

Features of Herd Immunity Against Hepatitis B (HBV) in the Territory of Republic of Sakha (Yakutia), Russian Federation

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There is new data on the prevalence and characteristics of population immunity against HBV among the indigenous population of the Republic of Sakha (Yakutia) of the Russian Federation. HBV infection in the risk group is significantly higher than in the normal population, in patients with type 2 diabetes, there is a high parenteral infection of HBV, HCV and HBV + HCV (71,5%, 10,8% and 7,5% respectively). It was shown that every other 3- 8 years among children and adults of Yakut population living in the Republic of Sakha (Yakutia) (hyperendemic region on HBV), vaccinated at birth against HBV, the frequency of detection of anti - HBs in protective concentrations (> 10 IU / l and higher) is - 72.2%. Saving anti-HBs in vaccinated for 8 years indicates a high efficacy of vaccines against hepatitis B.

Key words: infection, HBV, HCV, vaccination

Chronic hepatitis B (HBV) is a relevant problem of public health all over the world¹⁻³. This is due to the prevalence of hepatitis B virus in the world about 2 billion people are infected with it; there are over 500 million carriers of HBV, at 350 million. chronic infection is developed. However, about 100 thousand dies of fulminant hepatic failure. According to WHO, the next 10-20 years, chronic parenteral hepatitis become a major challenge to public health authorities, because it is expected an increase in the number of patients with liver cirrhosis (LC) for 60%, hepatocellular liver cancer (HCC) by 68% and increased mortality from liver disease in 2 times. If untreated, approximately at 20% of patients liver cirrhosis

(HC) is formed and with its subsequent development in complications. At another 20% of patients with compensated LC in the next 5 years decompensated disease develops^{4, 5, 6}.

In Russia, the situation on virus hepatitis (VH) with parenteral transmission mechanism of pathogens remains extremely unfavorable, which fully applies to the population of the Republic of Sakha (Yakutia). The Republic of Sakha (Yakutia) is unfavorable region on the incidence of viral hepatitis B and the level of HBsAg carriers in the population. On the territory of the republic for decades a high incidence of hepatitis B was recorded, in 2-3 times higher than the all-Russian performance^{7,8}. This is due to low socio-economic status of northerners, poor infrastructure, remoteness, small settlements and underdeveloped logistics base of health care institutions, which generally contributes to the spread of many infectious diseases, including virus hepatitis.

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Extreme climatic conditions of the North also contribute the frequent occurrence and chronization of inflammatory diseases of the liver. In Yakutia latency, low-symptom forms of chronic virus hepatitis are often observed. Due to the long latency of disease, carriage, chronic hepatitis is often diagnosed at later stages - liver cirrhosis, hepatocellular carcinoma of the liver⁹.

Proceeding from the above we set a goal: to explore the features of population immunity against hepatitis B (HBV) and make an analysis of the immunological effectiveness of vaccination in the territory of the Republic of Sakha (Yakutia) of the Russian Federation.

Materials and Methods

Field of study

Yakutia is located in North-East Asia within the 7603'-55029 'north latitude and 10503'-162051' east longitude. The area of Yakutia (3103.2 thousand. Km²) occupies 18% or almost 1/5 of the territory of the Russian Federation. The area of study is located in the Central part of Yakutia in Russia. West Point is located on the border with the Krasnoyarsk region (109°, 30'e. l.), East - on the border with the river Aldan (135°, 30' e. l.), South - 60° n. l., North - 64° n. l. According to the severity of the climate - this area is the cold pole of the northern hemisphere and the extremely sharp fluctuations in temperature. Long-term average January temperature in Oymyakon and Verkhoyansk are minus 49-50°C. In Oymyakon basin minimum temperatures reach minus 71°C and in Verkhoyansk minus 68°C, and in the central area to minus 66°. Summer is short, but relatively hot (in the most of the area is plus 36-38°C, on the coasts of seas plus is 29-32°C), with long sunshine (twenty-four hour polar day). The population of the republic according to Goskomstat Russia is 954,803 people. (2014). Population density - 0.31 pers. / Km² (2014). Ethnic composition: Yakut - 49.91%, Russian - 37.84%, other nationalities - 12.25% (Fig. 1).

Material of study

A survey is conducted in areas with compact living of the indigenous population of the Republic of Sakha (Yakutia) of the Russian Federation. Total 8038 people were surveyed, including: 1183 -adult, 2200 - adolescents, 3909 - school-age children ("indicative group"), 207 - recruiting young people, 539 - from risk group,

including: 205 health workers, 207 - patients Type 2 diabetes from the Republican endocrinology clinic and 127 patients were in the hospital examination in the clinic of the Research Institute of Health, North-Eastern Federal University for 5 years. Also persons vaccinated against hepatitis B: Adults - 160 school-age children - 205 were examined. Age of surveyed persons ranged from 7 to 70 years.

To compare the surveyed groups database of group of epidemiology and monitoring of chronic diffuse liver diseases from Research Institute of Health North-Eastern Federal University in 6108 the number of people were analyzed, among them children from 7 to 14 years - 2009, from 15 to 19 years - 1730 and older 20 years - 2360 people. Age of surveyed persons ranged from 7 to 83 years.

In the comparison group at the identification of markers of hepatitis B were donors, first applied in the service of a blood transfusion station c. Yakutsk (408 people).

Methods of survey: study of blood serum using enzyme immunoassay method for the detection of markers of parenteral virus hepatitis was conducted in immunology laboratory of the Research Institute of Health of North-Eastern Federal University. Laboratory diagnostics was in screening for markers of hepatitis B (HBsAg, aHBcor JgG), as well as marker postvaccination immunity against hepatitis B (HBsAg) a-HBs - qualitative and quantitative analysis in individuals vaccinated against hepatitis B;

- a) in the study applied the appropriate test system ZAO "Vector-Best";
 - b) Biochemical studies were conducted in patients with type 2 diabetes in laboratory of Yakut republican endocrinology clinic;
- Statistical methods: as a software statistical analysis of research materials software package Statistica 8.0 using the following statistical analysis methods was used: checking the normality of the distribution of quantitative traits using the Kolmogorov-Smirnov adjusted Lillieforsa and Shapiro-Wilk test; checking the equality of the population variance using Fisher's exact test; descriptive statistics; analysis of contingency tables; rank correlation analysis; nonparametric analysis of variance Mann-Whitney; test comparison

of proportions. Selected parameters listed below have the following notation: m - average, s - standard deviation, n - the volume of the analyzed subgroups. The critical value of the significance level was taken at 5%.

RESULTS

Indicators of population immunity of the indigenous population of the Republic of Sakha (Yakutia)

In the present study epidemiological studies on the prevalence of markers of parenteral hepatitis B infection and markers among vaccinated persons in Example of 4 settlements Ust-Aldan, Namsky and Gorny District is conducted.

As it is seen from fig. 2 we identified immunoglobulin G to HBsAg (antiHBcore-IgG class antibodies G to nuclear antigen) in the adult population (labor groups, indigenous and non-indigenous) in sentinel health (children aged 7-14 years and adolescents aged 15-17 years) among recruiting youth at-risk groups (health workers and dispensary patients on diabetes mellitus type 2). The proportion of infected persons among children - $15,3 \pm 8,4$; adolescents - $36,4 \pm 19,3$; recruiting young people - $45,1 \pm 9,4$; indigenous population - $39,7 \pm 7,6$; non-indigenous population - $37,9 \pm 10,1$; among labor groups - $38,8 \pm 11,0$; at risk group - $72,2 \pm 1,2$. Analysis of variance revealed statistically significant differences in proportion of infected persons among children, adolescents and adults ($F = 4,1$; $p = 0.03$). In risk group (health care professionals and patients with diabetes mellitus type 2) and among young people of recruiting age infection is significantly higher than in the control group (labor groups, indigenous people, non-indigenous population) - $F = 483,9$; $p < 0,001$. These findings have something in common with the conclusions of other researchers, where the risk of infection of medical workers in contact with human biological materials in the course of professional activity was high¹⁰.

As it is seen from fig. 3, Spearman rank correlation revealed that age-infection with hepatitis B virus (population immunity) increases ($r = 0,6$; $p = 0.02$), which is consistent with other studies. [11]. HBsAg carrier also increases with age ($r = 0,8$; $p = 0.03$).

Table 1. The immunological effectiveness of vaccination by the standard scheme vaccine "Virion" among the indigenous population (Yakuts) in Namsky region of Yakutia

Contingent	Total	HBsAg	aHcorJgG	AHBs+	aHBs-	Total	< 10 IU/l	10-100	100-500	500-1000	more 1000
Adults	124 %	8 6,5%	54 44%	89 72%	27 21,8%	116	0	31 25%	7 5,6%	0	48 38,7%
Children	62 %	1 1,6%	9 14,5%	44 71%	18 29%	44	0	18 41%	5 11,4%	0	21 47,7%

Table 2. HBV and HCV-infection in different population groups

	Diabetes mellitus (n=207)		Circulatory encephalopathy (n=88)		hi-square	P	Control group (n=9167)		hi-square	P
	abs.	%	abs.	%			abs.	%		
HBsAg	17	8,2	4	4,5	0,8	0,4	524	5,7	1,9	0,2
a-HBcor	148	71,5	42	60,9	2,2	0,1	163	15,9	276,6	<0,0001
a-HCV	10	10,8	2	2,6	3,2	0,07	92	2,3	23,6	<0,0001

Indigenous population vaccinated with a vaccine “Virion”

Among the surveyed adult population HBsAg was found in 6.5% of cases, a marker of infection aHVcorJgG - in 44% of cases, this suggests that in this locality (v. Homustah) epidemiological situation of hepatitis B is unfavorable. Of the 124 vaccinated adults surveyed by qualitative methods 89 persons have antibodies to hepatitis B hat is 72% of the total, while the absence of antibodies observed in 21.8% of the total vaccinated. After 3-7 years in the structure of the immune response of the vaccinated by the standard scheme persons with high (100-500 IU / L - 25%) and very high (more than 1000 IU / L -38.7%) protective antibody titers dominated. The geometric mean of antibody concentration in the observed group is -1783.5 + -73.5 IU / L. Perhaps the high concentration of antibodies are associated with the booster effect of the presence of immunoglobulin against hepatitis B core antigen - aHBcorJgG that is of particular interest in the study of immunology of post-vaccination immunity in the Far North (Table 1).

Among the vaccinated children of school age HBsAg detected in 1.6%, and markers of hepatitis B aHVcorJgG - in 14.5% cases. In total, after 3-8 years after completing full course of vaccination seroconversion was recorded in 71% of the 62 vaccinated children of school age, indicating the high immunogenicity of the used vaccine. It should be noted that 9,3% of the detected concentration of anti-HBs is lower the protective level (10 IU / L). At the same time, at 59.1% of children tensions of post-vaccination immunity can be regarded as high. At 52.4% of the schoolchildren anti-HBs is found in concentrations of from 101 to 1000 IU / l and more at 47.7% - 1000 IU / l. But the alarming fact is that 29% of children

antibody titer is absent after the vaccination course. It can be assumed that the children had contact with the infection or vaccination conducted not at the proper level, etc. It is important to note that none of the cases with children systemic complications of vaccination were not documented (Table 1).

Thus, among the Yakuts, vaccinated on a standard scheme of national vaccine “Virion”, after 3 - 8 years of the course of vaccination antibodies were detected in 71% of vaccinated. Protective antibody titer more 10 IU / l was detected in 25% of cases, high levels of antibody titer - more 100 IU / L were found in 44.3% of vaccinated.

Comparing hepatitis B infection among the adult population, in this case among vaccinated educators and health professionals of this settlement, the marker detection of infection with hepatitis B virus aHBcorJgG was higher than in children of school age ($\chi^2 = 40,2$; $p < 0,0001$).

Frequency of hepatitis B infection among risk groups on the example of patients with type 2 diabetes mellitus in the Yakut population

As the result of the study HBs-antigenemia (HBsAg) was detected in 8.2% of patients with diabetes The study HBs-antigenemia (HBsAg) was detected in 8.2% of patients with diabetes mellitus type 2. Most of the patients were infected with hepatitis B virus (HBV): at 71.5% an antibody to an korovskoy antigen HBV (a-HBcorIgG) were identified. Infection with hepatitis C virus (a-HCV) was detected in 10.8% of patients. At 7.5% of the patients was a mixed infection with hepatitis B and C. When comparing the frequency of hepatitis B virus in patients with diabetes mellitus and circulatory encephalopathy differences were not statistically significant (Table 2). In the control group HBs-antigenemia was slightly less (2.5%; $p = 0.2$), whereas the detection



Fig. 1. Republic of Sakha (Yakutia), Russian Federation

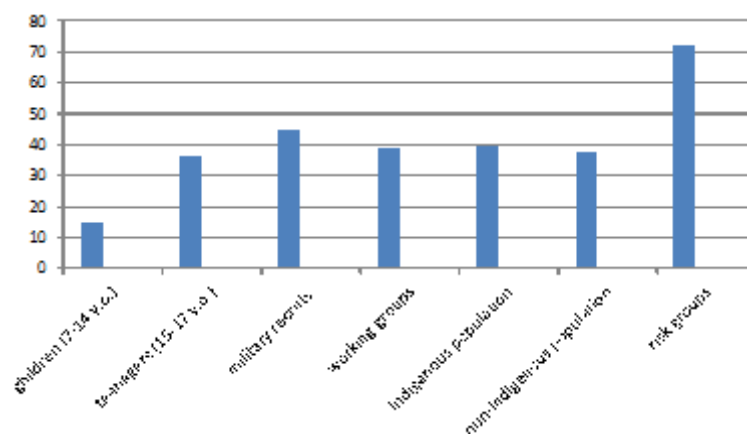


Fig. 2. The frequency of detection of a-HBcor IgG among different social groups (n = 7292)

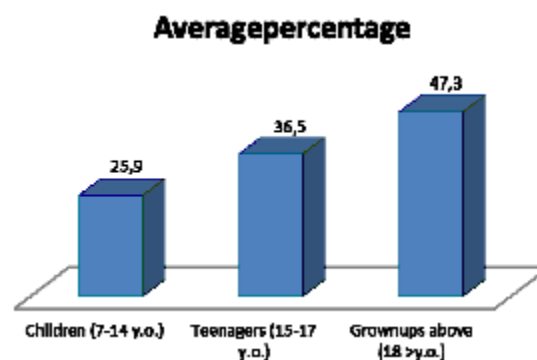


Fig. 3. Frequency of a-HBcor IgG depending on age

rate of a-HBcorJgG and a-HCV was much lower (4.5 and 4.7 fold, respectively, $p < 0.0001$).

CONCLUSIONS

1. There is new data on the prevalence and characteristics of population immunity against HBV among the indigenous population of the Republic of Sakha (Yakutia) of the Russian Federation. HBV infection in the risk group is significantly higher than in the normal population, in patients with type 2 diabetes, there is a high parenteral infection of HBV, HCV and HBV + HCV (71,5%, 10,8% and 7,5% respectively).
2. It was shown for the first time that every other 3- 8 years among children and adults of Yakut population living in the Republic of Sakha (Yakutia) (hyperendemic region on HBV), vaccinated at birth against HBV, the frequency of detection of anti - HBs in protective concentrations (> 10 IU / l and higher) is - 72.2%. Saving anti-HBs in vaccinated for 8 years indicates a high efficacy of vaccines against hepatitis B.

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