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# Exploring the Thyroid Gland Physiology in Relation to Thyroid Hormones: An Overview through the Lens of 3D Computational Biology

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***Abstract***

*The endocrine system plays a pivotal role in orchestrating and sustaining diverse physiological functions by manufacturing and releasing hormones, which function as vital chemical messengers within the body. Among the prominent endocrine glands, the thyroid gland holds a central position. Situated in the lower part of the neck, this gland adopts a butterfly-shaped structure. Its significance lies in the synthesis of three key hormones: thyroxine (T4), tri-iodothyronine (T3), and calcitonin. The thyroid hormones, T3 and T4, collectively referred to as thyroid hormone, are intricately crafted within the follicles of the thyroid gland. These hormones wield substantial influence over metabolic processes, playing a crucial role in regulating energy expenditure and the overall metabolic rate of the body. Their synthesis is a finely tuned process that contributes significantly to the maintenance of homeostasis. In addition to T3 and T4, the thyroid gland houses parafollicular cells, also known as C cells, interspersed between its follicles. These specialized cells take on the responsibility of producing calcitonin, a hormone with a distinctive role in the body's calcium homeostasis. Calcitonin functions by modulating calcium levels, ensuring that they remain within the normal range. By counteracting the actions of other hormones involved in calcium regulation, calcitonin contributes to the overall stability and health of the skeletal system. his intricate interplay of hormones originating from the thyroid gland underscores its multifaceted role in maintaining physiological equilibrium. From influencing metabolic activity to actively participating in calcium regulation, the thyroid gland serves as a linchpin in the delicate balance that defines optimal bodily function. Understanding the complexities of its hormone production provides profound insights into the broader landscape of endocrine control and its impact on overall well-being*

**Keywords:** Endocrine system, Hormones, Thyroxine, Tri iodo thyronine and Calcitonin.

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## INTRODUCTION

The thyroid gland produces two closely related hormones, thyroxine (T4) and triiodothyroxine (T3). These hormones exert their influence through thyroid hormone receptors α and β, playing a pivotal role in cell differentiation during development and contributing to the maintenance of thermogenic and metabolic homeostasis in adults. Autoimmune disorders affecting thyroid hormones can lead to thyrotoxicosis or result in glandular destruction and hormone deficiency, known as hypothyroidism. Additionally, benign nodules and various forms of thyroid cancer are relatively common and can be detected through physical examination.

Historically, iodine's presence in seaweed was discovered by Bernard Courtois in 1811, and in

 

1820, Jean-Francois Coindet established a link between iodine intake and goiter size. Gaspard Adolphe Chatin proposed in 1852 that endemic goiter could result from insufficient iodine intake, a concept later confirmed by Eugen Baumann's demonstration of iodine in thyroid tissue in 1896 [1].

The recognition of myxedema cases dates back to the mid-19th century (1870s), but its association with the thyroid was not established until the 1880s when myxedema was observed following thyroid gland removal (thyroidectomy). Confirmation came later in the late 19th century when individuals, including animals, exhibited symptom improvement after the transplantation of animal thyroid tissue. The severity of myxedema sparked interest in finding effective treatments for hypothyroidism, with early attempts at thyroid tissue transplantation showing some efficacy but often requiring repeated procedures.

In 1891, English physician George Redmayne Murray introduced subcutaneously injected sheep thyroid extract, followed by an oral formulation. Purified thyroxine emerged in 1914, and synthetic thyroxine became available in the 1930s, though desiccated animal thyroid extract remained widely used. Liothyronine was identified in 1952. Adjusting therapy for hypothyroidism proved challenging initially, but around 1915, the discovery that hypothyroidism caused a lower basal metabolic rate became a marker for therapy adjustments. In the 1950s, the serum protein-bound iodine test became the first helpful laboratory test for assessing thyroid status [2].

A significant breakthrough occurred in 1971 with the development of the thyroid-stimulating hormone (TSH) radioimmunoassay, providing a highly specific marker for assessing thyroid status. Subsequently, in 1972, a T3 radioimmunoassay was developed, followed by a T4 radioimmunoassay in 1974. These advancements revolutionized the precision of thyroid status assessment, guiding more accurate and targeted interventions for thyroid disorders.

## AIMS &OBJECTIVES:

To study the endocrinal physiology of Thyroid Gland wsr to Thyroid Hormones in detail.

## CONCEPTUAL STUDY

### Anatomy and Development

The thyroid, deriving its name from the Greek words "thyreos" (shield) and "eidos" (form), is composed of two lobes connected by an isthmus. Positioned anterior to the trachea, between the cricoid cartilage and the suprasternal notch, the thyroid is typically 12-20 grams in size, characterized by high vascularity, and exhibits a soft consistency. Situated posterior to each pole of the thyroid are four parathyroid glands, responsible for producing parathyroid hormone. During thyroid surgery, identification and careful handling of the recurrent laryngeal nerves along the lateral borders of the thyroid are essential to prevent injury and vocal cord paralysis [3].

The development of the thyroid gland originates from the floor of the primitive pharynx during the third week of gestation. It migrates along the thyroglossal duct to reach its final position in the neck, which accounts for rare occurrences such as ectopic thyroid tissue at the base of the tongue (lingual thyroid). This migration process typically commences around the 11th week of gestation [4].

Thyroid medullary C cells, producing the calcium-lowering hormone calcitonin, are derived from neural crest derivatives originating from the ultimobranchial body. These C cells are distributed throughout the thyroid gland, with higher density observed in the junction of the upper one-third and lower two-thirds of the gland. Although calcitonin's role in calcium homeostasis in humans is minimal, the significance of C cells lies in their involvement in medullary thyroid cancer [5].

The development of the thyroid gland is intricately regulated by the synchronized expression of various developmental transcription factors. These factors include thyroid transcription factor (TTF)-1,

 

TTF-2, and paired homeobox-8 (PAX-8), which are selectively expressed in the thyroid gland. While not exclusive to the thyroid, their combined action plays a crucial role in governing thyroid cell development and activating thyroid-specific genes like thyroglobulin (Tg), thyroid peroxidase (TPO), sodium iodide symporter (Na+/I-symporter or NIS), and the thyroid-stimulating hormone receptor (TSH-R). Mutations in these developmental transcription factors or their downstream target genes are rare causes of thyroid agenesis or dyshormonogenesis, though the origins of most forms of congenital hypothyroidism remain unknown [6].

Given that congenital hypothyroidism affects approximately 1 in 4000 newborns, neonatal screening is now a standard practice in most industrialized countries. Transplacental transfer of maternal thyroid hormone occurs before the fetal thyroid gland becomes functional, offering partial hormone support to a fetus with congenital hypothyroidism. Early replacement of thyroid hormone in newborns diagnosed with congenital hypothyroidism is crucial in preventing potentially severe developmental abnormalities [7].

The thyroid gland comprises numerous spherical follicles, each consisting of thyroid follicular cells surrounding secreted colloid—a proteinaceous fluid rich in thyroglobulin, the precursor to thyroid hormone. The thyroid follicular cells exhibit polarization, with the basolateral surface facing the bloodstream and the apical surface directed towards the follicular lumen. The heightened demand for thyroid hormone is regulated by thyroid-stimulating hormone (TSH), binding to its receptor on the basolateral surface of the follicular cells. This binding prompts the reabsorption of thyroglobulin from the follicular lumen and its subsequent proteolysis within the cytoplasm, resulting in the release of thyroid hormones into the bloodstream [8]

## **REGULSTION OF THE THYROID** AXIS

Thyroid-stimulating hormone (TSH), secreted by the thyrotrope cells in the anterior pituitary, plays a central role in regulating the thyroid axis and serves as a crucial physiological marker for thyroid hormone action. TSH is a 31-kDa hormone consisting of α and β subunits; the α subunit is shared with other glycoprotein hormones (luteinizing hormone, follicle-stimulating hormone, human chorionic gonadotropin [hCG]), while the β subunit is unique to TSH. The extent and nature of carbohydrate modification are influenced by thyrotropin-releasing hormone (TRH) stimulation, impacting the biological activity of the hormone.The thyroid axis exemplifies a classic endocrine feedback loop. Hypothalamic TRH stimulates the pituitary production of TSH, which, in turn, prompts thyroid hormone synthesis and secretion. Thyroid hormones exert negative feedback predominantly through thyroid hormone receptor β2 (TRβ2) to inhibit TRH and TSH production, establishing the "set-point" in this axis. TRH serves as the major positive regulator of TSH synthesis and secretion, with peak TSH secretion occurring approximately 15 minutes after the administration of exogenous TRH. While dopamine, glucocorticoids, and somatostatin can suppress TSH, they are not of major physiological significance unless administered in pharmacologic doses. Reduced levels of thyroid hormone elevate basal TSH production and enhance TRH-mediated stimulation of TSH. High levels of thyroid hormone predominantly regulate TSH in a pulsatile manner, displaying a diurnal rhythm with the highest levels occurring at night. However, these TSH fluctuations are relatively modest compared to its long plasma half-life of 50 minutes. As a result, single measurements of TSH are sufficient for assessing its circulating levels. Immunoradiometric assays, highly sensitive and specific, are used to measure TSH. These assays effectively differentiate between normal and suppressed TSH values, enabling the diagnosis of both hyperthyroidism (low TSH) and hypothyroidism (high TSH) [9]

## **THYROID HORMONE SYNTHESIS, METABOLISM, AND ACCTION**

Thyroid hormones originate from thyroglobulin (Tg), a sizable iodinated glycoprotein. Once secreted into the thyroid follicle, Tg undergoes iodination on tyrosine residues, which are then coupled through an ether linkage. The reabsorption of Tg into the thyroid follicular cell facilitates proteolysis, leading to the liberation of newly synthesized T4 and T3 [10].

 

**Iodine Metabolism and Transport**

The initial crucial step in thyroid hormone synthesis involves the uptake of iodine. Ingested iodine binds to serum proteins, primarily albumin, with unbound iodine being excreted in urine. The thyroid gland exhibits highly efficient iodine extraction from the circulation, exemplified by the uptake of 10-25% of a radioactive tracer (e.g., 123I) by the normal thyroid gland over 24 hours, a value that can escalate to 70-90% in Graves' disease. The basolateral membrane of thyroid follicular cells expresses the sodium-iodide symporter (NIS), which mediates iodine uptake. While NIS is most prominently expressed in the thyroid gland, lower levels are found in the salivary glands, lactating breast, and placenta. This regulated iodine transport mechanism allows adaptation to variations in dietary iodine supply, with low iodine levels increasing NIS expression and uptake, and high iodine levels suppressing both.

Selective NIS expression in the thyroid enables isotopic scanning, hyperthyroidism treatment, and thyroid cancer ablation using iodine radioisotopes without significant effects on other organs. Mutation of the NIS gene is a rare cause of congenital hypothyroidism, highlighting its pivotal role in thyroid hormone synthesis. Another iodine transporter, pendrin, located on the apical surface of thyroid cells, mediates iodine efflux into the lumen. Mutation of the pendrin gene leads to pendred syndrome, marked by defective iodine organification, goiter, and sensorineural deafness. Iodine deficiency is prevalent in various regions, including mountainous areas, central Africa, central South America, and northern Asia. Europe remains mildly iodine-deficient, and surveys suggest declining iodine intake in the United States and Australia. In regions with relative iodine deficiency, there's an increased prevalence

**Organification, Coupling, Storage, and Release**

Upon entering the thyroid, iodine undergoes a series of crucial processes. It is first trapped and transported to the apical membrane of thyroid follicular cells, where an organification reaction takes place. This reaction involves the enzymatic activity of thyroid peroxidase (TPO) and hydrogen peroxide generated by dual oxidase (DUOX) and DUOX maturation factor (DUOXA). The reactive iodine atom is then added to specific tyrosyl residues within thyroglobulin (Tg), a large dimeric protein weighing 660 kDa and comprising 2729 amino acids. The iodotyrosines within Tg are coupled via an ether linkage, and this reaction is dependent on the number of iodine atoms present in the iodotyrosines. Following coupling, Tg is reabsorbed into the thyroid cell, where it undergoes processing in lysosomes to release the thyroid hormones T4 and T3. Uncoupled mono- and diiodotyrosines (MIT, DIT) are deiodinated by the enzyme dehalogenase, contributing to the recycling of any iodide that has not been converted into thyroid hormones.

Disorders affecting thyroid hormone synthesis are a rare cause of congenital hypothyroidism. The majority of these disorders result from recessive mutations in TPO or Tg. However, defects have also been identified in other components such as the TSH receptor (TSH-R), sodium-iodide symporter (NIS), pendrin, hydrogen peroxide generation, and dehalogenase. Due to these biosynthetic defects, the thyroid gland is unable to produce adequate hormone levels, leading to elevated TSH levels and the development of a large goiter.

**TSH Action**

Thyroid-stimulating hormone (TSH) governs the function of the thyroid gland through the TSH receptor (TSH-R), a seven-transmembrane G protein-coupled receptor (GPCR). The TSH-R is linked to the α subunit of the stimulatory G protein (Gsα), initiating the activation of adenylyl cyclase and subsequent elevation in cyclic adenosine monophosphate (cAMP) production. Additionally, TSH induces phosphatidylinositol turnover by activating phospholipase C. The significance of the TSH-R is illustrated by the outcomes of mutations that may occur. Recessive loss-of-function mutations result in thyroid hypoplasia and congenital hypothyroidism. Conversely, dominant gain-of-function mutations lead to sporadic or familial hyperthyroidism, characterized by goiter, thyroid cell hyperplasia, and autonomous function. The majority of these activating mutations occur within the transmembrane

 

domain of the receptor, mimicking the conformational changes induced by TSH binding or the interaction of thyroid-stimulating immunoglobulins (TSI) seen in Graves' disease. Activation mutations of the TSH-R can also manifest as somatic events, triggering clonal selection and the expansion of affected thyroid follicular cells, ultimately resulting in autonomously functioning thyroid nodules.

### Other Factor that Influence Hormone Synthesis and Release

While thyroid-stimulating hormone (TSH) plays a predominant role in regulating the growth and function of the thyroid gland, various growth factors, primarily produced within the thyroid gland itself, also impact thyroid hormone synthesis. These factors encompass insulin-like growth factor β (TGF-β), endothelins, and various cytokines. Although the precise quantitative contributions of these factors are not fully elucidated, they hold significance in specific pathological conditions. For instance, acromegaly, characterized by elevated levels of growth hormone and IGF-I, is associated with goiter and a predisposition to multinodular goiter (MNG).

In autoimmune thyroid disease, certain cytokines and interleukins (ILs) contribute to thyroid growth, while others induce apoptosis. Iodine deficiency is linked to increased thyroid blood flow and the upregulation of the sodium-iodide symporter (NIS), enhancing more efficient iodine uptake. Conversely, excess iodide can transiently inhibit thyroid iodide organification, a phenomenon referred to as the Wolff-Chaikoff effect. In individuals with a normal thyroid, the gland typically escapes from this inhibitory effect, allowing iodide organification to resume. However, in patients with underlying autoimmune thyroid disease, the suppressive action of high iodide levels may persist

## THYROID HORMONE TRANSPORT AND METABOLISM

### Serum Binding Protein

T4 is released by the thyroid gland in approximately twenty times greater quantity than T3. Both hormones bind to plasma proteins, including thyroxine-binding globulin (TBG), transthyretin (TTR, previously known as thyroxine-binding prealbumin or TBPA), and albumin. The characteristics of these proteins are outlined in Table 1. Plasma-binding proteins serve to augment the pool of circulating hormones and prolong the delivery of hormones to specific tissue sites. While the concentration of TBG is relatively modest (1-2 mg/dL), its high affinity for thyroid hormones (T4 > T3) enables it to transport approximately 80% of the bound hormone. Albumin, with relatively lower affinity for thyroid hormones, boasts a higher plasma concentration (~3.5 g/dL), binding up to 10% of T4 and 30% of T3. On the other hand, TTR carries around 10% of T4 but a minimal amount of T3.

**Table 1.** Characteristics of circulation $T_4$ and $T_3$.

| Hormone Property | $T_4$ | $T_3$ |
|---|---|---|
| Serum concestrations<br>Total hormone<br>Fraction of total hormone in the unbound from<br>Unbound (free) hormone | <br>8 µg/dL<br>0.02%<br>$21+10^{-12}$ M | <br>0.14 µg/dL 0.3%<br>$6+10^{-12}$ M |
| Serum half-life | 7 d | 2 d |
| Fraction directly from the thyroid | 100% | 20% |
| Production rate, including peripheral conversion | 90 µg/dL | 32 µg/dL |
| Intracellular hormone fraction | ~20% | ~70% |
| Relative metabolic potency | 0.3 | 1 |
| Receptor binding | 10-10 M | 10-11 M |

When considering the impact of various binding proteins, approximately 99.98% of T4 and 99.7% of T3 are found to be protein-bound. T3 exhibits weaker binding compared to T4, resulting in a higher proportion of unbound T3 than unbound T4. However, the concentration of unbound T3 in circulation is lower due to its lower production levels and faster clearance when compared to T4. The unbound, or

 

"free," concentrations of these hormones are approximately ~2 x 10^11 M for T4 and ~6 x 10^12 M for T3, roughly aligning with the binding constants of these hormones to thyroid hormone receptors. It is generally believed that the unbound hormone is biologically available to tissues. Nevertheless, the homeostatic mechanisms that regulate the thyroid axis primarily focus on maintaining normal concentrations of unbound hormones as seen in Table 1.

### Abnormalities of Thyroid Hormone Binding Proteins

Various genetic and acquired anomalies can influence thyroid hormone binding proteins. X-linked thyroxine-binding globulin (TGB) deficiency results in markedly low total T4 and T3 levels. Despite this, individuals with this deficiency exhibit euthyroidism, with normal unbound hormone levels and TSH levels. It is crucial to recognize this condition to avoid attempts to normalize total T4 levels, as such efforts can lead to thyrotoxicosis due to rapid hormone clearance in the absence of TGB. Estrogen increases TGB levels by enhancing sialylation and delaying TGB clearance. Consequently, pregnant women or those using estrogen-containing contraceptives may experience elevated TGB levels, leading to increased total T4 and T3 levels while maintaining normal unbound hormone levels. This phenomenon partly explains why women with hypothyroidism may require higher doses of L-thyroxine replacement during pregnancy or estrogen treatment.

Mutations in thyroxine-binding globulin (TGB), transthyretin (TTR), and albumin can increase the binding affinity for T4 and/or T3, resulting in conditions known as euthyroid hyperthyroxinemia or familial dysalbuminemic hyperthyroxinemia (FDH). These disorders lead to increased total T4 and/or T3 levels while maintaining normal unbound hormone levels. The familial nature of these disorders and the normal TSH levels, rather than suppression, should prompt consideration of this diagnosis. FDH can be confirmed through tests measuring the affinities of radiolabeled hormone binding to specific transport proteins or by DNA sequence analyses of the abnormal transport protein genes.

Certain medications, such as salicylates and salsalate, can displace thyroid hormones from circulating binding proteins, temporarily affecting the thyroid axis by increasing free thyroid hormone levels. TSH is suppressed until a new steady state is achieved, restoring euthyroidism. Factors associated with acute illness can also displace thyroid hormones from binding proteins. The conversion of T4 to the more potent T3 is facilitated by deiodinase enzymes. Different types of deiodinases, such as type I and type II, play roles in various tissues, and their activities are influenced by factors like fasting, illness, trauma, medications, and contrast agents. Type III deiodinase inactivates T4, including in the sick euthyroid syndrome, a condition where its activation in muscle and liver occurs during periods of hypoperfusion, such as in severe illness. Additionally, rare cases of hypothyroidism in infants may be attributed to massive hemangiomas expressing type III deiodinase

## THYROID HORMONE ACTION

### Thyroid Hormone Transport

Thyroid hormones in the bloodstream can penetrate cells through passive diffusion or via specialized transporters like monocarboxylate transporter 8 (MCT8), MCT10, and organic anion-transporting polypeptide 1C1. Mutations in the MCT8 gene have been found in individuals with X-linked psychomotor retardation and thyroid function irregularities, characterized by low T4, high T3, and elevated TSH levels. Once inside cells, thyroid hormones primarily exert their effects by stimulating enzymatic responses within mitochondria. Additionally, these hormones may directly impact blood vessels and the heart through integrin receptors

### Nuclear Thyroid Hormone Receptors

Thyroid hormones exhibit a strong binding affinity to nuclear thyroid hormone receptors (TRs), which are present in most tissues with varying expression levels across organs. TRα is notably abundant in the brain, kidneys, gonads, muscle, and heart, while TRβ expression is relatively higher in the pituitary and liver. These receptors undergo variable splicing to generate distinct isoforms. Specifically,

 

the TRβ isoform, characterized by a unique amino terminus, is expressed selectively in the hypothalamus and pituitary, contributing to the feedback control of the thyroid axis. On the other hand, the TRα2 isoform carries a distinctive carboxy terminus that prevents binding with thyroid hormones; it is believed to function in inhibiting the activities of other TR isoforms.
The thyroid receptors (TRs) consist of a central DNA-binding domain and a C-terminal ligand-binding domain. These receptors specifically bind to DNA sequences known as thyroid response elements (TREs) located in the promoter regions of target genes. TRs can form homodimers or, more commonly, heterodimers with retinoic acid X receptors (RXRs). Upon activation, the receptor can either stimulate or inhibit gene transcription, depending on the regulatory elements within the target gene.

Thyroid hormones, T3 and T4, exhibit similar affinities for both TRα and TRβ. Nevertheless, structural distinctions in the ligand-binding domains offer the potential for developing selective agonists or antagonists, currently under investigation. T3 displays a 10-15 times greater binding affinity than T4, contributing to its heightened hormonal potency. Despite T4 being produced in excess, T3 predominantly occupies receptors due to peripheral tissue conversion of T4 to T3, increased T3 bioavailability in plasma, and the receptors' greater affinity for T3.

Upon binding to TRs, thyroid hormones induce conformational changes that alter interactions with auxiliary transcription factors. In the absence of thyroid hormone binding, aporeceptors bind co-repressor proteins, inhibiting gene transcription. Hormone binding releases co-repressors, allowing co-activators to enhance transcription. The discovery of TR interactions with corepressors explains how TR silences gene expression in the absence of hormone binding. Consequently, hormone deficiency profoundly impacts gene expression by causing both gene repression and the loss of hormone-induced stimulation. Targeted deletion of TR genes in mice has confirmed this concept, demonstrating a less pronounced effect than hormone deficiency alone

**Thyroid Hormone Resistance**

Resistance to thyroid hormone (RTH) is an autosomal dominant disorder characterized by elevated levels of thyroid hormones and inappropriately normal or elevated thyroid-stimulating hormone (TSH). Individuals with RTH generally do not exhibit typical hypothyroidism signs and symptoms due to partial hormone resistance, which is compensated by increased thyroid hormone levels. Clinical manifestations of RTH may include goiter, attention deficit disorder, a slight reduction in IQ, delayed skeletal maturation, tachycardia, and impaired metabolic responses to thyroid hormone.

Classic forms of RTH result from mutations in the TRβ gene. These mutations, located in specific regions of the ligand-binding domain, lead to the loss of receptor function. However, because the mutant receptors can still dimerize with retinoic acid X receptors (RXRs), bind to DNA, and recruit co-repressor proteins, they function as antagonists to the remaining normal TRβ and TRα receptors. This property, known as "dominant negative" activity, explains the autosomal dominant inheritance pattern.

Diagnosis is typically suspected in cases where unbound thyroid hormone levels are increased without TSH suppression. Similar hormone abnormalities may also be found in other affected family members, although about 20% of TRβ mutations arise de novo. DNA sequence analysis of the TRβ gene confirms the definitive diagnosis. RTH must be distinguished from other causes of euthyroid hyperthyroxinemia (e.g., familial dysalbuminemic hyperthyroxinemia) and inappropriate TSH secretion by TSH-secreting pituitary adenomas. In most cases, no treatment is indicated; the key is making the diagnosis to avoid inappropriate treatment for mistaken hyperthyroidism and to provide genetic counseling.

A distinct form of RTH is caused by mutations in the TRα gene. Affected patients exhibit clinical features resembling congenital hypothyroidism, including growth retardation, skeletal dysplasia, and severe constipation. In contrast to RTH caused by TRβ mutations, thyroid function tests show normal

 

TSH, low or normal T4, and normal or elevated T3 levels. These distinct clinical and laboratory features underscore the different tissue distribution and functional roles of TRβ and TRα. Optimal treatment for patients with RTH due to TRα mutations has not been established

## RESULT AND DISCUSSION

In India, thyroid disorders are prevalent and typically fall within the group of iodine-deficient disorders (IDDs). They are assessed based on total goiter rates and urinary iodine concentrations, commonly observed in school-aged children. Following the implementation of universal salt iodization programs in 1983, there has been a reduction in goiter prevalence in various regions of the country that were previously endemic. A 2004 WHO assessment categorized India as having 'optimal' iodine nutrition, with a significant proportion of households (83.2% urban and 66.1% rural) now consuming sufficient iodized salt. India is believed to be undergoing a transition from iodine deficiency to a state of sufficiency. A recent review of studies conducted in the post-iodization phase provides insights into the changing thyroid status of the Indian population. However, these studies are often confined to specific geographical areas or cities and are conducted in children with relatively small sample sizes. There have been no nationwide studies on the prevalence of hypothyroidism in India, either before or after iodization. A comprehensive, large-scale, cross-sectional study is needed to present an accurate representation of the evolving profile of thyroid disorders across the entire country, especially considering the post-iodization era.

## CONCLUSION

Hypothyroidism, a condition where every cell in the body has receptors for thyroid hormones, manifests across various organ systems, resulting in a broad range of symptoms. This necessitates individuals affected by hypothyroidism to depend on hormonal supplements throughout their lives. Despite the prevalent use of hormone replacement therapy (HRT), such as levothyroxine sodium, studies indicate that these treatments primarily elevate thyroid hormone levels in the bloodstream without addressing the root causes of the disease, namely inflammation and autoimmunity. The dependency on hormonal supplementation becomes a lifelong commitment for affected individuals. While HRT has seen significant advancements, the modern management of hypothyroidism still faces challenges, and patient satisfaction remains suboptimal. There is a growing realization that merely increasing thyroid hormone levels is not sufficient for comprehensive disease management. The need to delve into the underlying physiological mechanisms of thyroid hormone regulation becomes increasingly apparent to develop more effective therapeutic approaches. Understanding the intricate physiology of thyroid hormones is crucial for refining treatment strategies. Addressing the complexities of inflammation and autoimmunity may pave the way for innovative interventions that not only elevate hormone levels but also target the root causes of hypothyroidism. Advancements in treatment modalities that encompass a holistic approach to thyroid disorders are essential for enhancing patient outcomes and quality of life.

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