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Features of the State of Internal Organs and the Structure of Comorbidity in Deceased Persons with Alcoholic Liver Cirrhosis, Non-alcoholic Fatty Liver Disease at the Cirrhosis Stage and Alcoholic Liver Cirrhosis Associated with Insulin Resistance and Obesity

Introduction. A real problem of the present world is the study of the features of the course and management of diseases in comorbidity, which determines the individual prognosis for the patient, and has a significant impact on mortality rates at the general population level. The overwhelming majority of people with chronic non-infectious diseases have more than one pathological condition, which requires consideration of all interacting factors and risks [3]. Modern world basic recommendations focus not only on additional risk factors, but also on the association of diseases, which greatly worsen the recovery and lead to life expectancy decline. It is proved that concomitant diseases worsen not only the course of the disease, but also lead to its chronicity [4, 5]. Among the diseases that make up the polymorbid background, the diseases that have a common pathogenetic link with the underlying disorder or other dependence between them (anatomical proximity to the affected organs, causal relationship) deserve the greatest attention. However, the accidental combination of pathologies is not excluded [1, 2].

Today, the most common pathology among the chronic diffuse liver diseases is non-alcoholic fatty liver disease (NAFLD), which is diagnosed in 20-35% of the adult population, both in industrialized and developing countries [6, 9]. This disease has a long asymptomatic course. The initial manifestations of NAFLD are fatty hepatosis and steatohepatitis, often with obesity and insulin resistance. However, under adversity, the pathological process is transformed into the liver cirrhosis (LC) and may lead to hepatocellular carcinoma. The pathogenesis of NAFLD is complex and associated with a violation of lipid and carbohydrate metabolism, the development of oxidative stress, the immune-inflammatory response, activation of fibrosogenesis, apoptosis and vascular lesion. The same pathogenetic links are inherent in another, not less common, liver disease - alcoholic liver disease (ALD) [7, 8]. Often, in the initial stages of liver disorder, the combination of ALD and NAFLD is not recognized precisely because of the commonality of pathogenetic features. However, in later, advanced, stages with the development of fibrosis and LC, the combination becomes more apparent and manifests itself as systemic complications that are characteristic of each of the nosologies [10, 11]. Such comorbidity acquires the signs of a "deadly duo" characterized by irreversibility, prognostically unfavourable and progressive course.

The aim of the study. The aim of the work was to study the peculiarities of the the state of internal organs in deceased persons with alcoholic liver cirrhosis, non-alcoholic fatty liver disease at the cirrhosis stage and alcoholic liver cirrhosis associated with insulin resistance and obesity on the basis of analysis of protocols of pathoanatomical research.

Materials and methods. 216 protocols of the pathoanatomical study of patients with liver cirrhosis (LC) at the pathoanatomical department of the Ivano-Frankivsk Regional Clinical Hospital for the period of 2005-2018 have been analysed. The average age of patients was (54.0 ± 13.4) years: women - (46.3 ± 8.1) years, men - (58.9 ± 12.3) years, the average duration of the disease - (6.3 ± 1.7) years. By age, the patients were distributed

as follows: 79 young people (53 of them were men, 26 women), 103 middle-aged (76 men, 27 women), 34 elderly (23 men, 11 women). Among the deceased were: 69 (31.9 %) patients with alcoholic liver cirrhosis (ALC), (Group I), 42 (19.4 %) patients with NAFLD at the cirrhosis stage (Group II) and 105 (48.6 %) persons with ALC associated with insulin resistance and obesity (Group III).

The ALD was diagnosed according to the Adapted clinical guideline ″Alcoholic liver disease″ (State Expert Centre of the Ministry of Health of Ukraine, Ukrainian Gastroenterological Association, Kyiv, 2014) and the Order of the Ministry of Health of Ukraine dated November 6, 2014, No. 826 of the protocol on medical care in the specialty ″Alcoholic Hepatitis″.

NAFLD was diagnosed according to the Adapted clinical guidelines ″Non-alcoholic fatty liver disease″ and the Order of the Ministry of Health of Ukraine No. 826 dated November 6, 2014 ″Unified clinical protocol of primary, secondary (specialized) medical care: non-alcoholic steatohepatitis″, Recommendations of the European Association for the Study of Liver (EASL), insulin resistance and obesity was diagnosed according to the European Association for the Study of Diabetes (EASD), the European Association for the Study of Obesity (EASO).

According to the C. G. Child - R. N. Pugh score, among the patients of Group I with stage A, there were 6 (8.7 %) persons (Group IA), with stage B - 9 (13.0 %) persons (Group IB), with stage C - 54 (78.3 %) persons (Group IC); in Group II with stage A were 14 (42.9 %) persons (Group IIA), with stage B - 19 (45.2 %) persons (Group IIB), with stage C - 9 (11.9 %) patients (Group IIC); in Group III with stage A were 28 (26.6 %) persons (Group IIIA), with stage B - 34 (32.4 %) persons (Group IIIB), with stage C - 43 (41.0 %) persons (Group IIIC).

Exclusion criteria were the patients with detected LC of viral, toxic (except alcoholic), autoimmune genesis and metabolic diseases of the liver. Statistical processing of the obtained results was carried out using the software package Statistica v. 12.0, StatSoft, USA and Microsoft Exel. The parameters of parametric statistics - the arithmetic average (M) and the standard deviation (SD), were used. To determine the significance of the differences between the Groups in the distribution, close to normal, Fisher's exact test was used. Statistically significant differences were considered at $p < 0.05$.

Results and discussion. In all patients who died, according to the medical documentation, the signs of portal hypertension, hepatosplenomegaly, cytolytic, hepatodepressive, mesenchymal-inflammatory syndrome were revealed. Among the manifestations of hepatic hyperazotemia were hepatopulmonary syndrome in all patients, liver encephalopathy – in 91.7 % (198 out of 216) and hepatorenal syndrome - in 82.4 % (178 out of 216) of cases in patients with subcompensation and decompensation. The significant difference of the detection freaquency of the hepatorenal syndrome in Class B compared with Class A in Groups I, II and III, respectively, was detected, $p < 0.05$. Signs of cholestasis syndrome were found in 81.0 % (175 out of 216) of persons who died (table). The significant difference of the detection freaquency of the cholestatic syndrome in Group IIIA compared with Group IA was detected, $p < 0.05$. The significant difference of the detection freaquency of the cholestatic syndrome in Class B compared with Class A in Group III was detected, $p < 0.05$. The significant difference of the detection freaquency of the cholestatic syndrome in Class C compared with Class B in Groups I and II, respectively, was detected, $p < 0.05$. The significant difference of the detection freaquency of the hepatorenal syndrome and the cholestatic syndrome in Class C compared with Class A in Groups I, II and III, respectively, was detected, $p < 0.05$.

All patients with decompensation and 45.2 % (28 out of 62) of persons with subcompensation had ascites, and 14.7 % of patients with decompensation had ascites-peritonitis. The significant difference of the detection freaquency of the ascite in Class B compared with Class A in Groups II and III, respectively, was detected, $p < 0.05$. The significant difference of the detection freaquency of the ascite in Class C compared with Class A in Groups I, II and III, respectively, was detected, $p < 0.05$. The significant difference of the detection freaquency of the ascite in Class C compared with Class B in Groups I, II and III, respectively, was detected, $p < 0.05$. The significant difference of the detection freaquency of the ascites-peritonitis in Class C compared with Class A in Group III was detected, $p < 0.05$. The significant difference of the detection freaquency of the ascites-peritonitis in Class C compared with Class B in Group III was detected, $p < 0.05$.

Fatty digestive necrosis was diagnosed in 22.2 % (48 of 216) persons, lipodystrophy of the pancreas was in 33.3 %, 42.8, 61.1, 44.4, 52.6, 73.5, 42.6, 66.6 and 77.3 % of persons of IA, IIA, IIIA, IB, IIB, IIIB, IC, IIC and IIIC Groups respectively, atrophy of the pancreas - in 14.3 %, 16.7, 11,1, 21,1, 32,3, 27, 44,4 and 60,4 % of persons in IIA, IIIA, IB, IIB, IIIB, IC, IIC and IIIC Groups, respectively. The significant difference of the detection freaquency of the atrophy of the pancreas in Class C compared with Class B in Groups I and III, respectively, was detected, $p < 0.05$. Pancreonecrosis was diagnosed in all patients with ALD in stages A and B, and in 16.7 % (3 out of 18) and 2.9 % (1 out of 34) of patients with combination of ALD and insulin resistance and obesity in stages A and B. The significant difference of the detection freaquency of fat necrosis of the omentum and pancreatic necrosis in Class C compared with Class B in Group I was detected, $p < 0.05$.The significant difference of the detection freaquency of the pancreatic necrosis in Groups IIA and IIIA compared with Group IA was detected, $p < 0.05$. The significant difference of the detection freaquency of the pancreatic necrosis in Class B compared with Class A in Group II was detected, $p < 0.05$.

Division of detected pathoanatomical changes of internal organs depending on the stage of decompensation of liver cirrhosis (*n*; %; *p*)

Pathoanatomical changes of internal organs	LC class by C. G. Childe - R. N. Pugh score								
	IA, *n* = 6	IB, *n* = 9	IC, *n* = 54	IIA, *n* = 14	IIB, *n* = 19	IIC, *n* = 9	IIIA, *n* = 18	IIIB, *n* = 34	IIIC, *n* = 53
	abs/%	abs/%	abs/%	abs/%	abs/%	abs/%	abs/%	abs/%	abs/%
Cardiovascular system:									
-hydropericardium	3/50	9/100◊	54/100#	11/78.6	19/100	9/100	18/100*	34/100	53/100
-hypertensive illness	-	3/33.3	0/0°	9/64.3*	14/73.7	6/66.6	16/88.9*	29/85.3	34/64.6#○
-IHD	-	-	4/7.4	11/78.6*	13/68.4	9/100	14/77.8*	27/79.4	53/100#○
-atrial fibrillation	-	-	-	4/28.6	4/21.1	4/44.4	6/33.3	11/32.3	8/15.1°
-extrasystole	2/33.3	4/44.4	29/53.7	5/35.7	6/31.6	5/55.5	7/38.9	19/55.9	34/64.1#
-ischemic stroke in history	-	-	-	2/14.3	3/15.8	2/22.2	4/22.2	7/20.6	6/11.3
-myocardial infarction in history	-	-	-	4/28.6	4/21.1	2/22.2	4/22.2	5/14.7	6/11.3
-chronic venous insufficiency of the lower extremities vessels	-	1/11.1	11/20.4	1/7.1	3/15.8	3/33.3	3/16.7	5/14.7	21/39.6°
-atherosclerosis of the coronary arteries									
--lipidosis	1/16.7	2/22.2	13/24.1	12/85.7*	17/89.5	9/100	16/88.9*	31/91.2	53/100
--atheromatous plaque	-	-	-	9/64.3*	13/68.4	8/88.9	12/66.7*	26/76.5	48/90.6#
--complicated atherosclerotic plaque	-	-	-	2/14.3	3/15.8	2/22.2	5/27.8	10/29.4	17/32.1
--coronary artery stenosis by 10 %	-	-	-	3/21.4	6/31.6	3/33.3	5/27.8	11/32.3	21/39.6
--coronary artery stenosis by 30 %	-	-	-	2/14.3	3/15.8	2/22.2	3/16.7	6/17.6	13/24.5
--coronary artery stenosis by 50 %	-	-	-	1/7.1	2/10.5	1/11.1	2/11.1	5/14.7	7/13.2
--coronary artery stenosis by 90 %	-	-	-	-	2/10.5	-	3/16.7	4/11.8	0/0#○
- atherosclerosis of ileum arteries									
--lipidosis	-	2/22.2	26/48.1#	2/14.3	5/26.3	6/66.7#○	3/16.7	10/29.4	32/60.4#○
--atheromatous plaque	-	-	-	1/7.1	3/15.8	3/33.3	3/16.7	6/17.6	20/37.7°
--complicated atheromatous plaque	-	-	-	-	2/10.5	1/11.1	1/5.5	4/11.8	7/13.2
-atherosclerosis of the aorta									
--lipidosis	2/33.3	4/44.4	25/46.3	14/100*	19/100	9/100	18/100*	34/100	53/100
--atheromatous plaque	-	2/22.2	16/29.6	10/71.4*	15/78.9	7/77.8	11/61.1*	28/82.3	46/85.2#
--complicated atherosclerotic plaque	-	-	-	2/14.3	4/21.1	2/22.2	4/22.2	9/26.5	16/30.2
-closure of the valve									
--aortal	-	1/11.1	1/1.8	1/7.1	3/15.8	2/22.2	2/11.1	6/17.4	16/30.2
--mitral	-	-	1/1.8	1/7.1	2/10.5	1/11.1	3/16.7	6/17.4	12/22.6
-Ischemic abdominal syndrome	-	-	-	-	1/5.3	1/11.1	2/11.1	5/14.7	8/15.1
-Obliterating atherosclerosis of the lower extremities vessels	-	-	-	1/7.1	3/15.8	3/33.3	3/16.7	9/26.5	23/43.4#
-Atherosclerosis of the vessels of the base of the brain									
--lipidosis	-	-	2/3.7	7/50*	8/42.1	9/100#○	10/55.5*	27/79.4	51/96.2#○
--atheromatous plaque	-	-	-	3/21.4	4/21.1	5/55.5	5/27.8	14/41.2	37/69.8#○
-carotid arteriostenosis by 20 %	-	-	-	-	1/5.3	1/11.1	-	2/5.9	7/13.2
-the size of the left ventricle, (M ± SD)	1.59± 0.14	1.62± 0.15	1.53± 0.12	1.94± 0.16*	2.15± 0.19*	2.08± 0.17*	2.29± 0.16 *	2.25± 0.20*	2.14± 0.21*
-the size of the right ventricle, (M ± SD)	0.38± 0.03	0.38± 0.03	0.37± 0.03	0.41± 0.03	0.40± 0.03	0.41± 0.03	0.41± 0.03	0.42± 0.04	0.43± 0.04
Respiratory system:									
-hydrothorax	2/33.3	5/55.5	54/100#○	9/64.3	16/84.2	9/100#	13/72.2	31/91.2	53/100#
-pulmonary edema	2/33.3	4/44.4	54/100#○	8/57.1	16/84.2	9/100#	11/61.1	28/82.3	53/100#○
-pulmonary emphysema	-	-	3/5.5	2/14.3	3/15.8	2/22.2	5/27.8	11/32.3	19/35.8
-pneumonia	-	1/11.1	13/24.1	-	2/10.5	3/33.3	-	6/17.4	22/41.5#○
-pleurisy	-	-	5/9.2	-	1/5.3	2/22.2	1/5.5	3/8.8	15/28.3#○
-chronic bronchitis	-	2/22.2	18/33.3	2/14.3	6/31.6	9/100#○	5/27.8	17/50	53/100#○
Digestive system:									
-portal hypertension	6/100	9/100	54/100	14/100	19/100	9/100	18/100	34/100	53/100
-cytolytic syndrome	6/100	9/100	54/100	14/100	19/100	9/100	18/100	34/100	53/100
-hepatodepressive syndrome	6/100	9/100	54/100	14/100	19/100	9/100	18/100	34/100	53/100
-mesenchymal inflammatory syndrome	6/100	9/100	54/100	14/100	19/100	9/100	18/100	34/100	53/100
-hepatorenal syndrome	-	9/100◊	54/100#	-	19/100◊	9/100#	-	34/100◊	53/100#
-cholestatic syndrome	-	4/44.4	54/100#○	5/35.7	7/36.8	9/100#○	11/61.1*	32/94.1◊	53/100#
-ascite	-	3/33.3	54/100#○	-	6/31.6◊	9/100#○	-	19/55.9◊	53/100#○

-ascites-peritonitis	-	-	4/7.4	-	-	2/22.2	-	-	11/20.7#°
-fat necrosis of the omentum	6/100	9/100	7/12.9°	-	2/10.5	2/22.2	3/16.7	5/14.7	14/26.4
-splenomegaly	6/100	9/100	54/100	14/100	19/100	9/100	18/100	34/100	53/100
-exomphalos	-	-	13/24.1	-	4/21.1	4/44.4#	-	6/17.4	24/45.3#°
-esophageal varices									
Grade I	2/33.3	6/66.6	4/7.4	10/71.4	4/21.1◊	0/0#	13/72.2	7/20.6◊	0/0#°
Grade II	1/16.7	3/33.3	21/38.9	4/28.6	12/63.1◊	2/22.2°	5/27.8	18/52.9	17/32.1°
Grade III	-	-	29/53.7#°	-	3/15.8	6/66.6#°	-	9/26.5◊	36/67.9#°
--with bleeding	-	5/55.5◊	24/44.4#	-	7/36.8◊	5/55.5#	-	15/44.1◊	32/60.4#
- gastric varices	-	4/44.4	21/38.9#	6/42.8	8/42.1	6/66.6	11/61.1*	19/55.9	48/90.6#°
--with bleeding	-	-	13/24.1	-	2/10.5	3/33.3	-	9/26.5◊	19/35.8#
-chronic gastroduodenitis	6/100	9/100	54/100	14/100	19/100	9/100	18/100	34/100	53/100
-erosive gastroduodenitis	-	2/22.2	54/100#°	-	12/63.1◊	9/100°	-	27/79.4◊	53/100#°
-peptic ulcer of the duodenal bulb	1/16.7	2/22.2	9/16.7	2/14.3	3/15.8	4/44.4	3/16.7	6/17.4	7/13.2
-peptic ulcer of the stomach	-	1/11.1	2/3.7	-	2/10.5	1/11.1	1/5.5	4/11.8	4/7.5
-chronic hemorrhoids	1/16.7	2/22.2	24/44.4	2/14.3	6/31.6	4/44.4	4/22.2	11/32.3	31/58.5#°
- hemorrhoidal veins bleeding	-	-	4/7.4	-	-	1/11.1	-	3/8.8	7/13.2
-chronic pancreatitis	6/100	9/100	54/100	14/100	19/100	9/100	18/100	34/100	53/100
-pancreatic necrosis	6/100	9/100	0/0#°	0/0*	0/0◊	-	3/16.7*	1/2.9	0/0#
-lipodistrophy of the pancreas	2/33.3	4/44.4	23/42.6	7/42.8	10/52.6	6/66.6	11/61.1	25/73.5	41/77.3
-atrophy of the pancreas	-	1/11.1	27/50#°	2/14.3	4/21.1	4/44.4	3/16.7	11/32.3	32/60.4#°
- gallstone disease	-	1/11.1	8/14.8	2/14.3	3/15.8	2/22.2	4/22.2	9/26.5	17/32.1
-chronic cholecystitis	6/100	9/100	54/100	14/100	19/100	9/100	18/100	34/100	53/100
-cholangitis	-	-	2/3.7	-	-	2/22.2	-	1/2.9	15/28.3#°
-gallbladder hypotonia	1/16.7	2/22.2	11/20.4	3/21.4	4/21.1	2/22.2	4/22.2	12/35.3	19/35.8
-hepatocellular carcinoma	-	-	-	-	-	-	-	-	6/11.3°
Endocrine disorders:									
-diabetes mellitus I	-	-	-	-	-	-	-	1/2.9	2/3.8
-diabetes mellitus II	-	-	1/1.8	2/14.3	3/15.8	3/33.3	8/44.4	13/38.2	19/35.8
-thyroiditis	-	-	4/7.4	2/14.3	4/21.1	3/33.3	4/22.2	10/29.4	19/35.8
Urinary system:									
-chronic pyelonephritis	-	1/11.1	12/22.2	3/21.4	4/21.1	3/33.3	4/22.2	9/26.5	20/37.7
-kidney cyst	-	-	3/5.5	1/7.1	1/5.3	3/33.3	3/16.7	7/20.6	22/41.5#°
-CKD in the history	-	-	54/100#°	2/14.3	7/36.8	9/100#°	6/33.3	16/47	53/100#°
Nervous System:									
-encephalopathy	4/66.6	9/100	54/100	10/71.4	19/100◊	9/100	15/83.3	34/100◊	53/100#
-alcoholic delirium in the history	1/16.7	2/22.2	16/29.6	-	-	-	3/16.7	6/17.6	20/37.7°

* - the significant difference of the detection frequency of pathoanatomical changes in Groups II and III compared with Group I of the corresponding C. G. Child - R. N. Pugh Classes, $p < 0.05$; ◊ - the significant difference of the detection frequency of pathoanatomical changes of Class B compared with Class A in Groups I, II and III, respectively, $p < 0.05$; # - the significant difference of the detection frequency of pathoanatomical changes of Class C compared with Class A in Groups I, II and III, respectively, $p < 0.05$; ° - the significant difference of the detection frequency of pathoanatomical changes of Class C compared with Class B in Groups I, II and III, respectively, $p < 0.05$.

Varicose veins of the esophagus were detected in 97.2 % (210 out of 216) patients: the first degree - in 33.3 %, 71.4, 72.2, 66.6, 21.1, 20.6 and 7.4 % of persons in IA, IIA, IIIA, IB, IIB, IIIB, IC Groups, respectively; second degree - in 16.7 %, 28.6, 27.8, 33.3, 63.1, 52.9, 38.9, 22.2 and 32.1 % of people of IA, IIA, IIIA, IB, IIB, IIIB, IC, IIC and IIIC Groups respectively; the third degree - in 15.8 %, 26.5, 53.7, 66.6 and 67.9 % of persons of IIB, IIIB, IC, IIC and IIIC Groups, respectively. The significant difference of the detection frequency of the Grade I esophageal varices in Class B compared with Class A in Groups II and III, respectively, was detected, $p < 0.05$. The significant difference of the detection frequency of the Grade I esophageal varices in Class C compared with Class A in Groups II and III, respectively, was detected, $p < 0.05$. The significant difference of the detection freaquency of the Grade II esophageal varices in Class B compared with Class A in Group II was detected, $p < 0.05$. The significant difference of the detection frequency of the Grade II esophageal varices in Class C compared with Class B in Groups II and III, respectively, was detected, $p < 0.05$. The significant difference of the detection frequency of the Grade III esophageal varices in Class B compared with Class A in Group III was detected, $p < 0.05$. The significant difference of the detection frequency of the Grade III esophageal varices in Class C compared with Class A in Groups I, II and III, respectively, was detected, $p < 0.05$. The significant difference of the detection frequency of the Grade III esophageal varices in Class C compared with Class B in Groups II and III, respectively, was detected, $p < 0.05$.

The varicose veins of the stomach were in 42.8 %, 61.1, 44.4, 42.1, 55.9, 38.9, 66.6 and 90.6 % of the patients in IIB, IIIB, IC, IIC and IIIC Groups, respectively. The significant difference of the detection frequency of the gastric varices in Group IIIA compared with Group IA was detected, $p < 0.05$. The significant difference of the detection frequency of the gastric varices in Class C compared with Class A in Groups I and III, respectively, was detected, $p < 0.05$.

Bleeding from varicose veins of the esophagus was detected in 55.5 %, 36.8, 44.1, 44.4, 55.5 and 60.4 % of persons

of IB, IIB, IIIB, IC, IIC and IIIC Groups, respectively. The significant difference of the detection frequency of the esophageal varices with bleeding in Class B compared with Class A in Groups I, II and III, respectively, was detected, $p < 0.05$. The significant difference of the detection frequency of the esophageal varices with bleeding in Class C compared with Class A in Groups I, II and III, respectively, was detected, $p < 0.05$. IBleeding from the stomach veins was in 10.5 %, 26.5, 24.1, 33.3, and 35.8 % of the patients of IIB, IIIB, IC, IIC and IIIC Groups, respectively. The significant difference of the detection frequency of the gastric varices with bleeding in Class B compared with Class A in Group III was detected, $p < 0.05$. The significant difference of the detection frequency of the gastric varices with bleeding in Class C compared with Class A in Group III was detected, $p < 0.05$.

Bleeding from hemorrhoidal veins was in 8.8 %, 7.4, 11.1 and 13.2 % of persons of IIIB, IC, IIC and IIIC Groups, respectively.

Concomitant diseases with lesions of the gastrointestinal tract were the following: chronic gastroduodenitis in all patients who died, erosive gastroduodenitis in 22,2, 63,1, 79,4 % of people of IB, IIB, IIIB Groups, respectively and in all deceased patients with decompensation; peptic ulcer of the duodenal bulb - in 16.7 %, 14.3, 16.7, 22.2, 15.8, 17.4, 16.7, 44.4 and 13.2 % of persons IA, IIA, IB, IIB, IIIB, IC, IIC and IIIC Groups respectively; peptic ulcer of the stomach - in 5.5 %, 11.1, 10.5, 11.8, 3.7, 11.1 and 7.5 % of people of IIIA, IB, IIB, IIIB, IC, IIC and IIIC Groups, respectively; chronic hemorrhoids - in 16.7 %, 14.3, 22.2, 22.2, 31.6, 32.3, 44.4, 44.4 and 58.5 % of people with IA, IIA, IIIA, IB, IIB, IIIB, IC and IIIC Groups, respectively; exomphalos was in persons with subcompensation and decompensation in 28.7 % (51 out of 178) cases; chronic pancreatitis and chronic cholecystitis were found in all patients who died; gallstone disease was in 14.3 %, 22.2, 11.1, 15.8, 26.5, 14.8, 22.2 and 32.1 % of persons of IIIB, IC, IIC and IIIC Groups, respectively; gallbladder cholangitis was detected in 2.9 %, 3.7, 22.2 and 28.3 % of persons of IIIB, IC, IIC and IIIC Groups, respectively; gallbladder hypotonia was in 16.7 %, 21.4, 22.2, 22.2, 21.1, 35.3, 20.4, 22.2 and 35.8 % of cases in IA, IIA, IIIA, IB, IIB, IIIB, IC, IIC and IIIC Groups respectively. In 11.3 % (6 out of 53) persons of Group IIIC hepatocellular carcinoma was diagnosed. The significant difference of the detection ffrequency of the erosive gastroduodenitis, the pancreatic necrosis and the atrophy of the pancreas in Class C compared with Class A in Groups I and III, respectively, was detected, $p < 0.05$.

The significant difference of the detection frequency of the erosive gastroduodenitis in Class C compared with Class B in Groups I, II and III, respectively, was detected, $p < 0.05$. The significant difference of the detection frequency of the erosive gastroduodenitis in Class B compared with Class A in Groups II and III, respectively, was detected, $p < 0.05$. The significant difference of the detection frequency of the exomphalos, the Grade I esophageal varices, the gastric varices, the chronic hemorrhoids, the cholangitis and the hepatocellular carcinoma in Class C compared with Class B in Group III was detected, $p < 0.05$. The significant difference of the detection frequency of the exomphalos in Class C compared with Class A in Groups II and III, respectively, was detected, $p < 0.05$. The significant difference of the detection frequency of the chronic hemorrhoids and the cholangitis in Class C compared with Class A in Group III was detected, $p < 0.05$.

Among the diseases of the endocrine system, there was type 1 diabetes mellitus in 2.9 and 3.8 % of the patients of IIIB and IIIC Groups, respectively; type II diabetes mellitus - in 14.3 %, 44.4, 15.8, 38.2, 1.8, 33.3 and 35.8 % of people in IIA, IIIA, IIB, IIIB, IC, IIC and IIIC Groups , respectively; thyroiditis - in 14.3 %, 22.2, 21.1, 29.4, 7.4, 33.3 and 35.8 % of people in IIA, IIIA, IIB, IIIB, IC, IIC and IIIC Groups , respectively.

Concomitant diseases of the urinary tract organs were: chronic pyelonephritis in 21.4 %, 22.2, 11.1, 21.1, 26.5, 22.2, 33.3 and 37.7 % of persons of IIA, IIIA, IB, IIB, IIIB, IC, IIC and IIIC Groups respectively; kidney cysts - in 7.1 %, 16.7, 5.3, 20.6, 5.5, 33.3 and 41.5 % of patients of IIA, IIIA, IIB, IIIB, IC, IIC and IIIC Groups respectively; chronic kidney disease (CKD) according to the acts was diagnosed in 14.3 %, 33.3, 36.8, 47.0 % of people of IIA, IIIA, IIB, IIIB Groups, respectively, and in all patients with the stage of decompensation. The significant difference of the detection freaquency of the kidney cyst in Class C compared with Class A in Group III was detected, $p < 0.05$. The significant difference of the detection frequency of the kidney cyst in Class C compared with Class B in Group III was detected, $p < 0.05$. The significant difference of the detection frequency of the CKD in the history in the history in Class C compared with Class A in Groups I, II and III, respectively, was detected, $p < 0.05$. The significant difference of the detection frequency of the CKD in the history in Class C compared with Class B in Groups I, II and III, respectively, was detected, $p < 0.05$.

Among the disorders of the respiratory system in the deceased patients were: hydrothorax - in 33.3 %, 64.3, 72.2, 55.5, 84.2, 91.2 % of cases in IA, IIA, IIIA, IB, IIB, IIIB, IC, IIC and IIIC Groups, respectively; the pulmonary oedema - in 33.3 %, 57.1, 61.1, 44.4, 84.2, 91.2 % of persons in IA, IIA, IIIA, IB, IIB, IIIB Groups, respectively and in all deceased patients with the stage of decompensation; lung emphysema was detected in 14.3 %, 27.8, 15.8, 32.3, 5.5, 22.2 and 35.8 % of patients in IIA, IIIA, IIB, IIIB, IC, IIC and IIIC Groups , respectively; pneumonia - in 11.1 %, 10.5, 17.4, 24.1, 33.3 and 41.5 % of patients with the stage of subcompensation and decompensation; pleurisy - in 5.5 %, 5.3, 8.8, 9.2, 22.2 and 28.3 % of people iin IIIA, IIB, IIIB, IC, IIC and IIIC Groups, respectively; chronic bronchitis - in 14.3 %, 27.8, 22.2, 31.6, 50.0, 33.3, 100.0 and 100.0 % of cases in IIA, IIIA, IB, IIB, IIIB, IC, IIC and IIIC Groups, respectively. The significant difference of the detection frequency of the hydrothorax and the pulmonary edema in Class C compared with Class A in Groups I, II and III, respectively, was detected, $p < 0.05$.

The significant difference of the detection frequency of the hydrothorax in Class C compared with Class B in Group I was detected, $p < 0.05$. The significant difference of the detection frequency of the pulmonary edema in Class C compared with Class B in Groups I and III, respectively, was detected, $p < 0.05$. The significant difference of the detection frequency of the pneumonia and the pleurisy in Class C compared with Class A in Group III was detected, $p < 0.05$. The significant difference of the detection frequency of the pneumonia and the pleurisy in Class C compared with Class B in Group III was detected, $p < 0.05$. The significant difference of the detection frequency of the chronic bronchitis in Class C compared with Class A in Groups II and III, respectively, was detected, $p < 0.05$. The significant difference of the detection frequency of the chronic bronchitis in Class C compared with Class B in Groups II and III, respectively, was detected, $p < 0.05$.

Medical impression also included the disorders of the central nervous system, among which were: encephalopathy - in 66.6 %, 71.4, 83.3 % of people of IA, IIA, IIIA Groups, respectively, and in all patients with subcompensation and decompensation; alcoholic delirium - in 16.7 %, 16.7, 22.2, 17.6, 29.6 and 37.7 % of persons of IA, IIIA, IB, IIIB, IC and IIIC Groups, respectively. The significant difference of the detection frequency of the encephalopathy in Class B compared with Class A in Groups II and III, respectively, was detected, $p < 0.05$. The significant difference of the detection frequency of the encephalopathy in Class C compared with Class A in Group III was detected, $p < 0.05$. The significant difference of the detection frequency of the alcoholic delirium in the history in Class C compared with Class B in Group III was detected, $p < 0.05$.

Special attention should be paid to the analysis of changes in the cardiovascular system. In particular, hydropericardium as a manifestation of cirrhotic cardiac decompensation was observed in 50.0, 78.6 % of patients in IA, IIA Groups, respectively, and in all deceased patients of other Groups. The significant difference of the detection freaquency of the hydropericardium in Class C compared with Class A in Group I was detected, $p < 0.05$. The significant difference of the detection frequency of the hydropericardium in Class B compared with Class A in Group I was detected, $p < 0.05$. When comparing the size of the left ventricle in the deceased people, a significant increase in the Groups II and III ($p < 0.05$) was noticed, however, the size of the right ventricle did not differ in persons with different stages of compensation ($p > 0.05$).

Hypertension was concomitant in 64.3 %, 88.9, 33.3, 73.7, 85.3, 66.6 and 64.6 % of cases in IIA, IIIA, IB, IIB, IIIIB, IIC and IIIC Groups, respectively; people of IIA, IIIA, IIB, IIIB and IC Groups respectively ischemic heart disease (IHD) - in 78.6 %, 77.8, 68.4, 79.4, 7.4 % of people of IIA, IIIA, IIB, IIIB and IC Groups, respectively and in all persons of IIC, IIIC Groups who died. The significant difference of the detection frequency of the hypertensive illness and the IHD in Groups IIA and IIIA compared with Group IA was detected, $p < 0.05$. The significant difference of the detection frequency of the hypertensive illness and the IHD in Class C compared with Class A in Group III was detected, $p < 0.05$. The significant difference of the detection freaquency of the hypertensive illness in Class C compared with Class B in Groups I and III, respectively, was detected, $p < 0.05$.

The violations of the rhythm by atrial fibrillation type were recorded in the acts of pathological anatomical examination in 28.6 %, 33.3, 21.1, 32.3, 44.4 and 15.1 % of persons in IIA, IIIA, IIB, IIIB, IIC and IIIC Groups; according to the extrasystole type - in 33.3 %, 35.7, 38.9, 44.4, 31.6, 55.9, 53.7, 55.5 and 64.1 % of persons of IA, IIA, IIIA, IB, IIB, IIIB, IC, IIC and IIIC Groups, respectively. The significant difference of the detection frequency of the atrial fibrillation and chronic venous insufficiency of the lower extremities vessels in Class C compared with Class B in Group III was detected, $p < 0.05$. The significant difference of the detection frequency of the extrasystole in Class C compared with Class A in Group III was detected, $p < 0.05$.

The history of the deceased patients included an ischemic stroke in 14.3 %, 22.2, 15.8, 20.6, 22.2 and 11.3 % of cases in IIA, IIIA, IIB, IIIB, IIC and IIIC Groups, respectively, myocardial infarction - in 28.6 %, 22.2, 21.1, 14.7, 22.2 and 11.3 % of cases in IIA, IIIA, IIB, IIIB, IIC and IIIC Groups, respectively. Chronic venous insufficiency was in 7.1 %, 16.7, 11.1, 15.8, 14.7, 20.4, 33.3 and 39.6 % of persons in IA, IIA, IIIA, IB, IIB, IIIB, IC, IIC and IIIC Groups, respectively. The significant difference of the detection frequency of the chronic venous insufficiency of the lower extremities vessels in Class C compared with Class B in Group III was detected, $p < 0.05$.

The obliterating atherosclerosis of the lower limb vessels was observed in 7.1 %, 16.7, 15.8, 26.5, 33.3 and 43.4 % of the deceased of IIA, IIIA, IIB, IIIB, IIC and IIIC Groups , respectively . The significant difference of the detection frequency of obliterating atherosclerosis of the lower extremities vessels in Class C compared with Class A in Group III was detected, $p < 0.05$.

Ischemic abdominal syndrome was diagnosed in 11.1 %, 5.3, 14.7, 11.1 and 15.1 % of people of IIIA, IIB, IIIB, IIC and IIIC Groups, respectively.

Changes in the bloodstream were characterized by significant atherosclerotic lesions, especially in the deceased of Groups II and III. In particular, atherosclerosis of the coronary arteries at the stage of lipoidosis was in 16.7 %, 85.7, 88.9, 22.2, 89.5, 91.2, 24.1 % of persons of IA, стопчик, абзац, 5, рядок 6 - IIA, IIIA, IB, IIB, IIIB, IC Groups, respectively, and in all deceased of IIC and IIIC Groups; at the stage of an atheromatous plaque - in 64.3 %, 66.7, 68.4, 76.5, 88.9 and 90.6 % of persons in IIA, IIIA, IIB, IIIB, IIC and IIIC Groups, respectively ; at the stage of complicated atherosclerotic plaque - in 14.3 %, 27.8, 15.8, 29.4, 22.2 and 32.1 % of persons of IIA, IIIA, IIB, IIIB, IIC and IIIC Groups, respectively. People of Groups II and III had the narrowing of coronary arteries, mostly of the left. In particular, the narrowing of the coronary artery by 10 % was in 21.4 %, 27.8, 31.6,

32.3, 33.3 and 39.6 % of patients in IIA, IIIA, IIB, IIIB, IIC and IIIC Groups, respectively; by 30 % - in 14.3 %, 16.7, 15.8, 17.6, 22.2 and 24.5 % of persons in IIA, IIIA, IIB, IIIB, IIC and IIIC Groups, respectively; by 50 % - in 7.1 %, 11.1, 10.5, 14.7, 11.1 and 13.2 % of persons of IIA, IIIA, IIB, IIIB, IIC and IIIC Groups, respectively; by 90 % - in 16.7 %, 10.5 and 11.8 % of the people of IIIA, IIB and IIIB Groups, respectively. Atherosclerotic changes in the iliac artery were manifested by lipoidosis in 14.3 %, 16.7, 22.2, 26.3, 29.4, 48.1, 66.7 and 60.4 % of cases in IIA, IIIA, IB, IIB, IIIB, IC, IIC and IIIC Groups, respectively; atheromatous plaques - in 7.1 %, 16.7, 15.8, 17.6, 33.3 and 37.7 % of patients in IIA, IIIA, IIB, IIIB, IIC and IIIC Groups, respectively; complicated atheromatous plaques - in 5.5 %, 10.5, 11.8, 11.1 and 13.2 % of people of IIIA, IIB, IIIB, IIC and IIIC Groups, respectively.

The aortic aterosclerosis was recorded at the stage of lipoidosis in 33.3 %, 44.4 and 46.3 % of the people of IA, IB and IC Groups, respectively, and in all patients of Groups II and III; at the stage of atheromatous plaque - in 71.4 %, 61.1, 22.2, 89.5, 82.3, 29.6, 77.8 and 85.2 % of patients in IIA, IIIA, IB, IIB, IIIB, IC, IIC in IIIC Groups, respectively; at the stage of the complicated atheromatous plaque - in 14.3 %, 22.2, 21.1, 26.5, 22.2 and 30.2 % of people in IIA, IIIA, IIB, IIIB, IIC and IIIC Groups, respectively.

The changes in the valves of the heart were also detected. In particular, the sclerosis of the aortic valve was in 7.1%, 11.1, 11.1, 15.8, 17.4, 1.8, 22.2 and 30.2 % of patients of IIA, IIIA, IB, IIB, IIIB, IC, IIC and IIIC Groups, respectively; the mitral valve sclerosis - in 7.1 %, 16.7, 10.5, 17.4, 1.8, 11.1 and 22.6 % of people in IIA, IIIA, IIIB, IIIB, IC, IIC and IIIC Groups, respectively. The atherosclerosis of the base of the brain vessels at the stage of lipoidosis was found in 50.0 %, 55.5, 42.1, 79.4, 3.7, 100.0 and 96.2 % of persons in IIA, IIIA, IIB, IIIB, IC, IIC and IIIC Groups, respectively; at the stage of atheromatous plaque - in 21.4 %, 27.8, 21.1, 41.2, 55.5 and 69.8 % of persons of IIA, IIIA, IIB, IIIB, IIC and IIIC Groups, respectively. The narrowing of the common carotid artery by 20 % was revealed in 5.3 %, 5.9, 11.1 and 13.2 %, of cases in IIB, IIIB, IIC and IIIC Groups, respectively. The significant difference of the detection frequency of the lipidosis and atheromatous plaque of the coronary arteries and aorta, the lipidosis of the brain base vessels in Groups IIA and IIIA compared with Group IA was detected, $p < 0.05$. The significant difference of the detection frequency of the coronary arteries atheromatous plaque and the coronary artery stenosis by 90.0 % in Class C compared with Class A in Group III was detected, $p < 0.05$. The significant difference of the detection frequency of the ileum arteries lipidosis in Class C compared with Class A in Groups I, II and III, respectively, was detected, $p < 0.05$. The significant difference of the detection frequency of the ileum arteries lipidosis in Class C compared with Class B in Groups II and III, respectively, was detected, $p < 0.05$. The significant difference of the detection frequency of the coronary artery stenosis by 90.0 %, atheromatous plaque of the ileum arteries and the atheromatous plaque of the brain base vessels in Class C compared with Class B in Group III was detected, $p < 0.05$.

The significant difference of the detection frequency of the vessels of the brain base lipidosis in Class C compared with Class A in Group II was detected, $p < 0.05$. The significant difference of the detection freaquency of the vessels of the brain base lipidosis and atheromatous plaque in Class C compared with Class A in Group III was detected, $p < 0.05$. The significant difference of the detection frequency of the vessels of the brain base lipidosis in Class C compared with Class A in Group II was detected, $p < 0.05$. The significant difference of the detection frequency of the lipidosis of the brain base vessels in Class C compared with Class B in Groups II and III, respectively, was detected, $p < 0.05$.

The indicators of the size of the left ventricle were 1.22, 1.33 and 1.36 times higher in Groups IIA, IIB, IIC compared to patients of Groups IA, IB, IC, respectively ($p < 0.05$). The indicators of the size of the left ventricle were 1.44, 1.39 and 1.40 times higher in Groups IIIA, IIIB, IIIC compared to patients of Groups IA, IB, IC, respectively ($p < 0.05$). When comparing the indicators of the size of the right ventricle in Groups II and III compared to patients of Group I, depending on the compensation of the disease, no significant difference was found between the indices ($p > 0.05$).

The analysis of the pathoanatomical study maps of the deceased from LC was carried out. In all cases the signs of portal hypertension, hepatosplenomegaly, cytolytic, hepatodepressive, mesenchymal inflammatory, hepatopulmonary syndromes were revealed. All persons with subcompensation and decompensation had hepatotoxic syndrome. More than 80 % had symptoms of cholestasis, more than 90 % of people suffered from the liver encephalopathy. The disturbances in the digestive, respiratory, urinary, cardiovascular, endocrine and nervous systems were revealed.

All persons with decompensation, and about half of people with subcompensation had ascites. More than 70 % of those who suffered from fatty necrosis of the gland had pancreatic necrosis and peritonitis ascites. Lipodystrophy and atrophy of the pancreas were more pronounced in people with NAFLD and ALD associated with insulin resistance and obesity. The degree of severity of varicose veins of the esophagus and stomach corresponded to the degree of LC compensation; bleedings were observed in persons with stages B and C, especially in those who had a combination of ALD and insulin resistance and obesity. Concomitant diseases were chronic pancreatitis, chronic cholecystitis and chronic gastroduodenitis. 66.1 % of patients with subcompensation and all people with decompensation had erosive gastroduodenitis, 39.3 % of patients suffered from chronic hemorrhoids, 26.8 % of persons had gallbladder hypotonia, 21.3 % of people had gallstone disease, in 17.1 % of people was ulcer of duodenal bulb, 6.9 % of people had stomach ulcer, 9.3 % of people suffered from cholangitis. Hepatocellular carcinoma was detected in 5.3% of patients of Group III.

All patients suffered from respiratory system disorders. More pronounced changes were observed in those who combined ALD and insulin resistance and obesity: hydrothorax was in all persons with stage C, in 46.7 % of the patients of IA+B Group, in 75.7 % of patients of IIA+B Group and in 84.6 % in IIIA+B Group; the pulmonary edema was in all persons with stage C, in 40.0 % of people in IA+B Group, in 72.7 % of persons in IIA+B Group and in 75.0 % in IIIA+B Group; emphysema was in 4.3 % in Group I, 16.7 % in Group II and 33.3 % in Group III; pleurisy was in 7.2 and 7.1 % in Groups I and II with decompensation respectively and in 18.1 % in Group III; pneumonia was in the deceased with stages of subcompensation and decompensation in 22.2 % in IB+C Group, in 17.9 % of persons in IIB+C Group and in 32.2 % of persons in IIIB+C Group; chronic bronchitis was in one third of all patients of Group I, in 40.5 % in Group II and 57.1 % in Group III.

Atherosclerotic changes in the vascular bed were more pronounced in persons of Group II and especially of Group III, and were accompanied by more frequent development of complicated atherosclerotic plaque with narrowing of the lumen of the coronary and carotid arteries. Also people of Groups II and III had more often sclerosis of the aortic and mitral valve of the heart. Ischemic stroke was anamnestically recorded in cards of the deceased of Group II in 16.7 %, in Group III - in 16.2 %, myocardial infarction - in 23.8 % of patients of Group II and in 14.3 % in Group III. Among the concomitant diseases were: hypertension in 4.3, 69.0, 75.2 % of people in Groups I, II and III, respectively; coronary artery disease in 5,8, 78.6, 89.5 % of persons of Groups I, II and III, respectively; chronic venous insufficiency of the lower extremities vessels in 17.4, 16.7 and 27.6 % of persons in Groups I, II and III, respectively; obliterating atherosclerosis of the lower limbs vessels in 16.7 and 33.3 % of persons in II and III Groups, respectively; ischemic abdominal syndrome in 9.5 and 14.3 % of people in Groups II and III, respectively.

People who died from LC had rhythm disturbances; atrial fibrillation was in one third of all persons of Group II and in 18.1 % of Group III; ectopic heartbeat was in half of patients in Group I, in 38.1 and 39.0 % in Groups II and III, respectively. Among disorders of the urinary system, chronic pyelonephritis was detected in 25.9 %, kidney cysts - in 18.5 %, chronic kidney disease - in 25.0 % in Groups II and III (stage A), 43.4 % in Groups II and III (stage B) and all persons with stage C. Among the endocrine disorders were: type II diabetes mellitus in 19.0 % of patients of Group II and in 38.1 % of Group III, thyroiditis was found in 21.3 % of cases, preferably in combination of ALD and insulin resistance and obesity. Encephalopathy was in 76.3 % of patients with stage A and in all persons with stages B and C. Alcoholic delirium was in the history of one third of people in Groups I and III, respectively.

Analyzing the features of internal organs disorders and the structure of concomitant pathology in the deceased persons with ALD at the stage of cirrhosis of the liver associated with insulin resistance and obesity, it was revealed that along with the characteristic syndromes of liver cirrhosis (portal hypertension, hepatosplenomegaly, cytolytic, hepatodepressive, mesenchymal inflammatory, hepatopulmonary, hepatorenal, cholestatic, hepatic encephalopathy), disorders of the organs of the digestive, respiratory, urinary, cardiovascular, endocrine and nervous systems were more pronounced. With increasing decompensation of the disease, the number of concomitant pathologies increased. Each deceased with a combination of ALD and insulin resistance and obesity at the stage of subcompensation had more than four concomitant diseases, and at the stage of decompensation – more than six concomitant diseases. They had significant systemic atherosclerotic lesions of the vascular bed, which led to the development of acute vascular adverse events for one third of people. In 5.3 % of people with a combination of ALD and insulin resistance and obesity, hepatocellular carcinoma was detected.

Conclusions. In deceased persons with alcoholic liver disease at the stage of cirrhosis of the liver with insulin resistance and obesity the disorders of the organs of the digestive, respiratory, urinary, cardiovascular, endocrine and nervous systems were more pronounced. They had significant systemic atherosclerotic lesions of the vascular bed, which led to the development of acute vascular adverse events for one third of people.

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Features of the State of Internal Organs and the Structure of Comorbidity in Deceased Persons with Alcoholic Liver Cirrhosis, Non-alcoholic Fatty Liver Disease at the Cirrhosis Stage and Alcoholic Liver Cirrhosis Associated with Insulin Resistance and Obesity

N. Matkovska

Introduction. Today, the most common pathologies among the chronic diffuse liver diseases is non-alcoholic fatty liver disease (NAFLD) and alcoholic liver disease.

The aim of the study. The aim of the work was to study the peculiarities of the the state of internal organs in deceased persons with alcoholic liver cirrhosis (ALC), NAFLD at the cirrhosis stage and ALC associated with insulin resistance (IR) and obesity on the basis of analysis of protocols of pathoanatomical research.

Materials and methods. 216 protocols of the pathoanatomical study of patients with liver cirrhosis (LC). Among the deceased were: 69 (31.9 %) patients with ALC, 42 (19.4 %) patients with NAFLD at the cirrhosis stage and 105 (48.6 %) persons with ALC associated with IR and obesity.

Results. In deceased persons with ALC associated with IR and obesity, it was revealed that disorders of the organs of the digestive, respiratory, urinary, cardiovascular, endocrine and nervous systems were more pronounced. Each deceased with a combination of ALD and IR and obesity at the stage of subcompensation, had more than four, and at the stage of decompensation - more than six concomitant diseases. They had significant systemic atherosclerotic lesions (SAL) of the vascular bed. In 5.3 % of people with ALC associated with IR and obesity, hepatocellular carcinoma was detected.

Conclusions. In deceased persons with ALC with IR and obesity the disorders of the organs of the digestive, respiratory, urinary, cardiovascular, endocrine and nervous systems were more pronounced. They had significant SAL of the vascular bed, which led to the development of acute vascular adverse events for one third of people.

Keywords: comorbidity, non-alcoholic fatty liver disease, liver cirrhosis, alcoholic.

Особливості стану внутрішніх органів і структура коморбідних уражень у померлих із алкогольним цирозом печінки, неалкогольною жировою хворобою печінки на стадії цирозу та з алкогольним цирозом печінки, асоційованим з інсулінорезистентністю та ожирінням

Н. Р. Матковська

Вступ. Вивчення особливостей перебігу хвороб та курації хворих за умов коморбідності є загальносвітовою проблемою сьогодення, що не тільки визначає індивідуальний прогноз для хворого, але й суттєво впливає на показники смертності на загальнопопуляційному рівні. Більшість людей із хронічними неінфекційними недугами мають більш ніж одну хворобу, що потребує врахування усіх взаємодіючих чинників та ризиків. Сучасні базові світові рекомендації зосереджуються не лише на додаткових чинниках ризику, але й на асоціації хвороб, що значно погіршують умови одужання і призводять до скорочення тривалості життя. Доведено, що супутні хвороби не лише погіршують перебіг основної недуги, але й призводять до її хронізації. Серед коморбідних хвороб на найбільшу увагу заслуговують ті, що мають спільні патогенетичні ланки з основною недугою, чи іншу залежність між ними (анатомічна близькість уражених органів, причинно-наслідковий зв'язок). Але не виключається і випадкове поєднання хвороб.

Сьогодні найчастішим ураженням серед хронічних дифузних хвороб печінки визнано неалкогольну жирову хворобу печінки (НАЖХП), яка виявляється у 20,0–35,0 % дорослого населення як у індустріально розвинутих країнах, так і в країнах, що розвиваються. Хвороба тривалий час має безсимптомний перебіг. Початковими проявами НАЖХП є жировий гепатоз і стеатогепатит з інсулінорезистентністю та ожирінням. Проте за несприятливих умов патологічний процес трансформується у цироз печінки (ЦП) та може призвести до виникнення гепатоцелюлярної карциноми. Патогенез НАЖХП складний і асоційований із порушенням ліпідного та вуглеводного обміну, виникненням оксидативного стресу, імуно-запальної відповіді, активацією фіброзогенезу й апоптозу, ураженням судинного русла. Такі ж патогенетичні ланки властиві іншій поширеній хворобі печінки – алкогольній хворобі печінки (АХП). Часто на початкових стадіях ураження печінки поєднання АХП та НАЖХП не розпізнається саме через спільність патогенетичних механізмів. Проте на більш пізніх, заавансованих стадіях із виникненням фіброзу та ЦП поєднання стає більш очевидним і виявляється системними ускладненнями, характерними для кожної з нозологій. Така коморбідність набуває ознак «смертельного дуету», що характеризується незворотністю, негативним і прогностично несприятливим перебігом.

Мета. З'ясувати особливості змін внутрішніх органів і структури коморбідних уражень у померлих із алкогольним цирозом печінки (АЦП), НАЖХП на стадії цирозу та АЦП, асоційованим із інсулінорезистентністю та ожирінням, на основі аналізу протоколів патолого-анатомічного дослідження.

Матеріали й методи. Проаналізовано 216 протоколів патолого-анатомічного дослідження померлих на ЦП на базі патолого-анатомічного відділення Івано-Франківської обласної клінічної лікарні за період 2005–2018 рр. (серед них 64 жінки та 152 чоловіка). Середній вік хворих становив (54,0 ± 13,4) років: жінок – (46,3 ± 8,1) років, чоловіків – (58,9 ± 12,3) років, середня тривалість хвороби – (6,3 ± 1,7) року. Хворих розподілено за віком: 79 померлих були молодого віку (26 жінок, 53 чоловіки), 103 – середнього віку (27 жінок, 76 чоловіків), 34 – похилого віку (11 жінок, 23 чоловіки). Серед померлих було 69 (31,9 %) хворих на АЦП (I група), 42 (19,4 %) – на НАЖХП на стадії ЦП (II група) та 105 (48,6 %) – із поєднанням АЦП та інсулінорезистентності й ожиріння (III група).

АХП діагностували відповідно до адаптованої клінічної настанови «Алкогольна хвороба печінки» (Державний експертний центр МОЗ України, Українська гастроентерологічна асоціація, Київ, 2014) та Наказу МОЗ України № 826 від 06.11.2014 р. згідно з протоколом надання медичної допомоги за спеціальністю «Алкогольний гепатит». НАЖХП діагностували відповідно до адаптованої клінічної настанови «Неалкогольна жирова хвороба печінки» та Наказу МОЗ України № 826 від 06.11.2014 р. «Уніфікований клінічний протокол первинної, вторинної (спеціалізованої) медичної допомоги: неалкогольний стеатогепатит», Рекомендацій Європейської асоціації з вивчення печінки (EASL), інсулінову резистентність і ожиріння діагностували відповідно до рекомендацій Європейської асоціації з вивчення діабету (EASD), Європейської асоціації з вивчення ожиріння (EASO).

Відповідно до критеріїв C. G. Child – R. N. Pugh серед померлих I групи зі стадією А було 6 (8,7 %) хворих (IA група), зі стадією В – 9 (13,0 %) хворих (IB група), зі стадією С – 54 (78,3 %) хворих (IC група); серед померлих II групи зі стадією А було 14 (42,9 %) хворих (IIA група), зі стадією В – 19 (45,2 %) хворих (IIB група), зі стадією С – 9 (11,9 %) хворих (IIC група); серед померлих III групи зі стадією А було 28 (26,6 %) хворих (IIIA група), зі стадією В – 34 (32,4 %) хворих (IIIB група), зі стадією С – 43 (41,0 %) хворих (IIIC група).

Критеріями виключення були померлі з виявленим ЦП вірусного, токсичного (окрім алкогольного), автоімунного генезу, метаболічними хворобами печінки.

Статистичну обробку отриманих результатів проводили за допомогою пакета програмного забезпечення Statistica v. 12.0, StatSoft, США та Microsoft Exel. Використовували показники параметричної статистики – середнє арифметичне значення (M) і стандартне відхилення (SD). Для визначення значущості відмінностей між групами під час розподілу, близького до нормального, використовували точний критерій Р. Фішера. Статистично значущим вважали відмінності за $p < 0,05$.

Результати. У всіх померлих виявлено ознаки портальної гіпертензії, гепатоспленомегалії, цитолізного, гепатодепресивного, мезенхімально-запального, гепатопульмонального синдромів. У всіх померлих із субкомпенсацією і декомпенсацією був гепаторенальний синдром. Понад 80,0 % мали ознаки холестазу, понад 90,0 % – печінкову енцефалопатію.

Були ураження серцево-судинної системи, органів дихання, травлення, сечовиділення, ендокринної і нервової систем.

Атеросклерозні зміни судинного русла більш виражені у померлих II, і, особливо, III групи. Вони супроводжувалися частішим виникненням ускладненої атеросклерозної бляшки, звуженням просвіту вінцевих і сонної артерій. У померлих II і III груп частіше виявляли склерозування мітрального клапана та клапана аорти. Анамнестично ішемічний інсульт зазначений у картах 16,7 % померлих II групи, 16,2 % III групи, інфаркт міокарда – у 23,8 % померлих II групи та у 14,3 % III групи. Серед супутніх хвороб – гіпертонічна хвороба (у 4,3, 69,0 і 75,2 % померлих I, II і III груп відповідно); ішемічна хвороба серця (у 5,8, 78,6 і 89,5 % померлих I, II та III груп відповідно); хронічна венозна недостатність судин нижніх кінцівок (у 17,4, 16,7 та 27,6 % померлих I, II і III груп відповідно); облітеративний атеросклероз судин нижніх кінцівок (у 16,7 і 33,3 % померлих II і III груп відповідно); ішемічний абдомінальний синдром (у 9,5 і 14,3 % померлих II і III груп відповідно).

У померлих на ЦП виявляли порушення ритму, зокрема, фібриляція передсердь була у третини померлих II групи та у 18,1 % III групи; екстрасистолія була у половини померлих I групи, у 38,1 і 39,0 % померлих II і III груп відповідно.

У всіх померлих виявлено ураження дихальної системи. Більш виражені зміни спостерігали у померлих за поєднання АХП та інсулінорезистентності й ожиріння: гідроторакс був у всіх померлих зі стадією С, у 46,7 % – IA+B групи, у 75,7 % – IIA+B групи та у 84,6 % IIIA+B групи; набряк легень був у всіх померлих зі стадією С, у 40,0 % – IA+B групи, у 72,7 % – IIA+B групи та у 75,0 % IIIA+B групи; емфізема легень була у 4,3 % померлих I групи, у 16,7 % – II групи та у 33,3 % – III групи; плеврит був у 7,2 і 7,1 % померлих I і II груп із декомпенсацією відповідно та у 18,1 % померлих III групи; пневмонія була у померлих зі стадіями субкомпенсації та декомпенсації, з яких у 22,2 % померлих – IB+C групи, у 17,9 % – IIB+C групи та у 32,2 % – IIIB+C групи; хронічний бронхіт – у третини померлих I групи, у 40,5 % – II групи та у 57,1 % – III групи.

Асцит був у всіх померлих із декомпенсацією, а у померлих із субкомпенсацією – близько у половини. Понад 70,0 % померлих із жировими некрозами чіпця мали панкреонекроз і асцит-перитоніт. Ліподистрофія та атрофія підшлункової залози були більш виражені у померлих із НАЖХП і за поєднання АХП з інсулінорезистентністю та ожирінням. Ступінь вираженості варикозно розширених вен стравоходу та шлунка відповідав ступеню компенсації ЦП, а кровотечі спостерігались у померлих зі стадіями B і C та частіше виникали за поєднання АХП та інсулінорезистентності й ожиріння. Супутніми хворобами у всіх померлих були хронічний панкреатит, хронічний холецистит, хронічний гастродуоденіт. У 66,1 % померлих із субкомпенсацією та у всіх із декомпенсацією виявлено ерозивний гастродуоденіт, у 39,3 % – хронічний геморой, у 26,8 % – гіпотонію жовчного міхура, у 21,3 % – жовчно-кам'яну хворобу, у 17,1 % – виразку цибулини дванадцятипалої кишки, у 9,3 % – холангіт, у 6,9 % – виразку шлунка, у 5,3 % померлих III групи – гепатоцелюлярну карциному.

Цукровий діабет 2-го типу діагностований у 19,0 % померлих II групи та у 38,1 % померлих III групи, тиреоїдит – у 21,3 % померлих, переважно за поєднання АХП та інсулінорезистентності й ожиріння.

Діагностика уражень сечовидільної системи дала змогу виявити хронічний пієлонефрит у 25,9 % померлих, кісту нирок – у 18,5 %, хронічну хворобу нирок – у 25,0 % померлих II і III груп зі стадією A, у 43,4 % померлих II та III груп зі стадією B та у всіх померлих зі стадією C.

Енцефалопатія була у 76,3 % померлих зі стадією A та у всіх померлих зі стадіями B і C. Алкогольний делірій у анамнезі був у третини померлих I і III груп відповідно.

Аналіз особливостей і структури коморбідних уражень внутрішніх органів у померлих із АХП на стадії ЦП за поєднання з інсулінорезистентністю та ожирінням показав, що крім характерних для ЦП синдромів (портальної гіпертензії, гепатоспленомегалії, цитолізного, гепатодепресивного, мезенхімальнозапального, гепатопульмонального, гепаторенального, холестазного, печінкової енцефалопатії) частіше були ураження систем органів травлення, дихання, сечовиділення, а також серцево-судинної, ендокринної та нервової систем. У них виявлено значні системні атеросклерозні ураження судинного русла, що у третини померлих призвели до виникнення гострих судинних несприятливих подій. У 5,3 % померлих із поєднанням АХП на стадії ЦП та інсулінорезистентності й ожиріння виявлено гепатоцелюлярну карциному.

Висновки. У померлих із АХП на стадії ЦП за поєднання з інсулінорезистентністю і ожирінням частіше констатували ураження систем органів травлення, дихання, сечовиділення, а також серцево-судинної, ендокринної і нервової систем. У них виявлено значні системні атеросклеротичні ураження судинного русла, що у третини призвели до виникнення гострих судинних несприятливих подій.

Ключові слова: коморбідність, неалкогольна жирова хвороба печінки, алкогольний цироз печінки.

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