Review Article

The clinical picture of the damage to the organs of the hepatobiliopancreatic area in hypothyroidism

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ABSTRACT

Hypothyroidism is a clinical syndrome caused by hypofunction of the thyroid gland and characterized by a decrease in the content of thyroid hormones in the blood serum. Clinical manifestations of hypothyroidism can be diverse and depend on its etiology, the age of the patient, as well as the rate of development of thyroid hormone deficiency. The disease may have a pronounced clinical picture or, conversely, have no clinical manifestations and be detected randomly. Moreover, the signs of hypothyroidism very often mimic (mask) another pathology. Therefore, the diagnosis of hypothyroidism in some cases is difficult. In this work, a systematic analysis of the literature and clinical studies was carried out, and the negative effect of hypothyroidism in a patient on the liver, biliary system and pancreas was established. When analyzing the effect of hypothyroidism on the liver, no changes were observed in the organ itself. However, serum enzymes increased, such as aspartate aminotransferase, lactate dehydrogenase, and creatine phosphokinase. Violation of lipid metabolism in the liver with hypothyroidism can lead to obesity, which is never significant. Hypothyroidism revealed a violation of the biliary system and the development of cholelithiasis. There is a scientific study on the relationship between hypothyroidism and the formation of stones in the common bile duct.

Keywords: Hypothyroidism, Liver, Pancreas, Biliary system, Endocrine system

Introduction

The human endocrine system consists of endocrine glands that produce hormones that regulate the work of internal organs. One of the links of the endocrine system is the thyroid gland, which has close interaction with the hypothalamus and pituitary gland [1].

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The thyroid gland is considered the largest endocrine gland in the human body. It consists of two identical lobes and has a mass of about 15-20 grams in an adult. A list of the main hormones produced by the thyroid gland includes thyroglobulin (TG), thyroxine (T4), triiodothyronine (T3), and calcitonin [2]. Thyroid hormones regulate all metabolic processes in the body, so maintaining the physiological concentration of thyroid hormones is a prerequisite for normal growth, development and body functioning.

Thyroid hormones perform certain functions in the body:

1. Accelerate the processes of resorption and synthesis of bone tissue.
2. Have a stimulating effect on the processes of erythropoiesis.
3. Participate in the regulation of the work of the respiratory center.
4. Increase the sensitivity of receptors to catecholamines.

5. Have a positive chronotropic and inotropic effect on the myocardium and increase the number of catecholamine receptors in the myocardium.
6. Participate in thermoregulation processes.
7. Increase hormonal clearance and clearance of drugs, as well as metabolic rate.
8. Increase the oxygen demand of all body tissues (except the brain and spleen).
9. Contribute to the formation of bone and nervous systems in the fetus during the body's development [3].

At the same time, the regulation of thyroid function and the maintenance of a constant concentration of thyroid hormones are carried out by thyroid-stimulating hormone (TSH) produced by the pituitary gland.

Thyroid hormone deficiency reduces the formation of cellular enzymes and the oxygen demand of body tissues and slows down redox reactions. Thus, metabolic processes are disrupted. In cases when there is a decrease in the biological effect of thyroid hormones on organ tissues in the body or their persistent and long-term deficiency, hypothyroidism develops [4].

The following types of hypothyroidism are pathogenetically distinguished:

1. Thyrogenic or primary hypothyroidism.
2. Pituitary or secondary hypothyroidism.
3. Hypothalamic or tertiary hypothyroidism.
4. Peripheral or tissue hypothyroidism [5].

Depending on the severity of primary hypothyroidism, it is divided into:

1. Subclinical or latent (characterized by elevated TSH levels at normal T4 levels).
2. Manifest (reduced T4 levels, hypersecretion of TSH, clinical manifestations).
3. Compensated.
4. Decompensated.
5. Complicated (characterized by such severe complications as heart failure, effusion into serous cavities, cretinism, and secondary pituitary adenoma) [6].

Clinical manifestations of hypothyroidism have no specific symptoms and do not depend on the degree of thyroid hormone deficiency. Studies have shown that the faster hypothyroidism develops, the more vivid the clinical picture of the disease.

Anamnesis collection and physical examination of patients with hypothyroidism, in most cases, reveal the following signs: weakness, drowsiness, fatigue, lethargy, hypothermia, dry skin, there may be a pale jaundice skin tone, fragility and hair loss, periorbital edema, puffiness of the face, dry mouth, tooth decay, swelling of the tongue with dental prints, low or hoarse voice timbre, menstrual cycle disorders, paresthesia, constipation, bradycardia, hypertension, weight gain [7-9]. There is a gradual increase in clinical symptoms.

According to some authors, hypothyroidism may have symptomatic manifestations characteristic of the pathology of various organs and systems of the body [10]:

1. Respiratory in the form of sleep apnea syndrome, pleural effusion of unclear etiology, chronic laryngitis.
2. Dental in the form of periodontal tissue diseases, decreased salivation, high enamel damage, violations of tissue homeostasis in caries combined with periodontitis.
3. Neurological in the form of tunnel syndrome, carpal tunnel syndrome, and fibular nerve canal syndrome.
4. Psychiatric in the form of depression and dementia.
5. Cardiological in the form of arterial hypertension, dyslipidemia, and hydropericardium.
6. Gastroenterological in the form of biliary dyskinesia, cholelithiasis, chronic hepatitis, and jaundice.
7. Gynecological in the form of menstrual disorders, amenorrhea, polymenorrhea, hypermenorrhea, and dysfunctional uterine bleeding is observed.
8. Rheumatological in the form of polyarthritis, synovitis, and progressive osteoarthritis.
9. Hematological in the form of anemia of various genesis.

The absence of specific symptoms and the diversity of clinical manifestations of hypothyroidism complicates the timely diagnosis of the disease. The main diagnostic method is a hormonal study of the hypothalamic-pituitary-thyroid system.

Thus, studying the physiological role of the thyroid gland and the participation of thyroid hormones in the regulation of internal organs (pancreas, liver and biliary system) is important in understanding the clinical picture of hypothyroidism and timely diagnosis of the disease.

Disorders that occur in the biliary system, pancreas and liver against the background of ongoing hypothyroidism. Biliary system diseases are among the most common and severe digestive system diseases. The biliary system includes the bile ducts and gallbladder. In recent years, there has been an increase in the incidence of cholelithiasis among young people, men, and people with normal and underweight [11, 12].

According to scientific research, in the development of cholelithiasis, one of the important conditions is the oversaturation of bile with cholesterol, precipitation of cholesterol crystals and violation of the colloidal properties of bile with increased mucus production. In approximately 29.5% of cases (particularly after childbirth), small concretions spontaneously dissolve, and biliary sludge, including putty-like bile, disappears independently in 71% of patients. For the formation of biliary sludge and bile concretions, an important condition is to reduce the evacuation function of the gallbladder. When it is restored, sludge and small concretions are removed from the bladder through the bile ducts. The connection between hypothyroidism and the formation of stones of the common bile duct has been proved [13].

Study of the contractile function of the gallbladder and determination of the thyroid status of patients with cholelithiasis

In the course of various studies, it was revealed that among women with hypothyroidism, various diseases of the biliary system were diagnosed in 22% of the examined, of which cholelithiasis - was in 35% of cases. Cholelithiasis was detected in people over 60 in 54.5% of cases. Cholelithiasis was noted in 44.5% of patients with thyroid nodules, in 32.2% - with autoimmune thyroiditis and 22.2% - with primary and postoperative hypothyroidism, which is 3.5 times more common than in people with chronic cholecystitis. Structural changes in the thyroid gland were found in 41% of patients with various pathologies of the biliary system [14].

The authors of the study of the contractile function of the gallbladder and the determination of the thyroid status of patients with cholelithiasis conducted a clinical study involving 1010 patients. According to the study, it is known that ultrasound of the abdominal cavity (liver, gallbladder, pancreas) and thyroid gland was performed in 470 (47%) healthy individuals (average age of 45.2 ± 0.4 years) and 540 (53%) patients with cholelithiasis (GI), of which 354 (65.6%) women (average age 46.1 ±0.3 years) and 186 (34.4%) men (average age 46.9±0.9 years) **(Figure 1)**.

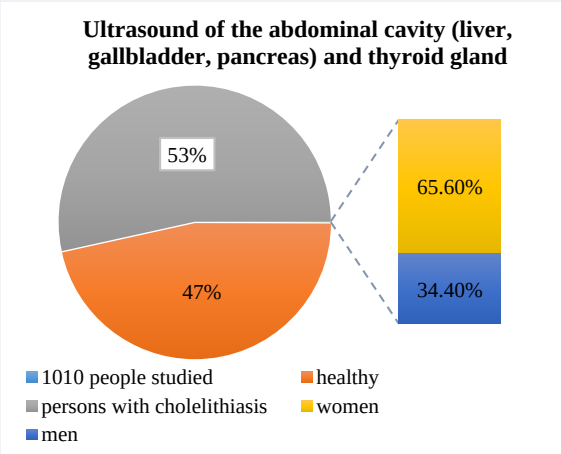
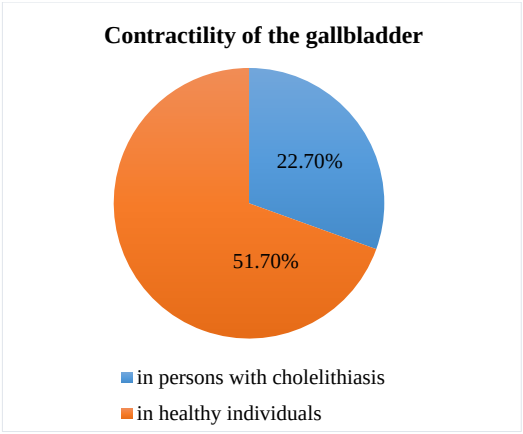


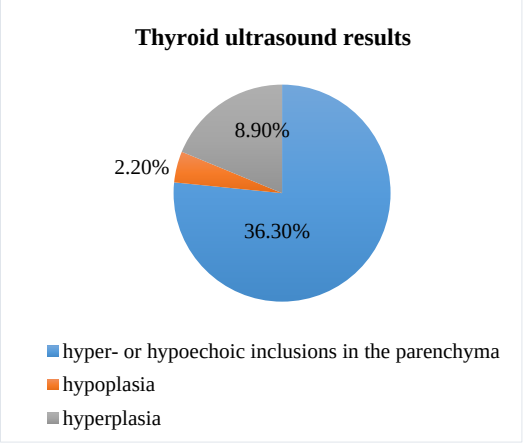
Figure 1. Distribution diagram of the studied patients

The gallbladder study included determining its length, width, wall thickness, and contractile function. The contractile function of the gallbladder was determined according to its volume on an empty stomach and after a choleretic breakfast (20 grams of sorbitol per 100 ml of water).

As a result of the study, it was revealed that the contractility of the gallbladder in persons with gallstone disease was significantly less (22.7%) than in healthy individuals (51.7%). Ultrasound of the thyroid gland revealed its hyperplasia in 8.9% of cases, hypoplasia — in 2.2%, and structural changes in the parenchyma in the form of hyper- or hypoechoic inclusions, regardless of the size of the thyroid gland, in 36.3% **(Figure 2)**.



a)



b)

Figure 2. The results of the study of the contractility of the gallbladder and ultrasound of the thyroid gland

In women with cholelithiasis, thyroid dysfunction was revealed in the form of changes in the level of thyroid hormones. Thyroid imbalance was noted in 177 (53.1%) women: of them, a low level of T3 with normal T4 and TSH content was registered in 1 (0.5%), a decrease in TSH with a normal amount of thyroid hormones - in 6 (3.2%), an increase in TSH levels - in 98 (52.1%). 72 (20.4%) were diagnosed with signs of hypothyroidism. No hormonal changes were detected among men. There was no dependence of bile concretions on the level of T3 and T4; patients with cholelithiasis had significantly higher TSH values than in the control group. In 23 (31.9%) women with thyroid hypofunction, concretions in the gallbladder formed 1-1.5 years after hypothyroidism detection **(Table 1)**.

Table 1. Results of thyroid ultrasound in patients with cholelithiasis

Name of the study	Quantity (% ratio)	Ultrasound of the thyroid gland	
Features of patients	540 (53%)	patients with cholelithiasis	
Gender		354 women (65.6%)	186 men (34.4%)
Average age		46.1 ± 0.3 years	46.9±0.9 years
Research results	177 (53,1%)	old thyroid imbalance	old had no hormonal changes
	1 (0,5%)	decreased T3 at normal T4 and TSH	

6 (3,2%)	decreased TSH at normal T3 and T4
98 (52,1%)	increased TSH
72 (20,4%)	signs of hypothyroidism
23 (31,9%)	in women with hypothyroidism concretions in the gallbladder formed after 1-1.5 years.

The results of the study showed that the etiology of stone formation is a violation of the contractile function of the gallbladder, and a decrease in the volume of bile ejected leads to changes in the enterohepatic circulation of bile acids and a decrease in their entry into the liver, creating conditions for accumulation of bile components and nucleation.

The liver is a multifunctional organ, the main function of which is to participate in metabolism processes. Despite its crucial role in metabolic processes, the structure and functional state of the liver in hypothyroidism remains insufficiently studied. In the liver, extra-thyroid formation of T3 from T4, enzymatic activation of steroid hormones, and biogenic amines are metabolized; inactivation of insulin, glucagon, and diuretic hormone occur. Hormones T3 and T4 are involved in the regulation of metabolism in liver cells - hepatocytes. This affects the functioning of the liver, and the liver, in turn, metabolizes thyroid hormones and regulates their systemic endocrine effects [15]. Disorders of the thyroid gland can lead to changes in the structure and functions of the liver, and liver diseases can cause abnormalities in the metabolism of thyroid hormones, contributing to the development of hypothyroidism [16].

According to scientific research, it was revealed that various liver diseases were diagnosed among patients with hypothyroidism. Of these, hypothyroidism is noted in 10-25% of patients with primary biliary cirrhosis of the liver. In 12% of those examined with autoimmune hepatitis, hypothyroidism is also a predisposing factor in the development of non-alcoholic fatty liver disease [17].

Experiments on laboratory animals with the use of drugs

In an experiment conducted on laboratory animals, it was revealed that after taking mercazolil for two months, destructive processes in the liver were noted on the second day after its cancellation: an increase in liver mass by 1.5 times, a decrease in the volume fraction of parenchyma, the appearance of necrosis foci. At the same time, no dystrophically altered hepatocytes were detected, which is explained by the rapid transition of dystrophic changes to necrotic ones. Against this background, the mass of activated Kupfer cells with high acid phosphatase activity increased 3 times, which indicates an increase in the phagocytic function of the system of hepatic macrophages eliminating necrotic masses. Despite these changes, the hepatocyte glycogen content did not change, and the total protein content increased. Presumably, this is due to compensatory activation of intra-lobular blood flow, as evidenced by the expansion of sinusoidal capillaries and an increase in their mass by 1.6 times. At the same time, no stagnant phenomena were observed, and 86% of sinusoids were free of blood [18].

In parallel with destructive processes, the activity of collagen genesis increased, and the mass of newly formed collagen increased 2.2 times. At the same time, the mass of small hepatocytes in the liver parenchyma decreased by 70%, and the mass of highly differentiated hepatocytes (having an average size) decreased by 65%, which may serve as evidence of the inhibition of their proliferation and differentiation. Moreover, if normally (in intact animals) the ratio of the mass of small cells to the mass of differentiated cells is 0.5, then with hypothyroidism, this ratio reaches 1.2, which indicates a decrease in the differentiation rate relative to the rate of cell proliferation. Based on the data obtained, it can be assumed that the regenerative capabilities of the liver in hypothyroidism are significantly reduced, and their quality and volume are not enough to restore the number of hepatocytes [19].

The pancreas is the link between the endocrine and digestive systems. The exocrine function of the pancreas communicates with the digestive system. The endocrine (endocrine) function is closely related to the endocrine glands and metabolic processes and is under the regulatory influence of thyroid hormones. Therefore, hypothyroidism disrupts the pancreas [20].

According to studies, patients with uncompensated primary hypothyroidism have pancreatic dysfunction in 65.1% of cases, which has clinical manifestations in the form of abdominal pain in 51.1% of cases, dyspepsia in 42.5%, structural changes of the organ in 37.5%. Pancreatic dysfunction is characterized by multidirectional changes in exocrine and endocrine functions, which worsened with an increase in the degree of decompensation of hypothyroidism with a relative increase in blood lipase, amylase and urine diastase, as well as a decrease in insulin and C-peptide levels. At the same time, there is an increase in insulin resistance, which decreases against the background of drug treatment [21]. According to some authors, one of the etiological factors in the development of the chronic process in patients with hypothyroidism may be functional insufficiency of the pancreas.

In order to correct pancreatic dysfunction in patients with uncompensated hypothyroidism, it is recommended to prescribe enzymes in combination with antihypoxic drugs, which help to improve the structural condition of the organ and exocrine function [22, 23]. The achievement of euthyroidism leads to the disappearance of symptoms of pancreatic dysfunction in the subclinical form of hypothyroidism, accompanied by a significant increase in the level of C-peptide [24-26].

Disorders occurring in the biliary system, pancreas and liver against the background of ongoing hypothyroidism are manifested in changes in the structure of organs and tissues, leading to disruption of metabolic processes and physiological functions of organs. The resulting changes may be reversible against the background of taking medications. Important in understanding the clinical picture of hypothyroidism and timely

diagnosis of the disease is the study of the physiological role of the thyroid gland and the participation of thyroid hormones in the regulation of internal organs (pancreas, liver and biliary system). Disorders that occur in the biliary system, pancreas and liver against the background of ongoing hypothyroidism are manifested in changes in the structure of organs and tissues, which leads to functional disorders in the work of organs and metabolic processes [27-33].

Clinical manifestations of hypothyroidism are very diverse and nonspecific. The clinical picture of hypothyroidism is characterized by the predominance of the state of inhibition of all vital functions in the human body and consists of a weakening of the activity of several organs, a decrease in metabolic processes and a complex of trophic disorders. The pronounced relationship between the state of the organs of the hepatobiliopancreatic region and the thyroid gland allows the clinician to determine pathological phenomena from the liver, biliary system and pancreas provoked by hypothyroidism [34]. Laboratory and instrumental studies, timely diagnosis of the disease, followed by the appointment of complex drug therapy, allow us to correct the changes that have occurred in organs and systems, thus preventing the development of complications [35].

Conclusion

Hypothyroidism is a clinical syndrome caused by hypofunction of the thyroid gland and characterized by a decrease in the content of thyroid hormones in the blood serum. Clinical manifestations of hypothyroidism can be diverse and depend on its etiology, the age of the patient, as well as the rate of development of thyroid hormone deficiency. The disease may have a pronounced clinical picture or, conversely, have no clinical manifestations and be detected randomly. In addition, signs of hypothyroidism very often mimic (mask) another pathology. Therefore, the diagnosis of hypothyroidism in some cases is difficult.

In this work, a systematic analysis of the literature and clinical studies was carried out, and the negative effect of hypothyroidism in a patient on the liver, biliary system and pancreas was established.

When analyzing the effect of hypothyroidism on the liver, no changes were observed in the organ itself. However, increased levels of serum enzymes such as aspartate aminotransferase, lactate dehydrogenase, and creatine phosphokinase were revealed. Violation of lipid metabolism in the liver with hypothyroidism can lead to obesity.

Thus, thyroid hormone deficiency affects many physiological functions and metabolic processes in the body, so changes in these organs and systems may be noted. Against the background of ongoing drug therapy, most of the changes are reversible.

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