



Cross-continental insights into liver cancer: an East vs. West epidemiology

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Liver cancer, encompassing both primary and secondary forms, presents a formidable global health challenge. According to the GLOBOCAN 2020 database, liver cancer ranks as the sixth most common cancer globally in terms of incidence, yet it stands as the third leading cause of cancer-related mortality worldwide (1). By 2040, liver cancer cases and deaths are expected to rise by 55.0% and 56.4%, respectively (2). The geographical distribution of incidence and mortality rates for these cancers varies, with the highest occurrence noted in Eastern Asia, Northern Africa, and South-Eastern Asia (2). This variation arises from a complex interplay of factors, encompassing sociodemographic aspects like age and gender, environmental exposures to viruses such as hepatitis B virus (HBV) and hepatitis C virus (HCV), and cultural habits including alcohol consumption (3,4).

Primary liver cancers, notably hepatocellular carcinoma (HCC) and intrahepatic cholangiocarcinoma (ICC), contribute significantly to the burden of this disease. The risk factors implicated in their development are both common and specific. Common risk factors include cirrhosis, chronic viral hepatitis infections (HBV and HCV), non-alcoholic fatty liver disease (NAFLD) and alcohol consumption (3,4). Specific risk factors for ICC include choledochal cysts, Caroli disease, primary sclerosing cholangitis and environmental toxins such as thorotrast (5).

Understanding the intricate interplay of risk factors and incidence trends is paramount for effective prevention strategies. Primary prevention efforts, such as widespread

vaccination against hepatitis B, have demonstrated significant success in reducing the incidence of HCC in endemic regions (6). Additionally, secondary prevention measures, such as regular screening protocols targeting high-risk populations of cirrhotic or chronic hepatitis patients, hold promise in detecting liver cancer at earlier, potentially curable stages (7).

An *et al.* conducted a study leveraging data from population-based cancer registries that cover 13.1% of China's population, aiming to evaluate the incidence of HCC and ICC across different demographics. This study not only looked at overall incidence but also analyzed variations by sex, geographic area, and age group. Furthermore, they conducted a comparative analysis of incidence trends with those observed in the United States between 2006 and 2015 (8).

The authors noted that in 2015, the incidence of HCC in China was approximately five times higher than that of ICC, with 301,500 new cases of HCC compared to 61,900 cases of ICC. This study stands out for its detailed reporting of incidence rates based on histological subtypes, focusing on the two most prevalent forms of liver cancer. The distinction in reporting by histological subtypes is crucial because, although HCC and ICC share many risk factors, there are specific ones unique to each that could account for the observed differences in incidence patterns. Additionally, for a shared risk factor, its impact can vary between HCC and ICC. For example, HBV presents a much higher risk

for developing HCC compared to ICC.

Gender-wise, males had significantly higher age-standardized rates (ASRs) of incidence for both cancers (HCC: 21.5% vs. 5.9%; ICC: 3.5% vs. 1.8%). The authors correctly highlighted the higher prevalence of hepatitis B and C infections in men (8.6% for HBV and 0.5% for HCV) compared to women (5.7% for HBV and 0.4% for HCV). As reported, these disparities are known to be influenced by a combination of hormonal, immunological, and viral factors, alongside gender-specific lifestyle habits, such as the higher incidence of unhealthy drinking in men (7.9%) versus women (3.3%) (9).

Additionally, rural areas showed higher ASRs than urban ones (HCC: 16.4% vs. 11.8%; ICC: 2.8% vs. 2.6%). The authors attributed this variation to a higher prevalence of hepatitis B infection in rural areas (7.3%) compared to urban areas (6.6%). Rural areas are more susceptible to higher rates of hepatitis B infection due to a combination of factors, including limited access to healthcare services, lower vaccination rates and reduced awareness about the disease. These challenges are compounded by socio-economic and cultural practices unique to rural settings, which can hinder effective prevention and treatment efforts (10).

The study reports a nationwide decrease in HCC incidence across all genders and ages in China, with the most significant decline observed among children aged 0 to 14 years. This trend is closely linked to the introduction and expansion of HBV vaccination, underscoring its vital role in combating liver cancer. Additionally, the authors highlight the importance of dietary improvements in reducing HCC incidence, particularly among the elderly, who did not benefit from neonatal HBV vaccination. This discussion raises concerns about the rising prevalence of NAFLD (11), a known precursor to HCC, exacerbated by unhealthy lifestyles. To address the increasing incidence of HCC, the implementation of appropriate dietary measures is essential (12), emphasizing the need for a comprehensive approach to effectively mitigate liver cancer rates.

The study also clearly contrasts the trends in ASRs of HCC and ICC incidence between China and the United States from 2006 to 2015. It highlights the annual decline in HCC incidence in China and the increase in both HCC and ICC incidences in the United States within the same timeframe. The authors correctly pinpointed that the contrasting situations likely stem from varying risk factors between the two countries. In China, HBV vaccination has led to a decrease in HBV prevalence, a major HCC risk factor, whereas in the United States, rising HCV infections

and the growing impact of NAFLD are significant contributors to the increasing HCC rates. Additionally, better HCC diagnosis, improved survival in cirrhotic patients, and rising diabetes and obesity rates may also play a role. The incidence rate of ICC in the United States has also doubled, driven by a rise in unhealthy lifestyles and enhanced disease awareness and detection efforts (13). Additionally, the worldwide surge in diabetes may also be affecting ICC rates.

An's study showcases several strengths, notably its use of data from 188 cancer registries that encompass 13.1% of China's population. This approach allows for a detailed and current overview of the incidence of HCC and ICC. Limitations of this study included the high percentage (50.8%) of cases with an unknown liver subtype due to inherent difficulties in diagnosing liver cancer histopathologically. Indeed, with unique histological traits of HCC contributing to sensitive and specific imaging features, multiphasic computed tomography (CT) or magnetic resonance imaging (MRI) have been accepted to serve as initial diagnostic tests (14).

In conclusion, An's study showed the importance of HBV vaccination as a key preventive measure against liver cancer, highlighting its role in effective health management. An also brought to light the significance of unique geographic risk factors responsible for the contrasting trends in liver cancer incidence between the United States and China.

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