

Non-alcoholic Fatty Liver Disease in Type 2 Diabetes: The Challenge of the Endocrinologist

Marin Pecani^{1*}, Thanas Furera¹, Agron Ylli¹

¹ Endocrinology Unit, University Hospital Center “Mother Theresa”, University of Medicine, Tirana, Albania.

Over the last decades, there has been a dramatic change of people's lifestyle toward a desk-bound life associated to high fat and rich sugar dietary intake, with significant consequences on human metabolism. Therefore, chronic metabolic diseases like obesity, type 2 diabetes (T2D) and non-alcoholic fatty liver disease (NAFLD) have erupted all over the world (1). Different studies have pointed out a significant association of T2D and NAFLD. The prevalence of NAFLD in T2D patients varies from 47% to 70% depending on the geographical region. In fact, diabetes, despite of being a risk factor for the development of NAFLD, also appears to accelerate its progression (2).

Pathogenesis of NAFLD in T2D is not completely elucidated but at the core of it, is insulin resistance leading to free fatty acid accumulation in liver cells progressing to lipotoxicity following inflammation and fibrosis (3). Specific gene variant such as the patatin-like phospholipase domain-containing 3 (PNPLA3) and transmembrane 6 superfamily member 2 protein (TM6SF2) have been found to have an important role in the development of NAFLD in T2D (4). The majority of the patients (48%-100%) are asymptomatic; in rare cases the disease can present with symptoms like fatigue and right upper quadrant pain. Liver enlargement, encountered in NAFLD – T2D patients is difficult to distinguish on physical examination because of concomitant obesity. Therefore, NAFLD in T2D is diagnosed casually due to liver enzymes alteration and/or incidental evidence of

hepatic steatosis during imaging modalities; i.e. ultrasound as the easiest accessible noninvasive method and with a low cost (3). On the other hand, the coexistence of NAFLD and T2D worsen insulin resistance, promotes dyslipidemia and makes difficult to achieve the preferred glycemic control predisposing the development of cardiovascular events (5).

At present, there is no specific treatment for NAFLD. In this regard, the challenge of the Endocrinologist would focus on two main roles. The main role is to prevent the evolvement toward non-alcoholic steatohepatitis (NASH) in T2D patients, through effective lifestyle modifications (increasing physical activity, lowering fat and sugar intake in diet, encouraging smoking and alcohol cessation) and the early use of antidiabetic drugs that have useful effects on the liver. The second crucial role of the endocrinologist is to identify further liver damage (fibrosis and/or possible cirrhosis) in T2D patients in order to refer the patient early to the hepatologist (6).

In conclusion, the challenge of the endocrinologist consists in improving the epidemic effect of NAFLD in patients with T2D. Since there are no specific drugs or methods in treating NAFLD and NASH – T2D patients, prevention is of crucial importance. Furthermore, promising multifunctional therapies and longitudinal studies exploring new glucose-lowering drugs are eagerly awaited, toward a better and personalized approach of the patient.

Acknowledgements: None declared.

Conflict of Interest Statement: The authors declare that they have no conflict of interest.

REFERENCES

1. Stefan N, Cusi K. A global view of the interplay between non-alcoholic fatty liver disease and diabetes. *Lancet Diabetes Endocrinol* 2022; 10(4):284-296.
2. Younossi ZM, Golabi P, de Avila L, Paik JM, Srishord M, Fukui N, et al. The global epidemiology of NAFLD and NASH in patients with type 2 diabetes: a systemic review and meta-analysis. *J Hepatol* 2019; 71:793-801.
3. Marušić M, Paić M, Knobloch M, Liberati Pršo AM. NAFLD, Insulin Resistance, and Diabetes Mellitus Type 2. *Can J Gastroenterol Hepatol* 2021:6613827.
4. Targher G. Is it time for non-alcoholic fatty liver disease screening in patients with type 2 diabetes mellitus?. *Hepatobiliary Surg Nutr* 2020; 9(2):239-241.
5. Xia MF, Bian H, Gao X. NAFLD and Diabetes: Two Sides of the Same Coin? Rationale for Gene-Based Personalized NAFLD Treatment. *Front Pharmacol* 2019; 6:10:877.
6. Kuchay MS, Misra A. Role of diabetologists in the management of nonalcoholic fatty liver disease: Primary prevention and screening/management of fibrosis and cirrhosis. *Diabetes Metab Syndr* 2022; 16(3):102446.