Neglected HBV/HDV Epidemic in Eastern Europe and Central Asia: Policy Modification Requirements for Effective Treatment and Elimination

Michael O. Favorov[1], Michael I. Mikhailov[2], Erkin I. Musabaev[3]

Coalition for Global Hepatitis Elimination, The Task Force for Global Health, Atlanta, Georgia, USA[1].

Medical Academy Postgraduate Professional Education, Ministry of Health, Russian Federation, Moscow, Russia[2].

Institute of Virology, Uzbekistan Ministry of Health, Tashkent, Republic of Uzbekistan[3].

Background:

Hepatitis D is a liver disease with both acute and chronic forms caused by the hepatitis D viroid (HDV) that requires the hepatitis B virus (HBV) for replication[1]. The HDV pathogen (discovered by M. Rizzetto and colleagues), is thought to cause the most severe form of viral hepatitis including countries of region of Eastern Europe and The Former Soviet Union[2] [4]. Among patients with chronic liver disease, HDV affects 70% of men aged about 40 years; although the route of HDV transmission is often unidentified, about 25% of those diagnosed have a family history of HBV, HDV, or both; 15% have a history of transfusion; and 10% have used drugs intravenously[5].

Patients with hepatitis delta rapidly progress (3–5 years) to liver cirrhosis and half of them go on to develop liver-related clinical complications with 50% liver decompensation after 3 years[4]. Hepatocellular carcinoma is diagnosed in 5%–10% of subjects 4 years after HDV infection. Liver transplantation is required by 20% of HDV patients and 5%–10% die within 2–10 years of diagnosis (usually in 3–5 years)[6].

The World Health Organization (WHO) estimates some 260 million people worldwide are living with (HBV) infection (defined as being HBsAg-positive) and about 20 million people in this group are infected with HDV[7].

Methods:

We reviewed available regional data on HBV/HDV infections. Sources included government reports, scientific publications, WHO reports, and other recorded data. We assessed HBV and HDV prevalence among populations in the UN-defined Eastern Europe and Central Asia (EECA) region. Regulatory government directives (Prikaz) on HBV and HDV testing, treatment, and prevention policies were also reviewed.

Results and discussion:

HDV hepatitis was found in all EECA countries but there were significantly different patterns in hepatitis B and D infections. Among identified HBsAg-positive donors and pregnant women anti-HDV were positive in 1% to 8% with increase of the prevalence from West to East.

Among people with chronic liver diseases (CLD) eastern European countries (the western part of the EECA region) had sporadic HDV infections; however, in the eastern part of the region (Central Asia, eastern Siberia) HDV infections occurred in 30% to 60% of patients with CLD, indicating that HDV is highly endemic in several countries (from west to east): Romania, Moldova, Turkmenistan, Uzbekistan, Tajikistan, the southern territories of Kazakhstan, and the Russian Federation provinces of Buryatia, Yakutia, and Tuva. Areas with intermediate HDV prevalence (about 10% of CLD) include the Caucasian sub-region, several southern provinces of the Russian Federation, and eastern Ukraine. CLD patients in Central Russia, including the highly populated Moscow and North-West subregions have low (~5%)

HDV prevalence. Poland, the Baltic countries, Belorussia, and western Russia and Ukraine have very low (<2%) HDV prevalence.

Based on available data, we estimate that more than 3 million people are infected with HBV in the EECA region. Up to 250,000 of those are also are infected with HDV. Based on of several HIV and viral hepatitis studies among persons who inject drugs, about 10% have HBsAg and about 10%-20% have delta infection markers.

There are mandatory HBV screening programs for donors and pregnant women in all countries in the region yet at least two-thirds of HBV-infected individuals do not know their HBV/HDV status prior to liver disease symptoms when they are tested for HBV.

HDV genotype [1] is predominant in the region and is similar to HDV RNA isolated nearby Western (Turkey) and Eastern (Mongolia) parts of the region.

Fortunately, a universal HBsAg vaccination significantly reduces HBV and HDV infections in EECA and prevents HBV/HDV in vaccinated groups. During the last 15-20 years, since the creation of national universal vaccination programs, acute hepatitis B has declined dramatically from 30% to 50% to less than 5 per 100,000 population. However, among those with acute HBV infections, the proportion of HDV co-infections distributed according to delta endemicity ranges from sporadic to 20%–25% in highly endemic areas. The ages of persons targeted by HBsAg vaccination programs vary by country—from newborns (all countries) to ages 15–20 years. Most adults, including those in high-risk groups, remain unprotected for HBV infection. That situation is especially alarming in hyperendemic HBV/HDV areas where the possibility of nosocomial transmission is still an issue. The system of government orders describing and determining the principles of diagnosis, prevention, and treatment for public health services in most of the regional EECA countries is largely outdated. Directives (Prikaz) on HBV/HDV management need significant modifications for alignment with World Health Organization and existing international standards for HBV/HDV elimination programs. Treatment management policy improvements are particularly important for hyper-endemic countries.

Conclusion:

Hepatitis B and D remain significant public health problems in many EECA countries. Within these countries an estimated quarter of a million people are super-infected with HDV and some 100,000 of them will likely have severe life-threating complications and premature deaths within 3–5 years. Thus, there is an urgent need for the adoption and implementation of international standards of treatment. The use of high-quality rapid testing in appropriate public health settings should become a part of the mandated algorithm for HBV diagnosis. To strengthen hepatitis B and D prevention/immunization programs for unvaccinated adults, plans need to be developed, introduced, and implemented. The combined use of available treatment options with advanced vaccination strategies will reduce HDV infections to levels achieved in Italy during last two decades.

References

1. Rizzetto M, Canese MG, Aricò S, Crivelli O, Trepo C, Bonino F, et al. Immunofluorescence detection of new antigen-antibody system (delta/anti-delta) associated to hepatitis B virus in liver and in serum of HBsAg carriers. Gut. [Internet]. 1977;18:997–1003. Available from: http://www.ncbi.nlm.nih.gov/pubmed/75123. Cited 29 Mar 2016.
2. Netesova IG, Swenson PD, Kalashnikova TV, Netesov SV, Favorov MO. HBsAg Subtypes Of Hepatitis B Virus (HBV) In Western Siberian Part Of Russia. Vir Issues 2004; 49:17-20.
3. Favorov MO, Nemechek V, Yashina TL, Nazarova OK, Lambert SB, Drobenuk J, Znoiko OO, Shkurko TV, Lvov DK, Onischenko GG, Fields HA,

Margolis HS. Current Epidemiological Trends Of Viral Hepatitis In Eastern Europe And The Former Soviet Union. Viral Hepatitis And Liver Disease (M. Rezzetto Et Al., Ed), Turin, Italy: Edizioni Minerva Medica, 1997. 555-558.

4. Yarasheva DM, Favorov MO, Yashina TL, Shakhgildian IV, Umarova AA, Sorokina SA, Kamardinov Khk, Mavashev VI. The Etiology Of Acute Viral Hepatitis In Tadjikistan In A Period Of Low Morbidity. Vopr. Virusol 1991;36:4546.
5. El Bouzidi K, Elamin W, Kranzer K, Irish DN, Ferns B, Kennedy P, Rosenberg W, Dusheiko G, Sabin CA, Smith BC, Nastouli E. epatitis delta virus testing, epidemiology and management: a multicenter cross-sectional study of patients in London. Clin Virol. 2015 May; 66:33-7.
6. Блохина Н.П. АКАДЕМИЯ МЕДИЦИНСКИХ НАУК ИНСТИТУТ ВИРУСОЛОГИИ имени Д.И.ИВАНОВСКОГО ЗДК, 616.36-002:616.07:616-071:616-08 Медицинские Диссертации http://medical-diss.com/medicina/hroniches-kiy-gepatit-delta-klinika-diagnostika-lechenie#ixzz5p8b8WBkB
7. Hepatitis D, 23 July, 2018 WHO Key facts: https://www.who.int/en/news-room/fact-sheets/detail/hepatitis-d