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INTERRELATIONSHIP BETWEEN LIVER FUNCTION, THYROID GLAND FUNCTION, OBESITY AND MICROBIOTA

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Summary. *Hypothyroidism affects metabolism and can be an important factor in the development of metabolic disorders. Metabolic-associated fatty liver disease (MASLD) and obesity occupy a special place in clinical practice due to the high risk of progression to cirrhosis and cardiovascular complications. Recent data suggest that intestinal dysbiosis may act as a key mediator in the pathogenesis of these conditions. This article reviews the pathogenetic mechanisms of the interaction of hypothyroidism, MASLD and obesity, as well as the role of microbiota as a potential target for therapeutic intervention, in particular with the help of probiotics and other corrective measures.*

Keywords: *MASLD, hypothyroidism, obesity, microbiota, bacterial overgrowth, intestinal permeability, probiotics.*

Obesity is a chronic proinflammatory disease that systemically affects normal physiology and metabolism, causing multiple diseases such as cardiovascular disease, diabetes (DM), metabolic-associated fatty liver disease (MASLD), and some cancers [1, 2]. Obesity is considered a major public health problem in the twenty-first century. The presence of obesity and abdominal adipose tissue distribution contribute to the formation of MASLD. Currently, hepatic MASLD and type 2 diabetes are metabolically associated diseases.

The aim of the work is to investigate the relationship between hypothyroidism, metabolic disorders (MASLD and obesity) and the state of the intestinal microbiota, as well as to substantiate the prospects of microbiota-oriented approaches in therapy.

Abdominal obesity plays a leading role in the development and progression of insulin resistance (IR). For the diagnosis of visceral obesity, the index waist circumference/hip circumference is used, which allows assessing the priority accumulation of fat in the abdominal fat depot [3]. According to the literature, body mass index (BMI) is an independent predictor of the development of fatty infiltration of the liver. Studies have shown that the prevalence of MASLD increases linearly with increasing BMI, reaching a 14-fold higher risk at a BMI of 37.5–40 kg/m² compared with the normal weight population [4]. As expected, the absolute risk is higher in patients with diabetes at any BMI. In particular, with regard to the risk of MASLD, the presence of diabetes in a normal weight population was equivalent to a 5–10 kg/m2 increase in BMI. In fact, up to 70% of patients with diabetes have fatty liver disease [5], and patients with MMASLD and diabetes have a higher degree of inflammation on liver biopsy and a faster evolution towards hepatocellular carcinoma. Data from the Rotterdam Study have shown that the coexistence of MASLD and diabetes is associated with a higher risk of developing liver fibrosis [6,7], and this process is not affected by age. Moreover, not only the presence of diabetes but also impaired carbohydrate tolerance are associated with an increased risk of developing diabetes in patients with MASLD [8, 9]. Finally, the presence of diabetes increases mortality in patients with MASLD [10]. On the other hand, it is important to mention that the presence of MASLD increases the risk of hyperglycemia and, in patients already suffering from diabetes, increases the risk of metabolic decompensation. Thus, the relationship between MASLD and insulin resistance is mutually aggravating [11]. Several studies have shown an association between MASLD with low body weight and metabolic risk factors such as dyslipidemia, hyperglycemia, and visceral obesity [12, 13, 14]. Moreover, fructose consumption and a cholesterol-rich diet have been associated with the development of MASLD [15, 16].

Thyroid hormones regulate energy metabolism, heat production, and oxidative processes. Hypothyroidism is characterized by a decrease in basal metabolic rate, which can lead to weight gain and fat accumulation. In addition, hypothyroidism contributes to the development of insulin resistance and changes in the blood lipid profile. [17].

The gut microbiota is an important regulator of metabolism and immune response. Dysbiosis, or a change in the composition of the normal flora, is associated with impaired intestinal barrier function, leading to the permeability of endotoxins into the systemic circulation. This process stimulates systemic inflammation and can worsen metabolic status, contributing to the development of both obesity and IBD. Correction of dysbiosis with probiotics, prebiotics, and dietary changes can positively affect metabolism and reduce systemic inflammation [18]. Steatohepatitis should be considered as a potential target for pharmacological treatment [19].

Metabolic status also contributes [20,21]. We found that in patients with MMASLD with excess body weight and obesity, increased leptin levels and decreased adiponectin levels in the blood serum were associated with an increase in the body

mass index and insulin resistance [22]. In excess body weight, proliferation and hypertrophy of adipocytes are accompanied by infiltration by macrophages with subsequent development of inflammatory reactions, resulting in changes in the metabolic activity of adipose tissue [23,24]. This is why a number of scientists consider pathological obesity to be a chronic systemic inflammatory process. These pathogenetic disorders also contribute to the development of sarcopenia in patients with MASLD, which forms a vicious circle in the liver-muscle system and contributes to an increase in cardiovascular risk [25,26].

Conclusion: Dysfunction of adipose tissue caused by low adiponectin and high leptin levels contributes to oxidative stress and inflammation underlying the pathogenesis of MASLD and cardiovascular complications [27,28,29,30]. The relationship between hypothyroidism, MASLD and obesity lies in common pathogenetic mechanisms, among which systemic inflammation plays a key role. Hypothyroidism contributes to a decrease in metabolism, which in turn entails obesity, and obesity is an important risk factor for the development of MASLD. The role of microbiota in this context is to regulate inflammatory processes and metabolism - changes in the composition of intestinal flora can aggravate or, conversely, reduce systemic inflammation [31,32]. A review of modern studies shows that correction of dysbiosis with probiotics can be a promising therapeutic strategy aimed at improving both metabolic status and liver function.

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ВЗАЄМОЗВ'ЯЗОК МІЖ ФУНКЦІЄЮ ПЕЧІНКИ, ФУНКЦІЄЮ ЩИТОВИДНОЇ ЗАЛОЗИ, ОЖИРІННЯМ ТА МІКРОБІОТОЮ

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Анотація. *Гіпотиреоз є одним із найбільш поширених ендокринних порушень у популяції України, що чинить суттєвий вплив на метаболічні процеси та виступає важливим предиктором формування метаболічних дисфункцій. Метаболічно-асоційована жирова хвороба печінки (МАСХП) та ожиріння посідають провідне місце в сучасній клінічній практиці у зв'язку з високою поширеністю та потенціалом прогресування до цирозу та серцево-судинних ускладнень. Накопичені дані свідчать про те, що дисбіоз кишечника може виконувати роль ключового медіатора у патогенезі зазначених станів. У даній статті представлено огляд патогенетичних механізмів взаємодії між гіпотиреозом, МАСХП та ожирінням, а також розглянуто мікробіоту як перспективну мішень для терапевтичних стратегій, зокрема із застосуванням пробіотиків та інших методів корекції.*

Ключові слова: *МАСХП, гіпотиреоз, ожиріння, мікробіота, надмірний ріст бактерій, проникність кишечника, пробіотики.*