INTRODUCTION

Approximately one third of the world’s population has serological evidence of past or present infection with hepatitis B virus (HBV) infection and 350 million people have chronic infection, causing 1 million deaths annually. About 5% of the HBV carriers have hepatitis D virus (HDV) super infection. The clinical association is due to the fact that the genome of HDV does not encode for its own envelope proteins. The HDV envelope consists of HBV surface proteins (HBsAg), and as a consequence HDV transmission occurs only in the presence of HBV. HDV replication seems to occur only in the liver, and all pathological abnormalities are limited to this organ. The clinical course of HDV infection may be variable. In general, the observed symptoms are more severe than those associated with other hepatitis viruses. It is estimated that up to 80% of all chronic patients with hepatitis delta will develop cirrhosis. This percentage is about three times higher when compared to that observed in hepatitis B patients.

The frequency of HDV associated fulminant hepatitis, the more severe form of the acute disease, is 10 times higher than the observed for other viral hepatitis. Seroprevalence studies in individuals positive for HBsAg show a non-uniform worldwide distribution of HDV. Cirrhosis and hepatocellular carcinoma (HCC) can develop at a younger age than in patients with chronic HBV infection alone. It is estimated that more than 15 million people are infected with HDV worldwide, and its prevalence is higher in Italy, Tunisia and in Middle East. Similar seroprevalence has been reported (15.3% anti-HDV positive) from Taiwan. In Pakistan, the frequency reported varies from 26.8% to 58.6% of patients infected with hepatitis B virus.

The aim of this study was to evaluate the frequency of HDV in various HBV-related liver diseases in hospitalized patients at Chandka Medical College Hospital, Larkana.

METHODOLOGY

The study was conducted at Medical Unit I, Chandka Medical College Hospital, Larkana, from July 2003 to June 2008. All the patients admitted with liver diseases were tested for HB surface antigen (HBsAg) and HCV antibody. HBV related liver cases were entered on especially constructed proforma. The studied variables included age, gender, and diagnosis of disease on the basis of liver function tests (LFTs), prothrombin time (PT), HB surface antigen (HBsAg) and HCV (Hepatitis C virus). If the HBsAg was positive, then anti-HDV antibodies were also tested. Hbc (core) antibodies were...
also tested wherever it was needed. Inclusion criteria for the study were patients of HBV related liver disorder aged 15-60 years. Exclusion criteria were co-infection with HCV and/or HIV, auto-immune hepatitis, alcoholic hepatitis, Wilson’s disease and haemochromatosis. This study was approved by the Ethical Review Committee of the hospital and all patients gave informed verbal consent before being enrolled in this study.

All results for continuous variables were expressed as mean and standard deviation (SD). The p-values for comparisons of categorical variables were generated by chi-square test for proportions and value of less than 0.05 were considered to indicate statistical significance. 95% confidence interval (CI) for assessing the HBV/HDV co-infection according to age groups and clinical diagnosis were estimated. All calculations were done with SPSS 15.0 (Statistical Package for Social Sciences, Chicago).

RESULTS

There were 774 patients with HBV related liver disease, 478 were males (57%) and 336 were females (43%). The mean age was 36.5 ± 14.39 for males and 34.03 ±13.16 years in females. Of the 774 cases, 183 were found to be reactive for anti-HDV antibodies, yielding an overall anti-HDV seropositivity of 23.6% (p = 0.001, 95% CI 1.71-1.85%) which was highly significant. Anti-HDV antibody was positive in 111 males and 72 females respectively (Table I), but the difference was not statistically significant (p=0.718). However, gender and clinical diagnosis was significant in cirrhosis (p= 0.001).

Table II shows the prevalence of HDV seropositivity in various age groups and clinical diagnosis and revealed higher in age group 20-40 years, and very significant in chronic liver disease like chronic hepatitis (p = 0.001) and cirrhosis (p = 0.001) as compared to the other age groups and acute hepatitis (p =0.029). There was a significant risk relationship between HDV seropositivity and subjects' clinical diagnosis, HDV infection being significantly higher in chronic liver disease, in age group 40-60 years than in the acute liver hepatitis.

DISCUSSION

The frequency of anti-HDV was 23.6%, indicating a high HDV infection in our area. This result was consistent with the studies reported (26.8%) from Karachi, and from Irabu Island, Japan.10,12 Similar seroprevalence of anti-HDV (22%) coexistent with HBs positive had been reported from Italy in 1987.6 The seroprevalence of anti-HDV in HBV related liver disorders have been reported at 11.5% and 10.6% from Iran and India respectively.13,14 In Turkey, the prevalence of anti-HDV serological markers were observed as 27.5% in HBV related chronic hepatitis.15 In Italy the prevalence of anti-HDV among HBs persons has declined from 22% in 1987 to 14% in 1992 and 8.2% in 1997.6 This has become possible because of improvement in socio-economic conditions and resources were utilized for active preventive measures, such as the use of disposable syringes, treatment of source and HBV immunization.

In other parts of the world, the seroprevalence of HDV among HBsAg-positive cases was 6.1%, 1.3%, 5.8%, 8.5%, 24.4% and 5.9% in Mongolia, rural Vietnam, Iran, South London, Bangladesh and India respectively.16-21 Lack of health education, poverty, poor sanitation, lack of proper hospital waste, the trend of frequent use of syringes even for trivial illness, quackery and lack of measures by public health department to tackle this issue seriously, probably contribute to the high frequency of HDV in this study.

Males (25.3%) were more infected than females (21.4%), consistent with earlier reports from Iran and Pakistan.10,18 It may be that males are exposed to various hazards while working over farmland and do not take precautions, as a result of that, they easily suffer from various infections. Routine use of multiple injections and intravenous drips even for trivial ailment seem to be an explanation. The anti-HDV antibody positivity in acute viral hepatitis patients in this study was in 23.6% as compared to studies like 3.1%, 16% and 8.1% from New Delhi, Mumbai and Turkey respectively.14,22,23

Table I: Frequency of 183 HDV patients among 774 HBV cases according to clinical diagnosis and gender.

<table>
<thead>
<tr>
<th>Gender</th>
<th>Diagnosis</th>
<th>Total</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>Acute hepatitis</td>
<td>27 (3.5)</td>
<td>111 (14.34)</td>
</tr>
<tr>
<td>Female</td>
<td>Chronic hepatitis</td>
<td>30 (3.88)</td>
<td>72 (9.30)</td>
</tr>
<tr>
<td></td>
<td>Cirrhosis liver</td>
<td>48 (6.2)</td>
<td>183 (23.6)</td>
</tr>
<tr>
<td></td>
<td>Ca liver</td>
<td>6 (0.77)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Table II: Distribution of 183 HDV patients among 774 HBV cases according to clinical diagnosis and age.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>&lt; 20 years N (%)</th>
<th>20-40 years N (%)</th>
<th>41-60 years N (%)</th>
<th>N (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute hepatitis</td>
<td>12 (1.5)</td>
<td>29 (3.74)</td>
<td>0</td>
<td>41 (5.3)</td>
<td>0.029</td>
</tr>
<tr>
<td>Chronic hepatitis</td>
<td>0</td>
<td>22 (2.84)</td>
<td>30 (3.87)</td>
<td>52 (6.7)</td>
<td>0.001</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>0</td>
<td>48 (6.2)</td>
<td>36 (4.65)</td>
<td>84 (10.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>Carcinoma liver</td>
<td>0</td>
<td>0</td>
<td>6 (3.3)</td>
<td>6 (0.7)</td>
<td>0.332</td>
</tr>
</tbody>
</table>
In chronic hepatitis and cirrhosis patients, anti-HDV antibodies were found in 24.7% and 22.2% cases respectively. Earlier, more or less similar seroprevalence of 21.4, 26.8 and 19, 32.5 percent have been reported from Mumbai, London, Chandigarh and Turkey respectively. In another study from Turkey, the total anti-HDV seropositivity among patients with chronic hepatitis B and hepatitis B-induced cirrhosis was the lowest (5%) in the west of the country and the highest in the southeast (27%) respectively. This reflects the difference in the regions of same country and failure to identify the reasons.

This study was hospital-based study; hence the figure does not reflect true frequency and severity of the disease. Moreover, the study was conducted in one units in single hospital which further confine its generalization.

**CONCLUSION**

HDV infection was frequent in hospitalized patients with HBV related liver disease. Therefore, practitioners and health care managers should be made aware of the risk of dual infection with HBV and HDV so as to reduce the risk by providing treatment and employ stringent preventive measures to decrease the chances of spread of these infections.

**REFERENCES**