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Changing epidemiology of hepatocellular carcinoma in Asia



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Hepatocellular carcinoma is a major problem in Asia because of the presence of multiple risk factors in the region such as endemicity of hepatitis B and significant contamination of foodstuff by aflatoxin in some areas. Another risk factor for HCC, chronic hepatitis C infection, in Asia is most significant in Japan, the only Asian country with more HCV than HBV-related hepatocellular carcinoma. As these risk factors can and are being modified by measures such as universal hepatitis B immunisation, successful treatment of HCV infections, reduction and improved surveillance of aflatoxin contamination of foodstuff, it is not surprising that the epidemiology of HCC in Asia is changing. All these are offset by the rising importance of NAFLD and NASH as chronic liver diseases and risk factors for HCC which contributes to the changing epidemiology of HCC in Asia.

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Introduction

Hepatocellular carcinoma (HCC) is one of the most common cancers worldwide and it is especially common in Asia. There were an estimated 782,000 new cases worldwide in 2012 of which 50% occurred in China alone [1]. In men, the highest rates of HCC in the world occur in Eastern and South-Eastern Asia with age-standardised rates (ASR) of 31.9 and 22.2 per 100,000 respectively [1]. In the context of HCC, the World Health Organisation (WHO) has classified chronic hepatitis B (CHB) infection, chronic hepatitis C (CHC) infection and aflatoxin as group 1 carcinogens [2,3]. Hepatitis B infection is endemic in most parts of Asia. Aflatoxin is a toxin produced by *Aspergillus* species in improperly stored maize and groundnuts especially in warm and humid conditions which are common in some regions of Asia. Thus, it is not surprising that HCC is prevalent in Asia.

However, the epidemiology of HCC in Asia has been changing. In 2012, the ASR of HCC in males in Eastern Asia was 31.9 per 100,000 compared to previously 35.5 per 100,000 in 2008 [1,4]. The importance of CHB as a cause of HCC is also declining due to the institution of successful hepatitis B vaccination programme in the region, offset by the rising significance of non-alcoholic steatohepatitis (NASH).

As an illustration, in our registry of 1,351 cases of HCC seen in the Department of Gastroenterology and Hepatology at the Singapore General Hospital over the past 3 decades, the proportion of cases associated with CHB infection has dropped from 71.9% in the pre-2010 era to 57.1% post-2010. In contrast, the proportion of non-viral, non-alcohol related HCCs (which connotes NASH aetiology in general) have risen from 16.6% to 27.8% over the same periods.

This article will examine and discuss these changing trends in the epidemiology of HCC in Asia.

Hepatitis B and HCC in Asia

Hepatitis B is endemic in Asia. In areas endemic for hepatitis B, up to 60–80% of HCCs are seropositive for markers of CHB infection [5,6]. A positive HBsAg serology is associated with excess relative risk of 10–30 times for the development of HCC [2,7–10]. Almost 90% of infants infected during the first year of life develop chronic infection, compared with 30% of children infected between 1 and 4 years and less than 5% of adult-acquired infection [11,12]. This is especially pertinent in Asia where the main mode of transmission of HBV infection is perinatally [13,14]. Furthermore, the risk of developing HCC is inversely related to the age of acquisition of HBV infection, being highest in individuals who acquired HBV infection perinatally [15,16]. Thus, HBV is an eminently modifiable risk factor for HCC in Asia [17]. Fig. 1 shows that HBV is the predominant cause of HCC in Asia except in Japan [18–22].

Changing epidemiology of HBV-related HCC

The HBV vaccine is highly efficacious. It has been shown to reduce the incidence of hepatocellular carcinoma and thus is recognised as the first cancer vaccine in mankind [23]. Many countries in Asia have implemented nationwide hepatitis B immunisation programmes [24]. The successful implementation of hepatitis B immunisation programmes have resulted in a significant decline in the seroprevalence of HBsAg in the country [25–27]. However, as these universal hepatitis B immunisation programmes were instituted only during the last couple of decades, the seroprevalence of HBsAg has fallen only in the younger aged population. For example, China started its universal hepatitis B immunisation programme in 1992. A subsequent nationwide HBV sero-epidemiological survey in 2006 showed that the HBsAg seroprevalence among children aged below 5 years old was less than 1.0% compared to a prevalence of 7.2% in those aged up to 60 years old [25]. Similarly, Singapore began universal HBV immunisation in 1987 and a subsequent seroprevalence study in 2010 showed that the HBsAg prevalence in young adults below 30 years of age was 1.1% compared to 4.1% previously and a separate survey showed HBsAg prevalence in children less than 17 years of age to be only 0.3% [27,28].

The successful lowering of the incidence of HBV infection by universal HBV immunisation has resulted in a progressively lower incidence of HCC. Taiwan started its universal HBV immunisation programme in 1984 following which the incidence of HCC in Taiwanese children aged 6–9 years of age declined from 0.52 per 100,000 for those born in the pre-universal HBV immunisation period between 1974 and 1984 to 0.13 per 100,000 for those born after the universal HBV immunisation programme

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