

Outpatient Management of Thyroid Disorders

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Abstract

Introduction: One of the major endocrine dysfunctions are diseases seen in the thyroid glands, where there could be an increase or decrease in the thyroid hormones being synthesized or circulated. There is an increased incidence of the condition in women as compared to men and it is critical to assess the condition accurately for its best management. However, management strategies for thyroid disorders continue to undergo constant evolution.

The Aim of Work: The study aimed to assess the information and practices regarding clinical management of thyroid disorders in the outpatient department. This review briefly outlines recent advances in managing thyroid disorders as well.

Methodology: The review is a comprehensive research of PUBMED from the year 1993 to 2019.

Conclusion: Thyroid diseases can span out to be life-long conditions that can be controlled by careful measures. Normalizing the normal blood levels of the thyroid hormones should be the goal of treatment. Pharmacological intervention is usually required in hyper and hypoparathyroidism. Antithyroid medications, beta-blockers, radioiodine and final resort being surgery can be used to treat the pathological condition.

Keywords: *Thyroid Disease; Outcomes; Clinical Practice; Thyroid Dysfunction*

Introduction

Thyroid hormones are responsible for the metabolism of the body, growth and homeostasis. Increased oxygen consumption is seen because of thyroid hormones in all tissues apart from the brain testes and spleen. They can stimulate carbohydrate usage, absorption of glucose, glycogenolysis and gluconeogenesis. Thyroid hormones help to maintain a healthy nervous and skeletal system. Under or over-activity of the thyroid hormones could cause variations in the other organ systems. The thyroid gland is located in between C5-T1, below the larynx in front of the trachea. It has four parathyroid glands in addition to that [1].

Outpatient endocrine departments see patients affected with thyroid diseases and disorders on a large scale. Endocrinologists need to have experience and expertise to report the conditions objectively and predict the outcomes [2,3]. Thyroid dysfunction is commonly seen affecting females with men to women ratio of 1:10. In addition to endogenous factors, the interaction between genetic predisposition and environmental factors can affect an organ-specific autoimmune response and increases the susceptibility to thyroid autoimmunity [4].

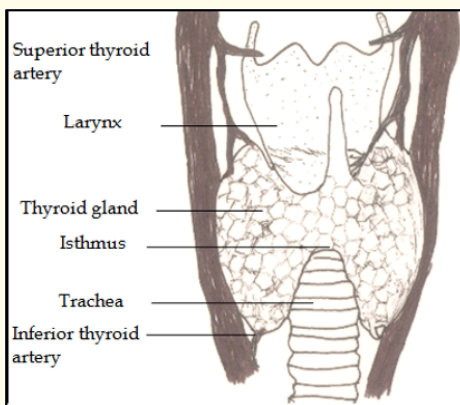


Figure 1: Thyroid gland anatomy with vessels [1].

About 2% of the female population autoimmune hyperthyroidism also known as Graves’ disease (GD), which has a characteristic presence of thyroid-stimulating antibodies (TSAb) (mimics the action of thyroid-stimulating hormone (TSH)) causes uncontrolled thyroid hormone production. Extra-thyroidal manifestation like thyroid eye disease can also be seen. In another 5% of the women population, autoimmune hypothyroidism (AH) is characterized by the presence of thyroid peroxidase (TPO) [5].

The most common cause of thyroid diseases seen universally is that of iodine deficiency. Overt thyroid dysfunction is dependent on the population’s iodine intake. Hashimoto’s disease and thyroid ablation is the main cause of hypothyroidism in developed regions and Graves’ disease (GD) and toxic adenoma (TA) are the common causes of thyrotoxicosis. Since there has been an improvement in modern testing, subclinical thyroid dysfunctions are diagnosed more than ever before [5].

Hypothyroidism

The thyroid-stimulating hormone (TSH- secreted from the anterior pituitary gland) regulates the function of the thyroid gland. The deficiency of this hormone can vary from severe to moderate. Overt Hypothyroidism (OH) is a severe deficit and subclinical hypothyroidism is the moderate form. The diagnosis of hypothyroidism may not be so evident, but a lookout for the following signs or symptoms must be done [6].

- Bradycardia
- Delayed ankle reflex
- Coarse and dry skin
- Weakness/lethargy
- Cardiac enlargement (on x-ray)
- Pallor of skin
- Impaired memory
- Constipation
- Poor heart sounds
- Slow speech
- Edema of eyelids
- Sensation of cold
- Decreased sweating
- Weight gain
- Hair loss
- Dyspnoea
- Peripheral edema
- Precordial pain
- Poor vision
- Cold skin
- Macroglossia
- Facial edema
- Coarseness of hair
- Hoarseness
- Anorexia
- Nervousness
- Menorrhagia
- Deafness
- Palpitations

Figure 2

Hashimoto’s thyroiditis and its fibrotic variant atrophic thyroiditis commonly attributes as permanent hypothyroidism which could require lifelong treatment with thyroxine (LT4). However, the table below shows the reversible causes of hypothyroidism [6].

Hashimoto’s thyroiditis	By decreasing thyroid-stimulating hormone receptor blocking antibodies
Postpartum thyroiditis	70% can become euthyroid in the first year
Subacute thyroiditis	Almost 100% become euthyroid
Iodine induced	Becomes normal when iodine is withdrawn
Drug-induced	Recovers when drugs are withdrawn
Post-ablative (surgery/RAI therapy)	Transient hypothyroidism occurs in some

Table 1: Hypothyroidism which can be reversed [6].

Pharmacological management

- Thyroxine replacement can be done by the following principles.
- Initially, LT4 (thyroxine) can be started off:
- 25 - 50 mg/day of in the elderly and cardiac patients
- 50-100 mg/day of LT4 in the young and healthy older patient.
- The dose can be increased to 4 - 6 weekly to aim for TSH “normalization” and symptom control.
- In those patients suspected with hypoadrenalism, Corticosteroid replacement should be started before LT4.
- In gluten sensitivity, pregnancy, and concomitant drug therapy, higher doses may be required.
- Clinical and biochemical monitoring should be done every 6 - 12 months [7].

Hyperthyroidism

Increased synthesis and secretion of thyroid hormones from the thyroid gland lead to hyperthyroidism and when there is the excess circulation of thyroid hormones, it is called thyrotoxicosis. Treatment modalities of hyperthyroidism include antithyroid drugs (ATDs), radioactive iodine ablation, and surgery. Hyperthyroidism can either be overt or subclinical. Low serum thyroid-stimulating hormone (TSH) concentrations and raised serum concentrations of thyroid hormones (thyroxine (T4), tri-iodothyronine (T3), or both) are the features of overt hyperthyroidism. On the other hand, in subclinical hyperthyroidism low serum TSH, but normal serum T4 and T3 concentrations are seen [8].

Graves’ disease

When the first episode of graves’ occurs, antithyroid drugs (ATD), radioactive iodine (RAI) therapy, and surgery may be used alone or in combination. ATD is recommended as the first line of therapy in patients who would require subsequent RAI or surgery or can be used as the only long term therapy [9].



Figure 3: Extrathyroidal features of Graves’ disease: marked chemosis and eyelid edemas; eyelid retraction, swelling, and exophthalmos [9].

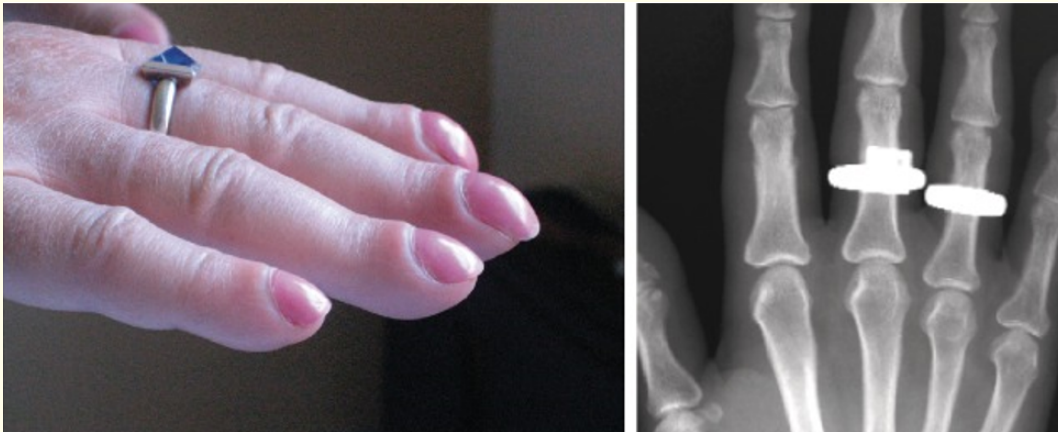


Figure 4: Extrathyroidal features of Graves' disease: soft-tissue edemas and clubbing; characteristic eroded bone margins of the phalanges [10].

Antithyroid drugs

Carbimazole (CMZ) and Propylthiouracil (PTU) are the usually used ethionamide ATD. They have a long half-life and can be absorbed easily and rapidly. Apart from the inhibition of the iodination of tyrosine in thyroglobulin, it can prevent the conversion of thyroxine (T_4) to triiodothyronine (T_3) in thyroid and peripheral tissues. This can be especially advantageous in severe thyrotoxicosis or thyrotoxic storm. However immunosuppressive effects can be seen with thionamides [8]. The regimen for Carbimazole (CMZ), methimazole (MMI) and propylthiouracil (PTU) for Graves' disease include [7]:

- "Titration regimen":
 - Start CMZ 40 mg/day (or equivalent doses of MMI or PTU).
 - Reduce gradually to maintain euthyroidism (for example, CMZ 5 - 10 mg/day).
 - Continue for 12 - 18 months.
- "Block and replacement regimen":
 - Start CMZ 40 mg/day or PTU 150 mg thrice daily.
 - Add thyroxine 100 - 150 mcg/day when euthyroid (at about 3 - 6 weeks).
 - Continue for 6 - 9 months.

Propranolol 20 - 80 mg thrice daily to block adrenergic effects in the initial few weeks. Skin reactions, arthralgias (sometimes heralding severe transient migratory polyarthritis), and gastrointestinal upsets are the side effects seen in 5% of the patients. The most undesirable and rare side effect is agranulocytosis [7].

RAI therapy

After adolescence, the first-line therapy for the first episode of GD is RAI therapy. This mode of treatment is common in recurrent diseases and the elderly population. In patients where surgery is contraindicated, RAI treatment is preferred. For up to 4 - 5 months after the RAI pregnancy should be avoided [7].

Surgery

In patients unwilling to go for RAI therapy, surgery is recommended. It can also be done in patients who develop severe side effects to ATD and in whom RAI is contraindicated [7].

Nodular thyroid disease, toxic adenoma (TA), and toxic multinodular goitre (TMNG)

Fine needle aspiration biopsy (FNAB), ultrasound and nuclear imaging, and biochemical tests are required to rule out malignancy. Suspicious regional lymph nodes should be sent for biopsy [11]. Follow-up throughout a lifetime is required in such cases. The management of such a condition include [12]:

1. For benign diseases, suppressive thyroxine therapy can be used (contraindicated in patients with suppressed T).
2. RAI therapy-the preferred method of treatment for TA and TMNG (Large non-functioning goiters may reduce in size).
3. Surgery-reserved for large goiters.
4. A major percentage of patients who undergo surgery or RAI therapy will be hypothyroid eventually and will require thyroxine therapy [7].

Drug-induced thyroid disease

Amiodarone

In such cases, CMZ/PTU (high dose) is given for 6 - 12 weeks and withdrawal of ATD attempted. When tests are inconclusive Corticosteroids need to be added to CMZ/PTU in mixed forms of AIT or response to ATD will be insufficient. Recurrent conditions can be treated with RAI therapy.

Lithium

Lithium induces hypothyroidism can be treated with thyroxine therapy.

Pregnancy and thyroid dysfunction

The strict control of thyroid homeostasis is required during the organogenesis of the fetus.

Hyperthyroidism

GD and gestational transient thyrotoxicosis (GTT) associated with hyperemesis gravidarum are the most common causes of hyperthyroidism seen in pregnant patients. Hyperthyroidism can lead to adverse maternal outcomes like [15]:

- Placental abruption
- Preterm delivery
- Heart failure or
- Thyroid storm.

And fetal outcomes like

- Low birth weight,
- Growth retardation
- Neonatal hyperthyroidism
- Stillbirth, and
- Fetal death.

Transient sometimes moderately severe thyrotoxicosis can be because the human chorionic gonadotrophin (HCG) is structurally related to TSH and high HCG activity are seen in women with hyperemesis. Short term ATD therapy may be required in patients who are TRAb -ve. The management includes [12]:

1. Due to a lack of teratogenesis, PTU is the preferred drug of choice [13].
2. TRAb should be checked early in pregnancy in patients with previous RAI or surgically treated GD

3. PTU 100-150 mg (thrice daily) should be given in patients who are thyrotoxic during pregnancy until they are euthyroid and the dose reduced rapidly until free T4 is at the upper limit of the reference range [14].
4. The transplacental transfer of TRAb can cause fetal thyrotoxicosis (tachycardia and growth retardation). Beta-blockers or ATD can be used in transient neonatal thyrotoxicosis [15].
5. Surgery should be avoided unless poor control resulting from poor compliance or side effects poses a risk to mother and child. The second trimester is the preferred timing for surgical intervention.

Patient status	Antibodies measurement
Euthyroid - previous antithyroid drug	Not necessary
Euthyroid ± T4 therapy and Previous radioiodine therapy/surgery	Check-in early pregnancy: if low or absent no further testing or if high: check fetus and check antibodies in last trimester
Receiving antithyroid drugs during pregnancy	Measure in last trimester

Table 2: Guidelines for measurements of TSH - receptor antibodies in a pregnant woman with grave's disease [14].

Hypothyroidism

Hypothyroxinaemia and subclinical and overt hypothyroidism can compromise maternal and fetal wellbeing. Impaired nonintellectual development of the child can be affected. During the first trimester, the adequate transfer of thyroxine must occur. The dose of LT4 should be increased by 50 - 100 mg/day in previously hypothyroid patients when the pregnancy is confirmed [14].

An immediate full replacement LT4 therapy is recommended in women without previous hypothyroidism where

1. Abnormal thyroid function-that is, TSH- 4 mU/l or free T4 below the reference range for gestational age irrespective of thyroid autoimmune status
2. Thyroid autoimmunity (TPOAb+ve) and TSH between 2 - 4 mU/l or free T4 in the low normal/low range.

There is a requirement to increase the LT4 dose as the pregnancy progresses. Evidence that hormones deficiency during maternity can lead to neurodevelopment also exists [7].

Postpartum thyroid dysfunction (PPTD)

PPTD is seen in half of the pregnant patients who are TPOAb+ve. Even though it could be a self-limiting disease, about one-third of the patients become permanently hypothyroid within the first year, and in the long term review the remaining patients are clinically or subclinically hypothyroid. Beta-blockers can help in symptomatic treatment in the early thyrotoxic phase. However, a temporary or permanent withdrawal of LT4 may be required. Post-partum thyroiditis being a common endocrinological condition, falls in the spectrum of autoimmune thyroid disorders [13].

Thyroiditis

A preexisting fungal, bacterial, or viral infection can get complicated by the presence of acute thyroiditis. A self- limiting form is that of De Quervain's thyroiditis which is subacute, commonly seen in women and is usually associated with a high erythrocyte sedimentation rate and decreased RAI uptake. Initially, beta-blockers can be used and later the LT4 therapy can be started. Subacute thyroiditis is usually painless [7].

Conclusion

A wide spectrum of diseases can be seen in thyroid dysfunctions, which are broadly under hypo and hyperthyroidism. There have been well-established treatment options in both these conditions but yet newer strategies are still evolving. Even though considerable advances have been made in understanding the immune system, thyroid immunity remains questionable. Debates regarding the optimal

range of TSH with thyroxine replacement, the duration of ATD for GD, and whether to treat subclinical disease are still ongoing. More evidence-based research for further insight into the conditions and newer modes of therapies must be researched. However, clinical experience will always remain invaluable in many situations. To maintain euthyroidism in patients, a lifelong follow up is required regardless of the treatment modality used [17].

Molecular biology has helped to study thyroid physiology better by creating hormone analogs that could be useful in obesity and other conditions. A scientific collaboration with the pharmaceutical field has improved treatment strategies.

Advances in thyroidology can result in increased clinical care and a rational understanding of the patients diagnosed with the condition.

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