Chronic Hepatitis in West and East

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Key Words

Chronic hepatitis • Hepatitis B virus • Hepatitis C virus • Cirrhosis • Hepatocellular carcinoma

Abstract

The main etiologies of chronic hepatitis (CH) worldwide are viral B and C infections. Progression of CH to end-stage liver disease has a significant impact on mortality and need for liver transplantation worldwide. This review will focus on differences in etiology, prevalence, clinical outcomes of CH and impact on public health issues between developed Western and developing Eastern countries. Despite achievements in treatment and prevention of viral hepatitis in Western countries, processes of globalization contribute to further spread of the infections. Further efforts towards the elimination of hepatic B virus transmission throughout implementation of vaccination programs and primary prevention of hepatitis C infection are still of high importance, especially in developing world.

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Introduction

The term chronic hepatitis (CH) means active, ongoing necroinflammatory disease of the liver persisting for more than 6 months that is detectable by biochemical and histological means [1–3]. Progression of CH to end-stage liver disease has a significant impact on mortality and

need for liver transplantation worldwide [4]. This review will focus on differences in etiology, prevalence, clinical outcomes and impact on public health issues of CH between Western and Eastern countries.

Classification

The first classification (1968) of CH distinguished cirrhotic and non-cirrhotic stages, and classified the disease according to the histological degree of disease activity into chronic persistent and chronic aggressive varieties [2]. The discovery of viral etiologies for CH substantiate a development of a new classification (1994), which included primary classification according to etiology, determination of disease severity, and stage of progression [3].

Causes

The most common cause of CH is viral infections of the liver (table 1). Other causes include autoimmune, drug-induced hepatitis, Wilson's disease, α_1 -antitrypsin deficiency and cryptogenic hepatitis. CH is also occasionally noted in conjunction with chronic alcohol abuse; however, current classification does not include alcoholic steatohepatitis, the same as non-alcoholic steatohepatitis, into the CH category due to different histology [1, 3].

Table 1. Causes of chronic hepatitis

Etiology
Viral hepatitis
Hepatitis B virus
Hepatitis C virus
Hepatitis D virus
Autoimmune hepatitis
Drug-induced hepatitis
Rare diseases
Wilson's disease
α_1 -Antitrypsin deficiency
Cryptogenic hepatitis

Viral Hepatitis

Hepatitis C virus (HCV) has been recognized as a major cause of chronic liver disease. In industrialized nations, low HCV seroprevalence rates have been reported (0.6% in Germany, 0.8% in Canada, 1.1% in France, and 1.8% in USA) in comparison to Asian countries (2.1% in Indonesia, 3.2% in China, and 2.4–6.5% in Pakistan) [5]. Six major genotypes of HCV have been identified [6]. In USA and Europe, genotype 1 is most prevalent (60–70%), while genotypes 2 and 3 are less common. In Eastern countries, genotype 3 is most common in India and the Far East, genotype 4 – in the Middle East, and genotype 6 – in Hong Kong and Vietnam. Genotype identification is clinically important because genotypes 1 and 4 are more resistant than genotypes 2 and 3 to the current standard interferon-based therapies.

In Western countries, hepatitis B virus (HBV) infection is relatively rare (prevalence rate <1%) and acquired primarily in adulthood, whereas the chronic HBV infection becomes an endemic in the Asia-Pacific region (prevalence rate >8%), causing hazardous public health problems [7]. Most infections in Asia occur from infected mother to child, and from reuse of unsterilized needles and syringes. HBV can be classified into eight genotypes [8]. Genotype A is mainly prevalent in Europe, North America, India, and Africa, while genotypes B and C are found in Asia, and genotype D is more common in Southern Europe, the Middle East, and India. Cirrhosis and hepatocellular carcinoma (HCC) are more frequent in carriers of genotype C than B [8]. However, despite increasing data on pathogenic differences among genotypes, the response to current antiviral treatments is only partly clarified, therefore routine HBV genotype testing in clinical practice is not recommended this time.

Hepatitis D virus (HDV) is a rare cause of CH. HDV is dependent on the hepatitis B virus and can only super-infect (in 5%) individuals with HBV infection [7]. Sero-logic studies have shown that HDV is found worldwide; however, the infection is endemic particularly in the Mediterranean area. Three major HDV genotypes are identified; genotype 1 is prevalent worldwide and genotype 2 in East Asia [9]. In the last decade, HDV infection has very rarely been encountered in the USA and Europe, and has markedly decreased also in some Asia countries, where HBV vaccination was implemented [10].

Autoimmune Hepatitis

Originally described in Northern Europeans and Northern Americans, autoimmune hepatitis (AIH) has a worldwide distribution. It was considered that AIH is a rare disease in Asian countries compared to the West; however, a recent study from Taiwan concluded that the incidence of AIH is much higher than previously presumed [11]. In Taiwan, as in Western countries, AIH type 1 is the predominant type of disease.

Drug-Induced Hepatitis

More than 1,000 drugs have been associated with idiosyncratic hepatotoxicity. Drugs like nitrofurantoin, minocycline and methyldopa have been described as being the cause of so-called 'drug-induced chronic active hepatitis' [12]. However, in the wide spectrum of drug-induced liver injury from fulminant liver failure to liver tumors, CH is a rare type of liver damage.

Rare Diseases

α_1 -Antitrypsin deficiency is a condition mainly affecting Caucasians, with only anecdotically cases in other ethnicities [13]. Contrarily, Wilson's disease is a genetic disorder that is found worldwide. Among more than 300 Wilson's gene distinct mutations, H1069Q missense mutation is the most common in Europe, and R778L in Japan [14].

Outcomes

Globally, 57% of cirrhosis and 78% of HCC cases were attributable to either chronic HBV or HCV infection [4]. In the USA, only 7 and 27% cases of cirrhosis are attributed to B and C virus, contrarily to China (66 and 32%, respectively). Most of HCC cases both in the USA and China are caused by HBV and HCV, however with opposite proportions (20 and 51% in the USA, and 72 and 22%

in China) [4]. Implementation of antiviral therapy can decrease the risk of liver decompensation and HCC for those already infected; however, in less-developed Eastern countries the opportunities for modern treatment might be limited. Starting in the 1990s, many Western and a few less developed countries implemented universal hepatitis B immunization and experienced measurable reductions in HBV-related diseases [10]. Primary prevention of hepatitis C infection should be directed on safer blood supply, safe injection practices in the developing world and decreasing of the number of people who start injection drug use worldwide [5].

Conclusions

In conclusion, the main etiologies of CH worldwide are viral B and C infections. There exist significant differences in the prevalence of viral CH and divergence in outcomes of the disease between Western and Eastern countries; however, processes of globalization contribute to further spread of the infections. Further efforts towards the elimination of hepatic B virus transmission throughout implementation of vaccination programs and primary prevention of hepatitis C infection are still of high importance, especially in the developing world.

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