We are IntechOpen, the world's leading publisher of Open Access books
Built by scientists, for scientists

6,900
Open access books available

186,000
International authors and editors

200M
Downloads

154
Countries delivered to

Our authors are among the
TOP 1%
most cited scientists

12.2%
Contributors from top 500 universities

CLARIVATE ANALYTICS
BOOK CITATION INDEX
INDEXED

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

Chapter

The Role of Ultrasound in Hypothyroidism, Technique, Differential Diagnosis and Follow-Up

Hakan Baş

Abstract

In hypothyroidism, which is as old as humanity, ultrasound has been the first and most important imaging examination in recent decades. This disease is involved in almost all steps in the spectrum from inflammatory diseases to cancer of the thyroid gland. Thyroid ultrasound is a critical tool in the differential diagnosis of hypothyroidism. If thyroid antibodies are negative. It is helpful to determine whether the thyroid is present and to visualize the parenchyma. In a hypothyroid patient, the US may lead to cost savings. If a typical autoimmune pattern is present on US, as a cost-reducing move, further investigations may not be required for the diagnosis of Hashimoto's thyroiditis. Moreover, the ultrasound image may contribute to the decision process whether to treat patients with positive antithyroid antibodies who are euthyroid or have only a mild subclinical hypothyroidism.

Keywords: Hypothyroidism, Ultrasonography, Color Doppler Imaging, Chronic lymphocytic thyroiditis, Thyroiditis, Hashimoto's thyroiditis

1. Introduction

Hypothyroidism that results from low levels of thyroid hormone is one of the most common endocrine disorders. It has various etiology and manifestations; when it is untreated, it increases morbidity and mortality. While the main cause of hypothyroidism is still iodine-deficient diet worldwide, it is autoimmune thyroid disease (also known as Hashimoto's thyroiditis) in regions where dietary iodine intake is sufficient. Today, it is successfully treated with exogenous thyroid hormone [1]. Hypothyroidism often accounts for a large part of the daily practice workload of endocrinology and radiology. Multidisciplinary communication is very important in the approach and management of this endocrine disorder. In the last 30–40 years, the most specific imaging tool in routine examination of thyroid gland diseases is ultrasonography (US). In this section, in hypothyroidism, details about the technique of thyroid US, "pattern recognition", which are important in differential diagnosis, and follow-up will be shared.

2. The thyroid ultrasonography

Ultrasound has become an essential complement to the examination today, while it was used as a new diagnostic tool in thyroid disorders in the 1960s [2]. Ultrasonography has changed the practice of medicine fairly. Relatively easy to use, no ionizing radiation, low cost, and bedside availability have made it invaluable in many clinical settings where patients with thyroid disease are evaluated. The superficial location of the thyroid gland in ultrasonography creates the advantage of high resolution to evaluate thyroid parenchyma and thyroid lesions. US is an indispensable examination in almost the entire spectrum of thyroid diseases. This proposition is similar for hypothyroidism. On the other hand, in thyroid US, specific pattern recognition of the various sonographic presentations of autoimmune diffuse thyroid disease, especially in the clinical presentation of hypothyroidism without antibodies, is completely required. It is also essential in determining whether a focal abnormality represents a true nodule that may require fine-needle aspiration biopsy or is part of an inflammatory process, often referred to as a pseudonodule [3]. The ultrasound, like other tests, should be used to confirm the differential diagnosis when a specific diagnostic question raised by clinical history and physical examination needs to be answered [4]. It should be correlated precisely

Figure 1.
(a) The lineer and convex transuders. (b) The ideal position of the patient is seen. Procedure is conducted with the patient lying supine with the neck in hyperextension with as much tolerated. Their shoulders can be supported with a rolled towel as seen.

with the other data. The justification of the request for thyroid ultrasound should be made by considering the patient history and laboratory results together.

2.1 The patient preparation, equipments and technique

For the thyroid gland ultrasound, no special preparation is required for the examination. However, the patient is requested to remove jewelry such as necklaces before the procedure. Fasting is not required.

Ultrasound studies of extracranial head and neck structures, including the thyroid gland, should first be performed with a linear transducer. The equipment should be set to utilize at the highest frequency, considering a balance between resolution and tissue penetration. Average frequencies of 7 to 15 MHz or higher are preferred, although some patients may require a lower frequency transducer for deep penetration. In addition, a curved transducer may be necessary to evaluate deep or large structures [5, 6]. The transducers are shown in **Figure 1a**.

The procedure is conducted with the patient lying supine with the neck in hyperextension as much as tolerated. Their shoulders can be supported with a rolled towel so that they can keep their necks comfortably in the hyperextension position [5]. The ideal position of the procedure is seen in **Figure 1b**. Upright or seated

Figure 2.
The examination steps. Firstly, the transducer is perpendicular to the neck long axis for the transverse plane. Then the transducer is turned mild oblique craniocaudally for the sagittal view of right and left lobes, respectively.

positioning may be helpful in patients who cannot tolerate neck hyperextension in the supine position [5, 7].

Water-based ultrasound gel reduces contact loss at the interface between the transducer and skin and improves image quality. It should be applied to the tip of the transducer rather than the patient's neck for patients' comfort. In addition, gel warmers can be used for the elderly and children (especially neonates), where heat loss may have important clinical consequences.

The lobes should be imaged in transverse and longitudinal planes and the isthmus in the transverse plane. Size should be obtained for each lobe, including the anteroposterior, transverse, and sagittal dimensions. In addition, the anteroposterior dimension of the isthmus should be measured in the transverse plane. Color Doppler images are obtained to supplement grayscale images in the appropriate clinical setting [5]. All the examination is illustrated in **Figure 2**. Assessment of the thyroid also includes imaging of the lymph node chain bilaterally for enlarged or abnormal lymph nodes, especially in levels III, IV and VI [6].

2.2 Ultrasound of the normal thyroid

The thyroid is a bilobed gland located anterior to the neck, in front of the trachea, and each lobe is located on either side of the trachea. Both lobes extend vertically and craniocaudally. The isthmus is the part of the gland just anterior of the trachea that connects the two lobes like a bridge. The trachea lies craniocaudal behind the isthmus in the form of an air-filled column. The carotid sheath consisting of the common carotid artery medially and the jugular vein laterally is observed on both posterolateral of the thyroid lobes. Visualized muscles deep in the skin-subcutaneous adipose tissue, sternohyoid, sternothyroid, sternocleidomastoid, and longus colli, also called strap muscles, cover the thyroid gland. The sternohyoid and sternothyroid lie on the anterior of the gland, the sternocleidomastoid lie anterolaterally, and longus colli muscles are located in the posterior of the gland. Another structure that can be seen better in the axial plane is the esophagus, which is located posterior to the left lobe and may sometimes contain air. The normal thyroid sonographic features in the transverse plane are shown in **Figure 3**.

Due to its colloidal content, the normal thyroid gland attenuates more sound beams than the strap muscles, and therefore sonographically appears hyperechoic. Normal thyroid echotexture is defined as uniform and homogeneous hyperechoic. It has a well-defined peripheral margin. In addition, the anterior margin of the thyroid gland is flat or concave. The anterior margin of the normal gland is presented in **Figure 4**.

The normal size of the thyroid gland varies according to the gender and height of the patients. Still, in adults, each lobe is approximately 5 x 2 x 2 cm in sagittal, anterior–posterior and transverse dimensions, respectively. The isthmus is measured in the transverse plane, and its normal size-upper limit is accepted as 0.3 cm. When these dimensions are exceeded, it is understood that the thyroid gland enlarges; this concept is called "goiter". Apart from measurements, some imaging findings can diagnose goiter. The bulge on the anterior surface of the lobes is a clue for diagnoses; as mentioned above, the surface is typically symmetrical and has a flat or concave appearance. The extension of the gland over the anterior surface of the common carotid artery in the transverse plane may be further evidence of gland enlargement. The normal thyroid gland can extend over the carotid surface without enlarging; in this case, the anterior contour shape is important. If it is flat or concave, goiter should not be diagnosed. The group in which the shape and contour of the gland are more important than the size is the children. The gland shape and contour are used to indicate gland growth rather than size [8]. There is no clear

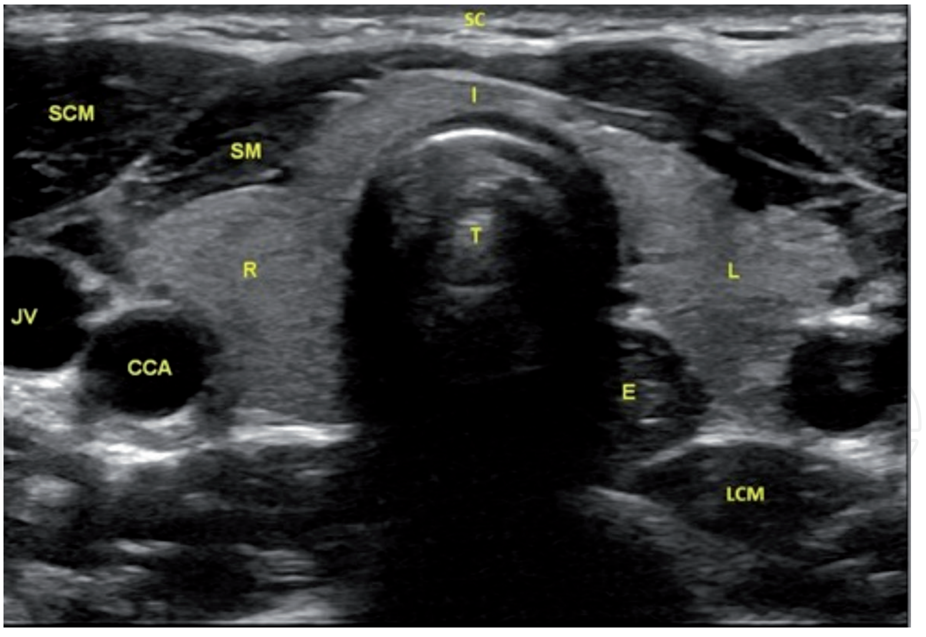

Figure 3.
The normal appearance of the thyroid gland in the ultrasonography examination is presented. (R: right lobe, L: left lobe, I: isthmus, T: trachea, E: esophagus, CCA: common carotid artery, JV: jugular vein, SM: strap muscle, SCM: sternocleidomastoid muscle, LCM: longus colli muscle, SC: subcutaneous tissue).

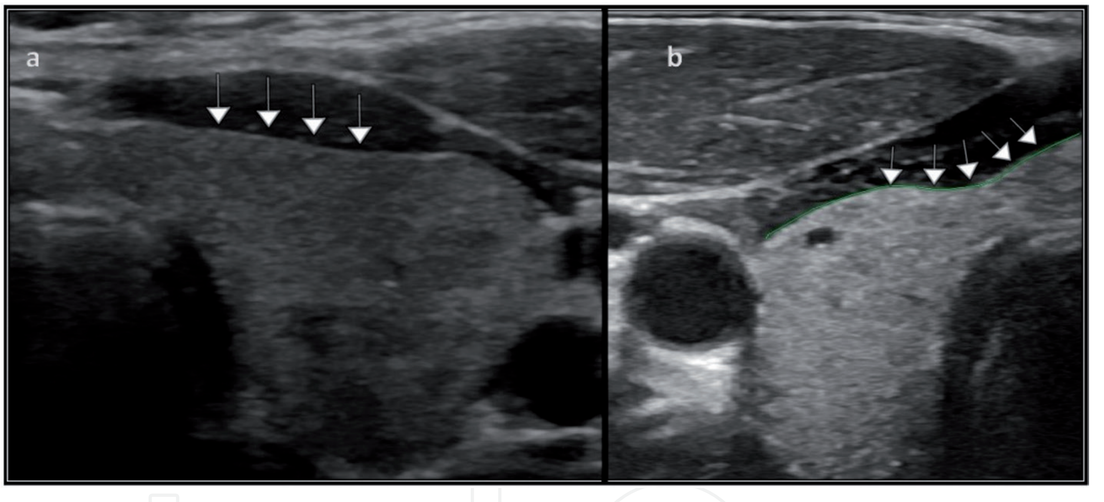

Figure 4.
(a) When the size of the gland is normal, the shape of the anterior surface (arrows) of the gland is nearly flat or (b) concave (green line and arrows). Please pay attention that there is no bulging anterior surface of the gland and no extension of the gland over the anterior surface of the common carotid artery in the transverse plane.

consensus on the normal dimensions of the thyroid in the pediatric population. When calculating the thyroid volume, the ellipsoid formula of width x length x height x 0.523 is used. In epidemiological studies, factors that affect pediatric thyroid size, such as ethnicity and local iodine burden/intake, can be counted [9, 10]. Neonatal thyroid volumes range from 0.84 ± 0.38 mL to 1.62 ± 0.41 mL [11]. The more practical method, the tracheal index, can be used. In the transverse plane, the transverse diameters of both lobes are summed and proportioned to the transverse diameter of the trachea. The normal range of the index is considered to be 1.7–2.4 [12]. Practical measurement methods for goiter are shown in **Figure 5**.

In the normal thyroid gland parenchyma, less than 5 vascular coding is expected in the sampling window at the lowest pulse repetition frequency (PRF) values without background noise on color Doppler ultrasound (CDI).

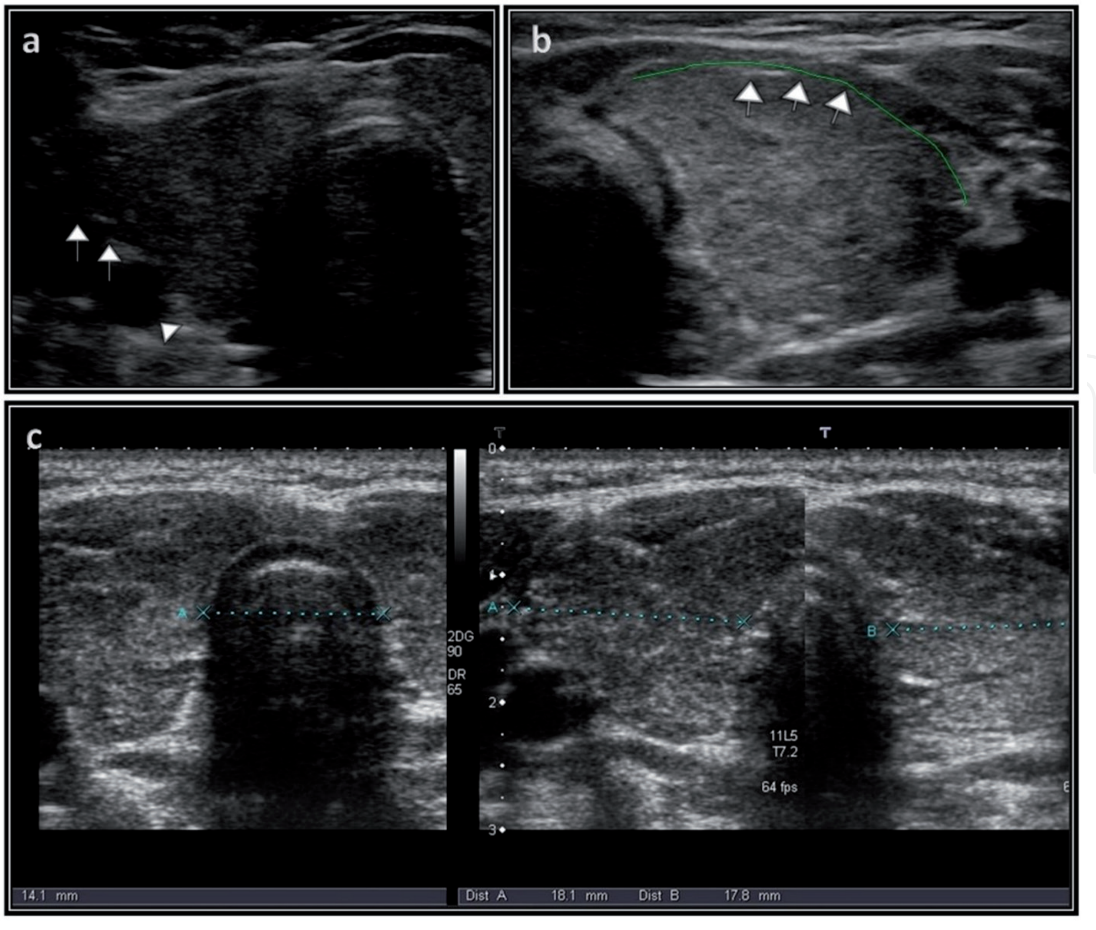

Figure 5.
Practical measurement methods for goiter There is an extension (arrows) of the gland over the anterior surface of the common carotid artery (arrowhead) in the transverse plane (a). The anterior surface (arrows) of the gland is bulging and convex (green line) (b). The right and left lobes dimensions in the transverse plane are 18.1 and 17.8 mm, respectively. The transverse diameter of the trachea is 14.1 mm. In the transverse plane, the transverse diameters of both lobes are summed and divided to the transverse diameter of the trachea. The tracheal index is calculated as 2,45 and interpreted as goiter. Cause normal range of the index is considered to be 1.7–2.4. This method is more appropriate for the pediatric population(c, Courtesy of Prof Dr. Suat Fitoz from his archive. Department of Pediatric Radiology, Ankara University School of Medicine, Ankara/Turkey).

3. Hypothyroidism

Hypothyroidism that results from low levels of thyroid hormone is one of the most common endocrine disorders. It has various etiology and manifestations; when it is untreated, it increases morbidity and mortality. The etiology of the hypothyrodism is seen in **Table 1**. While the main cause of hypothyroidism is still iodine-deficient diet worldwide, it is autoimmune thyroid disease (also known as Hashimoto's thyroiditis) in regions where dietary iodine intake is sufficient. Today, it is successfully treated with exogenous thyroid hormone [1]. According to the NHANESIII (National Health and Nutrition Examination Survey), based on a population study consisting of 12 years old and older, the prevalence of overt hypothyroidism among adults in the United States was 0.3% and subclinical hypothyroidism 4.3%. Female gender and increasing age were associated with presence of thyroid disorders and abnormality of thyroid lab results [13].

Basically, as related to the region, hypothyroidism etiologies are divided into two categories. If there is a problem with thyroid gland, it is named as "primary hypothyroidism". While the problem with hypothalamic-pitutary axis, it is named as "secondary (or central) hypothyoridism". The role of the ultrasound in

Primary hypothroidism
Fetal hypothyroidism (maternal thyroid-blocking antibodies, maternal antithyroid medication, maternal iodine deficiency, and iodine overload (such as from iodine-based antiseptics))
Congenital hypothyroidism *Transient* (maternal thyroid-blocking antibodies, maternal antithyroid medication, maternal iodine deficiency, and iodine overload (such as from iodine-based antiseptics)) *Permanent* • Thyroid dysgenesis (Agenesis, hemiagenesis, hypoplasia, and ectopia.) • Dyshormonogenesis
Iodine deficiency
Thyroiditis • Chronic lymphocytic thyroiditis (named as Hashimoto thyroiditis) • Subacute granulomatous thyroiditis (named as De Quervain disease) • Painless thyroiditis (Silent thyroiditis-Postpartum thyroiditis) • Suppurative thyroiditis • Drug-induced thyroiditis
Others Surgery, Thyroid radioactive iodine therapy, Radiotherapy to head or neck area
Secondary (central) hypothyroidism Neoplastic, infiltrative, inflammatory, genetic or iatrogenic disorders of the pituitary or hypothalamus.

Table 1.
The etiology of the hypothyrodism.

hypothyroidism reveals, when the etiology is primary hypothyroidism. Patients are usually referred to radiology clinics if elevated thyroid stimulating hormone (TSH) levels or palpable goiter are detected. In addition, also, when incidentally an abnormality is detected in the neck ultrasound, and for control purposes during pregnancy and before pregnancy.

With appropriate clinical history and laboratory results, ultrasonography in hypothyroidism can play an active role in differential diagnosis, follow-up, and treatment decision in some cases. For this reason, interdisciplinary communication should be at the highest level.

4. The role of thyroid ultrasound in hypothyroidism

In this section we will discuss ultrasound about findings, importance and role in differential diagnosis based on etiology of primary hypothyroidism.

4.1 Fetal hypothyroidism

Transplasental migration of maternal thyroid-blocking antibodies, and maternal antithyroid medication to fetus, maternal iodine deficiency on dietary, and iodine overload such as from iodine-based antiseptics can cause fetal hypothyroidism. Similar reasons may lead to transient congenital hypothyroidism in the newborn period after delivery. Fetal hypothyroidism is clinically associated with an increased risk of miscarriage and recurrent miscarriages, prematurity, impaired neurolation, and mental retardation.

In pregnancy, ultrasonography is a helpful tool to assess thyroid status in utero [7]. Ranzini et al. created the nomograms of fetal thyroid size by using the 5th, 10th, 50th, 90th, and 95th percentiles based on biparietal diameter and gestational age. They measured thyroid circumference without intraobserver or interobserver variability. It was found that variations in thyroid circumference measurements increased with both larger biparietal diameter and advancing gestational age. The context of this study is that fetal goiter may develop during pregnancy in women with Graves' disease and taking antithyroid drugs. Evaluation of goiter in the fetuses of these patients is important in terms of justifying the invasive and risky procedures such as amniocentesis, which is necessary for the determination of fetal thyroid hormone status [14]. In some case reports, fetal goiter and hypothyroidism have been investigated and it has been reported that it can be successfully treated with intraamniotic injections of tri-iodothyronine and thyroxine. It is thought that recognition and treatment of fetal goiter can reduce obstetric complications and improve the prognosis for normal growth and mental development of affected fetuses [15, 16]. Evaluation of fetal thyroid size in mothers with Graves' disease may also be useful in adjusting the dose of antithyroid medication and preventing fetal and neonatal goiter and hypothyroidism [7].

4.2 Congenital hypothyroidism

The incidence of congenital hypothyroidism is 1 in 1,400–4,000 newborns. Early diagnosis of hypothyroidism is very important by screening with the Guthrie test performed on the 5th postnatal day. After an abnormal Guthrie test, it is necessary to investigate the etiology and start hormone replacement therapy quickly to ensure proper neuronal and psychological growth [11]. Congenital hypothyroidism can be divided into two major categories: transient and permanent.

4.2.1 Transient congenital hypothyroidism

Transplacental migration of maternal thyroid-blocking antibodies and maternal antithyroid medication to the fetus, maternal iodine deficiency on dietary, and iodine overload such as from iodine-based antiseptics can cause transient congenital hypothyroidism in the newborn period after delivery. Newborns with transient congenital hypothyroidism do not need lifelong replacement therapy. Since this situation is temporary, no further imaging is required [17].

4.2.2 Permanent congenital hypothyroidism

Causes of permanent congenital hypothyroidism include thyroid dysgenesis responsible for about 80% of cases, dyshormonogenesis responsible for about 20%, and rarely seen hypopituitarism (not mentioned here). In congenital hypothyroidism, US examination is the primary method for distinguishing orthotopic from ectopic thyroid; then, further investigation is thyroid scintigraphy.

4.2.2.1 Thyroid dysgenesis

Athyreosis refers to an empty thyroid lodge caused by agenesis or ectopia and manifests as an empty fossa. In the presence of athyreosis, the presence of echogenic triangles, usually smaller than 5 mm, on both sides of the trachea, representing ultimobranchial and connective tissue residue, maybe misinterpreted as hypoplastic or dysplastic thyroid. This tissue, sometimes containing microcysts, does not flow or is minimal on color Doppler examination [18, 19]. The ultrasound finding of the athyreosis caused by agenesia is seen in **Figure 6**.

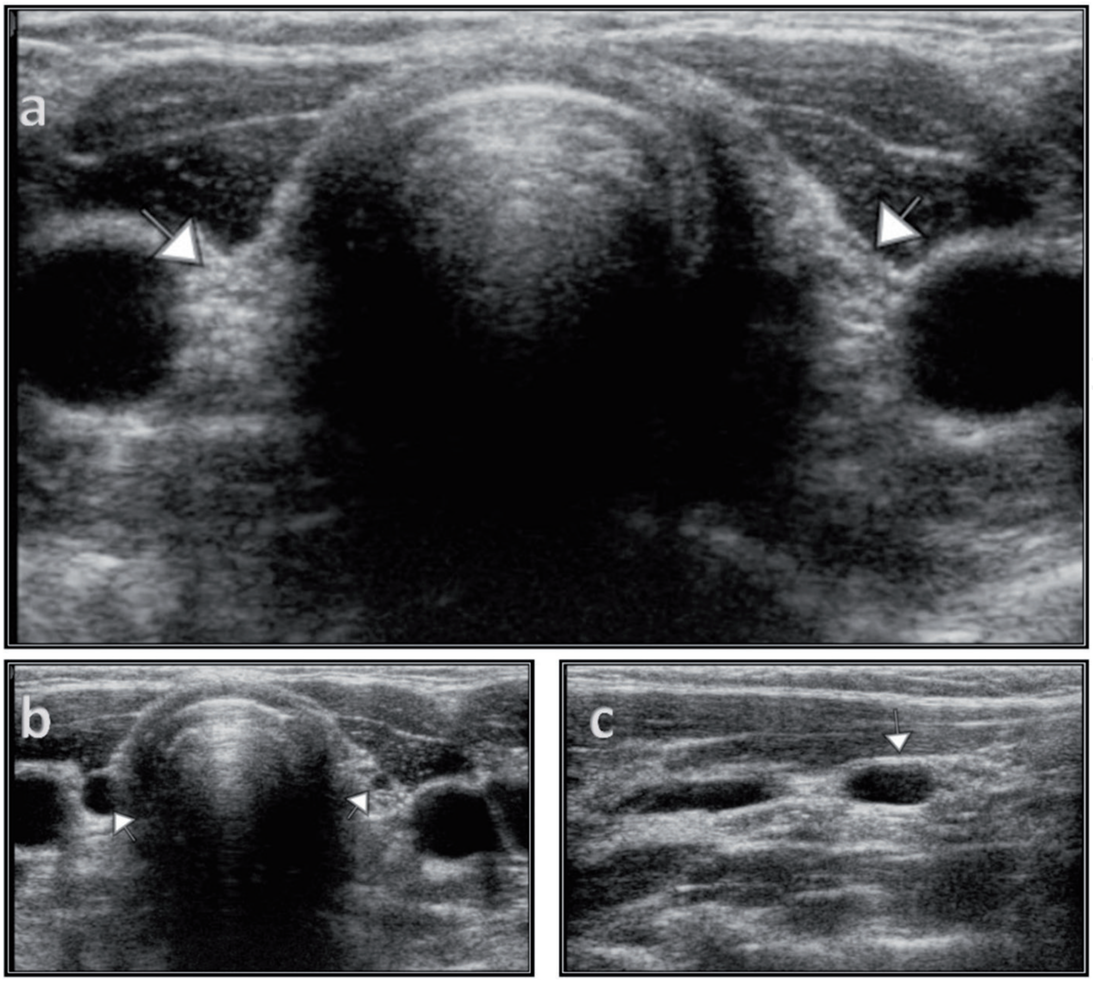

Figure 6.
(a) Athyreosis, empty thyroid lodge caused by agenesis. The arrows indicate echogenic triangles, representing ultimobranchial and connective tissue residue. (b) In the transverse and (c) sagittal planes, as in this case, there are bilateral cysts (arrows), also called ultimobranchial cysts, in the empty thyroid lodge. There is no flow on Color Doppler Imaging (not shown). (Courtesy of Prof Dr. Suat Fitoz from his archive. Department of Pediatric Radiology, Ankara University School of Medicine, Ankara/Turkey).

Due to the nature of thyroid gland embryology, when athyreoisis is detected in a patient, neck scans are required to search for the thyroid gland from the base of the tongue to the superior mediastinum in the midline on the embryological migration trace of the thyroid gland. The ectopic thyroid gland can be located in lingual, sublingual, hyoid, infrahyoid, and mediastinal. The lingual thyroid, the most common form of thyroid dysgenesis, accounts for 75% of the functioning tissues in cases of congenital hypothyroidism. On ultrasonography, ectopic thyroid tissue is well-defined oval shaped, and on color Doppler imaging it is usually hypervascular. Ectopia may initially be overlooked due to adequate hormone production in the neonatal period. In early childhood, hypothyroidism may become evident due to the increased need for thyroid hormone. Detection of the ectopic thyroid gland in scintigraphy depends on the size of the gland and whether it functions or not. Retrosternal, endolaryngeal, or endotracheal ectopic thyroids in the mediastinum are usually not detectable sonographically, in which case scintigraphic studies are required [11, 19–21]. Lingual ectopic thyroid cases are presented in **Figure 7**.

Athyreosis and residual echogenic tissues in the thyroid gland site observed in agenesis are unilateral in hemiagenesis. It can be detected incidentally in asymptomatic euthyroid patients, and in children with thyroid hemiagenesis, thyroid hormones may decrease during adolescence when the need for thyroid hormone is high. The absence of unilateral lobe and normal or goiter lobe on the opposite side can be observed on ultrasound. Scintigraphy can be used as a complement to exclude any additional orthotopic/ectopic functional thyroid tissue [20].

Thyroid hypoplasia, which is difficult to diagnose among thyroid dysgenesis, is responsible for 5% of congenital hypothyroidism cases. On ultrasound, the gland is usually hypoechoic, orthotopic (where it should be, not ectopic), normally shaped and normal in size or small for its age. Hypoplasia can be diagnosed in newborns with a tracheal index of less than 1.7 and a low uptake on scintigraphy [11]. The thyroid hemiaganesis and hypoplasia are demonstrated in **Figure 8**.

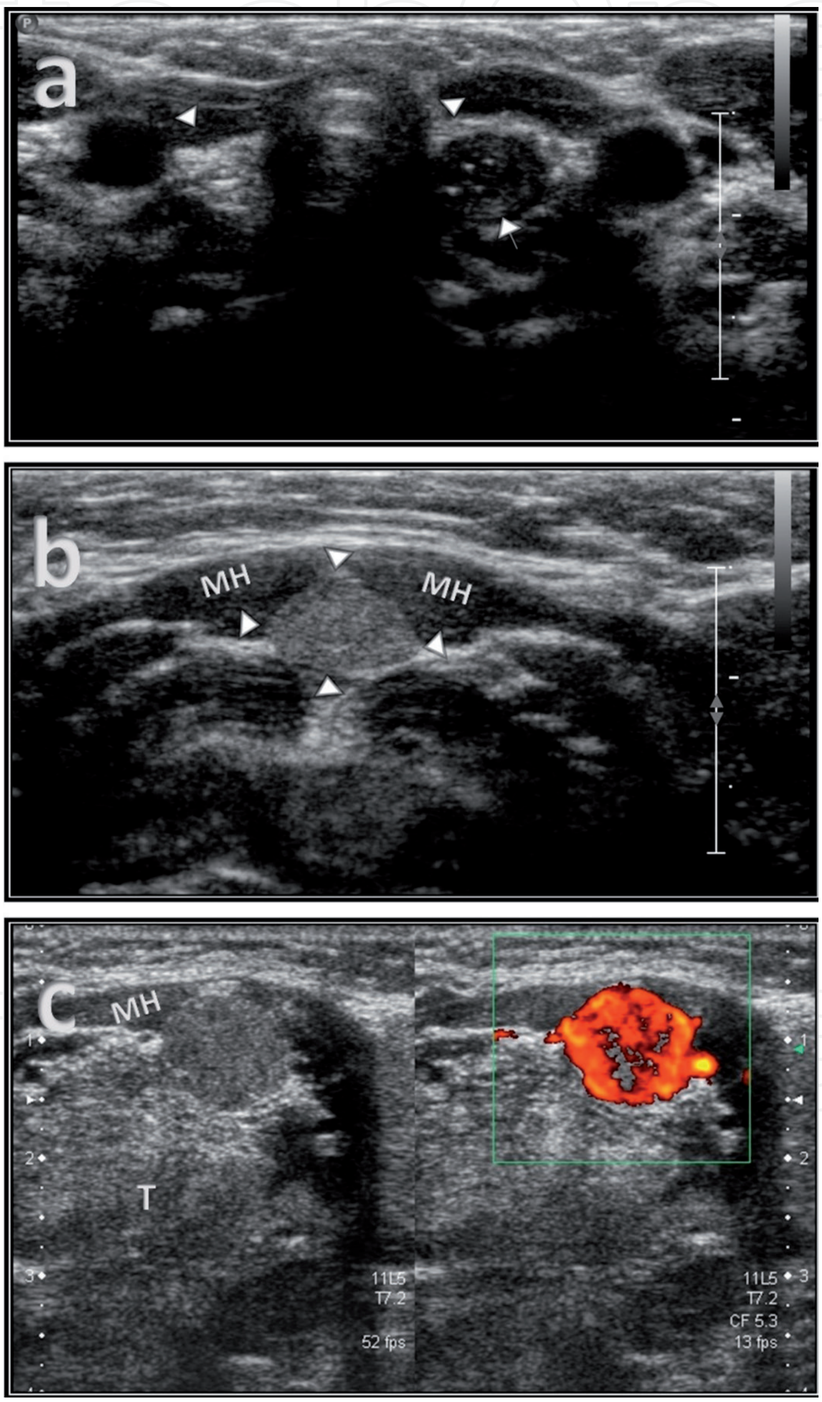

Figure 7.
(a) Athyreosis, empty thyroid lodge. The arrowsheads indicate echogenic triangles, representing ultimobranchial and connective tissue residue. The esophagus is more prominent (arrow). (b) The floor of the mouth superficial ultrasound examination, the lingual ectopic thyroid is seen as similar as normal thyroid echogenicity. (c) Another case of lingual ectopic thyroid is seen as ovoid, isoechoic, and hypervascular. (MH: Mylohyoid muscle, T: Tongue) (Courtesy of Prof Dr. Suat Fitoz from his archive. Department of Pediatric Radiology, Ankara University School of Medicine, Ankara/Turkey).

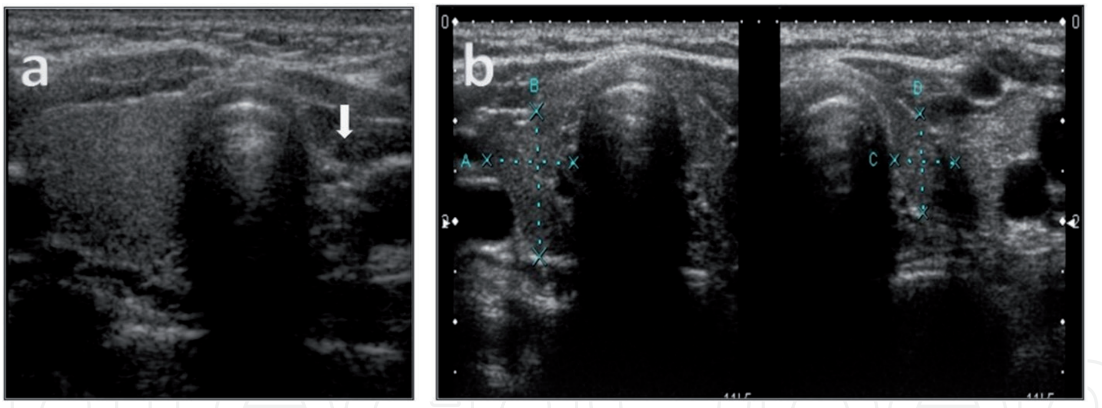

Figure 8.
(a) In hemiagenesis, athyreosis and residual echogenic tissue (arrow) is observed in the left thyroid gland site unilaterally. (b) The case of thyroid hypoplasia. The right and left lobes dimensions in the transverse plane are 11.3 and 7.9 mm, respectively. The transverse diameter of the trachea is 13,7 mm. The tracheal index was calculated as 1,4 and interpreted as hypoplasia. (Courtesy of Prof Dr. Suat Fitoz from his archive. Department of Pediatric Radiology, Ankara University School of Medicine, Ankara/Turkey).

4.2.2.2 Dyshormonogenesis

It constitutes 20% of congenital hypothyroidism. Dyshormonogenesis, in which the thyroid gland mostly has normal aspects and non-function, is characterized by defects in enzymatic processes in hormone production steps. The thyroid gland is orthotopically located. It may be of normal size and shape, or goiter may develop under thyroid-stimulating hormone. Since scintigraphic uptake may show differences due to deficiencies in different steps in dyshormonogenesis, uptake may be observed in some forms but not in some cases [20–22].

4.3 Iodine deficiency

Dietary iodine deficiency is still the most common cause of goiter and hypothyroidism in endemic areas of the world. Low hormone production after low iodine intake induces the elevation of thyroid-stimulating hormone. This causes diffuse and subsequently nodular goiter at the expense of maintaining the euthyroid state. Although iodine deficiency does not have a pathognomonic ultrasound finding, goiter with diffusely increased or multiple nodules could be detected on ultrasound.

4.4 Thyroiditis

Diffuse enlargement of the thyroid gland is a common finding. While iodine deficiency is still the most common cause of goiter and hypothyroidism worldwide, in the United States and other countries where dietary iodine intake is adequate, chronic lymphocytic thyroiditis (CLT) is the most common cause of goiter and hypothyroidism. CTL is also called Hashimoto's thyroiditis. Thyroiditis is the general definition of thyroid inflammation that can occur for many reasons. Although the spectrum of thyroiditis often overlaps in clinical, imaging, and laboratory findings, ultrasound is a very useful tool in evaluating thyroiditis as it provides information about the etiology and clinical course.

4.4.1 Chronic lymphocytic (Hashimoto's) thyroiditis (CLT)

Chronic lymphocytic thyroiditis is the most common form of thyroiditis in which autoimmunity plays a role in the pathogenesis. About 10% of the U.S. population and an estimated 25% of women over 65 exhibit antibodies to thyroid peroxidase. In Hashimoto thyroiditis, the thyroid cells are ruined through the cell and antibody-mediated immune process. The damage starts via the formation of antithyroid antibodies that attack the thyroid tissue and finally result in progressive fibrosis. Until late in the disease process, the condition is sometimes not diagnosed. The most common laboratory findings show elevated thyroid-stimulating hormone (TSH) and low thyroxine (T4) levels, along with increased antithyroid peroxidase (anti-TPO) antibodies. Women are affected 10 times more than men. The disease is frequently diagnosed between the 3rd and 5th decades [23]. The most important feature of the disease is the invasion of the thyroid gland parenchyma by lymphoplasmacytic cells. This situation reveals enlargement of the thyroid gland, heterogeneity, and diffuse decrease in echogenicity, among the most important findings on ultrasound. Sonographically, the clinical course ranges from heterogeneous and hypoechoic parenchyma to fibrosis and gland atrophy. Patients with chronic lymphocytic thyroiditis may develop primary thyroid lymphoma, representing less than 5% of all thyroid malignancies. Primary thyroid lymphoma should be suspected if an atrophic gland enlarges rapidly or especially in the presence of systemic symptoms [24].

There are studies in which high positive and negative predictive values of hypoechogenicity, indicating autoimmune disease and the risk of clinically significant hypothyroidism. It even may have an equal predictive value as the presence of thyroid autoantibodies for the development of hypothyroidism [25–28]. While positive antithyroid peroxidase antibodies are predictive of the clinical syndrome, a small subset of no more than 10–15% of the population has individuals with the clinically evident disease who are serum antibody negative [23]. Recognition of the ultrasonographic pattern of chronic lymphocytic thyroiditis in this subgroup may facilitate in determining the etiology and patient management.

4.4.1.1 Ultrasonographic patterns of Hashimoto's disease

The different appearance patterns can describe changes in CLT at different stages of the disease from early to late. The findings of chronic lymphocytic thyroiditis are presented in **Figure 9**. These patterns can be listed as hypoechoic and heterogeneous, pseudomicronodular, pseudomacronodular, markedly hypoechoic, and fibrosis-atrophy. These patterns do not represent an absolute sequential progression. Although fibrosis and atrophy are typically late manifestations, any other patterns may be seen early in the disease.

Normal thyroid tissue, as mentioned above, is hyperechoic compared to muscle tissue due to its iodine content. The thyroid gland has a uniformly homogeneous echogenicity. When the thyroid gland is exposed to lymphocytic infiltration, iodine-containing colloidal contents and normal cells in the parenchyma are destroyed. Lymphocyte infiltrates appear hypoechoic, similar to the low echo observed due to lymphocytes in lymphoid tissues. Hypoechogenicity formed by infiltrates together with normal hyperechoic areas causes a heterogeneous appearance in the gland. Both the degree of hypoechogenicity and heterogeneity varies with the distribution and severity of the lymphocytic infiltration.

When areas of hypoechoic lymphocytic infiltrate are more discrete, localized hypoechoic foci representing lymphocyte clusters are defined as pseudomicronodules. These pseudonodules are flame-shaped, hypoechogenic foci not exceeding 1 cm in size with a thin hyperechogenic fibrotic rim.

Pseudomacronodules, when the hypoechoic infiltrate areas are larger, the pseudonodules also appear larger, can often cause problems in distinguishing them from true nodules. When they are unilateral, nodule features should be examined in terms of malignancy association.

DOI: http://dx.doi.org/10.5772/intechopen.99989

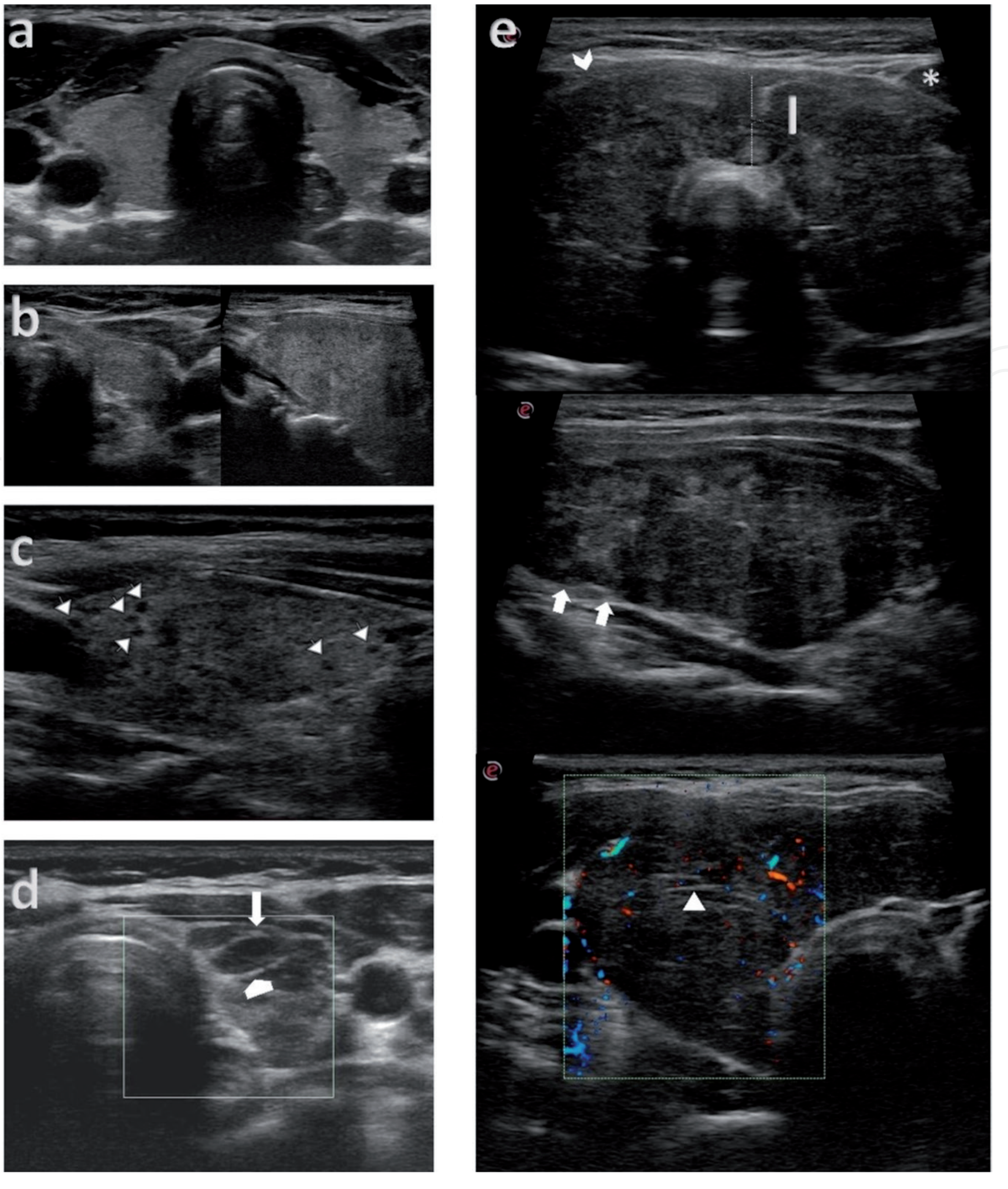

Figure 9.
Ultrasound findings of chronic lymphocytic thyroiditis. (a) The normal appearance of the gland for comparison. (b) Hypoechogenicity-heterogeneity pattern. The left lobe in the transverse and the right in the sagittal plane are shown. Hypoechogenicity formed by infiltrates and normal hyperechoic areas causes a heterogeneous appearance (relative according to a) in the gland. (c) Pseudomicronodular pattern. Hypoechoic lymphocytic infiltrate is discrete, localized hypoechoic foci (arrows) representing lymphocyte clusters are defined as pseudomicronodules that are flame-shaped, hypoechogenic foci not exceeding 1 cm in size with a thin hyperechogenic fibrotic rim. (d) Pseudomacronodular pattern. When the hypoechoic infiltrate areas are larger, the pseudonodules (arrow) also appear larger. Hyperechoic thin fibrotic septa (arrowhead) are observed in the periphery. (e) Markedly hypoechoic and fibrotic pattern. Gland sizes have increased, as can be seen from the isthmus (I) thickness. Bowing is observed in the anterior (arrowhead) of both lobes of the gland. The echogenicity of the gland is as low as the strap muscles indicated by asterisks. In the sagittal image, it is observed that the gland contours (arrows) are lobulated. In the Color Doppler Imaging, it was observed that the blood supply of the gland decreased. The thin echogenic linear formation indicated by the triangle represents fibrosis.

The markedly hypoechogenic pattern is typically seen as a large inflamed goiter. The thyroid parenchyma may be completely infiltrated with lymphocytes rather than discrete lymphocyte centres. The thyroid is equal to or more hypoechoic than adjacent muscle tissue. Thyroid lymphoma may have a very similar appearance and should be considered in the differential diagnosis, especially if there is rapid growth [24].

Finally, in the fibrosis-atrophy stage of progression of thyroid inflammation, fibrosis develops and appears sonographically as hyperechoic linear and curvilinear bands.

4.4.1.2 Doppler imaging findings of Hashimoto's disease

Color Doppler imaging (CDI) is a technique that complements the greyscale evaluation in thyroid ultrasonography and provides information about vascularity. The frequency shift that is constituted by increasing the frequency with the objects approaching the transducer and decreasing the frequency with the diverging ones, which is obtained by echoing the sound waves sent to the tissue, gives information about direction and speed. This phenomenon is also known as the "Doppler effect". CDI depends on the angle between the transducer and vessel and flow direction, whereas the "Power Doppler imaging (PDI)" is not. PDI is motion-sensitive and often amplifies the Doppler signal. It is independent of velocity, angle and flow direction. Allows slower flows to be detected with higher sensitivity than color Doppler. In the normal thyroid gland parenchyma, less than 5 vascular coding is expected in the sampling window at the lowest pulse repetition frequency (PRF) values without background noise on color Doppler ultrasound (CDI).

CDI findings may vary according to the stage of the disease. In the early and acute phase of the disease (usually in thyrotoxicosis, also known as Hashitoxicosis due to thyroid gland destruction), increased glandular blood supply may be observed, which may be due to trophic stimulation of TSH associated with the development of hypothyroidism. Doppler examination findings may show a diffuse hypervascularization pattern similar to Graves' disease during this time period. A decrease in Doppler signals will be observed in the advanced stages due to intense fibrosis and avascularity in Doppler examination. The Hashitoxicosis case is shown in **Figure 10**.

In Hashimoto's disease, there are cases with negative autoantibodies and hypothyroidism and a group with positive autoantibodies but without overt hypothyroidism. Sonographic and Doppler findings similar to Hashimoto's disease can be observed in euthyroid patients with positive anti-TPO autoantibodies. A study by Acar et al. found that only euthyroid individuals with high levels of antithyroid autoantibodies had similar sonographic structural and hemodynamic characteristics on Doppler examination, as observed in patients with Hashimoto's disease with hypothyroidism. They thought that structural and hemodynamic changes could begin much earlier than symptoms and hormonal imbalance [29].

4.4.1.3 Lymph nodes and microcalcifications in Hashimoto's disease

In the presence of Hashimoto's thyroiditis, one of the most common conditions encountered in thyroid ultrasonography is lymph nodes found in the central lymph node compartment and at levels III and IV. Knowing the characteristics of disease-associated reactive enlarging lymph nodes is important to avoid invasive unnecessary biopsies to rule out metastatic or lymphoproliferative diseases. A healthy lymph node consists of a hilum with fatty content and afferent-efferent vessels, which is hyperechoic on ultrasonography, and a more hypoechoic cortex with a thickness of less than 3 mm. Normal shape is fusiform. The normal ranges of lymph node sizes vary according to the station where the lymph node is located, and cut-off values are highly controversial. They are defined by the long and short axis dimensions obtained perpendicular to each other in the plane where the lymph node appears longest. Although there is no clear rule, 1 cm above the short axis is diagnosed pathologically in head and neck ultrasonography. As the short axis cut-off values get smaller, the sensitivity increases, and the specificity decreases, causing extra and unnecessary invasive procedures. Rather than the length of the short axis, the shape of the lymph node, the thickness of the cortex, and whether the fatty hilum can be distinguished are more important in defining the pathologies.

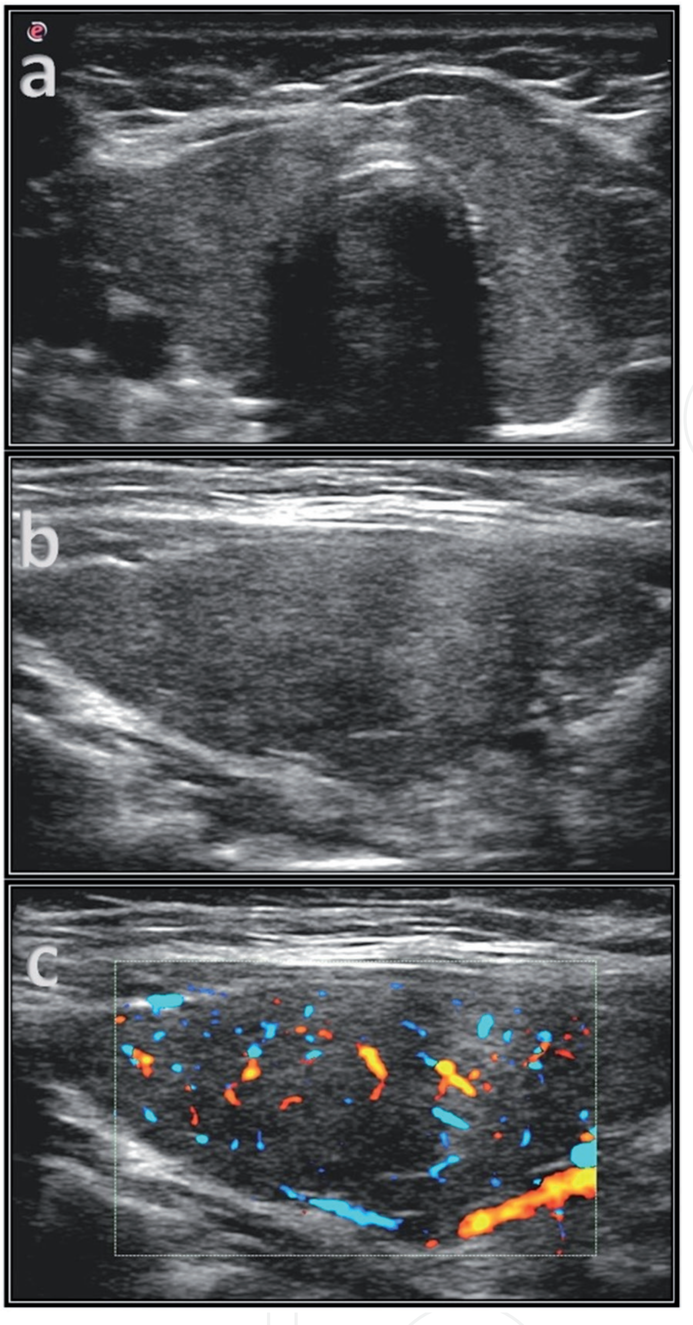

Figure 10.
A 37-year-old female patient is admitted with low TSH and high T4. In the thyroid ultrasound performed, (a) Diffuse decrease in echogenicity of the thyroid gland is observed in the transverse plane, and its echotexture is heterogeneous. (b) Similar findings are observed in the sagittal image. (c) Here, an increase in vascularity is observed in Color Doppler Imaging, which may be in the early or acute phase of the disease. The patient was diagnosed with Hashitoxicosis with clinical-laboratory and ultrasonographic findings.

Whether it is a metastatic or lymphoproliferative disease, infection or inflammatory processes such as Hashimoto, the lymph nodes become larger and more prominent. However, pathology is highly recognizable due to nuance differences such as shape, echo pattern and existence of fatty hilus. These features increase success in choosing the right patient for further examination.

It is lymph node enlargement, defined as reactive lymph node enlargement, defined in infectious and inflammatory diseases such as Hashimoto's. In fact, this is a diagnosis of exclusion. This name is given to lymph node enlargements in which malignant features such as ovoid or round shape, the fatty hilum could not be distinguished as hyperechoic due to infiltration, and blood supply from outside the hilum are excluded. The reactive lymph node should be fusiform, have a homogeneous hypoechoic cortex, and the fatty hilus should be distinguishable

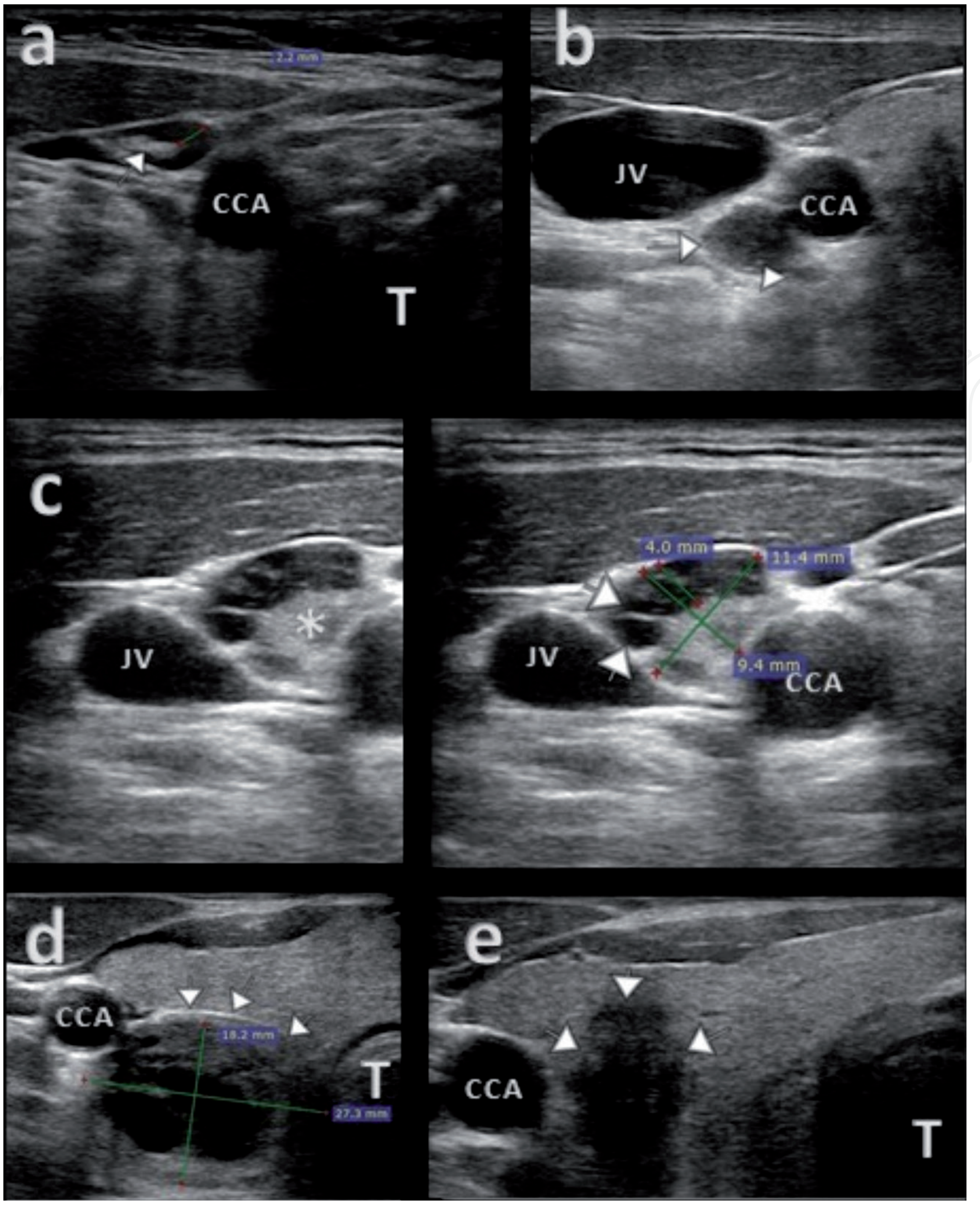

Figure 11.
Examples of lymph nodes that may be encountered during thyroid ultrasonography examination. a) Enlarged reactive lymph node at right cervical level III (most commonly observed in the pretracheal area, not shown here) secondary to the inflammatory process in Hashimoto's disease. Distinguishable hyperechoic fatty hilus marked with arrow. Homogeneous, hypoechoic cortex thinner than 3 mm. b-e) Images aquised from another patient. b) A pathologically enlarged lymph node (arrow) in the right cervical level III-IV, with a round shaped, hyperechogenic fatty hilus indistinguishable, with a small echogenic focus compatible with microcalcification (arrowhead). c) At right cervical level III, although the short axis is shorter than 1 cm (9.4 mm) and the fatty hilus (asteriks) can be distinguished, pathological lymph node is characterized by a heterogeneous and thicker (4 mm) than 3 mm cortex with cystic areas (arrows). d) Further inferiorly, at the right cervical level IV. Pathologically enlarged lymph node with cystic-solid component, with a short axis (18.2 mm) greater than 1 cm, preserved fat plane (arrows) intermediate with the thyroid, e) The source of all these metastatic lymph nodes is a malignant thyroid nodule located in the right lobe, with lobulated contour, markedly hypoechoic compared to the strap muscle, and taller-than-wide shaped. FNA was performed and the diagnosis of papillary thyroid cancer was confirmed cytopathologically.

as hyperechoic. Microcalcification and cystic changes (unless abscess formation secondary to suppurative lymphadenitis) is not observed in reactive lymph node enlargement. In this case, the pathognomonic findings of papillary thyroid cancer metastasis are considered, and it is necessary to look for a malignant nodule in the thyroid. In addition, reactive lymph nodes enlargements in Hashimoto's disease are located in the pretracheal and perithyroidal areas. In **Figure 11**, lymph nodes detected in thyroid ultrasonography examinations are observed.

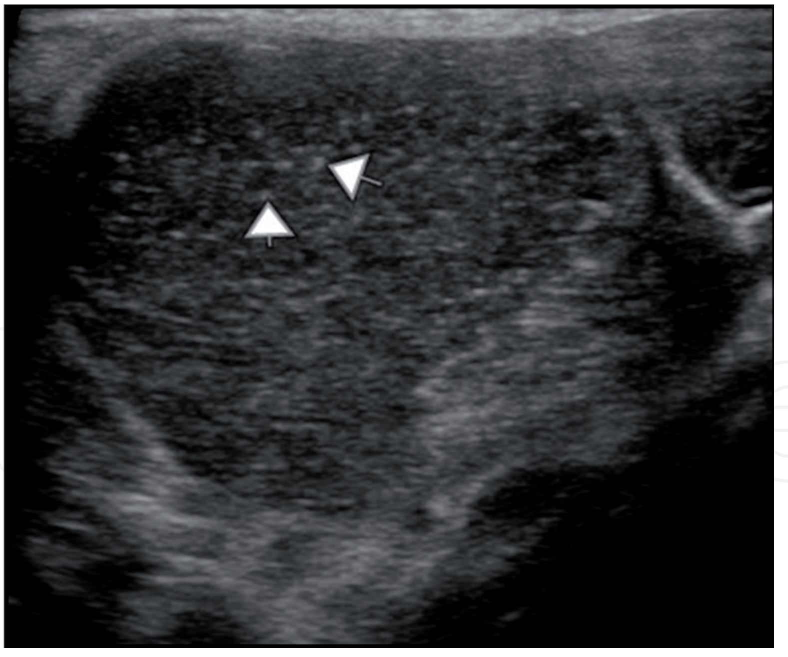

Figure 12.
Thyroid ultrasonography of a patient with Hashimoto's disease. At right lobe, numerous hyperechoic foci with a markedly hypoechoic background, 1–2 mm in size, with no acoustic shadow consistent with microcalcification (arrows). Biopsy was performed to rule out malignancy. The pathology result was reported as chronic lymphocytic thyroiditis.

One of the uncommon manifestations of Hashimoto's disease is diffuse microcalcifications. Microcalcifications are recognized as hyperechogenic foci with a 1–2 mm diameter that do not produce a posterior acoustic shadow. Undoubtedly, one of the pathognomonic findings of papillary thyroid cancer is microcalcification. Since it is a cancer finding, it causes diagnostic difficulties with its detection in Hashimoto's disease and makes fine needle biopsy mandatory to exclude malignancy. Especially when it is difficult to distinguish the pseudonodule from the true nodule, it may cause greater confusion. Cytopathological findings guide the correct diagnosis in such cases. The microcalcification in Hashimoto's Disease is shown in **Figure 12**.

4.4.2 Subacute granulomatous (De Quervain) thyroiditis

DeQuervain or subacute thyroiditis occurs due to the immune response following a viral or upper respiratory tract infection. The disease is often self-limited. However, its clinical presentation is an acute painful neck with systemic symptoms such as tender goiter, fever, fatigue, weight loss, high erythrocyte sedimentation rate or C-reactive protein, suppressed TSH level, and dysphagia. Patients may be hyperthyroid in the acute phase but usually become hypothyroid until they return to the euthyroid state after about 6 to 18 months. The typical ultrasound appearance of the gland is characterized by decreased vascularity of patchy, ill-defined hypoechoic areas in one or both lobes with involvement of the thyroid parenchyma. Sometimes the appearance is described as "lava flow" with diffuse and combined hypoechoic areas. Thus, the acute phase may show hypervascularity, while the subacute phase may reflect diffuse hypovascularity. The case of subacute granulomatous thyroiditis is demonstrated in **Figure 13**.

4.4.3 Painless thyroiditis (silent thyroiditis-postpartum thyroiditis)

Painless thyroiditis is a symptom-based classification, which includes both silent thyroiditis and postpartum thyroiditis. Silent thyroiditis is autoimmune and

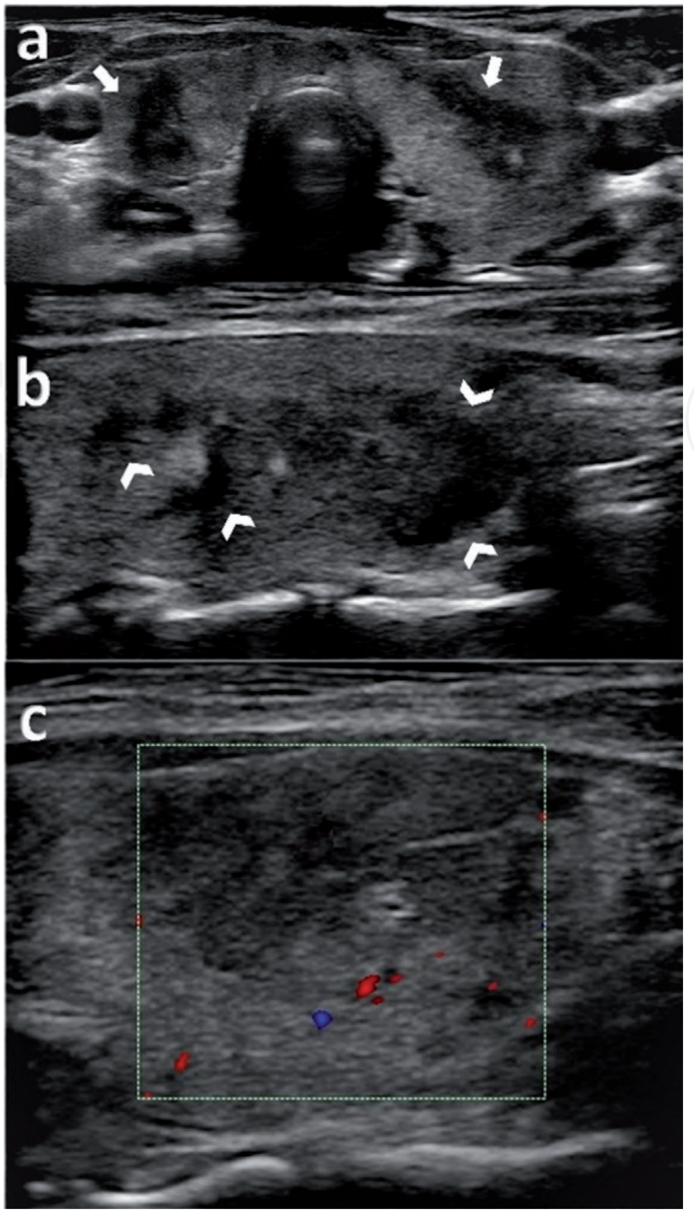

Figure 13.
A 40-year-old female patient presented with pain and tenderness in the anterior neck and general fatigue. It is understood from her history that he had a viral upper respiratory tract infection 2 weeks ago. Laboratory findings were high erythrocyte sedimentation rate, C-reactive protein and low TSH level. In the ultrasound; (a) In the transverse plane, there is an appearance like a focal nodular hypoechoic lesion (arrows) with unclear borders in both lobes. (b) The sagittal view of the left lobe shows that the lesion extends and spreads craniocaudal. Thus, with this finding, it was first understood that this was not a true nodule. Thyroiditis was considered as a preliminary diagnosis. Patchy hypoechoic areas are likened to "lava flows". (c) In addition, decreased blood supply in thyroiditis areas, as observed in Color Doppler examination, is another finding helpful in the diagnosis. It was diagnosed as De Quervain thyroiditis with clinical-laboratory and ultrasonographic findings.

considered a temporary form of Hashimoto's thyroiditis. They have lower thyroid autoantibody levels than those seen in Hashimoto's thyroiditis and frequently seen in women aged 30–50 years. Postpartum thyroiditis got this name because it occurs within 1 year after birth. It is seen in 10% of all pregnancies, and the recurrence rate in subsequent pregnancies is up to 70%. Patients may present either in the thyrotoxic phase, which is usually mild and lasts for 1–2 months or in the hypothyroid phase, typically transient, lasting 4–6 months. On ultrasound, hypoechogenicity is observed, as in other forms of autoimmune thyroid disease. Unlike Hashimoto's, hyperechoic fibrotic bands and marked hypoechogenicity are usually absent [30].

4.4.4 Suppurative thyroiditis

This type is a rare infection caused by a bacterial pathogen, seen in immunocompromised patients or children and young adults with branchial anomalies. A euthyroid patient may present with inflammation such as fever, sore throat, painful swelling, skin erythema, and lymphadenopathy. On ultrasound, an increase in blood supply to the thyroid gland is usually observed. Sometimes abscess formation can be observed [30].

5. Follow-up

The necessity of the ultrasonographic follow-up of the thyroid gland for hypothyroidism is debatable. However, when the antibodies are negative in the suspected cases, the ultrasonographic process of thyroiditis may be the sole evidence for chronic lymphocytic thyroiditis. Pattern recognition is a tool for diagnosis in such cases. In addition, subclinical hypothyroidism that may need treatment and other non-chronic thyroiditis outcomes can be determined by ultrasonographic follow-up.

Another follow-up reason is for malignancy that is occurred as papillary thyroid cancer (PTC) and primary thyroid lymphoma. Publications are showing that both malignancies are associated with hypothyroidism. Along with hypothyroidism, PTC suspected nodules have the same features (hypoechogenicity, microcalcifications, taller than wide shape etc) regardless of thyroid hormone state. The key role of the follow-up in hypothyroidism is that the nodule is true whether or not. If a new nodule develops malignance should be ruled out. Thereby the recording and the comparison with the old image is precious. Another malignancy is primary thyroid lymphoma. The risk increases with chronic lymphocytic thyroiditis. Once lymphocytes diffusely infiltrate the thyroid gland, the thyroid is equal to or more hypoechoic than adjacent muscle tissue. Thyroid lymphoma may have a very similar appearance and should be considered in the differential diagnosis, especially if there is rapid growth. It is often not easy to distinguish between the two situations. Therefore, the correlation of sonographic findings with systemic symptoms is important.

6. Conclusion

Ultrasonography is an indispensable complementary tool in hypothyroidism, which can be seen in almost all ages, from fetal life to geriatric age groups. Knowing the characteristic ultrasonographic findings of Hashimoto's disease, which is the most common cause of hypothyroidism in areas without iodine deficiency, is very important in diagnosis, especially in patients with negative thyroid autoantibodies. Hypoechogenicity should be remembered that it is the key finding in hypothyroidism. Such that; the predictive value is equal to that of autoantibodies. Another point that should not be overlooked when evaluating the thyroid gland is the cervical lymph nodes. Lymph nodes may reactively enlarge in diseases such as Hashimoto's disease as in malignancies. Rather than the size of the lymph node in the differentiation of reactive-malignancy, findings favoring reactive lymph node enlargements, such as fusiform shape, distinguishable echogenic fatty hilum, blood supply only from the hilum, homogeneous and thin cortex, and no changes such as cystic or microcalcification. Otherwise, a biopsy should be performed to exclude malignancy. One of the uncommon manifestations of Hashimoto's disease is diffuse microcalcifications. It causes diagnostic difficulties with its detection in Hashimoto's disease and makes fine needle biopsy mandatory to exclude malignancy. Although the details of the thyroid gland can be demonstrated by ultrasonography alone, it can never replace the evaluation of ultrasonography reinforced with clinical knowledge. This synergy will be possible by increasing interdisciplinary communication.

IntechOpen

IntechOpen

Author details

Hakan Baş
Department of Radiology, Occupational and Environmental Diseases Hospital, Ankara, Turkey

*Address all correspondence to: hakanbas7@outlook.com

IntechOpen

© 2021 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/3.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

References

[1] Patil N, Rehman A, Jialal I. Hypothyroidism. StatPearls. Treasure Island (FL): StatPearls Publishing Copyright © 2021, StatPearls Publishing LLC.; 2021.

[2] Fujimoto Y, Oka A, Omoto R, Hirose M. Ultrasound scanning of the thyroid gland as a new diagnostic approach. Ultrasonics. 1967;5(3):177-180.

[3] Milas M, Mandel SJ, Langer JE. Advanced Thyroid and Parathyroid Ultrasound. 2017.

[4] The thyroid nodule. Ann Intern Med. 1982;96(2):221-32.

[5] AIUM-ACR-SPR-SRU Practice Parameter for the Performance and Interpretation of a Diagnostic Ultrasound Examination of the Extracranial Head and Neck. J Ultrasound Med. 2018;37(11):E6-E12.

[6] Richman DM, Frates MC. Ultrasound of the Normal Thyroid with Technical Pearls and Pitfalls. Radiol Clin North Am. 2020;58(6):1033-1039.

[7] Blum M. Ultrasonography of the Thyroid. In: Feingold KR, Anawalt B, Boyce A, Chrousos G, de Herder WW, Dhatariya K, et al., editors. Endotext. South Dartmouth (MA): MDText.com, Inc.Copyright © 2000-2021, MDText.com, Inc.; 2000.

[8] Chanoine JP, Toppet V, Lagasse R, Spehl M, Delange F. Determination of thyroid volume by ultrasound from the neonatal period to late adolescence. Eur J Pediatr. 1991;150(6):395-399.

[9] Zimmermann MB, Hess SY, Molinari L, De Benoist B, Delange F, Braverman LE, et al. New reference values for thyroid volume by ultrasound in iodine-sufficient schoolchildren: a World Health Organization/Nutrition for Health and Development Iodine Deficiency Study Group Report. Am J Clin Nutr. 2004;79(2):231-237.

[10] Moradi M, Hashemipour M, Akbari S, Kor Z, Mirbod SA, Kooshanmehr MR. Ultrasonographic evaluation of the thyroid gland volume among 8-15-year-old children in Isfahan, Iran. Adv Biomed Res. 2014;3:9.

[11] Goldis M, Waldman L, Marginean O, Rosenberg HK, Rapaport R. Thyroid Imaging in Infants. Endocrinol Metab Clin North Am. 2016;45(2):255-266.

[12] Yasumoto M, Inoue H, Ohashi I, Shibuya H, Onishi T. Simple new technique for sonographic measurement of the thyroid in neonates and small children. J Clin Ultrasound. 2004;32(2):82-85.

[13] Hollowell JG, Staehling NW, Flanders WD, Hannon WH, Gunter EW, Spencer CA, et al. Serum TSH, T(4), and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). J Clin Endocrinol Metab. 2002;87(2): 489-499.

[14] Ranzini AC, Ananth CV, Smulian JC, Kung M, Limbachia A, Vintzileos AM. Ultrasonography of the fetal thyroid: nomograms based on biparietal diameter and gestational age. J Ultrasound Med. 2001;20(6):613-617.

[15] Agrawal P, Ogilvy-Stuart A, Lees C. Intrauterine diagnosis and management of congenital goitrous hypothyroidism. Ultrasound Obstet Gynecol. 2002;19(5):501-505.

[16] Khater C, Ceccaldi PF, Poujade O, Banigé M, Ottenwalter A, Luton D. Foetal thyroid dysfunction: treat the mother first! Horm Res Paediatr. 2015;83(2):136-140.

[17] Silva CT, Navarro OM. Pearls and Pitfalls in Pediatric Thyroid Imaging. Seminars in Ultrasound, CT and MRI. 2020;41(5):421-432.

[18] Sedassari AdA, de Souza LRMF, Sedassari NdA, Borges MdF, Palhares HMdC, de Andrade Neto GB. Sonographic evaluation of children with congenital hypothyroidism. Radiol Bras. 2015;48(4):220-224.

[19] Karakoc-Aydiner E, Turan S, Akpinar I, Dede F, Isguven P, Adal E, et al. Pitfalls in the diagnosis of thyroid dysgenesis by thyroid ultrasonography and scintigraphy. European Journal of Endocrinology. 2012;166(1):43-48.

[20] Hong HS, Lee EH, Jeong SH, Park J, Lee H. Ultrasonography of various thyroid diseases in children and adolescents: a pictorial essay. Korean J Radiol. 2015;16(2):419-429.

[21] Chang YW, Hong HS, Choi DL. Sonography of the pediatric thyroid: a pictorial essay. J Clin Ultrasound. 2009;37(3):149-157.

[22] Williams JL, Paul DL, Bisset G, 3rd. Thyroid disease in children: part 1: State-of-the-art imaging in pediatric hypothyroidism. Pediatr Radiol. 2013;43(10):1244-1253.

[23] Mincer DL, Jialal I. Hashimoto Thyroiditis. StatPearls. Treasure Island (FL): StatPearls Publishing Copyright © 2021, StatPearls Publishing LLC.; 2021.

[24] Kesireddy M, Lasrado S. Thyroid Lymphoma.

[25] Pedersen OM, Aardal NP, Larssen TB, Varhaug JE, Myking O, Vik-Mo H. The value of ultrasonography in predicting autoimmune thyroid disease. Thyroid. 2000;10(3):251-259.

[26] Raber W, Gessl A, Nowotny P, Vierhapper H. Thyroid ultrasound versus antithyroid peroxidase antibody determination: a cohort study of four hundred fifty-one subjects. Thyroid. 2002;12(8):725-731.

[27] Rago T, Chiovato L, Grasso L, Pinchera A, Vitti P. Thyroid ultrasonography as a tool for detecting thyroid autoimmune diseases and predicting thyroid dsfunction in apparently healthy subjects. J Endocrinol Invest. 2001;24(10):763-769.

[28] Rotondi M, Cappelli C, Leporati P, Chytiris S, Zerbini F, Fonte R, et al. A hypoechoic pattern of the thyroid at ultrasound does not indicate autoimmune thyroid diseases in patients with morbid obesity. Eur J Endocrinol. 2010;163(1):105-109.

[29] Acar T, Ozbek SS, Erdogan M, Ozgen AG, Demirel SO. US findings in euthyroid patients with positive antithyroid autoantibody tests compared to normal and hypothyroid cases. Diagn Interv Radiol. 2013;19(4):265-270.

[30] Dighe M, Barr R, Bojunga J, Cantisani V, Chammas MC, Cosgrove D, et al. Thyroid Ultrasound: State of the Art Part 1 - Thyroid Ultrasound reporting and Diffuse Thyroid Diseases. Med Ultrason. 2017;19(1):79-93.