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Alcoholic Liver Disease in Asia, Europe, and North America



Suthat Liangpunsakul[1,2] Paul Haber[3] Geoffrey W. McCaughan[4]

[1]Division of Gastroenterology and Hepatology, Department of Medicine, Indiana University School of Medicine, Indianapolis, Indiana; [2]Roudebush Veterans Administration Medical Center, Indianapolis, Indiana; [3]Drug Health Services, Royal Prince Alfred Hospital, Sydney Medical School, University of Sydney, Australia; and [4]Centenary Research Institute, AW Morrow GE/Liver Center Australian Liver Transplant Unit Royal Prince Alfred Hospital, University of Sydney, Australia

Alcoholic liver diseases comprise a spectrum of clinical disorders and changes in liver tissue that can be detected by pathology analysis. These range from steatosis to more severe signs and symptoms of liver disease associated with inflammation, such as those observed in patients with alcoholic hepatitis or cirrhosis. Although the relationship between alcohol consumption and liver disease is well established, severe alcohol-related morbidities develop in only a minority of people who consume alcohol in excess. Inter-individual differences in susceptibility to the toxic effects of alcohol have been studied extensively—they include pattern of alcohol consumption, sex, environmental factors (such as diet), and genetic factors, which vary widely among different parts of the world. Alcoholic liver disease is becoming more common in many parts of Asia, but is decreasing in Western Europe. Treatment approaches, including availability of medications, models of care, and approach to transplantation, differ among regions.

Keywords: Clinical Profiles; Alcoholic Liver Disease; Asia; Europe; North America.

Alcohol is consumed worldwide and has been used in many cultures for centuries.[1] When consumed in excess, it can cause diseases that place social and economic burdens on societies. In 2012, about 3.3 million deaths, or 5.9% of all global deaths, were attributed to alcohol consumption.[1] Alcohol-related health disorders are generally determined by the volume and quality of alcohol consumed and the pattern of drinking.[1]

Alcoholic liver disease (ALD) has been estimated to account for 48% of all deaths from cirrhosis.[2] It comprises a spectrum of disorders and pathologic changes in individuals with acute and chronic alcohol consumption, ranging from alcoholic steatosis to alcoholic hepatitis (AH) and cirrhosis. Alcoholic steatosis, once considered benign, is now recognized as a condition that can lead to advanced liver disease or cirrhosis.[3] Development of alcoholic steatosis depends on the dose and duration of alcohol intake. However, it is difficult to establish whether there is a threshold of alcohol intake required for development of fatty liver. Alcoholic steatosis can develop within 2–3 weeks in subjects who consume alcohol in the excessive range (120–150 g/d),[4] but can be reversed with abstinence. If alcohol consumption continues, some patients develop AH—the most florid manifestation of ALD, which is associated with high mortality.[5] Approximately 15%–20% of patients who drink alcohol excessively develop cirrhosis in their lifetime.[6]

Mortality from alcohol-associated cirrhosis in different countries correlates with per-capita alcohol consumption.[7,8] With recent changes in the economies and increases in mean incomes in developing regions of the world, there has been a rapid rise in per-capita alcohol consumption in countries such as China and India.[9,10] In fact, alcohol consumption is increasing faster in China than in other parts of the world.[9,11] The per-capita consumption of alcohol in India has increased by 55% during the past decade.[10] Based on these statistics, it is expected that the prevalence of ALD will increase globally. We review the similarities and differences in epidemiologic factors, patterns of alcohol consumption, risk factors, and clinical features of patients with ALD in different geographic regions, comparing countries in Asia with Europe and the United States.

Patterns of Alcohol Consumption

In comparing similarities and differences of ALD among different regions of the world, it is important to understand

Abbreviations used in this paper: **ADH, alcohol dehydrogenase; AH, alcoholic hepatitis; ALD, alcoholic liver disease; ALDH, aldehyde dehydrogenase; AUD, alcohol use disorder; AUDIT, Alcohol Use Disorders Identification Test; BMI, body mass index; CYP2E1, cytochrome P450 family 2 subfamily E member 1; DALY, disability-adjusted life years; IL, interleukin; WHO, World Health Organization.**

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CLINICAL ASPECTS

current and evolving patterns of global alcohol consumption. The World Health Organization (WHO) reported that in 2010, total alcohol per-capita consumption was highest in the developed world—mostly in the Northern Hemisphere.[12] Eastern Europe had the highest per-capita consumption per year, with 15.7 L/person (8.1 L/woman and 24.9 L/man).[2] The United States had per-capita consumption of 9.2 L/person (4.9 L/woman and 13.6 L/man).[12] By comparison, per-capita consumption values for China, India, Republic of Korea, and Japan were 6.7 L/person (2.2 L/woman and 10.9 L/man), 4.3 L/person (0.5 L/woman and 8 L/man), 12.3 L/person (3.9 L/woman and 21 L/man), and 7.2 L/person (4.2 L/woman and 10.4 L/man), respectively.[12] The total adult per-capita consumption in 2010, in liters of pure alcohol, is shown in Figure 1.[13]

In general, men that consume up to 2 drinks/d (1 drink/d for women) are defined as moderate drinkers.[14] Drinking at this level does not increase risk of organ injury. Daily consumption beyond these limits is considered to be heavy drinking, which can have adverse health and social outcomes.[15] This definition of chronic drinkers does not include the pattern of binge drinking—the definition varies among different geographic regions. The US National Institute on Alcohol Abuse and Alcoholism proposed a definition of binge drinking as the consumption of $\geq$5 drinks for men ($\geq$4 drinks for women) within 2 hours.[16] In the United Kingdom, binge drinking is defined as consuming $\geq$8 U for men ($\geq$6 U for women; approximately 5 or 4 American standard drinks, respectively).[17]

The WHO uses the patterns of drinking score (a composite measure of drinking patterns) to determine how people drink, instead of how much they drink, on a scale of 1 (least risky pattern of drinking) to 5 (most risky pattern of drinking).[18] Parameters used to create this indicator include quantity of alcohol consumed per occasion, festive drinking, proportion of drinking events that result in becoming drunk, proportion of drinkers who drink daily, drinking with meals, and drinking in public places. Eastern Europe had the highest pattern of drinking score (4.9),[2] whereas the score for the United States was 2—similar to countries in Asia, such as China, Japan, and Singapore.[18] India and Republic of Korea each had a score of 3.

In the United States in 2013, 86.8% of people 18 years or older reported that they drank alcohol at some point in their lifetime. Of these people, 24.6% stated that they engaged in binge drinking and 6.8% reported that they engaged in heavy drinking in the past month.[19] The percentage of men who had at least 1 heavy drinking day in the past year decreased from 31.6% in 1997 to 27.8% in 2006, then increased to 32.4% in 2009. Since the time period from 2009 to 2014, there has been no decrease or increase.[20] In the United Kingdom, the Health Survey for England reported that 57% of young men were binge drinkers.[21] Most European countries have had the same trend toward an increase in binge drinking, even in southern countries.[14] In Asia, alcohol consumption in China is increasing faster than other parts of the world.[11] A recent national survey found 56% of men and 15% of women to be current drinkers. Among them, heavy drinking was reported in 63% of men and 51% of women, whereas binge drinking occurred for 57% of men and 27% of women.[11] Alcohol use disorders (AUDs), defined as harmful patterns of drinking, such as alcohol dependence and abuse, have become a frequent problem linked to disturbances in mental and physical health and in social functioning in China.[11] There was a dramatic increase in the proportion of individuals with AUDs, from 0.45% in mid-1980s to 3.4% in mid-1990s,[11] with the lifetime prevalence of 9% during the years of 2001 to 2005.[22] India has also increased alcohol use, from 3.6 to 4.3 L/person/y.[13]

Unrecorded alcohol use varies greatly between countries, from <10% in wealthy and highly regulated nations to >50% in less well-developed nations.[23] Official statistics are typically based on taxation records of recorded consumption—these substantially underestimate total consumption, particularly in the developing world.[24] The chief concern regarding home brew is access to beverages with high alcohol content at relatively low cost. As a secondary concern, they may be contaminated with methanol, leading to life-threatening poisonings or consumption of other hepatotoxins, such as polyhexamethyleneguanidine, which has been linked to an outbreak of acute cholestatic liver injury in Russia.[23]

Prevalence and Burden of Alcoholic Liver Disease

Mortality from ALD, regardless of country, correlates with per-capita alcohol consumption.[7,8] Overall consumption or mean volume of alcohol consumed has been the usual measure of exposure, and that there is a dose–response relationship between the volume of alcohol consumed and risk of ALD.[25] A meta-analysis found that consumption of >25 g/d increased the relative risk of cirrhosis.[26] This threshold is in accordance with that from a study showing a significant increase in risk of cirrhosis with alcohol consumption of >30 g/d.[27] A separate study showed that recent drinking, rather than earlier-in-life consumption, was associated with the risk of alcohol-associated cirrhosis.[28]

Although studies correlate mean volume of alcohol consumption with ALD, several studies have associated risk with drinking patterns.[29] Binge drinking (too much too fast) and chronic excessive drinking (too much too often) are significant risk factors for ALD.[27,30] In addition to the quantity of alcohol consumption, there is controversy over whether risk of ALD depends on the type and pattern of alcohol intake, independent of absolute levels of consumption. Some studies have found red wine drinkers to have a lower risk of ALD than consumers of other beverages.[28,31] However, other studies produced contradicting results.[32,33]

Alcoholic Hepatitis

The precise incidence and prevalence of AH are unknown, partly because AH may be completely asymptomatic and thus remain undiagnosed. The available data on the burden of AH from each geographic region are difficult to compare, primarily because of the disparity in the studied