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STEATOHEPATITIS ASSOCIATED WITH METABOLIC SYNDROME

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Abstract
Steatohepatitis is an inflammation of the hepatic parenchyma that has aggravated the fatty transformation of the liver. The disease is asymptomatic for a long time. It can manifest itself as abdominal discomfort, pain in the right hypochondrium, dyspepsia, hepatomegaly, asthenic syndrome. It is diagnosed using biochemical blood analysis, ultrasound, static scintigraphy, liver fibroscopy, biopsy histology. Hepatoprotectors, biguanides, insulin sensitizers, anorexigenic drugs, statins, fibrates are used for treatment. It is possible to perform gastroplasty to correct weight. In case of severe liver failure, organ transplantation is necessary.

Keywords: steatohepatitis, metabolic syndrome.

Introduction

Steatohepatitis is a common non—infectious inflammatory liver disease that occupies 3-4 place in the structure of chronic progressive organ lesions. The prevalence of non-alcoholic forms of the disease in the population reaches 11-25%. In patients who are obese, pathology is 7 times more common than at normal weight. Alcoholic steatohepatitis is diagnosed in 20-30% of patients with chronic alcoholism. Pathology occurs in all age groups, but it is mainly detected after 45-50 years. The relevance of timely diagnosis of steatohepatitis is associated with a high probability of liver cirrhosis, which develops in 45-55% of patients in the absence of adequate therapy.

At present, the problem of fatty hepatosis (FH) is very relevant not only for hepatologists, but also for many specialists. Over the past decade, the incidence of liver steatosis has increased significantly. In the middle of the 20th century, it was observed in an average of 68% of cases in the urban population of developed countries, and at the end of the century - already in 15-20%. According to foreign authors (J. D. Browning, L. S. Sczepaniak), almost one third of the urban population suffers from FH. For every sixth liver biopsy with an unclear diagnosis, there is one case of FH. According to A. S. Loginov (1969), S. P. Lebedev (1980), about 30% of patients with liver damage have FH [18,21,28,29,30,32,42].

In the literature, FH is called by different names: fatty degeneration, fatty infiltration, fatty liver, liver dystrophy, liver steatosis [3,6,7,17,18,21,28,32,35,50]. However, the most common term is “fatty hepatitis”, and when talking about morphology, the term “fatty degeneration” is used. In a normal liver, the fat content does not exceed 1.5% of its mass, and it is not detected during a routine histological examination. Small drops of fat in hepatocytes begin to be detected by light microscopy if its amount increases to 2-5%, which is regarded as a pathological condition - fatty degeneration of the liver. If more than half of the hepatocytes contain fat drops that are larger than the cell nucleus, then the fat content in the liver is above 25% [1,21,32].

FH can develop as a result of exposure to a wide variety of factors. Among the etiologic factors leading to the development of FH, alcohol is of primary importance, followed by obesity and diabetes mellitus. The most probable causes of FH are the gastrointestinal and biliary tracts, intestinal bypass anastomosis, long-term parenteral nutrition, maldigestion and malabsorption syndrome, gluten enteropathy, Wilson-Konovalov disease, bacterial infections, viruses, and systemic diseases. In chronic infections, fatty liver dystrophy is detected in almost half of the cases [11,21,45,46,58,59,67,72].

FH also develops as a syndrome in diseases of the lungs, heart (congestive heart failure), cancer, severe purulent processes (E.M. Tareyev, 1948) and metabolic diseases (Cushing's syndrome, myxedema, thyrotoxicosis, acromegaly, gout, hyperlipidemia, hypothyroidism, hypo-β-lipoproteinemia) [21, 36,49]. Chemicals with hepatotoxic action (compounds of mercury, boron, barium, carbon, phosphorus, chromium, thallium, etc.) and many drugs (corticosteroids, estrogens, isoniazid, methotrexate, tetracyclines, salicylates, non-steroidal anti-inflammatory drugs) can cause FH. It can be caused by unbalanced nutrition, especially protein deficiency in the population of underdeveloped countries. Genetic predisposition is also not excluded in the development of FH [8,14,18, 25,26,30].

Fatty liver disease is often associated with gallbladder dyskinesia, especially gallstone disease. Chronic viral hepatitis, especially hepatitis C (genotype 3) is often accompanied by fatty liver disease. Canadian scientists noted that fatty liver disease was registered in 20% of cases after transplantation of the pancreatic islet apparatus [40,51]. Acute fatty liver of pregnancy is very rare [32]. Sometimes fatty liver disease develops in people without any reason [1,7,21].

By etiology, FH is classified as alcoholic and non-alcoholic, by time of occurrence as acute and chronic. Acute FH develops against the background of alcohol and drug poisoning and during pregnancy [39,52,57].

Depending on the diagnostic methods, alcoholic steatosis is detected with different frequencies. According to A. V. Kalinin, isolated alcoholic steatosis is detected in 50% of patients with alcoholism, according to L. G. Vinogradova (1991) - in 60-75%. According to S. Bellentano (2000), during an examination of 6917 people in Northern Italy, alcoholic steatosis was detected in the control group in only 16%, among "heavy drinkers" - in 46%, among the "obese" - in 76%, among "heavy drinkers and obese" - in 94% [8,18,29,30,39,43]. Viter V.I., Permyakov A.V. noted that when examining 100 corpses of people who died from acute ethanol poisoning, the analysis of histological data made it possible to establish the presence of liver disease in 73%, including FH in 65% [5].

Based on morphological features, fatty liver disease can be classified depending on the prevalence of fat droplets of a particular size: small-droplet, large-droplet, and mixed forms (Z.A. Bondar et al., 1970; 1971; S.D. Podymova, 1975) [29,32]. Large-droplet obesity is mainly observed in zone 3 (centrilobular) and is characterized by the presence of large single lipid droplets in the cytoplasm of hepatocytes with the nucleus shifted to the periphery of the cell. In small-droplet obesity, numerous small lipid droplets are detected in hepatocytes, with the nucleus located in the center of the cell. Mixed-type obesity should be classified as small-droplet [8,24].

H.Thaler (1982) distinguishes 4 forms of fatty degeneration: 1) focal disseminated, not manifested clinically; 2) pronounced disseminated; 3) zonal (in different parts of the lobule); 4) diffuse. S.D. Podymova (1993) offers her own version of classification: zero degree - small droplets of fat capture individual groups of liver cells; I degree - moderately expressed focal medium-, and large-droplet obesity of liver cells; II degree - moderately expressed diffuse small-, medium-, large-droplet, mainly

intracellular obesity; III degree - pronounced diffuse large-droplet obesity with extracellular obesity and the formation of fatty cysts. Obesity is considered as an independent risk factor and is associated with the development of fatty liver [21,22,38,48,50,58,59,66,68]. According to Brazilian researchers, among patients with a body mass index (BMI) of 35-40 kg/m^2, based on ultrasound examination (US), FH was detected in 75% of cases [61]. Abrams G.A., Kunde S.S. prove that when analyzing liver biopsy of patients with obesity, FH was detected separately in 30.3% of cases; with portal fibrosis - in 33.3%; NASH - in 36.4% [35]. According to other authors, FH was established in 87.1% of cases [60].

Theoretically, there are 4 mechanisms of fat accumulation in the liver due to: I. Increased intake of fat or fatty acids (FA) with food. Fat ingested with food is transported with blood, mainly in the form of chylomicrons. During lipolysis, FAs are released in adipose tissue. In adipocytes, they are included in triglycerides (TG), but some FAs can be released into the bloodstream and captured by the liver. The remains of chylomicrons also enter the liver; 2. Increased synthesis or inhibition of FA oxidation in mitochondria. Both of these processes increase TG production; 3. Impaired TG excretion from hepatocytes. TG excretion from hepatocytes includes binding to apoprotein, phospholipid, and cholesterol to form very low density lipoproteins (VLDL). Conjugation of TG with apoproteins occurs on the surface membranes of the endoplasmic reticulum with the participation of a number of enzymes and coenzymes called lipotropic factors. VLDL, which were secreted from the hepatocyte under the influence of lipoprotein lipase in the blood, are broken down into low-density lipoproteins and fatty acids; 4. Excessive amounts of carbohydrates entering the liver, which can be converted into fatty acids [1,7,10,12,30,41,62].

The reaction to alcohol is individual for each person. This is due to the genetically determined activity of enzymes, gender, age, ethnicity, etc. Thus, in women, the hormonal background contributes to an increase in the damaging effect of alcohol on the liver, and in half of the representatives of the Mongoloid race, toxic products of ethyl alcohol breakdown are neutralized significantly more slowly than in Europeans due to the presumably different degree of provision of the body with the enzyme alcohol dehydrogenase (AlcDH) [3,8,11,31,55]. Modern research does not allow us to make an unambiguous conclusion about the connection between the genes of the main histocompatibility complex and alcoholic liver disease. AlcDH is determined by five different genes located on chromosome 4. People with different AlcDH isoenzymes differ in the degree of alcohol elimination. Polymorphism of the most active forms of this enzyme, AlcDH2 and AlcDH3, may have a protective effect, since rapid accumulation of acetaldehyde leads to lower tolerance to alcohol. However, if such a person drinks alcohol, then more acetaldehyde is formed, which leads to an increased risk of liver disease [15,21,44,54,69].

In addition, alcohol is metabolized by microsomal cytochrome P450-II-E1. The gene encoding it has been cloned and sequenced, but the role of different variants of this gene in the development of alcoholic liver disease has not been studied. In case of enzymopathy in the cytochrome P-450 system, it is transformed into cytochrome P-420, which most activates the formation of free radicals and does not neutralize O_2- into hydroperoxide [8,27]. FH as a disease is most often diagnosed in middle and old age [4,8,16,19,21,23], more often in men than in women, by 2.7 times (S.D. Podymova). A number of authors noted cases of FH in children [11,43, 48,65,72].

In most cases, FH is asymptomatic, and only some patients experience moderate pain in the right hypochondrium. Pain in the liver area is usually associated with increased accumulation of fat in the liver and stretching of the liver capsule. The nature of other complaints is nonspecific. Depending on the

etiology, patients may have certain subjective and objective symptoms associated with the underlying disease. According to physical examination data, some patients have an enlarged liver with smooth edges. Palpation pain in the liver area is rare [7,9,16,17,21,32,47]. Biochemical blood tests reveal an increase in gamma-glutamyl transpeptidase (GGT) and only a slight increase in transaminase (ALT and AST) and alkaline phosphatase activity [7,18,21]. Bilirubin, albumin, and prothrombin levels are usually normal. Although a number of authors note a slight increase in bilirubin and a decrease in albumin. Significant help in the diagnosis of FH is provided by a violation of the glycemic profile, triglyceridemi, and an increase in cholesterol levels. Additionally, informative indicators may include urobilinogenuria and delayed retention of bromsulfalein. In one third of patients, a change in the thymol test and an increase in the level of a2-, b-, and gamma-globulins are noted [7,20,21,32,36,49].

Modern instrumental methods are used in the diagnosis of GI: ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), radionuclide hepatography and liver biopsy [4,6,7,13,17]. Ultrasound examination allows not only to assess the condition of the liver, but also to identify abnormalities in the gallbladder, liver vessels and pancreas. With ultrasound, the echogenicity of liver tissue can be normal or increased [2,3,4,7,32]. CT reveals a decrease in the absorption coefficient. When examining without contrast, the branches of the portal and hepatic veins are clearly visible. The absorption coefficient is less than that of the spleen and kidneys [30]. Fatty infiltration can also be detected with MRI [32]. Radionuclide examination of the absorptive and excretory function of the liver reveals a distinct decrease in absorption and a slowdown in excretion of dye [21].

Additional examination, including determination of immunological parameters, CT and liver biopsy, is prescribed if there are special indications [3]. Despite numerous studies of FH, the issues of pathogenesis and clinical features have not been sufficiently studied [42,45,71]. The patient examination program should be aimed at excluding other liver diseases, namely:

- viral infection (examine HBs-Ag, HCV-Ag);
- Wilson-Konovalov disease (examine the level of ceruloplasmin in the blood);
- congenital deficiency of b1-antitrypsin;
- idiopathic (genetic) hemochromatosis (examine iron metabolism, assess the condition of other organs);
- autoimmune hepatitis (assess the titers of antinuclear antibodies, antibodies to smooth muscles, it is advisable to study antimitochondrial antibodies and antibodies to liver and kidney microsomes) [8].

In most cases, the course of FH is favorable, especially when the etiologic factors are eliminated. Unfavorable prognostic indicators for this pathology include: severe and multiple disturbances in liver function tests, the presence of hepatocyte necrosis and disorders of regeneration processes; significant immunological disturbances; signs of cholestasis, portal hypertension syndrome [1,55,64].

The course of large droplet fatty liver is usually relatively benign. In small droplet obesity, the rate of progression of liver damage is higher, the prognosis is more serious.

Complications of liver steatosis include: development of steatohepatitis with progression to fibrosis and cirrhosis of the liver, formation of intrahepatic cholestasis with or without jaundice (obstructive intrahepatic intralobular cholestasis), development of transient portal hypertension, often with the presence of transient ascites and portocaval anastomoses, narrowing of intrahepatic venules and veins with the formation of Budd-Chiari syndrome (edema, ascites, signs of hepatocellular insufficiency)

[1,3,17,35,56,60]. Steatohepatitis with the development of liver cirrhosis can even lead to the development of hepatocellular carcinoma [48,53,63,72].

It is quite difficult to substantiate and systematize the treatment of FH given such a variety of causes. Modern approaches to treatment are aimed mainly at eliminating or weakening the factors leading to the development of FH, at relieving syndromes of impaired digestion and absorption, and at restoring the function of the liver and biliary system [7,9,10]. Drug therapy can significantly affect the consequences of steatosis, namely, reduce the level of lipid peroxidation, bind and inactivate toxic substrates in the hepatocyte as a result of increased synthesis of detoxifying substances: block the activity of mesenchymal-inflammatory reactions, slow down the progression of fibrosis [1,37]. During treatment, the use of certain drugs and alcohol abuse are excluded. Gradual, moderate weight loss is most effective in cases of FH development against the background of obesity and diabetes mellitus and is accompanied by positive dynamics of clinical and laboratory parameters, a decrease in the histological activity index. Rapid weight loss can lead to a worsening of the disease [8]. After eliminating the etiological factor, a course and symptomatic treatment is determined, and patients should be advised to remain under medical supervision for another year, and possibly longer. Every 2 months, the well-being and physical status should be assessed, once every 3 months, serum transaminase studies should be repeated, and an ultrasound should be performed once every 6 months. Treatment should be prolonged for 1 year or more [7].

Patients with FH are prescribed a diet rich in proteins (1 g of protein per 1 kg of body weight) and water-soluble vitamins, but poor in fats and, first of all, fatty acids formed during the thermal hydrolysis of fat, as well as carbohydrates to normalize the blood levels of glucose, lipids, and uric acid in the presence of corresponding disorders [1].

In some cases, with alcoholic etiology of the process, additional parenteral administration of water-soluble vitamins (B1, B2, B6, B12, PP, C) in generally accepted therapeutic doses for 10-14 days is required in addition to basic therapy [1,34,62]. The main indications for drug therapy of non-alcoholic metabolic liver damage are: development of steatohepatitis and steatosis of unknown etiology or the impossibility of stopping the action of etiological and additional risk factors for its development [1,62]. The choice of the drug is determined by: - the etiology of the process; - the leading pathogenetic mechanism of hepatocyte damage; - the level of mesenchymal-inflammatory reactions. In most cases, fatty liver is completely reversible provided that the causes leading to its formation are eliminated. It is this indisputable fact that should primarily attract the attention of both doctors and patients, since timely recognition of FH allows preventing the development of inflammation, which is much more difficult to treat [2,3,9].

The most important problem is to reduce alcohol consumption by the population. As is known, alcohol consumption has increased significantly over the past half century. An increase in alcohol consumption is observed throughout the world, especially in European countries, including Russia and the USA. According to WHO (2002), alcohol consumption and its consequences have also increased in recent years, especially in developing countries. In Mongolia, when comparing 2003 and 2002, a significant increase in alcoholic beverages was noted - alcohol by 23.7%, and wine and vodka - by 9.4%. According to statistics (1985-1997), alcohol abuse was found in 51.2% of cases among adults in Mongolia, with women accounting for 8%. At the same time, in recent years, a clear trend towards an increase in the number of patients with FH has been noted among the population of Mongolia, but its actual prevalence

remains unclear. The features of the etiology, pathogenesis and course of FH in Mongols, depending on the factors that form this pathology, have not been finally established. In this regard, there is a need to study the problem of FH using modern diagnostic methods.

References

1. Agofonova N.A., Volosheynikova T.V., Erigoryeva V.T., Yakovenko E.P. Metabolic liver diseases: non-alcoholic steatosis and steatohepatitis. Diagnostics and treatment. // Bol. org. pishchev. - 2004. - №2. http// www.pro-medicine.ru.
2. Batskov S.S. Fatty hepatitis - ways of pharmacological correction. // Materials of the symposium "Essential phospholipids in the treatment of liver damage". - Moscow, 1997. - P.19-21.
3. Bueverov A.O. Fatty liver: causes and consequences. // Popular medicine journal. - 2002. - T. 1, No. 4. http:/ /www.consilium-medicum.com.
4. Bueverov A.O., Maevskaya M.V. Some pathogenetic and clinical issues of non-alcoholic steatohepatitis. // Clinical prospects of gastroenterology, hepatology. - 2003. - No. 3. - P.2-7.
5. Viter V., Permyakov A.V., Naumov E.S., et al. Variants of thanatogenesis in acute alcohol intoxication. // Current aspects of forensic medicine. - 1999. - No. 5. - P. 128-133.
6. Eorshteyn E.S., Dudnik L.B., Maiore A.Ya., et al. Changes in the functional state of subcellular structures of hepatocytes in fatty hepatitis in clinical and experimental settings. // Advances in Hepatology / Ed. by A.F. Bluger. — Riga: Riga Medical Institute. — 1987. — P.158-173.
7. Grigoriev P.Y. Fatty hepatitis (fatty infiltration of the liver): diagnostics, treatment and prevention. // Bol. org. digestion. - 2002. - No. 1. - P.30-37.
8. Ivashkin V.T., Shulpekova Yu.O. Non-alcoholic steatohepatitis. // Bol. org. digestion. - 2000. - No. 2. - P. 41-45.
9. Kalinin A. V. Pathogenesis, clinical features and treatment of alcoholic liver disease. // Clinical prospects of gastroenterology, hepatology. - 2001. - No. 4. - P. 8-14.
10. Carneiro de Mura M. Non-alcoholic steatohepatitis. // Clinical perspectives of gastroenterology, hepatology. - 2001. - JN№ 3. - P.12-15.
11. Kirsanova A.S., Edemskiy A.V. Gastrointestinal complications in cystic fibrosis in children and their treatment. http: //mucoviscidos.com.ua
12. Klimov A.N., Nikulcheva N.G. Lipid and lipoprotein metabolism and its disorders. // Manual for doctors. St. Petersburg: Piter Kom, 1999. - 504 p.
13. Komarov F.I., Khazanov A.I. Guide to Gastroenterology. - M.: Medicine, 1995. - P.22-23.
14. Maevskaya M.V., Bueverov A.O. Old and new approaches to the treatment of alcohol disease. // Rus. journal of gastroenterology, hepatology, proctology. - 2003. - JN№ 6. - P.65-67.
15. Makarov V.K. Effect of alcohol on the lipid composition of blood serum in hepatitis B virus carriers. // Hygiene and Sanitation. - 2003. - J 1. - P.38-39.
16. Nikitin I.G., Storozhakov G.I., Fedorov I.G. et al. State of intestinal microflora in patients with non-alcoholic steatohepatitis. // RZHGGK. - 2002. - No. 5. - P.40-44.
17. Nimaeva D.E., Sizykh T.P. The nature of liver damage in type 2 diabetes mellitus. // Sib.med. zhurn. - 2002. - JN№ 6. - P.14-21.
18. Okorokov A.N. Diagnostics of diseases of internal organs. - M.: Medical literature. - 2002. - P.380-410.

19. Panchenko V., Ershov A., Zimovchenko G. et al. Hepatoprotective effect of eikonal in fatty hepatosis. http: //www.trinita.ru.
20. Petukhov V.A., Karalkin A.V., Ibragimov T.I., et al. Liver dysfunction and dysbiosis in fatty hepatosis and lipid distress syndrome and their treatment with Duphalac (Lactulose). // Russ. gastroenterological journal. - 2001. - No. 2. - P.93-104.
21. Podymova S.D. Liver diseases. - M.: Medicine, 1993.- 538 p.
22. Popova Yu.P., Fedortsova Yu.P., Shevyakova L.V., Beyul E.A. Excess body weight at a young age - a risk factor for the development of metabolic diseases. // Nutrition issues. - M.: Medicine. - 1989. - JJ 1. - P.1-15.
23. Svintsitsky A.S., Revenok E.N., Solovieva G.A., Tkachuk A.I. Evaluation of the effectiveness of the drug Livolin forte in the treatment of patients with fatty hepatosis. http:// www.health-ua.com.
24. Serov V.V. Morphological verification of chronic viral and alcoholic hepatitis. // RZHGGK. - 1998. - JJ 5. - P.26-29.
25. Serov V.V., Voinova L.V. Etiological and nosological assessment of liver pathology. // Rus. journal of gastroenterology, hepatology, proctology. - 2000. - JJ 2. - P.41-44.
26. Sizykh T.P., Efimova N.Yu. Aspirin bronchial asthma - a new type of hepatitis. // Liver, stress, ecology: Materials of the 1st Interrepublican Symp. - Novosibirsk-Irkutsk, 1994. - P.88-92.
27. Solongo B. The state of liver functions, lipid peroxidation and antioxidant protection in patients with aspirin asthma: Diss. candidate of medical sciences. - Barnaul, 2004. - 154 p.
28. Storozhakov G.I., Nikitin I.G., Banin B.B., et al. Fatty degeneration of hepatocytes and chronic HCV hepatitis. // Arch. pat. - 2000. - No. 6. - P.27-32.
29. Ulyanova V.V., Tkachev V.D., Chebanov S.M. Ultrastructure of the liver in fatty degeneration and initial stage of cirrhosis. // Diseases of the liver and biliary tract: Collection of scientific papers. - Moscow, 1982. - P.29-34.
30. Khazanov A.I. An important problem of our time - alcoholic liver disease. // Russian journal of gastroenterology, hepatology, proctology. - 2003. - No. 2. - P. 13-20.
31. Tserendash B., Shagdarsuren M. Elegniy butets, uil ajillagaa. UB.: Beat service, 2003, 80s.
32. Sherlock S., Dooley J. Diseases of the liver and biliary tract: Practical manual: Translated from English / Edited by Z.G.Aprosina, N.A.Mukhin. - M.: Geotar Medicine. - 1999. -864 p.
33. Erdenebayar L. Dontoh emgeg sutslal. - Ulaanbaatar, 2004. - pp. 174-178.
34. Yakovenko E.P., Grigoriev P.Ya. Chronic liver diseases: diagnostics and treatment. // RMZh. - 2003. - V. 11, J № 5. - P.291-296.
35. Abrams G.A, Kunde S.S, Lazenby A.J, et all. Portal fibrosis and hepatic steatosis in morbidly obese subjects: A spectrum of nonalcoholic fatty liver disease. // Hepatology. - 2004. -Aug, 40 (2). - P.475-483.
36. Alapont Puchalt B., Prosper Sierra M., Ricart Alvarez E., Navarro Hervas M. Hepatic steatosis associated with heterozygotic familial hypobetalipoproteinemia. // Gastroenterol Hepatol. - 2004. - April; 27(4). - P.256-259.
37. Angulo P. Treatment of nonalcoholic fatty liver disease. //Ann.Hepatol. - 2002. - J№ 1. - P.12-19.
38. Behrns K.E, Tsiotos G.G, DeSouza N.F, et al. Hepatic steatosis as a potential risk factor for major hepatic resection. // J. Gastrointest Surg. - 1998. - May-Jun, J№ 2 (3). - R.292-298 .
39. Bellentani S, Saccoccio G, Masutti F, et al. Prevalence of and risk factors for hepatic steatosis in Northern Italy. //Ann. Intern Med. - 2000. - Jan 18; 132(2). - P.112-117.

40. Bhargava R., Senior P.A, Ackerman T.E, et all. Prevalence of hepatic steatosis after islet transplantation and its relation to graft function. // Diabetes. - 2004. - May, 53 (5). -P.1311-1317.
41. Bradbury M.W, Berk P.D Lipid metabolism in hepatic steatosis. // Clin Liver Dis. - 2004. - Aug, 8(3). - P.639-671.
42. Browning J.D, Szczepaniak L.S, Dobbins R, et al. Prevalence of hepatic steatosis in an urban population in the United States: impact of ethnicity. // Hepatology. - 2004. - Dec: 40(6). - P.1387-1395.
43. Chan D.F, Li A.M, Chu M.N, et al. Hepatic steatosis in obese Chinese children. // Int J Obes Relat Metab Disord. - 2004. - Oct, 28 (10). - P. 1257-1263.
44. Charles SL Alcohol and the Liver. // Gastroenterology. -1994. - Vol. 106. - P.1085-1105.
45. Clark J.M, Diehl AM. Hepatic steatosis and type 2 diabetes mellitus. // Curr Diab Rep. - 2002. - June, 2 (3). - P.210-215.
46. Denis Marleau. Nonalcoholic Steatohepatitis (NASH). // Postgrad Med J. - 2000. - Vol. 76. - P.280-286.
47. Diehl A.M Nonalcoholic steatohepatitis. // Semin Liver Dis. - 1999. - 19(2). - P.221-229.
48. Festi D., Colecchia A., Sacco T., et al. Hepatic steatosis in obese patients: clinical aspects and prognostic significance. // Obes Rev. - 2004. - Feb, 5(1). - P.27-42.
49. Grassi M., Spada S., Conti R., et al. Hepatic steatosis: clinical-statistical study of patients diagnosed by histological or ultrasonographic methods. // Clin Ter. - 1998. - Jan-Feb, 149 (921). - P.53-60.
50. Howard J. Worman. Fatty liver. //www. medmark.org/gastrol Journals/News/Publiations
51. Hu K.Q, Kyulo N.L, Esrailian E, et al. Overweight and obesity, hepatic steatosis, and progression of chronic hepatitis C: a retrospective study on a large cohort of patients in the United States. // J. Hepatol. - 2004. - Jan, 40(1). - P. 147154.
52. Jolliet P., Leverve X., Pichard C. Acute hepatic steatosis complicating massive insulin overdose and excessive glucose administration. // Intensive Care Med. - 2001. - Jan, 27 (1). - P.313-316.
53. Kawaguchi K, Sakaida I, Tsuchiya M, et al. Pioglitazone prevents hepatic steatosis, fibrosis, and enzyme-altered lesions in rat liver cirrhosis induced by a choline-deficient L-amino acid-defined diet. // Biochem Biophys Res Commun. - 2004. - Feb, 27; 315(1). - P.187-195.
54. Kevin Walsh., Graeme Alexander. Alcoholic liver disease. http: //dir.yahoo.com /Health/Medicine/Gastroenterology/Journals/.
55. Kuntz E. Fatty liver - a morphological and clinical review. //Med.Welt. - 1999. - Vol. 50. - P.406-413.
56. Larrey D. From hepatic steatosis due to obesity to cirrhosis, in the absence of alcoholic intoxication. // Presse Med. -2003. - Mar 22, 32 (11). - P.512-518.
57. Letteron P., Fromenty B., Terris B., et al. Acute and chronic hepatic steatosis leads to in vivo lipid peroxidation in mice. // J. Hepatol. - 1996. - Feb, 24 (2). - P.200-208.
58. Luyckx F.H, Lefebvre P.J, Scheen A.J Non-alcoholic steatohepatitis: association with obesity and insulin resistance, and influence of weight loss. // Diabetes Metab. - 2000. - 26(2). - P.98-106.
59. Mohamed A. Metwally., Claudia O. Zein., Nizar N. Zein., Rochester MN Does High Body Mass Index Affect Hepatic Fibrosis, Steatosis and Inflammation in Patients with Chronic Hepatitis C? // J. Hepatol. - 2001. - 34.
60. Moretto M., Kupski C., Mottin CC, et al. Hepatic steatosis in patients undergoing bariatric surgery and its relationship to body mass index and co-morbidities. // Obes Surg. - 2003. - Aug, 13(4). - P.622-624.

61. Mottin C.C, Moretto M, Padoin AV, et al. The role of ultrasound in the diagnosis of hepatic steatosis in morbidly obese patients. // Obes Surg. - 2004. - May, 14(5). - P.635-637.
62. Niemela O., Parkkila S., Yla-Herttuata S., et al. Sequential acetaldehyde productiun, lipid peroxidation and fibrogenesis in micropig model of alcohol-induced liver disease. // Hepatology. - 1995. - Vol. 22. - P.1208-1214.
63. Ohata K., Hamasaki K., Toriyama K., et al. Hepatic steatosis is a risk factor for hepatocellular carcinoma in patients with chronic hepatitis C virus infection. //Cancer. - 2003. -Jun. 15, 97 (12). - P.2948-2950.
64. Pessayre D., Mansouri AM, Fromenty B. Nonalcoholic steatosis and steatohepatitis. Mitochondrial dysfunction in steatohepatitis. //Am. J. Physiol. - 2002. - Vol. 282. -P.193-199.
65. Rashid M., Roberts EA Nonalcoholic steatohepatitis in children. // J. Pediatr Gastroenterol Nutr. - 2000. - 30(1). - P.48-53.
66. Rinella ME, Alonso E, Rao S, et al. Body mass index as a predictor of hepatic steatosis in living liver donors. // Live Transpl. - 2001. - May, 7 (5). - P.409-414.
67. Sanyal AJ, Campbell-Sargent C, Mirshahi F, et al. Nonalcoholic steatohepatitis: association of insulin resistance and mitochondrial abnormalities. // Gastroenterology. - 2001. - 120(5). - P.1183-1192.
68. Sharma P., Balan V., Hernandez J., et al. Hepatic steatosis in hepatitis C virus genotype 3 infection: does it correlate with body mass index, fibrosis, and HCV risk factors? // Dig Dis Sci. - 2004. - Jan, 49(1). - P.25-29.
69. Simpson KJ Pathogenesis of alcoholic hepatic steatosis. // Addict Biol. - 1996. - 1(4). - P.363-370.
70. Thaler H. Zur Atiologie der Leberzirrhosen Therapiewoche. - 1976. - Bd 26, H. 5. - S.607-614.
71. Ueki K., Kondo T., Tseng Y.H, Kahn C.R Central role of suppressors of cytokine signaling proteins in hepatic steatosis, insulin resistance, and the metabolic syndrome in the mouse. // Proc Natl Acad Sci USA. - 2004. - Jul 13, 101(28). -P.10422-10427.
72. Youssef W., McCullough AJ Diabetes mellitus, obesity and hepatic steatosis. // Semin Gastrointest Dis. - 2002. - Jan, 13(1). - P.17-30.