Europasian Journal of Medical Sciences
EJMS
https://doi.org/10.46405/ejms.v3i2.255
Short Communication

Evaluation of liver enzymes and calculation of AST to ALT ratio in patients with acute viral hepatitis

Arun Pandeya[1], Naveen Kumar Shreevastva[1], Arun Dhungana[1], Anup Pandeya[2], Binita Pradhan[3]

Author Info:

[1]Assistant Professor, Department of Biochemistry, Kathmandu Medical College, Basic Sciences Block, Duwakot

[2]PhD Scholar, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand

[3]Associate Professor, Department of Emergency Medicine, Kathmandu Medical College, Kathmandu Nepal

***Corresponding Author:**

Mr. Arun Pandeya

Email: arnpandey@gmail.com

ABSTRACT

Background: Acute viral hepatitis is a common liver-associated abnormality encountered in clinical practice. The number of biochemical parameters is estimated to detect a hepatic abnormality, which can measure the severity and types of damage to hepatocytes, among which liver enzymes and bilirubin levels are assessed routinely which are raised in acute viral hepatitis.

Objective: This study aims to assess the liver enzymes, such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin, and calculation of AST to ALT ratio in acute viral hepatitis and to compare these parameters with the control group.

Methodology: This study included a total of 81 subjects diagnosed with acute viral hepatitis as cases and age and sex-matched, the same number of healthy subjects as control. Serum levels of AST and ALT, alkaline phosphatase (ALP), and bilirubin were analyzed using standard methods. Serum AST to ALT ratio was calculated. Data analysis was done using SPSS Version 17.0 and the results were expressed as mean ±standard deviation (SD).

Results: A mean serum activities of aminotransferases were statistically significantly raised in viral hepatitis compared to that in control.AST (514.85±350.66 VS 25.65±5.29; $p<0.001$) and ALT (781.65±525.69 VS 27.94±6.50; $p<0.001$). Similarly, serum levels of(ALP)were significantly increased in acute viral hepatitis compared to that in control (202.17±75.46 VS 98.83±27.99; $p<0.001$. However, a ratio of AST to ALT was decreased significantly (0.66±0.15 VS 0.94±0.21; $p= 0.001$) in acute viral hepatitis compared to that in control.

Conclusion: Both the aminotransferases and bilirubin levels are raised significantly, where, a rise in ALT is greater than a rise in AST, hence, the ratio of AST to ALT is decreased significantly in acute viral hepatitis than that in control. Thus, this decreased pattern of AST to ALT can diagnose acute viral hepatitis at an early stage and can help appropriate care and treatment to the patients.

Keywords: acute viral hepatitis, aminotransferases, AST to ALT ratio, liver function tests

QR Code	Article Info
Scan Me for Full Text	**Received**: 27 July 2021; **Accepted**: 30 December 2021; **Published Online**: 31 December 2021
View PDF	How to cite this article in Vancouver Style?
	Pandeya A, Shreevastva NK, Dhungana A, Pandeya A, Pradhan B. Evaluation of Liver Enzymes and calculation of AST to ALT ratio in patients with acute viral hepatitis. Europasian J Med Sci. 2021; 3(2):90-93. https://doi.org/10.46405/ejms.v3i2.255
	Disclaimer
	Conflict of Interest: None Declared; **Source of Support:** Nil
	Publisher's Note

Crossref 10.46405/ejms
https://doi.org/10.46405/ejms.v3i2.255

INTRODUCTION

Hepatitis which is most commonly caused by hepatitis viruses is an inflammatory condition of the liver showing the symptoms of jaundice, nausea, vomiting, and abdominal pain.[1] Viral hepatitis is one of the public health challenges in the world[2] and its prevalence in Kathmandu Nepal is 24.5%.[3] Several biochemical tests such as aminotransferases- alanine aminotransferase (ALT) and aspartate aminotransferase (AST), alkaline phosphatase (ALP), and bilirubin are evaluated to assess liver function tests[4] which help detect the integrity of hepatocytes. Similarly, an alteration of liver enzymes and bilirubin provides important information for the diagnosis of liver disease- hepatocellular damage or post-hepatic obstruction.[5,6]

Increased activity of ALT and AST in plasma mainly emphasizes hepatic cell damage due to either viruses or alcohol or ischemic conditions.[7] With the progression of the liver disease, intracellular ALT and AST are released on circulation, among which ALT is more specific to the liver. Also, ALT persists longer on plasma because of its higher half-life than that of AST.[8]

Viruses cause intrahepatic inflammation that disrupts the normal transport of conjugated bilirubin resulting in conjugated hyperbilirubinemia.[9] ALP being present on the surface of bile duct epithelial cells, any type of cholestasis leads to its release and makes its higher values on plasma.[6]

Nowadays, a ratio of the serum activities of AST to ALT, known as the De Ritis ratio is calculated which indicates different types of hepatitis based on etiology.[10] Early detection of viral hepatitis supports appropriate care and treatment which not only lowers the burden of disease but also improves the outcomes against the viral infection and helps treat the patient at the earliest. This study aimed to compare the various markers of liver function in acute viral hepatitis as well as to find the efficacy of the AST to ALT ratio in such patients.

MATERIALS AND METHODS

A Prospective study was conducted in Kathmandu Medical College Teaching Hospital from March 2019 to October 2019 and includes a total of 162 study population.

A convenient sampling technique was used and census sampling was done in patients who visited the medicine out-patient department and were diagnosed with acute viral hepatitis were enrolled as cases, similarly, age and sex-matched healthy subjects without any known hepato-renal diseases were included as controls. Any patients with other forms of hepatobiliary disorders, diabetes mellitus, hypertension, and renal disorders were excluded from the study. This study was ethically approved and informed oral consent was taken from all the participants.

Sample collection and estimation: Five ml of blood was drawn by venipuncture under aseptic

precaution in the fasting condition in a plain tube. The serum was separated and was transferred into a plastic tube. The activity of Serum ALT, AST, and ALP as well as the levels of bilirubin were estimated using Selectra Pro S auto analyzer using Elitech reagents. Values of AST and ALT >45IU/L; value of ALP >306 IU/L were considered as abnormal values.

Statistical Analysis: Statistical analysis was done using SPSS for Windows version 17.0. Results were expressed as mean ±SD. Comparison of variables between two groups was performed with Student's t-test for continuous variables. The p values < 0.05 were considered statically significant.

RESULTS

This study was carried out on 81 patients suffering from viral hepatitis as well as age and sex-matched same number of the control group were recruited for the study. The age and gender-wise distribution of the study participants are summarized in **table 1**.

Serum activities of aminotransferases- such as AST and ALT were raised significantly, however, a ratio of AST to ALT was decreased significantly in acute viral hepatitis compared to that in control. Serum activity of ALP as well as the levels of total and conjugated bilirubin were raised significantly in viral hepatitis compared to that in control, which is summarized in **table 2.** A very high number of cases with acute viral hepatitis (95.1%) had the AST to ALT ratio of <1 but a lesser number of controls had the ratio of AST to ALT <1 which is depicted in **table 3.**

Table 1: Age and gender-wise distribution of study participants

	Viral hepatitis (Mean±SD)	Control
Age (years) (Mean±SD)	46.77±12.24	45.72±12.76
Gender (Males%)	60 (74.1 %)	53 (65.4%)
(Females%)	21 (25.9 %)	28 (34.6%)

Table 2: Comparison of various biochemical parameters in acute viral hepatitis and the control group

Parameters	Viral hepatitis (Mean±SD)	Control (Mean±SD)	P-value
AST	514.85± 350.66	25.65± 5.29	<0.001
ALT	781.65± 525.69	27.94± 6.50	<0.001
AST/ALT	0.66±0.15	0.94±0.21	0.001
ALP	202.17±75.46	98.83±27.99	<0.001
Total Bilirubin	4.91± 1.64	0.71± 0.25	<0.001
Direct Bilirubin	2.15± 1.12	0.21± 0.16	<0.001

Table 3: Intervals of De Ritis ratio in viral hepatitis and control group

De Ritis	Viral Hepatitis	Control
0.5-0.99	77 (95.1%)	48 (59.3%)
≥1	4 (4.9%)	33 (40.7%)

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DISCUSSION

Findings of the present study revealed significantly increased levels of AST, ALT, ALP, and bilirubin in serum whereas a significantly reduced value of AST to ALT, the De Ritis ratio, in viral hepatitis compared to that in control. Aminotransferases, namely AST and ALT are the analytes that are commonly estimated for the assessment of Liver function tests. Among aminotransferases, AST is mainly present inside mitochondria of hepatocytes, RBCs, skeletal muscle cells, etc. whereas ALT is specifically present in the cytosol of the hepatocytes. Therefore, damage to hepatocytes will cause the release of these enzymes into plasma. The present study showed significantly raised levels of AST and ALT in viral hepatitis compared to that in control. Similar to the findings of the present study, a study conducted by Arthi et al. showed increased levels of AST and ALT in viral hepatitis.[11] Also, a study carried out by Ashraf-Uz-Zaman et al. found raised levels of AST as well as ALT in all types of viral hepatitis.[12] Though both the aminotransferases- AST and ALT are escalated in viral hepatitis, ALT is greater than that of AST due to which a ratio of AST to ALT, known as De Ritis ratio is most often below 1.0, and is in between 0.5 to0.7.[13] The present study also found a decreased AST to ALT ratio in viral hepatitis (0.66±0.15) compared to that in control (0.94) which is inconsistent with the findings of Arthi et al. and Benerji et al. [11,14]

Since, hepatitis virus damages the hepatic cell due to which hepatic enzymes, such as AST and ALT are released on plasma. Because the half-life of ALT on circulation is higher than the half-life of AST, the former remains on circulation for longer periods, which makes the higher activity of ALT on plasma, resulting in a lowered ratio of AST to ALT in viral hepatitis. Therefore, despite having more sophisticated techniques such as PCR, several-fold elevations in serum aminotransferases and a decline in AST to ALT ratio can be useful in diagnosing the etiology of acute hepatitis.[15]

Though the ratio of AST to ALT is altered due to alteration of either AST or ALT, its calculation is beneficial in a situation that even if serum levels of AST may be statistically insignificant in hepatitis of different etiology, the ratio differs significantly.[11] Moreover, in most cases of viral hepatitis, this ratio is below one, but an increase in this ratio may be a sign of progressing towards chronic hepatitis or cirrhosis. Even more, a raised ratio of AST to ALT only slightly above one suggests deterioration towards chronic viral hepatitis C to cirrhosis.[16]

Almost all cases (95.1%) with viral hepatitis showed a De Ritis ratio of less than one which indicates though both the aminotransferases are significantly raised in acute viral hepatitis, a rise in ALT is higher than a rise in AST making this ratio lesser than one. Inconsistent with the findings of this study, many studies have shown the ratio of AST to ALT lesser than one.[14,17] Therefore, a decrease in AST to ALT ratio (lesser than one) in acute viral hepatitis also gives a clue that the disease is being resolved at the time when testing occurs. And if the disease would not have been resolved, an AST/ALT ratio would not decrease.[18]However, a very small number of cases with acute viral hepatitis (4%) showed a De Ritis ratio of more than one. The cause for an increased ratio may be a sign of fulminant disease representing a lesser chance of prognosis. Even more, an increased ratio of AST to ALT of slightly above one hint for the progression of chronic viral hepatitis C to cirrhosis.[16]

Among the control group, only around 59% of the subjects showed the ratio of AST to ALT lesser than one whereas others showed this ratio more than one. A decrease in the ratio of AST to ALT, lesser than one, means increased concentration of ALT than that of AST on plasma, which may be explained in terms of the half-life of these enzymes. Since the half-life of ALT is higher in plasma (47 hours) than that of AST (18 hours).[15] Therefore, AST might have been rapidly cleared from the plasma making its lesser value which in turn results in decreased AST to ALT ratio.

Inconsistent with the previous studies,[11,17] a significantly increased ALP in viral hepatitis was found in this study. Since ALP in addition to the other sources is present on the surface of bile duct epithelial, thus, an intrahepatic obstruction or any type of inflammation may cause enhanced synthesis and release of ALP making its higher value in plasma.[6]Present study also showed a statistically as well as conjugated bilirubin in cases compared to that in control. Because viruses attack and thus damage the hepatocytes. Some viruses can lead to acute liver failure as well. The damaged hepatocytes may not either uptake bilirubin, or conjugate it properly or secrete it to the bile duct, thus, resulting in hyperbilirubinemia. Besides the damaging effect to hepatocytes, viruses can cause intrahepatic inflammation that disrupts the normal transport of conjugated bilirubin through biliary canaliculi and bile duct to intestine due to which regurgitation of bilirubin in blood results in conjugated hyperbilirubinemia.[9]

CONCLUSION

Estimation of liver enzymes and the ratio of AST to ALT is essential to understand the extent and types of liver damage and to diagnose viral hepatitis. Hence, this ratio is considered a reliable marker for the diagnosis of viral hepatitis. Since this study included some of the biochemical parameters only, further studies with a greater sample size as well as with many biochemical parameters are necessary for more accurate diagnosis and for differentiating viral hepatitis from other forms of liver diseases.

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