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Evaluation of Biochemical Parameters in Pregnant Women with thyroidism troubles

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Before the jury composed of:

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Dedication

بسم الله الرحمان الرحيم

To my beloved grandfather, may you rest in peace,

This day was one of your greatest dreams, and mine too. You always wished to see me graduate, to witness the result of my hard work and stand beside me with pride. It breaks my heart that you are not here to share this moment with me.

I wished with all my heart that you could see me today, hear my name, and celebrate this achievement with me. Though you left us last summer, your love, prayers, and belief in me never left my side.

I dedicate this thesis, this graduation, and this success to you.
You may be gone from my sight, but you will forever remain in my heart and in every achievement I reach.

I miss you deeply, and this moment will always belong to you too.

To my dear parents

My father, who guided me
To my mother, who always cared about my success

To my sisters, Nour and Malak
To my little brothers, Adem and Asser

you are my heart and my safe place; I wish you a life full of success, love, and dreams that come true.

To my entire family,

To those I love dearly: My English teachers miss Chenine Amira Chahrazed and Benaicha Faiza

To my dear friends, thank you for every shared moment and support; I wish you all a future filled with success and happiness.

And to all those who contributed, directly or indirectly, to making this work possible, I thank you.

Rania

الملخص

خلال فترة الحمل، تُعدّ التكيفات الفسيولوجية للغدة الدرقية ضرورية لتلبية الاحتياجاتا لأيضية المتزايدة لكل من الأم والجنين النامي.

مع ذلك، قد تُسبب أمراض الغدة الدرقية، وخاصة قصورالغدة الدرقية، مشاكل خطيرة للأم والجنين. تهدف هذه الدراسة إلى فحص وظائف الغدة الدرقية خلال فترة الحمل، مع التركيزبشكل خاص على قصورالغدة الدرقية والمؤشرات المناعية والكيميائية الحيوية المرتبطة به. تُسلّط هذه الورقة الضوءعلى وظائف هرمونات الغدة الدرقية (T4،T3) والعمليات التنظيمية التي تشمل هرمون تحفيزالغدة الدرقية (TSH) وهرمون موجهة الغدد التناسلية المشيمية البشرية (hCG). كما تُولى مؤشرات المناعة الذاتية، مثلا لأجسام المضادة لبيروكسيد الغدة الدرقية (anti-TPO) والأجسام المضادة للثيروجلوبولين،اهتمامًا خاصًا نظرًا لارتباطها غالبًا بنتائج حمل غيرمواتية.
بالإضافة إلى ذلك، تم تقييم الخصائص الكيميائية الحيوية مثل مستويات الهرمونات، وملامح الدهون، ومستوى السكرفي الدم.

تُبرزالنتائج كيف يؤثرخلل وظائف الغدة الدرقية على صحة الأم، والنموالعصبي للجنين، ونتائج الحمل. ولتجنب أي صعوبات، يُعد التشخيص المبكر والعلاج المناسب – وخاصة العلاج بالليفوثيروكسين – أمرًا بالغ الأهمية. تُبرزهذه الدراسة أهمية الفحص والمتابعة الدورية لوظائف الغدة الدرقية طوال فترة الحمل.

الكلماتالمفتاحية: قصورالغدةالدرقيةوفرطنشاطها،الغدةالدرقية،الحمل،هرموناتالغدةالدرقية،المؤشراتالحيوية.

Abstract

During pregnancy, physiological adaptations of the thyroid gland are essential to meet the increased metabolic demands of both the mother and the developing fetus.

However, serious problems for both the mother and the fetus can result from thyroid disease, especially hypothyroidism. This study's objective is to examine thyroid function during pregnancy, with a particular emphasis on hypothyroidism and the immunological and biochemical markers that are linked to it. The function of thyroid hormones (T3, T4) and regulatory processes involving TSH and hCG are highlighted in this paper. Autoimmune indicators, such as anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin antibodies, are given particular consideration since they are often linked to unfavorable pregnancy outcomes. Additionally assessed were biochemical characteristics such hormone levels, lipid profiles, and glycemia.

The results highlight how thyroid dysfunction affects maternal health, fetal neurodevelopment, and pregnancy outcomes. To avoid difficulties, early diagnosis and proper treatment—especially levothyroxine therapy—are essential. The significance of routine thyroid function screening and monitoring throughout pregnancy is highlighted by this study.

Keywords: Hypothyroidism and Hyperthyroidism, Thyroid, Pregnancy, Thyroid Hormones and Biochemical Markers.

Résumé

Pendant la grossesse, les adaptations physiologiques de la glande thyroïde sont essentielles pour répondre aux besoins métaboliques accrus de la mère et du fœtus en développement.

Cependant, les maladies thyroïdiennes, en particulier l'hypothyroïdie, peuvent entraîner de graves problèmes pour la mère et le fœtus. Cette étude vise à examiner la fonction thyroïdienne pendant la grossesse, en s'intéressant plus particulièrement à l'hypothyroïdie et aux marqueurs immunologiques et biochimiques qui y sont associés.
Le rôle des hormones thyroïdiennes (T3, T4) et les processus de régulation impliquant la TSH et l'hCG sont mis en évidence.
Les marqueurs auto-immuns, tels que les anticorps antithyroperoxydase (antiTPO) et anti-thyroglobuline, font l'objet d'une attention particulière car ils sont souvent liés à des issues de grossesse défavorables.
Les paramètres biochimiques, tels que les taux d'hormones, le profil lipidique et la glycémie, ont également été évalués.

Les résultats soulignent l'impact des dysfonctionnements thyroïdiens sur la santé maternelle, le développement neurologique du fœtus et l'issue de la grossesse. Afin d'éviter les complications, un diagnostic précoce et un traitement approprié, notamment par lévothyroxine, sont essentiels. Cette étude souligne l'importance du dépistage et du suivi réguliers de la fonction thyroïdienne tout au long de la grossesse.

Mots-clés: Hypothyroïdie et Hyperthyroïdie, Thyroïde, Grossesse, Hormones thyroïdiennes et Marqueurs biochimiques.

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List of abbreviations

ALT – Alanine Aminotransferase
AST – Aspartate Aminotransferase
ATP – Adenosine Triphosphate
T3: Triiodothyronine
T4: Thyroxine
FT3: Free Triiodothyronine
FT4: Free Thyroxine
hCG: human chorionic gonadotropin
TSH: Thyroid-stimulating hormone
TSH-R: Thyroid-releasing hormone receptor
TRAb: TSH-receptor antibodies
rT3: Reverse Triiodothyronine
TBG: Thyroxine binding globulin
TG/Tgb: Thyroglobulin
TPO: Thyroid peroxidase
TTR: Transthyretin
TRH: Thyrotropin-releasing hormone
T-reg: T regulatory
PVN: hypothalamic periventricular nucleus
cAMP: Adenylyl cyclase and intracellular
PKA: Protein kinase A
TRα: Thyroid hormone receptor alpha
TRβ: Thyroid hormone receptor beta
Gs-protein: Stimulatory G Protein
D1: Type 1 deiodinase
D2: Type 2 deiodinase
LDL: Low-density lipoprotein
IUGR: Intrauterine growth restriction
C5: fifth cervical vertebra
T1: first thoracic vertebra
DIT: Di-iodotyrosine
MIT: Mono-iodotyrosine
KI: Potassium iodide
MCT8: Monocarboxylate transporter 8
MCT10: Monocarboxylate transporter 10
TRE: Thyroid responsive element
BMR: Basal metabolic rate
RNA: Ribonucleic acid
IFN-γ:Interferon gamma
IL-1:Interfleukin-1
TNF-α: Tumor necrosis factor alpha
DIO3: Gene encoding type 3 iodothyronine deiodinase
DIO2: Gene encoding type 2 deiodinase
TSI: Thyroid-stimulating immunoglobulin
TBIl: Thyroid-binding inhibitory immunoglobulin

LMICs: Low-and middle-income countries
IVF: in vitro fertilization
IGF-1: Insulin-like growth factor-1
GH: growth hormone
RIA: Radioimmunoassay
ELISA: Enzyme-linked immunosorbent assay
PTC: Papillary thyroid carcinoma
FTC: Thyroid cancer with follicles
PDTC: Poorly differentiated thyroid carcinoma
MTC: Medullary thyroid carcinoma
l-T_4: levothyroxine

General Introduction

The thyroid gland is an essential endocrine organ that secretes triiodothyronine (T3) and thyroxine (T4), which control growth, metabolism, and cellular differentiation.These hormones influence gene expression, oxygen consumption, and basal metabolic rate in the majority of tissues.Thyroid function is extremely susceptible to physiological and metabolic changes since their synthesis depends on iodine intake and enzymatic activities within the thyroid follicular cells ***(Greenspan & Gardner, 2018; Guyton & Hall, 2021)***.TSH (thyroid stimulating hormone) is a stimulating hormone that controls the thyroidgland's hormone synthesis. The pituitary gland, a little gland near the base of the brain, secretes TSH.

This regulation is based on the thermostat principle, which states that as blood T3/T4 levels fall, as they do in hypothyroidism, blood TSH levels rise to encourage the thyroid to create mor e T3/T4.On the other hand, hyperthyroidism, which is frequently linked to autoimmune processes, can be brought on by dysregulation or an excess of T3/T4 in the blood. Hyperthyroidism also suppresses thyroid activity by lowering blood TSH levels ***(Brent,2012; Weetman, 2011)***.

Pregnancy induces significant hormonal and metabolic adaptations that affect thyroid physiology. Elevated human chorionic gonadotropin levels stimulate the thyroid gland, leading to decreased serum TSH concentrations, particularly during early gestation. Increased estrogen levels also raise thyroxine-binding globulin concentrations, modifying circulating thyroid hormone levels and requiring the use of gestational age-specific reference ranges for accurate assessment ***(Glinoer, 1997; Alexander et al., 2017)***. Normal fetal development and successful pregnancy outcomes depend on adequate maternal thyroid hormone levels, particularly during the first trimester when fetal thyroid function is still developing. Hormonal and immunological asses sent during pregnancy are crucial because pregnancy related immune modulation may also reveal or worsen autoimmune thyroid diseases ***(De Groot et al., 2012; Korevaar et al., 2017).***

The present study aims to assess thyroid hormonal parameters (TSH, FT3, and FT4), evaluate biochemical parameters associated with thyroid dysfunction during pregnancy, compare the biological variations observed in hypothyroid and hyperthyroid pregnant women, and emphasize the importance of early diagnosis and biological monitoring to improve maternal and fetal outcomes.

There are two main parts to this work. The first part provides the theoretical background and is divided into two chapters: the first covers the thyroid gland's anatomy, physiology, biochemistry, and pathophysiology, while the second covers physiological adaptations, thyroid function during pregnancy, and the effects of thyroid disorders on the health of the mother and fetus. The methodology, research population, data collection techniques, biochemical and hormonal parameters examined, statistical analysis, findings, discussion, and overall conclusion are all covered in the second part, which is devoted to the experimental investigation.

Part 01:

Theoretical part

Chapter 01: Thyroid Gland

I. **Definition**

The thyroid gland is an endocrine organ located in the neck that generates hormones that control calcium balance, growth, development, and metabolism.It originates from the foramen cec um during development, has two lobes joined by an isthmus, and weighs 15–25g in adulthood **(Bernard, 2025).**

The thyroid gland secretes thyroid hormones, which control the rate of the body's chemical functions (basal metabolism). Thyroid hormones influence basal metabolism in two ways:

- By stimulating almost all of the body's tissues to produce protein
- By increasing the amount of oxygen used by cells

Numerous essential body processes, including heart rate, the rate at which calories are burnt, s kin integrity, growth, heat production, fertility, and digestion, are influenced by thyroid hormones ***(Boucai, 2026).***

II. **Thyroid Hormones: Function and Role in Metabolic Regulation**

Thyroid hormones, especially thyroxine (T4) and triiodothyronine (T3), are vital endocrine regulators of cellular differentiation, growth, energy homeostasis, and systemic metabolism. While the thyroid gland secretes more T4, T3 is the physiologically active form that primarily modulates gene transcription by binding to nuclear thyroid hormone receptors (TRα and TRβ). Deiodinase enzymes (D1 and D2) convert T4 to T3 in peripheral tissues, ensuring tissue-specific control of thyroid hormone activity and metabolic adaption ***(Hall& Hall, 2021; Mullur et al., 2014).***

By boosting ATP turnover, oxidative phosphorylation, and mitochondrial activity, thyroid hormones raise basal metabolic rate. They increase oxygen consumption and Na+/K+-ATPase activity, which leads to increased thermogenesis and energy expenditure, especially in skeletal muscle and liver tissues ***(Hall, 2021; Brent, 2012).***

Thyroid hormones promote intestinal glucose absorption, hepatic gluconeogenesis, glycogenolysis, and lipolysis in the metabolism of fats and carbohydrates. Additionally, they boost cholesterol clearance and LDL receptor expression, which explains the hypercholesterolemia frequently seen with hypothyroidism. Proper metabolic response to physiological demands is ensured by these coordinated processes ***(Chaker et al., 2017; Mullur et al., 2014).***

In general, thyroid hormones integrate endocrine and dietary cues to maintain metabolic home ostasis, acting as key regulators of intermediate metabolism.Significant metabolic problems are caused by dysregulation, particularly in disorders like hypothyroidism and hyperthyroidism***(Chaker et al., 2017; Brent, 2012).***

III. Physiology of the Thyroid Gland

1. Structure of the Thyroid Gland

Located in the front of the neck, the thyroid gland is an essential endocrine gland that resembles a butterfly. The septae that dip from the capsule separate it into lobules. Numerous common components known as thyroid follicles make up the thyroid lobules. The anatomical and functional components of a thyroid gland are called thyroid follicles. These are spherical, and the wall is composed of several follicular cells, which are cuboidal cells. These follicular cells release thyroid hormone and are derived from the endoderm.

T4 and a trace amount of T3 make up thyroxine, the hormone that is in circulation. Both have different levels of stimulation on the target cells, even though the majority of T4 eventually transforms into the more active version T3. These hormones aid in controlling the body's BMR. The tiny C cells, sometimes referred to as parafollicular cells, are located either inside the wall of the thyroid follicles or in between them. These come from neural crest cells and release calcitonin, a polypeptide hormone that helps control blood and skeletal tissue calcium and phosphate levels.

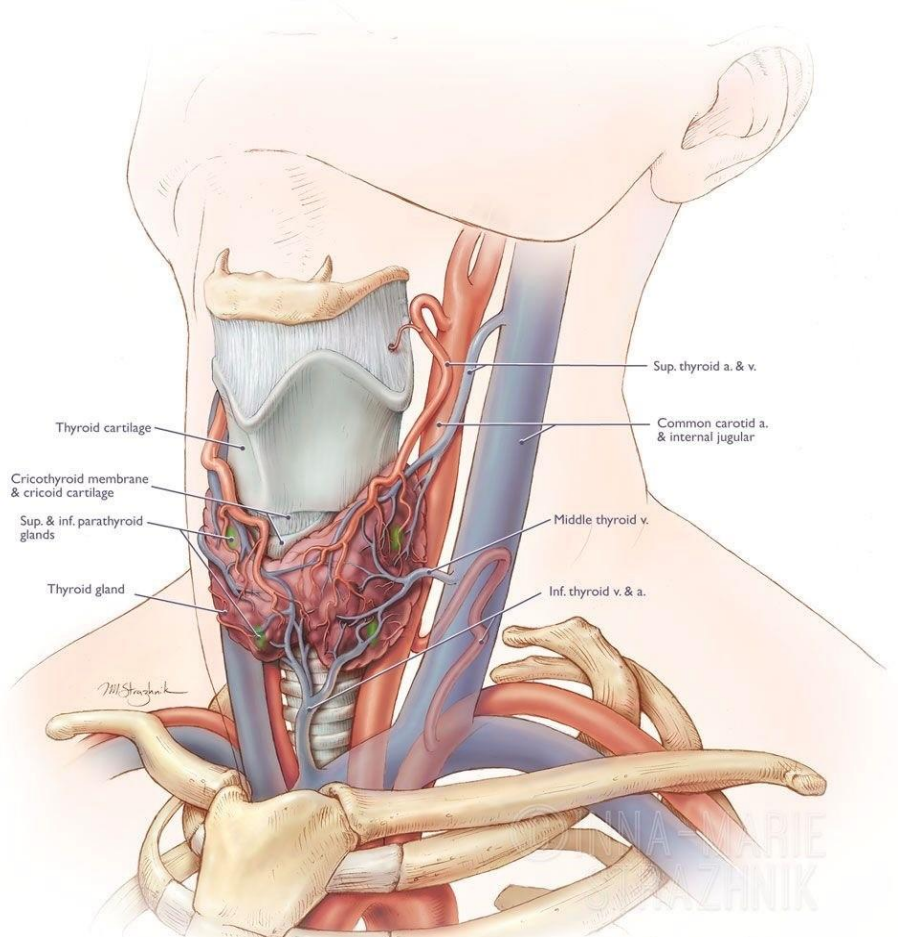


Figure 1. Position and structure of thyroid gland (Strazhnik, 2021)

2. Anatomy of the Thyroid Gland

The thyroid gland weighs approximately 25 g in adults and has an average volume of 6.6 ml. it is a highly vascular endocrine organ located in the anterior cervical region, inferior to the larynx and anterior to the upper tracheal rings ***(Standring, 2021; Mescher, 2021).*** It typically extends from the level of the fifth cervical vertebra (C5) to the first thoracic vertebra (T1) ***(Moore et al., 2018).***

The gland consists of two lateral lobes connected by a narrow isthmus that usually overlies the second to fourth tracheal rings ***(Standring, 2021; Moore et al., 2018).*** A pyramidal lobe may be present in some individuals, extending superiorly from the isthmus as a remnant of the thyroglossal duct ***(Standring, 2021).***

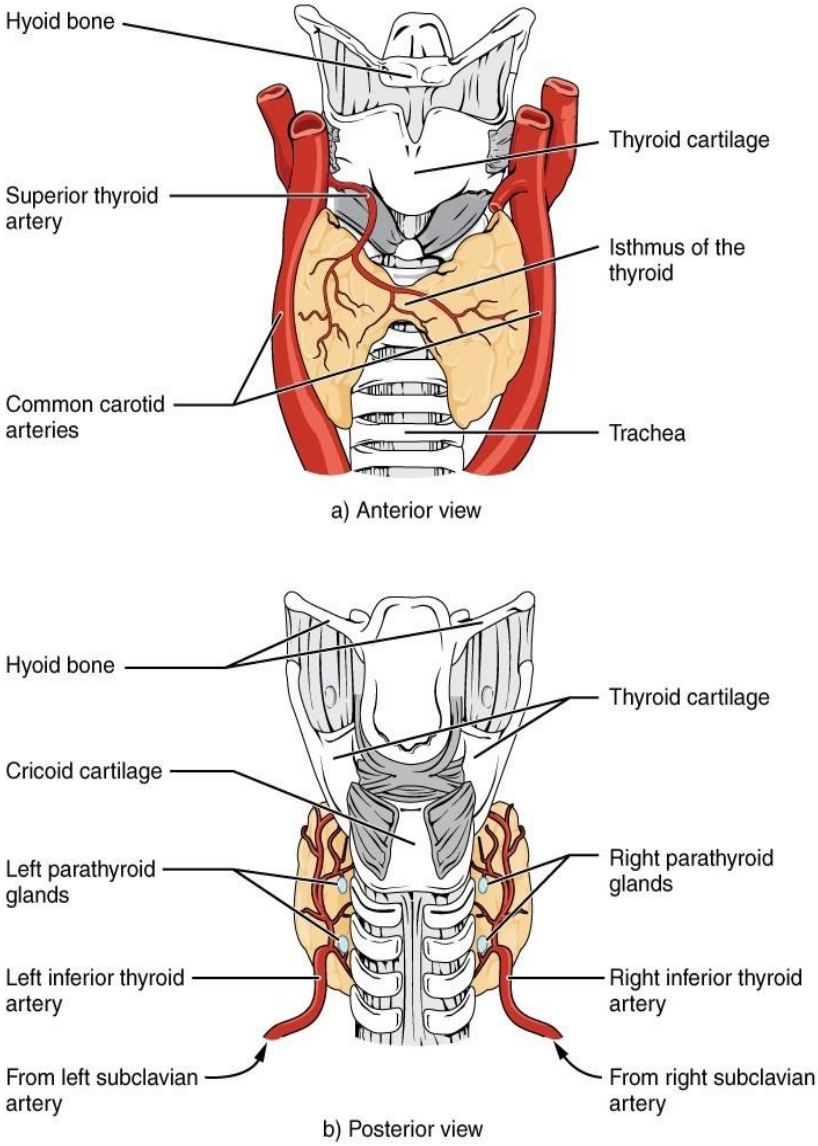


Figure 2. Anatomy of thyroid gland (University of Michigan Medical School © 2012).

Each lobe is roughly conical in shape, with each apex pointing superolaterally and their bases inferomedially (between the 4th and 5th tracheal rings). At their widest point, each lobe measures approximately 3 cm in the transverse plane and 2 cm in the anteroposterior plane (which corresponds to the thickness). The lobes are approximately 5 cm long. The isthmus lies above the 2nd or 3rd tracheal cartilages and measures 1.25 cm in both the transverse and vertical planes. In some individuals, a third lobe of the thyroid gland, called the pyramidal lobe, may be present. This is also a conical structure extending from the isthmus to the hyoid bone. In some cases, it may also originate from the inferomedial portion of either the left or right lobe. However, it is more commonly observed in the left lobe.

The main laryngeal cartilages provide a framework for the thyroid gland. Posteromedially, the gland is attached to the cricoid cartilage by the lateral thyroid ligaments. Additionally, the levatorthyroidis, a fibromuscular structure, also anchors the isthmus, or pyramidal lobe, to the hyoid bone ***(Khoudja, 2023).***

- Anteriorly, the thyroid gland is covered by the skin, superficial fascia, platysma muscle, and deep cervical fascia, and it lies deep to the infrahyoid (strap) muscles including the sternohyoid and sternothyroid muscles ***(Moore et al., 2018; Standring 2021).*** The gland is firmly attached to the larynx and trachea via the pretracheal fascia, explaining its upward movement during swallowing ***(Standring, 2021).***
- Posteriorly, each lobe is related medially to the trachea and esophagus, particularly on the left side where the esophageal impression is more evident ***(Moore et al., 2018).*** The recurrent laryngeal nerve ascends within the tracheoesophageal groove in close proximity to the posterior surface of the gland ***(Standring, 2021).*** The parathyroid glands are typically located on the posterior aspect of each thyroid lobe ***(Mescher, 2021; Standring, 2021).***

3. Histology of thyroid gland

Histologically, the thyroid gland is composed of numerous spherical follicles that represent its structural and functional units ***(Mescher, 2021).*** Each follicle is lined by simple cuboidal epithelium, known as follicular cells, which synthesize thyroglobulin and produce the thyroid hormones T3 and T4 ***(Mescher, 2021; Hall, 2021).***The follicular lumen contains colloid, a proteinaceous material rich in iodinated thyroglobulin ***(Hall, 2021).*** The height of follicular cells varies according to functional activity, becoming columnar during hyperactivity and flattened during hypoactivity ***(Mescher, 2021).*** Parafollicular (C) cells are located in the interfollicular spaces and secrete calcitonin, which plays a role in calcium homeostasis ***(Mescher, 2021).***

The gland is surrounded by a thin connective tissue capsule that sends septa inward, dividing the gland into lobules and providing a framework for blood vessels and nerves ***(Standring, 2021; Mescher, 2021).***

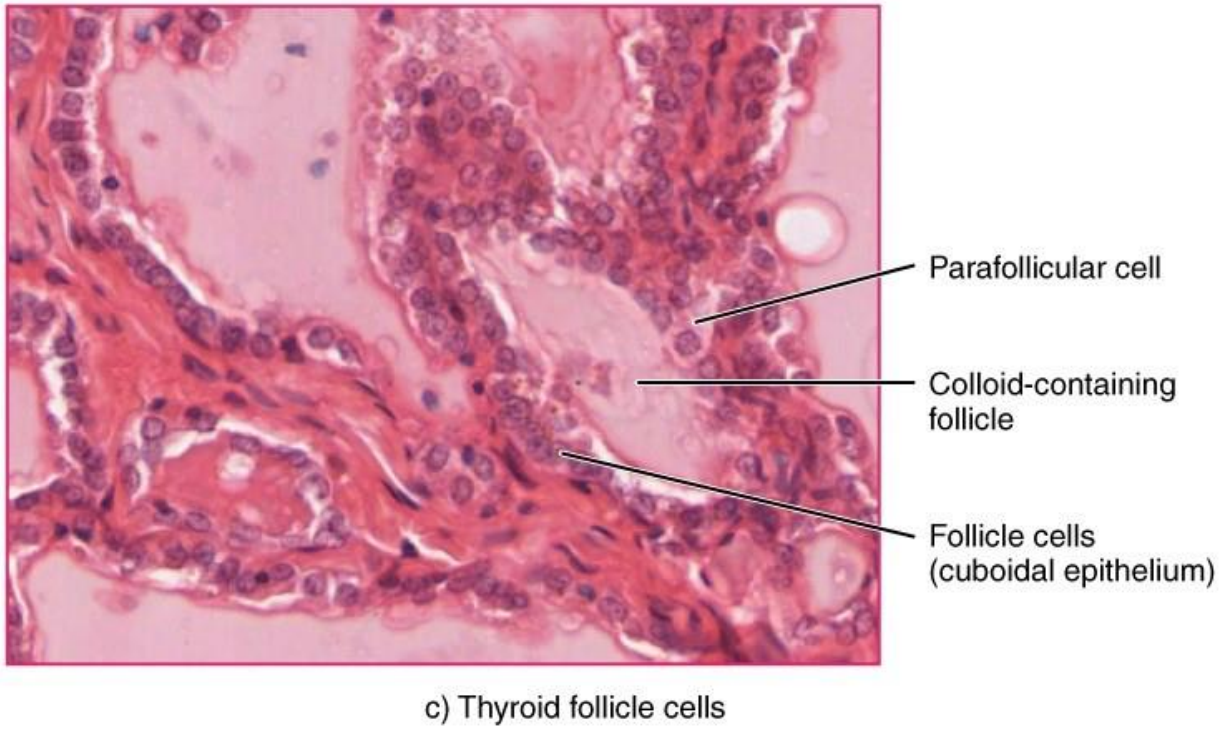


Figure 3. Histology of thyroid follicle cells University of Michigan Medical School © 2012).

IV. Biochemistry of thyroid hormones

1. Hormones Produced by the Thyroid Gland

Thyroid hormones (T3, T4) and calcitonin are produced and secreted by the thyroid gland, an endocrine organ that primarily controls development, metabolism, and calcium homeostasis. The thyroid gland's follicular cells, or thyrocytes, produce these hormones, which are then stored in the follicular colloid as thyroglobulin before being released into the bloodstream ***(Hall, 2021)***.

1.1. Thyroxine (T4 / Tetraiodothyronine)

Thyroxine (T4) is the primary hormone secreted by the thyroid gland, making up 80–90% of the total thyroid hormone production. It primarily acts as a prohormone that is transformed into the active hormone T3 in peripheral tissues such the liver, kidney, and skeletal muscle. It has comparatively little intrinsicbiological activity ***(Melmed, 2020;Goldfine, 2020).***

1.2. Triiodothyronine (T3)

Triiodothyronine (T3), the physiologically active form of thyroid hormone that binds to thyroi d hormone receptors in target cells and controls gene expression, is released by the thyroid gland in lesser amounts (about 10–20%).Rather than being directly secreted by the thyroid gland, the majority of the body's circulating T3 is actually created via peripheral deiodination of T4 ***(Braverman et al., 2021).***

1.3. Calcitonin

The thyroid gland's parafollicular (C) cells create calcitonin. Its primary role is to prevent bone resorption, which helps control blood calcium levels. acts as a hypocalcemic hormone, lowering renal calcium reabsorption and suppressing osteoclast activity to lower serum calcium.

In conclusion, the thyroid generates T4, T3, and calcitonin. T4 and T3 control growth, development, and metabolism, while calcitonin helps maintain calcium homeostasis ***(Boucai et al., 2026).***

2. Thyroid hormone synthesis

Thyroid hormones are basically two tyrosines linked together with the critical addition ofiodine at three or four positions on the aromatic rings. The number and position of theiodines is important ***(Mugesh et al., 2023).***

2.1. Iodine Metabolism

Iodine requirements range from 150 to 200 milligrams per day. Iodinated salt, seafood, grains, vegetables, and drinking water are its sources. There are 25–30 mg of iodine in the entire body. Iodine is present in every cell, but the thyroid gland stores 80% of it. The blood contains 5–10 μg/dL of iodine. Iodine is a rare soil component in the majority of the earth. Iodine levels are often lower in the upper parts of mountains. These regions, like the Himalayan region, are referred to as goitrous belts ***(Mugesh et al., 2023).***

Seaweeds are a commercial source of iodine. Goitrogens are food ingredients that inhibit iodine use. Cassava, maize, bamboo shoots, sweet potatoes, and beans all contain goitrogens. Thiocyanate, which is found in tapioca and cabbage, prevents the thyroid from absorbing iodine. Thiourea, which is present in mustard seeds, prevents thyroglobulin from becoming iodinated. Iodine's only biological function is in the synthesis of the thyroid hormones triiodothyronine (T3) and thyroxine (T4) ***(Mugesh et al., 2023).***

2.2. Tyrosines

Thyroglobulin is a big glycoprotein scaffold that provides tyrosines.Only a small number of th e 134 tyrosines included in a thyroglobulin molecule are actually utilized in the synthesis of T4 and T3 ***(Mugesh et al., 2023).***

2.3. Synthesis and Secretion of Thyroxine

Step 1. Iodine Uptake: Iodine is absorbed and concentrated by the thyroid gland (20–100x blood plasma levels). A sodium iodine symporter in the thyroid is responsible for capturing iodide from plasma. TSH stimulates this process ***(Mugesh et al., 2023).***

Step 2. Iodine Oxidation: The thyroid cell oxidizes the iodide it absorbs to produce active iodine. The only organ capable of carrying out this oxidation phase is the thyroid. Thyroperoxidase is the enzyme that catalyzes this. Hydrogen peroxide, which is generated by a NADPH-dependent process, is required for the reaction. TSH stimulates this second stage,

while antithyroid medications like methimazole, thiourea, and thiouracil hinder it ***(Mugesh and others, 2023).***

Step 3. Iodination: Then thyroglobulin (Tgb) is iodinated. The thyroid follicular cells produce thyroglobulin. With over 5000 amino acids (660 kD), it is a big protein. 10% of it is made up of carbs. The Tgb contains 115 tyrosine residues, of which 35 can be iodinated. In the follicular area, the intact Tgb molecule is undergoing tyrosine iodination. This results in the production of 3-monoiodotyrosine (MIT) and 3, 5-di-iodotyrosine (DIT) ***(Sharma et al., 2023).***

Step 4. Coupling: Some of the tyrosine residues in the thyroglobulin are aligned opposite each other, and arecoupled. When two DIT molecules coupled, one molecule of T4 isformed. T3 may be formed by de-iodination of outer ring of T4 by 5'-deiodinase. Under normal conditions, 99% of the hormone produced by the thyroid gland isT4. The T4 residues are now attached to the thyroglobulin molecule. The iodination andcoupling are taking place in the borders of the follicular cells ***(young &Arvan, 2026).***

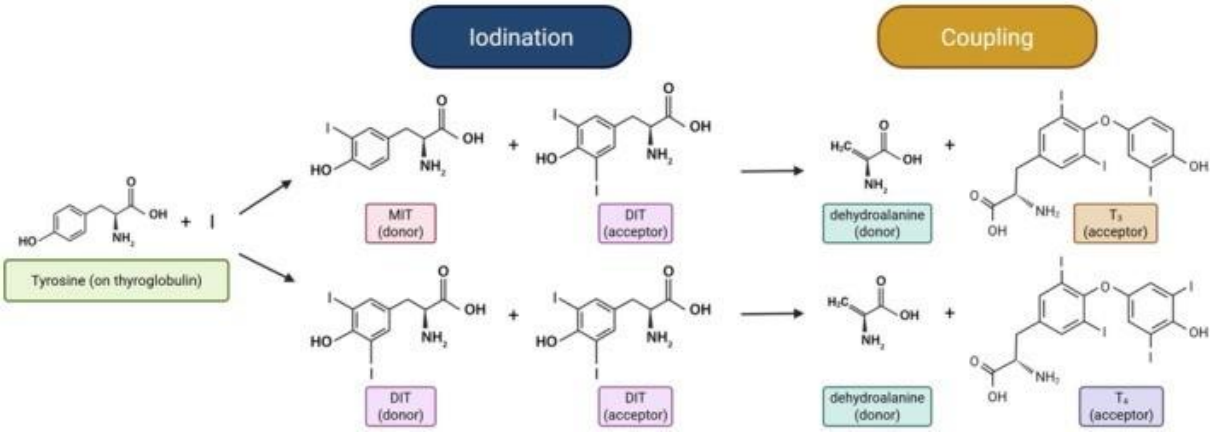


Figure 4. Synthesis of thyroid hormones: iodination and coupling reactions thyroglobulin (Young &Arvan, 2026)

Step 5. Storage: Because it is the only endocrine gland capable of storing significant amounts of the hormone, the thyroid gland is special.Each molecule of thyroglobulin has roughly eight T4 residues.The thyroid acini store it as a colloid ***(Cua et al., 2016).***

Step 6. Utilization: When necessity arises, thyroglobulin is taken up from the acinar colloid, into the cell bypinocytosis.

Step 7. Hydrolysis: Certain proteases hydrolyze the T4, releasing it. TSH significantly increases this activity.Potassium iodide (KI) is utilized as an adjuvant in hyperthyroidism because iodide inhibits this hydrolysis ***(Cua et al., 2016).***

Step 8. Release: This produces T4, which is then released into the circulation. De-iodination at position 5' occurs either within the thyroid cell or in the peripheral tissues to create T3. 5' deiodinase 5- deiodinase deiodinates the inner ring to create reverse T3 (rT3). It has very little biological activity.

Step 9. Salvaging of Iodine: Unused MIT and DIT are recovered and deiodinized so they can be used again within the cell ***(Cua et al., 2016).***

Step 10. Transport of Thyroid Hormones: Thyroid Hormone Transport Proteins carry thyroid hormones in plasma. Although they can be quickly released, the bound form is physiologically inert. About 80% of T4 and 60% of T3 are carried by the thyroxine binding globulin (TBG) (54 KD). Transthyretin (TTR), prealbumin (55 KD), and albumin (69 KD) are loosely linked to the other thyroid hormones.

V. Biochemistry of thyroid hormones

The hypothalamus-pituitary-thyroid axis is one of the numerous hormone regulation systems that identify an axis from the hypothalamus to the pituitary and finally to the peripheral target organs. The pituitary gland and the hypothalamus are physically near to one another. The infundibulum, which resembles a stalk, connects the pituitary gland, which is housed in the sella turcica, to the hypothalamus, which is situated near the base of the brain. Inhibitory and stimulatory hormones as well as other signal molecules can flow through the pituitary stalk's blood vessels and nerve fibers ***(Lechan et al., 2016; Santisteban and Costagliola, 2021).***

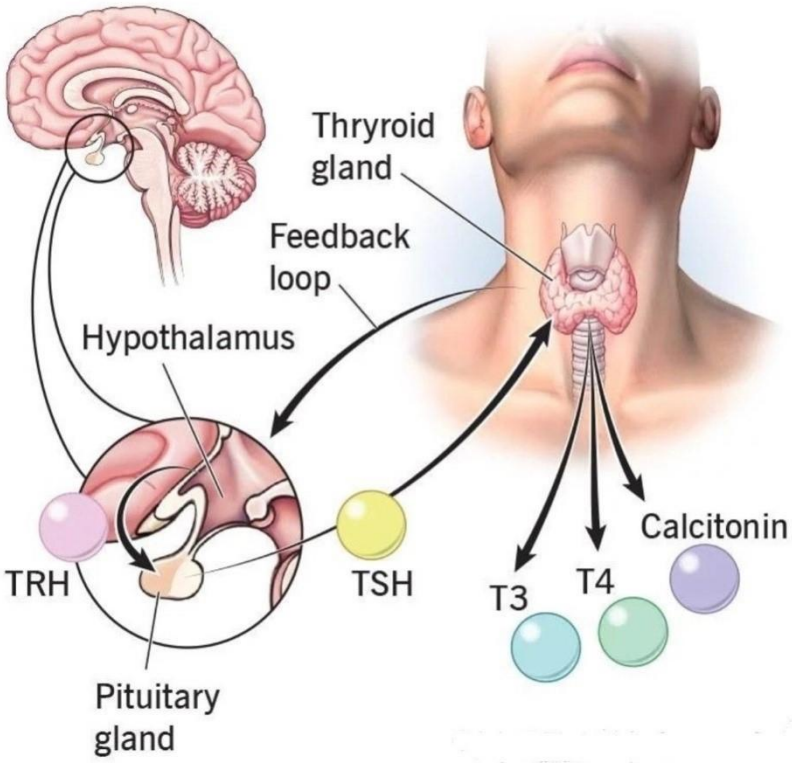


Figure 5. Structure of the hypothalamic-pituitry-thyroid axis (De Groot et al., 2012)

The circulating pituitary hormones regulate the stimulation or inhibition of the peripheral target organs. The various hypothalamus-pituitary-target organ axis systems interact in intricate and complex ways, and the integrated and interaction mechanisms of many of these systems are still unclear ***(Lechan et al., 2016; Santisteban and Costagliola, 2021).***

Because doctors must take into account the interplay between the axes rather than just the one that is currently being controlled, clinical care of patients with diseases involving one or more of these axes is difficult. This also applies to the hypothalamus-pituitary-thyroid axis, which is further complicated by a number of peripheral metabolic changes as well as protein breakdown and binding modifications ***(Feldt-Rasmussen, 2020).***

1. Functional Regulation of the Axis

The hypothalamus is where thyroid hormone regulation begins. Thyrotropin-releasing hormone (TRH) is released by the hypothalamus and travels to the anterior pituitary gland via the hypothalamic-hypophyseal portal system. Thyroid-stimulating hormone (TSH) is released when TRH activates thyrotropin cells in the anterior pituitary. The cell bodies in the hypothalamic periventricular nucleus (PVN) produce the peptide hormone known as TRH. Before TRH reaches the anterior pituitary, it can concentrate in the hypophyseal portal circulation, where these cell bodies project their neurosecretory neurons ***(Shahid et al., 2023).*** The thyroid-releasing hormone receptor (TSH-R) on the basolateral side of the thyroid follicular cell is where TSH attaches after being released into the circulation. Adenylyl cyclase and intracellular cAMP levels are activated when the Gs-protein coupled receptor TSH-R is activated. Protein kinase A (PKA) is activated by the elevated cAMP. PKA alters the activities of several proteins by phosphorylating them ***(Shahid et al., 2023).***

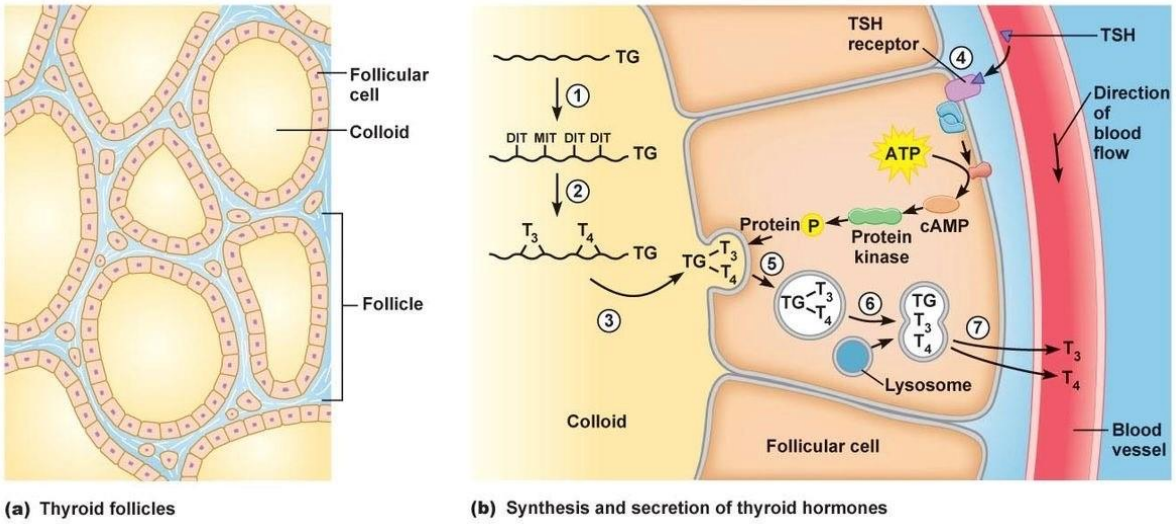


Figure 6. Thyroid follicle and hormone synthesis (Elaine et al., 2022).

2. Mechanisms of thyroid hormone synthesis

The five steps of thyroid synthesis are summarized below ***(Tab.01)***:

Table 1. Summary of thyroid hormone synthesis steps

Step	*Description*
1.Iodide Trapping	Iodide is trapped from the bloodstream into the thyroid gland.
2.Oxidation by TPO	Iodide is oxidized to iodine by thyroperoxidase.
3.Organification	Iodine is incorporated into tyrosine residues to form MIT and DIT.
4.CouplingReaction	MIT and DIT couple to form T3 and T4.
5.Storage and Release	T3 and T4 are stored and released into the bloodstream upon T SH stimulation.

Iodine plays a crucial role in thyroid function. An inadequate intake of iodine can lead to thyroid disorders such as goiter and hypothyroidism. Therefore, sufficient iodine consumption is necessary to maintain normal thyroid activity and proper hormone production.
The thyroid gland produces a big protein called thyroglobulin, which serves as the primary precursor for the synthesis of thyroid hormones. Tyrosine residues that are iodinated during the production of hormones are present. By promoting the metabolic processes necessary for the manufacturing of hormones, other significant proteins like thyroperoxidase also play a role in the process ***(Dalar, 2022).***

VI. Mechanism of Action of Thyroid Hormone

Only the free fractions can cross the cell membrane and affect intracellular metabolism. The hormone attaches to specific nuclear receptors. Then the receptor-hormone complex binds to the DNA. The T3 receptor complex binding sequence in the DNA or the thyroid responsiveelement (TRE) has been identified. The T3 binding results in increase in transcription rate ***(Brent, 2012).***

1. Metabolic Effects of Thyroid Hormones

- The hormone exerts action on every cell of the body. Calorigenic effect or thermogenesis is the major effect of thyroid hormone. This thermogenic effect is mediated by uncoupling of oxidative phosphorylation.
- Basal metabolic rate (BMR) is increased. Thyroxine increases cellular metabolism.
- Earliest effect of T4 is stimulation of RNA synthesis and consequent increase in protein synthesis. Higher concentration of T3 causes protein catabolism and negative nitrogen balance.
- Loss of body weight is a prominent feature of hyperthyroidism.

- Gluconeogenesis and carbohydrate oxidation are increased. Glucose tolerance test shows rapid absorption.
- Fatty acid metabolism is increased. Cholesterol degradation is increased and hence cholesterol level in blood is decreased, which is another hallmark of hyperthyroidism ***(Mullur et al., 2014).***

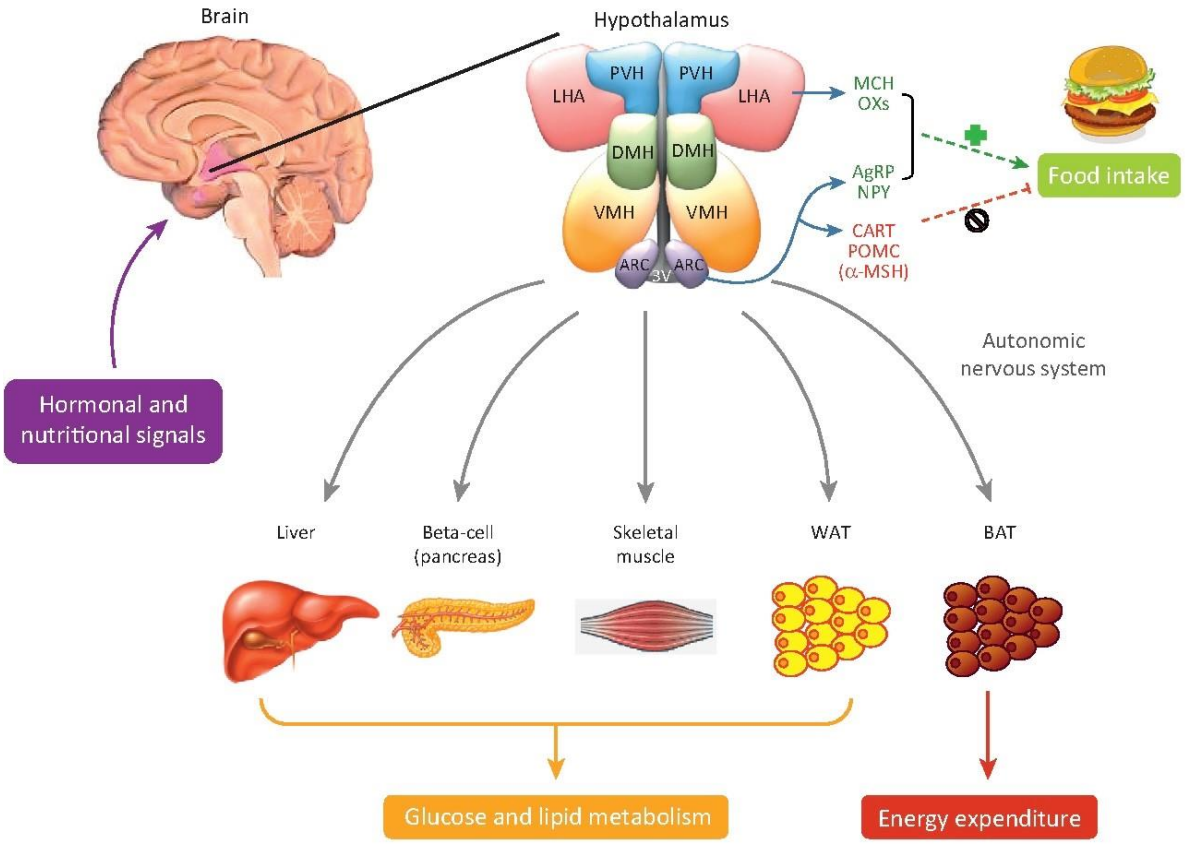


Figure 7. Schematic representation of the hypothalamus control of energy homeostasis and metabolism (Lopez et al., 2013)

1.2. Biological effects of thyroid hormones

1.2.1. Overall Impacts

Nearly every tissue in the body is impacted by thyroid hormones, namely triiodothyronine (T3) and thyroxine (T4). The control of energy balance and basal metabolic rate (BMR) is their main function. The physiologically active form, T3, binds to nuclear thyroid hormone receptors and modifies gene transcription, which affects enzyme activity and protein synthesis. By boosting mitochondrial activity and Na+/K+ ATPase activity, these hormones promote oxygen consumption and heat synthesis (thermogenesis).
Additionally, they control the metabolism of macronutrients:

Carbohydrates: promote glycogenolysis, gluconeogenesis, and glucose absorption

Lipids: lower serum cholesterol and increase lipolysis

Proteins: encourage adequate amounts of protein synthesis but cause excessive catabolism

Thyroid hormones are therefore crucial for preserving energy expenditure and metabolic balance ***(De Groot et al., 2012; Weetman, 2010).***

1.2.2. Impacts on Development and Growth

A. During pregnancy (In Utero): Thyroid hormones are essential for healthy growth during fetal life, particularly for the development of the central nervous system. The fetus is totally reliant on the mother's T4 throughout the early stages of pregnancy, which passes through the placenta. T3 controls:

- Migration and proliferation of neurons
- Synaptogenesis
- Myelination

Thyroid hormone deficiency at this crucial time can cause lasting neurological damage, including delayed psychomotor development and intellectual incapacity ***(Stagnaro-Green et al., 2011; Alexander et al., 2017).***

B. Following Birth: Thyroid hormones are still crucial for skeletal development and linear growth after birth. They work in concert with insulin-like growth factor-1 (IGF-1) and growth hormone (GH) to promote:

- Bone development
- Differentiating tissues
- Organdevelopment

Normal thyroid function is necessary to reach ideal adult height, however hypothyroidism in children causes growth retardation and delayed puberty ***(De Groot et al., 2012; LeRoith, 2014).***

1.2.3. Cardiovascularеffects

- The cardiovascular system is significantly impacted by thyroid hormones. Theyrise:
- Heart rate (beneficial chronotropic effect)
- Contractility of the heart (positive inotropic effect) - Heart output

Cardiovascular dysfunction is a result of these alterations ***(Jameson et al., 2016; De Groot et al., 2012).***

1.2.4. Impacts on the Nervous System

The neurological system's growth and operation depend on thyroid hormones. Theycontrol:

- Differentiatingneurons
- Axonal expansion
- Transmission through synapses

They affect mood, mental alertness, and cognitive performance in adults. Hypothyroidism islinkedto: - Slowing of cognition

- Impaired memory

- Depression

On the other hand, hyperthyroidism can cause irritation and anxiety. These outcomes demonstrate how thyroid hormones support healthy brain function ***(Stagnaro-Green et al., 2011).***

1.2.5. Impacts on Bone

By affecting osteoblast and osteoclast activity, thyroid hormones control bone remodeling. T3 induces: - Bone production by osteoblasts - Bone resorption by osteoclasts

Thyroid hormones are therefore necessary for preserving bone shape and density ***(Williams, 2013).***

1.2.6. Impacts on the Liver

Hepatic metabolism is significantly influenced by thyroid hormones. Theycontrol:

- The production and removal of cholesterol
- Metabolism of lipoproteins
- Serum cholesterol levels are lowered as a result of increased LDL receptor expression brought on by gluconeogenesis and glycogenolysis T3.

Reduced hepatic activity in hypothyroidism causes:

- Elevatedcholesterol
- Modifiedmetabolism of lipids

Thyroid hormones are therefore essential for preserving the liver's metabolic equilibrium ***(Yen, 2001).***

1.2.7. Impacts on the Digestive System

Digestion and gastrointestinal motility are stimulated by thyroid hormones. Theyrise: -

Peristalsis of the gut

- Digestive enzyme secretion In cases of hypothyroidism:
- Constipation results from decreased motility.
- Reduced absorption and digestion

The overall decrease in metabolic activity is reflected in these consequences ***(Cooper, 2003).***

1.2.8. Impacts on the Skin

Thyroid hormones affect the physiology of the skin by controlling:

- Turnover of the epidermis
- Activity of the sweat glands
- The function of hair follicles In cases of hypothyroidism:
- Skin becomes chilly, rough, and dry.
- Hair becomes fragile and may fall out.

Reduced metabolic activity and poor circulation are the causes of these alterations ***(Burman, 2015).***

2. Types of Thyroid Diseases

Thyroid diseases are classified into functional disorders, inflammatory diseases, structural abnormalities, and neoplastic conditions according to their pathophysiology and clinical presentation **(*Hall, 2021; Chakeret al., 2017*).**

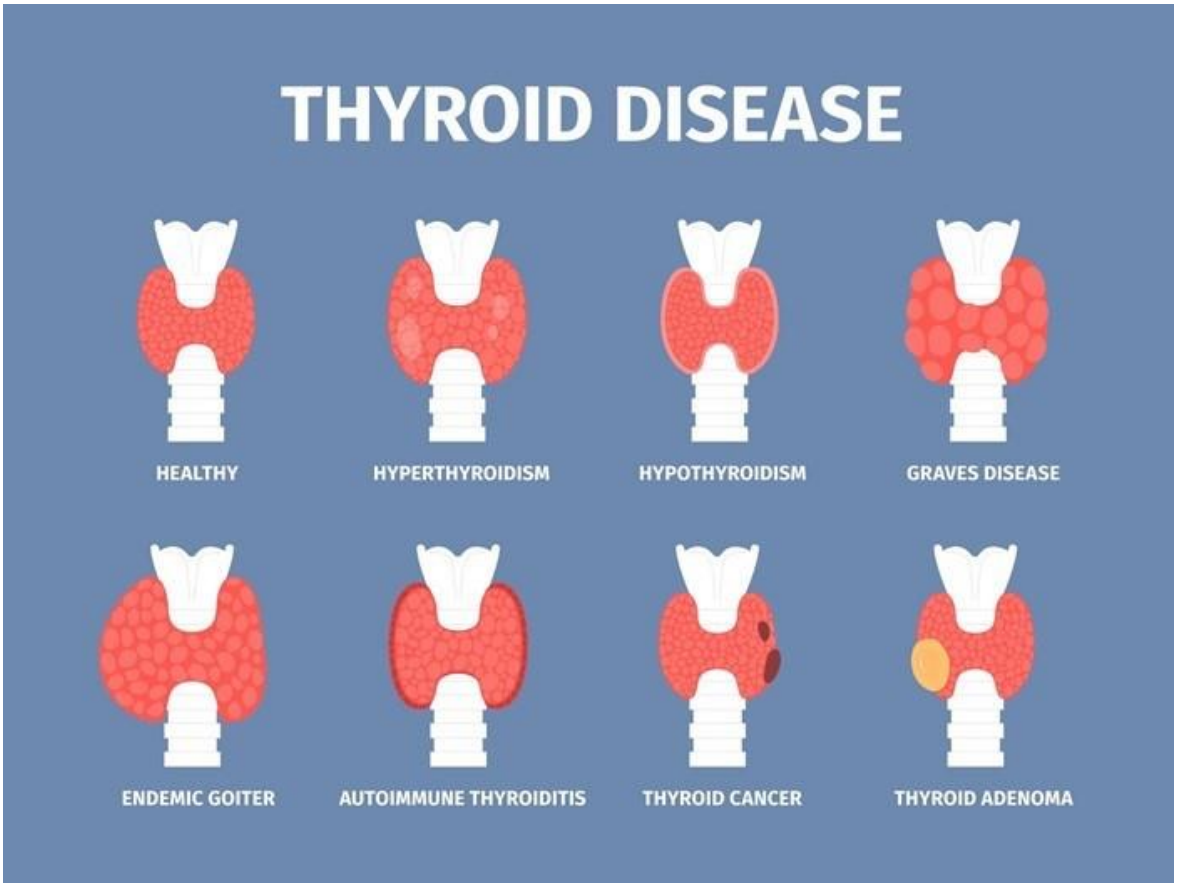


Figure 8. Types of thyroid diseases (Cleveland clinic and John Hopkins medicine 2022).

2.1. Functional Disorders

Hyperthyroidism and Hypothyroidism

2.2. Inflammatory Thyroid Diseases (Thyroiditis)

Both autoimmune and non-autoimmune types of inflammatory diseases exist. Usually caused by a virus, subacute thyroiditis manifests as a painful swelling of the thyroid. Immunemediated postpartum thyroiditis develops within a year of childbirth. A painless inflammatory inflammation that causes temporary thyroid impairment is called silent thyroiditis **(Brent, 2012; De Leo *et al.*, 2016).**

Chronic lymphocytic thyroiditis, or Hashimoto's: The most frequent cause of hypothyroidism in iodine-rich regions is autoimmune disorders, exhibits goiter, high TSH, low/normal TSH, and positive thyroglobulin and/or antithyroid peroxidase (TPO) antibodies.

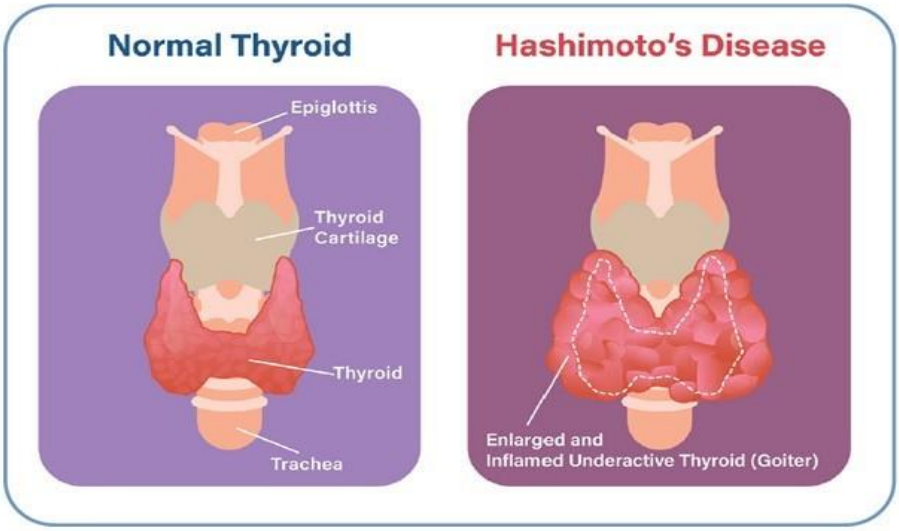


Figure 9. thyroid gland in both conditions « normal and affected by Hashimoto's thyroiditis » (Shawn et al., 2024)

Thyroid enlargement, or goiter:

-Diffuse goiter: a symmetrical, smooth enlargement linked to Hashimoto's illness, Graves' disease, iodine shortage, or compensation for mild hypothyroidism or hyperthyroidism.

-A multinodular goiter is an enlargement that has several benign nodules or areas of hyperplasia; it is frequently caused by an iodine imbalance or long-term TSH stimulation. Clinical impact: may bTe asymptomatic, raise aesthetic concerns, or compress adjacent structures (esophagus, trachea, recurrent laryngeal nerve), resulting in hoarseness, dysphagia, or dyspnea.

Thyroid Neoplasms: Thyroid neoplasms, which originate from the several cell types of the thyroid (primarily follicular cells and parafollicular/C cells), include both benign tumors and malignant thyroid malignancies. Some are aggressive and deadly, but the majority are slowmoving and very treatable.

2.3. Benign tumors of the thyroid

Adenoma follicular:

- Encapsulated, well-differentiated follicular cell tumor that appears on an isotope scan as a chilly or occasionally hot nodule.
- The majority is clinically quiet; capsular/vascular invasion on histology is what distinguishes them from less invasive follicular cancer.
- Other rare benign tumors include hyalinizing trabecular tumor, oncocytic (Hürthle cell) adenoma, and a few benign salivary gland-type tumors in the thyroid.

2.4. Differentiated thyroid carcinomas originating from follicular cells:

These tumors are typically iodine-avid and retain characteristics of normal follicular epithelium.

2.4.1. Papillarythyroidcarcinoma (PTC):

-Thyroid cancer is the most frequent (about 80% of cases in iodine-sufficient locations). -Appears as a solid or complicated nodule that frequently has psammoma bodies, Orphan Annie nuclei, and micro-macro-papillary features.

-Generally slow-growing, many individuals have lymph node metastases at diagnosis, but with appropriate treatment, overall survival is excellent.

2.4.2. Thyroid cancer with follicles (FTC):

-10–20% of thyroid cancers are the second most common.

-Displays microfollicles with vascular and/or capsular invasion under a microscope, which is crucial for diagnosis; it lacks the typical nuclear characteristics of PTC. -More likely to spread hematogenously (bone, lungs).

2.5. Poorly differentiated thyroid carcinoma (PDTC):

Aggressive, higher-grade tumors that have a poorer prognosis than PTC/FTC, less iodine uptake, and nested or trabecular patterns.

2.6. Medullarythyroidcarcinoma (MTC):

-Originates from calcitonin-secreting parafollicular (C) cells, Can be inherited (MEN–2A/2B, familial MTC) or sporadic (≈75%).

-Frequently manifests as a hard single nodule, perhaps accompanied by increased calcitonin and CEA; distant metastases and lymph nodes appear early.

2.6. Thyroid cancer that is anaplastic (undifferentiated):

-Thyroid follicular cells are the source of this highly aggressive, undifferentiated carcinoma, which accounts for only 1-2% of thyroid malignancies but is responsible for a disproportionate number of deaths.

-Usually manifests as a hard, rapidly growing neck mass, frequently accompanied with systemic symptoms and airway compression.

-Under a microscope, cells exhibit loss of thyroid-specific markers, sarcomatoid or spindlecell characteristics, and pronounced pleomorphism.

2.7. Additionaluncommonthyroidtumors:

-Carcinomas of the salivary gland (such as sclerosing mucoepidermoid with eosinophilia, secretory carcinoma, and mucoepidermoid).

-Cancers of the thymus and embryo (such as thyroblastoma, SETTLE, and intrathyroidal thymoma).

-Sarcomas of the thyroid and metastases from other malignancies (such as lung or renal cell).

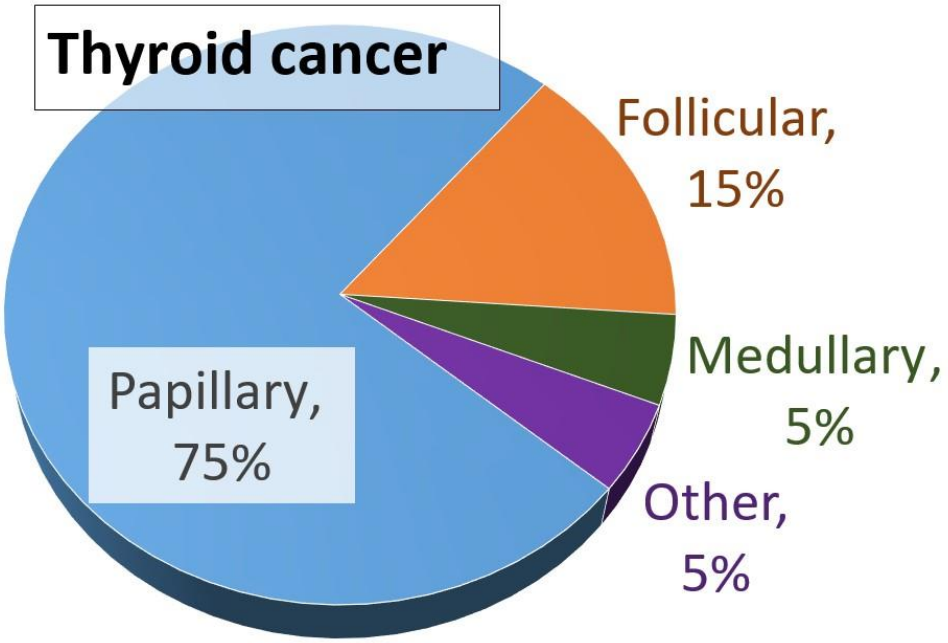


Figure10. Pie chart of thyroid cancer types by incidence (Häggström et al., 2021).

Chapter 02: Pregnancy and Thyroid Functions

I. Generality

Pregnancy is a dynamic period that is often associated with changes in thyroid hormone levels and an increase in the size of thyroid gland. After delivery, the normal thyroid returns to its' pre-pregnancy size after a few months. The cause of this increase in the thyroid are growth factors that are increased in pregnancy, like the hormone calcitonin. These growth factors are thought to also stimulate thyroid nodule growth so that they may enlarge during pregnancy, thus potentially increasing the concern of thyroid cancer and prompt additional testing ***(Vannucchi et al., 2017).***

The thyroid hormones are particularly important during pregnancy because they support both maternal metabolism and fetal growth and neurological development through increased hormone production. Key changes include gland enlargement, shifts in hormone-binding proteins, and stimulation by pregnancy hormones like Hcg***(Alexander et al., 2017).***

II. Importance of thyroid hormones in pregnancy

For a baby's brain and neurological system to develop normally, thyroid hormones are essential. Thyroid hormone levels during pregnancy are crucial for both the mother's health and the healthy growth and brain development of the unborn child. During pregnancy, the levels of thyroid hormone in the blood are significantly increased by two hormones: estrogen and human chorionic gonadotropin (hCG). The thyroid gland produces more thyroid hormones as a result of being stimulated by these hormones. During pregnancy, the thyroid gland may modestly grow in healthy women, but this is typically not noticeable to a doctor during a physical examination. ***(Kirti, 2024).***

Because certain pregnant symptoms and elevated thyroid hormone levels can coexist with thyroid illnesses, diagnosing thyroid issues during pregnancy can be difficult. However, some signs of hyperthyroidism or hypothyroidism are more obvious, which might lead your doctor to examine for these conditions. ***(Kirti, 2024).***

1. The effects of thyroid disorders on women (mothers)

A. Hypothyroidism:

- Without laboratory testing, the diagnosis may be postponed since symptoms like: exhaustion, cold intolerance, weight gain, constipation, dry skin, and depression frequently resemble those of a typical pregnancy ***(Alex et al., 2011).***
- If left untreated, complications: A higher chance of premature birth, anemia, placental abruption, miscarriage, stillbirth, and preeclampsia. Worsening metabolic state and cardiovascular strain (poor cardiac output) ***(Leslie et al., 2012).***
-

B. Hyperthyroidism: Uncontrolled hyperthyroidism may result in:

- Hypertension brought on by pregnancy, preeclampsia, heart failure, and thyroid storm (a potentially fatal condition).
- Low birth weight, preterm birth, and inadequate mother weight gain ***(Yew et al., 2023).***

C. Thyroiditis and postpartum thyroid disease:

- Postpartum thyroiditis (often autoimmune-like) can present as first a thyrotoxic phase, then a hypothyroid phase, causing fatigue, palpitations, weight changes, and mood disturbances in the early postpartum period ***(Pietro et al., 2012).***
- Women with autoimmune thyroid disease have higher risk of infertility, miscarriage, and obstetric complications ***(Roshini et al., 2024).***

2. The effects of thyroid disorders on the fetus and newborn

A. Hypothyroidism and hypothyroxinemia:

- The fetus's brain development during the first half of pregnancy is nearly entirely dependent on the mother's T_4; myelination, cortical maturation, and neuronal migration can all be hampered by maternal hypothyroidism or isolated low free T_4 ***(Leo et al., 2014).***
- Although these are lessened or avoided by early identification and treatment, long-term effects may include decreased IQ, impaired psychomotor development, and learning difficulties in the child ***(Leo et al., 2014).***
- Low birth weight, premature birth, and intrauterine growth restriction (IUGR) are also associated with maternal hypothyroidism ***(Sima et al., 2015).***

B. Graves' illness and hyperthyroidism:

- Fetal or neonatal hyperthyroidism (rapid heart rate, growth limitation, goiter, and even heart failure) is caused by maternal TSH-receptor antibodies (TRAb) that cross the placenta and stimulate the fetal thyroid ***(Shikha et al., 2025).***
- Although it is typically temporary as maternal antibodies disappear after birth, neonatal Graves' illness may necessitate special care ***(Shikha et al., 2025).***

Tab 2. *Maternal and fetal effects of thyroid disease in pregnancy* ***(Abiola et al., 2024).***

Aspect	***Mother (pregnantwoman)***	***Fetus / neonate***
Hypothyroidism (untreated)	Miscarriage, preeclampsia, anemia, preterm delivery, heart strain, marked fatigue.	IUGR, low birth weight, preterm birth, impaired cognitive and motor development if maternal T_4 is low early in gestation.
Hyperthyroidism (untreated)	Hypertension, heart failure, thyroid storm, preterm birth, low birth weight.	Fetal thyrotoxicosis or hyperthyroidism, fetal growth restriction, neonatal Graves' disease.
Normal pregnancy changes	TBG↑, TSH↓ early (due to hCG), free T_4 may transiently fall; thyroid workload ↑ 40–50%.	Fetus depends on maternal T_4 in early pregnancy; placental deiodinases and transporters filter and process thyroid hormones.

III. Biochemical emphasis

1. Pregnancy-related normal biochemical alterations

Total versus free hormones and TBG

- By mid-pregnancy, rising estradiol causes the liver to produce more sialylated TBG, which raises total T_4 and T_3 by about 1.5–2 times, but free T_4 may temporarily decrease before stabilizing ***(Violeta et al., 2025).***
- Due to the increased demand for thyroid hormone synthesis and secretion caused by this TBG-driven increase, daily T_4 output is increased by around 40–50%***(Shikha et al., 2025).***

hCG-induced reduction of TSH and elevation of TSH

- Early in pregnancy, hCG weakly interacts to the TSH receptor, activating thyroid follicular cells and enhancing iodine uptake and T_4/T_3 release. This results in a healthy decrease in TSH during the first trimester ***(Daniel G., 1997).***
- As a result, many women have low-normal TSH in the early stages of pregnancy, and thus may be mistakenly classified as "hyperthyroid" using non-pregnancy reference ranges ***(Angela M., 2012).***

Deiodination of the placenta

- Type 3 iodothyronine deiodinase (DIO3), which is expressed in the placenta, effectively "muzzles" the activity of thyroid hormones and shields fetal tissues from overexposure by converting T_4/T_3 to reverse (inactive) T_3 and T_2 ***(Köhrle J., 2004).***
- The physiologically active hormone that binds nuclear receptors and promotes gene transcription, T_3, can be simultaneously converted to T_3 by DIO2 in maternal and placental organs ***(Anee et al., 2017).***

2. The biochemistry of fetal transport and maternal metabolism

Maternalsubstrates and energetics:

a) Protein, fat, and glucose metabolism are all impacted by low T_4/T_3, which lowers basal metabolic rate.
b) Fatigue, dyslipidemia, and weight gain are all influenced by decreased lipolysis and glucose turnover.
c) These alterations may exacerbate insulin resistance and anemia by interfering with normal pregnancy metabolism ***(Anne et al., 2017***

Fetal hormone management and placental transport:

a) Before 10–12 weeks, the fetus's primary source of thyroid hormone is maternal T4 The placenta preferentially distributes T4 and uses membrane transporters (such as MCT8 and MCT10) and deiodinases to control the amount of T4 that reaches the fetal brain ***(Trace et al., 2012).***
b) Neuronal differentiation and myelination are hampered by reduced maternal free T4 in hypothyroidism or isolated hypothyroxinemiawhich restricts the substrate for fetal deiodination to T3 in the brain ***(Leo et al., 2014).***

3. Physiology of the fetal thyroid

The fetal thyroid gland begins as an outpouching in the midline of the anterior pharyngeal floor and moves caudally until it reaches its final location at 7 weeks of gestation. By 12 weeks of pregnancy, the fetal thyroid can trap iodine, and by 14 weeks, it can produce thyroxine. However, it takes until 18–20 weeks of gestation to see noticeable hormone secretion.

By 36 weeks of gestation, fetal TSH, T4, and TBG levels have progressively increased to adult levels. However, because placental type III deiodinase converts most fetal T4 to reverse T3, T3 and free T3 levels do not increase to adult levels; the fetal brain, which has high levels of type II deiodinase, is an exception.

While T3 and T4 transport can be significant, TSH transfer across the placenta is minimal. This is especially important for infants with congenital hypothyroidism, since research has revealed that their umbilical cord T4 levels can be as low as 50% of normal ***(Vulsma et al., 1989).***

In cases of congenital hypothyroidism, this transferred T4 may be essential for almost normal embryonic cognitive development. Thyroid stimulatory immunoglobulin (TSI), iodine, antithyroid medications, and TRH are also transferred transplacentally***(Tab.2) (Vulsma et al., 1989).***

Tab3. *Placental transfer of thyroid hormones, iodine and antibodie****s (Shlomo et al., 2020)***

Substance	***Transfer across placenta***
lodine	Transferred avidly across placenta, both by passive diffusion and by active transport
Thyroxine	Some transfer is seen, especially in the first trimester
TSH	Poorly transferred
TRH	Avidly transport edacross placenta
Antibodies	Anti Tpo, Anti TG, TSI, TBIl can all cause placenta freely and TSI can cause transient neonatal hyperthyroidism and TBIl can cause transient neonatal hypothyroidism.

IV. Difference between HYPOTHYROIDISM and HYPERTHYROIDISM

Hypothyroidism is when the thyroid gland does not produce enough thyroid hormones, whereas **Hyperthyroidism** is when the thyroid gland produces too much. The conditions have different symptoms and causes.

Thyroid gland is located in the middle of the neck. It generates hormones that control the metabolism of the body. Thyroxine and triiodothyronine are the two primary hormones produced by the thyroid.

When a person has a thyroid issue, their thyroid gland is not making enough hormones. The symptoms of **hypothyroidism** and **hyperthyroidism** are distinct. "Hyper" denotes excessive thyroid hormone production, whereas "hypo" denotes insufficient thyroid hormone production***(Pollock, 2023).***

1. Hypothyroidism

Slowed metabolism: Fatigue, cold intolerance, weight gain, constipation, dry skin, hair loss, and slowed reflexes are all signs of a slowed metabolism.

Cardiovascular: Bradycardia and potential hypertension.

Reproductive: infertility, heavier and more Irregular menstrual cycle (for women).

2. Hyperthyroidism

Nervousness, anxiety, insomnia, heat intolerance, perspiration, weight loss despite increased appetite, tremor, and palpitations are all signs of an accelerated metabolism.

Cardiovascular: arrhythmias, palpitations, and tachycardia.

Ocular (Graves') symptoms include: double vision in certain people and eye bulging (exophthalmos).

Tab.4 *Comparision of clinical features: Hypothyoidism vs Hyperthyroidism* ***(Pollock 2023).***

Feature	***Hypothyroidism***	***Hyperthyroidism***
Definition	Underactivethyroid gland	Overactivethyroid gland
Thyroid Hormones	Decreased levels of thyroid hormones (T3, T4)	Increased levels of thyroid hormones (T3, T4)
Symptoms	Fatigue, weight gain, feeling extra cold, constipation, hair loss, heavy and irregular periods, insomnia, brittle nails, muscle or joint pain	Fatigue, diarrhoea, hair loss, anxiety and nervousness, weight loss or gain, muscle weakness, insomnia, light and short periods
Causes	Autoimmunedisease, surgicalremoval, congenitalproblem, abnormal iodine levels, certain medications, thyroiditis	Autoimmunedisease, nodules, thyroiditis, abnormal iodine levels, overmedication

Part 02: Experimental part

I.Type and place of the study

In order to gather the clinical data, medical history, and biological test results needed for our research on thyroid disorders during pregnancy and the evolution of the associated biochemical parameters, we conduct an analytical study with patients using a questioning method.

This study was carried out during a two-month internship in the high-risk pregnancy department on the fifth floor of the Lala Kheira Mother and Child Specialized Hospital (Mostaganem, Algeria).

One general practitioner, one gynecologist, five nurses, the department head, and a supervisory assistant make up the medical team that oversees the department. A medical office, the department head's office, one treatment and care room, two restrooms, one intended for patients and the other for doctors and healthcare workers, as approximately twelve patient rooms with a capacity of nearly forty-two patients.

This area is devoted to managing and keeping an eye on high-risk pregnancies that need special medical care because of diseases or difficulties that could impair the mother's and/or the fetus's health, such as thyroid and endocrine issues.

II.Ethical Considerations

Before conducting this study, authorization and permission were obtained to access the highrisk pregnancy department at the Lala Kheira Mother and Child Specialized Hospital in order to collect the medical, clinical, and biological information necessary for this research work as part of our training and specialization in biochemistry.

Permission was given to review patients' medical charts and laboratory test results related to thyroid dysfunction during pregnancy. Additionally, patients were politely contacted and asked about their symptoms, medical history, family history, and personal information related to thyroid issues and pregnancy follow-up. With the patients' permission, all interviews and data collection were done with professionalism and respect.

Strict patient confidentiality and privacy were upheld throughout the study; no patient names or identifying information were revealed, and personal information and medical records were used only for academic and scientific purposes within the parameters of this research.

During hospitalization and medical follow-up, the department's medical and paramedical team upheld the patients' rights, safety, and dignity while providing ongoing ethical care and protection. The study was conducted in compliance with ethical guidelines pertaining to patient data confidentiality and medical research.

III. Population studied

1. Introduction

Our study included a population of 30 pregnant women presenting thyroid dysfunction during pregnancy. Among them, 15 patients were diagnosed with hypothyroidism and 15 with hyperthyroidism. The age of the patients ranged between 20 and 37 years.

In most cases, thyroid dysfunction was diagnosed during pregnancy, mainly at the beginning of gestation, between the 12th and 17th weeks of amenorrhea, corresponding to the third and fourth months of pregnancy. Some patients had a previous history of thyroid disorders before pregnancy that either developed or worsened into hypothyroidism or hyperthyroidism.

The included patients presented various clinical manifestations, often similar depending to the type of thyroid malfunction. While women with hyperthyroidism often displayed anxiety, weight loss, palpitations, and excessive perspiration, those with hypothyroidism typically displayed lethargy, weight gain, constipation, and cold sensitivity.

Furthermore, some individuals had concomitant conditions, especially gestational diabetes, which could affect how biochemical measures change during pregnancy.

2. Selectioncriteria

2.1. Inclusion Criteria

- Pregnant women diagnosed with thyroid dysfunction during pregnancy presenting with either: Hypothyroidism or Hyperthyroidism ▪Age range between 20 and 37 years.
- Patients hospitalized or followed in the high-risk pregnancy department of Lala Kheira Mother and Child Specialized Hospital.
- Patients who accepted to participate in the study and provided informed consent for data collection.

2.2. Exclusion Criteria

- Pregnant women with hypertensive disorders, including gestational hypertension and preeclampsia (HTA).
- Presence of severe obstetric complications likely to affect maternal hormonal and metabolic status.
- Multiple pregnancies: Twin pregnancies and Higher-order gestations (excluded due to their influence on hCG levels and thyroid hormone interpretation).
- Patients receiving medications known to interfere with thyroid function, including: Corticosteroids, Amiodarone, Lithium, Iodine-containing therapies.
- Patients with: Incomplete clinical information, Missing laboratory values (TSH, FT3, FT4) and Incomplete medical records.

- Patients who: Refused access to medical or personal data, who did not provide informed consent for participation.

These criteria were applied to minimize confounding factors and ensure that the observed biochemical and hormonal changes were primarily related to thyroid dysfunction during pregnancy.

IV. Questionnaire Method and data collection

A questionnaire approach was used to collect data in order to get comprehensive details regarding the clinical state of pregnant women who had thyroid dysfunction. Personal, clinical, biochemical, and hormonal information on hypothyroidism and hyperthyroidism during pregnancy were all included in the questionnaire.

Personal information gatheredincluded:

- ✓ Age ✓Weight ✓Height ✓Gestational age ✓Thyroid dysfunction diagnosis time: (Prior/Throughout pregnancy)

Health and Family Background:

- ✓ The evaluation comprised:Prior thyroid conditions
- ✓ Immune system disorders✓Diabetes
- ✓ Related or unrelated diseases ✓Thyroid dysfunction in the family to assess potential genetic causes

Clinical Symptom Evaluation:

The questionnaire looked into the clinical signs and potential causes of thyroid dysfunction. Among the symptomsreportedwere:

- ✓ Exhaustion ✓Variations in weight
- ✓ Heart palpitations ✓Anxiety ✓Constipation ✓Intolerance to cold

Depending on the type of thyroid condition, symptoms differed.

Laboratory and Biological Data:

The following biochemical and hormonal findings were gathered from laboratory analyses:

Hormonal characteristics:

- TSH

- FT3
- FT4

Ionogramparameters:

- Potassium (K^+)
- Na (sodium)
- Chloride (Cl^-)

Indicators of liver function: TGO (AST)/ TGP (ALT)

Therapeutic Follow-up: Treatment-related information was also collected:

- Type of treatmentused
- Most patients reported **levothyroxine therapy** as hormone replacement treatment.

V. Parametersstudied

1. Hormonal ParametersStudied

The hormonal assessment in this study was carried out in order to evaluate thyroid function in pregnant women diagnosed with hypothyroidism and hyperthyroidism. The analysis concentrated on measuring serum thyroid hormones and thyroid-regulating hormone using standard laboratory immunoassay methods.

1.1. Thyroid-Stimulating Hormone (TSH)

TSH was measured as the primary screening marker of thyroid function. Serum TSH levels were used to classify and monitor thyroid status in the studied population.

Within the framework of this research:

- Elevated TSH levels were thought to be a sign of hypothyroidism.
- Lower TSH levels were thought to be indicative of hyperthyroidism.

TSH measurement was routinely incorporated into all patient profiles and was regarded as the first-line metric for diagnosing and monitoring thyroid dysfunction during pregnancy.

1.2. Free thyroxine (FT4)

The physiologically active proportion of thyroxine in circulation was evaluated by measuring FT4 levels. Thyroid dysfunction was confirmed and its severity assessed using this measure.

Among the participants in the study:

- Low FT4 values were associated with hypothyroid cases.
- High FT4 values were associated with hyperthyroid cases.

To accurately classify thyroid health, FT4 values were read in conjunction with TSH levels, particularly in cases where isolated TSH abnormalities were observed.

1.3. Free Triiodothyronine (FT3)

In few situations, free triiodothyronine (FT3) was also measured to complete the thyroid profile and provide more details on peripheral thyroid hormone activity.

- Elevated FT3 levels were mainly observed in hyperthyroid patients.
- Reduced FT3 levels were occasionally noted in more severe hypothyroid cases.

When FT4 and TSH readings needed more explanation, FT3 was very helpful for verifying diagnosis and assessing the functional consequences of thyroid diseases.

❖ Analytical Approach and Interpretation in the Study

All hormonal measurements were interpreted according to pregnancy-adjusted reference ranges when available. Results were analyzed in correlation with clinical data and patient history in order to classify subjects into hypothyroid and hyperthyroid groups.

Throughout pregnancy, the hormonal profile (TSH, FT4, and FT3) was methodically employed as part of the diagnostic and monitoring approach. Particular attention was given to trimester-related physiological variations, especially in early pregnancy where hormonal fluctuations may influence interpretation.

Abnormal hormonal profiles were recorded and later correlated with maternal and obstetrical outcomes, including pregnancy complications and fetal development parameters.

2. Biochemical Parameters Studied

The biochemical investigation performed in this study aimed to evaluate the metabolic changes linked to thyroid dysfunction during pregnancy and their possible effects on outcomes for both the mother and the fetus. The selected biochemical parameters were analyzed from serum samples using standardized laboratory methods routinely employed in clinical biochemistry laboratories.

2.1. Glycemic parameters

To evaluate the metabolism of carbohydrates in pregnant women with thyroid impairment, blood glucose levels were examined. Because of their effects on insulin secretion, hepatic glucose production, and peripheral glucose consumption, thyroid hormones are crucial for maintaining glucose homeostasis.

Changes in thyroid function may contribute to disturbances in glycemic balance during pregnancy, increasing the risk of gestational metabolic complications. The evaluation of blood glucose was therefore included to identify possible associations between thyroid disorders and impaired glucose metabolism.

2.2. Lipid Profile

The lipid profile included the determination of:

- Total cholesterol
- Triglycerides
- High-density lipoprotein cholesterol (HDL-C)
- Low-density lipoprotein cholesterol (LDL-C)

In order to assess lipid metabolism abnormalities linked to hypothyroidism and hyperthyroidism during pregnancy, several parameters were examined.

Lipid synthesis, mobilization, and breakdown are all directly impacted by thyroid hormones. While hyperthyroidism is typically characterized by decreased lipid levels due to increased metabolic activity, hypothyroidism is frequently linked to hyperlipidemia, namely elevated total cholesterol and LDL-C concentrations.

The analysis of lipid parameters allowed the assessment of metabolic changes potentially related to thyroid hormonal imbalance.

2.3. Electrolyte Parameters (Ionogram)

The ionogram was performed to evaluate electrolyte and mineral balance in the studied patients. The analyzedparametersincluded:

- Sodium (Na^+)
- Potassium (K^+)
- Chloride (Cl^-)
- Calcium (Ca^{2+})

Endocrine dysfunction and decreased metabolic activity linked to thyroid disorders may impact electrolyte homeostasis. Pregnancy-related physiological changes may also be reflected in variations in these markers.

The total biochemical evaluation of maternal status included the electrolyte balance assessment.

2.4. Renal Function Parameters

Renal function was assessed through the measurement of serum:

- Urea
- Creatinine

These biomarkers were included to evaluate renal status and possible metabolic repercussions associated with thyroid dysfunction during pregnancy.

Thyroid conditions and pregnancy can both affect glomerular filtration rate and renal hemodynamics, which could result in differences in renal biochemical indicators. Further information about maternal metabolic adaptability was obtained by keeping an eye on these measures.

2.5. Hepatic Parameters

The evaluation of liver function comprised the measurement of:

- Aspartate aminotransferase (ASAT/AST)
- Alanine aminotransferase (ALAT/ALT)

These enzymes were examined to look for potential hepatic changes linked to thyroid problems or pregnancy-related issues. Hepatic metabolism is known to be influenced by thyroid hormones, and changes in liver enzyme activity may be caused by aberrant thyroid function.

❖**Biochemical Parameters' Analytical Significance**

Hormonal results and clinical information gathered from the patients were used to interpret the biochemical markers assessed in this investigation. Their research helped determine the severity of the disease and possible implications for the mother and fetus, as well as the investigation of metabolic disorders associated with thyroid dysfunction during pregnancy.

The combined study of hormonal and biochemical markers provided a comprehensive evaluation of the physiological and metabolic impact of hypothyroidism and hyperthyroidism throughout pregnancy.

VI. Methodology

The methodology of this study was based on clinical investigation, patient questioning, and laboratory analysis in order to evaluate the evolution of biochemical parameters associated with thyroid dysfunction during pregnancy.

Pregnant women with hypothyroidism or hyperthyroidism who were monitored at the highrisk pregnancy department of the Lala Kheira Mother and Child Specialized Hospital participated in the study.

A structured questioning technique was used to collect data, along with a review of the patients' medical records and test findings. Age, gestational age, trimester of diagnosis, personal and family medical history, thyroid dysfunction symptoms, linked disorders, treatment follow-up, and pregnancy evolution were among the data gathered.

1. Blood Collection

Qualified medical professionals collected venous blood samples under aseptic settings using sterile equipment and appropriate collection tubes based on the type of analysis needed. The hematological, hormonal, and biochemical tests required for the assessment and tracking of thyroid dysfunction during pregnancy were performed using the blood samples that were obtained.

2. Methods of Analysis

The assessment of hematological, hormonal, biochemical, and immunological parameters in pregnant women exhibiting thyroid dysfunction throughout pregnancy served as the foundation for this study's analytical methodology.

Venous blood samples obtained under suitable pre-analytical conditions and processed in accordance with standard laboratory protocols were used for the various analyses.

2.1. Hematological Parameters:

In order to evaluate the patients' overall hematological health and identify any anomalies related to pregnancy or thyroid dysfunction, hematological investigations were carried out using a Complete Blood Count (CBC/NFS). Among the assessedhematological, parameterswere:

- RBCs, or redbloodcells
- Hb, or hemoglobin
- Hematocrit (HCT)
- WBCs, or white bloodcells
- PLT, or platelet count

These values were helpful in detecting hematological abnormalities linked to endocrine diseases during pregnancy, such as anemia or inflammatory illnesses.

2.2. Hormonal Parameters

The main focus of this investigation was hormonal analyses, which were crucial for the identification, categorization, and monitoring of thyroid dysfunction during pregnancy.

Among the thyroid hormonal parameters that were assessed were:

- TSH, or thyroid-stimulating hormone
- FT4, or free thyroxine
- FT3, or free triiodothyronine

In order to evaluate thyroid gland function and track hormonal changes based on gestational age and the type of thyroid disease, several hormonal markers were examined.

2.3. Immunological Parameters

To assess the potential autoimmune cause of thyroid dysfunction, immunological studies were taken into consideration. The immunological parameter under investigation comprised: Antibodies against thyroid peroxidase (Anti-TPO).

Thyroid autoantibodies may be a sign of autoimmune thyroid conditions that are commonly linked to hypothyroidism during pregnancy.

2.4. Biochemical Parameters

Biochemical analyses were performed to evaluate metabolic disturbances associated with thyroid dysfunction and pregnancy evolution.

Among the biochemical parameters under investigation were:

- Blood sugar
- HbA1c, or glycated hemoglobin - Profile of lipids:
- Total cholesterol
- Triglycerides
- HDL cholesterol
- Low-densitylipoprotein

In order to evaluate metabolic alterations and potential correlations between thyroid conditions and other biochemical abnormalities during pregnancy, these measures were examined.

3. Statistical and Comparative Analysis

The results were gathered, categorized, and contrasted in accordance with:

- Thyroid dysfunction kind (hypothyroidism or hyperthyroidism)
- The trimester of gestation
- The patients' biological and clinical traits

In order to ascertain their clinical importance and connection to thyroid dysfunction, the analysis concentrated on the development and fluctuation of hormonal and biochemical indicators during pregnancy.

VII. Statistical analysis

The collected data were organized and analyzed using Microsoft Excel 2021. Qualitative data were displayed as numbers and percentages, whilst quantitative variables were portrayed as mean ± standard deviation (SD), minimum, and maximum values. Comparisons between groups were performed using the **Student's t-test**for quantitative variables. A **p-value < 0.05** was considered statistically significant.The results were summarized in tables and graphical representations to facilitate the description and comparison of the hormonal, hepatic, and electrolyte parameters among the study participants.

Part 03: Results and Discussion

I. Population related data

Thirty pregnant women with thyroid dysfunction, fifteen cases of hypothyroidism and fifteen cases of hyperthyroidismwere the subjects of data collection. Through a questioning technique related to the gathering of clinical and laboratory results, these patients were chosen to take part in the current study. Both hypothyroidism and hyperthyroidism accounted for around half of all recruited patients, indicating an equal distribution of thyroid problems within the research group.

1.1. Interpretation of the Distribution of Hypothyroidism and Hyperthyroidism Cases within the Study Population

The distribution of instances of hypothyroidism and hyperthyroidism in the pregnant population under study is shown in ***(Figure.12).***

The results show that hypothyroidism and hyperthyroidism are equally distributed, with 50% of the sample population falling into each category. The sample technique used in this study, which purposefully included both thyroid dysfunction categories in similar numbers to enable comparative analysis of their biochemical and hormonal profiles throughout pregnancy, is reflected in this balanced percentage.

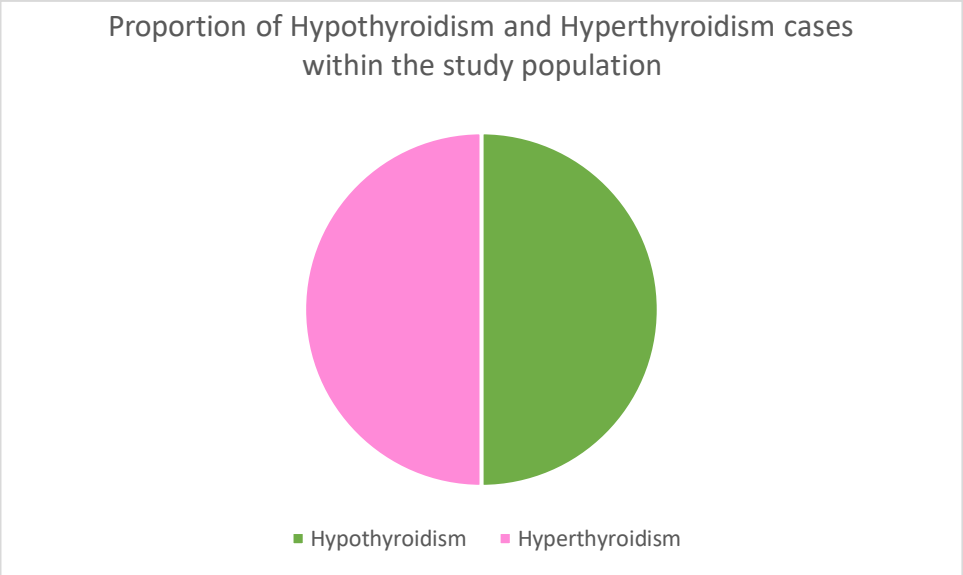


Figure.11 Proportion of Hypo/Hyperthyroidism cases within the study population.

A more comprehensive evaluation of thyroid dysfunction and its effects on maternal biochemical markers was made possible by the inclusion of both hypothyroid and hyperthyroid pregnant

women. A better comprehension of the hormonal changes and clinical signs connected to each thyroid condition during pregnancy is made possible by this comparative distribution ***(Alexander et al., 2017)***

1.2. Interpretation of Age Distribution of Hypothyroidism and Hyperthyroidism Cases

The distribution of hypothyroidism and hyperthyroidism cases among the pregnant women under study by maternal age groups is shown in ***(Figure13).***

According to the findings, thyroid dysfunction was seen in all of the study's reproductive age groups, which ranged from 20 to 37. Women between the ages of 25 and 34 had the highest frequency of instances, especially in the 25–29 and 30–34 age groups; women between the ages of 20 and 24 and 35–37 had lower frequencies.

In terms of thyroid dysfunction type, hypothyroidism and hyperthyroidism were found in all age categories, albeit there were minor differences. Women between the ages of 20 and 24 and 30 and 34 were slightly more likely to have hyperthyroidism, whereas women between the ages of 25 and 29 and 35 and 37 seemed to have hypothyroidism. In the population under study, the overall number of instances of hypothyroidism and hyperthyroidism stayed largely similar.

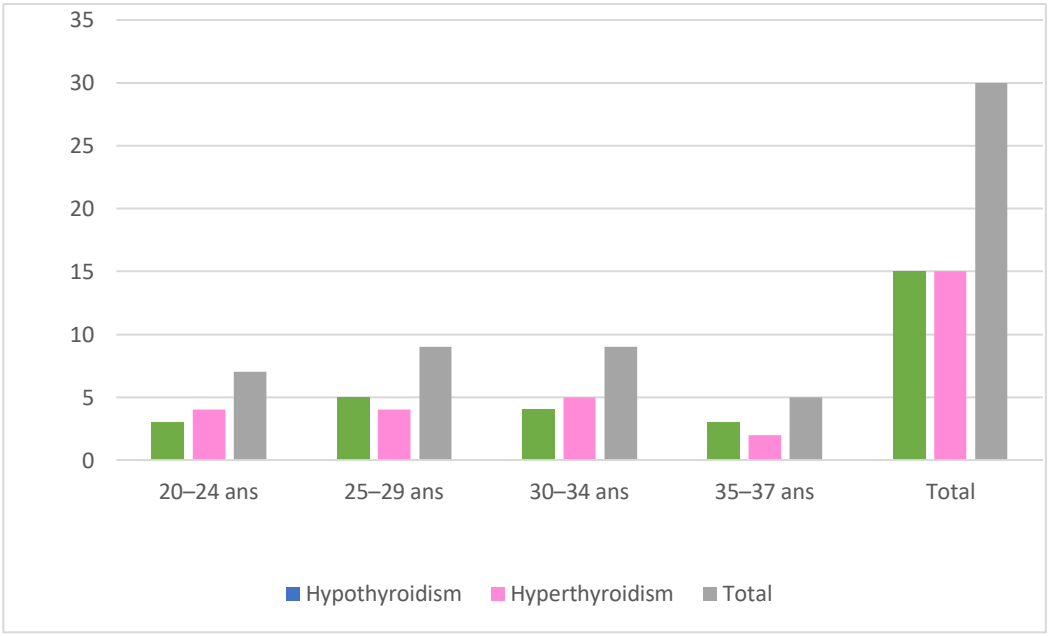


Figure.12 Distribution of Hypo/Hyperthyroidism cases across age groups.

These findings may be explained by the fact that thyroid dysfunction commonly affects women during reproductive age, particularly during pregnancy when major physiological and endocrine changes occur. Pregnancy induces significant modifications in thyroid function through increased estrogen concentrations and the stimulatory effect of human chorionic gonadotropin (hCG), which

may influence TSH and thyroid hormone concentrations and reveal previously undiagnosed thyroid disorders **(Alexander *et al.*, 2017)**.

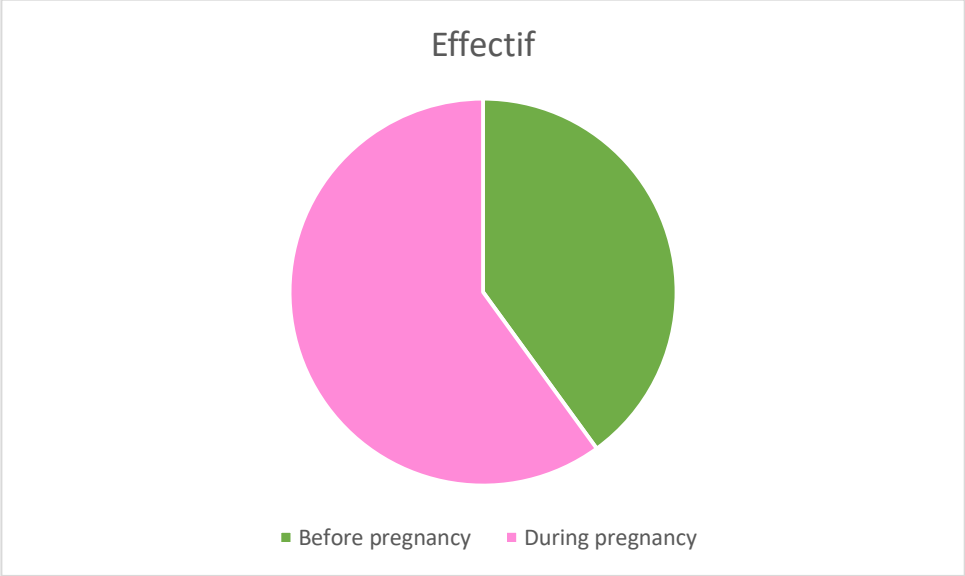
According to epidemiological studies, thyroid disorders are commonly diagnosed among women of reproductive age and pregnant populations, with maternal age typically ranging between the late twenties and early thirties. This is consistent with the study's finding that the majority of thyroid dysfunction cases occurred within the 25–34 age group **(Dong and Stagnaro-Green, 2019; Alexander *et al.*, 2017)**.

Furthermore, regardless of the mother's age, thyroid abnormalities can develop during pregnancy; however, some research indicates that an older mother may be more susceptible to thyroid dysfunction. **(Kıncı*et al.*, 2021)**.

Our study's comparatively balanced distribution of hypothyroidism and hyperthyroidism emphasizes the significance of thyroid screening and biochemical monitoring during pregnancy for early diagnosis and appropriate clinical management. It also reflects the deliberate inclusion of both categories within the chosen sample. **(Alexander *et al.*, 2017)**.

1.3. Distribution of Thyroid Dysfunction Diagnosis Before and During Pregnancy

The distribution of thyroid dysfunction diagnoses among the pregnant women under study by time of detection is shown in ***(Figure 14).***The data show that thyroid impairment was identified both prior to and during pregnancy. About 40% of the study group had been diagnosed before to



pregnancy, but the bulk of cases roughly 60% of the total were discovered during pregnancy.

Figure13. Distribution of Thyroid Dysfunction Diagnosis Before and During Pregnancy.

These results suggest that because of the significant physiological and hormonal changes that take place during gestation, pregnancy may aid in the identification or clinical manifestation of thyroid problems. Significant endocrine changes are linked to pregnancy, especially the effects of human chorionic gonadotropin (hCG) and elevated estrogen concentrations, which can alter thyroid hormone levels and identify thyroid disease that has not yet been identified ***(Alexander et al., 2017).***

The systematic biological monitoring and prenatal follow-up carried out during antenatal care, which enable early detection of hormonal abnormalities and thyroid disorders, may also account for the preponderance of diagnoses made during pregnancy observed in the current study ***(Korevaar et al., 2017).*** However, a considerable proportion of patients had been diagnosed prior to pregnancy, indicating the presence of pre-existing thyroid disease requiring continuous medical surveillance and hormonal monitoring throughout gestation. Early recognition and appropriate management of thyroid disorders before conception and during pregnancy are considered essential to optimize maternal and fetal outcomes.

In order to guarantee early identification and suitable therapeutic management of thyroid dysfunction, these results highlight the significance of thyroid screening and routine biochemical evaluation both before and throughout pregnancy.

II. Results - Hypothyoridism

Pregnant women with hypothyroidism were distributed unevenly throughout age groups. The group with the highest frequency (n=6) was 30–34 years old, followed by 35–39 years old (n=4) and 25–29 years old (n=3). The group with the lowest frequency (n = 2) was 18–24 years old. In general, women in their third and early fourth decades of life, the reproductive age range were more like ly to have hypothyroidism (***Figure 15***).

The study's findings regarding the prevalence of hypothyroidism in women between the ages of 30 and 34 are in line with the known epidemiology of thyroid dysfunction throughout reproductive age. Due to the increased hormonal and metabolic demands of pregnancy, thyroid problems are

relatively common among women of reproductive age and may manifest clinically. Elevated estrogen and hCG levels during pregnancy cause considerable thyroid stimulation, which may aggravate hormonal imbalance in sensitive women or disclose pre-existing thyroid disease. Maternal thyroid problems are often diagnosed during reproductive years and need to be closely monitored due to the potential repercussions for both the mother and the fetus, according to several scientists. These results highlight the significance of early thyroid screening and hormonal assessment during pregnancy, especially for women in age groups that are actively reproducing ***(Green and Pearce, 2012).***

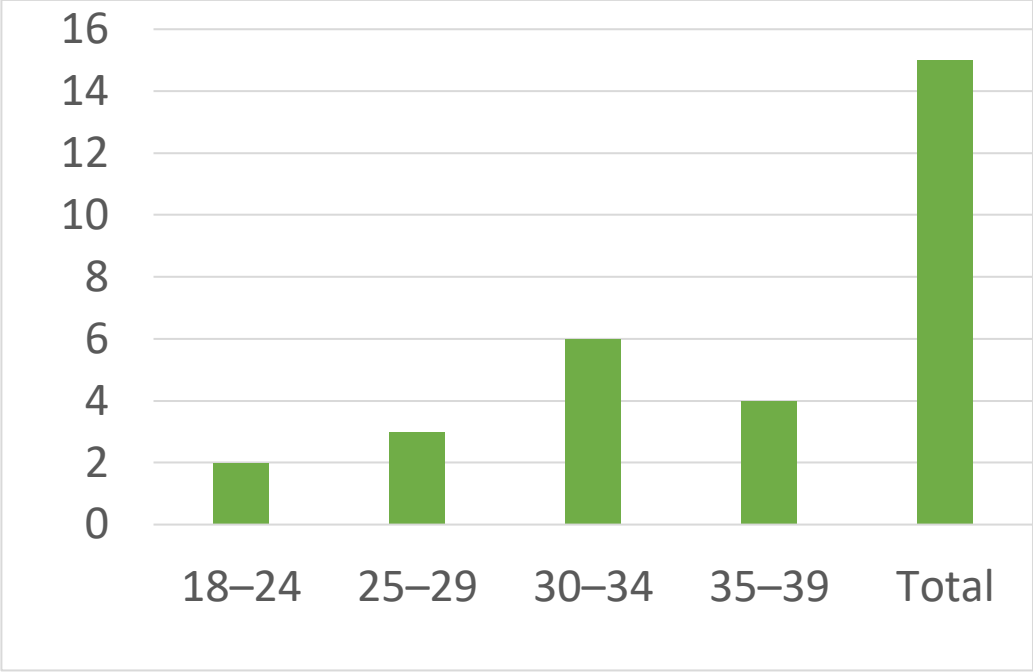


Figure14. Distribution of Hypothyroidism Cases According to Age Group.

The initial phase of our study focused on establishing the baseline demographic profile of the patient cohort presenting with thyroid dysfunction. The clinical and demographic characteristics are summarized in the table below**.**

Parameter	***Result***

The demographics of the study's pregnant hypothyroid women are shown in Table 1. With a mean age of 29.9 ± 4.4 years, the population was primarily young and of reproductive age.

The observed age distribution is consistent with the reproductive period, which is when thyroid diseases are most common and may have an impact on pregnancy outcomes. Thyroid physiology and gestational adaptability continue to be significantly influenced by maternal age.

Tab.5 Demographic Characteristics of the Study Population

Number of patients	15
Age range	19–38 years
Meanage	29.9 ± 4.4 years

1. Hormonal Parameters

The initial phase of our study focused on establishing the baseline demographic profile of the patient cohort presenting with thyroid dysfunction. The clinical and demographic characteristics are summarized in the table below.

The biochemical profiling revealed a mean serum Thyroid-Stimulating Hormone (TSH) concentration of *2.58±3.90 mIU/L*. The notably large standard deviation (*3.90 mIU/L*) highlights a high degree of inter-individual variability within the patient group, encompassing both standard euthyroid values and elevated subclinical/clinical thresholds. For peripheral thyroid hormones, the mean free thyroxine (FT4) level was measured at *16.21 ± 2.99 pmol/L*, while the mean free triiodothyronine (FT3) level exhibited a highly stable and tightly clustered distribution at *3.51± 0.05 pmol/L*.

Tab.6 Serum concentrations of thyroid-stimulating hormone (TSH) and free thyroid hormones.

Parameter	***Mean ± SD***
TSH	2.58 ± 3.90 mIU/L
FT4	16.21 ± 2.99 pmol/L
FT3	3.51 ± 0.05 pmol/L

Due to increased hormonal demand and fetal requirements, pregnancy causes significant physiological alterations in thyroid control. Variations in the degree of thyroid disease or therapy response among patients may be reflected in the TSH variability. Hormonal surveillance is especially crucial during pregnancy since thyroid hormones are critical for fetal neurodevelopment and maternal metabolism ***(Glinoer, 1997; De Groot et al., 2012).***

2. Ionogram and hepatic parameters

To assess the electrolyte and fluid balance of the patient cohort, serum concentrations of the primary extracellular and intracellular cations were measured. The quantitative data, expressed as mean values along with their respective standard deviations (Mean ±SD), are presented in the table below.

The biochemical evaluation of the serum ionogram revealed a mean sodium (Na+) concentration of 135.97 ±1.47 mmol/L.Th is indicates a highly uniform distribution with minimal variance across the cohort. Similarly, the mean serum potassium (K+) concentration was determined to be 3.64±0.05 mmol/L, demonstrating an exceptionally narrow standard deviation and reflecting stable circulating levels among the evaluated individuals.

Tab.7 Serum electrolyte profile of the study population

Parameter	***Mean ± SD***
Sodium (Na^+)	135.97 ± 1.47 mmol/L
Potassium (K^+)	3.64 ± 0.05 mmol/L

In the population under study, electrolyte balance seems to be largely maintained. Significant ion abnormalities are typically linked to severe hypothyroidism, despite the fact that thyroid hormones affect renal function and water-electrolyte homeostasis. Maintained electrolyte homeostasis is suggested by the comparatively steady sodium and potassium levels ***(Iglesias; Díez., 2009).***

To determine the metabolic and functional integrity of the liver within the study population, serum activities of key aminotransferases were quantified. The enzymatic values (Mean\pm SD) are detailed in the table below.

The assessment of hepatocellular enzymes showed a mean Aspartate Aminotransferase (TGO/AST) activity of ***22.88 ± 9.88 U/L***. The Alanine Aminotransferase (TGP/ALT) activity exhibited a lower mean value of ***15.46 ± 6.44 U/L***. Both parameters demonstrate moderate inter-individual variation within the sample group, as reflected by their respective standard deviations.

Tab.8 Serum hepatic transaminase profile

Parameter	***Mean ± SD***
TGO / AST	22.88 ± 9.88 U/L
TGP / ALT	15.46 ± 6.44 U/L

Thyroid hormone transport and metabolism are significantly influenced by the liver. Hepatic enzyme activity may be affected by metabolic changes in hypothyroidism, but the values found were within predicted ranges, indicating that the pregnant women under study had intact hepatic function ***(Malik and Hodgson., 2002).***

- ***Conclusion:***

In summary, the combined data captures a young, pregnant cohort experiencing early gestational thyroid stress but maintaining excellent homeostatic compensation. While individual variations in central signaling reveal that some women are transitioning into subclinical or primary gestational hypothyroidisma state requiring careful monitoring to safeguard maternal-fetal outcomesthematernal body is actively defending its metabolic equilibrium. This is demonstrated by highly stable peripheral thyroid hormone levels, confirming efficient peripheral conversion to meet the increased metabolic demands of pregnancy.

Crucially, this early gestational thyroid dysfunction has not triggered secondary gestational complications. Fluid and electrolyte balances remain tightly regulated within safe limits, and maternal liver function is entirely healthy. This intact hepatic profile ensures a stable metabolic infrastructure capable of supporting normal hormone conversion and clearance. Ultimately, these findings depict a pregnant population facing early thyroid insufficiency that is currently well-compensated, leaving vital organ functions, electrolyte balance, and peripheral tissue metabolism fully intact to support both mother and fetus.

III. Results - Hypethyroidism

The age distribution of pregnant women with hyperthyroidism showed variation among the studied age groups. The 30–34 years age group represented the highest frequency (n=6), followed by 35–39 years (n=4) and 25–29 years (n=3), while the 18–24 years group presented the lowest frequency (n=2). These findings indicate that hyperthyroidism occurred predominantly among women in the third decade of reproductive life.

The study's findings about the prevalence of hyperthyroidism in women between the ages of 30 and 34 are consistent with the epidemiological profile of thyroid disease throughout reproductive age. Women of childbearing age are frequently affected by hyperthyroidism, especially autoimmune types like Graves' disease, which can become clinically apparent during pregnancy due to increased metabolic demand and physiological stimulation of the thyroid gland by human chorionic gonadotropin (hCG).

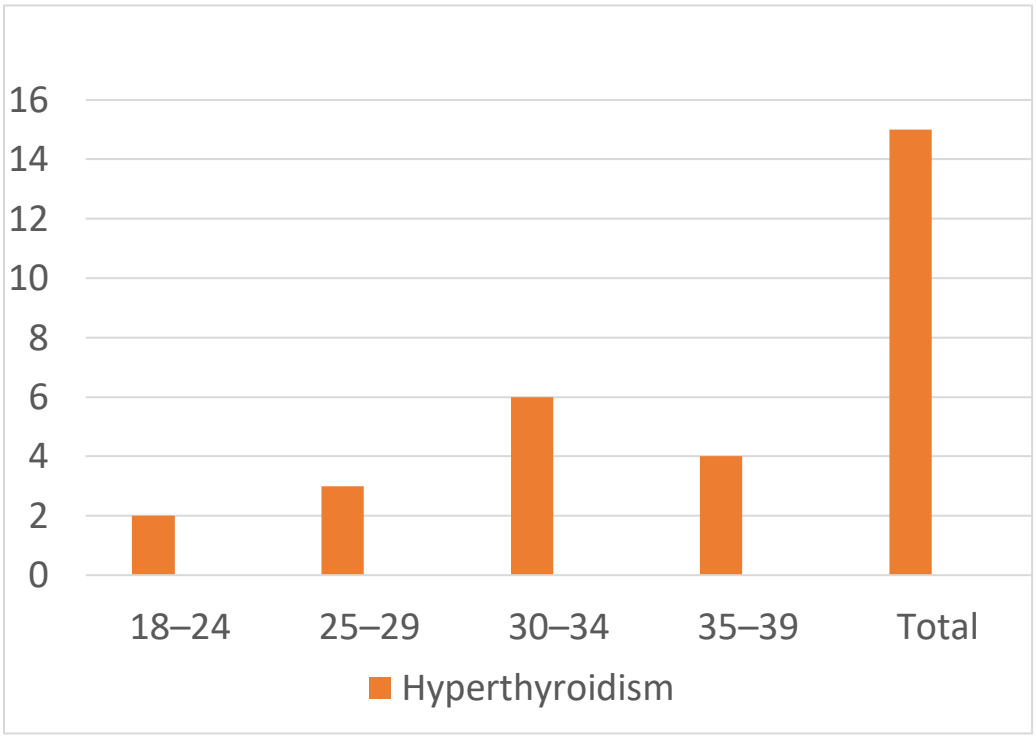


Figure.15 Distribution of hyperthyroidism cases across age groups

Endocrine changes brought on by pregnancy may exacerbate latent dysfunction or reveal pre-existing thyroid problems. Several publications have reported similar findings, highlighting the fact that thyroid abnormalities are common during the reproductive years and necessitate careful hormonal management to minimize consequences for both the mother and the fetus. These results highlight the significance of early thyroid function evaluation and biological monitoring during pregnancy ***(De Groot et al., 2012).***

- The primary characteristic of hyperthyroidism is excessive thyroid hormone production, which raises FT4 and FT3 levels and suppresses TSH.
- The study's 15 hyperthyroid individuals' biochemical profiles varied, indicating varying degrees of thyroid malfunction.
- The cases were categorized as severe overt, overt, mild to moderate, and mild/subclinical hyperthyroidism based on hormonal data.
- Additionally, some individuals displayed related biological alterations, such as abnormalities in liver enzymes and electrolytes.
- These results demonstrate that, in addition to thyroid hormones, hyperthyroidism can impact several other biochemical markers.
- The following sections go into further detail about each category and its biological traits.

Patients 2, 5, and 10 present a strong suppression of TSH levels (0.001–0.01 mIU/L), accompanied by elevated FT4 (21.1–28.0 pmol/L) and FT3 (3.5–6.2 pmol/L). Electrolyte analysis reveals mild hyponatremia in certain cases, with sodium values around 133–134 mmol/L, while potassium remains at the lower end of the normal range. Liver function tests show variability, including a notable increase in TGP in Patient 2 (83.60 U/L) (***Table 9***).

Tab.9 Patients with severe overt hyperthyroidism.

Patient	***Age***	***TSH***	***FT4***	***FT3***	***Na^+***	***K^+***	***TGO***	***TGP***
P2	38	0.001	21.1	3.50	133.5	3.40	35.00	83.60
P5	38	0.01	24.8	5.8	137.3	3.62	17.25	9.39
P10	18	0.01	28.0	6.2	134.7	3.70	32.62	15.71

These findings are consistent with a severe overt form of hyperthyroidism, reflecting a complete suppression of TSH due to negative feedback and a significant increase in circulating thyroid hormones. This hormonal profile indicates a state of increased metabolic activity, which may contribute to mild disturbances in electrolyte balance and potential hepatic involvement. The elevated TGP observed in patient2 May indicate thyroid-induced liver dysfunction or associated metabolic overload ***(Ross et al., 2016).***

Patients 4, 7, 11, 13, and 14 have high FT4 (23.5–26.0 pmol/L) and FT3 (5.5–5.9 pmol/L) along with decreased TSH levels (0.02–0.08 mIU/L) (***Table 10***). Although a little drop in sodium is seen in a few instances, electrolyte results are generally constant. Liver enzyme levels can indicate either slight to moderate elevations or stay generally within normal ranges.

Tab.10 Patients with overt hyperthyroidism.

Patient	***Age***	***TSH***	***FT4***	***FT3***	***Na^+***	***K^+***	***TGO***	***TGP***
P4	30	0.08	23.5	5.6	137.1	3.60	30.22	15.47
P7	28	0.05	25.2	5.9	134.2	3.61	13.2	14.5
P11	32	0.06	24.0	5.5	133.7	3.60	32.62	15.53
P13	33	0.02	25.5	5.7	136.7	3.63	17.25	9.40
P14	30	0.04	26.0	5.9	138.0	3.61	38.28	26.36

These findings point to classical overt hyperthyroidism, which is defined by a definite excess of thyroid hormone that is less severe than in the preceding group. A compromised hypothalamic-pituitary feedback response is seen in the ongoing suppression of TSH. While the moderate changes in liver enzymes indicate a limited degree of hepatic metabolic stress, minor electrolyte fluctuations may indicate the start of systemic metabolic consequences ***(Ross DS et al., 2016).***

Patients 6, 9, 12, and 15 exhibit slightly higher FT4 and FT3 values along with a modest drop in TSH levels (0.09–0.20 mIU/L) (***Table 11***). There are no notable abnormalities, and electrolyte measurements are mostly within normal levels. Results for liver enzymes show very slight variations and no abnormalities that are clinically significant.

Tab.11 Patients with Mild to Moderate Hyperthyroidism.

Patient	***Age***	***TSH***	***FT4***	***FT3***	***Na^+***	***K^+***	***TGO***	***TGP***
P6	30	0.12	21.9	5.4	137.1	3.60	38.28	26.39
P9	29	0.20	20.5	4.9	134.8	3.64	15.2	13.01
P12	31	0.10	22.3	5.3	135.8	3.61	17.22	9.40
P15	27	0.09	23.0	5.4	135.3	3.61	13.2	14.5

These results are in line with an early or compensated form of hyperthyroidism, which is characterized by an excess of thyroid hormone that is still partially controlled. Pituitary feedback is still partially functioning, as seen by the slight suppression of TSH. The slight biochemical alterations imply that there is little systemic involvement at this point, which could be indicative of an early or perhaps curable stage of the illness ***(Melmed et al., 2016).***

While FT4 and FT3 are still within the near-normal range, Patient 8 has a slightly lower TSH level (0.30 mIU/L). Tests for liver function and electrolyte balance typically show only slight, isolated variations (***Table 12***).

Tab.12 Patients with Mild / Subclinical Hyperthyroidism Pattern.

Patients	***Age***	***TSH***	***FT4***	***FT3***	***Na^+***	***K^+***	***TGO***	***TGP***
P8	24	0.30	19.8	4.8	137.4	3.80	10.68	27.8

When thyroid hormone concentrations are still mostly within reference ranges but early pituitary suppression is noticeable, this pattern may indicate a subclinical or early hyperthyroid condition. It

can be a sign of thyroid malfunction in its early stages or a moment of potential healing. Clinical monitoring is usually advised in this situation instead of prompt, aggressive action ***(Ross et al., 2016).***

- **Conclusion:**

With a consistent pattern of suppressed TSH and high FT4 and FT3 values, this research of 15 hyperthyroid individuals confirmed thyroid hormone excess and disruption of the hypothalamic-pituitary-thyroid axis.

The majority of patients had obvious overt biochemical profiles, and the cases varied from mild/subclinical to overt and severe hyperthyroidism.

A few metabolic alterations were also noted, such as low-normal potassium, mild hyponatremia, and sporadic elevations in liver enzymes (TGO/TGP), which are indicative of the systemic consequences of excess thyroid hormone.

Overall, the results demonstrate that hyperthyroidism is a systemic illness that is evaluated using a combination of TSH, FT4, and FT3 measurements.

General Conclusion

The completion of this research work, conducted within the Faculty of Natural and Life Sciences at Abdelhamid Ibn Badis University of Mostaganem, highlights the critical intersection between biochemistry and maternal-fetal health. By bridging theoretical literature with practical clinical data, this study underscores the profound importance of the thyroid gland in maintaining body balance during pregnancy.

Thyroid hormones play a fundamental role as master regulators of metabolism, cellular energy, and early neurological development in utero. During pregnancy, the maternal body undergoes significant hormonal shifts that heavily increase the metabolic workload on the thyroid. When the thyroid reserve is inadequate to meet this demand, it triggers dysfunctions that can compromise both maternal health and proper fetal development, leading to serious obstetric and cognitive risks if left untreated.

Our field study at the Lalla Kheira Mother and Child Hospital in Mostaganem successfully illustrated these connections. The clinical and biological data confirmed that pregnancy often acts as a direct unmasker of silent thyroid insufficiencies, as the majority of cases were diagnosed during gestation. From a biochemical perspective, the results showed that while thyroid-stimulating hormones varied, the maternal body actively worked to stabilize vital functions. Electrolyte balances and liver functions remained well-compensated, proving that the body deploys effective defense mechanisms to protect major organs during early or managed thyroid stress.

In conclusion, this work capitulates the vital necessity of a healthy thyroid axis for a safe pregnancy. While the maternal body is highly resilient and capable of protecting its core metabolic functions, the equilibrium remains fragile. Ultimately, these findings emphasize the immense importance of early and systematic thyroid screening during the first trimester, allowing for timely medical interventions to safeguard the long-term well-being of both mother and child.

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