

A Cross-Sectional Study On The Viral Etiology Of Acute Hepatitis In Children

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ABSTRACT

Background: Acute viral hepatitis is also considered a significant cause of morbidity in children especially in developing countries, where contaminated water, poor sanitation and inconsistent availability of preventive health care facilities are major factors in the continuation of transmission. Hepatitis A virus (HAV) and hepatitis E virus (HEV) are significant contributors to acute hepatitis, and hepatitis B virus (HBV) and hepatitis C virus (HCV) can play a role in the disease burden.

Objective: To determine the frequency of different viral etiologies of acute hepatitis among children presenting to a tertiary care hospital.

Methods: This cross-sectional study was conducted in the Department of Pediatrics, MTI Hayatabad Medical Complex/Khyber Girls Medical College, Peshawar, from October 2025 to April 2026. All 292 children with acute viral hepatitis aged 1–15 years were recruited using non-probability consecutive sampling. Children with chronic liver disease and those with drug-induced hepatitis were not included. Chemiluminescent microparticle immunoassay (CMIA) was used for HAV IgM, HBsAg, anti-HCV and anti-HEV IgM testing to determine viral etiology. The data were analyzed using SPSS version 22.0, with p-value ≤ 0.05 as a statistically significant value.

Results: The mean age of the participants was 7.64 ± 3.78 years, and 168 (57.5%) were males. HAV was the most frequently identified viral etiology, accounting for 181 (62.0%) cases, followed by HEV in 48 (16.4%), HBV in 25 (8.6%) and HCV in 12 (4.1%). No tested viral marker was detected in 26 (8.9%) children. Viral etiology showed a significant association with age group ($p < 0.001$) and residence ($p = 0.024$), whereas no significant association was observed with gender ($p = 0.879$).

Conclusion: HAV was the predominant viral cause of acute hepatitis among children, followed by HEV, whereas HBV and HCV were comparatively uncommon. The findings emphasize the continued importance of improved sanitation, safe drinking water, early recognition and preventive measures for reducing childhood viral hepatitis.

Keywords: Acute viral hepatitis; Children; Hepatitis A; Hepatitis B; Hepatitis C; Hepatitis E; Viral etiology.

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middle income countries, especially in children, where sanitation and safe drinking water facilities may not be available and where preventive services may be limited.

The types of viruses that are more likely to be associated with contaminated food and water and poor personal hygiene and sanitation are the hepatitis A virus and hepatitis E virus (3,4). HAV is an important cause of acute viral hepatitis in children and is typically a self-limited disease, but sometimes leads to serious hepatitis and acute liver failure. A hospital based study in Pakistan revealed that HAV was a significant proportion of acute viral hepatitis in children, underscoring the role of HAV in the local paediatric population (5).

Symptoms of acute viral hepatitis can range from constitutional symptoms to frank jaundice. Children can show symptoms of jaundice, fatigue, loss of appetite, nausea, vomiting, abdominal discomfort, dark urine and raised serum aminotransferase levels. This may not be as specific in young children and laboratory confirmation is essential to determine the underlying viral cause (2,6). The determination of etiology has implications for the management of patients, counselling, prevention and surveillance.

Hepatitis A is a common childhood problem but different types of hepatitis viruses are common in different parts of the world. In addition, HEV is known to be a significant cause of acute viral hepatitis in regions of the world where sanitation is poor and water supplies are contaminated (7,8). For this reason HBV and HCV are of special concern as they may lead to chronic infection and chronic liver disease, cirrhosis and HCC. While an effective vaccine aimed at the routine prevention of HCV is not yet available, the epidemiology of HBV has been significantly modified in children through preventive vaccination (1,9).

Recently, renewed attention has also been directed toward acute hepatitis in children because clusters of severe hepatitis without evidence of the conventional hepatitis A–E viruses were reported internationally. These cases emphasized the need to broaden the scope of etiological investigation while presuming all cases of pediatric hepatitis were due to the more common hepatotropic viruses. Possible causes for these outbreaks included the adenovirus and other infectious agents, but how these agents might be contributing to the outbreaks was still unclear (6, 10).

Despite the global attention given to viral hepatitis, the pattern of specific viral etiologies among children may differ according to geography, sanitation, vaccination coverage, socioeconomic circumstances and exposure patterns. Local data on the relative frequencies of HAV, HBV, HCV and HEV are therefore important for developing appropriate diagnostic, preventive and public-health strategies. The present study was consequently conducted to determine the frequency of different viral etiologies of acute hepatitis among children presenting to the Department of Pediatrics, MTI Hayatabad Medical Complex, Peshawar. This objective is consistent with the original study protocol.

2. METHODOLOGY

A **cross-sectional study** was conducted in the Department of Pediatrics, MTI Hayatabad Medical Complex/Khyber Girls Medical College, Peshawar. The study was carried out from October 2025 to April 2026. Ethical approval was obtained from the Hospital Research and Ethical Committee/Institutional Review Board of Hayatabad Medical Complex, Peshawar, under Approval No. 2441, dated 11 February 2025. Approval of the research protocol was also obtained from the College of Physicians and Surgeons Pakistan (CPSP), Research Evaluation Unit, under Ref. No. CPSP/REU/PED-2023-021-7966, dated 19 October 2025. Written informed consent was obtained from the parents or legal guardians of all enrolled children before participation, and confidentiality of patient information was maintained throughout the study.

A total of 292 children were included in the study. The sample size was determined with the WHO sample size calculator with a 95% confidence level, a prevalence of hepatitis C virus infection of 2.5 and an absolute precision of 5%. Participants were recruited using consecutive sampling which is a non-probability sampling technique. Children between 1 and 15 years of age with acute viral hepatitis based on the operational criteria set were included. Drug-induced hepatitis, defined by a history of drug exposure and chronic liver disease (CLD) were excluded.

Acute viral hepatitis was the condition when the eyes turned yellow for less than 14 days, and AST/ALT was increased more than three times the upper normal limit (UUNL) ($\text{AST/ALT} \geq 120 \text{ IU/L}$) and/or bilirubin was increased (Bilirubin $> 2.5 \text{ mg/dL}$). Viral etiology was determined using serological testing. Hepatitis A was diagnosed with the presence of HAV IgM, Hepatitis B was diagnosed with the presence of HBsAg, Hepatitis C was diagnosed with the presence of anti-HCV and Hepatitis E was diagnosed with the presence of HEV IgM. All such markers were analyzed by a chemiluminescent microparticle immunoassay (CMIA).

Ethical approval was obtained and children who met the eligibility criteria and presented to the pediatric indoor unit of MTI Hayatabad Medical Complex were enrolled. Their parents/guardians

Demographic data, such as age, gender, length of symptoms, place of residence, father's occupation, mother's education, and socioeconomic status of the family was taken. A complete clinical history was taken and a thorough physical examination was performed. Viral serology was ordered and blood samples were drawn to find the source of acute hepatitis. All necessary information was recorded on a proforma that had been specially designed.

All the data were entered and analyzed in SPSS version 22.0. The Shapiro-Wilk test was used to evaluate normality of quantitative variables such as age, weight, height and duration of symptoms. Data on normally distributed variables were reported as mean $\pm$ standard deviation, and for data on variables that were not normally distributed, the median and interquartile range (IQR) were reported. Characteristics of categorical variables such as gender, place of residence, fathers occupation, mothers education, socioeconomic status and viral etiology were given as frequencies and percentages. The results were stratified by age, gender, duration of symptoms, place of residence, father's occupation, mother's educational level and socioeconomic position of the family to assess potential effect modifiers. After stratification, the relationships of categorical variables with viral etiology were analyzed by Chi-square test, using Fisher's exact test when the number of cells in the table was five or less. A p-value of < 0.05 was deemed to be statistically significant.

3. RESULTS

Overall, 292 children with acute hepatitis were studied. Participants' age ranged from 1 to 15 years (7.64 ± 3.78). The largest proportion, 118 (40.4%), belonged to the 6–10-year age group, followed by 96 (32.9%) aged 1–5 years and 78 (26.7%) aged 11–15 years. There were 168 (57.5%) males and 124 (42.5%) females, giving a male-to-female ratio of approximately 1.35:1. There were 173 (59.2%) rural residents and 119 (40.8%) urban residents in the study population. The median time from onset of symptoms to presentation was 6 days (IQR: 4–9 days). The mean body weight and height were 24.18 ± 10.46 kg and 121.37 ± 22.84 cm, respectively.

Table 1. Demographic and baseline characteristics of children with acute hepatitis (n=292)

Variable	n (%) / Mean $\pm$ SD
Age, years	7.64 ± 3.78
Age group	
1–5 years	96 (32.9)
6–10 years	118 (40.4)
11–15 years	78 (26.7)
Gender	
Male	168 (57.5)
Female	124 (42.5)
Residence	
Rural	173 (59.2)
Urban	119 (40.8)
Weight, kg	24.18 ± 10.46
Height, cm	121.37 ± 22.84
Duration of symptoms, days, median (IQR)	6 (4–9)

For parental and socioeconomic factors, 145 (49.7%) children came from low-income families, 105 (36.0%) middle income families and 42 (14.4%) high-income families. The maternal education showed that 99 mothers (33.9%) were illiterate, 78 mothers (26.7%) had primary education, 67 mothers (22.9%) had secondary education and 48 mothers (16.4%) had matriculation or higher education. Employment/job was the most common paternal occupation followed by business/employment and unemployment.

Table 2. Socioeconomic and parental characteristics of participants (n=292)

Characteristic	n (%)
Father's occupation	
Job	137 (46.9)
Business	96 (32.9)
Unemployed	59 (20.2)

Low	145 (49.7)
Middle	105 (36.0)
High	42 (14.4)

Laboratory studies showed that hepatitis A virus was the most common viral cause, found in 181 (62.0%) children. Hepatitis E was identified in 48 (16.4%) cases, hepatitis B in 25 (8.6%), and hepatitis C in 12 (4.1%). Four viral markers were not found in 26 children (8.9%). Therefore, 266 (91.1%) were found to have at least one of the hepatitis viruses investigated.

Table 3. Distribution of viral etiology among children with acute hepatitis (n=292)

Viral etiology	n	%
Hepatitis A (HAV IgM positive)	181	62.0
Hepatitis E (HEV IgM positive)	48	16.4
Hepatitis B (HBsAg positive)	25	8.6
Hepatitis C (anti-HCV positive)	12	4.1
None of the tested viral markers detected	26	8.9
Total	292	100.0

Positive HAV IgM, HBsAg, anti-HCV, and HEV IgM are used to diagnose hepatitis A, hepatitis B, hepatitis C, and hepatitis E respectively, and are detected by chemiluminescent microparticle immunoassay. There was a significant association between age group and viral etiology ($\chi^2=28.82$, $p<0.001$). Hepatitis A had more cases in children aged 1-5 years (75.0%) than in those aged 6-10 years (65.3%) or in those aged 11-15 years (41.0%). On the other hand, relatively more of hepatitis B, hepatitis C and hepatitis E were present in older children.

Table 4. Viral etiology according to age group (n=292)

Viral etiology	1–5 years n (%)	6–10 years n (%)	11–15 years n (%)	Total
Hepatitis A	72 (75.0)	77 (65.3)	32 (41.0)	181
Hepatitis B	4 (4.2)	8 (6.8)	13 (16.7)	25
Hepatitis C	2 (2.1)	4 (3.4)	6 (7.7)	12
Hepatitis E	8 (8.3)	20 (16.9)	20 (25.6)	48
No tested viral marker	10 (10.4)	9 (7.6)	7 (9.0)	26
Total	96 (100.0)	118 (100.0)	78 (100.0)	292

$\chi^2 = 28.82$, $p < 0.001$

Upon examining the viral etiology by gender, the most common infection was still hepatitis A, in both males and females. HAV was identified in 108 (64.3%) males and 73 (58.9%) females. Gender was not found to be statistically significant with viral etiology ($p=0.879$).

Table 5. Distribution of viral etiology according to gender

Viral etiology

groups with the highest prevalence in children from low-income households. But the overall difference of socioeconomic category vs. viral etiology was not statistically significant at the conventional level ($p=0.089$).

Table 7. Viral etiology according to socioeconomic status

Viral etiology	Low (n=145)	Middle (n=105)	High (n=42)	p-value
Hepatitis A	99 (68.3)	63 (60.0)	19 (45.2)	
Hepatitis B	8 (5.5)	10 (9.5)	7 (16.7)	
Hepatitis C	4 (2.8)	5 (4.8)	3 (7.1)	
Hepatitis E	25 (17.2)	17 (16.2)	6 (14.3)	
No tested viral marker	9 (6.2)	10 (9.5)	7 (16.7)	
Total	145 (100.0)	105 (100.0)	42 (100.0)	0.089

Overall, the findings demonstrated that HAV represented the dominant viral cause of acute hepatitis in the pediatric population, accounting for almost two-thirds of all cases. HEV was the second most frequently identified virus, while HBV and HCV were comparatively uncommon. Viral etiology differed significantly across age groups and urban/rural residence, whereas no meaningful difference was observed according to gender.

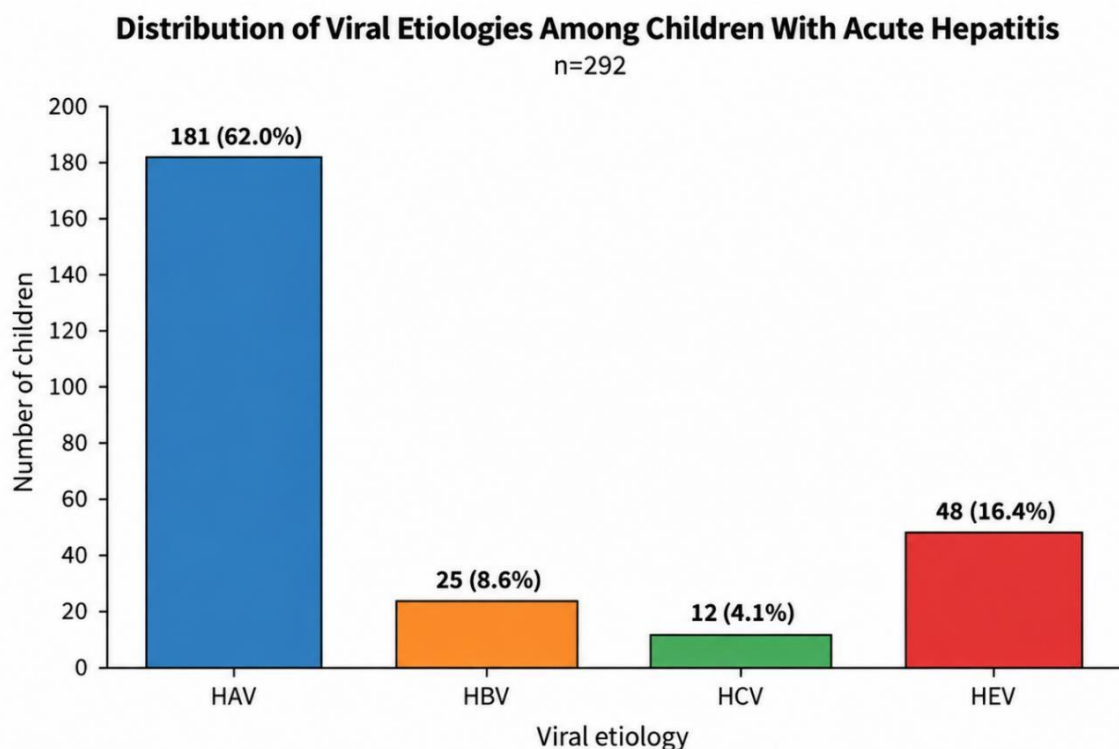


Figure 1. Distribution of viral etiologies among children presenting with acute hepatitis (n=292).

Figure 1. Frequency distribution of hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), and hepatitis E virus (HEV) among children with acute hepatitis (n=292).

4. DISCUSSION

The present study demonstrated that hepatitis A virus (HAV) was the predominant viral etiology of acute hepatitis in children, accounting for 62.0% of the cases, followed by HEV (16.4%), HBV (8.6%), and HCV (4.1%). These findings indicate that enterically transmitted hepatitis viruses, particularly HAV, continue to account for a substantial proportion of acute hepatitis among children in this setting. A hospital-based study by Rasheed et al. involving 200 children with acute viral hepatitis similarly reported HAV infection in 75% of cases, with the 6–10-year age group being the most frequently affected (11). The comparatively high frequency of HAV in both studies may reflect continued exposure through contaminated food or water and inadequate sanitation in settings where HAV remains endemic. A systematic review of pediatric acute liver failure also demonstrated that HAV was an important infectious etiology among children in developing countries, further emphasizing its continuing clinical significance (12).

HEV was the second most common viral infection, accounting for 16.4% of the children. While HEV has been described more clinically, its importance in the pediatric population in endemic populations should not be overlooked. Zaki et al. studied 180 children with acute hepatitis and reported HEV positivity in children; this highlights the importance of screening for HEV in the evaluation of acute hepatitis in children (13). It is possible that some of the relatively high HEV frequency seen in our study is associated with the same environmental routes of transmission of HAV (e.g. fecal contamination of drinking water). The co-circulation of HAV and HEV therefore suggests that improved sanitation, access to safe drinking water and hygiene measures would help to decrease the burden of acute viral hepatitis in children.

The incidence of HBV (8.6%) and HCV (4.1%) was significantly lower than that of HAV and HEV and were rare. Part of this difference in HBV contribution among children may be explained by routine childhood HBV vaccination. At a global level, a significant decline in HBsAg prevalence in children aged less than 5 years and a gradual increase in the coverage of hepatitis B vaccines have been found, but there are large differences across regions (14). HCV was also a small proportion of the acute hepatitis in our study. In a systematic review and meta-analysis, Indolfi et al. reported a pooled HCV seroprevalence of 0.87% among children with no identifiable risk factors, which varied greatly between geographic regions and was slightly higher in older children (aged > 11 years) (15). While HBV and HCV were less prevalent causes of acute presentation in this study, their presence may have implications for persistent infection and long-term liver disease and is clinically important.

There was a significant correlation between age group and the viral etiology ($p < 0.001$). HAV accounted for 75.0% of cases in children aged 1–5 years, 65.3% of cases in children aged 6–10 years, but decreased to 41.0% in children aged 11–15 years. By contrast, a higher proportion of older children were infected with HBV, HCV, and HEV. This variation implies that the pattern of exposure may vary by age. HAV is predominant in children, which is similar to what is seen in endemic areas, and perhaps other viral agents can be present in the older age groups, giving them more exposure. More recently, the significance of the clinical heterogeneity of acute hepatitis in children has been indicated. In children, conventional HAV–HEV markers were missing in many children with acute hepatitis of unknown origin during the international outbreak of acute hepatitis in 2021–2022 and other viral–immune–mediated processes (adenovirus, adeno-associated virus 2) were investigated (16–18). These reports underscore the need to consider a wide-ranging diagnostic strategy when routine viral markers are negative.

Viral etiology ($p = 0.024$) was also highly associated with residence, with 68.2% of children in rural areas being found to be infected with HAV and 52.9% of those in urban areas. This difference could be due to differences in sanitation, water quality, household conditions, and exposure to fecal–oral transmission, but these individual exposures were not measured directly in the present study and cannot thus be determined as causes. In contrast, there was no significant correlation between viral etiology and gender ($p = 0.879$), indicating that exposure to the major hepatotropic viruses was not strongly sex-dependent in this population. However, modern studies of the causes of acute hepatitis in children have also highlighted the importance of the simultaneous influence of diverse environmental, infectious and host factors, which do not necessarily be attributed to a specific demographic feature (19). More recently, it has been shown that HAV can cause clinically severe liver failure in children, although most infections are self-limited (20).

The findings of this study have important implications for both clinical practice and preventive health. Testing for HAV and HEV should continue to be an integral part of the initial work-up of children with acute hepatitis in areas with enterically transmitted hepatitis, and screening for HBV and HCV should still be done due to the potential for longer-term effects. Actions that promote safe drinking water, sanitation, food hygiene and appropriate vaccinations could help even further cut childhood hepatitis. There were a few shortcomings in the study. The study was performed in a single tertiary-care hospital, which restricted the extent to which its findings can be generalized to the broader population, and was a cross-sectional study; thus, temporal and causal inferences were not possible. In addition, only the hepatitis viruses examined in the study protocol were examined, so other viral, metabolic, autoimmune or unknown factors could have played a role in other cases with negative results for the tested viral markers. More comprehensive etiological testing and environmental risk factor evaluation is recommended in larger multicenter studies.

5. CONCLUSION

Hepatitis A virus was the most common viral cause of acute hepatitis among children, accounting for nearly two-thirds of cases, followed

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