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SERIOUS COMPLICATIONS OF CHRONIC VIRAL HEPATITIS AND THE URGENCY OF THEIR CONTROL

Zamira Fayzullaeva Rakhmatovna[1], Umidakhon Nazaralieva Shukhrat qizi[2], Kumisay Usenbaeva Samatovna[3].
[1]Head teacher of the department of Microbiology, Virology and Immunology of the Tashkent Medical Academy.
[2,3]Student of the Tashkent Medical Academy
e-mail: nadyakxon@gmail.com[2] , kumisayusenbaeva@gmail.com[3]

Abstract. One of the new public health issues that requires immediate attention is viral hepatitis. The disease can advance from an unintentional discovery to potentially fatal disorders such liver cirrhosis, and its appearance varies at the time of diagnosis. It is one of the uncommon disorders that can cause the body to become inflamed for a long time and may not show symptoms right away. It makes a significant contribution to the worldwide healthcare burden. The burden of viral hepatitis is comparable to that of HIV and tuberculosis in terms of mortality. Viral hepatitis causes 1.4 million deaths every year. The WHO set an ambitious goal to eradicate viral hepatitis by 2030, but there are still many obstacles to overcome, such as disparities in healthcare access, reaching at-risk populations, and providing access to screening and effective treatment. The stigma associated with viral hepatitis still exists and needs to be addressed. The WHO goal of global elimination by 2030 is a commendable goal, but it is still ambitious, and the coronavirus 2019 pandemic has definitely halted progress. This review article will focus on hepatitis A to E, highlighting issues that have been resolved in the field over the past ten years, those that still need to be resolved, and providing recommendations for future research and problem solving. Along with other infectious diseases like HIV, malaria, and tuberculosis, it is one of the biggest global public health concerns. The main distinction is that, particularly in underdeveloped nations, there are relatively few preventive approaches for viral hepatitis. It has the potential to become the next hidden pandemic because to its diverse presenting levels, lack of resources for diagnosis and treatment, and rapidly growing burden. The authors of the current review sought to gather the existing worldwide hepatitis prevention methods, disease surveillance procedures, and key findings from the national hepatitis control program in order to provide some recommendations.

Keywords. Viral hepatitis B, viral hepatitis A, epidemiology, guidelines, cirrhosis, chronic HCV infection.

Introduction. Viral hepatitis is a pathologic condition in which the liver becomes inflamed as a result of a hepatitis virus infection. With 248 million cases of hepatitis B and 71 million cases of hepatitis C worldwide, it significantly increases

the strain on healthcare systems. It is one of the most significant global public health issues, along with other infectious diseases including HIV, malaria, and tuberculosis. HIV caused 1.4 million deaths in 2016, according to the World Health Organization's Progress report on HIV, viral hepatitis, and sexually transmitted infections. Of all the deaths linked to viral hepatitis, 48% and 47% of the deaths were caused by the hepatitis B virus (HBV) and HCV, respectively. The World Health Organization (WHO) has set out an ambitious global elimination strategy for viral hepatitis, with the goal of eliminating viral hepatitis as a public health threat by 2030. Furthermore, one of the leading causes of death for persons living with HIV (PLHIV) is viral hepatitis. According to estimates, there are 2.75 million HIV-HCV coinfections and 2.6 million HIV-HBV coinfections among PLHIV worldwide. The fact that viral hepatitis prevention has been chosen as Target 3 of the 2030 Agenda for Sustainable Development, which highlights the urgent need to prevent and manage viral hepatitis, indicates how important it is [1-5]. Despite the fact that viral hepatitis still kills over 1.4 million people annually, we have made significant progress in understanding the epidemiology of viral hepatitis and associated treatment strategies during the past ten years, with perhaps the most notable advancements occurring in the treatment of chronic hepatitis C, which is now curable with a brief course of all oral antiviral therapy. Hepatitis B vaccination, facilitating safe injection and blood transfusion practices, encouraging safe sex, treating hepatitis B, and curing hepatitis C are among the key interventions for viral eradication that have been identified. Modeling studies, however, indicate that up to 80% of high-income nations will fall short of the WHO goal. Hepatitis A-E will be the subject of this review article, which will highlight issues that have been resolved in the field during the last ten years, identify issues that still need to be fixed, and offer ideas for future research and problem-solving strategies. The effect of the coronavirus 2019 (COVID-19) pandemic on viral eradication will also be covered [6-10]. Overall, hepatitis B infection causes for 30 % of cirrhosis and 45 % of hepatocellular carcinoma. Hepatitis C has a higher chronic asymptomatic prevalence of 55–85 %, with 15–30 % developing liver cirrhosis within 20 years. Approximately 2-4 percent of people with cirrhosis will develop hepatocellular carcinoma in their lifetime. About 25% of liver cancer cases globally are caused by hepatocellular carcinoma. At about 93.45 deaths per 100,000, some countries have one of the highest documented hepatocellular carcinoma mortality rates in the world. Given the scope and gravity of the issue, most people concur that all parties involved—including governments and funding organizations—must give viral hepatitis prevention and control the same level of attention as they do HIV, TB, and malaria [11-17]. And there have been calls by various agencies, associations and groups for an organized global response with well-articulated policies and strategies to address this largely forgotten problem. The World Health Organization has proposed a comprehensive approach by outlining four strategic axes to guide viral hepatitis response in member countries. In this study, we used this framework to examine the existing level of response in some countries. The objective is to review the policy environment, strategy and implementation and regulation of hepatitis B & C prevention, care, and treatment activities and bring the identified gaps to the

attention of relevant stakeholders and policymakers.We suggest that a health facility should have a rapid diagnostic kit for screening, a suitable lab for confirmation, a strong Health Management Information System (HMIS) portal for data management, and frequent workshops for doctors and lab technicians [18-23].

The main purpose of this presented analytical manuscript is a brief commentary on many years of scientific research on the serious complications of chronic viral hepatitis and the relevance of combating them.

Global strategies: hepatitis B and C testing guidelines. The first is the Global Health Sector Strategy (GHSS) on Viral Hepatitis, 2016–2021, which aims to help fulfill the 2030 Agenda for Sustainable Development. It covers the first six years of the post-2015 health agenda, 2016-2021, building on the Prevention and Control of Viral Hepatitis Infection: Framework for Global Action and on two resolutions on viral hepatitis adopted by the World Health Assembly in 2010 and in 2014. The plan covers all five hepatitis viruses (hepatitis A, B, C, D, and E), with a special focus on hepatitis B and C, owing to the extremely severe public health burden they represent. By 2030, this plan aims to eradicate viral hepatitis as a threat to public health [1, 4, 6]. In order to achieve a 65% reduction in mortality, 90% of infected individuals must be diagnosed and 80% of diagnosed cases must be treated (Fig. 1). Three major developments necessitated changes to this strategy, which was last updated in 2016. These developments included the evolution of DAA regimens, the reduction in the need for genotyping following the approval of DAA medications that are pan-genotypic, and the rapid rollout of treatment in low- and middle-income countries as a result of the significant cost reduction of DAAs. These guidelines entail evidence-based recommendations for program managers and healthcare providers for treating persons with chronic HCV infection [7, 11, 14, 15].

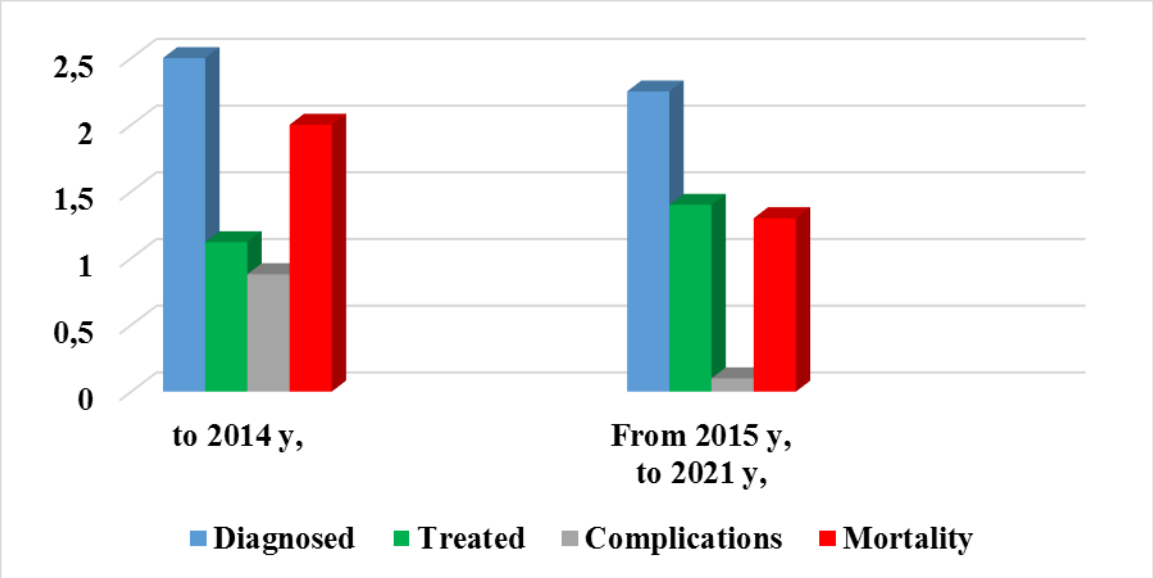

Figure 1. Effectiveness of the global strategy for the diagnosis, treatment and prevention of viral hepatitis.

Monovalent vaccination against hepatitis B. In nations with low and moderate endemicity, the World Health Organization advises monovalent hepatitis B immunization as a catch-up measure. In high burden nations like some countries with low economic, it is predicted that large-scale regular vaccination of babies lowers transmission. Nonetheless, this immunization can help high-risk groups, including as waste handlers and medical personnel. However, the monovalent vaccine is currently out of reach for most people in need due to its high cost. Therefore, as a family-based self-care strategy, the government needs to promote generic, inexpensive hepatitis B immunization in the community. The present availability of new second-generation Directly Acting Antivirals (DAAs), such as simeprevir and sofosbuvir, and their above 90% hepatitis C cure rate are predicted to understate the necessity for hepatitis C vaccine. However, the necessity of creating a hepatitis C vaccine is justified by concerns about treatment resistance, inadequate efficiency for various genotypes, the high cost, and adverse effects. The vaccination experiment is currently a public health priority and has advanced to the testing stage on an animal model, which shows promise [7-12].

Therapy for persistent infections. The majority of published information on the management of chronic HEV infection comes from studies and case series involving SOT recipients. About one-third of patients have been shown to benefit from a 30% reduction in immunosuppressive dosage. Ribavirin and PEGylated interferon both work well to treat persistent HEV infection. Ribavirin monotherapy is the recommended treatment since interferon raises the risk of organ rejection in transplant recipients. Six months after ribavirin monotherapy ended, 64% of patients were HEV RNA negative, according to a systematic study. Although the ideal dosage and length of treatment are still up for debate, three-month courses have been the most widely utilized. Ribavirin monotherapy, at a median dose of 600 mg/d for 3 months, produced SVR in 78% of cases, according to a multi-center case series of 59 transplant recipients infected with HEV [18-22]. Issues that still need to be resolved. Absence of ribavirin response: Managing non-response to ribavirin is the primary issue that needs to be resolved in connection to persistent HEV infection. An other medication for treating persistent HEV infection is sofosbuvir. In a case report, it had no impact in improving viraemia, but it has demonstrated promise in preventing HEV replication in vitro. In a subsequent research, nine patients receiving sofosbuvir monotherapy showed a slight decrease in viral load, but no viral eradication was accomplished. In a patient with a chronic hepatitis E infection, convalescent plasma was also tested; however, it had no effect on HEV RNA levels [9-14].

Methods for hepatitis b infection control and prevention. The excellent practice guidelines that can successfully stop the spread of HBV are covered in this

article. Beginning with the first dose of the hepatitis B vaccine given immediately after birth, followed by full vaccination during infancy and the use of catch-up vaccination programs for children, it uses examples of international and US programs in HBV vaccination (such as Alaska) to show how effective infant vaccination strategies can achieve this goal.

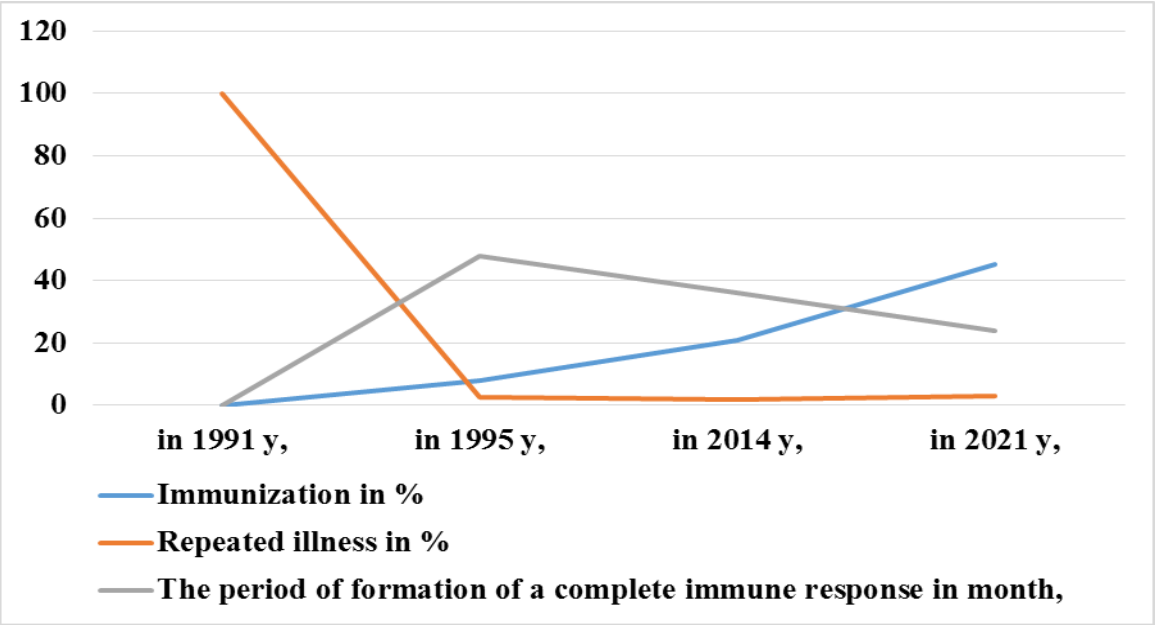

Figure 2. Methods for hepatitis b infection control and prevention.

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It also demonstrates how programs that target people who are most at risk of contracting HBV can stop acute icteric HBV infection and transmission in this age group [3-7]. International Vaccine Policy. The Expanded Programme on Immunization (EPI) Global Advisory Group suggested in 1991 that hepatitis B vaccination be incorporated into national immunization programs by 1995 for nations with a prevalence of 8% or more HBV carriers and by 1997 for those with a lower prevalence. The hepatitis B vaccine was made available countrywide in 184 countries by the end of 2014. As the most economical method of preventing and controlling hepatitis B, the WHO advises using monovalent HBV immunization within 24 hours of birth and then finishing the HBV vaccine series within 6 to 12 months (Fig 2.). This approach lowers the population's pool of chronic carriers while offering future birth cohorts the earliest protection available [17-21].

Recommendations. Since the program is using preexisting healthcare infrastructure, it should be ensured that the healthcare facility that is designated as a treatment center is provided with rapid diagnostic kits for screening, machinery required for lab investigation, drugs, and a well-developed Health Management Information System (HMIS) portal. For optimal use, screening kits should be distributed by program management units in a systematic manner, which involves

distributing the kits in tiers by going from top to bottom. In addition to antenatal and preoperative screening, free screening kits should be made available for key and bridge populations. It is important to research the population's willingness and the results of hepatitis screening. A well-established procedure should be in place for notifying patients who test positive for quick diagnostic tests, conducting auxiliary and confirmatory testing, and treating them. For greater results, a decentralized strategy could be used. Many treatment centers (district hospitals) lack the facilities necessary for basic laboratory tests to treat viral hepatitis, such as coagulation profile (PT/INR); some centers do not have an HMIS portal, and in other centers, doctors are unaware of the program that has provided the logistics, despite the availability of screening kits and medications. These problems could be fixed by a well-designed HMIS portal [7-14]. To have well-focused and responsible employees at every level, the focus of these seminars needs to be expanded to include program managers, data entry operators, and peer supporters. Infrastructure and human resource development should be coordinated with capacity-building. Specialty resources should be carefully nominated for training, with an emphasis on internists from facilities that have human and infrastructure resources available. It is essential to regularly monitor and conduct evaluation meetings and visits in order to identify the program's implementation shortcomings and strengths at the local level. Lastly, state steering committees ought to update each state's operational guidelines in light of the ground reports. Publication of these reports is also advised in order to spread best practices and problem-solving techniques [15-21].

Discussion. A pathologic condition known as "viral hepatitis" occurs when an infection caused by a hepatitis virus results in liver inflammation. With 248 million hepatitis B and 71 million hepatitis C infections worldwide, it significantly adds to the strain on healthcare systems around the world. On par with other infectious diseases like HIV, malaria, and tuberculosis, it is one of the most significant global public health concerns. In 2016, 1.4 million people died from HIV, viral hepatitis, and other sexually transmitted illnesses, according to the World Health Organization's Progress report on these conditions. 96% of all deaths linked to viral hepatitis were caused by the hepatitis B virus (HBV) (48%) and HCV (47%), respectively [1-3]. Furthermore, one of the leading causes of death for persons living with HIV (PLHIV) is viral hepatitis. According to estimates, there are 2.75 million HIV-HCV coinfections and 2.6 million HIV-HBV coinfections among PLHIV worldwide. The fact that viral hepatitis prevention has been chosen as Target 3 of the 2030 Agenda for Sustainable Development, which highlights the urgent need to prevent and manage viral hepatitis, indicates how important it is. This article's objective is to evaluate the state of national programs and policies for managing, preventing, and controlling viral hepatitis. The authors' goal is to gather the existing

worldwide hepatitis plans, illness monitoring methods, and key findings from the national hepatitis control program. They also hope to provide some recommendations 4, 5, 9, 11, 14]. The World Health Organization advises viral hepatitis surveillance that covers mortality from liver disease sequelae, such as cirrhosis and HCC, as well as the incidence of acute hepatitis and the prevalence of HBV and HCV. In order to define the objective of eradicating viral hepatitis as a public health issue by 2030, the GHSS uses mortality reduction among HBV and HCV cases as one of its criteria. Therefore, it is essential to establish methods for measuring mortality associated to HBV and HCV. At first, mortality was calculated solely from acute infection deaths; however, it neglected mortality from chronic liver disease caused by hepatitis virus infection, including cirrhosis and HCC [15-18]. With the program being in its fourth year, a few problems have been experienced in successfully executing it. The primary priority is infrastructure and material management. For the timely acquisition and distribution of supplies, accurate planning for the estimation of medications and fast diagnostic kits is crucial. Another significant obstacle is the mobilization of human resources for efficient service delivery in every district. Focus areas that require an urgent call to action include the best possible acquisition of high-quality testing kits, expanding viral load testing, reporting on the MIS platform, routine program monitoring and evaluation, and supporting supervision at all levels [11, 17, 19, 20, 24].

Conclusions. Over the past ten years, there have been significant advancements in the field of viral hepatitis, especially in relation to the treatment and cure of hepatitis C. As we work to eradicate viral hepatitis worldwide, the gastroenterology and hepatology community must concentrate on identifying the undiagnosed and enrolling them in treatment programs while continuing to develop innovative treatments with the ultimate goal of curing the disease.

Many other low-income nations are paying little attention to viral hepatitis and the illness burden it causes. The international community provides little in the way of financial assistance and technical advice. Nonetheless, a global movement is propelling advancements in the response to viral hepatitis on a global scale. Many countries' response to the illnesses has been uneven thus far, and the nation lacks the structures and resources required for a comprehensive and successful response. Therefore, the nation must develop policies and plans in the areas of disease surveillance, screening and identification of risk groups, hepatitis B vaccination at birth, and care and treatment. Enhancing the accessibility of viral hepatitis data, gaining access to affordable generic medications, and creating treatment protocols are also essential.

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