Research Article

Viral Load by RT-PCR as a Marker of Severity in Children with Hepatitis A

Dr Ayub Ansari[1], Dr Shrish Bhatnagar[1], Dr Tasleem Raza[1]

Author's Affiliation:
1- Department of Pediatrics, Era's Lucknow Medical College and Hospital, India.

Correspondence:
Dr Shrish Bhatnagar, Professor and Head, Department of Pediatrics, Era's Lucknow Medical College and Hospital, Lucknow Sarfarzganj, Hardoi Road, Lucknow Pin 226003 Ph: 0 9648234797 drshrishbhatnagar@gmail.com

Received on: 06-Dec-19

Accepted for Publication: 31-Dec-19

Abstract:

Objectives: To study the association between severity and viral load in children suffering from acute Viral A Hepatitis.

Methods: 50 patients of Acute Viral A Hepatitis were enrolled into the study. They were divided into acute hepatitis (Group I), severe acute hepatitis (Group II) and fulminant hepatitis (Group III), based on PT time and Hepatic encephalopthy. Viral load was assessed by Real Time PCR using quantitative assay.

Results: Majority of the patients belonged to acute hepatitis. HAV viral load of Group III (3.94±0.61 log copies/ml) and Group III (3.54±0.82 log copies/ml) was found to be statistically significantly higher than that of Group I (1.85±0.51 log copies/ml). Correlation between HAV viral load and Prothrombin time was found to be strong and statistically significant.

Conclusion: Children suffering from Acute Viral A Hepatitis with high viral load have a poor prognosis.

Keywords : Children, Hepatits A, RT PCR.

INTRODUCTION

The prevalence of hepatitis A virus has been reported to be between 30- 90% in children aged 10 years 1,2 Acute phase of infection, in general remains uneventful, however, severe cases require hospitalization and a few of them can lead to conditions like fulminant hepatic failure (3). In the recent years, an interest has been generated to evaluate whether severity of viral hepatitis caused by hepatitis A virus is dependent on the viral load. Now a days the estimation of load of viral organisms by Real-Time Polymerase Chain Reaction (RT-PCR) has become easier and precise (1,2). There is preliminary evidence available showing a significant but variable association between hepatitis A viral load and disease severity (1,2,3) However, all these studies have generally been done in small group of adult population only. Keeping in view the wider implications of severity of Hepatitis A virus in pediatric patients, the present study was planned with an aim to find out association between severity of Viral Hepatitis A and viral load in a pediatric population at a North Indian tertiary care centre.

MATERIAL AND METHODS

The prospective study was carried out among pediatric patients aged 1 to 18 years with confirmed viral hepatitis caused by Hepatitis A virus (HAV) between March 2015 to December 2016. In 145 cases of acute viral hepatitis ELISA based serological test were done for Hepatitis A, B, E and C. 50 patients presenting with fever, malaise, jaundice, nausea, vomiting, anorexia and right upper quadrant pain or raised transaminases (especially ALT) and

confirmed positive only for IgM HAV by ELISA method were included in the assessment. Informed consent and clearance from institutional ethical committee was taken. ECR/717/Inst/UP/2015/RR-18

Demographic details, immunization history, dietary preferences, hygiene status and presenting complaints were noted. Anthropometric measurements were performed. Vital recording and thorough clinical examination was done. Viral load was assessed by Real Time PCR (Applied Bio systems) using quantitative assay.

All the patients were divided into following three groups depending on the severity of viral hepatitis, *viz.* :(7, 9)

Group I: Acute Hepatitis (AH) (raised hepatic enzymes with PT >40% with no hepatic encephalopathy)

Group II: Severe Acute Hepatitis (SAH) (PT <40% with no hepatic encephalopathy)

Group III: Fulminant Hepatitis (FHF) (PT <40% with hepatic encephalopathy)

All the patients were followed up till the recovery or mortality. Association between viral load and disease severity and viral load and outcome was assessed.

DATA ANALYSIS

The data was analyzed using Statistical Package for Social Sciences (SPSS) version 15.0. Data was been represented as frequencies (Nos.) and percentages (%) for categorical data and as mean and standard deviation for continuous data. Chi-square test had been used for categorical and Analysis of variance / Independent samples "t" test had been used for comparing the parametric data in different groups. The confidence level of the study was kept at 95%, hence a "p" value less than 0.05 indicated a statistically significant association.

RESULTS

Out of 50 patients included in the study, majority were patients of acute hepatitis “Group I” (n=34; 68%), 9 (18%) were patients of severe acute hepatitis “Group II” and rest 7 (14%) were of Fulminant hepatic failure “Group III”.

Fever and loss of appetite were the most dominant prodromal symptoms across all groups. Children with FHF had significantly longer duration of jaundice (8.57$\pm$ 1.90) days than the other two groups (Table 1).

Difference in mean haematological and biochemical variables of above three groups was found to be statistically significant for only Prothrombin Time, INR, Total serum bilirubin, Direct serum bilirubin. (Table 2)

HAV viral load of Group III (3.94$\pm$0.61 log copies/ml) and Group II (3.54$\pm$0.82 log copies/ml) was found to be statistically significantly higher than that of Group I (1.85$\pm$0.51 log copies/ml) (Table 3).

Correlation between HAV viral load and prothrombin time was found to be strong and statistically significant. (Figure 1).

Both the mortalities during the period of study were from Group III. They both had at a high viral load of 4.2 and 3.9 log copies/ml at admission.

DISCUSSION

In present study, 50/145 (34%) cases of acute viral hepatitis were of hepatitis A. Duration of jaundice was significantly higher in cases with FHF group.

In present study, coagulation factors showed a significant association with severity of acute viral hepatitis A. It was observed that PT and INR values were significantly higher in FHF failure group as compared to rest of 2 groups. This finding is an established fact as demonstrated by various studies of Kim *et al.* (3), Newsome *et al.*

(10) and hence prothrombin time has been taken as a criteria for segregation between severe and non-severe viral hepatitis (1).

The mean viral load showed a significant difference among the 3 groups, it was found to be higher in severe acute hepatitis (3.54±0.82) and fulminant liver failure (3.94±0.61) as compared to that in acute hepatitis (1.85±0.51) groups. Contrary to the findings of present study, Sainokami *et al.*(7) reported viral load ≥4 log copies/mL to be present in 63.0% of mild and 75% of severe acute hepatitis cases but did not find this difference to be significant statistically. However, Fujiwara *et al.* (9) in their study found a similar incremental trend of viral load as observed in present study. They reported mean admission viral load to be 2.65±1.65, 3.82±1.20 and 4.19±1.03 logcopies/ml in acute hepatitis, fulminant hepatitis and severe acute hepatitis cases. Lee *et al.* (11) in their study showed mean viral load to be 4.7 logcopies/ml in severe acute hepatitis cases as compared to 3.3 logcopies/ml in mild acute hepatitis cases, thus showing a significant association between viral load and severity of disease. In a study by Rezende *et al.* (1) low or reduced HAV load was found to be associated with FHF. They attributed it to a strong immunological response in FHF patients. The peak viral load in patients with liver failure may have been underestimated in previous study because they reached the peak viral load before admission (12). Both the cases who expired were of FHF group and had viral load ~4.0 log copies/ml. A strong positive correlation was observed between viral load and prothrombin time. Similar to results in present study, a significant mild correlation between prothrombin (%) and viral load was also observed by Lee *et al.* (11)

CONCLUSION

Thus we conclude that a child suffering from HAV related acute viral hepatitis with a prolonged duration of jaundice (>8 days) and deranged Prothrombin Time coupled with high viral load of HAV has a poor prognosis.

The study is the first work of its type in pediatric patients of Indian subcontinent. The findings in present study, despite of a preliminary basis are encouraging and endorsed the findings of previous works in adult population. Further studies in different patient groups with larger sample size and sequential monitoring of viral load might help to substantiate the pool of knowledge on this issue.

ACKNOWLEDGEMENTS Nil

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