



## 22. THE ROLE OF LEPTIN IN THE PATHOGENESIS OF METABOLIC DYSFUNCTION-ASSOCIATED FATTY LIVER DISEASE

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**Introduction.** Metabolic dysfunction-associated fatty liver disease (MAFLD) has become one of the leading causes of end-stage liver disease. Its pathogenesis is not fully understood, but leptin may contribute to the development and progression of this disease, by multiple pathogenic pathways. Leptin, a polypeptide primarily synthesized by adipocytes, is mainly responsible for maintaining energy homeostasis. Circulating leptin levels reflect primarily body energy stores and secondarily acute changes in energy intake.

**Aim of study.** To elucidate the role of leptin in the pathogenesis of MAFLD.

**Methods and materials.** There have been relevant articles related to leptin, adipose tissue, and metabolic dysfunction-associated fatty liver disease, published between 01.01.2020-01.11.2023, on search engines PubMed and ScienceDirect.

**Results.** In the beginning, leptin was described as an anti-obesity hormone, but the studies revealed that leptin has pleiotropic effects. It is involved in body weight control, glucose metabolism, immune function, and metabolic programming. In a healthy state, leptin has anti-steatotic effects, preventing lipids storage in the liver and promoting their mobilization. Moreover, leptin improves insulin sensitivity, and suppresses hepatic glucose production and lipogenesis. The leptin level is directly proportional to the amount of adipocytes. Even though most of the MAFLD patients have an increased body mass index and high leptin level, it promotes lipotoxicity, insulin resistance, and up-regulation of proinflammatory cytokines. One reason could be the development of leptin resistance that provides a critical link between adipose tissue, liver, insulin resistance, and inflammation. In this way, hyperleptinemia and leptin resistance contribute to worsening hepatic steatosis and promote the progression to steatohepatitis and liver fibrosis.

**Conclusion.** Leptin represents a key milestone in the pathogenesis of MAFLD, which is considered the hepatic manifestation of the metabolic syndrome. Leptin level is positively associated with the severity of MAFLD and could be used as an independent predictor of the presence or development of this disease.

**Keywords.** Leptin, adipose tissue, fatty liver disease.