

STATE OF VIRAL HEPATITIS CARE IN 16 COUNTRIES OF CENTRAL AND EASTERN EUROPEAN REGION

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SUMMARY

Objectives: Survey was conducted to assess state of viral hepatitis care in Central and Eastern Europe (CEE).

Methods: Representatives of 16 CEE countries completed on-line survey in April–May 2017 that collected information on basic epidemiology and availability of key services for HCV and HBV infections. Sources of information provided ranged from national surveillance data to expert opinion.

Results: The burden of viral hepatitis varied between countries, ranging from 6,500 to 2 million for HCV and from 10,000 to 3 million for HBV. Access to routine HCV RNA testing and genotyping was reported by 11 and 9 countries, respectively. HCV resistance testing was available in 7 countries. Direct acting antivirals (DAAs) were available in 13 countries, most frequently Sofosbuvir and Ledipasvir/Sofosbuvir (12 countries apiece) and Ombitasvir/Paritaprevir/Dasabuvir (9 countries). HBV DNA testing and HBV genotyping were routinely available in 10 and 7 countries, respectively. Eleven countries reported available treatment with Tenofovir.

Conclusions: There are gaps in viral hepatitis care in CEE. Despite the availability of registered modern drugs for HCV and HBV, the access to treatment is limited. Ensuring quality health care is essential to reduce the epidemic and achieve the WHO's goal of eliminating viral hepatitis as a major public health challenge.

Key words: viral hepatitis, Central and Eastern Europe, HCV, HBV

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INTRODUCTION

Viral hepatitis due to hepatitis B virus (HBV) and hepatitis C virus (HCV) represent major health challenge globally. Both viruses can cause chronic hepatitis that may lead to cirrhosis and hepatocellular carcinoma (1, 2). The World Health Organization (WHO) estimates that there are more than 300 million people living with chronic HBV and HCV infection globally including 29 million people living in the WHO European Region resulting in 171,000 deaths annually (3, 4).

Currently available prevention and treatment modalities make the goal of viral hepatitis elimination technically feasible (5). This includes highly effective vaccine against HBV, antiviral drugs to control HBV and new generation direct acting antivirals (DAAs) curing >95% of HCV infections (1, 6). However, there are important challenges to overcome, including gaps in prevention, diagnosis and treatment (3).

Latest global hepatitis report shows that only 9% of people living with HBV and 20% of people living with HCV are aware of their status (3). Only 8% of those diagnosed with HBV and HCV infections received antiviral therapy (3). Access to effective

treatment is substantially hampered by high costs of both HBV and HCV drugs (7), which are often inaccessible to all patients through health systems. While prevention can reduce the rate of new infections, the number of chronically infected persons would remain high for years, therefore, ensuring testing, virological monitoring and unrestricted access to treatment is crucial for achieving elimination goal.

We conducted survey to assess state of viral hepatitis care within the Euroguidelines in Central and Eastern Europe (ECEE) Network Group, which was formed in 2016 to promote dissemination of European standards of care in HIV and viral hepatitis in Central and Eastern Europe (CEE) (8).

MATERIALS AND METHODS

On-line survey was constructed to elicit information related to HCV and HBV care in CEE region. The survey asked respondent to answer 17 question, including 2 general questions about the country of residence and occupation, 8 questions about HCV epidemiology and availability of HCV diagnostic and treatment

services, and 7 questions about HBV epidemiology and availability of HBV diagnostic and treatment services. Questions were primarily pre-defined multiple choice questions with an option to provide free text response in “Other” section. Questions were reviewed by field experts for content validity. Survey content is provided in Table 1. Informed consent was not sought as survey did not collect any identifiable private information about the respondent or any other individual.

Data collection took place in April–May 2017. Overall 17 respondents participated from 16 CEE countries (Albania, Armenia, Bosnia and Herzegovina, Bulgaria, Croatia, Estonia, Georgia, Greece, Hungary, Poland, Republic of Moldova, Romania, Serbia, Slovenia, Turkey, Ukraine). Majority of respondents (76%) were HIV or other specialty clinicians, there were two epidemiologists, a head of national reference laboratory and a manager of national programme. Respondents were asked to provide the source of

Table 1. Survey content

No	Question	Answers
1	What is your country?	Text
2	What is your current occupation?	a) HIV clinician b) Other specialty clinician c) Epidemiologist d) Other (to be specified)
3	What is the number of HCV infected persons in your country?	Number
4	Which group is dominating among HCV positive persons?	a) People who inject drugs b) Medical procedure in anamnesis c) Unknown d) Other (to be specified)
5	Which groups are routinely tested in public healthcare system for HCV infection (anti-HCV antibodies)?*	a) Blood and organ donors b) Populations at risk e.g. PWID, MSM, sex workers c) Medical procedure in anamnesis d) Pregnant women e) Other (to be specified)
6	Do you have access to routine HCV RNA testing?	a) Yes b) Periodically c) No
7	Do you have access to routine HCV genotyping?	a) Yes b) Periodically c) No
8	Do you have access to routine HCV resistance testing?	a) Yes b) Periodically c) No
9	Describe antiviral treatment available for HCV infection in public health care (free of charge):	a) DAA original products b) DAA generic products c) Interferon + RBV only d) No treatment is available
10	Do you have DAA drugs available in your country infection in public health care (free of charge)?*	a) Simeprevir (SMV) b) Boceprevir (BCV) c) Sofosbuvir (SOF) d) Ledipasvir/Sofosbuvir (LED/SOF) e) Daclatasvir (DCV) f) Elbasvir/Grazoprevir (EBR/GZR) g) Ombitasvir/Paritaprevir/Ritonavir + Dasabuvir (OMB/PTV/r + DAS) h) Other
11	What is the number of HBV infected persons in your country?	Number

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No	Question	Answers
12	Which group is dominating among HBV positive persons?	a) Injecting-drug users
		b) Persons with medical procedure in anamnesis
		c) Unknown
		d) Other (to be specified)
13	Which groups are routinely tested in public healthcare system?*	a) Blood and organ donors
		b) Populations at risk e.g. IDU, MSM, sex workers
		c) Medical procedure in anamnesis
		d) Pregnant women
		e) Other (to be specified)
14	Do you have access to routine HBV DNA testing?	a) Yes
		b) Periodically
		c) No
15	Do you have access to routine HBV genotyping?	a) Yes
		b) Periodically
		c) No
16	Which antiviral treatment is available for HBV infection in public health care?*	a) Tenofovir
		b) Entecavir
		c) Lamivudine
		d) Interferon
		e) Other (to be specified)
17	Describe availability in public health care for end stage liver disease treatment*	a) Liver transplantation for HIV negative
		b) Liver transplantation for HIV positive
		c) None
		d) Other (to be specified)

* Multiple answers possible

information, which ranged from national survey and surveillance data to expert opinion.

RESULTS

Among 17 respondents 13 (76.5%) were either HIV or other specialty clinicians, among remaining four persons – two were epidemiologists, one head of national reference laboratory and one programme manager.

The burden of viral hepatitis varied between countries with estimated 10,000 to 3 million individuals with HBV and from 6,500 to 2 million HCV infections. Based on provided data, at least 5 million people live with HBV and 3.7 million with HCV infection in CEE region. Injection drug use was the major risk factor for HCV infection, reported by 9 (52.9%) countries, while HBV was most frequently associated with history of medical procedures – 8 (50%) countries.

Blood and organ donors were screened for both infections in all countries. Screening policies for other populations varied by country. Pregnant women were screened for HBV in 12 (75.0%) and for HCV in 9 (56.3%) countries. Populations at risk were screened for HBV in 10 (62.5%) and for HCV in 12 (75.0%) countries. Only 4 (25.0%) countries had policy of screening

people with history of medical procedures both for HBV and HCV infections (Fig. 1).

Not all countries ensure routine access to molecular diagnostic methods (Fig. 2). HBV DNA testing and HBV genotyping was routinely available in 10 (62.5%) and 7 (43.8%) countries, respectively. HCV RNA testing was routinely accessible in 11 (68.8%) countries, with 9 (56.3%) countries ensuring access to HCV genotyping.

Eleven (68.8%) countries reported availability of treatment with Tenofovir for HBV infection (Fig. 3). DAAs for HCV in-

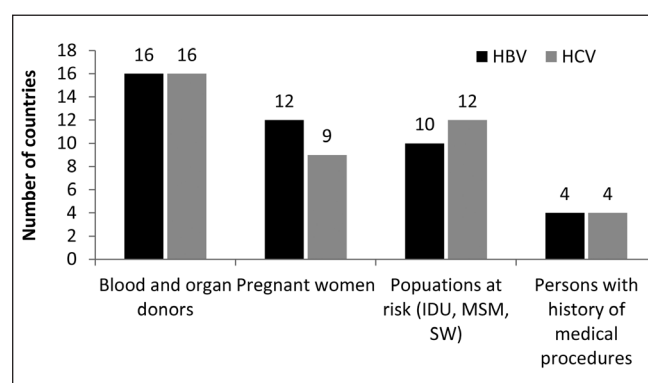


Fig. 1. Populations routinely screened for HBV and HCV.

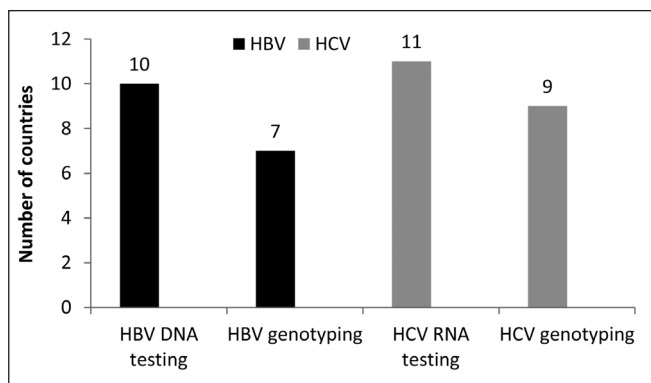


Fig. 2. Routine availability of molecular diagnostics.

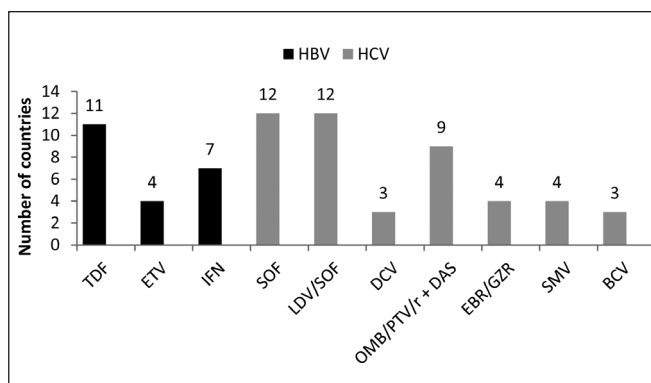


Fig. 3. Routine availability of HBV and HCV medicines.

TDF – Tenofovir; ETV – Entecavir; IFN – Interferon; SOF – Sofosbuvir; LDV/SOF – Ledipasvir/Sofosbuvir; DCV – Daclatasvir; OMB/PTV/r + DAS – Ombitasvir/Paritaprevir/Ritonavir + Dasabuvir; EBR/GZR – Elbasvir/Grazoprevir; SMV – Simeprevir; BCV – Boceprevir

fection were available in 13 (81.4%) countries. Most commonly available DAAs were Sofosbuvir (12 countries, 75.0%), Ledipasvir/Sofosbuvir (12 countries, 75.0%) and Ombitasvir/Paritaprevir/Ritonavir + Dasabuvir (9 countries, 56.3%).

DISCUSSION

This was the first survey to evaluate access to hepatitis care in CEE region primarily from the clinicians' perspective. Our survey indicates that there are gaps in viral hepatitis care that need to be addressed in order to improve surveillance and treatment and thus make the elimination goal feasible. Action plan for the health sector response to viral hepatitis in the WHO European Region, unanimously approved by all member states in 2016, provides roadmap towards hepatitis elimination with measurable targets to be achieved across the continuum of hepatitis services.

It is agreed that successful engagement in the continuum depends on testing, which is the gateway to treatment and care. Survey showed existing testing policies and practices may result in missed opportunities to diagnose both HBV and HCV. For example, while eight countries identified persons with history of medical procedures as the dominant in HBV, only 4 countries reported availability of routine testing for this population. People who inject drugs and pregnant women are also missed in screening programmes in some CEE countries. It should be noted that

gaps in hepatitis testing are also visible in more affluent parts of Europe and as a result only 13% of HBV-infected persons and 30% of HCV-infected individuals are diagnosed in the entire European region (3, 9).

The price is considered to be the key driver affecting access to diagnostic and treatment services in general, therefore, economic situation in CEE should be taken into account. Based on the World Bank classification, of 16 countries participating in this survey majority (11 countries) have lower- or middle-income economies. Five countries are classified as high income, yet their per capita gross national income (GNI) is significantly lower than average of the European Union (World Bank, GNI per capita, Atlas method*).

Current economic situation in surveyed countries may explain limited accessibility of molecular diagnostics for HBV and HCV. With regard to treatment, all countries reported availability of some treatment. For HBV, Tenofovir most commonly available drug, with Entecavir use reported by 4 countries (including 3 high income countries). It should be noted that in non-EU member CEE countries Tenofovir is available as generic product at significantly lower price as compared to originator, but at the same use of Tenofovir for HBV might be limited to HIV co-infected populations (10).

Uptake of HCV treatment is low in the entire WHO European region, with only 5% of those diagnosed receiving treatment (3). Coverage declines as we go from the West to the East as it was demonstrated in recent publications, including the EuroSIDA report that showed twice as lower uptake of DAA based treatment in CEE countries compared to Western and Northern Europe among HIV/HCV co-infected persons (11, 12). High price of new generation DAAs results in restricted prescriptions not only in middle-income countries, but also in high-income settings. Analysis of data from countries in the European Union and European Economic Area, and Switzerland identified that nearly half of these countries restricted reimbursement of DAA based treatment to more advanced stages of liver disease, and further 17% had restrictions related to active substance use (13).

High prices and restricted access resulted in emergence of so call "buyer's clubs" that implies importation of low cost generic DAAs from countries producing these drugs through voluntary licensing (14). Importation schemes had been documented in the European region and it has been suggested that these drugs are as effective as originator products (15).

Limitations should be acknowledged. Survey had narrow representation of key stakeholders and it was primarily limited to clinicians. Inclusion of policy makers and civil society representatives might have brought different perspective. Survey covered only testing and care aspects of viral hepatitis without addressing primary prevention, which remains essential component of comprehensive response measures. Reports indicate that there is need for improving HBV immunization in children and especially among key populations at risk along with improving access to harm reduction services (3, 16). Another limitation is that not all countries of CEE region participated in the survey and we might have missed important data. For example, the Czech Republic has made important progress in providing HCV treatment, reimbursing all currently available DAAs (17), and

*<https://data.worldbank.org/indicator/NY.GNP.PCAP.CD>

providing HBV treatment to 14% of those eligible, which is well above the regional average (18).

It should be noted that response to viral hepatitis, especially to HCV, has been scaling-up in CEE region and substantial progress has been made in many countries after conducting the survey. In most of the surveyed countries reimbursements for DAAs are available, however, minimum fibrosis stage based restrictions remain in many countries (19). Georgia has been leading in terms of HCV treatment uptake with up to 50,000 persons initiating DAA treatment (20). HCV treatment uptake has been increasing in other countries as well including Poland, Romania and Ukraine. However, overall progress in the region remains unsatisfactory (21). Less progress has been made in treating HBV, with an estimated <1–5% of eligible patients receiving treatment, with the highest coverage reported in Turkey (14%) and Slovenia (17%) (18).

CONCLUSIONS

Our study provides important insights into the state of viral hepatitis care in CEE region and can serve as a benchmark for assessing the future progress. There is clear need for improving access to testing and treatment through stronger commitment and political leadership. Innovative approaches for financing response activities should be identified including through public-private partnerships and market oriented mechanisms. Lessons learned from HIV field should be explored in hepatitis field including voluntary pooled procurement, which has been shown to be effective in significantly reducing prices of HIV medicines (22). In summary, momentum for hepatitis elimination continues to grow and the opportunity needs to be seized to turn this momentum into effective action.

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Conflict of Interests

None declared

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