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Diagnosis and Prediction of Liver Fibrosis in Chronic Viral Hepatitis C in Hiv-Infected

Khadieva Dora Isakovna
Bukhara State Medical Institute named after Abu Ali ibn Sino, Uzbekistan, Bukhara, st. A. Navoi

Abstract: Liver lesions in children with HIV infection remain a pressing problem due to the frequency of their occurrence and the diverse etiology of the diseases. HIV is considered 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.

Keywords: HIV, infection, viral hepatitis, treatment, liver, fibrosis.

Relevance of the topic

HIV is considered 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.

Despite significant advances in diagnosis, prevention and treatment, HIV infection and parenteral viral hepatitis are socially significant diseases that influence, among other things, the demographic situation in the country [1-3]. The relevance is determined by the wide distribution of these infections, the variety 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; 71 million people worldwide have CHC; more than one million new cases and 1.34 million deaths from this infection are recorded annually [7-9]. This is more than the human immunodeficiency virus (HIV/AIDS)-related mortality rate of 1 million [11–13]. CHC is becoming a significant 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 co-infected with hepatitis C virus and HIV are the main source of HIV/HCV in infancy and childhood [14]. In the case of coinfection of HIV 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].

In children, fibrosis progresses at a slow rate, so there are few established reliable risk factors for disease progression [26-29]. The development of progressive liver disease in these patients occurs infrequently until the duration of infection exceeds 30 years [30].

However, during HIV infection, the phenomenon of aggressive fibrogenesis of the liver occurs, so 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.

Purpose 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.

Research objectives:

1. Based on retro- and prospective analysis, study the structure and features of liver lesions in HIV-infected children of the Bukhara region for the period from 2018-2022.

2. Assess the epidemiological and clinical and laboratory features of co-infection (HIV and HCV) in children.
3. To establish the frequency and severity of fibrotic changes in liver tissue in co-infected children based on data obtained from indirect elastometry. To study the cytokine profile of patients with HIV/HCV to identify predictors of liver fibrosis.
4. Identify risk factors for the progression of CHC in children with HIV infection by constructing multivariate regression models based on clinical, anamnestic, laboratory and instrumental data, and develop an index of the likelihood of developing fibrosis.
5. Taking into account the data obtained on predictors of liver fibrosis, create an algorithm for monitoring children with HIV/HCV coinfection to prevent disease progression.

Research methods

Laboratory research methods. Among the patients examined, the main method of detecting HIV infection (in children over 18 months old) was testing using enzyme-linked immunosorbent assay (ELISA) or chemiluminescence immunoassay (CHLA). Testing for HIV using the AIDS ELISA method is carried out on an automatic enzyme immunoassay analyzer "ELISYS" model "ELISYS QUATRO" (Human GmbH, Germany) (photometric method), as well as on a photometer for microplates "Mark" version "iMark" (BioRad Laboratories , Inc., USA) (photometric method). Testing for HIV using the CHLA method is carried out on an immunochemical modular analyzer for in vitro diagnostics “ARCHITECT i2000 sr mobdule” (Abbott, USA) (chemiluminescence method). To confirm a positive ELISA result, the immunoblotting (IB) method is used. This method allows you to detect antibodies to HIV-1 or HIV-2 in the test sample of blood serum (plasma) 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 nonspecific reactions. The IB method is based on the method of indirect enzyme immunoassay, which makes it possible to determine the spectrum of antibodies to HIV proteins. All children underwent a clinical blood test, the level of erythrocytes, leukocytes, platelets, hemoglobin, hematocrit, differentiation of leukocyte 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, gammaglutamyl transpeptidase, alkaline phosphatase, total cholesterol, glucose, urea, creatinine, total protein, albumin.

Statistical research methods.

Statistical processing of the research materials was carried out using parametric and nonparametric analysis methods. Accumulation, adjustment, systematization of initial information and visualization of the results obtained were carried out in Microsoft Office Excel spreadsheets. Statistical analysis was carried out using the IBM SPSS Statistics version 26 (USA) application package. To check whether the distribution of the characteristic corresponds to the normal law, the Shapiro-Wilk test was used. In the case of describing quantitative indicators with a normal distribution, arithmetic means (M) and standard deviations (SD) were calculated. Sets of quantitative indicators whose distribution differed from normal were described using the values of the median (Me), 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 test was used (if the distribution of characteristics corresponded to the normal law) and the Mann-Whitney test (otherwise).

Comparison of three groups for quantitative indicators, the distribution of which differed from normal, was performed using the Kruskal-Wallis test. Group medians were compared using the independent samples median test (Median Test).

Conclusion

According to the regional registry, as of March 30, 2023, 784 patients with chronic hepatitis C were registered in the Bukhara region. Moreover, only 389 people had a diagnosis of CHC confirmed by RNA PCR for hepatitis C, of which 86 were children and adolescents under 17 years of age inclusive. The absolute majority are men, who accounted for 63.7%, women – 36.3%, respectively. For the period from 2014 to 2022. In AIDS, 22 children with coinfection with HIV and HCV were observed. In addition, information about patients with CHC is entered into the monitoring system for patients with viral hepatitis C "Register of Patients with Viral Hepatitis C". In 90-95% of cases, CHC in early childhood occurs in anicteric, subclinical and inapparent forms with a high frequency of chronicity. According to all researchers, the frequency of chronic HCV infection is high, from 40-56% to 81% or more [7, 12]. In childhood, chronicity most often forms as a primary chronic process during vertical infection of the child from the mother. 118 Between 1% and 4% of children with CHC are at risk of developing cirrhosis, while fibrosis and severe inflammation may occur in 15% with CHC [36, 35]. Advanced stages of liver fibrosis in children with CHC develop in the presence of concomitant pathology (hematological diseases, obesity, oncopathology, co-infection with HIV, HBV) [11, 27]. In HIV infection, the phenomenon of aggressive liver fibrogenesis occurs, so the study of fibrotic processes in the liver and the rate of their progression in children is extremely relevant. Despite the high reliability of the results, liver puncture biopsy has a number of limitations in pediatric practice and the risk of complications, especially in patients with severe liver damage accompanied by hemostasis disorders [11, 35]. In recent years, the search for non-invasive methods for diagnosing fibrosis has been carried out in several directions. Despite the fact that at the present stage much attention is paid to reducing the rate of progression of HIV infection and CHC, and non-invasive methods for diagnosing fibrosis are being actively developed, many unresolved issues remain. In particular, identifying regional characteristics and causes of liver damage in children with HIV. It is necessary to identify factors contributing to the progression of HIV/HCV co-infection and study groups of children at high risk for the development of liver fibrosis. A generalization of the management features of children at high risk of liver damage is required. Further study of the mutual influence of the two infectious diseases is necessary; improving approaches to timely diagnosis of fibrosis, predicting its development, as well as reducing the rate of progression of HIV and HCV. In this connection, we undertook this study. The purpose of the study was to develop an algorithm for timely diagnosis and prediction of the development of liver fibrosis in chronic hepatitis C in 119 HIV-infected children based on the study of clinical diagnostic markers and serum predictors.

Conclusions

In the structure of liver lesions in HIV-infected children of the Bukhara region, CHC predominated (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 co-infection in children were the perinatal route of infection - 90.5%, the predominance 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 undulating hyperenzymemia. Every fifth coinfected child had high levels of HCV RNA. Among concomitant diseases, half of the patients had lesions of the nervous system, and a quarter had cognitive and intellectual-mnestic disorders.

According to indirect elastometry of the liver, 32% of children with HIV/HCV had fibrosis of varying severity, among them patients with fibrosis stage F1 in accordance with the METAVIR scale predominated. 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 multi-infection and with HIV/HCV coinfection. A correlation analysis revealed a moderately close relationship between IL-6 and the level of HCV RNA $r = 0.506$ ($p = 0.006$), as well as with the fibrosis index APRI $r = 0.42$ ($p = 0.0260$). TNF-alpha does not affect the formation of liver fibrosis in co-infected children, in contrast to data obtained in adults. When constructing multivariate regression models of disease progression, risk

factors were identified: low adherence to therapy; persistence of HIV replication after 24 weeks of ART; high level of HCV RNA; ALT and AST>2 normal and wave-like hyperfermentemia; 126 increase in indices: APRI > 0.5 and FIB-4 > 1.45; the presence of hepato- and splenomegaly; concomitant gastrointestinal diseases. Prediction of the formation of liver fibrosis is based on the calculation of the index: with a value of ≤ -13 points, a low risk of developing fibrosis is noted, with an index of ≥ +13 points, a high risk (diagnostic accuracy of the Ac method = 89.5%).

The monitoring algorithm for a child with HIV/HCV co-infection includes early diagnosis of diseases; early start of ART; monitoring the level of adherence; determination of non-invasive markers of fibrosis; assessment of disease progression and the possibility of liver fibrosis formation.

REFERENCES

1. Choi Y.J., Kim J.H., Koo J.K., Lee C.I., Lee J.Y., Yang J.H., Ko S.Y., Choe W.H., Kwon S.Y., Lee C.H. Prevalence of renal dysfunction in patients with cirrhosis according to ADQI-IAC working party proposal. Clin. Mol. Hepatol. 2014;20:185–191. doi: 10.3350/cmh.2014.20.2.185.
2. Oblokulov Abdurashid Rakhimovich Mukhammadieva Musharraf Ibrokhimovna Sanokulova Sitora Avazovna Khadieva Dora Isakovna. (2023). CLINICAL AND LABORATORY FEATURES OF SPONTANEOUS BACTERIAL PERITONITIS IN PATIENTS WITH VIRAL LIVER CIRRHOSIS. *Journal of Advanced Zoology*, *44*(S-2), 3744–3750. Retrieved from http://jazindia.com/index.php/jaz/article/view/1716
3. Russ K.B., Stevens T.M., Singal A.K. Acute Kidney Injury in Patients with Cirrhosis. J. Clin. Transl. Hepatol. 2015;3:195–204.
4. Allegretti A.S., Ortiz G., Wenger J., Deferio J.J., Wibecan J., Kalim S., Tamez H., Chung R.T., Karumanchi S.A., Thadhani R.I. Prognosis of Acute Kidney Injury and Hepatorenal Syndrome in Patients with Cirrhosis: A Prospective Cohort Study. Int. J. Nephrol. 2015;2015:108139. doi: 10.1155/2015/108139.
5. Cholongitas E., Senzolo M., Patch D., Shaw S., O'Beirne J., Burroughs A.K. Cirrhotics admitted to intensive care unit: The impact of acute renal failure on mortality. Eur. J. Gastroenterol. Hepatol. 2009;21:744–750. doi: 10.1097/MEG.0b013e328308bb9c.
6. Barbaud A., Waton J., Herbeth B., Bursztejn A. C., Bollaert M., Schmutz J. L., et al. (2014). Comparison of cytokine gene polymorphism in drug-induced maculopapular eruption, urticaria and drug reaction with eosinophilia and systemic symptoms (DRESS). J. Eur. Acad. Dermatol. Venereol. 28 (4), 491–499. 10.1111/jdv.12130
7. Barrett J. S., Fossler M. J., Cadieu K. D., Gastonguay M. R. (2008). Pharmacometrics: a multidisciplinary field to facilitate critical thinking in drug development and translational research settings. J. Clin. Pharmacol. 48 (5), 632–649. 10.1177/0091270008315318
8. Ibrokhimovna, M. M. . (2024). Improvement of Primary Prophylaxis and Treatment of Spontaneous Bacterial Peritonitis Complicated in Virus Etiology Liver Cirrhosis. Journal of Intellectual Property and Human Rights, 3(4), 19–25. Retrieved from http://journals.academiczone.net/index.php/jiphr/article/view/2506
9. Elmurodova A.A. (2023). Viral Hepatitis Delta: An Underestimated Threat. *Texas Journal of Medical Science*, *26*, 1–3. Retrieved from https://zienjournals.com/index.php/tjms/article/view/4610
10. Oblokulov Abdurashid Rakhimovich Mukhammadieva Musharraf Ibrokhimovna Sanokulova Sitora Avazovna Khadieva Dora Isakovna. (2023). CLINICAL AND LABORATORY FEATURES OF SPONTANEOUS BACTERIAL PERITONITIS IN PATIENTS WITH VIRAL LIVER CIRRHOSIS. Journal of Advanced Zoology, 44(S2), 3744–3750. Retrieved from http://www.jazindia.com/index.php/jaz/article/view/1716

11. Mukhammadieva M.I. (2022). Modern clinical and biochemical characteristics of liver cirrhosis patients of viral etiology with spontaneous bacterial peritonitis //Texas Journal of Medical Science. – 2022.- P. 86-90
12. Abdulloev Mukhriddin Ziyodulloevich. (2023). Modern Therapy of Viral Hepatitis. Texas Journal of Medical Science, 26, 66–69. Retrieved from https://www.zienjournals.com/index.php/tjms/article/view/4636
13. Abdulloev Mukhriddin Ziyodulloevich. (2023). Modern Therapy of Viral Hepatitis. Texas Journal of Medical Science, 26, 66–69. Retrieved from https://www.zienjournals.com/index.php/tjms/article/view/4636
14. Mukhammadieva M.I. (2023). Вирус этиологияли жигар циррози беморларида спонтан бактериал перитонит билан асоратланишнинг профилактикаси ва давосини такомиллаштириш//Oriental Renaissance: Innovative, educational, natural and social sciences. - 2023.-P.947-953.
15. Oblokulov A.R., M.I.Mukhammadieva.(2022). Clinical and biochemical characteristics of liver cirrhosis patients of viral etiology with spontaneous bacterial peritonitis//Academicia Globe: Indersciense Research.-2022.- P. 210-216.
16. M. R., M. ., & S. A., S. . (2022). Features of the Course of Contagious Giardiasis Associated with Giardiasis. Miasto Przyszłości, 26, 186–189. Retrieved from https://miastoprzyszlosci.com.pl/index.php/mp/article/view/464
17. Sanokulova Sitora Avazovna. (2023). COVID-19 IN CHILDREN. Academia Science Repository, 4(06), 25–32. Retrieved from https://academiascience.com/index.php/repo/article/view/843
18. Sanokulova Sitora Avazovna. (2023). Acute Kidney Injury in Critically Ill Cirrhotic Patients with Spontaneous Bacterial Peritonitis. Texas Journal of Medical Science, 25, 65–70. Retrieved from https://zienjournals.com/index.php/tjms/article/view/4502
19. Sanokulova Sitora Avazovna. (2023). Factors of Development of Hepatorenal Syndrome in Patients with Liver Cirrhosis of Viral Etiology. Texas Journal of Medical Science, 26, 4–9. Retrieved from https://www.zienjournals.com/index.php/tjms/article/view/4611
20. Авазовна, С. С. . (2023). Факторы Развития Гепаторенального Синдрома У Больных Циррозом Печени Вирусной Этиологии. AMALIY VA TIBBIYOT FANLARI ILMIY JURNALI, 2(12), 1–8. Retrieved from https://www.sciencebox.uz/index.php/amaltibbiyot/article/view/8673
21. Санокулова, Ситора Авазовна ОСОБЕННОСТИ ТЕЧЕНИЯ КОНТОГИОЗНЫХ ГЕЛЬМИНТОВ АССОЦИИРОВАННОГО С ЛЯМБЛИОЗОМ // ORIENSS. 2023. №2. URL: https://cyberleninka.ru/article/n/ocobennosti-techeniya-kontogioznyh-gelmintov-assotsiirovannogo-s-lyambliozom (дата обращения: 12.12.2023).
22. Jalilova, A.S. (2022). THE SPREAD OF CIRRHOSIS OF THE LIVER BY ETIOLOGICAL FACTORS. Oriental renaissance: Innovative, educational, natural and social sciences, 2 (6), 253-257.\
23. A. A., E., A. S., D., & A., M. S. (2022). Modern Approaches to Treatment of Chronic Giardiasis. Central Asian Journal of Medical and Natural Science, 3(2), 102-105. Retrieved from https://www.cajmns.centralasianstudies.org/index.php/CAJMNS/article/view/631
24. Облокулов, А., & Муҳаммадиева, М. (2022). КЛИНИКО-ЛАБОРАТОРНАЯ ХАРАКТЕРИСТИКА СПОНТАННОГО БАКТЕРИАЛЬНОГО ПЕРИТОНИТА ПРИ ЦИРРОЗЕ ПЕЧЕНИ ВИРУСНОЙ ЭТИОЛОГИИИ. Журнал вестник врача, 1(3), 66–69. извлечено от https://inlibrary.uz/index.php/doctors_herald/article/view/2016
25. Oblokulova Z.I, Oblokulov A.R, & Jalilova A.S. (2022). Diagnostic Significance of Hepatic Fibrosis in Patients with Extrahepatic Chronic Viral Hepatitis C. Central Asian Journal of Medical

and Natural Science, 3(3), 438-443. Retrieved from https://www.cajmns.centralasianstudies.org/index.php/CAJMNS/article/view/806

26. Aslonova.M.R. (2022). Determination of suicidality against the background of Parasitic Diseases in children // INTERNATIONAL JOURNAL OF PHILOSOPHICAL STUDIES AND SOCIAL SCIENCES. – 2022.- P. 9-12.
27. Jalilova, A. S. (2022). Approaches to Etiotropic Therapy of Covid-19 in Outpatient Patients. INTERNATIONAL JOURNAL OF HEALTH SYSTEMS AND MEDICAL SCIENCES, 1(1), 41-44.
28. Mukhtarova Sh.A. (2022) Age-related features of clinical manifestations of giardiasis // International journal of medical sciences and clinical research 2022;17-21.
29. Jalilova A.S. (2022). FEATURES OF CLINICAL MANIFESTATIONS OF CYTOMEGALOVIRUS INFECTION IN CHILDREN. International Journal of Medical Sciences And Clinical Research, 2(09), 12–16. https://doi.org/10.37547/ijmscr/Volume02Issue09-04
30. Raximovich, O. A., Sadilloyevna, J. A., Abdulloyevna, M. S., & Farxodovich , R. F. (2022). Microbiological Indicators of Patients with Confirmed Sars-Cov-2 - Infection. Central Asian Journal of Medical and Natural Science, 3(2), 289-294. https://doi.org/10.17605/OSF.IO/9CFP6
31. Жалилова А. С. Дилноза Саётовна Косимова. Клинико–Лабораторная Характеристика Пациентов С Covid-19 И Предиктор Антибактериальной Терапии //CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES. – 2021. – С. 81-86.
32. Abdulloyevna, M. S. . (2023). Tez-Tez Kasal Bo'lgan Bolalarda O'tkir Respirator Kasalliklarning Klinik-Laboratoriya Xususiyatlari. AMALIY VA TIBBIYOT FANLARI ILMIY JURNALI, 2(12), 29–34. Retrieved from https://sciencebox.uz/index.php/amaltibbiyot/article/view/8680
33. Muxtorova, S. A. (2022). Clinical and laboratoriya features of acute respiratory disease in frequently ill children. Web of scientist: International scientific research journal, 1026-1030.
34. Mukhtarova, S. H. (2022). A.(2022) AGE-RELATED FEATURES OF CLINICAL MANIFESTATIONS OF GIARDIASIS. INTERNATIONAL JOURNAL OF MEDICAL SCIENCES AND CLINICAL RESEARCH, 17-21.
35. Mukhtorova Shokhida Abdulloevna. (2023). Microbiological Indicators of Patients Infected with SarsCov-2. Texas Journal of Medical Science, 21, 41–45. Retrieved from https://www.zienjournals.com/index.php/tjms/article/view/4116
36. Mukhtorova Shokhida Abdulloevna. (2023). CYTOMEGALOVIRUS INFECTIONS IN CHILDREN WITH PRIMARY AND SECONDARY IMMUNE DEFICIENCIES. Academia Science Repository, 4(06), 23–28. Retrieved from http://academiascience.com/index.php/repo/article/view/832
37. Aslonova.M.R. (2023). VITAMIN DEFICIENCY CASES RESULTING FROM PARASITIC DISEASES // Galaxy International Interdisciplinary Research Journal.-2023.-P. 404-409
38. Mukhtorova Shokhida Abdulloevna. (2023). CHARACTERISTIC FEATURES OF THE COURSE OF CITOMEGALOVIRUS INFECTION IN CHILDREN. Galaxy International Interdisciplinary Research Journal, 11(4), 484–487. Retrieved from https://giirj.com/index.php/giirj/article/view/5150..
39. Raximovich, O. A., Sadilloyevna, J. A., Abdulloyevna, M. S., & Farxodovich , R. F. (2022). Microbiological Indicators of Patients with Confirmed Sars-Cov-2 - Infection. *Central Asian Journal of Medical and Natural Science*, *3*(2), 289-294. https://doi.org/10.17605/OSF.IO/9CFP6
40. Ш. А, М. (2023). Профилактика Сезонного Распространения Орви Среди Детей Раннего Возраста. AMALIY VA TIBBIYOT FANLARI ILMIY JURNALI, 2(12), 22–28. Retrieved from https://www.sciencebox.uz/index.php/amaltibbiyot/article/view/8678