

Health ecology: factors of spread and consequences of viral hepatitis manifestation

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Abstract. The features of viral hepatitis B (HB) and C (HC) in the initial making of these diagnoses in three age groups of men and women (25-30, 31-55 years old for women and 31-60 years old for men, over 55 for women and 60 years old for men) were studied. High levels of bilirubin in the blood serum in all groups indicated damage of the functions of hepatocytes, especially in men with hepatitis B, in women with hepatitis C. The high ALT activity indicated an increase in cytolytic processes in liver hepatocytes in all groups with viral HB and HC, especially in men of the younger group, in women of the younger and middle-aged groups. The high concentration of AST indicated early stages of HC infection in all age groups, especially in the younger group of men with liver, heart, kidney and muscle damage. A positive thymol test in all groups of men and women with HB and HC indicated a shift in the protein balance along the path of pathologically enhanced synthesis of γ -globulins in hepatocytes and the removal of albumins from the body. The concentration of β -lipoproteins in the blood serum only in men of the younger group with hepatitis C corresponded to the norm, in other groups with HB or HC this parameter exceeded it by an average of 1.5 times, noting a violation of lipid metabolism in hepatocytes of the liver.

1 Introduction

The analysis of publication activity on the study of chronic viral hepatitis B (CHB) and C (CHC) shows the interest of researchers in this problem, since the receipt of new data opens up a wide prospect for expanding and deepening knowledge in the field of features of the manifestation of viral hepatitis [1, 2]. Viral hepatitis affects all age and social groups of the population. Taking into account the breadth of their spread, the level of morbidity, the severity of their course, the frequency of development of chronic forms and the economic damage they cause, they belong to one of the leading places among viral infections [3, 4]. All types of viral hepatitis are registered in Russia. They occupy one of the leading places in human infectious pathology [3, 5]. Experts attribute Russia to regions of the world with low endemicity for hepatitis E, with average-for hepatitis A, B, C, D, assessing these data to a certain extent conditionally. Since their accuracy depends on the quality of diagnostics and completeness of registration of all cases of the population infection [5]. The prevalence of viral hepatitis in Russia is estimated by the official indicators of registration of the incidence of acute hepatitis CHA, CHB and CHC in the population and by the frequency of detection of serological markers of infection [6, 7].

For each form of viral hepatitis, markers have been established – specific biological and specific compounds that cause morphofunctional changes in the human body, for which they are successfully diagnosed [8, 9, 10].

The lack of accurate official statistics on CHB and CHC in Russia does not give a complete understanding of the level of their spread due to the low level of medical activity of the population. In some territories of Russian regions there are millions of hepatitis B and C virus carriers [11, 12].

The reaction of the blood system to viral infection of the body is always aimed at eliminating damage in it and restoring the original state of homeostasis. Protective reactions of the blood system, during primary infection with hepatitis C or B viruses, are characterized by a high level of manifestation of protective reactions with simultaneous damage to vital organs and systems of the body itself – the liver, heart, and muscle apparatus [4, 6, 7]. These points actualize the study of the reactivity of the blood system to viral load in different age groups of the population, which causes hepatitis B and C.

The purpose of the work is to study the response of the blood system to viral load caused by primary infection of the adult human body with hepatitis B or C.

2 Experimental

To achieve this goal in the parameters of immunoenzyme analysis (IEA) the characteristics of the system response of blood viral load in the serum of antibodies at initial diagnosis of viral hepatitis B or C in mature persons were examined:

150 men and 150 women, three age groups (25-30 years old, 31-55 years old for women and 31-60 years old for men, over 55 for women and 60 years old for men)

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who had been confirmed primary diagnosis of "hepatitis" or "hepatitis C" in the Regional Infectious Clinical hospital named by E. Pavlovsky (Belgorod). Accordingly, 6 groups of 50 people each were formed as a result of a random sequence of their admission to the diagnostic examination, taking into account age and gender, and confirmation of the diagnosis-hepatitis B or C. These types of VH are almost always marked by tension of the blood system functions and disorders in the immune system [6, 7, 13]. Timely and correctly performed diagnostics of the response to the viral load of the white blood system based on the severity of IEA parameters, taking into account biochemical markers, allows us to assess the functional status of the subjects at the time of diagnosis confirmation – VHB or VHC [6, 7]. The reactivity of the blood system in examined subjects of all age and gender groups was assessed for the presence of hepatitis B or C pathogens [7, 11]. Thus, VHB was found by the presence of corresponding markers of hepatitis B (HBsAg, AHBcor, AHBcorM, AHBc) or hepatitis C (NS3, NS4, NS5, core). The detection of viral hepatitis antibodies was performed on the basis of detection of a complex of structural and non-structural viral peptides using solid-phase of IEA [5, 8, 12].

The nature of the course of viral infection and the degree of liver dysfunction were assessed by biochemical parameters: concentrations of aminotransferases (ALT and AST) in blood serum, bilirubin, B-lipoproteins, protein metabolism (thymol test) [10, 14]. For early diagnosis of viral hepatitis, it is important that the activity of the ALT enzyme increases in the prodromal period and against the background of viral hepatitis its concentration in the blood serum on average can increase by 8-10 times, and the AST enzyme-by no more than 2-4 times [6, 7].

The study conducted a comparative analysis of the features of the manifestation of viral hepatitis B and C in different age and sex groups of the adult population. The initial revealed average immunological and biochemical indicators are considered on the basis of their comparison with standard age-sex norms typical for men and women. All the original individual data were statistically processed using descriptive statistics of the computer software package "Statistica 10" with the determination of the values of the average (M), standard error (m) and standard deviation (σ).

3 Results and discussion

Features of manifestation in men and women infected with VHB or VHC, who have a positive result for the presence of their corresponding markers in their blood serum, are presented in table I. Among both sex groups, at each age, the markers identified individuals not only with acute exacerbation of HB, but also with signs of a slow current chronic form of infection and even recovering.

All individuals with a positive result for HC were found to have a virus replication process, some of them showed signs of current or even past infection.

This data indicated a low level of medical activity of the examined different age groups, who only with pronounced pathological manifestations of liver function disorders passed the necessary diagnosis or were accidentally detected with VH after passing a medical examination.

The results of the IEA for viral hepatitis B and C in men and women of three age groups allowed us to note that all age groups do not have a proper level of knowledge about the ways of spreading viral hepatitis and there is a lack of formed skills to be protected against them.

In each age group of women and men infected with the pathogen HB, the concentration of bilirubin in the blood exceeded the physiological norm, indicating that the degree of pathological changes in men with increasing age was higher (see table I). The analysis of the detected average values of bilirubin showed that the concentration of bilirubin exceeded their physiological norm on average from 33% to 58%, respectively, in the age range. In all age groups of women, the increased bilirubin amount was close in value, exceeding the norm by 39-45%.

Similarly, in groups of men and women with hepatitis C, the concentration of bilirubin in the blood was shown within the upper limit of the norm, and in women of all age groups, its indicator was higher, and in comparison, with the groups of men, it was shown in a wider range (table II).

In women of the middle age group, the level of total bilirubin was higher ($p < 0.05$) than in the group of 20-30 years old.

Thus, the increased level of bilirubin in the blood serum indicated a pronounced functional tension of liver cell functions in all age groups, especially in men with hepatitis B, and in women with hepatitis C, especially in the group of 20-30 years old.

A highly sensitive indicator of hepatocyte cytosis is the activity of infected enzymes-alanine aminotransferases (ALT) and aspartate aminotransferases (AST) in the blood serum, which characterize the severity of the inflammatory process in the liver. The development of a cytological process in the liver of a patient with viral hepatitis is accompanied by an increase in serum ALT activity to a greater extent and AST to a lesser extent.

In all age groups infected with hepatitis B, the indicator ALT in plasma was higher than normal in men of junior and senior age groups in 1,8 times, and women have 2.4 and 2 times respectively in the middle and older groups (table III). The highest indicator of ALT against the norm was established in men of middle-aged group – 2 times, and in women of junior group – 3 times.

Table 1. IEA results for viral Hepatitis B and C in men and women of three age groups

| Markers (the number of cases of positive reaction) | | | | | |
|---|----|--------------------------------|----|--------------------------|----|
| 25-30 years old | | 31-60 / 31-55 years old | | More than 61 / 56 | |
| M | F | M | F | M | F |
| 50 | 50 | 50 | 50 | 50 | 50 |
| HBsAg – the main marker, detected starting from 3-5 weeks of infection | | | | | |
| 11 | 10 | 8 | 12 | 10 | 14 |
| Confirming test for hepatitis B AHB – a previous infection or the presence of post-vaccination immunity | | | | | |
| 38 | 41 | 48 | 45 | 42 | 47 |
| Markers of hepatitis B: a sign of ongoing replication of the virus, a sign of current and past infection | | | | | |
| 50 | 50 | 50 | 50 | 50 | 50 |
| AHBcIgM- active replication and acute infection found 1-2 weeks after HBsAg detection | | | | | |
| 13 | 11 | 17 | 12 | 8 | 6 |
| AHBcIgM sum-chronic infection | | | | | |
| 44 | 35 | 42 | 48 | 48 | 45 |
| AHBeIgM- acute period of infection | | | | | |
| 50 | 50 | 50 | 50 | 50 | 50 |
| HBeAg- high blood infection, an indicator of active replication of hepatitis B | | | | | |
| 50 | 50 | 50 | 50 | 50 | 50 |
| Anti-VHC- the main marker of infection | | | | | |
| 42 | 34 | 37 | 43 | 41 | 36 |
| A-HCV- spectrum - sign of ongoing virus replication, sign of current and past infection | | | | | |
| 126 | 32 | 25 | 40 | 19 | 25 |
| A-HCVcIgM- chronic hepatitis C (reactivation phase) | | | | | |

Table 2. The concentration of bilirubin in Blood Serum in men and women with Hepatitis B

| Age male/female | Total bilirubin, $\mu\text{mol/l}$ $M \pm m$ (min-max) | |
|--------------------|---|-------------------------------|
| | Men | Women |
| Hepatitis B | | |
| 20-30 | 24,8 \pm 2,14 10,2-70,4 | 25,9,0 \pm 2,66 8,1-74,7 |
| 31-60 / 31-55 | 27,1 \pm 2,52 9,0-78,6 | 25,8 \pm 2,32 9,7-73,8 |
| More than 61 / 56 | 28,5 \pm 2,62 11,2-75,6 | 26,0,1 \pm 4,03 9,4-77,8 |
| Hepatitis C | | |
| 20-30 | 22,8 \pm 3,75 10,4-68,8 | 28,8 \pm 2,90 9,0-84,1 |
| 31-60 / 31-55 | 21,8 \pm 2,40 9,2-72,0 | 21,0 \pm 1,62* 8,7-70,8 |
| More than 61 / 56 | 19,7 \pm 2,02 9,1-82,8 | 23,3 \pm 2,33 9,1-76,6 |

* Note: the normal level of bilirubin in the blood serum is 7-17.2 mmol / l. * - $p < 0.05$.

Table 3. The Concentration of ALT in Blood Serum in men and women infected with Hepatitis B

| Age male/female | ALT, Un/l ($M \pm m$, min-max) | |
|--------------------|-------------------------------------|-----------------------------|
| | Men | Women |
| Hepatitis B | | |
| 20-30 | 80,4 \pm 9,54 19-192 | 110,5 \pm 10,46 25-288 |
| 31-60 / 31-55 | 92,3 \pm 8,23 20-288 | 76,1 \pm 9,10 18-195 |
| More than 61 / 56 | 79,4 \pm 9,62 22-184 | 68,0 \pm 10,2 16-202 |
| Hepatitis C | | |
| 20-30 | 85,0 \pm 9,64 28-330 | 89,6 \pm 9,10 13-268 |
| 31-60 / 31-55 | 108,8 \pm 8,91 29-346 | 96,8 \pm 6,44 14-188 |
| More than 61 / 56 | 90,0 \pm 7,84 21-152 | 95,2 \pm 8,86 17-210 |

* Note: the normal ALT level is equal in men – up to 45 Un/l, in women – up to 34 Un/l.

The enhanced cytological process in the liver was characteristic of all groups of patients with hepatitis C, especially men of the middle and older groups and women of all age groups. These changes were close in value and on average exceeded the norm by 2.4-2.6 times, indicating that they had negative changes in internal organs, including the kidneys, liver, heart and skeletal muscles (see table III). ALT output from the liver had a negative effect on these organs of the body in men and women. The activity of this enzyme in all groups infected with hepatitis B exceeded the norm, especially in women of the younger and middle age groups it exceeded on average 2.5 times, and in men of the younger group - 2 times. It is known that when a person is infected with viral hepatitis, ALT concentration in serum is significantly higher than AST concentration by almost 2-2.5 times. On average, the normal concentration of AST in women reaches 31 Un/l, in men it is higher – up to 37 Un/l.

In men and women infected with hepatitis B, the concentration of the AST enzyme in the blood serum was increased against the norm (table IV).

Higher concentration of the AST enzyme was in women of the younger and middle-aged groups - almost 2 times higher than their values in the older group. The values of AST concentration in men of the older and middle groups were lower by 25% and 29% against women of the same age.

In men and women with hepatitis C, the values of AST concentration in the blood serum exceeded the norm, but in men of all groups, compared with women's groups, they were the most significant. Concentration of AST in men of the younger group exceeded the norm by almost 3 times, and in older groups by 2.6 and 2.2 times, indicating early stages of VHC infection, usually occurring without pronounced clinical symptoms.

The most pronounced individual values of serum AST concentrations were observed in men and women infected

with hepatitis C in all age groups. They pointed to the manifestation of pronounced negative shifts in functions not only in the liver, but also in other vital organs.

The concentration of β -lipoproteins in the blood serum in all groups of men and women infected with VHB was reduced against the norm (table V).

Table 4. Serum AST concentration in men and women infected with Hepatitis B

| Age male/female | AST, Un/l (M \pm m, min-max) | |
|--------------------|--------------------------------|----------------------------|
| | Men | Women |
| Hepatitis B | | |
| 20-30 | 78,2 \pm 8,84 25-202 | 97,8 \pm 9,02 17-278 |
| 31-60 / 31-55 | 70,8 \pm 9,21 17-198 | 90,6 \pm 10,36 23-198 |
| More than 61 / 56 | 53,8 \pm 7,24 16-172 | 51,2 \pm 9,32 18-192 |
| Hepatitis C | | |
| 20-30 | 117,6 \pm 10,42 23-356 | 76,0 \pm 8,31 22-152 |
| 31-60 / 31-55 | 97,4 \pm 7,42 16-358 | 80,7 \pm 4,66 22-189 |
| More than 61 / 56 | 80,4 \pm 6,20 20-148 | 74,1 \pm 6,22 23-220 |

* Note: the normal concentration of AST in the blood serum in men is up to 37 U/l, in women up to 31 U/l

The concentration of β -lipoproteins in the blood serum corresponded to the norm, in other groups of men and women it was reduced against the norm by an average of 1.5 times, indicating a violation of lipid metabolism only in the younger group of men infected with HCV due to the disorders of liver hepatocyte functions.

Table 5. Serum concentration of B-Lipoproteins in men and women Infected with Hepatitis B

| Age male/female | β -lipoproteins, % (M \pm m, min-max) | |
|--------------------|--|--------------------------|
| | Men | Women |
| Hepatitis B | | |
| 20-30 | 48,0 \pm 2,80 22-74 | 45,0 \pm 3,77 26-59 |
| 31-60 / 31-55 | 40,8 \pm 2,22 27-60 | 47,2 \pm 3,13 27-94 |
| More than 61 / 56 | 50,1 \pm 4,59 28-100 | 43,8 \pm 3,38 33-58 |
| Hepatitis C | | |
| 20-30 | 64,0 \pm 11,4 23-238 | 49,2 \pm 3,57 31-69 |
| 31-60 / 31-55 | 43,0 \pm 3,12 22-81 | 48,1 \pm 2,66 23-71 |
| More than 61 / 56 | 52,0 \pm 3,04 29-59 | 47,6 \pm 4,22 25-94 |

* Note: normal blood serum lipoproteins are 65-75%

Conducting a thymol test (MacLagan test) is aimed at earlier detection of infection with viral hepatitis B and C. The negative value of the intake corresponds to its norm and is 0-4 units. M. value of the intake is higher than 4 units. It is regarded as a positive test that indicates a violation of the protein composition in the blood serum, in particular associated with viral hepatitis.

According to the average values, a positive thymol test was detected in all age groups of men and women with

hepatitis B, but in the middle-aged groups its values were higher and indicated violations of protein metabolism in the body due to pathological changes under the influence of viral load in liver hepatocytes (table VI).

According to the average values a positive thymol test was found in all age groups of men and women with hepatitis C and its values were most pronounced in the middle-aged group of men and women; they were slightly higher in value in all age groups of men with hepatitis B. In all groups of women with hepatitis C the values of the thymol test were more significant, indicating a marked violation of protein metabolism associated with VH.

Table 6. Indicators of thymol test in blood serum in men and women with hepatitis B or C

| Age male/female | Thymol test, un. (M \pm m, min-max) | |
|--------------------|--|----------------------------|
| | Men | Women |
| Hepatitis B | | |
| 20-30 | 4,6 \pm 0,46 1,2-14 | 4,2 \pm 0,29 1,8-7,0 |
| 31-60 / 31-55 | 6,6 \pm 0,62 1,3-19 | 5,1 \pm 0,30 2,1-12,4 |
| More than 61 / 56 | 4,5 \pm 0,41 2,1-11 | 4,4 \pm 0,30 2,6-7,1 |
| Hepatitis C | | |
| 20-30 | 4,4 \pm 0,39 2,1-16,8 | 5,2 \pm 0,52 1,7-12,2 |
| 31-60 / 31-55 | 4,2 \pm 0,37 1,3-17,2 | 5,1 \pm 0,54 1,5-19,8 |
| More than 61 / 56 | 4,0 \pm 0,22 1,6-4,8 | 4,6 \pm 0,38 2,0-14,1 |

Taking into account that the liver plays a leading role in protein metabolism in the body, pathological changes in hepatocytes when infected with hepatitis provides the removal of a large number of albumins from the body and an increase in serum γ -globulins. The positive value of the test persists for a long time after the recovering from hepatitis – from 6 months to a year, so it allows to evaluate the process of restoring the functional state of the liver.

4 Conclusion

High serum levels of bilirubin in all groups of men and women with viral hepatitis caused damage to the functions of hepatocytes, especially in men with hepatitis B and women with hepatitis C. High concentration and activity of ALT aminotransferase in blood serum indicated enhanced cytological processes in liver hepatocytes in all groups of men and women with viral VHB and HC, especially pronounced in men of the younger group, women of the younger and middle-aged groups. The concentration of AST aminotransferases exceeded the norm in all groups of men and women and was the most pronounced in infected with HC, indicating that their functions of the liver, the heart, kidneys, and muscles were damaged. In men of the younger group with HC, the concentration of aminotransferases exceeded the norm by almost 3 times, and in older men by 2.6 and 2.2 times, corresponding to earlier stages of infection of the body.

A positive thymol test showed a shift in the protein balance in all age groups of men and women with viral hepatitis towards a pathological increase in the synthesis of γ -globulins in liver hepatocytes and the removal of albumins from the body.

The concentration of β -lipoproteins in the blood serum only in the younger group of men infected with hepatitis C corresponded to the norm, in the other groups infected with VHB or HC hepatitis, it on average exceeded the norm by 1.5 times, indicating a violation of lipid metabolism in liver hepatocytes.

References

1. V.A. Isakov, V.V. Pokrovsky, "Russia is on the verge of a hepatitis B epidemic," Problems and prospects of the global fight against the virus, Pediatrician's Practice, (2006)
2. I.V. Mayev, T.E. Polunina, E.V. Polunina, Clinical medicine, **11**, pp. 12-18 (2009)
3. V.G. Akimkin, S.V. Skvortsov, A.A. Enaleeva [et al.], World of viral hepatitis, **7-8**, pp. 5-6 (2000)
4. S.Yu. Karpov, P.E. Krel, Clinical Medicine, **31**, pp. 14-19 (2005)
5. Z.G. Aprosina, Chronic viral hepatitis. Moscow: Meditsina, (2002)
6. M. Amjad, V. Mudgal, M. Faisal, Laboratory medicine, **44**, pp. 292-299 (2013)
7. N.D. Yushchuk, E.A. Klimova, O.O. Znoiko [et al.], Russian journal of gastroenterology, Hepatology and Coloproctology, pp. 23-26 (2010)
8. A.N. Burkov, T.V. Blinova, A.N. Mayansky, G.M. Lapshina, Viral hepatitis and their diagnostics in immunoassay systems: Methodological recommendations, N. Novgorod, (1998)
9. N.V. Dunaeva, E.V. Esaulenko, Questions of Virology, **51**, 10-14 (2006)
10. V.K. Pimenov., A.Yu. Afanasiev., A.A. Kolobov [et al.], Questions of Virology, **6**, 44-47 (2000)
11. A.Yu. Afanasiev, V.K. Pimenov, S.V. Zubov [et al.], Phase of hepatitis C flow according to the data of dynamic control of the spectrum of antibodies to the hepatitis C virus. Hepatitis B, C, D and G-problems of studying diagnosis, treatment and prevention. Moscow, (1997)
12. A.V. Ivanov, A.O. Kochetkov, Advances in biological chemistry, **45**, 37-86 (2005)
13. E.L.Krasavtsev, S.V. Zhavoronok, V.M. Mitsura, A.P. Demchilo, Microbiology, **2**, pp. 57-61 (2006)
14. A.F. Bluger, Structure and function of the liver in epidemic hepatitis. SYNTETG, (2017)