



## PATTERNS AND OUTCOMES OF DRUG-INDUCED LIVER INJURY IN HEPATITIS A: A PROSPECTIVE OBSERVATIONAL STUDY FROM A TERTIARY CARE CENTER IN NORTH INDIA.

Zeeshan Ahmad Wani<sup>1</sup>, Rameez Raja Najar<sup>1\*</sup>, Afrah Nasir<sup>1</sup>, Muzamil Majeed<sup>1</sup>

<sup>1</sup>GMC Srinagar, Jammu and Kashmir UT, India 190010

Corresponding author: Rameez Raja Najar

---

### Abstract

#### Background:

Hepatitis A virus (HAV) infection is typically self-limiting, but atypical presentations and complications like drug-induced liver injury (DILI) can complicate its course. This study analyzes the pattern, frequency, and impact of DILI among patients with HAV and its role in the progression to severe liver outcomes.

#### Aims and Methods:

This prospective observational study was conducted over a one-year period at a tertiary care center in North India (Kashmir), including 105 patients aged 8–45 years diagnosed with HAV-related hepatitis. The study focused on clinical features, biochemical parameters, patterns of DILI, associated use of complementary and alternative medicine (CAM), response to corticosteroids, and severe outcomes such as acute liver failure (ALF), liver transplantation, and mortality. Statistical analysis was conducted using SPSS software; a p-value <0.05 was considered statistically significant.

#### Results:

Out of 105 patients, 5 (4.76%) developed DILI. All DILI cases had a history of CAM intake prior to admission. These patients presented with exaggerated cholestatic patterns (serum bilirubin >20 mg/dL in 60% of DILI cases) and markedly elevated liver enzymes (mean ALT: 2950 u/L). DILI was associated with a prolonged cholestatic course in 80% of cases and contributed to deterioration in 2 of the 3 ALF patients. Steroid therapy led to a favorable response in 100% of the 60 patients treated, including 4 of the 5 DILI patients. Among the ALF cases, one patient with suspected DILI-related exacerbation required liver transplantation, one responded to plasma exchange, and one died despite supportive care.

#### Conclusion:

DILI is an under-recognized but important contributor to atypical and severe courses of HAV infection. A detailed drug and CAM history is crucial in HAV patients. Early recognition and corticosteroid therapy may mitigate DILI-induced liver injury. Further multicentric studies are needed to understand the pathogenesis and management of DILI in viral hepatitis.

**Keywords:** Hepatitis A, Drug-induced liver injury, Complementary and alternative medicine, Cholestasis, acute liver failure, Steroids.

## Introduction

Hepatitis A virus (HAV) infection, caused by a nonenveloped RNA virus of the Picornaviridae family, is typically a self-limiting illness. While the majority of cases resolve uneventfully, a subset develops atypical manifestations including prolonged cholestasis, relapsing hepatitis, or rarely, acute liver failure (ALF)[1].

Drug-induced liver injury (DILI) is an increasingly recognized complication in viral hepatitis and is often linked with the intake of unregulated complementary and alternative medicines (CAM), especially in developing countries. DILI can worsen the course of hepatitis, mimicking or amplifying the cholestatic pattern or even triggering ALF[2,3].

This study explores the frequency and clinical patterns of DILI in patients with HAV and examines its impact on disease severity and outcomes.

## Materials and Methods

This prospective observational study was conducted over one year in a tertiary care hospital in Kashmir, North India. A total of 105 patients aged 8–45 years presenting with HAV infection (confirmed via serology) were included. Data Collection was done on inpatient basis ,collected demographics and age of presentation, Use of CAM prior to admission. History and clinicobiochemical parameters including jaundice, hepatomegaly, Liver function tests (LFTs) and coagulogram (INR/PT). Patients were diagnosed with DILI based on temporal association with drug/CAM intake, biochemical pattern (e.g., hepatocellular, cholestatic, mixed), and exclusion of other causes. Patterns of DILI and severe outcomes was noted over a study period. Use of steroids ,clinical response and associated severe outcomes in the form of Acute liver failure(ALF), liver transplantation, mortality observed over 1 year were noted. Statistical Analysis was done using SPSS software was used. Frequencies, means, and proportions were calculated. A p-value <0.05 was considered statistically significant.

## Results

### a) Biochemical Profile of DILI Cases

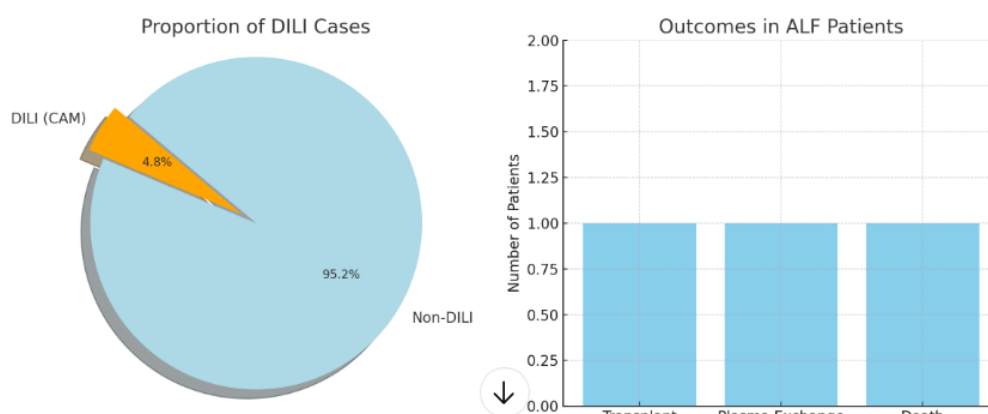
Out of 105 patients, 5 (4.76%) developed DILI. All DILI cases had a history of CAM intake prior to admission. These patients presented with cholestatic patterns of liver injury with serum bilirubin exceeding >20 mg/dL in 60% of DILI cases and showed markedly elevated liver enzymes with mean ALT: 2950 u/L. DILI was associated with a prolonged cholestatic course in 80% of cases and contributed to deterioration in 2 of the 3 ALF patients as shown in Table 1.

**Table 1. Summary of DILI and pattern of its injury in acute Viral hepatitis**

|                                           |                 |
|-------------------------------------------|-----------------|
| Total patients                            | 105             |
| DILI cases (CAM-related)                  | 5 (4.76%)       |
| Mean ALT (U/L)                            | 2950            |
| Serum bilirubin >20 mg/dL (DILI)          | 3 (60%)         |
| Prolonged cholestatic course (DILI)       | 4 (80%)         |
| DILI patients with ALF                    | 2 of 3          |
| DILI patients receiving steroids          | 4 of 5          |
| Favorable steroid response (all patients) | 60 of 60 (100%) |

## b) Association with Acute Liver Failure

Out of 105 patients, CAM-related DILI was seen in 4.76%~4.8%. 3 patients developed Acute liver failure(ALF). Among the ALF cases, one patient with suspected DILI-related exacerbation required liver transplantation, one responded to plasma exchange, and one died despite supportive care as is shown in figure



**Figure 1. DILI incidence and its associated outcomes in Acute Hepatitis.**

## c) Response to Steroid Therapy

Steroid therapy led to a favorable response in 100% of the 60 patients treated, including 4 of the 5 DILI patients. This suggests a potential benefit of corticosteroids in selected cases of DILI, especially when an immune-mediated mechanism is suspected.

## Discussion:

In this study, we enrolled 105 patients, of which Drug induced liver injury (CAM) was observed in 5 cases (4.76%). All of them gave history of CAM intake. Previous studies have highlighted the role of CAM in DILI pathogenesis [4,5]. The DILI subgroup in our cohort demonstrated cholestatic pattern, with serum bilirubin exceeding 20 mg/dL in 60% of cases and mean ALT levels reaching 2950 U/L. These biochemical patterns reflect an exaggerated hepatic injury, comparable to reports from other DILI registries, particularly those related to herbal and dietary supplements [6,7]. Moreover 80% of DILI cases followed a prolonged cholestatic course which is inconsistent with previous studies suggesting that CAM-related DILI may have a delayed or sustained resolution phase [8]. Importantly, DILI contributed to clinical deterioration in 2 of the 3 patients who progressed to acute liver failure (ALF), reinforcing the severe impact such injuries can have when superimposed on pre-existing hepatic stress. One ALF patient required liver transplantation, while another responded favorably to plasma exchange. The third patient succumbed despite maximal supportive care. This highlights the variable and often unpredictable trajectory of DILI, particularly in severe presentations. Steroid therapy was administered to 60 patients in our cohort and demonstrated a favorable response in all treated cases, including 4 of the 5 DILI patients. While corticosteroids remain controversial in idiopathic or viral hepatitis, they have shown potential benefit in immune-mediated DILI or in cases with significant inflammation on liver histology [9]. Our findings lend support to the selective use of steroids in DILI, particularly when clinical and biochemical features suggest an immune-allergic mechanism. Our results have got clinical implications particularly in resource limited settings where DILI especially CAM intake is widespread. Early identification of DILI in viral hepatitis is essential to prevent progression to severe liver injury. Furthermore, clinicians should maintain a high index of suspicion for CAM-induced DILI in patients presenting with acute or cholestatic hepatitis patterns, especially when accompanied by rapid clinical decline.

Limitations of this study include the small number of DILI cases, lack of histological confirmation and the challenges in establishing definitive causality between CAM intake and DILI given the multifactorial nature of liver injury are acknowledged. Future multicentric studies incorporating liver biopsy and standardized causality assessment (e.g., RUCAM) would provide deeper insights.

**Conclusion:** CAM related DILI on top of viral hepatitis presents with severe cholestatic liver injury and ALF in some cases. Our study lend support to the selective use of steroids in DILI, particularly when clinical and biochemical features suggest an immune-allergic mechanism. Early recognition and high index of suspicion could help in improving outcomes and prevent progression.

## References

1. Cyriac Abby Philips, Philip Augustine, Sasidharan Rajesh et al. Complementary and Alternative Medicine-related Drug-induced Liver Injury in Asia J Clin Transl Hepatol. 2019 Sep 28;7(3):263-274.
2. Desmond Chun Hwee Teo, Patricia Suet Leng Ng, Siew Har Tan et al. Drug-induced liver injury associated with Complementary and Alternative Medicine: a review of adverse event reports in an Asian community from 2009 to 2014. BMC Complement Altern Med. 2016 Jul 7;16:192
3. Luke Hillman, Michelle Gottfried, Maureen Whitsett, Jorge Rakela et al. Clinical Features and Outcomes of Complementary and Alternative Medicine Induced Acute Liver Failure and Injury. Am J Gastroenterol. 2016 Apr 5;111(7):958-965.
4. Navarro VJ, Khan I, Björnsson E, Seeff LB, Serrano J, Hoofnagle JH. Liver injury from herbal and dietary supplements. *Hepatology*. 2017;65(1):363-373.
5. Teschke R, Frenzel C, Schulze J, Eickhoff A. Herbal hepatotoxicity: challenges and pitfalls of causality assessment methods. *World J Gastroenterol*. 2013;19(19):2864-2882.
6. Chalasani NP, Maddur H, Russo MW, Wong RJ, Reddy KR. ACG Clinical Guideline: Diagnosis and Management of Idiosyncratic Drug-Induced Liver Injury. *Am J Gastroenterol*. 2021;116(5):878-898.
7. Philips CA, Paramaguru R, Joy AK, et al. Clinical outcomes, histopathology and HLA typing in drug-induced liver injury (DILI) due to antituberculosis treatment. *Liver Int*. 2018;38(10):1830-1838.
8. Björnsson ES. Drug-induced liver injury: an overview over the most critical compounds. *Arch Toxicol*. 2015;89(3):327-334.
9. Lucena MI, Andrade RJ, Kaplowitz N, et al. Phenotypic characterization of idiosyncratic drug-induced liver injury: the influence of age and sex. *Hepatology*. 2009;49(6):2001-2009.