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DOI 10.25789/YMJ.2025.92.17

УДК 616.36-006.6-071(571.56)

EFFECTIVENESS OF AN INTERDISCIPLINARY APPROACH TO EARLY DIAGNOSIS OF HEPATOCELLULAR CARCINOMA

The implementation in the Republic of Sakha (Yakutia) of a set of measures aimed at eliminating parenteral viral hepatitis and improving the provision of medical care to the adult population with oncological diseases has had a significant impact on the effectiveness of hepatocellular carcinoma diagnosis. Patients with advanced fibrosis and cirrhosis of the liver require special attention, as it is in this group of patients that the highest proportion of fatalities is observed, as well as the greatest burden on the healthcare system budget.

The aim of the study was to evaluate the impact of an interdisciplinary approach on the etiological verification of the diagnosis and the effectiveness of HCC detection using the example of the Republic of Sakha (Yakutia).

Materials and methods. A retrospective analysis was conducted of data from 632 patients with HCC in the Republic of Sakha (Yakutia) who were examined and treated at the Yakutsk Republican Oncology Dispensary, and an analysis of the incidence rate based on official statistics before and after the introduction of the interdisciplinary approach.

Results and discussion. Due to improved screening, the proportion of patients with viral hepatitis markers increased 2.5 times and approached 70%. Clinical and laboratory diagnosis of liver cirrhosis improved, which is extremely important when choosing a treatment strategy for a patient. The rate of early diagnosis at stage I according to the TNM classification increased from 5.1% to 12.0% over 5 years. The increase in the proportion of patients with early-stage HCC opens up broad opportunities for the use of local tumor destruction methods and is expected to increase the overall survival of patients. It has been shown that an interdisciplinary approach reduces the time it takes to refer a patient from an infectious disease specialist to an oncologist and improves the quality of morphofunctional diagnosis of the liver.

Conclusion. The experience of the Republic of Sakha (Yakutia) shows that improving dispensary observation of risk groups and continuity in patient management within the framework of interdisciplinary cooperation between specialists is a promising direction that can ensure early diagnosis of HCC and improve treatment outcomes.

Keywords: hepatocellular carcinoma, early diagnostics, malignant neoplasms, organization of medical care.

For citation: Sleptsova S.S., Malov S.I., Sleptsov S.S., Nikiforov P.V., Gumennikova M.S., Panferova E.I., Malov I.V. Effectiveness of an interdisciplinary approach to early diagnosis of hepatocellular carcinoma. Yakut Medical Journal, 2025; 92(4): 76-80. https://doi.org/10.25789/YMJ.2025.92.17

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Introduction. Due to its widespread prevalence and alarming growth rate, hepatocellular carcinoma (HCC) has become a pressing health care issue. Among malignant neoplasms, HCC ranks fifth in the world in terms of prevalence and second in terms of mortality, second only to colorectal cancer [1]. Every year, more than 600,000 patients worldwide die from HCC [1].

As a rule, HCC develops against a background of fibrotic changes in the liver and directly depends on the duration, severity, and stage of the disease. In 80–90% of cases, HCC develops against a background of liver cirrhosis (LC) [8]. An exception is viral hepatitis B, in which the virus genome integrates into the hepatocyte genome and has oncogenic properties [18].

In most countries around the world, hepatitis B and C viruses play a leading role in the development of HCC. Due to vaccination of the population in all countries of the world, its significance as a risk factor for HCC has significantly decreased. Therefore, the emphasis in the structure of etiological significance has shifted towards hepatitis C. The pathogenesis of HCC in hepatitis C involves the development of liver cirrhosis as the first stage, against which the risks of HCC increase many times over. Thus, even after the elimination of the virus as a result of antiviral therapy, patients remain at risk of developing HCC, which is 2.1% per year for Child-Pugh class A cirrhosis and 7.8% per year for class B cirrhosis [11].

The absence of clinical symptoms in the early stages and, consequently, late diagnosis have led to high mortality rates and low treatment effectiveness for HCC. Thus, in 2023, the total number of newly diagnosed patients with HCC in Russia was 6,321 and the number of deaths from malignant liver tumors was 10,571. This fact indicates that the diagnosis was often made post-mortem. It is worth noting that 78.2% of the identified patients were in stages III-IV of the disease [4]. At the same time, in cases of early diagnosis and radical treatment, the 5-year survival rate of patients increases to 70% [15, 16].

In this regard, improving dispensary observation of risk groups and continuity

in the management of patients within the framework of interdisciplinary cooperation between specialists appears to be a promising direction capable of ensuring early diagnosis of HCC and improving treatment outcomes.

The aim of the study was to evaluate the impact of an interdisciplinary approach on the etiological verification of the diagnosis and the effectiveness of HCC detection using the example of the Republic of Sakha (Yakutia).

Materials and methods. A retrospective analysis was conducted of data from 632 patients with HCC in the Republic of Sakha (Yakutia) who were examined and treated at the Yakutsk Oncology Dispensary between 2019 and 2023. Men predominated among the patients observed. For comparative assessment, parameters such as gender, age, presence of viral hepatitis B, C and D, liver cirrhosis, and HCC stage according to the TNM scale were selected. The choice of the periods being compared (2019 and 2023) is due to the introduction of a number of regional regulatory documents in the Republic of Sakha (Yakutia) after 2019 aimed at improving the detection of viral hepatitis, HCC, patient routing, and interdisciplinary collaboration among specialists. To assess the long-term incidence and staging of patients with HCC, we used official statistics for the Republic of Sakha (Yakutia) [5], in which malignant neoplasms (MN) of the liver and intrahepatic bile ducts (IBD) are grouped under code C22.

Statistical processing was performed using the "Statistica" software package, version v.10. Student's t-test and chi-square ($\chi 2$) were used to analyze differences between groups. The indicators in the tables are presented as the frequency of occurrence of the indicator (%) or the mean value with standard error (M ± m). The mean value, standard deviation, and median were calculated. Statistical significance was assessed at $p \leq 0.05$.

Results and discussion. As in the rest of the world, the incidence of malignant liver tumors is growing annually in the Russian Federation. Thus, since 2007, an increase in this indicator has been observed in both men (Fig. 1) and women (Fig. 2). Moreover, this oncopathology occurs in men 2.2-2.7 times more often. In the Sakha Republic (Yakutia), incidence rates in both sexes significantly exceed the national average, which cannot but cause concern [3, 4]. Despite the heterogeneity of indicators in the Sakha Republic (Yakutia) from year to year and a clear predominance of men, among people diagnosed with the disease, a trend towards a decrease in incidence rates among women in this subject of the Russian Federation is observed (Fig. 2), which is confirmed by the regression equation y = 11.599 - 0.1673x.

HCC is a multifactorial disease, the risks of developing which are determined by a combination of congenital and modifiable risk factors [8]. It is clear that today, HCC should be viewed not so much as an independent disease, but as a sequential change in pathological conditions (hepatosis → hepatitis → liver fibrosis → cirrhosis → hepatocellular carcinoma) that fall within the competence of various internal medicine specialists. Given the leading role of viral agents, this sequence also determines the patient's path from one specialist to another: therapist/general practitioner → infectious disease specialist/gastroenterologist → oncologist. The lack of a well-thought-out referral system for these patients leads to late diagnosis and low five-year survival rates for patients with hepatocellular carcinoma associated with hepatitis B and C [6, 9].

In this regard, based on Order No. 116n of the Ministry of Health of the Russian Federation dated February 19, 2021 "On the Approval of the Procedure for the Provision of Medical Care to the Adult Population with Oncological Diseases" for 2020-2023, a number of regulatory documents were adopted in the Republic of Sakha (Yakutia) aimed at improving the dispensary observation of patients with viral hepatitis, the diagnosis and treatment of oncological diseases, namely:

- Order of the Ministry of Health of the Republic of Sakha (Yakutia) No. 01-07/1074 dated August 6, 2020, "On the Organization of Region-Specific Screening Studies of Persons in Groups at Increased Risk of Cancer";
- Order of the Ministry of Health of the Republic of Sakha (Yakutia) dated No-

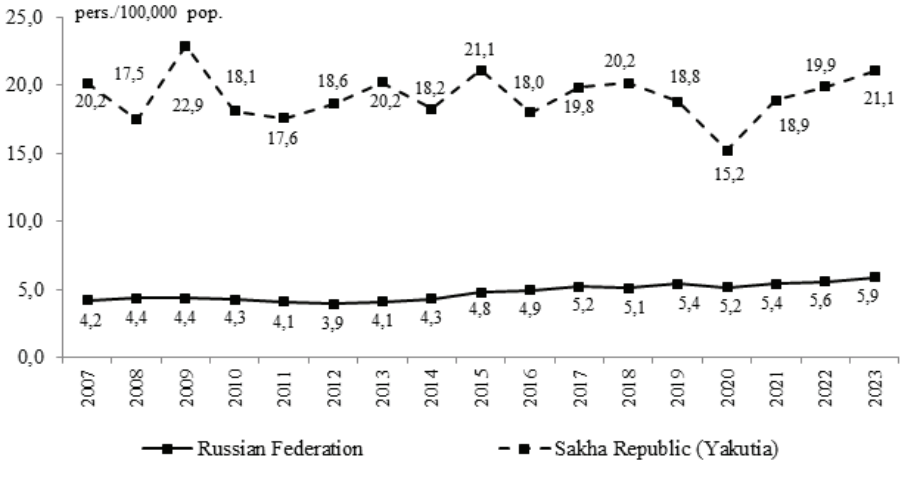

Fig. 1. Standardized incidence rate of liver cancer in men in the Russian Federation and Yakutia (2007-2023)

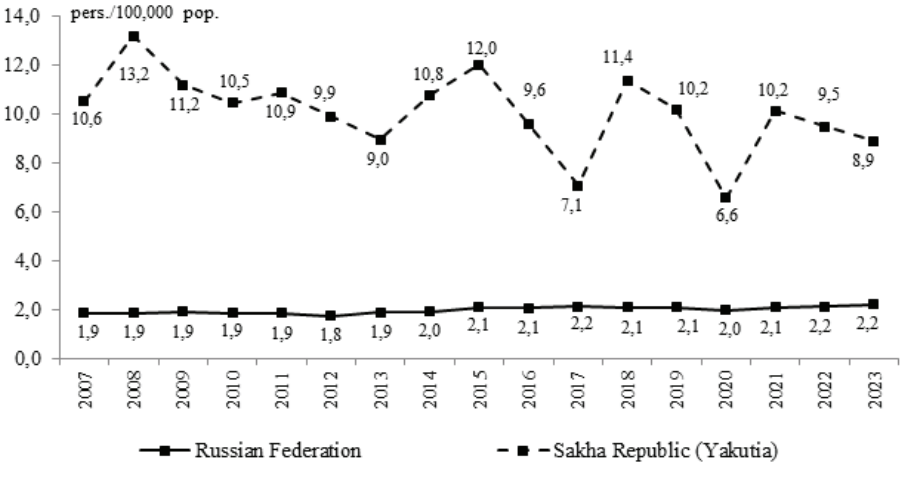

Fig. 2. Standardized incidence rate of liver cancer in women in the Russian Federation and Yakutia (2007-2023)

vember 2, 2020, No. 01-07/1607 "On the organization of dispensary observation of adults with oncological diseases in the Republic of Sakha (Yakutia)";

- Order of the Ministry of Health of the Republic of Sakha (Yakutia) dated October 6, 2021, No. 01-07/1368 "On the organization of medical care for patients with chronic viral hepatitis in the Republic of Sakha (Yakutia)";

- Order of the Ministry of Health of the Russian Federation No. 168n dated March 15, 2022, "On the Approval of the Procedure for Dispensary Observation of Adults";

- Order of the Ministry of Health of the Republic of Sakha (Yakutia) dated March 15, 2023, No. 01-07/509 "On the organization of specialized medical care for patients with chronic viral hepatitis in the Republic of Sakha (Yakutia)".

Later in the period under review, the following orders of the Ministry of Health of the Republic of Sakha (Yakutia) came into force: "On the implementation of measures aimed at improving the provision of medical care to the adult population with oncological diseases in the Republic of Sakha (Yakutia)" (dated July 24, 2024, No. 01-07/1179), "On improving medical care for adult patients with chronic viral hepatitis in the Republic of Sakha (Yakutia)" (dated February 6, 2025, No. 01-07/239-OD), as well as the order of the Government of the Republic of Sakha (Yakutia) "On the approval of the regional program "Fighting cancer in the Republic of Sakha (Yakutia) for 2025-2030" (dated June 30, 2025, No. 503-r).

All these regulatory acts should have a significant impact on improving patient routing and interdisciplinary interaction between related specialists. Patients with risk factors, primarily viral cirrhosis of the liver, are subject to a specific algorithm of observation and examination, which significantly reduces the time required for examination. Dispensary observation of patients with chronic viral hepatitis (CHV) and cirrhosis of the liver of viral etiology is carried out on an outpatient basis by an infectious disease doctor, or in his absence, by a district therapist, general practitioner (family doctor). The results of the patient's examination are sent in electronic format to the State Budgetary Institution of the Republic of Sakha (Yakutia) "Yakutsk Republican Center for the Prevention and Control of AIDS and Infectious Diseases" to decide on the appointment of antiviral therapy and monitoring to achieve a sustained virological response. In chronic hepatitis C, this type of treatment should be prescribed for up to 1 year. However, patients with se-

Comparative characteristics of patients with HCC before and after the introduction of an interdisciplinary approach in the Republic of Sakha (Yakutia)

Indicator		Total (n = 280)	2019 (n = 138)	2023 (n = 142)	P
Male (M), n (%)		158 (56.4)	74 (53.6)	84 (59.2)	0.351
Female (F), n (%)		122 (43.6)	64 (46.4)	58 (40.8)	
F:M ratio		1:1.3	1:1.2	1:1.5	
Age of men (M+m), years		63.7±0.9	63.8±1.3	63.7±1.3	>0.05
Age of women (M+m), years		69.5±0.8	68.6±1.1	70.5±1.1	>0.05
Total with hepatitis, n (%)		132 (47.1)	35 (25.4)	97 (68.3)	**<0.001**
of which:	hepatitis C, n (%)	67 (50.7)	21 (60.0)	46 (47.4)	0.203
	Hepatitis B, n (%)	31 (23.5)	5 (14.3)	26 (26.8)	0.135
	Hepatitis B+D, n (%)	27 (20.5)	7 (20.0)	20 (20.6)	0.939
	Hepatitis B+C, n (%)	4 (3.0)	2 (5.7)	2 (2.1)	0.635
	Hepatitis B+D+C, n (%)	3 (2.3)	0	3 (3.1)	0.256
Cirrhosis of the liver, n (%)		112 (40.0)	15 (10.9)	97 (68.3)	**<0.001**
TNM stage I, n (%)		24 (8.5)	7 (5.1)	17 (12.0)	**0.04**
TNM stage II, n (%)		64 (22.9)	33 (23.9)	31 (21.8)	0.679
TNM stage III, n (%)		110 (39.3)	64 (46.4)	46 (32.4)	**0.017**
TNM stage IV, n (%)		82 (29.3)	34 (24.6)	48 (33.8)	0.093

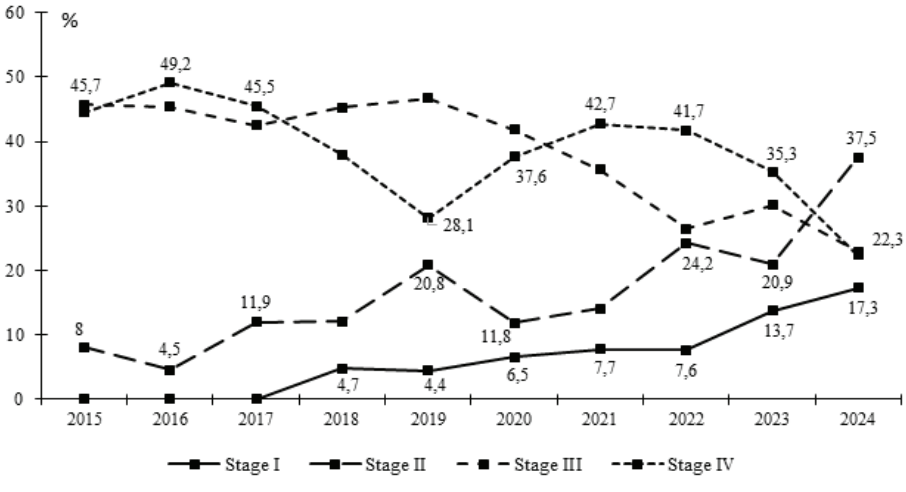

Fig. 3. Distribution of patients with HCC diagnosed in Yakutia by stage (2015-2023)

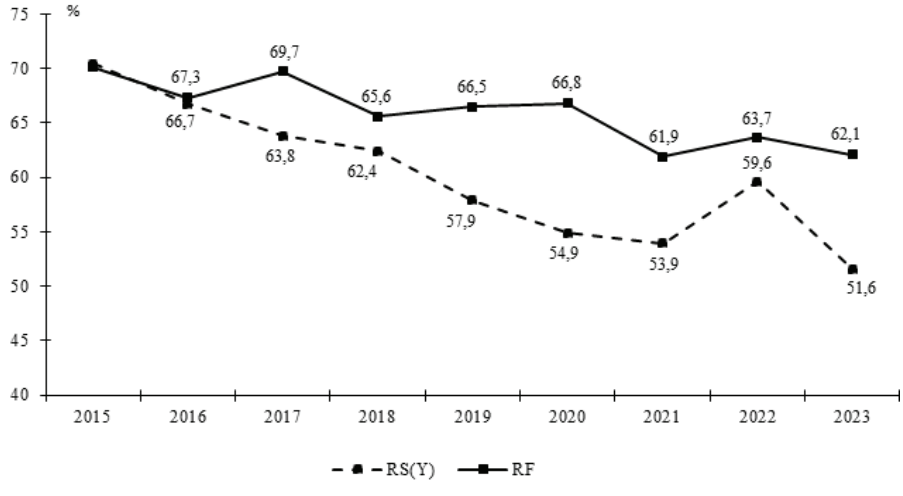

Fig. 4. One-year mortality of patients with HCC in the Russian Federation (RF) and Yakutia (Republic of Sakha (Yakutia)) (2015-2023)

vere fibrosis or cirrhosis of the liver, due to the high risk of developing HCC, are subject to lifelong monitoring by a gastroenterologist or therapist with mandatory examinations every 6 months, including ultrasound examination of the abdominal organs and determination of the level of a specific tumor marker.

It is important to note that in recent years, Yakutia has seen positive trends in increasing the coverage of antiviral therapy for people with hepatitis. In 2024, 1,198 people with chronic hepatitis C and 262 people with chronic hepatitis D received a full course of treatment, which exceeds the 2023 figures by 2.8 and 1.7 times, respectively.

For comprehensive centralized monitoring of patients at risk for HCC, a federal registry of patients with viral hepatitis was launched in Yakutia on September 1, 2024. Thanks to this data, specialists from medical organizations can track the availability of examinations and treatment for their patients and monitor the timeliness of antiviral therapy prescriptions.

As can be seen from Table 1, the implementation of measures aimed at improving the provision of medical care to the adult population with cancer in the Republic of Sakha (Yakutia), including the formation of interdisciplinary interactions, over a five-year period has led to a significant improvement in the etiological interpretation of the causes of liver damage and the quality of assessment of the functional and morphological state of the liver. Due to improved screening, the proportion of patients with markers of viral hepatitis increased 2.5 times and approached 70%, which corresponds to the literature data for the Euro-Asian region [2, 12, 13]. The inclusion of infectious disease specialists and gastroenterologists in the process of monitoring patients was accompanied by an improvement in the clinical and laboratory diagnosis of liver cirrhosis, which is extremely important when choosing a treatment strategy for a patient, as well as in the early differential diagnosis of focal liver lesions.

One of the key indicators of the effectiveness of dispensary observation of patients from risk groups is the early diagnosis of HCC. The proportion of patients diagnosed at stage I according to TNM at the Yakutsk Oncology Dispensary over 5 years increased 2.4 times (Table), and in the Republic of Sakha (Yakutia) as a whole, 3.9 times (Fig. 3). This indicates the effectiveness of primary health care in terms of cancer awareness and prevention, primarily on the part of infectious disease specialists, therapists, and gastroenterologists.

An important informative criterion for diagnostic effectiveness is one-year mortality, i.e. the proportion of patients who died from HCC within the first year after diagnosis among patients registered in the previous year (Fig. 4). This indicator depends on the regularity of dispensary observation, which is confirmed by the increase in the detection of persons with stage III-IV liver cancer in 2021-2022 in the republic, associated with quarantine restrictions on routine examinations of persons, including those from risk groups.

The five-year survival rate of patients with HCC diagnosed during the study period increased by 1.7 times and amounted to 18.3% and 31.9%, respectively, confirming the positive impact of the organizational and managerial measures taken.

In accordance with current regulations, each patient with a confirmed cancer diagnosis is subject to review by a multidisciplinary team to determine the treatment strategy. It should be noted that an interdisciplinary approach is important not only for the early diagnosis of HCC, but also after confirmation of the diagnosis, in the treatment of concomitant complex pathologie with different morpho-functional statuses of liver damage. A significant reduction in mortality ($p<0.01$) and an increase in 3-year survival to 92% in patients with HCV-associated HCC after achieving a sustained virological response [10, 14, 17,] was made possible solely through the coordinated interdisciplinary collaboration of oncologists and infectious disease specialists. Given the unfavorable situation in the region with regard to chronic viral hepatitis and its outcomes (cirrhosis of the liver and hepatocellular carcinoma), it is necessary to further expand access to antiviral therapy for people with chronic viral hepatitis B, C and D, early initiation of antiviral therapy regardless of the stage of fibrosis, rational use of compulsory health insurance funds and regional programs. It is precisely this approach that ensures the timely and safe administration of antiviral therapy and directly determines the improvement of the oncological prognosis.

Conclusion. The literature data and the republic's experience in implementing an interdisciplinary approach to the routing and clinical observation of patients with HCC allow us to recommend its widespread use. It is necessary to continuously improve the rules for routing patients with chronic viral hepatitis in order to decentralize the provision of medical care and expand access to treatment. The question remains open as to how the introduction of an interdisciplinary approach will affect the overall survival of patients with HCC. The answer to this question requires prospective observation of patients and careful analysis, and the authors of the article hope to continue the research in the foreseeable future.

The authors declare no conflict of interest.

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HYGIENE, SANITATION, EPIDEMIOLOGY AND MEDICAL ECOLOGY

DOI 10.25789/YMJ.2025.92.18

УДК 615/38-082:612.111.7

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DETECTION OF ANTIBODIES TO THE HEPATITIS B VIRUS CORE ANTIGEN IN DONORS OF YAKUTIA AS A METHOD OF ENHANCING VIRAL SAFETY

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The article presents the results of the study on antibodies to the hepatitis B virus core antigen (anti-HBcore) among donors of the Republican Blood Transfusion Station during the period of 2021–2024. The purpose of this study is to determine the most effective method of identification and exclusion from blood donation of individuals with latent infection and past hepatitis B virus infection. In addition, the article reviews virus-safe blood components procurement, reduction of discarded blood and minimization the risk of post-transfusion complications during hematransfusions.

Throughout the study period, the overall detection rate of anti-HBcore was 26.3%, with no statistically significant gender-based difference (25.3% in men vs. 28.2% in women; p = 0.912). Donor age appeared to be one of the main factors influencing anti-HBcore prevalence. The findings indicate that routine anti-HBcore testing at every donation made by the age group of over 30-35 years old is recommended.

Keywords: donor, hepatitis B virus, hepatitis B core antibodies, hematransfusion safety.

For citation: Gerasimova V.V., Davydova L.E., Ermolaev A.R., Ivanova A.A., Chulakova N.A. Detection of antibodies to the hepatitis B virus core antigen in donors of yakutia as a method of enhancing viral safety. Yakut medical journal. 2025; 92(4): 80-83. https://doi.org/10.25789/YMJ.2025.92.18

Introduction. An essential prerequisite of hemotransfusion therapy is the assurance of the infectious safety of blood and its components [7, 10, 13]. At present, in Russia, the cases of HIV, hepatitis B virus (HBV), or hepatitis C virus (HCV) transmission to recipients are not being registered [8,12]. This is largely due to continuous monitoring of all stages of the process, thorough and attentive donor selection, proper blood testing, and pathogen inactivation. According to official data, in 2020, out of 1,205,295 donors in Russia, more than 9,000 cases of infections were detected: HIV (9.4%), HBV (18.8%), HCV (37.8%), and syphilis (37.3%) [3, 4].

The prevalence of chronic HBV infection in the Republic of Sakha (Yakutia) remains consistently high and exceeds the average national level by 2.3 times. In 2024, 214 new cases of chronic HBV were reported in the republic, with an incidence rate of 21.45 per 100,000 popu-