Hepatitis D: surveillance and epidemiological situation in the Russian Federation

Olga Isaeva

Mechnikov Research Institute for Vaccines and Sera, Russian Medical Academy of Continuous Professional Education, Moscow

> October 25 2018 Moscow

Hepatitis D virus (HDV)

- HDV is a causative agent of hepatitis with parenteral route of transmission
- HDV is a viroid-like agent, the satellite for HBV
- HDV is the only one viroid-like agent that is infectious for human (other viroids infect plants)
- HDV infection is productive only in presence of HBV infection (coinfection or superinfection)
- Efficacy of HBsAg expression influences the replication of HDV





Prevalence of delta infection and genetic diversity of HDV (genotypes I-VIII) in the world



Pascarella S. and Negro F. Hepatitis D virus: an update // Liver International. – 2011. – Vol. 31. – P. 7-21.

Globalization and migration as major factors contributing to hepatitis delta transmission



Therapeutic options for chronic hepatitis D

- 1. HBV polymerase inhibitors are not effective;
- 2. Pegilated IFN-α: cure rate 25-27%;
- 3. Pegilated IFN- α + nucleos(t)ide analogues: cure rate 23-47%;
- 4. Clinical trials for new antivirals:
- viral entry inhibitor (Myrcludex B);
- Inhibition of post-translational modification of HDV antigen (LHDAg prenylation inhibitors): reduction of viral load for 0,75-1,25 log IU/ml
- No specific anti-HDV vaccine is available in near future

Epidemiological surveillance in the Russian Federation:

Hepatitis **B**

Continuous monitoring of the dynamics of the epidemic process (including a long-term analysis of morbidity), factors and conditions influencing disease spread, coverage of immunization, population immunity, circulation of the pathogen in order to assess the situation and timely management decisions.

Hepatitis D

- There is no specific notification for hepatitis D in surveillance system; all cases are reported in combined statistic for hepatitis B.
- in regions endemic for hepatitis D, it is imperative to assess the epidemiological situation, identify trends in the epidemic process, and make timely effective management decisions that <u>prevent the</u> occurrence and spread of HDV.
- In endemic regions: all HBsAg positive should be tested for anti-HDV

Russian Federation (N=6149)



Methods:

- 1. Enzyme immunoassay detection of HBsAg and anti-HDV
- 2. PCR amplification of *R0* region fragment (400 nt) covering the 3' end of the *HD* gene.
- 3. Direct sequencing of amplified DNA fragments

HBsAg prevalence in different age groups of general population in the Russian Federation



Prevalence of HBsAg in healthy population in studied regions of RF



Prevalence of anti-HDV among HBsAg positive individuals in general population of Tyva Republic



Prevalence of HDV in different age groups of general population in Tyva (regardless of HBsAg status) (N=1086)

| Age groups | Ν | Anti-HDV | | HDV RNA | |
|------------|------|----------|-----|---------|-----|
| | | n | % | n | % |
| <1 | 97 | 0 | 0 | 0 | 0 |
| 1-4 | 109 | 0 | 0 | 0 | 0 |
| 5-9 | 113 | 0 | 0 | 0 | 0 |
| 10-14 | 107 | 2 | 1.9 | 0 | 1.9 |
| 15-19 | 105 | 4 | 3.8 | 4 | 1.9 |
| 20-29 | 102 | 4 | 3.9 | 3 | 2.9 |
| 30-39 | 103 | 5 | 4.9 | 3 | 2.3 |
| 40-49 | 112 | 6 | 5.4 | 1 | 0.7 |
| 50-59 | 115 | 2 | 1.7 | 1 | 0.8 |
| > 60 | 123 | 4 | 3.3 | 2 | 1.6 |
| Total | 1086 | 27 | 2.5 | 14 | 1.3 |

Intrafamilial transmission of HBV and HDV





Phylogenetic analysis with a timescale for HDV R0 region (353 nt) **Timescale in years** (sequences obtained in 2009 and 2014)



300 200 100



State report 2018. On the state of sanitary and epidemiological well-being of the population of the Russian Federation in 2017.

Russian Federation:

4.7-fold decrease in incidence rates of acute hepatitis B in 2017 compared to 2008;

Chronic hepatitis B incidence in 2017: 44.42 per 100,000 population

Republic Tyva, incidence rates in 2017: Acute hepatitis B: <u>0.32 per 100,000</u> <u>population</u>. Not among the subjects of the Russian Federation with the highest incidence rates.

<u>Chronic hepatitis B: 76.95 per 100,000</u> <u>population.</u> One of the 10 regions of the Russian Federation with the highest incidence rates.



The aim of current research in Tyva – development of a action plan for optimization of the system of diagnosis, control and prevention of viral hepatitis D, based on knowledge of the epidemiology, genetic diversity and microevolution of the pathogen, the clinic features of this infection in an endemic region of the Russian Federation (Tyva Republic). Time-scaled phylogenetic analysis using a Bayesian likelihood-based algorithm for HBV sequences of overlapping region of S and P genes (700 nt). Sequences obtained in Tyva 2008-2009 (in red). Timescale in years. Confidence indexes are shown in tree nodes. Blue bars reflect error

-15000

-12500



Time-scaled phylogenetic analysis using a Bayesian likelihood-based algorithm for for HDV R0 region (353 nt) **Timescale in years** (sequences from Tyva (in blue) obtained in 2009 and 2014).

300

200

100





Prospects for the analysis of the full genome of HDV

- The study of microevolution of HDV in the host organism during long-term follow up.
- Determination of the role of polymorphism in HDV genome in disease progression and outcomes of chronic hepatitis D.
- Determination of HDV transmission routes in endemic region and investigation of itrafamiliar infection clusters.
- Reconstruction of the history of HDV spread in endemic regions for better understanding of its high prevalence in certain areas.

Thank you for your attention!