Hepatitis C Virus Antibodies In Nigerians With Hepatocellular Carcinoma
S Mustapha, M Bolori, N Ajayi, H Nggada, U Pindiga, W Gashau, M Khalil

Abstract
Objective: The aim of the study is to determine the frequency of antibodies to hepatitis C virus among Nigerian patients with hepatocellular carcinoma.

Method: The study was prospective. Patients with histologically confirmed hepatocellular carcinoma were studied. Sera of the patients were tested for hepatitis C virus antibodies using a third generation ELISA.

Results: A total of 108 patients consisting of 81 males and 27 females were studied, giving a male to female ratio of 4:1. Their ages ranged from 22 to 75 years with a mean of 48 years (SD±13.0). The highest incidence of hepatocellular carcinoma was found among those aged 40-49 years. A total of 19 patients (17.6%) were positive for HCV antibodies. There was no significant difference in the frequencies of these antibodies between the male and female patients.

Conclusion: HCV plays a significant role in the etiology of hepatocellular carcinoma in Nigeria. Therefore, patients with chronic hepatitis C should be screened for HCC on regular basis.

INTRODUCTION
Hepatocellular carcinoma (HCC) is one of the commonest malignant tumours in Tropical Africa. It represents the commonest malignancy in Nigerian males. Hepatitis B virus (HBV) has been shown to be the most important etiological factor for HCC in Nigeria and the rest of sub-Saharan Africa. Hepatitis C virus (HCV) is generally thought to play a lesser significant role in the etiology of HCC in this region compared to Western countries where up to 50% of HCC patients have been reported to have evidence of HCV infection.

The aim of this study is to determine the frequency of antibodies to HCV among Nigerian patients with HCC.

METHODOLOGY
One hundred and eight (108) patients with HCC seen at the University of Maiduguri Teaching Hospital were prospectively studied. The diagnosis of HCC was confirmed by histology following a Menghini needle biopsy or fine needle aspiration cytology (FNAC). The presence of anti-HCV antibodies was tested using a third generation ELISA method (Murex Diagnostic Ltd., UK). Underlying cirrhosis was diagnosed either histologically or clinically by the presence of ascites, esophageal varices or distended abdominal veins. Data were expressed as mean ± SD. Statistical analysis were done using Chi square test. A p value of ≥ 0.05 was considered significant.

RESULT
Out of the 108 patients studied, 81 were males while 27 were females giving a male to female ratio of 4:1. Their ages ranged from 22 to 75 years with a mean of 48.3 years (SD±13.0). The highest incidence of the disease was found in those aged 40-49 years (Table 1). Nineteen patients (17.6%) were positive for HCV antibodies while 72 (66.7%) were positive for hepatitis B surface antigen (HBsAg). These rates were significantly higher (p<0.001) than among blood
donors at the hospital who were used as controls (HCV antibodies and HBsAg prevalence rates of 2.3% and 12.9% respectively among blood donors). Eight patients (7.4%) were positive for both HCV antibodies and HBsAg.

Table 2 shows the distribution of HCV antibodies sero-prevalence among the different age groups. The highest prevalence was among the 40-49 years age group. History of blood transfusion was obtained in only 3 (15.8%) of the HCV positive patients. On the other hand, 11 of them (57.9%) had scarification marks/tattoos or ear-piercing. There was no significant difference in the HCV antibodies prevalence between the male and female patients (18.4% versus 16.8%) \( p > 0.1 \).

Seventeen (89.5%) of the patients had clinical or histological evidence of cirrhosis, and 3 of them (15.8%) had a history of significant alcohol ingestion.

**Figure 1**
Table 1: Age and Sex Distribution of 108 HCC Patients

<table>
<thead>
<tr>
<th>Age groups(years)</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 - 29</td>
<td>17</td>
<td>2</td>
<td>19</td>
<td>17.6</td>
</tr>
<tr>
<td>30 - 39</td>
<td>12</td>
<td>4</td>
<td>16</td>
<td>14.8</td>
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<tr>
<td>40 - 49</td>
<td>19</td>
<td>8</td>
<td>27</td>
<td>25.0</td>
</tr>
<tr>
<td>50 - 59</td>
<td>19</td>
<td>6</td>
<td>25</td>
<td>23.1</td>
</tr>
<tr>
<td>60 - 70</td>
<td>10</td>
<td>4</td>
<td>14</td>
<td>13.0</td>
</tr>
<tr>
<td>≥ 70</td>
<td>4</td>
<td>3</td>
<td>7</td>
<td>6.5</td>
</tr>
<tr>
<td>Grand Total</td>
<td>81</td>
<td>27</td>
<td>108</td>
<td>100</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Our study showed that 19 (17.6%) of the HCC patients were positive for HCV antibodies. This is similar to an earlier finding reported from southern Nigeria\(^8\). It is however much lower than in western countries and Japan where prevalence rates of 50-75% were reported\(^6, 7, 9\). On the other hand, 66.7% of our patients were positive for HBsAg, which shows that HBV plays a more significant role than HCV in the etiology of HCC in this region.

Only 3 (15.8%) of the HCV positive patients had ever received blood transfusion. However, 11 (57.9%) of the patients had scarifications, tattoos or ear piercing which indicates that these are possibly the main means of transmitting the virus in this environment. The prevalence of HCV antibodies in the general population in Nigeria ranges from 2.3 to 8.4 percent\(^{10, 11, 12}\) which is higher than in Europe and the United States where prevalences ranging from 0 to 1.8% were reported\(^{13, 14, 15}\). In spite of this, the frequency of HCV among western patients with HCC is higher than in sub-Saharan Africa because HBV and aflatoxin account for most cases HCC in this region\(^3, 4, 5\).

Eight of the HCV antibodies-positive patients were co-infected with HBV. This is significant since the two viruses are believed to be synergistic in the etiology of HCC\(^16\). Three of patients also had history of significant alcohol ingestion; therefore the etiologic role of alcohol cannot be ruled out in these patients. However, since these patients had co-existing
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macronodular cirrhosis, HCV may be the more likely etiology for HCC.

The mechanism by which HCC causes liver cancer has not been determined. The virus may cause cancer directly or indirectly through liver inflammation and regeneration associated with chronic hepatitis. Unlike HBV, HCV does not integrate into the DNA of patient's hepatocytes; therefore a direct mechanism of carcinogenesis would most likely involve the effect of viral protein on cell growth. HCV-related liver cancer almost always occurs in the presence of liver cirrhosis. This is consistent with the findings of this study which showed that 89.5% of the HCV-positive HCC patients had underlying cirrhosis. This suggests the importance of indirect mechanisms such as inflammation, fibrosis and hepatocyte regeneration in the development of cancer. The hypothesis has been put forward that malignant transformation occurs in cirrhosis when nodules within the cirrhotic liver become dysplastic.

Although HBV is the major etiological factor for HCC in Nigeria, our findings indicate that HCV is also an important cause of HCC. Therefore, patients with chronic hepatitis C should be screened for HCC on a regular basis using serum alpha-fetoprotein and ultrasound scan in the hopes of detecting this cancer early. In addition, efforts should be made to reduce the transmission of HCV through health education to reduce high risk behavior such a scarification/tattooing using unsterilized instruments.

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