ABSTRACT

Although primary liver cancer is rare, its incidence rate has been rising quickly in Canada, more than tripling since the early 1980s. This cancer is more common in men than women, and the age-specific incidence rates in men have been increasing significantly in all age groups from 40 years of age onward. The death rate has followed a similar upward trajectory, in part because of the low 5-year survival rate of 18% in both sexes. Infection with the hepatitis B or C virus continues to be the most common risk factor, but other factors may also play a role. Risk reduction strategies, such as viral hepatitis screening, have been recommended in other countries and warrant consideration in Canada as part of a coordinated strategy of disease prevention and control.

KEY WORDS

Liver cancer, surveillance, risk factors, trends, prevention

1. INTRODUCTION

Primary liver cancer originates in the bile ducts, blood vessels, or connective tissue of the liver. Worldwide, this cancer is the fifth most common among men and the seventh most common among women. Primary liver cancer remains relatively uncommon in Canada, accounting for an estimated 1% of all new cancer diagnoses and deaths in 2012, but it is a rising cause of cancer-related deaths and liver transplants. We used data from the Canadian Cancer Registry to examine the incidence and mortality trends for primary liver cancer between 1980 and 2007.

Our review shows that incidence and mortality rates have increased substantially in Canada since the early 1980s (Figure 1), particularly for hepatocellular carcinoma (HCC), which is the predominant histologic type, comprising about 70% of new cases. The incidence rate is higher in men than in women, and in men, it tripled to 6.8 from 2.2 per 100,000 between 1980 and 2007 and is projected to increase into the future. An examination of age-specific incidence rates in men shows the highest incidence occurring among those 70–79 years of age, although statistically significant rate increases have occurred in all age groups examined (that is, 40+ years) since 1980 (Figure 2). The death rate has followed a similar upward trajectory, reflecting the poor prognosis with this cancer and the late-stage at which it is commonly detected. The 5-year relative survival in all stages of the disease is currently only 18% in Canada.

2. RISK FACTORS

The major risk factor for primary liver cancer is infection with viral hepatitis. Chronic infection with hepatitis B virus (HBV) accounts for approximately 23% of HCC cases in developed countries, but the percentage is much higher in the developing world, including Southeast Asia and sub-Saharan Africa.

FIGURE 1 Age-standardized incidence and mortality rates (per 100,000) of primary liver cancer, Canada, 1980–2007. Primary liver cancer incidence was defined as C22.0, and mortality, as C22.0, C22.2–C22.7. *p < 0.05 (statistically significant). AAPC = average annual percentage change, calculated using the JoinPoint Regression Program (version 3.5.4: U.S. National Cancer Institute, Bethesda, MD, U.S.A.).
Patients with chronic HBV have a risk of developing liver cancer that is 20–100 times higher than that for uninfected individuals. Chronic inflammation and repeated cellular regeneration is thought to be the mechanism by which such cases develop, typically after 25–30 years of HBV infection. Most HBV infections in the developing world are transmitted from mother to child at birth, but worldwide, the virus is also commonly transmitted between sexual partners or through household contact or other activities (for example, needle-sharing) that result in exposure to contaminated blood or body fluids.

Chronic infection with hepatitis C virus (HCV), believed to be associated with exposure to contaminated blood, is a more pertinent risk factor for non-HBV-related liver cancers in developed countries, especially in high-risk populations such as injection drug users and blood transfusion recipients. Some cases of HCV infection are also attributable to immigration from high-prevalence countries such as Egypt, Italy, and Japan.

In the United States and some northern European countries, more than half of HCC cases are found to be both HBV- and HCV-negative, implying that other risk factors may play a role. Those factors include alcohol-related cirrhosis of the liver, fatty liver disease associated with obesity, diabetes, smoking, and oral contraceptives. Less-common risk factors include hereditary hemochromatosis, α1-antitrypsin deficiency, primary biliary cirrhosis, autoimmune hepatitis, Wilson disease, and nonalcoholic steatohepatitis.

3. PRESENTATION AND DIAGNOSIS

The asymptomatic nature of liver cancer means that patients often present with late-stage or advanced malignancy. Symptoms at presentation can include abdominal pain, abdominal mass, and on occasion, paraneoplastic syndromes, including hypercalcemia, watery diarrhea, hypoglycemia, and erythrocytosis. Routine ultrasonographic screening of patients with chronic viral hepatitis or cirrhosis may identify asymptomatic early-stage disease that is amenable to treatment and, conceivably, improve survival. Further details can be found in the recently published Canadian recommendations for the clinical management of HCC.

4. RISK REDUCTION

In 2008, the U.S. Centers for Disease Control and Prevention (CDC) published updated guidelines for broadening HBV screening to all individuals in the United States who have lived or were born in world regions with intermediate or high HBV prevalence. Recommendations by the U.S. Institute of Medicine were also recently expanded to include community-based programs for HBV screening, testing, and vaccination services for immigrants. The CDC also recently released draft guidelines proposing a one-time HCV test for people in the United States born between 1945 and 1965, many of whom are unaware that they are infected with the virus.

Similar national strategies have not been implemented in Canada, but other options have been recommended, including catch-up HBV immunization for adolescents, screening for HBV in adults and children immigrating from at-risk regions, and prompt screening and treatment of household contacts of liver cancer patients. Those efforts could be complemented with efforts to reduce stigma and to raise awareness in at-risk populations about chronic HBV and HCV infection. Such efforts could include developing a national education and awareness campaign targeting the general public and at-risk communities, creating a national advocacy plan to educate policymakers about the importance of viral hepatitis infections, and ensuring that health care professionals are educated about whom to vaccinate for HBV and to screen for both HBV and HCV.

Primary health care providers can play an additional important role by providing culturally relevant education about the risk factors for liver cancer to their patients as part of the range of disease prevention and control activities outlined in Table 1.

5. IMPLICATIONS

Liver cancer trends in Canada are partly a result of greater immigration from areas of the world in which liver cancer and HBV are endemic. Census data indicate an ongoing rise in immigration from Asia, with immigrants from other regions of the world making up a smaller percentage of all new arrivals to Canada. There is also some evidence of declining...
liver cancer incidences in high-risk countries\cite{11,12}, which might be the result of control of aflatoxin exposure and improvements in coverage with childhood HBV immunization\cite{13}. How such changes will affect the burden of liver cancer in Canada and other developed countries in relation to chronic HCV infection and fatty liver disease has yet to be seen.

6. SUMMARY

Incidence and mortality rates for primary liver cancer are among the fastest rising for all cancers in Canada, which represents an increasing concern. The role of chronic viral hepatitis infection—together with the potential roles of other risk factors—poses many challenges and calls for a coordinated strategy of disease prevention and control.

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8. CONFLICT OF INTEREST DISCLOSURES

The authors have no financial disclosures to make and no conflicts of interest to report.

9. REFERENCES


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