розробка та впровадження сучасних інтегрованих підходів до моніторингу ВІЛ-інфекції, вивчення впливу соціальних детермінант здоров'я на поширення хвороби, а також оцінка ефективності просвітницьких та профілактичних програм серед ключових груп населення.

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ОЦІНКА РІВНЯ ТРАНСАМІНАЗ НА РІЗНИХ СТАДІЯХ МЕТАБОЛІЧНО-АСОЦІЙОВАНОЇ СТЕАТОТИЧНОЇ ХВОРОБИ ПЕЧІНКИ

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EVALUATION OF TRANSAMINASE LEVELS IN DIFFERENT STAGES OF METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE

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Abstract. *In this study, the pathogenetic mechanisms that cause the development of liver tissue inflammation with subsequent increase in liver enzymatic function, development of non-alcoholic steatohepatitis and liver fibrosis were described. The levels of ALT and AST depending on the stage of progression of MASLD were identified and described.*

Keywords*: metabolic dysfunction-associated steatotic liver disease, transaminases, AST, ALT, nonalcoholic steatohepatitis, liver fibrosis.*

Introduction. Metabolic dysfunction-associated steatotic liver disease (MASLD) is a multisystemic disease beyond the liver that can increase the risk of heart failure, obstructive sleep apnoea, and malignancy and can result in an increase in cancer-related and cardiovascular disease mortality [1]. Histologically, MASLD manifests itself with the formation of hepatic steatosis – the accumulation of fatty inclusions in at least 5% of hepatocytes and/or an increase in triglyceride levels above 55 mg/g of liver without signs of hepatocellular damage [2]. The next step in the pathogenesis of MASLD is the further progression of steatosis with the formation of nonalcoholic steatohepatitis (NASH) [3]. NASH is characterized by the development of adipose tissue inflammation due to the induction of a local and systemic immune response [4]. Typical histological features of NASH are, first of all, macrovesicular steatosis, mixed lobular inflammation and hepatocellular ballooning [5]. It has been shown that the degree of fat accumulation correlates with the activation of hepatic stellate cells, so steatosis was considered an independent activator of fibrogenesis. The subsequent development of oxidative stress, mitochondrial dysfunction, production of adipokines, proinflammatory cytokines and bacterial endotoxins were considered as a "second blow", leading to hepatocyte damage and the development of inflammation [6]. The next link in the progression of MASLD is the further progression of NASH with the formation of liver fibrosis (LF). The central factor in the development of LF is the activation of hepatic stellate cells (Ito cells), localized in the perisinusoidal space of Disse, with their subsequent differentiation into proliferative fibrogenic myofibroblasts [7]. Extracellular inflammatory processes with the participation of macrophages, hepatic sinusoidal endothelial cells, T-killers, platelets have an additional effect on the activation of stellate cells [8].

MASLD is currently the most common chronic liver disease worldwide and the main cause of elevated serum hepatic transaminases [9]. Asymptomatic elevation of liver enzymes is a possible clinical manifestation of MASLD. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are most closely associated with hepatic fat accumulation and are most commonly found in the cytoplasm of hepatocytes [10]. ALT and AST aminotransferases are liver enzymes involved in the transfer of amino groups of aspartate and alanine to ketoglutaric acid and are markers of hepatocellular injury [11]. ALT and AST levels depending on the stage of progression and duration of MASLD, so the study of these transaminases is clinical importance for the diagnosis of MASLD.

Objective: Study of the enzymatic status of the liver in patients with MASLD depending on the stage of its progression.

Materials and methods. 42 patients with MASLD were studied, who were divided into the following groups: group 1 – 10 patients with hepatic steatosis, group 2 – 10 patients with NASH; group 3 – 10 patients with LF in stage F 0-1 and group 4 – 11 patients with LF in stage F 1-2. Fibrosis stages F3 and F4 were not detected in the patients involved in the study. The control group consisted of 20 relatively healthy individuals. The average age of all examined patients was (46.23±9.3) years.

Results and their discussion. The average AST levels in patients with hepatic steatosis were (34.6±9.4) U/L, in patients with NASH – (42.4±8.7) U/L, in patients with LF F0-1 – (43.7±10.4) U/L and in patients with LF F1-2 – (44.2±7.4) U/L. A significant difference in AST levels was recorded when comparing the level of the studied enzyme between the subgroup of patients with hepatic steatosis in comparison with the groups of patients with NASH, LF F0-1 and LF F1-2 ($p_1<0.05$, $p_2<0.05$, $p_3<0.05$). The average ALT levels in patients with hepatic steatosis were (55.3±8.4) U/L, in patients with NASH – (68.7±9.7) U/L, in patients with LF F0-1 – (74.2±7.6) U/L and in patients with LF F1-2 – (76.8±8.9) U/L. A significant difference in ALT levels was recorded when comparing the levels of the studied enzyme between each subgroup with different stages of progression of MASLD with the control group ($p<0.01$). Also, a significant difference in ALT levels was recorded when comparing the levels of the studied indicator in the subgroup of patients with hepatic steatosis with the subgroups of patients with NASH, LF F0-1 and LF F1-2 ($p_1<0.01$, $p_2<0.05$, $p_3<0.05$). It should be noted that when comparing the levels of AST and

ALT between subgroups of patients with LF F0-1 and LF F1-2, no significant difference in the studied parameters was found (p_1>0.05, p_2>0.05). Previous studies demonstrate that the presence of elevated levels of ALT and AST are associated with increased mortality in patients with liver diseases, including MASLD [12-14]. These data are also consistent with our study findings. A significant increase in the levels of AST (p<0.01) and ALT (p<0.01) was found in patients with MASLD in the NASH stage compared to patients with MASLD in the stage of hepatic steatosis, which indicates the influence of the development of the inflammatory process in the liver tissue on the progression of the MASLD stages.

Conclusions and prospects for further research. A significant increase of AST and ALT levels in the subgroup of patients with hepatic steatosis compared with the subgroups of patients with NASH, LF F0-1 and LF F1-2 confirms the relationship between the development of the inflammatory process and fibrogenesis in the liver tissue with an increase in the activity of hepatic transaminases in patients with MASLD. Considering the small group of patients, further multicenter prospective studies are needed to study and predict the influence of serum hepatic transaminases on the risk of cardiovascular diseases developing in patients with MASLD.

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