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UDC: 612.335.3 - 616 - 053

METABOLICALLY ASSOCIATED FATTY LIVER DISEASE AND THYROID HYPOFUNCTION: GENETIC ASPECTS

https://doi.org/10.5281/zenodo.18562288

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Abstract: *Metabolically associated fatty liver disease is the most common chronic liver disease, characterized by pathological changes in liver cells, with hepatic fat accumulation and impaired metabolism.*

Thyroid hypofunction is a common endocrine disorder characterized by a deficiency of thyroid hormones, which negatively affects the body's overall metabolic balance.

Studies have shown that genetic predisposition factors, hereditary mutations, polymorphisms, and epigenetic mechanisms play an important role in the development of thyroid hypofunction and hepatic steatosis. Molecular genetic investigations, including analyses of gene expression changes and nucleotide sequence variations, are of fundamental importance. Based on genetic markers, it becomes possible to assess patients' disease risk and to develop personalized diagnostic and therapeutic strategies. It is also important to substantiate the relationship between the clinical manifestations of metabolically associated fatty liver disease and thyroid hypofunction and their genetic determinants. The results of genetic research play a crucial role in disease prevention, early diagnosis, and effective treatment. In modern medicine, it is necessary to propose practical recommendations aimed at reducing disease progression and improving patients' quality of life through the implementation of genetic counseling, molecular diagnostics, and preventive strategies.

Studying the genetic basis of these two conditions is important not only at the research level but also in clinical practice, as it contributes to the development of personalized medicine and modern therapeutic approaches.

Keywords*: Metabolically associated fatty liver disease, thyroid hypofunction, genetic predisposition, molecular genetic research, epigenetics, personalized diagnostics.*

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RELEVANCE

Metabolically associated fatty liver disease and thyroid hypofunction are chronic pathological conditions that negatively affect the body's overall metabolism and the function of all organs and systems. Metabolically associated fatty liver disease is characterized by degenerative and functional disorders of hepatocytes and may have various etiologies, including viral, toxic, metabolic, or genetic factors. At the same time, thyroid hypofunction adversely affects metabolic processes in the body—particularly the metabolism of lipids, proteins, carbohydrates, minerals, and vitamins—which in turn leads to impairment of liver function.

In recent years, scientific research has focused on identifying the relationship between metabolically associated fatty liver disease and thyroid hypofunction, highlighting the central role of genetic determinants in this process. For example, mutations or decreased expression of genes involved in thyroid hormone synthesis and secretion (such as TSHR, TPO, and TG) may lead to hypofunction. At the same time, the genetically determined vulnerability of hepatocytes contributes to the development of metabolically associated fatty liver disease, as impairments in hepatic metabolic and detoxification processes result in the accumulation of toxins and metabolites in the body.

The genetic basis of metabolically associated fatty liver disease and thyroid hypofunction is important not only for understanding pathological processes but also for early diagnosis and the development of individualized treatment strategies. In this context, genetic markers and molecular diagnostic methods serve as advanced tools in clinical practice. From this perspective, the identification of genetic factors and the mechanisms of their phenotypic manifestation represent one of the most relevant scientific issues in modern medicine.

The clinical manifestations of metabolically associated fatty liver disease and thyroid hypofunction depend on multiple factors and are not limited solely to genetic predisposition. Environmental conditions, dietary habits, exposure to toxic substances, chronic diseases, and stress factors collectively influence the rate of disease progression and severity. Therefore, alongside the identification of genetic determinants, it is essential to conduct clinical diagnostics and functional tests in an integrated approach.

The main objective of the study is to investigate the potential for identifying genetic factors involved in the development of metabolically associated fatty liver disease and thyroid hypofunction, and to examine associated clinical conditions, advanced diagnostic methods, and genetics-based personalized treatment approaches.

LITERATURE REVIEW

The study of metabolically associated fatty liver disease and thyroid (thyroid gland) hypofunction, particularly their genetic basis, has gained significant

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attention in recent years within clinical endocrinology and molecular genetics research.

The literature review indicates that the co-occurrence of metabolically associated fatty liver disease and thyroid hypofunction is often associated with genetic predisposition. Studies have shown that mutations in genes involved in tyrosine kinase signaling, deiodinases, and hepatic metabolism increase the risk of developing metabolically associated fatty liver disease (Zhang et al., 2021). In addition, genetic alterations of the thyroid gland, particularly polymorphisms in the TSHR, TG, and TPO genes, play a significant role in the development of hypothyroidism (Jameson & De Groot, 2019). These genetic factors exacerbate lipid metabolism disorders associated with hepatic steatosis and promote the development of steatosis and fibrosis in hepatocytes.

Recent molecular studies have enhanced the identification of the hereditary characteristics of hepatic steatosis through the use of advanced genetic methods, including genome-wide association studies (GWAS), exome sequencing, and the analysis of molecular markers (Eslam et al., 2018). These approaches help to better understand the pathogenetic mechanisms underlying the development of hepatic steatosis in combination with thyroid hypofunction. Research indicates that certain genetic variants alter hepatic lipid metabolism and the activity of thyroid hormone receptors, thereby intensifying the clinical manifestations of hepatic steatosis and hypothyroidism.

Studies indicate that the hereditary component of hepatic steatosis and thyroid hypofunction is evident not only at the molecular level but also in family histories. For example, in patients with familial hypothyroidism and hepatic steatosis, genetic investigations allow for the detection of a high prevalence of mutations (Park et al., 2020). At the same time, the association between hepatic steatosis and thyroid hypofunction is intensified by metabolic syndrome, insulin resistance, and disorders of lipid metabolism, reflecting the multifactorial genetic and epigenetic nature of these diseases.

The study of the genetic aspects of metabolically associated fatty liver disease and thyroid hypofunction is important not only for diagnosis and prognosis but also for the development of personalized treatment strategies. Using genetic markers and molecular diagnostic tools, it is possible to identify high-risk individuals, initiate treatment at an early stage, and prevent the progression of hepatic steatosis. In clinical practice, a combined approach involving liver biopsy, genetic testing, and assessment of thyroid function is recommended as an effective means of determining disease etiology.

The genetic aspects of metabolically associated fatty liver disease and thyroid hypofunction are multifaceted and are being extensively studied through molecular, clinical, and epidemiological

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research. Scientific literature on this topic highlights the mechanisms of their concomitant development, genetic predisposition, and the diagnostic significance of molecular markers, thereby enabling targeted disease prevention and the development of personalized treatment strategies.

The study employs clinical and experimental methods, with a systematic analysis of patients' genetic profiles, biochemical parameters, and endocrine functions. The research subjects include patients diagnosed with metabolically associated fatty liver disease and thyroid hypofunction, whose medical histories are examined while taking into account congenital and hereditary factors, as well as environmental and nutritional influences.

For genetic investigations, blood samples are used to obtain high-quality DNA, which is analyzed using polymerase chain reaction (PCR), sequencing, and genotyping techniques. The results are then compared with previously identified genetic markers. Clinical-hormonal and biochemical analyses are also applied to determine hormone levels and liver enzyme activity in patients. The use of statistical and bioinformatics tools enables the evaluation of the significance of genetic data, their association with phenotypic disease manifestations, and the analysis of potential polygenic and monogenic factors, thereby contributing to a better understanding of the hereditary mechanisms underlying metabolically associated fatty liver disease and thyroid hypofunction.

The studies are aimed at identifying the genetic basis of metabolically associated fatty liver disease and thyroid (thyroid gland) hypofunction, and the obtained data allow for a better understanding of the phenotypic expression and molecular mechanisms of these diseases. During the research, it is particularly relevant to conduct a comprehensive analysis of genetic markers, specifically polymorphisms in genes involved in thyroid hormone synthesis, including thyroid peroxidase (TPO), thyroglobulin (TG), and the sodium/iodide symporter (NIS; SLC5A5), as well as genes affecting liver function, such as patatin-like phospholipase domain-containing protein 3 (PNPLA3) and transmembrane 6 superfamily member 2 (TM6SF2), in both patients and a healthy control group.

Studies have demonstrated a high frequency of the PNPLA3 I148M and TM6SF2 E167K variants in patients with metabolically associated fatty liver disease. These polymorphisms disrupt hepatic lipid metabolism and increase the risk of developing metabolically associated fatty liver disease. At the same time, in patients with thyroid hypofunction, a high prevalence of mutations in the TPO and TG genes has been identified, which adversely affects the synthesis and secretion of thyroid hormones.

The combination of polymorphisms was also reflected in the clinical status of

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patients. For example, individuals with concomitant hepatic steatosis and thyroid hormone deficiency showed a greater predisposition to metabolic syndrome, weight gain, and dyslipidemia, demonstrating the complex interaction between genetic predisposition and epigenetic factors.

Scientific research on the interrelationship between metabolically associated fatty liver disease and thyroid hypofunction is ongoing. Mutations in the TPO and TG genes lead to reduced thyroid hormone levels, which in turn affect hepatic lipid metabolism and glycemic balance. At the same time, polymorphisms in PNPLA3 and TM6SF2 create a predisposition to the development of metabolically associated fatty liver disease, which, when combined with thyroid hormone deficiency, exacerbates clinical manifestations.

Genetic markers play an important role in clinical practice by supporting diagnostic decision-making and individualized treatment strategies. For example, the presence of the PNPLA3 I148M variant can be used as an indicator for monitoring lipid metabolism and assessing liver function, while mutations in the TPO and TG genes may help predict the risk of thyroid hormone deficiency and guide the development of a personalized therapeutic plan. In particular, Eslam et al. (2019) reported that the PNPLA3 polymorphism is associated with an increased disease risk in patients with metabolically associated fatty liver disease, whereas a high frequency of TPO mutations is observed in thyroid hypofunction.

In addition, for patients with a genetic predisposition to thyroid hypofunction, it is recommended to implement comprehensive monitoring of liver and thyroid function, along with dietary therapy, individualized physical activity and exercise intensity, and a personalized pharmacological treatment plan, which helps to reduce the risk of complications.

Substantiating the interrelationship between the genetic determinants of metabolically associated fatty liver disease and thyroid hypofunction is highly relevant and holds significant scientific and practical value for clinical diagnosis, prevention, and the development of individualized treatment strategies.

CONCLUSION

The study of the genetic basis of metabolically associated fatty liver disease and thyroid (thyroid gland) hypofunction is of great importance in shaping clinical diagnostic approaches and treatment strategies. Genetic predisposition, that is, hereditary factors, together with various metabolic and molecular mechanisms, play a key role in the development of these diseases.

Genetic studies demonstrate the interrelated development of metabolically associated fatty liver disease and thyroid hypofunction. Thyroid hormone deficiency may suppress hepatic metabolism, impair the activity of liver enzyme systems, and promote the

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development of hepatic steatosis. At the same time, genetic forms of fatty liver disease can directly influence thyroid hormonal processes, playing an important role in the formation of primary and secondary hypofunction.

In the evaluation of metabolically associated fatty liver disease and thyroid hypofunction, the use of genetic testing, molecular diagnostics, and biomarkers in clinical practice helps to reduce the risk of complications and mortality and enables the initiation of effective treatment at early stages of the disease. Genetics-based preventive measures, including genetic counseling, identification of high-risk individuals, and their regular monitoring, play a significant role in disease prevention.

It should be emphasized that the study of genetic aspects is relevant not only for individualized treatment but also for the development of health improvement and preventive strategies. Future research conducted in collaboration with genetic centers and clinical laboratories will enable the identification of how genetic markers and polymorphisms influence disease severity, duration, and response to therapy.

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