Frequency of deaths in hepatitis C virus infected hepatocellular carcinoma patients and its relationship with raised serum alpha-fetoprotein levels

Fida Hussain Shaikh,1 Shaista Zeb,2 Sultan Ahmed Chandio,3 Alvina Munaf,4 Muhammad Aamir Ghori,5 Mohammad Sadik Memon,6 Asif Ali Burney7

Abstract

Objectives: To determine the frequency of deaths in hepatitis C virus infected hepatocellular carcinoma patients, and its relationship with raised serum alpha-fetoprotein levels.

Methods: The cross-sectional study was conducted at Isra University Hospital, Hyderabad, Pakistan, between March 2013 and April 2014, and comprised all patients diagnosed with hepatitis C virus and hepatocellular carcinoma over 30 years of age. Blood sample was drawn for the measurement of serum Alfa fetoprotein levels. Data was analysed using SPSS 16.

Results: The mean age of the 165 patients was 55.49±11.67 years. The mean tumour size was 5.63 ± 2.14 cm. Of the total, 31(18.8%) patients had tumour size <3cm, 65(39.4%) 3-5cm and 69(41.8%) >5cm. The mean serum Alfa fetoprotein level was 7641.0±3665.32 IU/ml. Overall mortality rate was 70(41.9%). Tumour size >5cm was significantly associated with mortality (p=0.016).

Conclusion: Serum Alfa fetoprotein levels were a useful tool for the detection of hepatocellular carcinoma in hepatitis C virus patients.

Keywords: Hepatitis C virus, Hepatocellular carcinoma, Alpha fetoprotein levels. (JPMA 66: 34; 2016)

Introduction

A potential earliest predictable oncofoetal marker is serum Alphafetoprotein (AFP) level. During early phase of life, large amount of AFP is produced by the foetal liver, but its production stops soon after birth. Synthesis of AFP is seen in hepatocellular carcinomas (HCCs) and hepatoblastomas, and that is why it is extensively used in clinical field as a prognostic marker in hepatitis C Virus (HCV)-related HCC.1 Burden of HCV and its related complications continue to rise in the world. World Health Organisation (WHO) estimated a prevalence of about 3% in 1999 with 170 million people worldwide affected by HCV.2 Malignant Hepatoma or HCC cause primary malignancy of the liver and represent the third leading cause of cancer-related deaths worldwide among them; around 80% of the HCV-related HCC are reported in the developing countries of Asia.3 It is already well known that the progression and development of HCC is closely related to HCV, predominantly in cirrhosis, and that is why proper regular examination and assessment with serum AFP levels should be performed to evaluate the prognosis in patients with HCV-related HCC.4

The current study was planned to investigate the frequency of deaths caused by elevated serum AFP levels in HCV-related HCC patients.

Patients and Methods

The prospective cross-sectional study was conducted at the Department of Gastroenterology and Hepatology, Isra University Hospital, Hyderabad, Pakistan, from March 2013 to April 2014, and comprised all patients of HCV-HCC of age ≥30 years of either gender who volunteered to take part in the study. Patients with fulminant hepatic failure, HCC caused by infection other than HCV, end-stage renal disease (ESRD), those were lost to follow-up, and the ones not willing to participate were excluded.

Structured questionnaires were used to collect the relevant information, including demography, measurement of serum AFP levels, and after six weeks, patients were followed up over the phone to see the outcome.

A blood sample was drawn for the measurement of serum AFP levels in all patients who were either admitted to hospital or were visiting the outpatient department (OPD) at the time of the study.

Data was analysed using SPSS16. Frequencies and percentages were computed for qualitative variables like gender, mortality rate, economic and educational status. Numerical variables such as age, levels of serum AFP, and
tumour size were presented as mean ± standard deviation. P>0.5 was considered statistically significant.

**Results**

Out of 165 patients, 145 (86.8%) were men and 20 (12.2%) were women. The overall mean age was 55.49±11.67 years. The mean duration of HCV was 28.17±14.23 years and that of HCC was 10.54±8.33 years. The mean tumour size was 5.63±2.14 cm. Of the total, 31 (18.8%) patients had tumour size <3 cm, 65 (39.4%) 3-5 cm and 69 (41.8%) >5 cm.

**Table**: Demographic characteristics.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total 165</th>
<th>Mean ± SD</th>
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<tbody>
<tr>
<td>Age—Years</td>
<td>55.49±11.67</td>
<td></td>
</tr>
<tr>
<td>Duration of HCV</td>
<td>28.17±14.23</td>
<td></td>
</tr>
<tr>
<td>Duration of HCC</td>
<td>10.54±8.33</td>
<td></td>
</tr>
<tr>
<td>Serum AFP - IU/ML</td>
<td>7641±3665.32</td>
<td></td>
</tr>
<tr>
<td>Size of Tumour - cm</td>
<td>5.63±2.14</td>
<td></td>
</tr>
<tr>
<td>Number Percent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>145</td>
<td>86.80%</td>
</tr>
<tr>
<td>Female</td>
<td>20</td>
<td>12.20%</td>
</tr>
<tr>
<td>Education Status</td>
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<tr>
<td>No Schooling</td>
<td>32</td>
<td>19.40%</td>
</tr>
<tr>
<td>Primary</td>
<td>47</td>
<td>28.50%</td>
</tr>
<tr>
<td>Secondary</td>
<td>55</td>
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</tr>
<tr>
<td>Graduation</td>
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<td>18.80%</td>
</tr>
<tr>
<td>Socioeconomic Status</td>
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<td></td>
</tr>
<tr>
<td>Lower</td>
<td>20</td>
<td>12.10%</td>
</tr>
<tr>
<td>Middle</td>
<td>95</td>
<td>57.60%</td>
</tr>
<tr>
<td>Upper</td>
<td>50</td>
<td>30.30%</td>
</tr>
</tbody>
</table>

HCV: Hepatitis C Virus  
HCC: Hepatocellular Carcinoma  
AFP: Alfa fetoprotein.

>5 cm. The mean serum AFP level was 7641.0±3665.32 IU/ml (Table). Overall mortality rate was 70 (41.9%) (Figure-1) at six weeks of follow-up. Tumour size >5 cm was significantly associated with mortality (p=0.016) (Figure-2).

**Discussion**

HCC is one of the most prevalent liver carcinomas associated with high mortality rates both in developed and developing countries even after all the advancement in treatment strategies. The aetiology of HCC varies worldwide; in Pakistan HBV is the most common cause of HCC. Clinical studies have revealed potential relationship between AFP levels and the progression of HCC. Patients infected with HCV infection require close monitoring of their disease progression by having the levels of AFP assessed on a regular basis. Most studies have documented the association of an elevated serum AFP level in patients with HCV as a potential biomarker to determine the development of HCC.5,6

In our study, majority of the HCV-HCC patients had AFP levels over 400 IU/ml. Similar findings were observed in a local study,7 as well as an international study.8

In a north Indian study, AFP levels were raised in 65% HCC cases; the highest level recorded being 580ng/ml.9 In a south Indian study, elevated AFP levels were observed in 47.4% cases.10 These results correlate well with our study.

In the current study, mean tumour size was 5.63±2.14 cm, while the mean serum AFP level was 7641.0±3665.32 IU/ml which is in line with earlier studies.1,10 Overall mortality in our study was seen in 41.9% while one study reported a much lower 18.7%; this difference is probably because of different lifestyle, hospital facilities, education.

Figure-1: Mortality rate in patients of HCV-HCC (Total [N=165]).

HCV: Hepatitis C Virus  
HCC: Hepatocellular Carcinoma.

Figure-2: Association of tumour size with mortality rate (Total [N=165]).
and socio-economic status as well as awareness regarding the disease.

In our study, tumour size >5cm was found to be the significant cause of mortality in HCC patients (p=0.016). This finding was similar to a local study.¹

Conclusion
Serum AFP levels were a useful tool for the detection of HCC. HCV-HCC patients with elevated AFP levels revealed higher mortality rates and had significant association with large tumour size.

References