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Phenotypes of Non-Alcoholic Fatty Liver Disease in Different Regions of the Russian Federation, Diagnostic and Therapeutic Approach in Clinical Practice

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Aim: to present data on the prevalence of various phenotypes of non-alcoholic fatty liver disease (NAFLD), the features of its diagnosis and treatment in various regions of the Russian Federation following a meeting of chief gastroenterologists.
Key points. Non-alcoholic fatty liver disease (NAFLD) holds the leading position among non-infectious liver diseases in the Russian Federation, its prevalence is 37.3 % and does not tend to decrease.
To get information on various aspects of NAFLD diagnosis and treatment, opinion of 18 chief external regional gastroenterologists and leading specialists in the field of liver diseases was studied by analyzing the responses to questions specially formulated for them. Information on the situation in the Ural, Privolzhsky, Southern, Central and Northwestern Federal Districts was obtained. Regional statistics on the prevalence of NAFLD and its certain phenotypes (steatosis, steatohepatitis, cirrhosis), diagnostic instruments and treatment approaches which are used in clinical practice, as well as on the most common associated conditions was presented.
Conclusions. The collected information allows to improve both administrative and treatment and diagnostic-related activities in managing patients suffering from this disease.
Keywords: non-alcoholic fatty liver disease, prevalence, phenotypes, diagnosis, treatment, regions of the Russian Federation
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Фенотипы неалкогольной жировой болезни печени в различных регионах Российской Федерации, диагностические и лечебные подходы в клинической практике

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Цель: представить данные о распространенности различных фенотипов неалкогольной жировой болезни печени (НАЖБП), особенностях ее диагностики и лечения в различных регионах Российской Федерации по итогам встречи главных специалистов-гастроэнтерологов.
Основное содержание. НАЖБП лидирует среди неинфекционных заболеваний печени в РФ, ее распространенность составляет 37,3 % и не имеет тенденции к снижению.

Для получения информации о разных аспектах диагностики и лечения НАЖБП было изучено мнение 18 региональных главных внештатных специалистов-гастроэнтерологов и ведущих специалистов в области заболеваний печени посредством анализа ответов на специально сформулированные для них вопросы. Была получена информация о ситуации в Уральском, Приволжском, Южном, Центральном и Северо-Западном федеральных округах. Представляет большой интерес региональная статистика по распространенности НАЖБП и ее отдельных фенотипов (стеатоз, стеатогепатит, цирроз), диагностических инструментах и лечебных подходах, которые используются в клинической практике.

Выводы. Полученная информация дает возможность усовершенствовать административные и лечебно-диагностические мероприятия в ведении пациентов с НАЖБП.

Ключевые слова: неалкогольная жировая болезнь печени, распространенность, фенотипы, диагностика, лечение, регионы РФ

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Among non-infectious liver diseases in the Russian Federation and worldwide, non-alcoholic fatty liver disease (NAFLD) takes the first place. Its leading position has been maintained for at least 10 years, despite active studies in search for medicinal products with maximum efficacy and efforts in controlling its main underlying condition i.e. obesity/overweight. Why is it still impossible to cope with this problem, just as the medical community solved the problem of treating hepatitis C? The response is probably that NAFLD is a multifactorial disease with complex multicomponent pathogenesis and a big number of associated conditions. Moreover, clinical course of NAFLD is also influenced by other liver damage risk factors which can be present in the same patient: regular alcohol consumption, administration of potentially hepatotoxic medicinal products, etc. To apply a correct approach to a patient with the NAFLD in the conditions of Russian clinical practice, it is important to understand the opinion of practitioners from the regions of our vast country differing in climatic conditions, cultural patterns and habits, dietary habits and prevalence of other diseases. For this purpose, opinion of external regional gastroenterologists and leading specialists in the field of liver diseases on local NAFLD statistics, its most common phenotypes, diagnostic and therapeutic approaches to patients was studied.

Chief regional gastroenterologists and leading specialists in the field of liver diseases were offered to fill in an online questionnaire compiled using a special form. The responses were generalized, analyzed and given in the article.

Fifty chief external regional specialists received an invitation to complete the questionnaire. Eighteen specialis took part in the survey and provided their data.

Information about the survey participants:

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Therefore, data on the situations in Belgorod and Belgorod Region, the Republic of Bashkortostan, Kirov Region, Krasnodar Krai, Moscow and Moscow Region, Nizhny Novgorod Region, Orenburg Region, Privolzhsky Federal District (PFD), Rostov Region, Saint Petersburg, Samara and Samara Region, Saratov Region, Sverdlovsk Region, Tambov Region, Ural Federal District (UFD), Chelyabinsk and Chelyabinsk Region were obtained.

If we combine these geographical areas into bigger blocks, then information was obtained from 4 specialists from the UFD with its details on Yekaterinburg, Sverdlovsk Region, Chelyabinsk and Chelyabinsk Region; information was also received from 7 specialists on PFD (Nizhny Novgorod Region, Samara Region, Saratov Region, the Republic of Bashkortostan, Kirov Region, Ulyanovsk Region, Orenburg Region); information on local statistics in the Southern Federal District (Rostov Region, Krasnodar Krai) was obtained from 2 specialists; as of the Central Federal District, the information was received from 3 specialists responsible for Moscow, Tambov Region and Belgorod and Belgorod Region, there are also data on Northwestern Federal District (Saint Petersburg) received from 1 specialist.

NAFLD Epidemiology

According to the published data, overall prevalence of NAFLD worldwide is 25.2 % [1]. In Russia, according to multicenter study DIREG2, the prevalence of NAFLD in outpatients accounted for 37.3 %. Herewith, 80.3 % of these patients were diagnosed with steatosis, while steatohepatitis was diagnosed – in 16.8 % of patients and only 2.9 % of patients had cirrhosis. The most common risk factors in the NAFLD population were dyslipidemia (Fredrickson Type II) observed in 75.9 % of patients, hypertension registered in 69.9 % of patients and hypercholesterolemia in 68.8 % of patients. [2]. In 2019 data on the incidence of NAFLD in outpatient polyclinic of one medical center were obtained which accounted for 24.9 % [3]. For the citizens of Moscow (a population-based study) this parameter accounts for 7.4 %. Analysis of the NAFLD risk factors in general population (citizens of a big industrial city) showed the results which were similar to that in

DIREG study: the risk factors included obesity and hypercholesterolemia [4].

As for the regions of the Russian Federation, it is quite difficult to obtain information on the NAFLD statistics, especially on its phenotype, which is driven by objective reasons (the principles for statistical accounting and coding liver diseases).

Individual parameters of the Central Federal District can be found in literature. In Moscow Region individual Register of Patients liver disorders was created. This statistical tool allows to collect information on diagnosed liver diseases at any stage, and to assess the contribution of a specific etiological factor. According to the Register, the number of patients who complained of any liver pathology for the first time from 2011 to 2017 was 21,228, of which the number of patients with liver cirrhosis of any etiology was 2244 (10.5 %), and 22 patients (1 %) had cirrhosis due to NAFLD. Data on NAFLD and its phenotypes prevalence are being processed and prepared for publication at present [5]. Clinics named after V.Kh. Vasilenko of the Sechenov University, Hepatology Department (Moscow) have published own statistical data on analysis of documentation of patients who sought medical attention in 2013, 2014 and 2017 (2459 patients in total); their number was compared by nosological forms at each time interval. Almost two-fold increase both in proportion and the total number of patients with NAFLD was observed from 2013 to 2017. In 2013, 163 patients sought medical advice at the Hepatology Department, in 2014 and 2017 the number was 151 and 276, respectively [6].

Results of Specialists Survey

The first question was about NAFLD prevalence in the region of a specialist's responsibility.

According to the results of the survey, in the PFD average NAFLD prevalence accounts for 50 % on average as the primary and secondary diagnosis in the outpatient gastroenterology practice. In some regions of the PFD this figure ranges from 25 % (Orenburg Region) to 70 % (Samara and Samara Region), in other regions of the PFD it accounts for 30 % (Nizhny Novgorod Region), 38 % (Kirov Region) and 40 % (the Republic of Bashkortostan). Overall, these numbers are comparable and concordant with the results of DIREG2 study and NAFLD prevalence in the outpatient practice in the Russian Federation in general.

In the Southern Federal District NAFLD is registered rarer: in Krasnodar Krai it accounts for 17 % of which primary disease was diagnosed in 2 % of cases while comorbidity was diagnosed in 14.8 %. It is not possible to obtain targeted statistics in the Rostov Region, as all liver diseases are summarized, i.e. this is 13,539 patients for 2021 according to ICD 10 diagnoses codes K70-K76.

In the Ural Federal District, the prevalence of NAFLD is 37 % which also coincides with similar number in the Russian Federation in general. More detailed information was received for Sverdlovsk Region where the number of patients with NAFLD is about 1 case per 100 patients admitted to hospital and 8 cases per 100 outpatients.

Central Federal District is presented by the following data: it is the Clinics named after V.Kh. Vasilenko at Sechenov University (Moscow), where the proportion of patients with NAFLD is 30 % of those seeking medical advice in the field of hepatology; Tambov Region where only data on reporting 1324 cases of NAFLD in 2022 are available; Belgorod and Belgorod Region provide information that 3000 patients with NAFLD are monitored by gastroenterologists in this region which allows to describe its phenotypes.

Data on the Northwestern Federal District were provided by an expert from Saint Petersburg. According to St. Petersburg Medical Informational and Analytical Center of the Healthcare Committee of Saint Petersburg, 10,133 patients sought medical advice in 2022 with "Fatty (change of) liver, not elsewhere classified" (K76.0), which accounts for 181 patients per 100,000 population and 58.5 % in the structure of liver diseases.

The second question to the specialists was as follows: Which NAFLD phenotypes do you encounter in your practice in percentage: steatosis, steatohepatitis, cirrhosis?

In the PFD doctors report steatosis in 70 % of cases, steatohepatitis — in 25 % of cases and cirrhosis — in 5 % of cases. In individual regions of the PFD these values are as follows: Orenburg Region — steatosis — 70 %, steatohepatitis — 27 %, cirrhosis — 3 %; Samara and Samara Region — 75 %, 20 %, and 5 %, respectively; Kirov Region — 85 %, 14 %, and 1 %. The overall trend indicates that most commonly doctors report steatosis in their clinical practice, NAFLD as an etiological factor of liver cirrhosis is reported in less than 5 % of cases.

In the Southern Federal District steatosis is also the most commonly reported phenotype of NAFLD which is supported by data from Krasnodar Krai, i.e. 70 %, while steatohepatitis is observed in 24 % of cases and cirrhosis in 6 % of cases.

In the Ural Federal District the prevalence of NAFLD phenotypes is conventional: steatosis accounts for 74 %, steatohepatitis accounts for 22 % and cirrhosis accounts for 4 %. More detailed information was received for Sverdlovsk

Region where the proportion phenotypes differs and patients with steatohepatitis prevail and account for 60 %, while the number of patients with steatosis is 30 % and with cirrhosis it is 10 %. For Chelyabinsk Region this distribution is as well preserved: steatosis, steatohepatitis and cirrhosis account for 40 %, 55 % and 5 %, respectively.

Central Federal District: Tambov Region demonstrates conventional distribution of NAFLD phenotypes: steatosis – 80 %, steatohepatitis – 15 %, cirrhosis – 5 %. Data from Belgorod and Belgorod Region are comparable with those from the Clinics named after V.Kh. Vasilenko (Moscow): steatosis is rarer than steatohepatitis: 30 % and 50 %, respectively for Belgorod

Table 1. Results of survey among regional specialists on the incidence of NAFLD-associated pathologies

Таблица 1. Результаты опроса региональных специалистов о частоте ассоциированных с НАЖБП патологических состояний

Area of responsibility (city, district, region)	Which comorbidities are most commonly associated with NAFLD in your region in percentage (%) (a combination of several factors is possible)?							
	Obesity/overweight	Cardiovascular diseases	Lipid spectrum disorders (percentage)	Respiratory system disorders (sleep apnea, etc.)	Musculoskeletal system disorders	A combination of NAFLD with systemic/excessive alcohol consumption	A combination of NAFLD with drug-induced/toxic liver injuries	Other (please specify)
Chelyabinsk, Ural	80	80	80	80	90	100	90	diabetes
Nizhny Novgorod Region	30	10	10	10	10	15	10	5
Samara region, Samara	52	48	72	10	32	10	3	a combination with T2DM 36 %
Chelyabinsk region	98	50	70	10	20	20	10	Carbohydrate metabolism disorders
Privolzhsky Federal District	60/30/10 (normal weight)	50	70	5	60	20	20	GERD 40 %
Rostov region	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Belgorod region, Belgorod	70	60	70	40	70	40	30	Diabetes mellitus, insulin resistance 80 %
Republic of Bashkortostan	10	3	2	2	5	10	10	5
Kirov region	80	19	19	1	1	1	1	–
Sverdlovsk Region	80	80	80	5	10	50	50	combination with Diabetes mellitus – 50 %
Tambov region	70	50	10	10	30	50	10	diabetes
Krasnodar Krai	75	25	30–40	5	10–15	15–20	1–3	Cancer of various localization – 20 to 25 %
Ulyanovsk region	30	10	7	8	25	40	8	Alcohol + DILI
Ural Federal District	52	67	73	31	74	62	35	combination with GERD in 60 %
Orenburg region	90	90	100	10	10	70	25	Genetic predisposition
Saratov region	70	87	80	32	56	15	34	–
In-patient hospital, Moscow	90	30	70	10	20	40	10	Diabetes mellitus, hyperuricaemia
Saint Petersburg	90	80	90	10	20	30	15	Inflammatory bowel disease (15 to 20 % of patients)

Table 2. Results of survey among regional specialist on the diagnostic tools used for diagnosing different NAFLD phenotypes: steatosis, steatohepatitis, fibrosis and cirrhosis

Таблица 2. Результаты опроса региональных специалистов о том, какие диагностические инструменты используются для диагноза различных фенотипов НАЖБП: стеатоза, стеатогепатита, фиброза и цирроза

Area of responsibility (city, district, region)	**Which diagnostic methods do you use for diagnosis (several methods can be listed)?**			
	***Steatosis**	***Steatohepatitis**	***Fibrosis**	***Cirrhosis**
Chelyabinsk, Ural	Ultrasound	Laboratory methods	Elastometry	Biopsy
Nizhny Novgorod Region	Laboratory tests, ultrasound	Laboratory tests, ultrasound	Laboratory tests, ultrasound	Laboratory tests, ultrasound
Samara region, Samara	Ultrasound, lipid spectrum assay	Ultrasound, lipid spectrum assay, functional liver test, carbohydrate metabolism assay	Ultrasound, elastometry	Ultrasound, color Doppler mapping of the portal system, abdominal CT, MRI
Chelyabinsk region	Ultrasound	Ultrasound, elastometry, laboratory tests	Elastometry, biopsy, laboratory tests	Elastometry, histology
Privolzhsky Federal District	Transabdominal ultrasound	Complete blood count, enzymes, CRP, ferritin	Real-time elastometry, Fibrotest (rare)	Real-time elastometry, biopsy
Rostov region	Ultrasound, MRI, laboratory tests	Ultrasound, MRI, laboratory tests	Elastometry	Ultrasound, MRI, laboratory tests, EGD, elastometry
Belgorod region, Belgorod	Fibroscan, SCT, fibrotest, lipid profile	Laboratory tests: AST, ALT, bilirubin, GGT, ALP, lipid profile, HOMA-index, fibrotest, fibroscan, SCT	Fibroscan, fibrotest	Laboratory tests: AST, ALT, bilirubin, GGT, ALP, cholinesterase, lipid profile, HOMA-index, fibrotest, fibroscan, SCT, abdominal ultrasound
Republic of Bashkortostan	Abdominal ultrasound, fibro-elastometry	Abdominal ultrasound, fibro-elastometry	Abdominal ultrasound, fibro-elastometry	Abdominal ultrasound, fibro-elastometry, Doppler ultrasound of the liver, spleen
Kirov region	Ultrasound	Ultrasound, MRI	Ultrasound, MRI, elastography, liver biopsy	Ultrasound, MRI, liver biopsy
Sverdlovsk Region	Fibroscan, elastometry, blood biochemistry, lipid spectrum	Fibroscan, elastometry, blood biochemistry, lipid spectrum	Fibroscan, elastometry, blood biochemistry, lipid spectrum	Fibroscan, elastometry, blood biochemistry, lipid spectrum, abdominal CT, FGDS
Tambov region	Abdominal ultrasound	Abdominal ultrasound	Elastometry	Abdominal ultrasound, abdominal CT
Krasnodar Krai	Abdominal ultrasound, CT for other pathology	Biochemistry (ALT, AST, GGT, ALP), in expert cases – liver puncture biopsy	Elastometry, in expert cases – liver puncture biopsy	Abdominal ultrasound, abdominal CT, EGD (for Esophageal varices detection), CBC (detection of anemia, leukopenia, thrombocytopenia), biochemistry (ALT, AST, bilirubin, GGT, ALP, cholinesterase)
Ulyanovsk region	Ultrasound, laboratory tests, (biochemistry – lipid spectrum, cytolysis, cholestasis markers)	Ultrasound, laboratory tests, (biochemistry – lipid spectrum, cytolysis, cholestasis markers)	Ultrasound, Sonoelastography, Fibroscan, non-invasive diagnostic tests (NFS, FIB4, ELF, Fibrotest), liver biopsy, portal pressure measurement	Ultrasound, Sonoelastography, Fibroscan, non-invasive diagnostic tests (NFS, FIB4), portal pressure measurement

End of table 2. Results of survey among regional specialist on the diagnostic tools used for diagnosing different NAFLD phenotypes: steatosis, steatohepatitis, fibrosis and cirrhosis

Окончание таблицы 2. Результаты опроса региональных специалистов о том, какие диагностические инструменты используются для диагноза различных фенотипов НАЖБП: стеатоза, стеатогепатита, фиброза и цирроза

Area of responsibility (city, district, region)	Which diagnostic methods do you use for diagnosis (several methods can be listed)?			
	*Steatosis	*Steatohepatitis	*Fibrosis	*Cirrhosis
Ural Federal District	Abdominal ultrasound; CAP	Abdominal ultrasound; CAP; blood biochemistry; liver biopsy	Elastometry (Fibroscan), liver biopsy	Elastometry (Fibroscan), liver biopsy, EGD
Orenburg region	Biochemistry, ultrasound, fibro elastography	Biochemistry, ultrasound, fibro elastography	Biochemistry, ultrasound, fibro elastography	Biochemistry, ultrasound, fibro elastography
Saratov region	Ultrasound, biochemical tests	Ultrasound, biochemical tests, elastometry	Elastometry	EGD, ultrasound, blood biochemistry, MRI
In-patient hospital, Moscow	Ultrasound, CT, elastometry	Biochemistry, liver biopsy	Elastometry, non-invasive calculation index	Clinical examination
Saint Petersburg	Liver ultrasound, biochemical blood test, lipid profile assessment, insulin resistance evaluation, rating scale (steatosis index, etc)	Liver ultrasound, biochemical blood test, lipid profile assessment, insulin resistance evaluation, rating scale (steatosis index, etc.)	Liver ultrasound, biochemical blood test, lipid profile assessment, insulin resistance evaluation, CT, MRI, Fibro Max test, FibroScan test (elastometry), rating scales (fibrosis rating scale), liver biopsy (if indicated)	Liver ultrasound, biochemical blood test, lipid profile assessment, insulin resistance evaluation, CT, MRI, Fibro Max test, FibroScan test (elastometry), liver biopsy (if indicated)

Region and 20 % and 50 % for Clinics named after V.Kh. Vasilenko. According to the data provided by these specialists, the proportion of patients with liver cirrhosis is higher as well: 20 % for Belgorod Region and 30 % for Clinics named after V.Kh. Vasilenko. These differences are due to the fact the statistics is provided for inpatients.

According to the literature data on the Register of Moscow Region [5], cirrhosis due to NAFLD is accounted for 1 % of cases.

Northwestern Federal District is represented by the data from Saint-Petersburg, where NAFLD phenotypes are distributed as follows: hepatic steatosis — 80 %, steatohepatitis — 18 %, liver cirrhosis — 2 %.

The third question: Which comorbidities are most commonly associated with NAFLD in your region in percentage (%) (a combination of several factors is possible).

The results of responses to this question are provided in Table 1.

As a comment to the table it should be noted that experts work in different healthcare facilities, different regions of the Russian Federation which influences the results of response to the question.

Most commonly the NAFLD is combined with overweight and obesity. For all regions and districts this parameter is over 70 %, similar trend is traced for dyslipidemia (Table 1). Issues related to sleep apnea are reported in about 30 % of patients with NAFLD, various changes in musculoskeletal system are also presented in most cases in the regions of the Russian Federation.

As besides NAFLD liver injury associated with excessive alcohol consumption is relevant for the Russian Federation population, the specialists were asked to specify the proportion of patients with NAFLD with second serious liver damage risk factor.

According to the specialists, a combination of NAFLD with alcohol consumption, i.e. dual diagnosis ALD/NAFLD accounts for more than 50 % of cases in the UFD: overall in the region the number is as high as 62 %, in Chelyabinsk it accounts for 100 % and in Sverdlovsk Region — for 50 %.

In the Northwestern Federal District, a combination of NAFLD with excessive alcohol consumption is reported in 30 % of cases. The numbers are lower in the PFD and Krasnodar Region,

i.e. 20 % on average. It is difficult to summarize data on Moscow considering the specificity of the work of specialists participating in the survey. For Belgorod and Belgorod Region this number is 30 %.

The next question to the specialists: which methods are used to diagnose hepatic steatosis, steatohepatitis, fibrosis and cirrhosis?

Almost all the specialists use ultrasound for steatosis diagnosis which does not contradict with international clinical recommendations; to diagnose steatohepatitis only three specialists mention liver biopsy; to diagnose liver fibrosis transient elastometry is widely used, cirrhosis is diagnosed according to the rules of routine clinical practice (Table 2).

Table 3 provides responses of the specialists to questions about the role of ademetionine in NAFLD treatment, the phenotypes it is prescribed for and the medicinal products it is combined with.

When analyzing the responses it is important to note that in different regions of the Russian Federation specialists pay attention to the consideration that changing patient's lifestyle is a priority for medical care. Pharmacotherapy is prescribed for clear indications and ademetionine is actively used at different disease stages (for different phenotypes). More than a half of the specialists assign ademetionine the leading role in NAFLD treatment ("leading role", "first place", "highest priority", "first place in severe patients", for over 50 % of patients, etc.). Also specialists note that its role is important in cholestatic types of NAFLD, when it is combined with excessive alcohol consumption and drug-induced liver injury. About 40 % of chief specialists noted individually that they prescribe ademetionine at early stages, at steatosis stage, in case of changes in liver enzymes.

Ademetionine in NAFLD treatment

The primary mechanism of action of ademetionine (SAM) is related to its ability to donate its methyl group during transmethylation and transsulfuration, thus facilitating formation of glutathione which is the main cellular antioxidant which neutralizes exo- and endotoxins [7]. The synthesis of SAM has been often shown to be reduced in patients with a chronic liver disease due decreased *MAT1A* expression and inactivation of MAT isoenzymes coded by it [8]. The experiment demonstrated that the absence of *MAT1A* gene results in increased levels of triglycerides, fatty acids, including the oxidized ones, ceramides and in decreased SAM and metabolites levels. Of no little importance is the fact that SAM administration provided for reduction of the signs of non-alcoholic steatohepatitis [9]. In the study by A.Yu. Baranovsky et al. (2010) [10] efficacy of original ademetionine in treatment of patients with non-alcoholic steatohepatitis was demonstrated. The work by L. Baiming et al. (2011) [11] also demonstrated the efficacy of SAMe in NAFLD. In observational study, 62 patients with NAFLD were divided into two groups with the first group receiving ademetionine 500 mg twice daily for 8 weeks and group of comparison receiving Vitamin C 100 mg 3 times daily. Study results showed that SAM facilitates the decrease of ALT, AST, improvement of clinical symptoms. Authors notes that SAM also influenced the lipid spectrum parameters, i.e. it reduced triglycerides and cholesterol levels.

Considering that according to the specialists' assessment, a significant proportion of patients in the Russian Federation has a combination of NAFLD with excessive alcohol consumption, data from A. Diaz Belmont et al., G.Vendeimale et al. [12, 13] that orally prescribed SAM provided for significant increase in glutathione hepatic levels both in patients with alcoholic liver injury and in patients with pathology not resulting from alcohol consumption vs. placebo are important.

The study by Z.M. Younossi et al. (2022) demonstrated that fatigue in patients with NAFLD which is usually attributed to sleep disorder, depression and cardiovascular diseases can have a negative impact on the health condition-related quality of life and on clinical outcomes, in particular, it can increase the risk of mortality by more than two-fold. Therefore, it is important to recognize the fatigue in patients with NAFLD and to use effective treatment methods [14]. The review of 16 studies involving 3238 patients studying SAM use in liver diseases conducted by K.L. Raikhelson et. al showed statistically significant positive impact of SAM on increased fatigue. This effect was observed irrespectively of the route of administration and the duration of the drug product use. According to the data from the studies, the effect of SAM on fatigue in patients with liver diseases is dose-dependent and can preserve after the end of treatment course [15].

Thus, a thorough analysis of NAFLD phenotype and disease-associated conditions, especially patients' geography in the Russian Federation allows to select optimal combination or monotherapy keeping in mind that lifestyle modification is of utmost importance in achieving professional success.

Conclusion

Non-alcoholic fatty liver disease holds the leading position among non-infectious liver diseases in the

Table 3. The role of ademetionine in NAFLD treatment
Таблица 3. Значение адеметионина в лечении НАЖБП

Area of responsibility (city, district, region)	5. What role does ademetionine play in treating patients with NAFLD in your practice?	6. For which NAFLD phenotype do you prescribe ademetionine?	7. At which stage of NAFLD patient management do you prescribe ademetionine?	8. Do you use ademetionine 1) as monotherapy (please specify No. 1 in the response below) 2) in combination with other medicinal products (please specify number 2 in the response below and clarify other drugs and the reasons)
Chelyabinsk, Ural	1st place	For any	Starting with steatosis	2
Nizhny Novgorod Region	Major	All	In case of laboratory abnormalities	more often in combination with other drugs
Samara region, Samara	The drug product of choice – 1st place	For all	Starting with steatosis	1, 2 – UDCA, treatment of comorbidities
Chelyabinsk region	Adjuvant therapy, additional component to recommendations on body weight management; when the disease is accompanied by alcoholic liver disease, drug-induced liver injury	Steatohepatitis	At any stage	1, 2 – in combination with GLP-1 receptor agonists
PFD	It takes the first place in treating severe patients, patients with steatohepatitis and cholestasis	Combination with ALD, intrahepatic cholestasis	In severe patients first (drug-induced cholestasis, steatohepatitis with cholestasis)	2 (with UDCA) effect on various pathogenetic components
Rostov region	Leading role	for all	At all	2 – UDCA
Belgorod region, Belgorod	Lifestyle, dietary habits, physical activity, body weight decrease if ademetionine is indicated. It is most commonly prescribed for steatohepatitis, cirrhosis accompanying NAFLD	More often prescribed for combination with drug-induced, toxic liver injury	In case of moderate to severe cytolytic syndrome	1
Republic of Bashkortostan	2	1	In case of changes in liver enzymes	with UDCA
Kirov region	It is used.	For any	at initial stages	A case-by-case approach to a patient is used
Saint Petersburg	The drug is prescribed for steatohepatitis and more severe NAFLD phenotypes, alongside with biguanides, thiazolidinediones, hypolipidemic therapy, UDCA, essential phospholipids	Indicated for steatohepatitis and more severe NAFLD phenotypes. At the stage of steatosis, drug therapy for NAFLD is not indicated.	If necessary – at the stage of development of steatohepatitis, fibrosis and cirrhosis	Rarely used as monotherapy. It is prescribed in combinations for comorbid pathology: as a rule, such patients have concomitant diseases: metabolic syndrome, cardiovascular diseases, cholelithiasis, diabetes mellitus, etc., which also require the appointment of appropriate therapy
Tambov region	Leading role	Steatohepatitis	For in-patient care	2 – with UDCA
Krasnodar Krai	The drug is widely used: 60 %	NASH	For in-patient care the drug is prescribed intravenously, when shifting to out-patient stage the drug is prescribed in the form of tablets	2, more often with UDCA as this drug products have different therapeutic targets

End of table 3. The role of ademetionine in NAFLD treatment
Окончание таблицы 3. Значение адеметионина в лечении НАЖБП

Ulyanovsk region	One of key positions	Almost for all	In-patient + Out-patient treatment	I use in as monotherapy (1) and in combination with UDCA drug products (in case of cholestasis, biliary sludge, hyperglycemia, in complex therapy with statins)
Ural Federal District	Leading role	Metabolically associated fatty liver disease; combination of NAFLD with ALD; combination of NAFLD with drug-induced liver injury	Out-patient, day hospital, in-patient	1 (50 %) / 2 (50 %) – Vitamin E or UDCA
Orenburg region	Leading role	Steatohepatitis	Steatohepatitis treatment	Either as monotherapy or in combination with UDCA
Saratov region	54 % of patients are treated with ademetionine	NASH	NASH	2 – with UDCA
In-patient hospitals				
In-patient hospital, Moscow	Minimal	In combination with asthenic syndrome	At any stage, in case of secondary asthenic syndrome	1
In-patient hospital, Sverdlovsk Region	Minimal	For asthenic syndrome	Minimum	weight decrease, physical exercise

Russian Federation. To solve this issue effectively, detailed statistical information about the regions of our country is required. For this, opinion of 18 experts who are external regional gastroenterologists and leading specialists in the field of liver diseases was studied by analyzing the responses to questions specially formulated for them. Information on the situation in the Ural, Privolzhsky, Southern, Central and Northwestern Federal Districts was obtained. According to multicenter study DIREG2, the overall prevalence of NAFLD in outpatients in Russia is comparable with NAFLD prevalence worldwide and accounts for 37.3 % and 25.24 %, respectively [1, 2]. NAFLD division into phenotypes in most districts and regions studied in the survey also complies with the data for the Russian Federation provided in DIREG2 study: over 50 % of patients have steatosis, about 10 to 20 % of patients have steatohepatitis and 1 to 5 % of patients have liver cirrhosis. The specificity of the work of the Clinics named after V.Kh. Vasilenko, and other specialized facilities demonstrate a big proportion of patients with severe forms of NAFLD and high proportion of cirrhosis (up to 30 %). Among associated conditions overweight and obesity, dyslipidemia and cardiovascular diseases prevail. In most case regional statistics coincides with the Russian Federation statistics and literature data worldwide. The fact that 30 to 50 % of patients with NAFLD in different regions consume excessive amount of alcohol which forces to search for special therapeutic approaches for them, in particular when selecting optimal pharmacological treatment, comes under notice.

Due to its confirmed efficacy, ademetionine can be used in patients with NAFLD at all disease stages (steatosis, steatohepatitis, fibrosis) and firmly occupies a niche among hepatotropic drug products in the present-day practice. Ademetionine is also recommended for treating patients with NAFLD and concomitant risk factors. Such risk factors include alcohol consumption, lipid profile disorders, i.e. hypercholesterolemia, hypertriglyceridemia, increased fatigue. The obtained results are important material for the analysis of further actions to optimize administrative, diagnostic and clinical work.

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