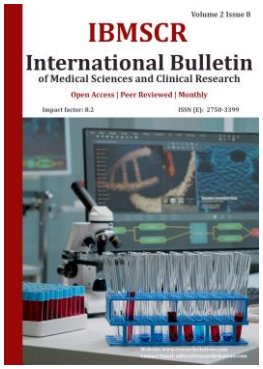

ASSESSMENT OF THE DEVELOPMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE BY CLINICAL AND LABORATORY MARKERS

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The urgency of the problem. Currently, non-alcoholic fatty liver disease (NAFLD) is one of the most common diseases in hepatology, leading to a deterioration in the quality of life, disability and death. The overall prevalence of NAFLD in the population ranges from 10 to 40% [1,3,5,6,7]. In the normal course of NAFLD, 12-40% of patients with hepatosis develop non-alcoholic steatohepatitis after 8-13 years. Of these, 15% of patients develop liver cirrhosis and liver failure. Of 7% of patients with liver cirrhosis, hepatocellular carcinoma develops within 10 years [2,3,5]. The heterogeneity of NAFLD leads to the absence of a single generally accepted standard of treatment for such patients. Of course, all overweight patients should be advised to reduce their weight by eating a low-calorie diet and exercising regularly, and the effect of the latter seems to be more significant. An unhealthy lifestyle is the main cause of NAFLD [3,4,5,8].

Purpose of the study: To determine the clinical and laboratory features of non-alcoholic fatty liver disease at the stage of fatty hepatosis and steatohepatitis.

Materials and research methods. To solve the set tasks, 98 patients with NAFLD were examined, including 67 (68.3%) patients at the stage of liver steatosis (HS) and 31 (31.6%) patients with steatohepatitis (SG). Of these, 45 (46%) men and 53 (54%) women aged 20 to 75 years (average age 49.2 ± 4.2). The research results were recorded in the developed clinical information cards (questionnaire). When selecting patients, we considered the criteria for including and not including patients in the study. Criteria for the inclusion of patients in the study: - men and women aged 20 - 75 years; - the presence of fatty hepatosis and steatohepatitis; - the presence of a signed informed consent. The criterion for not including from the survey was alcohol consumption in patients with fatty liver disease. We considered the data of the anamnesis (absence of alcoholic beverages consumption regularly). We also used a special CAGE questionnaire [3,5]. We compared the results obtained in the course of the study with the indicators of the control group, formed of 24 apparently healthy individuals aged 20 to 65 years, who had no abnormalities in the hepatobiliary system. The diagnosis of non-alcoholic fatty liver disease was made on the basis of anamnesis, laboratory tests, and ultrasound examination of the liver. To detect NAFLD, ultrasound of the hepatobiliary system and liver elastography were performed. Lipid metabolism was studied in terms of serum cholesterol (CS), high density lipoproteins (HDL), low density lipoproteins (LDL), very low-density lipoproteins (VLDL) and triglycerides (TG). The LDL and VLDL values were calculated using the formula: VLDL = TG / 2, LDL = CHCR- (VLDL + HDL). Based on the results obtained, the atherogenic coefficient (CA) was calculated using the formula: CA = CS LDL + CS VLDL / HDL. Determination of the degree of obesity was carried out according to the Quetelet index, calculating it using the formula: BMI = weight (kg) / height (m2). The results

obtained were processed statically using the Student's t-test and the difference was considered significant in those cases when p <0.05 was expressed.

Results and discussion. According to the results of our study, the ratio of women to men was 1.3: 1. To assess the characteristics of clinical manifestations, the first duty was to outline the circle of the leading symptoms of NAFLD, which constitutes the essence of the disease. Only then did they proceed to the analysis of each symptom of the disease. At the same time, two of the most important, in our opinion, qualities of clinical signs of NAFLD were subjected to a more thorough analysis: the frequency of occurrence and the degree of their perception. The results are shown in Table 1.

Table 1.

Comparative assessment of the frequency of manifestations of clinical signs of NAFLD

№	Symptoms	HS (n = 67) abs %	SH (n = 31) abs %
1	Aching pain, discomfort in the area right hypochondrium	33 —— 49,2±6,1	18 —— 58,06±8,8
2	Nausea	28 —— 41,7±6,02	18 —— 58,06±8,8
3	Heartburn	35 —— 52,2±6,1	19 —— 61,2±8,7
4	eructation	32 —— 47,7±6,1	21 —— 67,7±8,3
5	flatulence	31 —— 46,2±6,09	19 —— 61,2±8,7
6	constipation	21 —— 31,3±5,6	17 —— 54,8±8,9
7	Mushy chair	20 —— 29,8±5,5	12 —— 38.7±8,7
8	increased fatigue, general weakness	23 —— 34,3±5,7	15 —— 48.3±8,9

The complex of the main clinical sign's characteristic of NAFLD consisted of the following factors: aching pain, discomfort in the right hypochondrium, heartburn; nausea, belching, flatulence, constipation, mushy stools, fatigue, general weakness. As can be seen from Table 1, clinical signs of steatohepatitis in non-alcoholic fatty liver disease occur with a high frequency. Of these, aching pain, discomfort in the right hypochondrium 58.06%. When studying the functional state of the liver, we were interested in the state of lipid metabolism of NAFLD. Lipid metabolism indicators are presented in Table 4.

Table 2.

Indicators of lipid metabolism in patients of the examined groups

Index	CG (n=24)	MG (n=98)	P
Cholesterol (mmol / L)	5,12±0,04	7,3±0,08	0,005
Cholesterol VLDL (mmol / l)	0,37±0,06	0,92±0,02	0,001
Cholesterol LDL (mmol / l)	3,26±0,07	4,62±0,12	0,001
Cholesterol HDL (mmol / L)	1,32±0,04	0,82±0,06	0,001
Triglycerides (g / L)	0,93±0,02	1,96±0,08	0,001
Atherogenic coefficient (CA)	2,72±0,04	6,5±1,12	0,03

Disorders of lipid metabolism in NAFLD are one of the cardinal signs of the disease [3]. According to our data, severe HCS (more than 6 mmol / L) was recorded more often. Dyslipidemia in NAFLD was characterized by an increase in the level of triglycerides more than 1.9 mmol / L and in which the level of HDL cholesterol is <1 mmol / L. These disorders turned out to be more noticeable, which indicated more severe disorders of lipid metabolism. Lipid metabolism indicators are presented in the table. Judging by the data in Table 5, in patients with NAFLD at the stage of steatosis and hepatic steatohepatitis, significant changes in lipid metabolism were revealed towards an increase in cholesterol (p = 0.005), VLDL cholesterol (p = 0.001), LDL cholesterol (p = 0.001), TG (p = 0.001), CA (p = 0.03) and a decrease in HDL (p = 0.001). The results obtained indicate the presence of atherogenic dyslipidemia in NAFLD patients at the stage of steatosis and steatohepatitis. Atherogenicity is a concept that reflects the relationship between bad and good fats. The atherogenic index markedly exceeded the permissible values in all examined patients. In order to assess the functional state of the liver in NAFLD at the stage of fatty hepatosis and steatohepatitis, the parameters of pigment metabolism, cytolysis and cholestasis were studied (Table 3). Biochemical studies were carried out to determine the activity of alanine aminotransferase (ALT) and aspartate aminotransferase (AST), γ-glutamyl transpeptidase (GGTP), alkaline phosphatase (ALP), the content of total bilirubin and its fractions.

Table 3.

Indicators of transaminase levels in the group of examined

Index	CG (n=24)	HS (n=67) 1	SG n=31 2	P_{1-2}
Total protein (g / l)	65,22±0,21	75,2±3,2	78,2±3,8	> 0,05
Albumin g / l	53,2±1,0	45,2±2,2	44,2±2,2	> 0,05
Total bilirubin μmol / l	10,6±0,2	13,6±6,2	19,2±5,2	0,01
Binding bilirubin μmol / l	3,5±0,5	3,8±0,8	4,1±1,6	0,02
ALT (unit / l)	17,6±0,96	27,6±8,7	88,6±31,7	0,001
AST (unit / l)	20,9±1,1	20,9±7,7	48,2±23,7	0,001
alkaline phosphatase ALF (unit / l)	121,9±5,9	132,9±21,9	150,0±28,8	0,02
γ-ГТТП (unit)	24,9±1,1	34,9±12,7	71,9±41,7	0,001
Glucose (mmol / l)	4,3±0,8	5,9±0,9	6,45±0,65	> 0,05

The level of bilirubin was significantly increased relative to the indicators of the control group. The activity of HS cytolysis indices, the AST level reached 20.9, the ALT - 27.6. With steatohepatitis, there are higher ALT values 88.6 and AST 48.2 than in healthy individuals and patients with hepatic steatosis, so ALT in NASH exceeds 6-8 norms, AST exceeds 3-4 norms, with HS ALT exceeds 1- 2 norms, AST does not change significantly. The ALP activity in the SP was 132.9 U / L, which corresponded to the standard values (Table 3). The increase in alkaline phosphatase activity is 1.5-2.5 higher in patients with SH. Indicators of carbohydrate metabolism: the level of glucose in the blood serum was significantly increased (p> 0.05) in the patients we observed, since in the observation group in 25 patients (25.51%), among the comorbidities, there was a violation of tolerance to carbohydrates.

Thus, on the basis of the studies carried out, clinical signs of aching pain, discomfort in the right hypochondrium, belching, heartburn, increased fatigue, general weakness and laboratory for the activity of cytolysis indicators in steatohepatitis, there are higher ALT, AST, ALP values than in patients with hepatic steatosis. The main differential difference between non-alcoholic steatosis and steatohepatitis, available in clinical practice, may be the severity of the biochemical syndrome of cytolysis. Dyslipidemia (hypertriglyceridemia, decreased HDL, increased LDL) occurs in about 65-85% of patients.

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