

Emerging trends in pediatric viral hepatitis: Case studies and insights

Abstract

Background: Viral hepatitis is a leading cause of liver disease in children, primarily caused by hepatitis A, B, and C viruses.^{1,2} Since 2022, there has been a rising number of pediatric hepatitis cases with unclear origins, indicating the potential emergence of new etiologies.³ This study aimed to analyze the increasing trends of viral hepatitis in children, with a particular focus on hepatitis C. It included data from a regional hospital registry in Dnipro, Ukraine, that documented 167 children diagnosed with viral hepatitis C and B, highlighting the challenges of diagnosis and treatment. Additionally, the study presents illustrative cases to demonstrate clinical variability and systemic barriers, offering a comprehensive overview of the issue.^{4,5}

Methods: A retrospective analysis of clinical and laboratory data from 167 children aged 2–18 years with viral hepatitis was conducted. Barriers to care, treatment outcomes, and the utility of direct-acting antiviral (DAA) therapies were assessed. Three illustrative cases were presented to highlight the diverse clinical challenges and outcomes.⁶

Results: In a study of 167 children, 86% were diagnosed with chronic hepatitis C (CHC), and 14% with chronic hepatitis B (CHBV). Of the 106 treated for CHC with direct-acting antiviral agents (DAA), 105 achieved a sustained virologic response (SVR) within 12 weeks. All 16 patients treated for CHBV, using pegylated interferons, entecavir, or lamivudine, reached undetectable DNA levels or significant viral load reductions, with normalized ALT and AST levels. Barriers to care included low public awareness, high diagnostic costs, and logistical delays. Three case studies highlight challenges such as severe acute hepatitis, chronic infections, and unknown causes.^{7,8}

Conclusion: Addressing gaps in awareness, diagnostic processes, and access to pediatric-appropriate medications is critical for improving outcomes in pediatric hepatitis. Continued research is needed to address the rising burden of acute hepatitis cases of unknown etiology.^{9,10}

Keywords: viral hepatitis C, children, pediatric formulations, velpatasvir, public health, adenoviruses

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Shostakovych-Koretska Liudmyla

Infectious Diseases, Dnipro State Medical University, Ukraine

Correspondence: L Shostakovych-Koretska, Infectious Diseases, Dnipro State Medical University, Ukraine, Tel +380675638335, Email shost3@gmail.com

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Introduction

Viral hepatitis is a major global health issue, affecting millions of children worldwide.^{1–4} Hepatitis A, B, and C viruses are the most common causes of acute and chronic hepatitis in pediatric populations.^{4,11} However, since 2022, an increasing number of children have been presented with hepatitis symptoms but tested negative for known hepatotropic viruses (A–E). This suggests the emergence of new causes.^{12,13} potentially linked to non-hepatotropic viruses such as adenoviruses or SARS-CoV-2.^{5,13} The burden of chronic hepatitis, particularly hepatitis C, remains underdiagnosed and undertreated due to barriers such as limited awareness, high diagnostic costs, and delayed access to medications. The management of chronic hepatitis, particularly hepatitis C, remains a challenge due to limited public awareness, logistical barriers, and the delayed availability of antiviral medications.¹⁴

This study aimed to analyze the increasing trends of viral hepatitis in children, with a particular focus on hepatitis C. It included data from a regional hospital registry in Dnipro, Ukraine, that documented 167 children diagnosed with viral hepatitis C and B, highlighting the challenges of diagnosis and treatment. Presenting illustrative case studies helps to highlight the range of clinical challenges and outcomes associated with pediatric hepatitis C. This approach provides a comprehensive understanding of the issue and explores the

effectiveness of modern treatment strategies, particularly direct-acting antivirals (DAAs), in managing patients with hepatitis C.^{8,15}

Methods

This retrospective observational study analyzed data from the regional infectious diseases hospital registry in Dnipro, Ukraine. Data were collected from medical records at a Regional Infectious Diseases Hospital in Dnipro, Ukraine. Treatment regimens, outcomes, and systemic barriers were analyzed. The study involved 167 children aged 2 to 18 years who were diagnosed with hepatitis C. Gender Distribution: 52% male, 48% female. Both CHVB and CHVC cases were evaluated to capture the full spectrum of disease presentation and management.^{15,16} Out of the 167 children, 106 received treatment and continued with follow-up care.

Illustrative cases: Three specific cases were selected to provide an in-depth exploration of different aspects of the problem:

- Severe acute hepatitis in a pregnant adolescent and her newborn.
- Chronic hepatitis C managed with direct-acting antivirals (DAAs).
- Acute hepatitis of unknown etiology presenting a complex diagnostic challenge.

Results

The hospital registry includes 167 children diagnosed with chronic viral hepatitis. Among this group, 144 were identified as having chronic hepatitis C virus (CHVC), while 23 were diagnosed with chronic hepatitis B virus (CHVB). Out of the 144 children with CHVC, 106 received treatment with pan-genotypic direct-acting antivirals (DAAs). Treatment for the 16 patients with CHVB involved pegylated interferons, entecavir, or lamivudine. All patients continued to receive follow-up care. Treatment outcomes: Among the 106 patients treated for CHVC, 105 achieved a sustained virologic response (SVR) within 12 weeks. Viral RNA was cleared in all cases except for one patient, who did not show a sustained response. Normalization of liver enzymes occurred in all treated children. For patients with CHVB, all demonstrated either undetectable DNA or significant reductions in viral loads along with normalization of ALT and AST levels.

Additionally, two cases of hepatitis C resolved spontaneously without antiviral therapy. Analysis of the hospital registry indicated that not all cases of viral hepatitis are diagnosed and treated on time, with several factors contributing to these delays in diagnosis and treatment for children with hepatitis:

- I. Awareness: Low public knowledge regarding appropriate medical services and specialists for hepatitis
- II. Cost: High expenses associated with additional testing provided by private laboratories
- III. Provider knowledge: Insufficient understanding among family doctors and pediatricians about accessible treatment options funded by public health resources
- IV. Logistical barriers: Uncertainty in regional responsibilities for the management and registration of pediatric hepatitis cases
- V. Formulation availability: A shortage of pediatric formulations of antiviral medications.

Case studies

Case 1: Acute Hepatitis C in a pregnant adolescent

A 17-year-old pregnant girl, at 38 weeks gestation, was admitted to a perinatal center with complaints of nausea, fever, right upper quadrant pain, and jaundice over the past week. Her previous pregnancy weeks were unremarkable. Serological testing for hepatitis A, B, C, D, and E yielded negative results. Further tests for autoimmune hepatitis and herpes infections, along with imaging, were conducted. Due to worsening intoxication and hyperbilirubinemia, she underwent a cesarean section. A positive PCR test for HCV RNA then confirmed acute viral hepatitis C, severe course.

Over the postpartum period, her liver markers normalized, and she was discharged after two weeks for outpatient follow-up. The newborn girl weighed 3150 g and measured 51 cm, showing no significant deviations in vital functions or laboratory parameters. Testing revealed positive antibodies and HCV RNA presence. Following discharge, she was monitored by an infectious disease specialist and pediatrician. At six months, follow-up testing did not detect HCV RNA; by 18 months, results confirmed spontaneous viral elimination, with no signs of chronic liver disease observed.

Case 2: Chronic Hepatitis C management

A 9-year-old girl with perinatal HCV infection had been under monitoring since age 3, with no prior detailed examinations.

Laboratory analyses indicated positive HCV antibodies and a viral load of 700,000 IU/mL. Tests for hepatitis B, A, D, and E were negative, with genotype 3 identified. Elevated ALT (85) and AST (50) levels were noted, while liver elastography indicated F0-F1 fibrosis.

Given her treatment-naïve status and the absence of cirrhosis, a course with Sofosbuvir (400 mg) and Velpatasvir (100 mg) daily for 12 weeks was recommended. The treatment proceeded without adverse effects. Follow-up at 4 and 12 weeks indicated no detection of HCV RNA, with normalized liver function tests.

Case 3: Unidentified etiology of acute hepatitis

A 5-year-old girl presented to the hospital with jaundice and symptoms of acute hepatitis on day 8 of the illness. Before jaundice, she experienced diarrhea and mild upper respiratory symptoms. Hospital examination revealed critically elevated bilirubin (>300 µmol/L) and ALT (1000 IU/L), AST (950 IU/L). Tests for hepatotropic viruses; A, B, C, viruses were negative, including tests for herpes viruses and COVID-19. Coagulation tests indicated moderate hypocoagulability, with AFP levels alarmingly high at 17,000 IU/mL.

She was transferred to a regional facility ICU for further evaluation, where extensive imaging ruled out oncological or obstructive pathologies and autoimmune hepatitis. Treatment included, corticosteroids, lactulose, and other supportive measures. The Diagnosis established was acute hepatitis of undetermined etiology, severe form. The patient showed gradual improvement over three weeks, with normalized bilirubin and transaminase levels and reduced AFP levels.

Discussion

The increasing incidence of hepatitis in children, including cases with unknown etiology, reflects a shifting epidemiological landscape. Potential links to adenoviruses and COVID-19 highlight the need for comprehensive research.^{7,9,17} Direct-acting antivirals (DAAs) such as Sofosbuvir and Velpatasvir have transformed chronic hepatitis C treatment, offering high efficacy and tolerability even in children.^{1,5,18} The findings of this study underline a concerning increase in hepatitis cases among children, including those without detectable hepatotropic viral markers. The emergence of cases linked to potential non-hepatotropic viruses, such as adenoviruses and SARS-CoV-2, underscores the need for broader diagnostic strategies and further research into new viral etiologies. These unexplained cases not only pose diagnostic challenges but also suggest that we may be facing an evolving epidemiological landscape where traditional diagnostic methods may no longer suffice. Globally, cases of acute hepatitis in children with unknown etiology have drawn attention, as evidenced by the clustering of such reports since 2022. This highlights the urgent need for international collaboration to understand whether these cases represent new viral strains, immune-mediated responses, or environmental exposures. This study reaffirms the efficacy and safety of pan-genotypic direct-acting antivirals (DAAs), such as Sofosbuvir and Velpatasvir, in children aged 3 years and older. These medications have transformed the treatment landscape for chronic hepatitis C (CHC), offering high sustained virologic response (SVR) rates with minimal side effects. In our cohort, all 105 children treated with DAAs achieved SVR within 12 weeks, regardless of genotype or baseline viral load. This is consistent with global data supporting DAAs as the standard of care. However, early antiviral therapy for acute hepatitis C (AHC) remains controversial. Current guidelines, including those by the World Health Organization (WHO), recommend a watch-and-wait approach for AHC, given that up to 30% of cases may achieve spontaneous clearance.^{2,18}

This was reflected in our study, where 2 children with AHC experienced natural resolution of the infection without antiviral therapy. Balancing the benefits of early treatment against the likelihood of spontaneous clearance is critical, especially in resource-limited settings where prioritization of antiviral medication for chronic cases may be more cost-effective. Barriers to care remain significant, including public awareness, diagnostic costs, and logistical issues.^{8,14,15} Addressing these challenges requires systemic reforms, increased education efforts, and improved access to diagnostics and pediatric antiviral formulation.^{16,18}

Conclusion

Pediatric viral hepatitis, whether chronic or acute, presents a complex public health challenge. Although advancements in treatment offer hope, systemic barriers must be addressed to improve outcomes. To tackle the issue of chronic hepatitis, we need better early diagnostic measures and streamlined processes to ensure timely access to antiviral therapy. It is crucial to enhance awareness among parents and healthcare providers about new treatment options for viral hepatitis in children, especially for those aged three and older. Continued research into unexplained acute hepatitis and enhanced public health strategies are essential to address this evolving issue.

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Conflicts of interest

The author declares there is no conflict of interest.

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