Hepatitis E Super Infection

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In this study, 100 sera of hospitalized jaundiced patients were assayed for the presence of anti-HEV IgG by enzyme immunoassay and for HBsAg and anti-HCV by serological techniques. Out of 25 HBsAg positive patients, 3 (12%) were positive for anti-HEV IgG and out of 12 anti-HCV positive patients 4 (33%) showed positivity for anti-HEV IgG.

Key words. Enterically transmitted non-A, non-B hepatitis, HBsAg, anti-HCV, ELISA.

A wide variety of infections can involve the liver e.g. infections mono-nucleosis caused by Ebstein bar virus, Cytomegalovirus, Herpes Simplex Virus particularly in children and immunosuppressed patients, yellow fever mainly in Africa with a high mortality. Even Rubella, Adenovirus or Enterovirus infections can involve the liver during course of the disease.

Unless otherwise specified, the term viral hepatitis is reserved for infection of the liver caused by a small (but growing) group of viruses having a particular affinity for liver. These are hepatitis A, B, C, D, E, and G viruses. Their spectrum of effects on the liver is wide, ranging from a mild exposure with clearance of the virus and life long immunity to acute fulminating hepatitis or exposure with no active disease but chronic changes in the liver resulting in cirrhosis or even carcinoma.

Viral hepatitis has traditionally been divided into infectious hepatitis (Hepatitis A and Hepatitis E) and serum hepatitis (hepatitis B, C, D, and G). Faeco-oral viral transmission occurs in hepatitis-A and E. No carrier state exists in both these conditions. Parenteral and percutaneous viral transmission occurs in hepatitis, B, C and D. Carrier state occurs in all these three types of hepatitis.

HEV is the main cause of sporadic and epidemic types of viral hepatitis in our set up. It is reported that it is responsible for 77% of cases of AVH. HEV is faeco- orally transmitted and initially affects the gut. The infection results in viraemia and virus reaches the target organ (liver). The causative virus is excreted through the gut in faecal material. The virus passes from faeces of infected persons into the sewage. Whenever there are chances for the contamination of the portable water with HEV containing sewage, outbreaks of HEV infection may occur. The incubation period of the disease is on an average 40 days and the highest attack rate is seen in the young adults while equally affecting both the sexes. The disease is usually mild in nature and is self-limiting, without any ensuing long term sequelae. However, it can be fatal in pregnant females if it affects during third trimester, it may lead to high mortality and frequent foetal losses. Although hepatitis E causes mild illness which is self-limiting and without any chronic sequelae. However, rarely cases of fulminant hepatic failure and sub acute hepatic failure are seen in this particular hepatitis. It has been suggested that such cases are due to super infection of hepatitis E in chronic hepatitis B carriers superficially resembling acute hepatitis B. Combined infections with non-A, non-B hepatitis agents and hepatitis B virus are responsible for serious forms of hepatitis.

Patients and methods
This study enrolled 100 cases of acute hepatitis diagnosed on clinical grounds. Admitted jaundiced patients were selected from Jinnah Hospital, Services Hospital and Mayo Hospital, Lahore. Cases of obstructive Jaundice were excluded by ultrasonographic examination. Past and present history was inquired by the patients.

About 3-6 ml of serum was obtained from each case. Haemolysed samples were excluded. The samples were collected and stored at 2-8°C if the assays was to be performed within 5 days. For longer periods, samples were aliquoted and stored at –20°C. Repeated freeze-thaw cycles were avoided.

All sera along with positive and negative controls were tested in 3 batches for anti-HEV IgG in an ELISA utilizing recombinant antigens (Abbott). All results were read with the help of spectrophotometer which was blanked with a substrate at 492nm. Absorbance of the specimen was related to the cutoff value for detection of anti-HEV IgG.

All sera were also tested for HBsAg and anti-HCV by serological technique.

Results
A total of 100 sera of jaundiced patients were assayed for the presence of anti-HEV-IgG by enzyme immuno assay. Out of the 100 sera tested 22(22%) showed positivity for anti-HEV IgG. Out of these positive patients 70 were male patients and 30 female patients. 100 sera were also tested for HBsAg and anti-HCV by serological techniques. 25 were positive for HBsAg and 12 were positive for anti-HCV. Out of 25 HBsAg positive 3 (12%) were reactive for anti-HEV IgG and out of 12 anti-HCV positive patients 4 (33.3%) were positive for anti-HEV IgG.

So super infection with HEV was seen in 12% of the cases of HBV and in 33.3% of the hepatitis C patients.
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Table 1. Correlation of IgG anti-HEV antibodies in HbsAg positive patients

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<thead>
<tr>
<th>HbsAg (n=100) positive</th>
<th>IgG anti-HEV positivity in HbsAg positive patients (n=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. %age</td>
<td>No. %age</td>
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<tr>
<td>25</td>
<td>25.0</td>
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Table 2. Correlation of anti-HEV IgG antibodies in anti-HCV positive patients.

<table>
<thead>
<tr>
<th>Anti-HCV positive</th>
<th>IgG anti-HEV positivity in HbsAg positive patients (n=12)</th>
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</thead>
<tbody>
<tr>
<td>No. %age</td>
<td>No. %age</td>
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<tr>
<td>12</td>
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Discussion

Hepatitis E virus has been recognized as the major aetiological agent of enterically transmitted non-A, non-B (ET NANB) hepatitis. It is now well established that HEV is responsible for major outbreaks of ET-NANB hepatitis in India, Pakistan, Bangladesh, Nepal, Burma, Algeria, Somalia, Sudan, Ivory coast and Mexico. The introduction of assays for the detection of HEV has further expanded the scope of our knowledge regarding the viral causes of hepatitis. Hepatitis E is responsible for mild, self limiting illness with no chronic sequelae. However, superinfection of hepatitis E in patients with fulminant hepatitis.

In our study, out of 100 hospitalised jaundiced patients 22(22%) were found to be positive for anti-HEV-IgG. 25(25%) were positive for HbsAg and 12(12%) were positive for anti-HCV. Among 25 HbsAg positive patients 3(12%) showed positivity for IgG anti-HEV and out of 12 anti-HCV positive patients 4(33.3%) were reactive for IgG anti-HEV. The result of our study demonstrated significant super infection of hepatitis-E in patients of hepatitis B and C. Another reported incidence of dual infection by hepatitis B and E virus is 10%. A similar study by Halfon showed anti-HEV positivity in 16 out of 147 patients. Among HEV antibody positive patients 7 of 16(43.7) were also anti-HCV positive and 1 of 6.2% was HbsAg positive.

These results suggest that patients with hepatitis B and C virus infection could also be infected by HEV. In such cases of super infection or dual infection clinical picture instead of being mild and self limiting, will be fulminant and with chronic sequelae.

References