

## Editorial

### Prevention of hepatocellular carcinoma

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Among approximately 650,000 people who die from hepatocellular carcinoma (HCC) each year, at least two-thirds live in Asia<sup>1</sup> and there is a continuation of long-term increases in its incidence.<sup>2</sup> Hepatitis B Virus (HBV)<sup>3</sup> and hepatitis C Virus (HVC)<sup>4</sup> are the major risk factors for development of HCC and co-infection has been found to have additive effect in meta-analysis.<sup>4</sup> High HBV-DNA levels have been reported to be associated with the development of HCC in patients infected with hepatitis B even with normal ALT values.<sup>5</sup> In Pakistan, a higher prevalence of HCC in patients with HBV has been noted in the poor socio-economic class<sup>6</sup>

Besides viruses, chronic alcohol use, cigarette smoking especially when in combination with either HBV or HCV<sup>7</sup> and non-alcoholic fatty liver disease (NAFLD)<sup>8</sup> have been identified as a important non viral risk factors for occurrence of HCC. Food and water-borne carcinogens including aflatoxins have contributed to unusually high rates of HCC in parts of China and sub-Saharan Africa.<sup>9</sup> Most cases of HCC develop on a pre-existing chronic liver disease, usually due to HCV, HBV or alcohol.<sup>8</sup>

Considering all these factors, we can view important preventive strategies in this regard. Prevention and early treatment of viral diseases is a vital step which should be taken. A vaccine that protects against HBV infection was licensed in 1969 and is now one of the most widely used vaccine. National vaccination programs, especially in Taiwan, have dramatically reduced the HBV infection and carriers, with a concomitant decrease in the incidence of HCC in the vaccinated populations.<sup>10</sup> Appropriate treatment of HBV infection with antivirals has reduced the titers of HBV in the blood and thereby greatly reduced the risk of chronic liver disease and HCC.<sup>11</sup>

Prevention of HCV by screening blood donors, universal precautions against blood contamination in health-care settings and reducing HCV transmission from unnecessary injection use are vital.<sup>1</sup> The risk of HCC is reduced among patients with HCV who achieve sustained virological response (SVR) with antiviral therapy.<sup>12</sup> Analysis of 14 studies, involving thousands of patients developing SVR with antiviral treatment showed reduced HCC risk in patients with an SVR, compared with nonresponders.<sup>12</sup>

Although chronic infection with hepatitis B virus and/or hepatitis C virus are the most important risk factors for hepatocellular carcinoma (HCC) worldwide, other causes of cirrhosis can also lead to HCC. High prevalence of alcoholism and the worldwide obesity epidemic (and associated fatty liver disease) are important non-viral liver diseases which are expected to increase in future.<sup>8,9</sup> Thus, appropriate public health measures to reduce the population's exposure to known etiologic agents, or early therapeutic intervention for 'at-risk' individuals before development of cirrhosis (e.g. in hereditary hemochromatosis and Wilson's disease) should be emphasized. Synergistic effect between smoking and HBV or HCV infection on the risk of HCC has been observed and thus, chronic carriers of HBV or HCV are recommended to avoid smoking.<sup>7</sup>

Since HCC arises from the background of cirrhosis, it can be useful to look for its early development with periodic surveillance. Thus, certain high risk groups like Asian males >40, females >50 with HBV or HBV cirrhosis, all non-hepatitis B cirrhosis patients should be offered surveillance.<sup>12</sup> It is recommended that these patients should have ultrasonography and alpha fetoprotein every 6-12 months.<sup>12</sup>

In conclusion, infant hepatitis B vaccination, screening blood for HCV and avoidance of unnecessary therapeutic injections are most cost effective means to prevent hepatitis and ultimately HCC. Widespread application of HCC surveillance may be helpful in prevention of HCC.

## REFERENCES

1. Farrell GC, Chan HL, Yuen MF, Amarapurkar DN, Chutaputti A, Fan JG, et al. Prevention of hepatocellular carcinoma in the Asia-Pacific region: consensus statement. *J Gastroenterol Hepatol* 2010;25:657-63.
2. Centers for Disease Control and Prevention (CDC). Hepatocellular carcinoma - United States, 2001-2006. *MMWR Morb Mortal Wkly Rep* 2010;59:517-20.
3. Khokhar N, Aijazi I, Gill ML Spectrum of Hepatocellular Carcinoma at Shifa International Hospital, Islamabad. *J Ayub Med Coll Abbottabad* 2003;15:1-4.
4. Cho LY, Yang JJ, Ko KP, Park B, Shin A, Lim MK, et al. Co-infection of hepatitis B and C viruses and risk of hepatocellular carcinoma: systematic review and meta-analysis. *Int J Cancer* 2010 Mar 15. [Epub ahead of print].
5. Kumada T, Toyoda H, Kiriyama S, Sone Y, Tanikawa M, Hisanaga Y, et al. Incidence of hepatocellular carcinoma in patients with chronic hepatitis B virus infection who have normal alanine aminotransferase values. *J Med Virol* 2010;82:539-45.
6. Parvez T, Anwar MS. Factors other than Hepatitis B Virus responsible for Hepatocellular Carcinoma in lower social class. *J Coll Physicians Surg Pak* 2002;12:268-70.

7. Chuang SC, Lee YC, Hashibe M, Dai M, Zheng T, Boffetta P. Interaction between cigarette smoking and hepatitis B and C virus infection on the risk of liver cancer: a meta-analysis. *Cancer Epidemiol Biomarkers Prev* 2010;19:1261-8.
8. Petta S, Craxi A. Hepatocellular carcinoma and non-alcoholic fatty liver disease: from a clinical to a molecular association. *Curr Pharm Des* 2010;16:741-52.
9. Fan JG, Farrell GC; Asia-Pacific Working Party for Prevention of Hepatocellular Carcinoma. Prevention of hepatocellular carcinoma in nonviral-related liver diseases. *J Gastroenterol Hepatol* 2009;24:712-9.
10. Plymoth A, Viviani S, Hainaut P. Control of hepatocellular carcinoma through hepatitis B vaccination in areas of high endemicity: perspectives for global liver cancer prevention. *Cancer Lett* 2009;286:15-21.
11. Eun JR, Lee HJ, Kim TN, Lee KS. Risk assessment for the development of hepatocellular carcinoma: According to on-treatment viral response during long-term lamivudine therapy in hepatitis B virus-related liver disease. *J Hepatol* 2010;53:118-25.
12. Bruix J, Sherman M. AASLD Practice Guidelines. Management of hepatocellular carcinoma. *Hepatology* 2005;42:1208-36.

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