Prevalence of Hepatitis C virus infection among children with liver disease

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Abstract

The prevalence of hepatitis C virus infection in children with chronic liver disease (CLD) and neonatal cholestasis syndrome (NCS) has been determined in the present study.

All the cases of CLD and NCS attending the Pediatric Gastroenterology clinic between Oct 2004 to Oct 2006 were included in this study and the sera of the patients was tested for anti-HCV antibodies by an ELISA based third generation diagnostic kit.

Of the total of 86 patients enrolled in the study, 50 were cases of CLD and 36 were cases of NCS. There were only 2 patients positive for anti-HCV antibody out of total 86 cases. The first sero-positive case was among the patients of CLD and the second sero-positive child was a patient of NCS.

The prevalence of hepatitis C virus infection in children with CLD and NCS in our region is 2.0% and 2.8%, respectively.

Keywords: Chronic liver disease, Neonatal Cholestasis Syndrome, Hepatitis C virus, Prevalence and Children

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Introduction

Worldwide more than 130 million people are chronically infected by hepatitis C virus (HCV) infection [1]. Among the hepatotropic viruses HCV is most likely to cause chronic infection. Only a small proportion of HCV infected individuals are children. The prevalence of HCV infection increases with age in the general population and is lower among adolescents (0.4%) than among adults (2.5%) [2]. It is estimated that the seroprevalence of anti-HCV is 0.2% in children younger than 12 yrs of age and 0.4% in those between 12-19yrs of age [3]. The course of HCV infection in children can be acute or sub-acute to prolonged, with frequent progress to chronicity (30-60%) [4]. Chronic HCV infection is a major cause of CLD in children [5].

The rate of progression to chronicity may depend on the route of transmission ranging from 60% and 80% in post-transfusion and vertically acquired HCV infection respectively [6].

Chronic hepatitis C in children may be either asymptomatic or may present with jaundice, hepatomegaly and chronic biochemical evidence of hepatitis (raised serum transaminase levels). Diagnostic tests for HCV infection are broadly grouped as serological assays for detection of anti-HCV antibodies and molecular tests for detection of viral particles. Among the serological assays, the third generation Enzyme Immunoassay (EIA) is nowadays used for detection of anti-HCV antibodies. It has a sensitivity of 97% and can detect antibodies within 4-10 weeks after infection. Among the molecular tests, PCR test and b DNA (branched chain DNA) test are used to detect specific viral nucleic acid (HCV RNA) sequence.
Methods

This study was conducted from Oct 2004 to Oct 2006 and the subjects were children with CLD and infants with NCS, presenting to the Pediatric Gastroenterology clinic. Children presenting with clinical features suggestive of liver dysfunction or cirrhosis of more than 3 months duration, supported by laboratory and/or histological evidence of CLD or of less than 3 months duration with histological evidence of chronic liver injury where taken as CLD cases. Infants less than 6 months of age presenting with jaundice starting in neonatal period or later with conjugated hyperbilirubinemia (i.e. the direct bilirubin fraction of > 15% of total or absolute level more than 2 mg/dl) persisting beyond 14 days of life were taken as NCS cases. In all these patients of CLD and NCS, complete workup for liver disease was planned out. A detailed history and physical assessment with investigative workup was done for all the cases as per the protocol followed in the GE clinic. The estimation of anti-HCV antibodies was done for all the cases in the Department of Microbiology. This was done by an Enzyme Linked Immunosorbent Assay (ELISA) based third generation diagnostic kit i.e. HCVMicrolisa manufactured by J.Mitra and Co Ltd. HCV Microlisa is an in-vitro third generation enzyme immunoassay for qualitative detection of antibody to HCV (anti-HCV Ab) in human serum or plasma. Percutaneous liver biopsy was done after taking informed consent with a 16 or 18 gauge Trucut liver biopsy needle in 26 out of 50 cases of CLD and 14 out of 36 cases of NCS.

Results

The baseline characteristics of 50 children with CLD and 36 children with NCS enrolled in the study are summarized in table 1. In the CLD group there were 37 (74.0%) males. There was a bimodal distribution of cases with peaks in 1-3 years and 6-12 years age group with median age being 5yrs 10 months. In the NCS group, there were 31 (86.1%) males with the median age group of 2 months. Jaundice as a presenting feature was seen in 31 (62.0%) of the CLD cases and in 34 (94.4%) of the NCS cases. In the CLD group, mean serum bilirubin level was 3.87± 4.39 mg/dl and mean direct bilirubin fraction was 2.90 ± 2.91 mg/dl. Whereas in NCS group, the mean total serum bilirubin level was 11.47 ± 8.11 mg/dl and mean direct bilirubin fraction level was 5.94 ± 3.15 mg/dl. Percutaneous liver biopsy was done in 26 out of total of 50 patients of CLD and in 14 out of total of 36 cases of NCS. Others either did not give consent for biopsy or deranged PT did not allow us to perform it. Of the 26 children with CLD, 12 had chronic hepatitis, 7 had cirrhosis, 3 had fibrosis, 2 each had storage disorder and vascular malformation. Of the 14 infants with NCS, biopsy showed neonatal hepatitis in 8 cases, extra hepatic biliary atresia in 2 cases, cholestasis in 3 cases and cirrhosis in 1 case. On serological testing for HBsAg and anti-HCV antibody, it was found in the CLD group, 7 cases (14.0%) were positive for HBsAg and the highest prevalence was in the age group of 13-144 months with 5 cases positive for HBsAg out of 24 cases. In the NCS group 2 (5.5%) were positive for HBsAg out of which 1 was in the age group of 1-3 months and the other positive case was in the age group of 4-6 months. Out of 50 CLD cases, anti-HCV antibody was present in only 1 case (2.0%). She was a 10 years old female child who presented with fever, night blindness, jaundice and abdominal distension. Hepatosplenomegaly and ascites was present on clinical examination. In the NCS group, only 1 case was positive for anti-HCV antibody giving a prevalence of 2.8%. The seropositive case was a 3 months old male child who presented with jaundice and acholic stools since day 10 of life. Hepatosplenomegaly and skin bleeds were present on examination. He was a preterm baby with no significant antenatal or family history. Table 2 and 3 depict the prevalence of HBsAg and anti-HCV antibody in different age groups of CLD and NCS cases respectively.

Table 1: Clinical and laboratory profile of the CLD and NCS cases.

<table>
<thead>
<tr>
<th></th>
<th>CLD (n=50)</th>
<th>NCS (n=36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age (months)</td>
<td>70(7-144)</td>
<td>2 (0.5-6)</td>
</tr>
<tr>
<td>Male gender</td>
<td>37 (74.0%)</td>
<td>31 (86.1%)</td>
</tr>
<tr>
<td>Mean wt Z score (SD)</td>
<td>-2.04±1.07</td>
<td>-1.94±1.32</td>
</tr>
<tr>
<td>Mean Ht Z score (SD)</td>
<td>-2.34±1.46</td>
<td>-2.32±2.28</td>
</tr>
<tr>
<td>Deranged transaminases (%)</td>
<td>35(70.0)</td>
<td>31 (86.1%)</td>
</tr>
<tr>
<td>Hypoproteinemia (%)</td>
<td>19(38.0%)</td>
<td>16 (44.0%)</td>
</tr>
<tr>
<td>Deranged prothrombin time (%)</td>
<td>31(62.0%)</td>
<td>23(63.8%)</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>------------</td>
<td>------------</td>
</tr>
<tr>
<td>HBsAg (%)</td>
<td>7 (14.0%)</td>
<td>2 (5.5%)</td>
</tr>
<tr>
<td>Anti-HCV antibody (%)</td>
<td>1(2.0%)</td>
<td>1(2.8%)</td>
</tr>
</tbody>
</table>

Table 2: Prevalence of HBsAg and anti-HCV antibody in different age groups of CLD cases

<table>
<thead>
<tr>
<th>No of cases with CLD</th>
<th>Age group</th>
<th></th>
<th></th>
<th></th>
<th>Total (%) (n=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤12 months (n=9)</td>
<td>12-36 months (n=14)</td>
<td>37-72 months (n=6)</td>
<td>3-144 months (n=24)</td>
<td></td>
</tr>
<tr>
<td>HBsAg positive</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>7 (14)</td>
</tr>
<tr>
<td>Anti HCV Ab positive</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1 (2)</td>
</tr>
</tbody>
</table>

Table 3: Prevalence of HBsAg and anti-HCV antibody in different age groups of NCS cases

<table>
<thead>
<tr>
<th>No of cases with NCS</th>
<th>Age group</th>
<th></th>
<th></th>
<th></th>
<th>Total (%) (n=36)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;1 months (n=11)</td>
<td>1-3 months (n=17)</td>
<td>4-6 months (n=8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HBsAg positive</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2 (5.5)</td>
</tr>
<tr>
<td>Anti HCV Ab positive</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1 (2.8)</td>
</tr>
</tbody>
</table>

Discussion

With only 2 cases positive for anti-HCV antibody out of total of 86 cases, our study showed a low prevalence of HCV infection in children with CLD and NCS, which is 2.0% in the CLD group and 2.8% in the NCS group. A global update [7] has shown that the prevalence of anti-HCV antibody in the general population varies from 1.03% to 5.3% in different geographical regions of the world.

The recent NHANES study (the National Health and Nutrition Examination Survey) conducted between 1999 and 2002 reported a prevalence of 1.6% of anti-HCV positive cases from a sample of 15079 healthy subjects in USA [8]. HCV infection in India has a population prevalence of around 1% [9]. Irshad et al [10] reported the prevalence of anti-HCV antibody in healthy individuals from Delhi to be 1.5%.

Only a small proportion of HCV infected individuals are children. In healthy pediatric population, the prevalence of hepatitis C varies from 0% to 0.9%[11]. A study from Pakistan of 3533 healthy children aged between 1-15 years of age showed a prevalence of anti-HCV antibody of 1.6% [12]. The literature of the prevalence of HCV infection in children with chronic liver disease (CLD) and neonatal cholestasis syndrome (NCS) is scarce especially from India. Most of the studies have shown a low prevalence of anti-HCV antibody in children with chronic liver disease (CLD) and neonatal cholestasis syndrome (NCS). Yachha et al [13] in their study to determine the etiological spectrum of hepatobiliary disorders in northern India found that out of 85 cases of CLD, only 3 were anti-HCV positive giving a prevalence of 3.5%. In the same study they had 60 cases of NCS out of which none were anti-HCV antibody positive. The results of this study are almost similar to the present study. The study by Yachha et al [13] done at a North Indian centre close to the area of the present study also utilizes the detection of anti-HCV antibody as the test for diagnosis of HCV infection.
In a prospective study from Pakistan, hepatitis B was the leading cause of CLD in children (24%) whereas none of the children in this study were anti-HCV antibody positive [14]. Monein et al [15] in a diagnostic evaluation of 70 cases of NCS found none of the patients to be anti-HCV antibody positive. The sensitivity of the third generation ELISA for anti-HCV antibody is almost 97% but the specificity could be as low as 40-50% especially in low risk groups [16]. The PCR RNA for virus isolation has specificity of 97% [17]. The limitation of our study is that we have used only anti-HCV antibody for diagnosis of HCV infection as a result of which we may have missed some cases of HCV infection such as children with immunodeficiency, HIV co-infection or leukemia. Moreover, anti-HCV antibodies passively derived from mother may persist till 12 to 18 months of age so diagnosis in infancy needs confirmation by detection of HCV RNA. We conclude as pointed out by other studies the prevalence of HCV infection in children with chronic liver disease and neonatal cholestasis syndrome is very low.

References


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