

## CLINICAL PREDICTORS OF PROLONGED CHOLESTASIS IN ADOLESCENT HEPATITIS A: A CROSS-SECTIONAL STUDY

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### Abstract

**Background:** Even though overall results are positive, persistent cholestasis is a rare but clinically significant consequence of acute hepatitis A that contributes to extended morbidity.

**Objective:** To identify clinical and laboratory predictors of prolonged cholestasis among adolescents hospitalized with acute hepatitis A.

**Methods:** this Cross sectional study conducted at Department Of Medicine, MTI-Hmc, Peshawar from Jan 2023 to june 2023.involving teenagers with serologically confirmed acute hepatitis A between the ages of 10 and 19 was carried out at Hayatabad Medical Complex in Peshawar. Conjugated hyperbilirubinemia (total bilirubin >5 mg/dL) that lasted longer than four weeks was considered prolonged cholestasis. Biochemical parameters and clinical characteristics were examined. Independent predictors were found using logistic regression.

**Results:** 18 (12%) of the 150 teenagers experienced persistent cholestasis. Female sex (aOR 3.1; 95% CI

1.1–8.7; p=0.03), peak total bilirubin >15 mg/dL (aOR 4.8; 95% CI 1.7–13.6; p=0.003), and severe pruritus

(aOR 2.9; 95% CI 1.0–8.4; p=0.046) were independent predictors.

**Conclusions:** In teenagers with acute hepatitis A, prolonged cholestasis is strongly predicted by higher bilirubin levels, female gender, and severe pruritus. Supportive management and follow-up may be guided by early detection.

**Keywords:** Hepatitis A Virus,Cholestasis, Prolonged,Adolescent Health,Bilirubin

### Introduction

Acute viral hepatitis is still mostly caused by the hepatitis A virus (HAV), particularly in areas with poor water and sanitation [1]. Atypical symptoms including recurrent hepatitis, fulminant hepatic failure, and protracted cholestasis have been documented, despite the fact that infections in children typically resolve on their own [2, 3]. Even though the prognosis is benign, prolonged cholestasis greatly impairs quality of life and recovery time. It is defined by chronic jaundice, pruritus, dark urine, and pale stools that remain longer than four weeks after the initial sickness [4,5].In different cohorts, the reported incidence of persistent cholestasis following HAV infection varies from 3% to 15% [6–8]. Although the precise pathogenesis is unknown, it may involve decreased bile flow and immune-mediated hepatocellular canalicular damage [9]. Certain genetic variants in bile transporter genes (ABCB4, ABCB11), female gender, and advanced age have all been identified as host factors [10,11]. A cholestatic pattern and a delayed recovery have also been linked to

elevated initial bilirubin levels and noticeable pruritus [12,13]. Despite having unique physiological and psychosocial traits, the teenage group is still understudied, with the majority of literature concentrating on children or adults [14]. Finding clinical indicators of persistent cholestasis in this age group may enhance prognosis counseling, cut down on pointless treatments, and encourage focused supportive care [15]. In order to determine clinical and biochemical predictors of persistent cholestasis among teenagers hospitalized with acute hepatitis A in a tertiary care setting in Peshawar, Pakistan, this cross-sectional study was created.

### **Objective**

To identify clinical and biochemical predictors associated with prolonged cholestasis in adolescents with acute hepatitis A.

### **Methods**

#### **Study design and setting:**

This was a hospital-based cross-sectional study conducted at the Department Of Medicine, MTI-Hmc, Peshawar from Jan 2023 to June 2023.

#### **Participants:**

Adolescents aged 10–19 years with serologically confirmed acute HAV infection (positive anti-HAV IgM) were included.

#### **Exclusion criteria:**

Patients with co-infection (HBV/HCV), drug-induced liver injury, chronic liver disease, hemolytic anemia, or incomplete data were excluded.

#### **Definition of prolonged cholestasis:**

Prolonged cholestasis was defined as persistence of predominantly conjugated hyperbilirubinemia with total bilirubin >5 mg/dL beyond four weeks from diagnosis, in the absence of biliary obstruction on ultrasound [16].

#### **Data collection:**

Clinical variables (age, gender, pruritus, fever, abdominal pain, dark urine, pale stools) and laboratory parameters (ALT, AST, ALP, total and direct bilirubin) were extracted from hospital records.

#### **Statistical analysis:**

SPSS version 26 was used to analyze the data. Categorical data were reported as frequency (%), and continuous variables as mean  $\pm$  SD or median (IQR). Chi-square or the t-test were used to compare independent variables. Multivariable logistic regression was used to find independent predictors of persistent cholestasis for variables with  $p < 0.1$ . Statistical significance was defined as  $p < 0.05$ .

### **Results**

Out of 150 adolescents, 12% developed prolonged cholestasis. Female sex (61.1%), severe pruritus (55.6%), and peak total bilirubin levels above 15 mg/dL (median 18.2 mg/dL) were significantly associated with prolonged cholestasis ( $p < 0.05$ ). The multivariable logistic regression identified peak bilirubin >15 mg/dL (aOR 4.8,  $p = 0.003$ ), female sex (aOR 3.1,  $p = 0.03$ ), and severe pruritus (aOR 2.9,  $p = 0.046$ ) as independent predictors. ALP levels exceeding twice the upper limit of normal were also linked to prolonged cholestasis ( $p = 0.04$ ), highlighting important clinical indicators for early intervention and management.

**Table 1. Baseline characteristics of study population**

| Variable                                      | Overall<br>(n=150) | Prolonged<br>cholestasis (n=18) | No prolonged<br>cholestasis (n=132) | p-<br>value |
|-----------------------------------------------|--------------------|---------------------------------|-------------------------------------|-------------|
| Age (years, mean $\pm$ SD)                    | 15.2 $\pm$ 2.1     | 16.0 $\pm$ 1.8                  | 15.1 $\pm$ 2.1                      | 0.08        |
| Female, n (%)                                 | 62 (41.3)          | 11 (61.1)                       | 51 (38.6)                           | 0.048       |
| Severe pruritus, n (%)                        | 36 (24.0)          | 10 (55.6)                       | 26 (19.7)                           | 0.002       |
| Peak total bilirubin (mg/dL),<br>median (IQR) | 8.6 (5.1–<br>15.8) | 18.2 (12.5–24.7)                | 7.4 (4.9–10.8)                      | <0.001      |
| ALT (IU/L), median (IQR)                      | 560 (320–<br>980)  | 430 (210–760)                   | 580 (340–990)                       | 0.12        |
| ALP >2 $\times$ ULN, n (%)                    | 44 (29.3)          | 9 (50.0)                        | 35 (26.5)                           | 0.04        |

The baseline and clinical features of 150 teenage hepatitis A patients are compiled in Table

1. 18 (12%) of the patients had prolonged cholestasis, with a larger percentage of females (61.1%) than males ( $p = 0.048$ ). Prolonged cholestasis was substantially correlated with severe pruritus (55.6%) and considerably raised peak total bilirubin levels (median 18.2 mg/dL,  $p < 0.001$ ). Furthermore, while variations in ALT levels were not statistically significant, the extended cholestasis group had greater ALP levels that exceeded twice the upper limit of normal ( $p = 0.04$ ).

**Table 2. Multivariable predictors of prolonged cholestasis**

| Predictor                | Adjusted Odds Ratio (aOR) | 95% CI   | p-value |
|--------------------------|---------------------------|----------|---------|
| Peak bilirubin >15 mg/dL | 4.8                       | 1.7–13.6 | 0.003   |
| Female sex               | 3.1                       | 1.1–8.7  | 0.03    |
| Severe pruritus          | 2.9                       | 1.0–8.4  | 0.046   |

The multivariable logistic regression analysis that found independent determinants of persistent cholestasis in teenage hepatitis A is shown in Table 2. The best predictor was peak bilirubin levels over 15 mg/dL (aOR 4.8, 95% CI 1.7–13.6,  $p = 0.003$ ). Higher risks of persistent cholestasis were also substantially correlated with female sex (aOR 3.1,  $p = 0.03$ ). The clinical significance of severe pruritus in disease monitoring is highlighted by the fact that it also independently predicted extended cholestasis (aOR 2.9,  $p = 0.046$ ).

## Discussion

In this study, 12% of adolescents with acute HAV infection developed prolonged cholestasis, consistent with international reports ranging between 3% and 15% [1,6,8]. The best predictor was peak bilirubin >15 mg/dL, which indicates a more severe cholestatic biochemical reaction [17]. This is consistent with the findings of Kwon et al. [10] and Saboo et al. [4], who similarly found a correlation between longer disease duration and higher baseline bilirubin levels. In line with results from adult studies by Coppola et al. [3] and Alebaji et al. [2], female sex was another independent predictor that may be related to hormonal regulation of bile secretion and immune response [11]. As also reported by Gökçe et al. [7], severe pruritus at beginning predicted protracted cholestasis, where pruritus indicated increased bile acid accumulation and slower resolution [12]. Intrahepatic

bile stasis, immune-mediated canalicular injury, and genetic polymorphisms affecting bile acid transporters (ABCB4, ABCB11) are probably involved in the pathophysiology [9,10]. Additionally, viral variables including genetic variations may be involved, according to recent research [18]. UDCA and corticosteroids are showing positive results in certain refractory instances, and management is still supportive [13,14]. Similar patterns were observed in the alleviation of symptoms in our population. Our study's strengths include its analytical technique and targeted adolescent population. Retrospective design, a single-center setting, and the absence of genetic or viral characterization are among the limitations. However, the results provide clinically significant indicators that can direct at-risk teen surveillance and counseling. Early identification of cholestasis-prone patients reduces needless interventions and anxiety by enabling prompt beginning of antipruritic medicine, reassurance, and follow-up.

## Conclusion

In adolescents with hepatitis A, chronic cholestasis is significantly predicted by higher peak bilirubin (>15 mg/dL), female sex, and severe pruritus. Clinicians can provide early counseling and better follow-up planning by being aware of these risk factors.

## Authors Contribution

**Concept & Design of Study:** Muhammad Bilal Khattak<sup>1</sup>

**Drafting:** Jahanzeb Khan Afridi<sup>2</sup>

**Data Collection & Data Analysis:** Hameed ullah<sup>3</sup>

**Critical Review:** Muhammad khadim<sup>4</sup>

**Final Approval of version:** Zaynab<sup>5</sup>

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