ABSTRACT

Hepatitis B Virus (HBV) is one of the leading cause of cirrhosis and hepatocellular carcinoma worldwide. The virus has 10 different genotypes and has a specific geographic distribution for each genotype. Viral genotypes and certain mutations in the viral genome are associated with differential clinical features and therapeutic response. It is also evident that during HBV infection certain host genetic factors play major role in determining the outcome of infection and also impact the outcomes of antiviral therapy. IL28B plays an important role in the outcome of HBV infection and it could inhibit the viral replication. There are some functional genetic variants in IL28B gene which regulate the expression of IL28B. These genetic variants played significant role in predicting the antiviral therapy response and disease progression. There are several case control studies across the globe which are investigating the role of these functional variants on disease progression and antiviral therapy outcomes. In current study the available data on the genetic analysis of IL28B variants and their impact on HBV disease progression or antiviral therapy response is analyzed. The results showed that most of the studies including only small number of study participants hence the low sample number impact the power of statistical analysis. It is proposed that in future the case control studies must be conducted on large scale so statistical results can be justified and will be of help in clinical settings.

Key words: IL-28B; HBV; Ethnicity; Genetic analysis; Case-control studies

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DEAR EDITOR

The major recent breakthrough in genetics and hepatology is the role of variations found in the region of interleukin-28B (IL28B), the gene coding for the IL28B protein, also known as interferon (IFN)-λ3. The genetic variations in this region are highly predictive of pegylated INF alpha (Peg-IFN-α) and ribavirin (RBV) therapy response and viral clearance in different ethnic groups of chronic hepatitis C patients[1]. Recently there are growing numbers of studies on investigating the role of these genetic variations in different ethnic groups and Peg-IFN-α and RBV treatment response in hepatitis B patients.

A report published by Holmes et al (2013) showed that IL28B genotype (rs12979860) is not a useful predicting marker for treatment outcome in Asian chronic hepatitis B patients treated with pegylated interferon-α. The study includes very small number of patients as well control subjects. Conclusion of the study based
Table 1 Summary of studies investigating IL-28B polymorphic variants association with HBV disease susceptibility, progression and Interferon ribavirin therapy response.

<table>
<thead>
<tr>
<th>Year</th>
<th>Ethnicity</th>
<th>Patients (n)</th>
<th>Control (n)</th>
<th>Conclusion/Association with IL-28 Polymorphism</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>Italian</td>
<td>292</td>
<td>244</td>
<td>Positive association with disease susceptibility</td>
<td>9</td>
</tr>
<tr>
<td>2011</td>
<td>Taiwanese</td>
<td>140</td>
<td>150</td>
<td>No association with disease progression</td>
<td>7</td>
</tr>
<tr>
<td>2011</td>
<td>Chinese</td>
<td>283</td>
<td>47</td>
<td>Positive association with disease susceptibility and chronicity</td>
<td>8</td>
</tr>
<tr>
<td>2012</td>
<td>Chinese</td>
<td>49</td>
<td>49</td>
<td>No association with disease susceptibility</td>
<td>9</td>
</tr>
<tr>
<td>2012</td>
<td>Taiwanese</td>
<td>133</td>
<td>-</td>
<td>No association with disease progression and chronicity</td>
<td>10</td>
</tr>
<tr>
<td>2012</td>
<td>Chinese</td>
<td>512</td>
<td>-</td>
<td>Positive association with Interferon ribavirin therapy response</td>
<td>11</td>
</tr>
<tr>
<td>2012</td>
<td>Chinese</td>
<td>651</td>
<td>226</td>
<td>No association with disease susceptibility</td>
<td>12</td>
</tr>
<tr>
<td>2012</td>
<td>Not differentiated</td>
<td>205</td>
<td>-</td>
<td>Positive association with Interferon ribavirin therapy response</td>
<td>13</td>
</tr>
<tr>
<td>2012</td>
<td>Netherlands</td>
<td>95</td>
<td>-</td>
<td>No association with HBeAg seroconversion</td>
<td>14</td>
</tr>
<tr>
<td>2011</td>
<td>Chinese Han</td>
<td>406</td>
<td>203</td>
<td>Preventive effect on disease progression</td>
<td>15</td>
</tr>
<tr>
<td>2011</td>
<td>Taiwanese</td>
<td>115</td>
<td>-</td>
<td>No association with HBeAg seroconversion</td>
<td>16</td>
</tr>
<tr>
<td>2011</td>
<td>Italian</td>
<td>292</td>
<td>344</td>
<td>Positive correlation with viral infection</td>
<td>17</td>
</tr>
<tr>
<td>2011</td>
<td>Chinese</td>
<td>342</td>
<td>144</td>
<td>No correlation with the outcome of HBV infection</td>
<td>18</td>
</tr>
</tbody>
</table>

on 52 patients and 32 controls from Asian ethnicity; study groups were further divided into 4 different groups on ethnic basis. The study includes 8, 14, 22, 8 patients of Cambodian, Chinese, Vietnam and other ethnic background respectively. Similarly the control group from Cambodian, Chinese, Vietnam and other ethnicity includes 7, 9, 11 and 5 individuals respectively. The Caucasian and African study groups includes 7, 1 patients and 2, 2 healthy control respectively[6]. The results showed that CC IL28B genotype was the major prevalent genotype and was present in 85% patients and 83.3% healthy individuals followed by CT genotype which was present in 15% patients and 13.9% controls. Genotype TT prevalence was 0% in cases and 2.8% in controls; the very low prevalence was may be due to very small number of investigated individuals. On the basis of these results authors concluded that IL-28B polymorphism (rs12979860) has no association with pegylated interferon therapy outcomes in HBV patients with Asian ethnic background.

The findings of other reports analyzing the role of IL-28B polymorphic variants on HBV infection susceptibility and therapy outcomes from different groups are conflicting but were based on comparatively larger number of patients and controls (Table 1)[18-38]. A recent report by Chen et al[39] investigated the IL-28B Gene polymorphism association and the Progress of Hepatitis B Infection in Han Chinese. Irrespective of results; the study includes 3 patients and a healthy group of 406, 406, 393 and 244 individuals respectively. A summary of all available studies in PubMed investigating the role of IL-28B polymorphism with respect to HBV infection is given in Table 1. The main problem of case control studies for genetic analysis of host genetic markers is the number of individuals being analyzed. The studies based on small number of samples like 1, 2, 7, 8 individuals may showed statistically false positive or false negative association. Therefore care should be taken while concluding such kind of studies. It is highly recommended that this kind of investigation must include larger study groups and should be done on larger scale.

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