ETIOLOGICAL STUDY OF ACUTE HEPATOCELULAR JAUNDICE WITH SPECIAL REFERENCE TO ACUTE VIRAL HEPATITIS IN NORTH EAST INDIA
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HOW TO CITE THIS ARTICLE:
Roslin Loitongbam, Anup Kumar Das, Premashish Kar, Mitul Bora, Swarup Ranjan Dey. “Etiological Study of Acute Hepatocellular Jaundice with Special Reference to Acute Viral Hepatitis in North East India”. Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 40, September 01; Page: 10069-10075, DOI: 10.14260/jemds/2014/3306

ABSTRACT: BACKGROUND: Acute viral hepatitis (AVH) due to Hepatitis-A virus infection (HAV) and Hepatitis E virus infection (HEV) are considered as a major public health problem and is an important cause of morbidity and mortality both in developing and developed countries. Acute hepatocellular jaundice can be caused by viral hepatitis, drugs, toxins, other infections and alcohol. AIM: To determine the etiology of acute hepatocellular jaundice in a tertiary care hospital of North East India and to study the biochemical changes in cases of acute hepatocellular jaundice of different etiologies. SUBJECTS AND METHODS: The study involved 121 patients of hepatocellular jaundice admitted in different medicine wards of Assam Medical College and Hospital over a period of one year. Detailed clinical and biochemical investigations were carried out. Samples were tested for routine hemogram, liver function tests and serology for different hepatotropic viruses. RESULTS: Of all cases, 82 were of viral and 39 cases were of non-viral origin. Overall, maximum cases of acute hepatocellular jaundice occurred in third and fourth decade of life. HAV (39.02%) was most common cause, followed by HEV (18.29%), HBV (4.88%) and hepatitis C (1.2%). Among non-viral cases, 20 (51.28%) were due to Falciparum malaria, 7 (17.9%) due to drugs, 6 due to alcohol, 4 due to leptospira and 2 cases were due to mushroom poisoning. Serum bilirubin, ALT, AST, alkaline phosphatase (ALP) and PT were more altered in AVH group compared to non-viral group. CONCLUSION: Hepatitis A remains the commonest cause of acute hepatocellular jaundice and there is also an increasing trend for higher age group of hepatitis A infection as opposed to malaria in non-viral acute hepatitis. Biochemical changes were more marked in AVH. KEYWORDS: Hepatocellular jaundice, acute viral hepatitis, prevalence, North East India.

INTRODUCTION: Although acute hepatocellular jaundice can be caused by variety of diseases like acute viral hepatitis, drugs and toxins including alcohol, acute viral hepatitis (AVH) is still considered to be the commonest cause. Acute viral hepatitis (AVH) remains a public health problem both in developed and developing nations including India despite the availability of vaccines, prophylactic measures and improved sanitations.

HAV has a worldwide distribution and affects infants and young children in developing countries but epidemics are rare; whereas HEV is mostly restricted to tropical countries and affects older children and young adults and hence, epidemics are common.¹-² In developing countries like India, HAV and HEV are both hyper endemic.³

Exposure rates over a period of time are different in different parts of the country and in different socio-economic groups.¹ But the whole scenario of acute hepatocellular jaundice has been changing, especially that of acute viral hepatitis in North Eastern region during the last few years due to increased incidence of multiple blood transfusions, unprotected sexual exposure, intravenous drug...
use and other socioeconomic factors. In addition, multiple infections e.g. B&C, A&B etc are increasingly being reported. Higher rates of viral infection are found in chronic alcohol users too.

Few studies describing the pattern of hepatitis viruses are available from Northern India mainly from Delhi and Chandigarh [4,5].

And very few have been conducted in this region, which looked into the full spectrum of hepatotropic viruses as the etiology. As this tertiary care hospital renders services to not only Assam but to entire North Eastern states, this study will probably reflect the whole scenario and spectrum of acute hepatocellular jaundice including non-viral causes as well in the North Eastern populations.

With these backgrounds our study was undertaken to evaluate the different causes of acute hepatocellular jaundice, to determine the incidence of different hepatotropic viruses and other causes in this region and to study the biochemical changes in these cases.

SUBJECTS AND METHODS: This study was conducted with patients >12 years of age suffering from acute hepatocellular jaundice admitted in various wards of Assam Medical College and Hospital, Dibrugarh for a period of one year.

Any patient presenting with acute onset jaundice with or without prodromal symptoms who had predominantly raised conjugated hyperbilirubinemia and disproportionate rise of AST, ALT > 3 times upper normal value, compared to serum alkaline phosphatase (SAP) were taken up for this study. Patients who developed encephalopathy after the onset of icterus were considered to have acute hepatic failure [6].

Patients who did not have a known chronic liver disease, past abdominal surgeries and co-existing illness (congestive cardiac failure, surgical jaundice, proven malignancies, liver abscess, hemolytic anaemia) were only included. Written informed consent was taken from patients or guardians. The institutional ethics committee approved the study.

Relevant clinical information was collected from each patient and included presenting complaints, food habits, socio-economic status, drug history, alcohol abuse, and any significant past history. Clinical examination included general physical and systemic examination, with special emphasis on icterus, fever, blood pressure, presence of organomegaly and ascites, and presence of signs of hepatic encephalopathy. Basic investigations including complete hemogram and renal function tests were done in all cases.

Complete liver function test (LFT), prothrombin time (PT) and ultrasonography were done on admission for each patient. Upper limit of normal for AST and ALT was taken as 40 IU/L and for alkaline phosphatase as 170 IU/L.

All patients were tested for IgM anti HAV (using HAVAB EIA kit, Abbott laboratories, USA), HBsAg (using Eliscaan micro ELISA strips, Ranbaxy diagnostics, England), anti-HCV (using INNOTEST HCV antibody iii kit), and IgM anti HEV antibody (using GLD-HEV IgM EKISA kit, Genelabs diagnostics, Singapore). IgM anti-HBc, HBV DNA and HCV RNA was done in patients who were HBsAg positive and anti-HCV positive respectively.

All patients were followed up for complete clinical and biochemical recovery. Standard care treatment was given for acute symptoms like nausea, vomiting, abdominal pain where indicated.

Statistical Methods: History, clinical, and biochemical data were collected from all patients. The prevalence of hepatitis viruses were analyzed by Fisher’s exact test. Two tailed tests were used and a P < 0.05 was considered to be statistically significant.
RESULTS: A total of 121 cases of acute hepatocellular jaundice were seen during the period of study. Out of this 82 cases (67.77%) were of viral and 39 cases (32.33%) of non-viral origin. There was a male preponderance with male to female ratio of 2.5:1 indicating less exposure of female populations. Maximum cases of acute hepatocellular jaundice were seen in 30-50 years age group with a mean age of 48.5 years.

Among cases of viral origin, hepatitis A was the commonest cause in 32 (39.02%), followed by hepatitis E in 15 (18.29 %) and hepatitis B in 4 (4.88%) cases. There was only one case of acute hepatitis C. Mixed infection was seen in 4 cases (A+E in two cases, B+E and B+A in one case each respectively) [Table].

Hepatitis A constituted 47.05 % and 23.5% of all cases of acute viral hepatitis in the age group 20-30 and 31-40 years, followed by hepatitis E in 23.5% and 11.1% in this respective age group. In the older age groups, 41-50 and 51-60 years, hepatitis E was the commonest (46.3%) infection, followed by hepatitis A (18.1%) [Table].

In majority of the cases of AVH (82.93%) patients used unsafe source of drinking water, which includes 71.8% cases of HAV and 93.33% cases of HEV.

Among non-viral causes malaria was the commonest cause (20 cases, 51.28%), followed by drugs mainly ATT and paracetamol (7 cases), alcohol (6 cases), and leptospira in four cases.

Prolonged cholestasis was seen only in one patient in the non-viral group compared to seven cases in viral group (all related to HAV). Majority (77.2%) of the patients with prolonged cholestasis had raised serum alkaline phosphatase, up to three times the upper limit of normal while only three cases had risen above three times the upper limit of normal reference range.

The mean serum bilirubin in AVH group was 14.11 mg/dl compared to 7.01 mg/dl in non-viral group. 61 (74.39%) cases had serum ALT in the range of 500-1200 IU/L on admission and only 18 (21.95%) cases had a value less than 500 IU/L and rest three cases had a value greater than 1200 IU/L.

In cases that developed acute liver failure during the study period, HAV was found to be the commonest cause again (65%, 11/20), followed by HEV virus infection (25%, 5/20), HBV virus (5%, 1/20) and combined HAV & HEV infection(5%, 1/20). No acute liver failure occurred in isolated hepatitis C infection.

DISCUSSION: In this study AVH was the most common cause of acute hepatocellular jaundice. Majority (68.3%) of the AVH cases belonged to the age group of 20-40 years. Kaur et al in 2003 also found out that AVH was most common in the age group of 20-40 years [7].

We found HAV (39.02%) as the commonest etiology followed by HEV (18.29%) which is significant as other Indian studies have shown contradicting results where hepatitis E is the commonest cause of sporadic AVH among Indian adults[7,8,9] while Malathi S et al from south India have reported that HAV is common in children with AVH,[10]

Most Indian studies have shown a low prevalence of this virus among adult Indians [7,11-12]. But we found a third of our adult patients were infected with hepatitis A, being particularly high in third and fourth decade of life.

With improvement of the socioeconomic conditions of the communities, a shift in the age of acquiring HAV infection has been seen from childhood to older age groups in India and globally.
Chadha et al, compared the etiology of sporadic and fulminant viral hepatitis a decade apart and found an increase in hepatitis A incidence in adults, especially, in those who developed fulminant hepatic failure (from 3.5% to 10.6%).[8]

Our patients were generally from tea garden community and hilly areas, who were non-immune to hepatitis A infection. Our study implies that hepatitis A continues to be an important cause of acute hepatocellular jaundice and is also the leading cause of acute viral hepatitis in adults, in North East India. In the present study, co-infection was seen in 4 cases (4.87%) of all AVH cases. Two cases had co-infection of hepatitis A & E and another one case each had hepatitis A & B, and hepatitis B & E. Kaur et al in Ludhiana also found a similar rate of co-infection of hepatitis B & C and Hepatitis B & E in their study.[7]

Hepatitis E was most prevalent in the age group of 20-30 years. Hepatitis A was found to be the major cause of acute liver failure as opposed to other studies from India where hepatitis E was the leading cause.[4,13,14-16] Biochemical parameters were more markedly raised in those patients who had a viral origin in compared to non-viral diseases.

Prolonged cholestasis was seen only in eight patients and majority of them were related to hepatitis A infection. But prolonged cholestasis was commonest in hepatitis E as documented in earlier studies.[17] The duration of illness was usually less than four weeks in majority (72.9%) of our patients but was longer (even more than eight weeks) in those patients who developed co-infection with other viruses.

In the non-viral group (n: 39), malaria continues to be an important cause of acute hepatitis (51%) followed by drugs (18%). Comparatively, the altered LFTs were less marked than those in AVH. All the cases of malaria were Pf positive severe malaria. Malarial hepatopathy is a well-known extra-cerebral complication, but carries a good prognosis when treated promptly.

CONCLUSION: AVH is the leading cause of acute hepatocellular jaundice in North East India, HAV being the most common cause, including acute liver failure. This suggests a geographical difference of AVH from other Indian reports. AVH is still a major health problem in our part of the country.

The reduced incidence of Hepatitis E and age wise shift pattern of hepatitis A indicates the improvement in living standards of North East populations. Malaria and hepatotoxic drugs like ATT also cause a considerable number of acute hepatitis but are milder compared to AVH.

REFERENCES:
Liver function tests

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<tr>
<th>Liver function tests</th>
<th>Viral group (Mean±SD) mg/dl</th>
<th>Non-viral Group (Mean±SD) mg/dl</th>
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<tr>
<td>Total Bilirubin</td>
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<td>Direct bilirubin</td>
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<td>Indirect bilirubin</td>
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<td>AST</td>
<td>492.92±656.70</td>
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<td>ALT</td>
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<td>Alk phosphatase</td>
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<td>Prothrombin time</td>
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<td>12.87±0.87</td>
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</table>

Table 2: Comparison of biochemical parameters between viral and no viral groups
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Date of Submission: 13/08/2014.
Date of Peer Review: 14/08/2014.
Date of Acceptance: 25/08/2014.
Date of Publishing: 29/08/2014.