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# DIAGNOSIS OF LIVER FIBROSIS IN CHRONIC VIRAL HEPATITIS C IN HIV-INFECTED CHILDREN

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**Abstract: General Background:** Chronic viral hepatitis (CH) poses a significant challenge in contemporary healthcare, leading to severe liver diseases such as cirrhosis and hepatocellular carcinoma. **Specific Background:** Among the known hepatotropic viruses, hepatitis B, C, D, and G are implicated in chronic liver conditions, with hepatitis C virus (HCV) being particularly concerning in co-infected populations, such as children with HIV. **Knowledge Gap:** While the progression of liver fibrosis in CH is well-documented, the interplay of risk factors affecting fibrosis progression in HIV-infected children remains underexplored. **Aims:** This study aims to assess the risk factors influencing liver fibrosis in children diagnosed with chronic hepatitis C and co-infected with HIV, emphasizing the need for timely diagnosis and management. **Results:** Preliminary findings indicate that HIV co-infection significantly exacerbates the progression of liver fibrosis in children with chronic hepatitis C, highlighting age, immune status, and viral load as critical factors. **Novelty:** This research provides novel insights into the unique clinical presentation of liver disease in pediatric HIV-positive populations, which is often overlooked in current literature. **Implications:** The implications of this study are profound, suggesting that healthcare providers must prioritize regular screening for liver fibrosis in this vulnerable demographic to improve clinical outcomes and inform therapeutic strategies. Addressing this issue could lead to enhanced management protocols for co-infected children, ultimately reducing morbidity associated with chronic liver disease.

**Keywords**: Chronic Viral Hepatitis, Fibrosis, Liver Cirrhosis



## Introduction

### Relevance of the topic

Liver damage in children with HIV infection remains a pressing issue due to its frequency of occurrence and diverse etiology of diseases [1-3]. HIV is considered to be the cause of many hepatobiliary disorders; hepatotropic effects can be exerted by chronic viral hepatitis B and C, opportunistic infections, in addition, there is a direct effect of the human immunodeficiency virus and the hepatotoxic effect of antiretroviral therapy (ART) drugs [4]. Despite significant advances in diagnostics, prevention and treatment, HIV infection and parenteral viral hepatitis are socially significant diseases that affect, among other things, the demographic situation in the country [1-3]. The relevance is determined by the widespread prevalence of these infections, the diversity of clinical forms, the significant frequency of adverse outcomes, as well as the commonality of epidemiological, social and economic factors [4-6].

Viral hepatitis C is a global health problem, with 71 million people worldwide having CHC, more than one million new cases and 1.34 million deaths from this infection registered annually [7-9]. This is more than the mortality associated with the human immunodeficiency virus (HIV/AIDS), which is 1 million people [11-13]. CHC is becoming a serious cause of morbidity and mortality among

people living with HIV [25]. This also applies to pediatric patients, given the perinatal route of transmission of pathogens. Mothers coinfected with the hepatitis C virus and HIV are the main source of HIV/HCV in infancy and childhood [14]. In the case of HIV coinfection with the hepatitis C virus (HCV) in the mother, the frequency of perinatal transmission of HCV increases from 6 to 20%, as a result, the child can be infected with two viruses simultaneously [15-19]. Most children with HCV in Russia are infected vertically from infected mothers [20-23].

However, in HIV infection, there is a phenomenon of aggressive liver fibrogenesis, therefore, the study of fibrotic processes in the liver and the rate of their progression in children is relevant, and the possibilities of their scientific and practical implementation are of undoubted interest.

**The aim of the study:** to develop an algorithm for timely diagnosis and prediction of the development of liver fibrosis in chronic viral hepatitis C in HIV-infected children based on the study of clinical diagnostic markers and serum predictors.

## Methods

Laboratory research methods. Among the examined patients, the main method for detecting HIV infection (in children over 18 months) was testing using enzyme-linked immunosorbent assay (ELISA) or immunochemiluminescent assay (ICLA). HIV testing by ELISA in AIDS is carried out on the ELISYS automatic enzyme-linked immunosorbent assay analyzer, model ELISYS QUATRO ( Human GmbH , Germany) (photometric method), as well as on the photometer for microplates " Mark " version " iMark " (" BioRad Laboratories , Inc. , USA) (photometric method). HIV testing by the IHLA method is performed on a modular immunochemical analyzer for in vitro diagnostics «ARCHITECT i2000 sr mobdule » (« Abbott », USA) (chemiluminescence method). To confirm a positive ELISA (ILA) result, the immune blotting (IB) method is used. This method allows to detect antibodies to HIV-1 or HIV-2 in the studied blood serum (plasma) sample due to interaction with HIV 1 antigens (env1: gp160, 120, 41; pol : p 31, 51; gag : p 24,17), or HIV 2 ( env 2: gp 36, 105), applied to the test strip , and thus confirm the seropositivity of the sample or identify possible non-specific reactions. The IB method is based on the indirect enzyme immunoassay method, which allows to determine the spectrum of antibodies to HIV proteins. All children underwent clinical blood analysis, the level of erythrocytes, leukocytes, platelets, hemoglobin, hematocrit, differentiation of leukocytes into populations and a number of other indicators were determined. During the study, the following biochemical blood parameters were determined: ALT, AST, total bilirubin and its fractions, gamma-glutamyl transpeptidase , alkaline phosphatase, total cholesterol, glucose, urea, creatinine , total protein, albumin.

## Results and Discussion

Statistical analysis was performed using the IBM SPSS Statistics 26 version (USA) software package. The Shapiro-Wilk test was used to check whether the distribution of a feature complied with the normal law . In the case of describing quantitative indicators that had a normal distribution, the arithmetic mean values (M) and standard deviations (SD) were calculated. Sets of quantitative indicators whose distribution differed from normal were described using the median values ( Me ), the first and third quartiles (Q1; Q3). Nominal data were described with absolute values and percentages. Differences between the assessed groups were considered statistically significant at $p < 0.05$.

To compare quantitative indicators in two independent study groups, the Student's t-test was used (in the case of the distribution of features corresponding to the normal law) and the Mann-

Whitney test (otherwise). Comparison of three groups by a quantitative indicator, the distribution of which differed from the normal one, was performed using the Kruskal-Wallis test . The medians of the groups were compared using the median test for independent samples ( Median Test ).

## Conclusion

In the structure of liver lesions in HIV-infected children of the Bukhara region, CHC was predominant (64.6%). Less common were CMV hepatitis (12.3%) and hepatotoxic effects of ART (23.1%), which were characterized by the absence of signs of fibrosis in the liver tissue.

The epidemiological features of HIV/HCV coinfection in children were the perinatal route of infection - 90.5%, the prevalence of genotype 1 of the hepatitis C virus - 57.1%. Clinical and laboratory features of CHC were characterized by the presence of asthenovegetative syndrome (85.7%), hepato- (28.6%) and splenomegaly (57.4%), and wave-like hyperenzymemia . Every fifth coinfected child had a high level of HCV RNA. Among the concomitant diseases, half of the patients had lesions of the nervous system, and a quarter had cognitive and intellectual-mnestic disorders.

According to indirect liver elastometry, 32% of children with HIV/HCV had fibrosis of varying severity, among them, patients with fibrosis stage F1 according to the METAVIR scale prevailed. It was revealed that the most significant predictors of liver fibrosis were IL-4 and IL-6. An increase in IL-4 relative to the norm was established in patients with HCV monoinfection and with HIV/HCV coinfection . Correlation analysis revealed a moderate relationship between IL-6 and the HCV RNA level r=0.506 ( p= 0.006), as well as with the APRI fibrosis index r=0.42 ( p= 0.0260). TNF-alpha does not affect the formation of liver fibrosis in coinfected children, in contrast to the data obtained in adults. When constructing multivariate regression models of disease progression, the following risk factors were identified: low adherence to therapy; persistence of HIV replication after 24 weeks of ART; high HCV RNA levels; ALT and AST>2 norms and undulating hyperenzymemia ; 126 increase in indices: APRI > 0.5 and FIB-4 > 1.45; presence of hepato- and splenomegaly ; concomitant gastrointestinal diseases. Prediction of liver fibrosis development is based on index calculation: with a value ≤ -13 points, a low risk of fibrosis development is noted, with an index ≥ +13 points - a high risk (diagnostic accuracy of the Ac method = 89.5%).

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