Spectrum of Alcoholic Liver Disease

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KEYWORDS

• Alcoholic liver disease • Epidemiology of alcohol abuse • Alcoholic hepatitis
• Risk factors for alcoholic liver disease

KEY POINTS

- Alcoholic liver disease is a major cause of socioeconomic and health problems in the developed world.
- The risk of alcoholic liver disease is affected by gender, age, genetics, drinking patterns, and obesity.
- The spectrum of alcoholic liver disease includes simple steatosis, acute alcoholic hepatitis, and alcoholic cirrhosis.

INTRODUCTION

Liver disease from excessive alcohol consumption is an important cause of morbidity and mortality worldwide. Fermented beverages were first made in the Neolithic era (10,000 BC), and subsequently, the relationship between alcohol and a variety of health and socioeconomic problems has become increasingly evident.[1] According to the World Health Organization (WHO), 3.3 million people die of alcohol-related causes annually.[2] Despite public knowledge of its potential adverse effects, alcohol consumption has increased and, with it, morbidity and mortality from alcoholic liver disease (ALD).[3] ALD comprises a spectrum of injury, including simple steatosis, acute alcoholic hepatitis, and cirrhosis. Rather than being distinct disease entities, these pathologic processes frequently overlap.

EPIDEMIOLOGY OF ALCOHOLIC LIVER DISEASE

ALD has been extensively studied for many years. However, an improved understanding of chronic viral hepatitis and nonalcoholic fatty liver disease has altered the interpretation of prior decades of epidemiologic data concerning the health effects of alcohol abuse. It is estimated that approximately 67.3% of the adult United States

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population drinks alcohol and 7.4% meet criteria for alcohol abuse.[4] Globally, the WHO estimates that individuals older than age 15 years drink an average of 6.2 L of pure alcohol per year (Fig. 1); the equivalent of 13.5 g per day (Table 1). There is great regional variability in alcohol consumption caused by socioeconomic, cultural, and religious factors, with the highest levels in Europe and the Americas and the lowest levels in south-east Asia and eastern Mediterranean countries.[2] As a result, the burden of alcohol-related disease and disability is highest in the developed world. A small proportion of drinkers consume most of the alcohol imbibed; for example, in the United States, 20% of drinkers are responsible for 80% of alcohol consumption.[4] In 1998, estimated alcohol-related health-care costs in the United States were $26.5 billion, and in 2005 an estimated 1.152 million life-years were lost from premature mortality caused by alcohol-related disorders.[4,5]

Age and Alcoholic Liver Injury

People often start drinking alcohol at a young age, and, as a result, ALD may affect individuals of any age. Based on years of life lost because of premature mortality, ALD is most often seen in persons aged 45 to 54 years, followed by those aged 35 to 44 years.[5] Recently, there has been an increase in alcohol abuse among the elderly, with up to 10% to 15% of elderly primary-care patients meeting criteria for alcohol abuse; as a result, this subpopulation has experienced an increase in alcohol-related hospitalizations and deaths from alcoholic cirrhosis.[3,6]

Gender and Alcoholic Liver Injury

Men consume significantly more alcohol than women and consequently have 9 times more alcohol-related liver disease.[7] However, women are more vulnerable to the hepatotoxic effects of alcohol and, compared with men, have greater than twice the relative risk of ALD and cirrhosis for any given alcohol intake.[8] Women who consume 7 to 13 alcoholic beverages each week are at risk of developing ALD, compared with 14 to 27 for men. Female gender also is considered an independent risk factor for fibrosis progression in individuals with simple steatosis.[9]

Ethnicity, Genetics, and Alcoholic Liver Disease

The effect of ethnicity on the development and outcome of ALD is an important issue complicated by the changes in public reporting practices regarding race over time. Mortality data that distinguished between Hispanic and non-Hispanic white people showed that white Hispanic men had the highest death rates from cirrhosis (with mention of alcohol) followed by black non-Hispanic men, with Hispanic men of Mexican origin at highest risk.[10,11] Hispanic men also seem to develop ALD including alcoholic hepatitis and cirrhosis at a significantly younger age than do white non-Hispanic men.[12] American Indians and native Alaskans had a significantly higher mortality from chronic ALD compared with white people.[13]

Recently, genome-wide association studies found that the patatinlike phospholipase-domain containing protein 3 (PNPLA3) gene is associated with increased hepatic fat content and an increased risk of developing both alcoholic and nonalcoholic fatty liver disease.[14] A meta-analysis found that the PNPLA3 polymorphism increases the risk of developing the entire spectrum of ALD and is associated with increased disease severity.[15] The PNPLA3 polymorphism seems to be more prevalent in persons of native-American ancestry from South America compared with non-native South Americans; for example, those of Spanish, European, and African ancestry.[16] A high frequency of PNPLA3 variants and a strong association of these variants with increased serum alanine aminotransferase (ALT) levels has been found in indigenous Mexican and