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Current Status of Liver Diseases in Korea:
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Current status of liver diseases in Korea: Toxic and alcoholic liver diseases

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= Abstract =

The study of the epidemiology of toxic liver injury has been limited in Korea. The number of hospitalizations for toxic liver injury has been estimated to be 2,400 persons per year. About 30~40% of fulminant hepatitis was attributed to toxic hepatitis. The frequent causative agents of toxic hepatitis in Korea are herbal medicines (34~40%), folk remedies (23~34%), and prescribed medicines (24~55%). However, the most common agents causing severe liver injury including fulminant hepatitis are herbal medicine and folk remedies. Antituberculosis drugs and acetaminophen are two common causes of fulminant hepatitis among prescribed drugs. Alcohol is one of the leading causes of chronic liver disease in Korea. No nationwide study on the epidemiology of alcoholic liver disease (ALD) has been carried out, but 7~31% of cirrhosis has been reported to be alcoholic in a few single-center studies. Alcohol could be a risk factor for the development of hepatocellular carcinoma (HCC) in chronic viral hepatitis. Several studies have shown that alcohol increased the risk of HCC in liver cirrhosis with HBsAg or anti-HCV. Furthermore, alcoholic cirrhosis with occult hepatitis B virus infection increased the risk of HCC.

Key words: Liver failure, Acute; Liver transplantation; Carcinoma, Hepatocellular; Liver cirrhosis; Epidemiology

Abbreviations: HCC, hepatocellular carcinoma; DALY, disability-adjusted life years PYs, person-years; ALD, alcoholic liver disease; ADH, alcohol dehydrogenase; ALDH, aldehyde dehydrogenase; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus

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Studies on the epidemiology of toxic liver injury have been limited in Korea. In a preliminary multicenter study, the number of hospitalizations for toxic liver injury was estimated to be 2,400 persons per a year.¹ About 30–40% of fulminant hepatitis has been attributed to toxic hepatitis, and toxic hepatitis was found to be one of the most common causes of fulminant hepatic failure leading to liver transplantation.^{2,3}

The most frequent causative agents of toxic hepatitis in Korea have been reported to be herbal medicines (34–40%), folk remedies (23–34%), and prescribed medicines (24–55%).^{4,6} The ingredients of such herbal medicines and folk remedies were unknown in most cases,^{4,6} but *Polygonum multiflorum* Thunberg, *Artemisia capillaris* and *Dictamnus dasycarpus* have been reported to cause toxic liver injuries.^{4,5,7–9} Antibiotics and non-steroid anti-inflammatory drugs were common in prescribed drugs.^{4,5} Antituberculosis drugs,¹⁰ antifungal agents,^{11–12} anti-convulsants,⁶ propylthiouracil,¹³ azathioprine,⁵ and albendazole¹⁴ were also reported to cause toxic liver injuries. Ticlopidine was reported to induce cholestatic liver injury.¹⁵ Raw carp juice ingestion could induce acute toxic hepatitis and acute renal failure.¹⁶ Occupational exposure of chemicals including trichloroethylene and dimethylformamide was also reported to induce toxic hepatitis.^{17,18} Several mushroom poisonings (*Amanita virosa*, *Amanita phalloides*, *Amanita subjunquillea*) were also important causes of severe hepatitis.¹⁹ However, the most common agents causing severe liver injury including fulminant hepatitis were herbal medicine and folk remedies.^{2,3} Antituberculosis drugs and acetaminophen were two common causes of fulminant hepatitis among prescribed drugs.³

The diagnosis of toxic hepatitis was based on a RUCAM (Roussel Uclaf Causality Assessment Method) score in most studies.^{4,6} Toxic hepatitis appeared more frequently in women than men, and was prevalent in the sixth and the seventh decades of life. Jaundice was the most common symptom. A hepatocellular injury pattern (50–80%) was more common than cholestatic (7–23%) or mixed injury (13–32%).^{4,5} The overall prognosis of toxic hepatitis was favorable, but patients with underlying liver disease underwent an unfavorable clinical course. The prognostic factors of toxic hepatitis were serum bilirubin and albumin at presentation.^{4,6}

Alcohol is one of the leading causes of chronic liver disease in Korea. 73.3% of adult Korean men and 36.2% of adult Korean women drink alcohol more than once a month.²⁰ The quantity of alcohol consumption increased from 5.02 kg per person in 2001 to 5.64 kg in 2004. As alcohol consumption was increasing, the socioeconomic loss attributed to alcohol also increased from 2.58% of GDP in 2000²¹ to 2.9% in 2004.²² The disability-adjusted life years (DALY) of alcoholic cirrhosis was estimated to be 798.2 person-years (PYs) per 100,000 Korean men and 149.3 PYs per 100,000 Korean women in the 2000s.²³ The DALY of hepatocellular carcinoma (HCC) associated with alcohol was estimated to be 655.2 PYs per 100,000 Korean men and 126.2 PYs per 100,000 Korean women in the 2000s.²³ Despite the heavy burden of alcoholic liver diseases (ALD) on public health, there have been few studies on ALD in Korea and the data on ALD is limited.

No nationwide study has addressed the epidemiology of ALD, but only a few single-center studies have been conducted retrospectively. Seven percent of cirrhosis was reported to be alcoholic in the 1980s,²⁴ but 31% was reported to be alcoholic cirrhosis in the 1990s²⁵ and 26% in the 2000s.²⁶ However, the direct comparison of this individual data may be inappropriate because the prevalence of ALD can differ depending on whether the hospital is a referral or a community-based one and whether it is located in a rural or an urban area.

The liver histology of chronic alcoholics varied. 10.3–23.9% of chronic alcoholics had pure steatosis, 23.1–69% had alcoholic fibrosis, and 19–23.1% had cirrhosis.^{27–28}

The association of genetic polymorphism of alcohol metabolizing enzyme with alcoholic liver disease has been investigated by several groups. Genetic polymorphism of aldehyde dehydrogenase (ADH)2 and ADH3 was not associated with the development or the severity of alcoholic liver disease. However, aldehyde dehydrogenase (ALDH)2*2 and cytochrome P4502E1 c2 were significantly lower in alcoholic cirrhosis than the controls, and the absence of these alleles was a significant risk factor for heavy drinkers.²⁹⁻³²

Alcohol could be a risk factor for the development of HCC in chronic viral hepatitis. The seroprevalence of HBsAg and anti-HCV in alcoholic patients with cirrhosis was reported to be 29% and 10.5%, respectively.³³ Several studies have shown that alcohol increased the risk of HCC in cases of liver cirrhosis with HBsAg³⁴ or anti-HCV.³³ Alcoholic cirrhosis with occult hepatitis B virus infection increased the risk of HCC.³⁵

There has been little study on the treatment of alcoholic liver diseases in Korea. Regarding liver transplantation, the alcohol relapse rate was 50% in patients who were abstinent from alcohol for less than 6 months, whereas it was 9.1% in patients who remained abstinent for 6 months.³⁶

Severe alcoholic hepatitis had a poor prognosis. A study in the 2000s showed that the 90-day mortality of alcoholic hepatitis was 16.2%, and a higher Child-Pugh score and discrimination function were associated with increased in-hospital mortality.³⁷

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