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Clinical-epidemiological and pathogenetic features of viral hepatitis C in the hemodialysis departments

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Background. *Today, the programmed hemodialysis belongs to the clinical medicine area where patients are at a constant risk of viral hepatitis infection. This is associated with surgical interventions on the vessels, fairly frequent transfusions of blood components, and regular hemodialysis*

procedures. But in recent years, the ratio of reported cases of viral hepatitis B and C in patients on programmed hemodialysis has changed significantly. With an abrupt increase in the incidence of viral hepatitis C, there is a decrease in the number of registered viral hepatitis B cases.

The aim. *To study the clinical, epidemiological and pathogenetic features of viral hepatitis C in hemodialysis units.*

Material and methods. *A multicenter study was conducted that enrolled the patients from the Programmed Hemodialysis Units in Tashkent and the regional departments of the Republic of Uzbekistan. The study involved 395 patients on programmed hemodialysis for 7.5 ± 0.7 years. The age of patients was 43.5 ± 0.91 years. The diagnosis of chronic viral hepatitis C was made on the basis of medical history, clinical and laboratory data, and detection of anti-HCV IgG and RNA-HCV in blood.*

Results. *When analyzing the clinical examination and laboratory test results of 395 patients, the parenterally transmitted viral infection markers were detected in 181 patients (45.8%). The analysis of the overall incidence of viral hepatitis showed that chronic viral hepatitis C had the highest rates and was found in 125 patients (31.6%). The analysis of the chronic viral hepatitis C course in the presence of the end-stage chronic renal disease showed that in 11 (34%) of 32 patients of the Main group the disease proceeded as a fulminant form of chronic renal-hepatic failure with the development of adverse outcomes. Twenty seven patients (84%) in this group developed progressive anemia. In 16 patients (50%), persistent polyserositis developed in the form of hydrothorax, ascites, and pericarditis, which reflected the aggravating effect of chronic viral hepatitis C on the course of chronic renal disease.*

Conclusions. *In Hemodialysis Units, both in the city of Tashkent, and in the regional departments of the Republic of Uzbekistan, the incidence of chronic viral hepatitis C prevails, having the form of a pathological process with a minimally low activity. Chronic viral hepatitis C has an aggravating effect on the course of the underlying disease with the development of adverse outcomes.*

Keywords: chronic viral hepatitis C, program hemodialysis, viral hepatitis, end-stage chronic renal disease

CRF, chronic renal failure

CVH *B*, chronic viral hepatitis *B*

CVH *C*, chronic viral hepatitis *C*

CVH D, chronic viral hepatitis Delta

ESRD, end-stage chronic renal disease

HIV infection, infection caused by the human immunodeficiency virus

The scientific advances of recent decades have helped to significantly expand the understanding of the chronic hepatitis *C* pathogenesis and its outcomes, which made it possible to develop effective methods to diagnose the disease, determine the main therapeutic trends in the treatment and significantly improve the prognosis [1]. In recent years, the ratio of the recorded cases of viral hepatitis *B* and *C* has changed significantly.

Today, the programmed hemodialysis belongs to the field of clinical medicine where patients are at a certain risk of being infected with viral hepatitis. This is associated with surgical interventions on the vessels, rather frequent transfusions of blood components, and regular hemodialysis procedures. Due to an extensive use of vaccination against hepatitis *B* in high-risk groups, including in hemodialysis units, the ratio of reported cases

of viral hepatitis *B* and *C* in patients on hemodialysis has significantly changed. With the dramatic increase in the incidence of hepatitis *C*, there has been noted a decrease of registered hepatitis *B* cases. [2-5]. A severe nature of the pathology in patients with chronic renal failure (CERF) with the aggravating impact of undercurrent infections on the course of the underlying disease with worsening the prognoses of treatment underlines the urgency of this problem.

The general transmission route for viral hepatitis *B* and *C* leads to the formation of associated forms of the disease in patients with end-stage chronic renal failure (ESRD). Meantime, the number of studies conducted to investigate the problem has clearly been insufficient, and their data are very contradictory [6–9].

The purpose of the study was to investigate the clinical, epidemiological, and pathogenetic characteristics of viral hepatitis *C* in hemodialysis units.

Material and methods

A multicenter study included the patients of hemodialysis units in Tashkent and Regional Departments of the Republic of Uzbekistan; 395 patients who had been on programmed hemodialysis for 7.5 ± 0.7 years were examined. The age of the patients was 43.5 ± 0.91 years; there were 132 (33%) women, and 263 (67 %) men. The development of ESRD was formed as a result of chronic glomerulonephritis in 244 patients (61.7%), and chronic pyelonephritis in 64 (16.2%) patients. The diagnosed conditions were as follows: polycystic kidney disease in 18 (4.6%) cases, urolithiasis in 4 (1%), nephrosclerosis in the presence of diabetes mellitus in 60 (15.2%),

systemic red lupus in 3 (0.79%); and there was the diagnosis of gout in 2 cases (0.51%).

Clinical characteristics of the chronic viral hepatitis *C* (CVH *C*) course against the underlying ESRD (the main group) were studied in 32 patients in the Specialized Hemodialysis Unit at the Research Institute of Epidemiology, Microbiology, and Infectious Diseases of the Republic of Uzbekistan. Control group I consisted of 36 patients with chronic viral hepatitis *C* without a concomitant disease, and control group II consisted of 30 ESRD patients without CVH *C.* The groups were comparable by age and gender. The patients of the main group and control group I were comparable in CVH *C* disease duration. All patients underwent clinical and laboratory examinations, including the liver and kidney ultrasonography.

The diagnosis of CVH *C* was made on the basis of patient's medical history, clinical and laboratory data, and the detection of anti-HCV IgG in blood (by ELISA). The viral load and the virus *C* genotype were determined by the real-time polymerase chain reaction, Rotor Gene (Corbet Research, Australia) using the RIBO-sorb AmpliSens® kits (Russia). To exclude getting mixed infection, all patients underwent testing of blood serum for HBs Ag, anti-HDV, and the human immunodeficiency virus infection (HIV infection), using enzyme-linked immunosorbent assay. Based on the recommendations of Order No. 542 of August 27, 2018, issued by the Healthcare Ministry of the Republic of Uzbekistan, the pathological process activity was graded by the severity of the cytolytic syndrome according to the levels of alanine aminotransferase and aspartate aminotransferase in blood: minimal - 1.5–2 higher than normal, low - 2-3 times higher than normal, and moderate - from 3 to 5 higher than normal; severe - above 5 norms.

To identify significant differences between the mean values of different data cumulative parameters of initially compared patient groups, the Student's test was used. Graphics was made using Excel and Windows software packages.

Results

The examination of 395 patients revealed the presence of parenterally transmitted viral infections in 181 patients (46 %). A total incidence of monoinfections was detected in 153 (85%) patients, and the mixed-associated forms of hepatitis were found in 28 patients (15%). Thus, the revealed mixed-associated forms of hepatitis were as follows: chronic viral hepatitis *B* (CVH *B*) + CVH *C* in 16 (4%) patients, CVH *B* + chronic viral hepatitis Delta (CVH D) in 8 (2%), and CVH *C* + HIV in 4 (1%) patients. Among the patients with monoinfections, CVH *B* was seen in 23 (6%), CVH *C* was found in 125 (32%), and HIV infection was observed in 5 patients (1%) (Fig. 1).

The analyzed overall morbidity with viral hepatites showed that the highest incidence was determined in CVH C that was identified in 125 patients (32%). The patient distribution with regard to virus C genotypes was as follows: there were 70 (56%) patients with the 1st genotype, 24 (19%) with the 2nd genotype, and 31 patients (25 %) with the 3rd genotype. Thus, in the majority of patients (55%), the disease was caused by the 1st genotype virus.

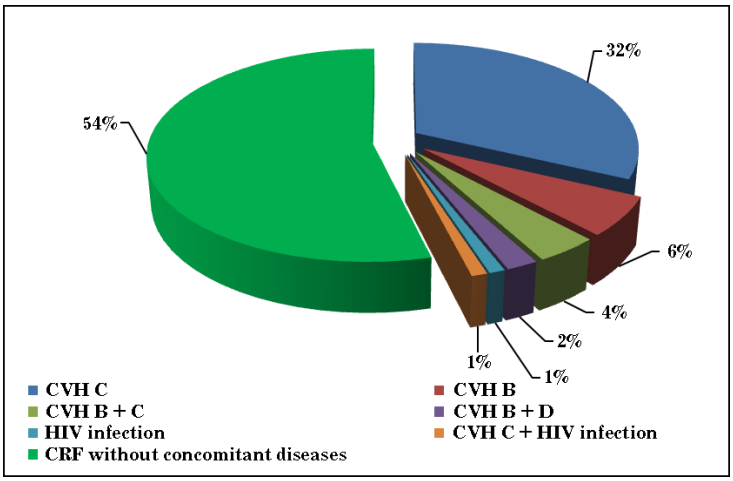

Fig. 1. The prevalence of viral hepatitis in hemodialysis units

The data of the patients' clinical and laboratory examination aimed at assessing the activity of the pathological process are presented in Fig. 2. It was established that CVH *C* and CVH *B* monoinfections occured predominantly with minimally low activity in 87% and 95% of patients, respectively. The mixed infections of CVH *B* + CVH *C* in 69% of patients, CVH *B* + CHAD in 63% of patients, and CVH *C* + HIV in 18% of patients proceeded with moderate activity of the pathological process. It should be noted that in no case of viral hepatitis a marked activity of the pathological process was seen, which was possibly a specific feature of the course of CVH *B*, CVH *C*, and CVH D in the presence of ESRD in the patients on program hemodialysis.

Fig. 2. The distribution of patients with viral hepatitis by the activity of the pathological process in the liver

Next, we studied the clinical course of CVH *C* in ESRD patients (Table 1); they were found to have more frequent intoxication symptoms, such as persistent weakness, nausea, and lack of appetite, compared to the

ESRD patients without CVH *C*, the difference was statistically significant ($p < 0.05$). We also revealed a significantly ($p < 0.05$) higher incidence of anemia and polyserositis in the form of ascites, pericarditis, hydrothorax in this group of patients. The transient edematous syndrome was characteristic of the ESRD patients without CVH *C;* it was well corrected after adequately performed dialysis, while 8 (25%) ESRD patients with CVH *C* demonstrated persistent edema uncorrectable by dialysis, which was obviously associated with an impaired protein-synthetic liver function in this group of patients.

In the main group, 22 patients (69%) showed the liver enlargement, and 8 (25%) patients had the spleen enlargements, which were also comparable to the parameters of control groups I and II. Meanwhile, in the ESRD patients with CVH *C*, skin itching occurred significantly more often ($p < 0.05$) with the normal levels of bilirubin and its fractions. With a statistically significant higher incidence of anemia ($p<0.05$), 27 patients (84%) of the main group, compared to the patients of control groups I and II, showed a decrease in dialysis tolerance in the form of hypertensive crises and cardiovascular failure.

Table 1. The frequency of clinical symptoms in patients with chronic viral hepatitis C against the end-stage chronic renal disease

Clinical symptoms	**Control group I CVH *C* n = 36**	**Main group ESRD with CVH *C* n = 32**	**Control group II ESRD without CVH *C* n = 30**
Weakness, occasional	30 (83%)	4 (13%) *	9 (30%) **
Weakness, continuous	6 (17%)	28 (88%) *	21 (70%) **
Nausea	2 (5.5%)	14 (44%) *	6 (20%) **
Lack of appetite	2 (5.5%)	23 (72%) *	6 (20%) **

Liver enlargement	2 (5.5%)	22 (69%) *	4 (13%) **
Spleen enlargement	0	8 (25%) *	0 **
Ascites	0	8 (25%) *	0 **
Hemorrhagic syndrome	0	13 (40%) *	2 (6.7%) *
Arterial hypertension	0	18 (56%) *	19 (63%)
Cardiovascular failure	4 (11%)	13 (40%)	6 (20%) *
Hydrothorax	0	4 (12.5%) *	0 **
Anemia	3 (8%)	27 (84%) *	22 (73%)
Pericarditis	0	8 (25%) *	2 (6.7%) **
Polyserosites	0	4 (13%) *	2 (6.7%) **
Polyneuropathy	3 (8%)	21 (66%) *	14 (46.7%)
Itchy skin	3 (8%)	21 (66%) *	9 (30%)

Note: * Statistically significant differences in patient values between the Main and Control I groups
** Statistically significant differences in patient values between the Main and Control II groups

The analyzed CVH *C* course in ESRD (Fig. 3) showed that in 11 (34%) ESRD patients of the main group, the disease proceeded as a fulminant form of chronic renal-hepatic failure with the development of adverse outcomes. Twenty seven (84%) patients of this group developed progressive anemia; 16 patients (50%) developed persistent polyserosites in the form of hydrothorax, ascites, and pericarditis, which reflected an aggravating impact of CVH *C* on the ESRD course.

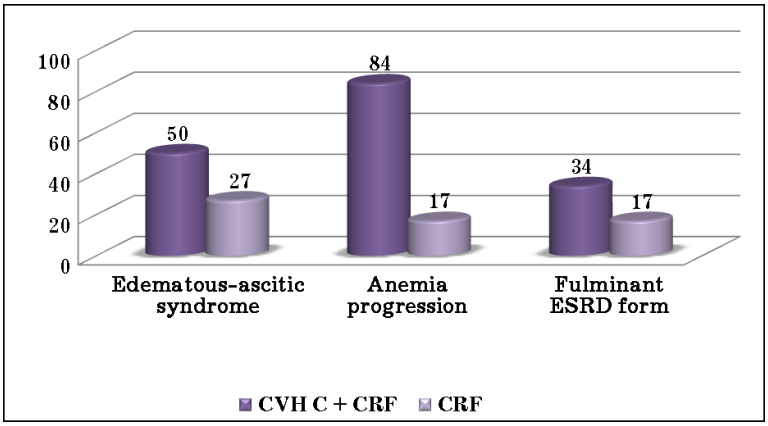

Fig. 3. Specific features in the course of chronic viral hepatitis C against the end-sage chronic renal disease

Discussion

In the ESRD patients treated with program hemodialysis, CVH *C* was found to occur with the highest incidence compared to other parenterally transmitted viral infections, and proceed mainly with a minimally low activity of the pathological process. Some authors [6, 7] have explained the low-symptom course of CVH *C* in ESRD patients with the fact that these patients are systematically treated with hemodialysis, which results in a regular removal of viruses and their metabolic products from the bloodstream and, consequently, the level of viremia decreases. On the other hand, the patients of hemodialysis units have a low level of immune defense [8–10], which, in our opinion, might be the cause of a sluggish of chronic hepatitis, since viral hepatitis *B, C,* and Delta are immune-mediated viral infections and the severity and intensity of their clinical course correlate with the degree of a host immune response.

The above dictates the need for a regular examination for the detection of viral hepatitis in ESRD patients in order to conduct a timely antiviral therapy and reduce the incidence of viral hepatitis in hemodialysis units.

Conclusions

1. In the patients with the end-stage chronic renal disease who are being treated in hemodialysis Units both in Tashkent and in the Regional Departments of the Republic of Uzbekistan, the chronic viral hepatitis C prevails in the incidence among parenterally transmitted viral hepatitis.

2. Chronic viral hepatitis *C* against the underlying end-stage renal disease proceeds mainly with minimally low activity of the pathological process.

3. Chronic viral hepatitis *C* has an aggravating impact on the course of the underlying disease with the development of adverse outcomes.

4. The results of this study provide the reasons for the implementation of mandatory testing of ESRD patients for the markers of chronic hepatitis and the administration of a timely antiviral therapy.

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