IMMUNOPATHOGENESIS OF NON-ALCOHOLIC FATTY LIVER DISEASE IN METABOLIC SYNDROME

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Relevance

The prevalence of non-alcoholic fatty liver disease (NAFLD) in different countries ranges from 10–24% in the general population and reaches 55–74% among individuals with excess body weight. Numerous studies have demonstrated that NAFLD, including non-alcoholic steatohepatitis (NASH), is closely associated with components of metabolic syndrome. Current concepts of NAFLD pathogenesis describe a “two-hit” model, which includes initial accumulation of triglycerides in hepatocytes due to impaired β-oxidation, followed by secondary inflammatory injury mediated by proinflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6). The progression from steatosis to steatohepatitis and cirrhosis is closely related to the functional state of the antioxidant defense system and genetic predisposition.

Objective

To study the production of proinflammatory cytokines IL-6 and TNF-α, as well as the functional state of antioxidant capacity in patients with non-alcoholic fatty liver disease at the stage of steatohepatitis associated with metabolic syndrome.

Materials and Methods

A total of 114 patients diagnosed with NAFLD associated with metabolic syndrome were examined. Among them, 43% were men and 57% were women, with a mean age of 47.2 years. Patient selection was performed using a random sampling method and included assessment of family history, genetic predisposition, smoking and alcohol consumption status, epidemiological history of viral hepatitis, physical activity level, dietary habits, psychological and diabetic status, arterial hypertension, and comorbid conditions. All patients underwent comprehensive clinical, biochemical, and instrumental examinations, including abdominal ultrasound and liver elastometry. Serum levels of IL-6 and TNF-α were determined using enzyme-linked immunosorbent assay (ELISA) test kits (“Cytokine” and “Protein Contour”, Saint Petersburg). Total antioxidant capacity (TAC) of blood serum was assessed by ELISA using Cayman Chemical test kits.

Results

The analysis demonstrated a significant increase in proinflammatory cytokine production in patients with NASH. Serum IL-6 levels in patients with NASH reached 4.21±0.20 pg/ml, which was 15.5 times higher than in healthy individuals (0.270±0.02 pg/ml). TNF-α production was also markedly elevated in the patient group (0.704±0.03 pg/ml) compared with healthy controls (0.049±0.003 pg/ml), exceeding control values by 14.3 times. At the same time, total antioxidant capacity of blood serum in patients with NASH was significantly reduced (0.079±0.03 mM/l) compared with healthy individuals (0.380±0.03 mM/l), representing a 4.8-fold decrease.

Conclusion

Patients with non-alcoholic steatohepatitis associated with metabolic syndrome exhibit pronounced activation of proinflammatory cytokine production (IL-6 and TNF-α) accompanied

by a significant reduction in total antioxidant capacity of blood serum. These findings suggest that oxidative stress and immune-mediated inflammation play a key role in the pathogenesis of NASH and provide a rationale for the inclusion of antioxidant agents in the pathogenetic treatment of this category of patients.

Table 1. Laboratory Parameters in Patients with Non-Alcoholic Steatohepatitis

▪ **Parameters**	▪ **Healthy individuals (n=20)**	▪ **Patients with NASH (n=114)**
▪ **IL-6, pg/ml**	▪ 0.270±0.02	▪ 4.21±0.20*
▪ **TNF-α, pg/ml**	▪ 0.049±0.003	▪ 0.704±0.03*
▪ **Total antioxidant capacity, mM/l**	▪ 0.380±0.03	▪ 0.079±0.03*

*Note: ***p<0.05 – statistically significant difference compared with healthy controls.***