normalizing thyroid dysfunction. This will provide much more options to treat thyroid dysfunction. Long-term effectiveness studies of the substances are needed to optimize the treatment length.

ACKNOWLEDGEMENT: Nil

CONFLICTS OF INTEREST: The authors declare no conflict of interest.

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How to cite this article:
Tewari I, Bhatt P and Singh S: Different treatment approaches used in autoimmune thyroid disease: a comprehensive review. Int J Pharm Sci & Res 2023; 14(5): 2173-82. doi: 10.13040/IJPSR.0975-8232.14(5).2173-82.