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Hepatocellular carcinoma epidemiology



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ABSTRACT

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Primary liver cancer (namely hepatocellular carcinoma, HCC) is worldwide the fifth most common cancer in men and the seventh one in women, and it represents the third most frequent cause of cancer death. HCC rates are particularly high in eastern/southeastern Asia and in Africa, intermediate in Southern Europe, and low in most high-income countries. Persistent infections by HBV or HCV are the main recognized risk factors for HCC. Aflatoxin exposure is also an important risk factor for HCC development in Africa and eastern Asia. In high-income countries heavy alcohol drinking, tobacco smoking, overweight, diabetes, familial/genetic factors, and selected dietary aspects, have a relevant role. Updated geographic patterns and time trends in mortality from HCC in Europe, USA, Japan, and Australia are provided in the present review, together with an overview of relevant etiologic factors for HCC and main measures for the prevention of this neoplasm.

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Introduction

The epidemiology of liver cancer is made complex by the difficulty to separate the large number of secondary tumours from primary liver cancers [1]. In most populations, the major histological type of primary liver neoplasm is hepatocellular carcinoma (HCC), other forms including adult cholangiocarcinoma originating from the intrahepatic biliary ducts, angiosarcoma from the intrahepatic blood vessels, and childhood hepatoblastoma [2–4].

Primary liver cancer (namely HCC) is one of the most frequent malignancies in the world: it ranks as the fifth most common cause of cancer in men and the seventh one in women, with an estimated number of new cases of 520,000 and 230,000 respectively for men and women in 2008 [5]. Age-standardized rates (world population) are particularly high in eastern and south-eastern Asia (over 20/100,000 men and over 10/100,000 women) and middle and western Africa (15–20/100,000 men and about 8–19/100,000 women); in most high-income countries, including the Americas, Australia, and western and northern Europe, rates are below 7.5/100,000 men and below 2.5/100,000 women, while intermediate rates (around 10/100,000 men and 3/100,000 women) are observed in Southern Europe. Rates are 2–3 folds higher in men than women, the difference being generally larger in high-incidence than in low-incidence areas. Liver cancer incidence has substantially increased in North America and Northern Europe, while it has been decreasing in some high-risk countries from Asia [6–8]. Although almost half liver cancers worldwide are from China, there are scanty incidence data on liver cancer from this country; aflatoxin is its second cause after persistent infection with hepatitis B virus (HBV) and hepatitis C virus (HCV) in China, and its control is responsible for some likely recent falls in rates [9].

Five-year survival from liver cancer was about 15% in the USA in 2002–2008 [8], about 12% in Europe in 2000–2007 [10], and even lower (about 5% in 2002) in low-income countries [11]. Given its poor prognosis, the estimated number of deaths from liver cancer is not appreciably different from that of new cases (about 500,000 in men and 220,000 in women in 2008) and liver cancer represents the third most frequent cause of cancer death worldwide (the second one in low-income countries) [5].

Although liver cancer is a rapidly evolving and fatal disease for which treatment is still unsatisfactory, there is sufficient knowledge for effective primary prevention [2–4]. Indeed, causal factors have been identified for three major histological types of primary liver cancer, i.e., HCC, cholangiocarcinoma, and angiosarcoma. Persistent infections by HBV or HCV — which account for over three-quarters of all liver cancer cases in the world — result in chronic liver damage, which can play an important role in liver cancer development. In the minority of liver cancers in which viral infection is not involved, exposures that also damage the liver, as heavy alcohol consumption, or may be directly genotoxic, as tobacco smoke or aflatoxin, are of relevant importance.

In the present review, we provide some descriptive information on the geographic patterns and time trends in mortality from primary liver cancer (namely HCC) in major European countries, the European Union (EU) as a whole, and, for comparison purpose, in the USA, Japan, and Australia. Moreover, we give an overview of major environmental risk factors for this neoplasm, including established ones, as HBV and HCV infections, heavy alcohol drinking, tobacco smoking, aflatoxin, as well as selected dietary factors, overweight/obesity, diabetes, and use of oral contraceptives (OC) [2–4,12]. Familial and genetic factors are also considered.

Mortality from hepatocellular carcinoma

Over the last few decades, mortality from HCC has been considerably variable across Europe [13,14]. Mortality from primary liver cancer (namely HCC) in the EU overall, after an increase in the early 1990's, started to decline since 1994, with a decline by 1.9% per year in men and by 3.4% in women [15]. Between 2002 and 2007, overall EU mortality rates (age-standardized on the world population) from HCC decreased from 3.9 to 3.6/100,000 men and from 0.93 to 0.77/100,000 women. Male mortality substantially decreased in Italy (by 4% per year in men and by 5% in women); appreciable declines were also observed in the Czech Republic, France (after the mid 1990's), and Spain (after 2000) (Fig. 1). In contrast, recent trends were upwards in Germany, the UK, a few other northern European countries, and Portugal, particularly in men. Mortality rates remained approximately stable in Austria for both sexes, and in Finland, Germany, and Portugal for women. Mortality rates in middle-age population

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