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AN INTEGRATED CLINICAL-ECHOGRAPHIC APPROACH TO CHRONIC VIRAL HEPATITIS IN CHILDREN

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Abstract.

Chronic viral hepatitis (CVH) in children causes prolonged liver inflammation, structural and functional impairment, fibrosis development, and an increased risk of cirrhosis. Conventional clinical and laboratory methods do not always provide sufficient information for an objective assessment of pathological activity or the severity of parenchymal structural changes.

Objective. *To improve the diagnosis of chronic viral hepatitis in children through the application of modern ultrasound technologies in comprehensive patient examination.*

Materials and Methods. *A retrospective study was conducted in 112 children aged 3-18 years with CVH, including 87 (77.7%) with HBV, 18 (16.1%) with HCV, and 7 (6.2%) with HDV. Diagnostic methods comprised clinical, biochemical, and serological assessments together with comprehensive ultrasound examinations, including high-frequency grayscale sonography, Doppler ultrasound, 3D/4D sonography, multislice B-mode ultrasonography of the liver, and elastography with fibrosis staging according to the METAVIR scale. The study was conducted in accordance with the principles of the Declaration of Helsinki (2013 revision) and was approved by the Local Ethics Committee of Tashkent State Medical University, with informed consent obtained from the legal representatives of all participants. Statistical analysis included correlation analysis, Student's t-test, and Fisher's F-test, with statistical significance set at $p < 0.05$; data were processed using SPSS Statistics version 26.0. This work was carried out as part of the Tashkent State Medical University research project «Development and Improvement of Non-Invasive Diagnostic Methods for Chronic Diffuse Liver Diseases in Children» (2021-2025).*

Results. *The severity of liver structural changes correlated significantly with clinical and laboratory indicators of disease activity, the most informative markers being liver size, echostructure heterogeneity, blood flow parameters in the portal and hepatic vessels, and quantitative elastometry. This comprehensive approach enabled stratification of CVH activity into minimal, moderate, and severe categories and improved diagnostic accuracy.*

Conclusions. *The integrated clinical-sonographic approach employing modern ultrasound technologies provides an informative, reproducible, and safe means of assessing CVH in children, while standardization of morphometric and hemodynamic criteria enhances diagnostic accuracy and optimizes treatment strategies.*

Keywords: *Chronic Viral Hepatitis; Children; Ultrasound; 3D/4D Sonography; Elastography; Liver Fibrosis; Clinical-Sonographic Diagnosis.*

Introduction

Chronic viral hepatitis (CVH) in children remains a significant problem in pediatric hepatology, since hepatitis B, C, and D viruses can cause prolonged, often asymptomatic liver inflammation that leads to progressive parenchymal fibrosis, organ dysfunction, and an increased risk of cirrhosis in adolescence and adulthood [1, 2]. The long-term, largely subclinical course of the disease complicates early diagnosis and timely initiation of therapy [3, 4].

Chronic viral liver diseases are among the most pressing problems in modern medicine, given their high prevalence and the risk of progression to cirrhosis and hepatocellular carcinoma (Figure 1), with timely diagnosis and appropriately selected treatment strategies playing a key role in improving patient prognosis and quality of life [5].

Clear patient management algorithms are therefore of particular importance, encompassing the stages of diagnosis, determination of disease activity (Figure 2), selection of optimal therapy, and subsequent dynamic monitoring [6].

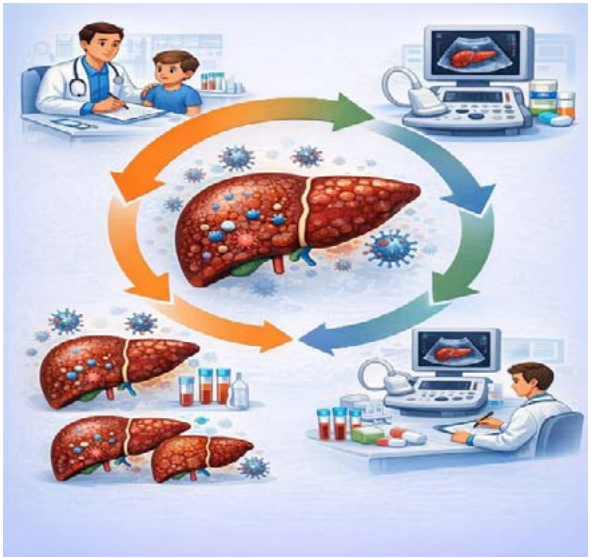

Figure 1. Diagnostic algorithm for chronic viral liver diseases

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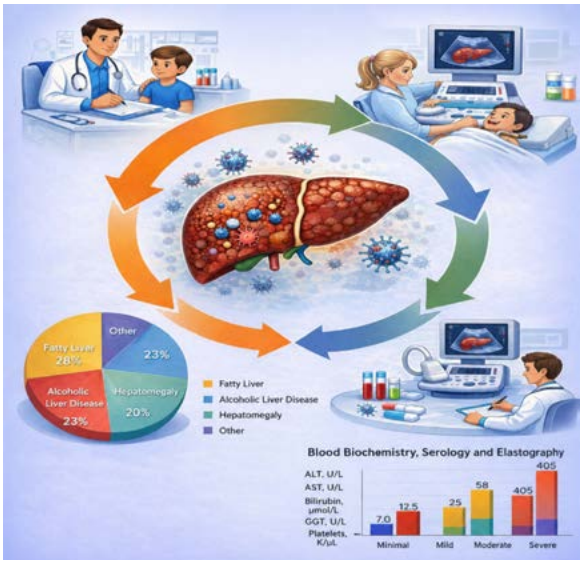

Figure 2. Treatment and dynamic monitoring algorithm for patients with chronic viral liver diseases

Conventional diagnostic methods, including history-taking, clinical examination, biochemical testing, and serological blood analysis, can detect infection and assess its activity, but do not always provide sufficient information about the morphological state of the liver, the severity of fibrosis, or the characteristics of hepatic-portal hemodynamics [7, 8].

Significant progress has recently been made in the development of non-invasive liver imaging methods, particularly ultrasound technologies, which offer high informativeness, safety, and reproducibility in children [9, 10]. Comprehensive ultrasound methods – including high-frequency grayscale sonography, Doppler ultrasound, 3D/4D sonography, multislice B-mode ultrasonography of the liver, and elastography – enable objective assessment of fibrosis severity, inflammatory activity, and portal hemodynamics [11, 12].

Although these technologies have been introduced into clinical practice, standardization of techniques and quantitative criteria for assessing disease activity in children remains insufficient [13, 14]. An integrated approach is particularly valuable, providing a systemic understanding of liver status, enabling stratification of patients by disease activity, and predicting disease dynamics [15, 16]. In pediatric practice, age-related anatomical and physiological features of the liver and spleen, variability in hemodynamic parameters, and the specific manifestations of viral infection across different age groups must all be taken into account [17, 18].

Objective. To improve the diagnosis of chronic viral hepatitis in children through the application of modern ultrasound technologies in comprehensive patient examination.

Materials and Methods

Study Design and Setting. This retrospective clinical and instrumental study involved 112 children aged 3-18 years with CVH, examined at the Hepatology Department of the Republican Specialized Scientific and Practical Medical Center of Pediatrics, Ministry of Health of the Republic of Uzbekistan, and at the Department of Medical Radiology No. 2, Tashkent State Medical University.

Patient Characteristics. Of the 112 children, 87 (77.7%) had HBV, 18 (16.1%) had HCV, and 7 (6.2%) had HDV, with disease activity categorized as minimal in 28 patients (25.0%), moderate in 48 patients (43.0%), and severe in 36 patients (32.0%).

Diagnostic Methods. Assessment of disease activity included evaluation of clinical symptoms; biochemical parameters (ALT, AST, bilirubin, alkaline phosphatase, GGT, total protein); serological markers (HBsAg, anti-HCV, anti-HDV, etc.); and comprehensive ultrasound examination of the liver and spleen. Echographic diagnostics comprised high-frequency grayscale sonography, Doppler ultrasound of the hepatic and portal vessels, 3D/4D sonography for volumetric and dynamic analysis, multislice B-mode ultrasonography of the liver, and elastography with quantitative fibrosis assessment according to the METAVIR classification.

The study was conducted in accordance with the principles of the Declaration of Helsinki (2013 revision), and the protocol was approved by the Local Ethics Committee of Tashkent State Medical University, with informed consent obtained from the legal representatives of all participants.

Statistical analysis was performed using correlation analysis, Student's t-test, and Fisher's F-test, with statistical significance set at $p < 0.05$; data processing was carried out using SPSS Statistics version 26.0.

This study was conducted as part of the Tashkent State Medical University research project «Development and Improvement of Non-Invasive Diagnostic Methods for Chronic Diffuse Liver Diseases in Children» (2021-2025).

Results and Discussion

The study included 112 children aged 3-18 years with chronic viral hepatitis: 87 (77.7%) with HBV, 18 (16.1%) with HCV, and 7 (6.2%) with HDV, with disease activity categorized as minimal in 28 children (25.0%), moderate in 48 children (43.0%), and severe in 36 children (32.0%).

Although clinical and laboratory abnormalities were present, ultrasonography in children with minimal CVH activity identified significant deviations in gallbladder parameters, including wall thickening, heterogeneous content, and folds in the fundus, body, and neck regions; this finding suggests that ultrasound is less sensitive than clinical and laboratory data at this stage of disease activity (Figure 3, Figure 4).

Figure 3. Liver echogram: moderate portal vein dilation (arrows).

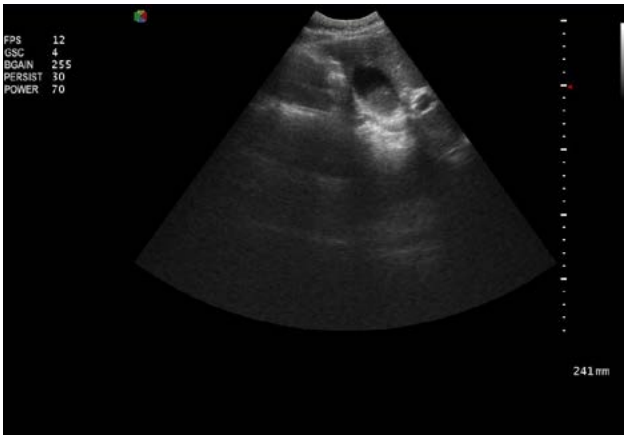

Figure 4. Echogram of a congested gallbladder.

Grayscale sonography findings for the liver and spleen in children with moderate CVH activity differed significantly from those observed in patients with minimal activity. In moderate CVH, the liver parenchyma exhibited a fine-grained structure in 45 ± 4.59% of patients, a medium- grained structure in 41 ± 4.54%, and a coarse-grained heterogeneous structure in 14 ± 3.21%, the latter being characteristic of connective tissue elements and corresponding to a morphological pattern of portal tract infiltration by various cellular elements together with increased collagen fibers, densification, and collagenization of reticular fibers. Liver echogenicity was mildly increased in 10 ± 2.77% of children, moderately increased in 28 ± 4.15%, and markedly increased in 62 ± 4.48%. Vascular pattern abnormalities also differed significantly from those observed in moderate CVH activity.

Hepatic vessels remained well delineated in 72±4.15% of patients, whereas 28±4.15% exhibited various changes in vascular architecture, including loss of definition, vessel thinning, an enhanced vascular pattern, and vessel wall thickening. The portal vein diameter ranged from 5 mm to 8 mm in 44 ± 4.59% of patients, from 9 mm to 12 mm in 39 ± 4.51%, and was 12 mm or greater in 17 ± 3.47%, with a diameter exceeding 9 mm regarded as an indirect sign of portal hypertension. In cases of portal hypertension, ultrasound of the hepatic vessels revealed wall abnormalities such as thickening, tortuosity, and regions of deformation of the vessel lumen.

Gallbladder abnormalities, including wall thickening, were detected in 82 ± 3.5% of patients with moderate CVH activity (Figure 5); a perifocal reaction – characterized by wall thickening exceeding 3 mm and a «double contour» appearance of the wall – was observed in 24 ± 3.94% of patients. Heterogeneous content was noted in 71 ± 4.19%, and folds in the fundus, body, and neck regions were present in 7 ± 4.19%. Splenic echostructure abnormalities included increased echogenicity in 71 ± 4.3% of patients and parenchymal densification in 66 ± 1.41%. The splenic vein diameter was up to 6 mm in 77 ± 3.8% of patients and exceeded 7 mm in 23 ± 3.89%, with thickened walls, tortuosity at the splenic hilum, and narrowing of the vessel lumen within the parenchyma (Figure 6).

In severe CVH activity, gallbladder wall thickening and bile stasis were characteristic findings (Figure 7).

Figure 5. Liver echogram: gallbladder wall thickening in moderate chronic viral hepatitis

Figure 6. Splenic echogram: splenomegaly in moderate chronic viral hepatitis

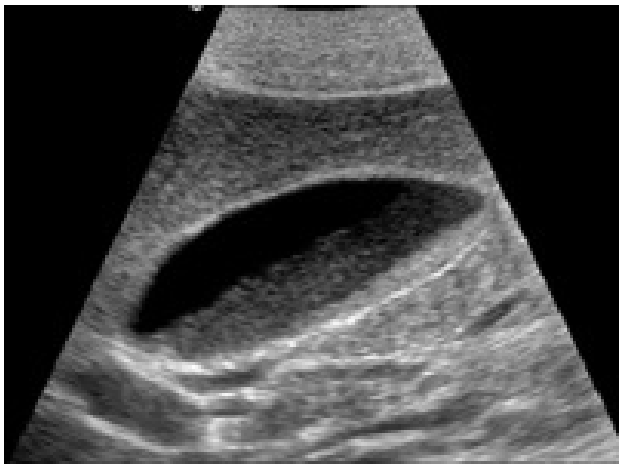

Figure 7. Echogram of thickened gallbladder walls and bile stasis in severe chronic viral hepatitis

Hepatic vessels remained distinct in 10 ± 3.25% of patients and appeared indistinct in 66±5.13%, manifesting as disrupted vascular pattern integrity, wall thickening, and tortuous contours, while peripheral vessel branches were not visualized in 24 ± 1.33% of children. The portal vein diameter exceeded 9 mm in 41 ± 5.33% of patients

and 12 mm in 33 ± 5.10%, and did not exceed 5-8 mm in 26 ± 1.49% (Figure 8).

Figure 8. Echogram of a dilated portal vein in severe chronic viral hepatitis

The spleen retained a crescent shape in 57±5.1% of patients with severe CVH activity, whereas in 43±5.37% it acquired a biconvex shape with rounded edges as a result of organ enlargement, likely associated with increased splenic thickness and width.

Increased echogenicity and parenchymal densification of the spleen, attributable to connective tissue deposition, were observed in all cases (100%).

The diagnostic accuracy of comprehensive echographic methods in detecting liver contour changes in children with chronic viral hepatitis was evaluated (Figure 9).

Grayscale sonography provided objective information for identifying liver contour abnormalities, with no significant difference in informativeness between 3D/4D technology and multislice B-mode ultrasonography of the liver. In some cases, B-mode ultrasound created the impression of thickening of the liver capsule along the diaphragmatic surface; this finding was not confirmed by 3D or 4D echographic visualization and instead resulted from reverberation artifacts arising from air-filled lung tissue, with no independent diagnostic value.

Liver Size Changes. Ultrasound measurements of liver size differed from the findings of physical examination and varied according to the degree of disease activity in children with CVH. Hepatomegaly was already evident at minimal CVH activity and progressed with increasing disease severity, while in severe CVH a disproportion of liver lobes predominated, manifesting as a pronounced increase in the size of the caudate lobe relative to the right and left lobes.

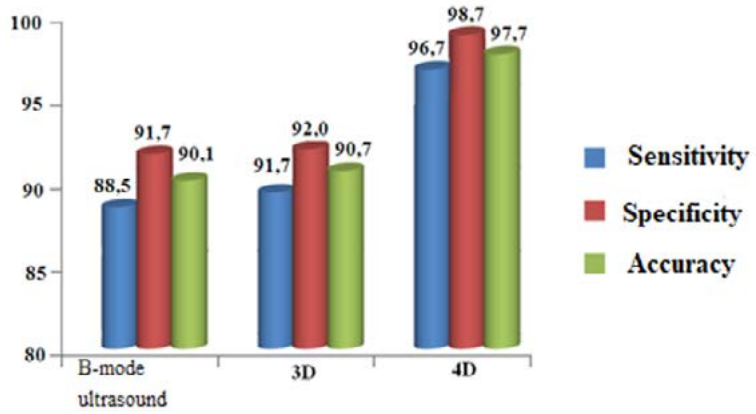

Figure 9. Diagnostic accuracy of comprehensive echographic methods in detecting liver contour changes in children with CVH (%).

In children with minimal CVH activity, two parameters tended to increase: the craniocaudal dimension (CCD) of the left lobe and the thickness of the left lobe. In moderate CVH, there was an increase in the OVD of the right lobe, while the remaining liver parameters – thickness of the right lobe, CCD of the left lobe, and thickness of the left lobe – showed a significant increase compared with minimal activity.

The diagnostic informativeness of the methods used was calculated accordingly (Figure 10).

The findings indicate that the various grayscale sonography methods provide differing yet qualitatively similar information regarding changes in liver shape and size, with grayscale sonography demonstrating the highest diagnostic accuracy for these features, although the differences in informativeness between 3D/4D technologies and multislice B-mode ultrasound were minimal.

Liver Parenchymal Structure Changes. The parenchymal changes identified in this study were both diffuse and focal, with diffuse abnormalities ranging from 10.0 ± 4.2% to 79 ± 5.6% and focal changes ranging from 10.0 ± 4.6% to 83.0 ± 5.2%.

On ultrasound, diffuse changes in liver tissue manifested as increased parenchymal echogenicity, granularity, and heterogeneity, together with altered acoustic characteristics in the porta hepatis region. Increased echogenicity in this region, confirmed by morphological examination, was a sign of periportal fibrosis. A consistent increase in the frequency of detected diffuse liver changes was observed with increasing disease activity.

In multislice B-mode ultrasonography of the liver, diffuse parenchymal changes appeared as poorly demarcated hyper- or hypoechoic areas, while elastography, through qualitative and quantitative assessment of liver stiffness, enabled clarification of the degree of fibrosis and diffuse liver changes in children with CVH.

The diagnostic accuracy of comprehensive echographic methods in detecting diffuse parenchymal structural changes of the liver in children with chronic viral hepatitis is presented in Figure 11.

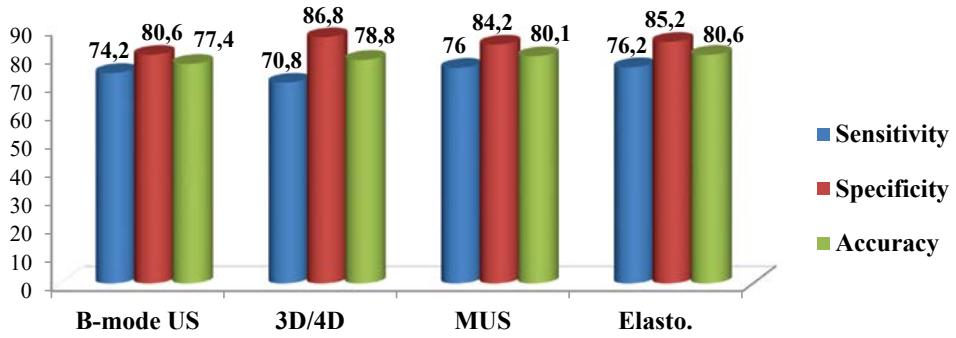

Figure 11. Diagnostic accuracy of echographic methods in detecting diffuse liver parenchymal changes in children with CVH (%).

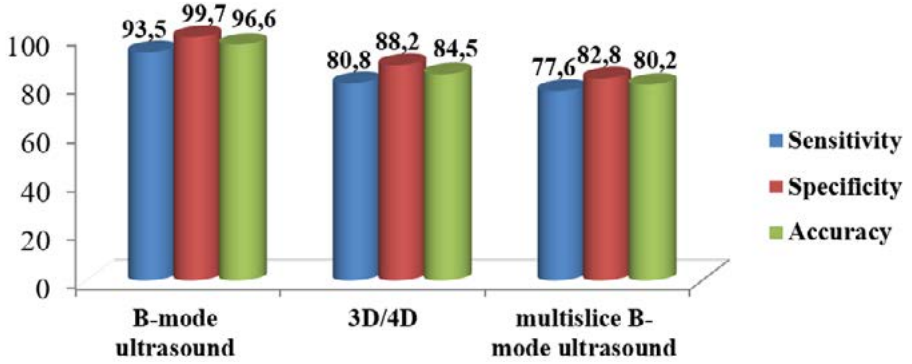

Figure 10. Diagnostic accuracy of echographic methods in detecting liver size changes in children with CVH (%).

As shown in the diagram, the highest diagnostic informativeness was achieved with elastography and multislice B-mode ultrasonography of the liver.

Although diffuse parenchymal changes can be assessed echographically using any ultrasound visualization method, quantitative stiffness indices are provided specifically by ultrasound elastography.

Ultrasound did not allow differentiation of the diffuse parenchymal changes characteristic of chronic viral hepatitis of different etiologies, since features such as parenchymal hyperechogenicity, increased granularity, and heterogeneity cannot be used to determine the type or etiology of the chronic hepatic process.

Increased echogenicity in the periportal area, confirmed by morphological examination, indicated periportal fibrosis. Comparison of the echographic findings with the biochemical test results likewise revealed no statistically significant correlation; however, an overall consistent increase in the frequency of detected diffuse liver changes was observed with progression of disease stage.

Clinical and laboratory parameters correlated significantly with disease severity: children with severe CVH activity exhibited higher levels of ALT, AST, gamma-GTP, and bilirubin, together with pronounced changes in blood protein composition, whereas in minimal disease activity, biochemical parameters were either within normal limits or only slightly elevated, indicating a latent course of the disease process.

Echographic examination revealed the following patterns. High-frequency grayscale sonography enabled detection of liver and spleen enlargement as well as parenchymal echostructure heterogeneity, both proportional to the severity of disease activity. High-frequency grayscale sonography enabled detection of liver and spleen enlargement as well as parenchymal echostructure heterogeneity, both proportional to the severity of disease activity. Doppler ultrasound showed that, in moderate and severe CVH activity, signs of portal hypertension were present, including increased linear and volumetric blood flow velocity in the portal vein and elevated resistive indices of the hepatic and splenic arteries.

The use of 3D and 4D sonography enabled volumetric and dynamic visualization of the liver, assessment of the depth and extent of pathological changes, identification of fibrotic areas, and clarification of vascular architecture, while multislice B-mode ultrasonography of the liver provided high-precision, layer-by-layer examination of the liver and spleen, detection of diffuse parenchymal changes, and accurate localization of fibrotic zones.

Elastography with quantitative assessment of fibrosis enabled stratification of children by disease activity: mean liver stiffness was 5.4-7.2 kPa for minimal activity, 7.3-9.3 kPa for moderate activity, and 9.4-12.2 kPa for severe activity. These values showed a significant correlation with clinical, laboratory, and grayscale sonography data, confirming the high informativeness of the integrated approach.

A comprehensive assessment of all parameters – including clinical, laboratory, and echographic data – allowed for an objective determination of the degree of chronic viral hepatitis activity in children and identification of key markers for patient stratification. The most informative markers were liver and spleen size, parenchymal echostructure heterogeneity, portal hemodynamics parameters, and quantitative elastometry data.

Thus, the study demonstrated the high efficacy of the integrated clinical-echographic approach, which provides reproducible, objective, and non-invasive assessment of the severity of chronic viral hepatitis in children and optimizes patient monitoring and treatment strategies.

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The results confirm the high clinical significance of the integrated approach to CVH diagnosis in children [19, 20]. While standard biochemical and serological parameters are informative for confirming the diagnosis, they do not always allow for an objective assessment of the liver's morphological state [21]. Comprehensive ultrasound – including grayscale sonography, Doppler ultrasound, 3D/4D sonography, and multislice liver ultrasound – revealed structural and functional changes correlating with the activity of the inflammatory process [22, 23].

Elastography with quantitative fibrosis assessment showed high informativeness in stratifying patients by disease activity [24, 25]. This aligns with international literature recognizing elastography as a promising non-invasive method for fibrosis assessment [26]. The integrated approach enables detection of latent structural changes, objective assessment of dynamics, and prediction of the risk of fibrosis progression and portal hypertension [27].

The development of digital technologies and AI opens prospects for automated analysis of echographic data in pediatric hepatology [28-30]. The implementation of standardized protocols for comprehensive echography in pediatric practice ensures improved diagnostic accuracy, better patient stratification, and optimization of clinical decisions.

Conclusions

1. The integrated clinical-echographic approach using high-frequency grayscale sonography, Doppler ultrasound, 3D/4D sonography, multislice liver ultrasound, and elastography is an informative, reproducible, and safe method for assessing CVH in children.

2. Comprehensive assessment of clinical, laboratory, and ultrasound parameters allows for objective determination of the degree of pathological activity and stratification of patients into groups with minimal, moderate, and severe activity.

3. Liver elastography with quantitative fibrosis assessment according to METAVIR demonstrates high sensitivity and specificity, correlating with clinical and laboratory data: Emean for minimal activity – 5.4-7.2 kPa, moderate activity – 7.3-9.3 kPa, severe activity – 9.4-12.2 kPa.

4. Modern ultrasound technologies enable early detection of structural and hemodynamic abnormalities, allow prediction of fibrosis progression and portal hypertension, and support the optimization of monitoring and treatment strategies.

5. Development of a standardized protocol for comprehensive clinical-echographic diagnosis improves the accuracy and objectivity of disease severity assessment in children with CVH.

Future Research Prospects. It is advisable to develop automated algorithms for processing 3D/4D echographic and elastography data to improve the accuracy and reproducibility of fibrosis assessment. A promising direction is the comparative study of the informativeness of comprehensive echography with magnetic resonance imaging and multislice computed tomography. Long-term observation of children with varying degrees of CVH activity will allow for the evaluation of fibrosis progression and the effectiveness of individualized therapy. Integration of ultrasound data with laboratory and genetic markers will create the basis for a comprehensive prognostic model.

Author Contributions. F. Inoyatova – concept and design of the study, scientific supervision, clinical management of patients, final approval of the manuscript; G. Yusupaliyeva – collection of clinical data, performance and interpretation of ultrasound examinations, statistical data processing, manuscript editing; S. Davlatov – methodological consulting, critical review of the manuscript content, coordination of the author team's work; R. Navruzov – analysis of radiological data, contribution to writing the «Materials and Methods» and «Discussion» sections; K. Sherkulov – participation in the interpretation of results, critical editing of the manuscript. All authors reviewed the final version of the manuscript and consented to its publication.

Conflict of Interest. The authors declare no conflict of interest related to the preparation and publication of this article.

Use of Artificial Intelligence. Artificial intelligence tools were not used in the preparation of this manuscript.

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ІНТЕГРОВАНИЙ КЛІНІКО-ЕХОГРАФІЧНИЙ ПІДХІД ДО ХРОНІЧНИХ ВІРУСНИХ ГЕПАТИТІВ У ДІТЕЙ

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Резюме.

Хронічні вірусні гепатити (ХВГ) у дітей супроводжуються тривалим запаленням печінки, порушенням її структури та функції, розвитком фіброзу та ризиком цирозу. Традиційні клініко-лабораторні методи не завжди дозволяють об'єктивно оцінити ступінь активності патологічного процесу та вираженість структурних змін паренхіми.

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Мета. Удосконалення діагностики хронічних вірусних гепатитів у дітей шляхом застосування сучасних технологій ультразвукових досліджень у системі комплексного обстеження хворих.

Матеріали та методи. Ретроспективне дослідження 112 дітей віком 3-18 років із ХВГ: ХГВ – 87 (77,7%), ХГС – 18 (16,1%), ХГD – 7 (6,2%). Діагностика включала клінічні, біохімічні та серологічні методи, а також комплексне УЗД: високочастотну серошкальну ехографію, доплерографію, 3D/4D ехографію, мультизрізову ехогепатографію та еластографію з оцінкою фіброзу за шкалою METAVIR. Дослідження виконано відповідно до принципів Гельсінської декларації ВМА (редакція 2013 року). Протокол схвалено локальним етичним комітетом ТашГМ У. Інформовану згоду законних представників пацієнтів отримано від усіх учасників. Використані статистичні методи: кореляційний аналіз, критерій Стьюдента, F-критерій Фішера; рівень достовірності $p<0,05$. Обробка даних – SPSS Statistics версії 26.0. Робота виконана в рамках НДР ТашГМУ «Розробка та вдосконалення неінвазивних методів діагностики хронічних дифузних захворювань печінки у дітей» (2021-2025 рр.).

Результати. Вираженість структурних змін печінки достовірно корелювала з клінічними та лабораторними показниками активності. Найбільш інформативними маркерами виявилися: розміри печінки, неоднорідність ехоструктури, показники кровотоку в портальних і печінкових судинах, кількісна еластометрія. Комплексний підхід дозволив стратифікувати ступінь активності ХВГ (мінімальна, помірна, виражена) і підвищив точність діагностики.

Висновки. Інтегрований клініко-ехографічний підхід із використанням сучасних ультразвукових технологій є інформативним, відтворюваним і безпечним методом оцінки ХВГ у дітей. Стандартизація морфометричних та гемодинамічних критеріїв підвищує точність діагностики та дозволяє оптимізувати тактику лікування.

Ключові слова: хронічний вірусний гепатит; діти; ультразвукове дослідження; 3D/4D ехографія; еластографія; фіброз печінки; клініко-ехографічна діагностика.

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