

Chapter II

9

LIVER AND BILE DUCT  
ICD-10 C22, C24

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**Incidence**

Liver cancer is the fifth most common malignant disease in males worldwide and is the major cause of death from cancer. It accounts for an estimated 442 119 new cases each year among men and 184 043 among women. Mortality attributable to liver cancer was estimated at 416 882 deaths in men and 181 439 in women. The geographical distribution of liver cancer varies greatly worldwide, perhaps more than any other major tumour site (Ferlay *et al.*, 2004). The disease is relatively uncommon in developed countries. In the developing world, in contrast, liver cancer is very common, accounting for more than 80% of the global liver cancer cases with high rates in Sub-Saharan Africa, East and Southeast Asia, and Melanesia; China alone accounts for 55% of the worldwide incidence. The incidence among men is over twice that among women.

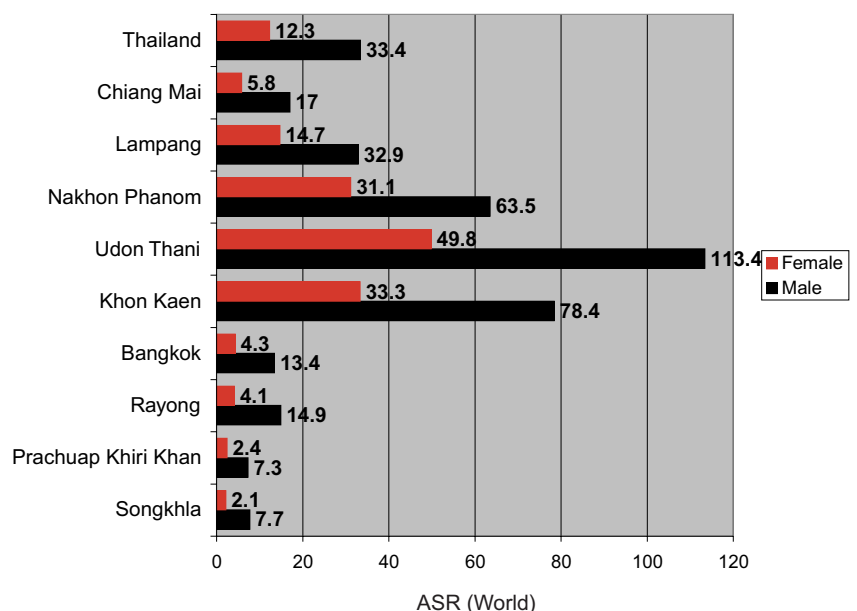
Most of primary cancers of the liver (PLC) are of epithelial cell

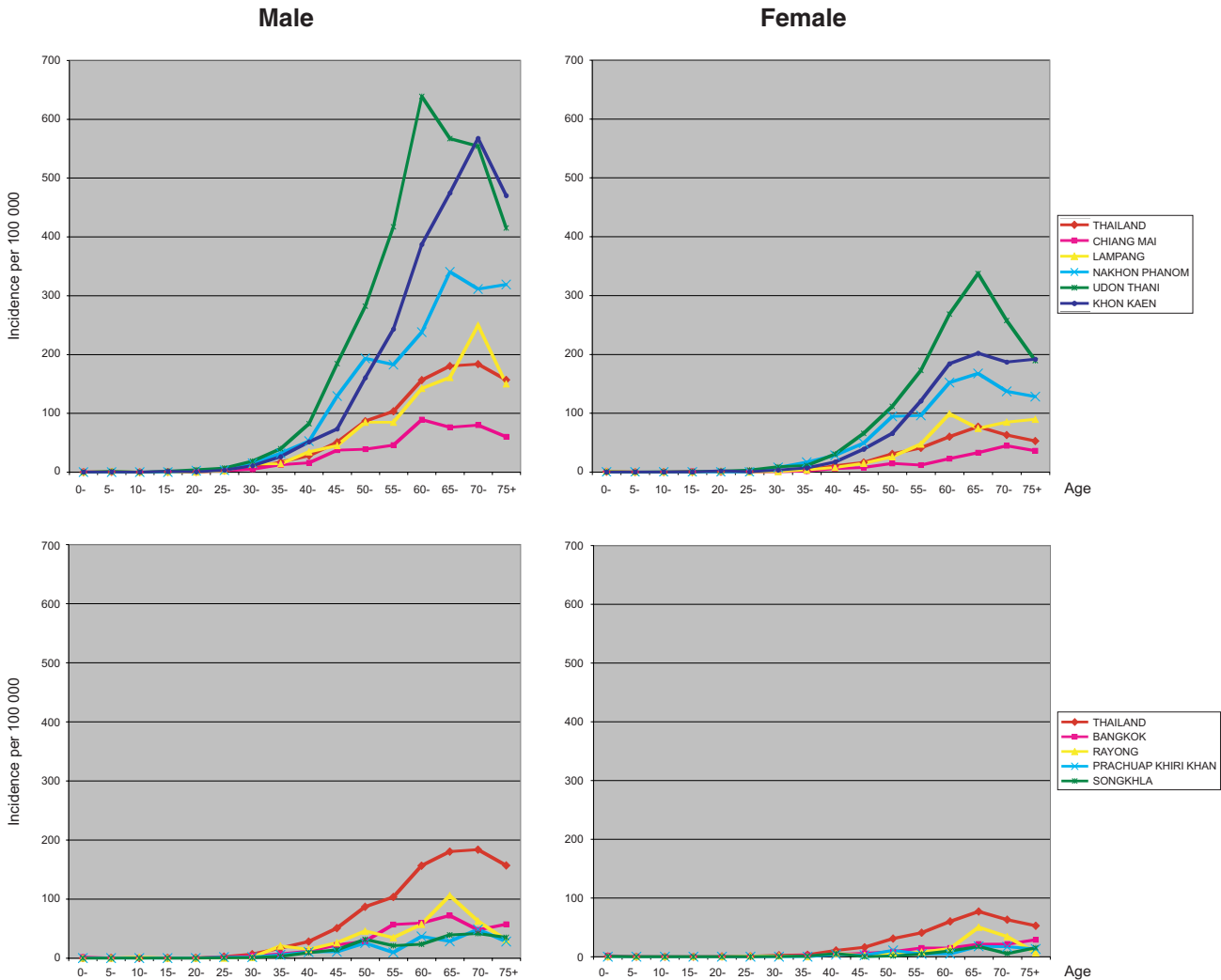
origin, either from hepatocytes or intrahepatic bile duct cells. (Hamilton and Aaltonen, 1999). Hepatocellular carcinoma (HCC) arises from hepatocytes and accounts for 80% of all PLC. Other tumor types include intrahepatic cholangiocarcinoma (tumors of that part of the bile duct epithelium located within the liver), hepatoblastoma (a malignant embryonal tumor of childhood) and angiosarcoma (arising from blood vessels) are relatively rare.

The incidence of HCC in Japan, the UK, the USA and several Nordic countries has increased over the past two decades and has become progressively associated with younger age groups (Bergstrand and Venook, 2000). Hepatocellular carcinoma is almost always lethal, survival from time of diagnosis often being less than six months; only 10% of patients survive five years or more.

Cholangiocarcinoma (CCA) is relative rare in most populations but is second among primary can-

**Figure 2.9.1** Liver and bile duct cancer in different regions, 1998-2000



**Figure 2.9.2** Age-specific incidence rates of liver and bile duct cancer, 1998-2000

cers of the liver. CCA accounts for an estimated 15% of liver cancers worldwide (Nakanuma *et al.*, 1999) and 7.7% of malignant tumors of the liver in the United States. The variation in geographical distribution of this cancer is marked. It accounts for a considerable fraction in Indochina countries such as Thailand, an endemic area for *Opisthorchis viverrini*, and Far East Asia, an endemic area for *Clonorchis sinensis* (Parkin *et al.*, 1993). A relatively high percentage of CCA is also seen in Hong Kong and Italy. The male:female ratio ranges from 1.1:1 to 2.2:1 (Parkin *et al.*,

1997). An increasing trend for mortality from CCA in non - endemic areas for liver flukes has been noted in all regions of the world (Patel, 2002).

PLC is the most frequent malignancy in Thailand with an estimated 11 581 new cases (ASR = 40.5 per 100 000 population in males, ASR = 16.3 in females) in 1990 (Vatanasapt *et al.*, 1993) and 11 868 new cases (ASR = 37.4 in males, ASR = 15.5 in females) in 1993 (Deerasamee *et al.*, 1999). It is the leading cancer in males and the third in frequency in females. There is a very marked regional

variation, with the highest incidence in the Northeast. The age - standardized incidence rate (ASR) of liver cancer in Udon Thani is the highest. The incidence rate reported from registries in Thailand ranged between ASR = 7.3 (Prachuap Khiri Khan) and ASR = 113.4 (Udon Thani) in males, and from ASR = 2.1 (Songkhla) to ASR = 49.8 (Udon Thani) in females (Figure 2.9.1). The age distribution of liver cancer patients is similar in reports from all centers in Thailand. The age - specific incidence rates of liver cancer increase at older ages and reach the peak around the

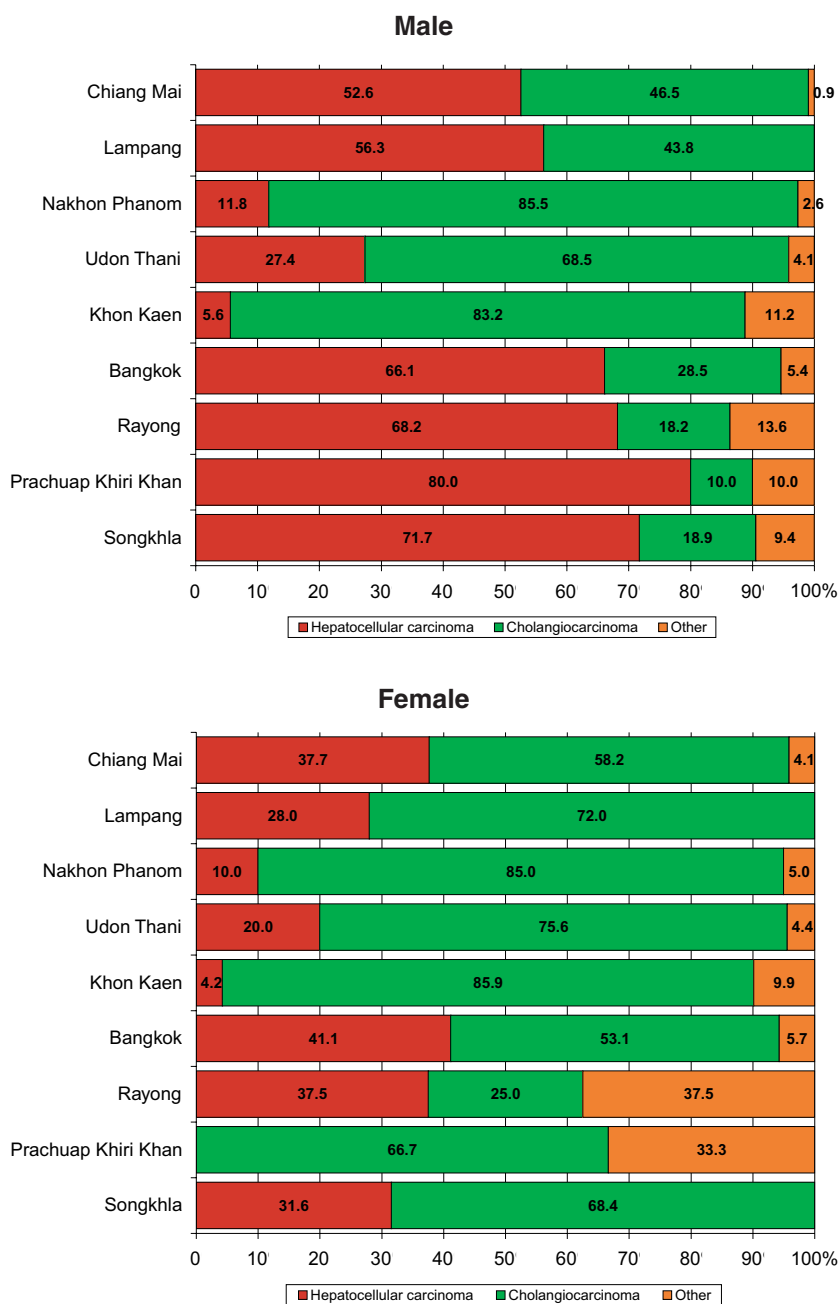
age of 65 (Figure 2.9.2).

PLC in adults are of two main histological types: HCC and CCA (including intrahepatic CCA and extrahepatic adenocarcinoma). There is considerable geographic variation, as a result of the very striking pattern of occurrence of cholangiocarcinoma, which varies more than 12 folds between regions, while the frequency of hepatocellular cancer is more or less constant in different parts of the country (Srivatanakul *et al.*, 1988). In 1998-2000, the percentage of different microscopic types of liver cancer (based on ultrasound, CT scan, cytology and histology results) varies greatly between regions (Figure 2.9.3). The proportion of CCA among PLC cases is highest in Nakhon Phanom, 85.5% in males and 85.0% in females (Figure 2.9.3).

**Risk factors**

The large differences in the pattern of liver cancer incidence between developed and developing countries imply different priorities for prevention. About 80% of liver cancer worldwide are caused by HBV, HCV, and liver flukes (Jones, 1997; Srivatanakul *et al.*, 2004). Most of HCC cases in the high risk areas (Sub-Saharan and South Africa, East Asia and Melanesia) chronic infection with HBV is the principal underlying cause, with the exception of Japan which has high prevalence of HCV infection. HBV vaccination has become a powerful tool in reducing cirrhosis and HCC. In western countries, the low risk areas (North and South America, South-Central Asia, Northern Europe, Australia and

**Figure 2.9.3** Histological types of Liver and bile duct cancer, 1998-2000



New Zealand), chronic alcohol abuse is a major etiological factor. Cholangiocarcinoma has a different geographical distribution, with highest incidence in the north-eastern Thailand. It is caused by chronic infection with the liver fluke, *Opisthorchis viverrini*, which is ingested through infected raw

cyprinoid fish. It has been demonstrated that HCV infection is a potentially strong risk factor for CCA in Japan (Kobayashi *et al.*, 2000), Italy (Donato *et al.*, 2001), the United States (Shaib *et al.*, 2005) and recently has also been shown in Thailand (Srivatanakul *et al.*, 2006 unpublished result).