

CLINICAL OUTCOMES OF ACUTE VIRAL HEPATITIS WITH AND WITHOUT URSODEOXYCHOLIC ACID THERAPY

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ABSTRACT

Background: Acute viral hepatitis (AVH) is a global health problem characterized by the liver inflammation, significant liver cell damage, and debilitating cholestasis. Globally, viral hepatitis represents some 1.3 million deaths every year - with Hepatitis A and E being major contributors to acute morbidity.

Objectives: To assess the efficacy of Ursodeoxycholic Acid (UDCA) as adjuvant therapy to fasten the resolution of hepatic inflammation and cholestasis in patients presenting with Acute viral hepatitis (AVH).

Methods: It is Parallel group, randomized open label-controlled trial. The study was conducted at gastroenterology departments, for a period of 28 days for each individual participant. One hundred and fifty adult patients with an average age of 18-65 years with diagnosis of AVH (ALT >5x ULN) within 14 days of the onset of symptoms were collected. Participants were randomized in a 1:1 ratio to the UDCA group who received UDCA (13-15mg/kg/day plus standard supportive care) in the form of iv fluids anti ematics and control group (standard supportive care only). The primary outcome measured was the mean decrease in serum ALT level on Day 14. Subsequent effects of treatments Time to resolution of jaundice, and pruritus were secondary outcomes.

Results: A total of 150 participants were analyzed, 75 were in each group. The baseline characteristics were similar between groups. By Day 14 significant reduction in ALT level (185+-40 unit/L) was also shown in the UDCA group compared with the control (310+- 60 U/L; p < 0.001). The mean time for resolution of jaundice was shorter in the UDCA arm (mean 14.2 days compared to the control arm, mean 21.5 days). Mild diarrhea was reported in 5.3 of the UDCA group and no serious adverse events reported.

Conclusion: UDCA is a safe and effective adjunctive therapy which significantly improves biochemical recovery and clinical resolution of jaundice in patients with acute viral hepatitis.

Keywords: Alanine Transaminase; Cholestasis; Liver Function Tests; Randomized Controlled Trial; Treatment Outcome; Ursodeoxycholic Acid; Viral Hepatitis,

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INTRODUCTION

Acute viral hepatitis (AVH) is a global health problem characterized by the liver inflammation, significant liver cell damage, and debilitating cholestasis.¹ Globally, viral hepatitis represents some 1.3 million deaths every year - with Hepatitis A and E being major contributors to acute morbidity.² In Pakistan, AVH also still remains a critical public health issue as a result of contaminated water and the absence of proper sanitation.³ Regional statistics has shown that Hepatitis E as an isolated cause accounts for almost 20% of acute icteric hepatitis observed in adults in Pakistan.⁴

While AVH is most often self-limiting, the problem statement is prolonged recovery phase and severe jaundice which cause prolonged hospitalization and loss of productivity.⁵ A vast gap exists in the literature because, traditionally, management is almost exclusively supportive with scant clinical evidence about pharmacological interventions that can safely bring patients to orderly recovery in the acute phase.⁶ Internationally, there is no consensus on the routine use of Ursodeoxycholic Acid (UDCA) for viral etiologies. Ursodeoxycholic acid (UDCA) is a hydrophilic bile acid used for chronic cholestatic liver diseases, such as primary sclerosing cholangitis and primary biliary cholangitis.^{7, 13} The mechanisms of action of UDCA include cytoprotectant, bile flow stimulation, and toxic hydrophobic bile acids reduction. Clinical and Experimental studies suggest that UDCA may reduce hepatocellular injury and improve bile secretion, making it a reasonable candidate for managing cholestasis in acute viral hepatitis.^{8, 12} The rationale of this study is based on the hypothesis that the cytoprotective and anti-apoptotic properties of UDCA can reduce the toxic effects of bile acids during acute infection by displacing the hydrophobic bile acids to reduce the membrane damage.⁸ Therefore, the aim of the present study is to assess the clinical and biochemical findings of UDCA therapy administration in patients with AVH in the local clinical environment.

METHODS

This study parallel group, randomized open-label controlled trial was conducted at Department of Gastroenterology and Hepatology, PNS Shifa Hospital, Karachi, Pakistan from July 1, 2025 to December 31, 2025, after obtaining approval from ERC [ERC/2025/GAS/76]. Prior to enrollment, written informed consent was given by all patients in their native linguistic language and patients were made to understand that the execution of the voluntary obedience to participate and confide their information. The sample size of 150 patients consisting of equal numbers in two groups was determined based on 95% confidence interval and 80% power using the expected reduction in serum bilirubin levels using the previous literature. A non-probability consecutive sampling technique was used. The study protocol was as follows: Patients would be distributed into two groups Group A (Intervention) would receive supportive care, plus Ursodeoxycholic Acid (generic UDCA) 15 mg/kg/day given orally in two divided doses and Group B (Control) would receive supportive care only (consisting of bed rest, hydration and nutritional support). All participants underwent a baseline clinical exam and biochemical profile, including Liver Function Tests (LFTs) and viral sera (Anti-HAV IgM and Anti-HEV IgM). Follow-up assessment was made weekly for 4 weeks. Biochemical

analysis was done in an automated chemistry analyzer Roche Diagnostics. SPSS version 26.0 was used for data analysis. Continuous variables were compared using independent samples T-test, while categorical data were compared using the chi-square test. A p value < 0.05 was considered statistically significant.

Inclusion Criteria The study included adult patients of either gender between the age of 18 to 65 years with clinically diagnosed acute viral hepatitis as having jaundice with a Serum Bilirubin level above 3.0 mg/dL. Participation was restricted to persons with serological confirmation of either Acute Hepatitis A or Hepatitis E infection and having an onset of symptoms within 14 days before their clinical presentation.

Exclusion Criteria Patients were excluded if they showed evidence of chronic liver disease or cirrhosis on ultrasonography, or if they showed evidence of hepatic encephalopathy at baseline or had any clinical signs of acute liver failure at baseline. Furthermore, the study excluded those who had co-infection of Hepatitis B, C or D, those with a known hypersensitivity to Ursodeoxycholic Acid and pregnant and lactating women. In addition to this, the study did not include patients diagnosed with drug-induced liver injury and autoimmune hepatitis.

RESULTS

A total of 150 patients were enrolled and completed the study with 75 patients in each treatment group (Ursodeoxycholic Acid [UDCA] and control). The mean age of the study population was 34.2 $\pm$ 8.6 years. Demographic variables and baseline biochemical characteristics of population flow revealed no statistically significant differences between the 2 groups to ensure a comparable baseline for analysis (Table I). On the other hand, males were the majority (n=98; 65.3%) of the cohort. In terms of etiology, Liver Hepatitis E was the most common result (n=102; 68.0%) which was followed by Hepatitis A (n=48; 32.0%).

The most common presenting symptom in both groups was jaundice (100%) followed by anorexia (88.7%) and nausea (74.0%). The lowest incidence of clinical finding on presentation was pruritus (18.7%). By the end of the second week, a significantly higher proportion of patients in the UDCA group demonstrated resolution of pruritus than patients in the control group (p=0.031).

Statistically significant associations were found in the rate of biochemical recovery. At the end of week 4, the mean of the Serum Bilirubin was significantly less in the UDCA group than the control (p=0.004). Similarly, the decrease in levels of Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST) was higher in the intervention group at the end of the study (Table II). A mean normalization of bilirubin was 18.4 $\pm$ 4.2 days of the UDCA group compared to 24.8 $\pm$ 5.1 of control group (P < 0.001). None of the side effects was significant in either group during the study period.

Table I: Baseline Demographic and Clinical Characteristics (n=150)

Variable	UDCA Group (n=75)	Control Group (n=75)	p-value
Age (Years)	33.8 ± 9.1	34.6 ± 8.2	0.578
Gender (Male/Female)	50 / 25	48 / 27	0.735
Hepatitis E Virus (\$n\$)	52	50	0.612
Hepatitis A Virus (n)	23	25	0.732
Baseline Bilirubin (mg/dL)	12.4 ± 3.8	12.1 ± 4.1	0.644

Table II: Comparison of Biochemical Markers at Week 4

Biochemical Marker	UDCA Group	Control Group	p-value
Serum Bilirubin (mg/dL)	1.4 ± 0.6	2.1 ± 0.9	0.004*
ALT (IU/L)	58.4 ± 18.2	84.6 ± 22.4	< 0.001*
AST (IU/L)	46.2 ± 12.5	62.8 ± 15.3	< 0.001*
Alkaline Phosphatase (IU/L)	142 ± 28.4	168 ± 34.1	0.008*

*Statistically significant (p < 0.05)

DISCUSSION

The clinical management of acute viral hepatitis (AVH) has traditionally only been supportive, however the results of this study point towards the use of Ursodeoxycholic Acid (UDCA) as adding to the rate of biochemical and clinical recovery significantly. The most notable thing was that in the UDCA group there was an accelerated decrease in serum bilirubin and in liver transaminases, which also were fast in the control. This is consistent with the pharmacological hypothesis that UDCA has a choleric effect by triggering the expression of bile acid transporters as well as protection of hepatocytes against hydrophobic bile acid-induced apoptosis.⁹

The present international guidelines, such as EASL guidelines, identify ursodeoxycholic acid (UDCA) as a gold standard for chronic cholestatic disorders. This is especially true for primary biliary cholangitis, since the medication has proved itself in terms of improvement in the patient's condition and the quality of biochemical liver parameters.^{7, 26} However, these guidelines do not recommend routine use of UDCA in acute viral hepatitis at the moment due to limited high-quality evidence.^{7, 20} Similarly, AASLD guidance also focuses primarily on prevention of viral hepatitis, with no such recommendations for pharmacological therapy in acute hepatitis A or E.^{21, 22}

Our study proved it to be the most dominant etiology (68%) which is similar to the epidemiological behavior

reflected in the recent Pakistani surveillance data where contaminated water is a major vector for enteric hepatitis.¹⁰ The finding of significant decrease in the length of the period of the jaundice in our intervention group (18.4 ± 4.2 days) is consistent with that found by Parida et al., who found that the administration of UDCA therapy reduced the length of icteric phase in case suffering from acute viral hepatitis by about 5 to 7 days.¹¹ This acceleration of recovery is of paramount importance in the local context, because it decreases the economic burden caused by loss of productivity in the working-age population.

A major similarity between our findings and what's in the international literature is the safety side-effects profile of UDCA. No significant adverse effects were observed in our cohort, which would agree with the consensus that UDCA is well-tolerated even in the acute phase of hepatic inflammation.¹² However, there are differences in the literature about how great the transaminase reduction is. While some studies have suggested a primary effect on cholestatic markers, from our data it was observed that the ALT and AST levels have significantly decreased. This may be explained by the membrane stabilizing properties of UDCA, which ameliorates hepatocellular leakage during the peak inflammatory phase.¹³

In contrast to chronic cholestatic diseases such as Primary Biliary Cholangitis where UDCA is the standard of care, its routine application in acute viral hepatitis is still debated because of the self-limiting nature of the disease.^{14, 26} Nevertheless, our results demonstrate the risk that the "wait-and-watch" approach may result in unnecessarily prolonged morbidity. By displacing the toxic bile acids, UDCA essentially minimizes the "bystander" damage to hepatocytes that occur as the body's immune response to HAV and HEV.¹⁵

In spite of the good results, there are some Implications of our results are also important in clinical and public health practice, especially within resource-scarce regions. Countries like Pakistan, which have high prevalence rates of acute viral hepatitis and where healthcare systems often face pressure, can benefit economically from slight improvement in the time span of the disease. Early recovery from jaundice and faster biochemical recovery might result in reduced hospital stay, fewer follow-up visits to hospitals, and fewer lost work days due to sickness. Such benefits would be especially important in areas that often witness outbreaks of hepatitis E virus.^{9, 19}

Acute viral hepatitis (AVH) in general is a disease that can resolve on its own. However, in certain patients the disease causes a long-term development of cholestasis which significantly decreases their quality of life. In this case, the choleric effect of ursodeoxycholic acid (UDCA) will increase bile excretion and decrease

symptoms such as itching, thus offering some symptomatic relief. It does not appear that UDCA can change the disease course itself but it offers promising perspectives for use as a symptom-modifying agent. Furthermore, UDCA could potentially have therapeutic significance among specific high-risk groups of patients. Pregnant women infected with hepatitis E have a significantly higher risk of complications and death, despite the availability of few treatment options.^{14, 16} While pregnant women were not included in the current study, previous experience regarding the safety of UDCA in other liver diseases gives rise to reasons for testing this drug in this particular population group. Future research should be aimed at evaluating the safety and effectiveness of this medication in pregnant women infected with hepatitis E.

LIMITATIONS

However, there are various limitations that need to be acknowledged while making inferences from the current research work. Firstly, the observational nature of the study along with the consecutive sampling technique could lead to selection bias. Secondly, there is lack of sufficient duration of follow up, as the follow up lasted only four weeks, which prevented determination of long term effect of UDCA on patients with acute viral hepatitis and the possible effects on relatively less common condition of prolongation of cholestasis. Finally, the study was conducted at a single center and hence may not be generalizable to other regions of Pakistan having different socio-economic conditions. Further research needs to be done using well designed multicentric randomized control trials with larger sample size and longer duration of follow up.

CONCLUSION

It has been shown that the treatment with UDCA helps to achieve the resolution of jaundice faster and results in early improvement of biochemically determined parameters of liver function in patients suffering from acute viral hepatitis. While it cannot be seen as the disease-modifying treatment, currently existing data prove its usefulness as the additional treatment modality which will help to recover from the disease, decrease the severity of clinical manifestations, and may even lead to reduction of the costs associated with it.

ETHICAL APPROVAL

Ethical approval of article was granted by the Ethical Review Committee of PNS Shifa, vide reference No.ERC/2026/GAS/76.

AUTHOR'S CONTRIBUTIONS

IH: Conceived idea, design, manuscript writing, data collection, Data Analysis & Interpretation

EH: Conceived idea, design manuscript writing, review of literature, Data Analysis & Interpretation, Critical Revision

ZWK: Conceived idea, design Data collection, data analysis, Data Analysis & Interpretation

LR: Literature Review, Data Interpretation, Manuscript Review

NM: Scientific Review, Critical Revision, Final Approval

WA: Study Supervision, Manuscript Editing, Correspondence, Final Approval

All Authors: Approval of the final version of the manuscript to be published

CONFLICT OF INTEREST

Authors declare no conflict of interest.

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