Epidemiology of Biliary Lithiasis in Europe

Biliary lithiasis can be defined as the presence of concrements in the gallbladder, the biliary ducts, or both. These concrements can be stones (>3 mm) or biliary sludge containing particles of smaller size. Biliary lithiasis and gallstone disease are two exchangeable umbrella terms for the same condition. Gallstone disease can be asymptomatic or associated with chronic or acute symptoms. Symptomatic disease is more common when gallstones are present than when biliary sludge alone is present [1].

In Europe, biliary lithiasis has probably been common since antiquity. Egyptian mummies were also found to have suffered from biliary concrements. However, the physicians in the ancient Greek and Roman age often did not recognize gallstones as the cause of biliary symptoms. Galen’s writings, for example, fail to mention biliary stones. In pre-Roman cultures, the flow of bile was considered important as a metaphor for nutrition and digestion. Ancient medications, on the other hand, often contained ground gallstones taken from oxen, which were used as a remedy for various conditions. Only after these times was the importance of gallstones understood [2], and it was probably Antonius Benivenius, in his book on hidden causes of death (De abditis morborum causis, published 1528), who first described an autopsy-verified case of acute cholecystitis leading to death.

As the prevalence of biliary disease is different in different ethnic groups, it seems worthwhile to summarize epidemiologic data for each continent separately [1–3]. With very few exceptions, sonographic imaging has been used in all epidemiologic studies to detect biliary lithiasis. In spite of some differences in disease definition and observer experience, population-based studies using abdominal sonography as a screening tool allow meaningful comparisons among different subgroups and populations around the world. One study from Siberia found a good correlation between sonography and autopsy as detection methods [4].

One of the largest epidemiologic studies on this topic was the Multicenter Italian Study of Cholelithiasis (M.I.COL.), which sonographically screened nearly 30,000 patients [5]. The main results are shown in Figure 2.1. When these results recorded in the Mediterranean region are compared against results recorded in Central or Northern Europe [6], any differences noted are small, suggesting that the ethnic origin of Europeans is sufficiently similar to justify the expectation of similar prevalences of biliary stones throughout Europe, providing other key risk factors do not differ among the different countries. Nowadays, socioeconomic background, culture, and life expectancy are quite similar in all European countries. The epidemiology of biliary diseases is therefore relatively uniform throughout Europe.
Epidemiology of Biliary Lithiasis Outside Europe

In the Americas, disease prevalence within the population varies with ethnic origin [7]. Northern American whites suffer from gallstone disease with a frequency similar to that observed in Europeans. However, much higher prevalences have been found in different Indian American populations [8], such as the Pima, the Chippewa [9], and the Micmac [10] in North America and the Mapuche in South America [11]. Owing to the American Indian admixture in Mexico, standardized disease prevalence is relatively similar to that in North America or Canada [7, 12]. In each subgroup, ancestry is an important explanatory variable [13] and must be considered when such patients need care.

Epidemiologic data relating to Asian populations are quite contradictory: gallstones are found much more frequently in Chinese [14, 15] than in Japanese [16] populations. Comparison with Europeans indicates that biliary diseases in Asians have slightly different etiology and pathology. A large proportion of biliary calculi in Asians are brown pigment stones, and such stones are often found in the intrahepatic bile ducts (i.e., hepatolithiasis). Since biliary tract infestation with parasites is responsible for some of these stones, the prevalence of biliary lithiasis also depends on the availability of antiparasitic drugs in these countries. This may go some way toward explaining the variations in disease prevalence in Asia. Genetic factors also have to be considered.

Unfortunately, virtually no data are available on the prevalence of biliary lithiasis in Africa. Probably because of their lifestyle, the Bantu and the Masai have one of the lowest prevalences anywhere in the world [17]. In the USA, black Americans still have a slightly lower prevalence of biliary lithiasis [7], which shows that both genetic and environmental factors are responsible for disease development.

Unchangeable Risk Factors

Age is certainly one of the most important risk factors for biliary lithiasis [18, 19]. Children under the age of 16 rarely develop gallstones. In adults, prevalence steadily increases (Fig. 2.1). This increase is largely independent of gender, although in women there seems to be a slight decrease in prevalence during the perimenopausal years.

Female gender is an important risk factor for biliary lithiasis [20, 21]. In general, the life-time risk of biliary lithiasis is 2 or 3 times higher for a European woman than for a European man. Owing to relatively lower estrogen levels after menopause, the female predominance is less prominent in older age groups. On the other hand, any estrogen medication before or after the menopause increases the risk of biliary lithiasis. Parity and breastfeeding have also been found to be associated with biliary lithiasis [22].

Although it is evident from epidemiologic data that there is an hereditary component in biliary diseases, little is known about the genetics of gallbladder stones [23–25]. Some studies have assessed the genetic component in biliary lithiasis by analyzing possible target genes [26–28]. These genes may act by indirect metabolic pathways (obesity, cholesterol metabolism, etc.) or have a direct effect on biliary lithogenesis (biliary cholesterol hypersecretion, supersaturation, and crystallization, or bile stasis).

Other risk factors of lesser importance include Crohn’s disease [29] and liver cirrhosis [30]. Biliary sludge may also be found after the administration of ceftriaxone or after liver transplantation.

Modifiable Risk Factors and Disease Prevention

Obesity dramatically increases the likelihood of gallstone development [19, 31, 32].