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Changes of four common non-infectious liver diseases for the hospitalized patients in Beijing 302 hospital from 2002 to 2013

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ABSTRACT

The implementation of a hepatitis B vaccination program in China has led to a significant decline in the prevalence and incidence of liver diseases secondary to hepatitis B virus over the past two decades. With recent changes in the economy and increases in average incomes in China during the same period, there has been a rapid rise in per capita alcohol consumption and an epidemic of obesity. We hypothesized that the burden of liver diseases in China has shifted from infectious to non-infectious etiologies. We retrospectively analyzed the data of 20,378 patients who were hospitalized in Beijing 302 hospital between 2002 and 2013. We found that the total admission rate secondary to alcoholic liver disease (ALD), non-alcoholic liver disease (NAFLD), autoimmune liver disease (AILD), and drug-induced liver injury (DILI) was 10.7%. ALD was the leading cause of inpatient hospitalization (3.9% of total admissions). The rate of inpatient admission for ALD, AILD, and DILI increased by 170%, 111%, and 107%, respectively during the study period. Chinese herbal medicine was the primary cause of DILI in our subjects. The burden of non-infectious liver diseases has increased over the last decade among hospitalized patients in a large tertiary hospital in China. The increase in the rate of admission for ALD and DILI from Chinese herbal medicine suggests that strategies to reduce harmful use of alcohol and increase awareness and education on the use of herbal medicine are needed.

Introduction

The implementation of a hepatitis B vaccination program in China has led to a significant decline in the prevalence and incidence of liver diseases secondary to hepatitis B virus over the previous two decades (Luo, Li, & Ruan, 2012). With recent changes in the economy and increases in average incomes in China during the same period, there has been a rapid rise in per capita alcohol consumption and an epidemic of people being overweight and obese (Gordon-Larsen, Wang, & Popkin, 2014; Hao, Chen, & Su, 2005; Sun, Ma, Han, Pan, & Xu, 2014).

Alcohol consumption is increasing faster in China than in other parts of the world (Hao et al., 2005; Tang et al., 2013). 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 in 57% of men and 27% of women (Tang et al., 2013). A dramatic increase in the proportion of individuals with alcohol-use disorder was also observed, from 0.45% in the mid-1980s to 3.4% in the mid-1990s (Tang et al., 2013).

The recent data from the Chinese National Surveys on Students' Constitution and Health showed a significant and continuous increase in the prevalence of obesity in children and adolescents during 1985–2010 (Sun et al., 2014). In another survey of 18,059 participants, the prevalence of obesity, defined by those with body mass index (BMI) $\geq$25 kg/m^2 nearly tripled from 11.7% in 1991 to 29.2% in 2009 (Gordon-Larsen et al., 2014). The increase in obesity prevalence has coincided with the epidemic of metabolic syndrome (MetS) (Roth, Qiang, Marbán, Redelt, & Lowell, 2004; Wang et al., 2013).

Alcoholic liver disease (ALD) has been estimated to account for 48% of all deaths from cirrhosis (Rehm, Samokhvalov, & Shield,

Abbreviations: AILD, autoimmune liver disease; ALD, alcoholic liver disease; DILI, drug-induced liver injury; HBV, hepatitis B virus; MetS, metabolic syndrome; NAFLD, non-alcoholic fatty liver disease.

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2013). It comprises a spectrum of pathologic changes, ranging from alcoholic steatosis to alcoholic hepatitis (AH) and cirrhosis, in individuals who consume alcohol in excess (Sozio, Liangpunsakul, & Crabb, 2010). There is a dose-response relationship between the quantity of alcohol consumed and risk of ALD (Rehm et al., 2010). A meta-analysis found that consumption of more than 25 g/day of alcohol increased the relative risk of cirrhosis (Corrao, Bagnardi, Zambon, & Torchio, 1998). Non-alcoholic fatty liver disease (NAFLD) is one of the most common chronic liver diseases worldwide (Chalasani et al., 2012). Two of the major risk factors associated with NAFLD are obesity and the presence of metabolic syndrome, MetS (Marchesini et al., 2001, 2003).

Because the lifestyle of the Chinese population is undergoing drastic changes following China's rapid economic growth (Wang et al., 2013), we hypothesized that the burden of liver diseases in China has shifted from infectious (i.e., HBV) to non-infectious or life style-related etiologies (i.e., alcohol and MetS). To test this hypothesis, we conducted a retrospective study of all hospitalized patients in a large tertiary hospital specializing in liver diseases in Beijing, Beijing 302 Hospital, to determine the burden and magnitude of non-infectious liver diseases.

Materials and methods

Study subjects

Demographic data, clinical presentations, and laboratory tests of all subjects (20 years old or older) with liver diseases who were admitted into the Liver Unit at the Beijing 302 hospital from Jan. 1, 2002 to Dec. 31, 2013 were analyzed. Our analyses primarily focused on those with ALD and NAFLD. In addition, we also included two non-infectious liver diseases, autoimmune liver disease, as well as drug-induced liver injury (DILI). All subjects were referred to Beijing 302 Hospital because of abnormal hepatic panels. After investigations, the diagnoses were made based on the standard practice guidelines (Danan & Benichou, 1993; Li, Fan, et al., 2011; Li, Jiang, et al., 2011; Lindor et al., 2009; Manns et al., 2010). Excessive alcohol consumption was defined as men who consumed more than 140 g/week of alcohol or women who drank more than 70 g/week of alcohol (Li, Fan, et al., 2011; Li, Jiang, et al., 2011). NAFLD was diagnosed in those with abnormal transaminase in the absence of excessive alcohol consumption and other possible etiologies such as viral hepatitis, iron overload, and use of medications associated with hepatotoxicity, with the radiographic imaging compatible with hepatic steatosis, based on the recommendation guidelines by the Consensus statement from the Study Group of Liver and Metabolism, Chinese Society of Endocrinology (Gao & Fan, 2013). AILD was diagnosed based on the antibody profiles, and in this study AILD consisted of primary biliary cirrhosis, autoimmune hepatitis, and the overlap syndrome between the two conditions (Lindor et al., 2009; Manns et al., 2010). DILI was diagnosed by exclusion of the known causes of liver diseases and by detailed history taking, notably on medical exposure and the onset of abnormal liver chemistries. The primary objective of our study was to determine the non-infectious liver diseases (ALD, NAFLD, AILD, and DILI)-related admission rate and their trends over a decade from 2002 to 2013. The secondary objective was to determine the inpatient mortality of these 4 non-infectious liver diseases. The study was approved by the Ethics Committee of Beijing 302 Hospital, and the study conformed to the Helsinki Declaration of 1977.

Statistical analysis

The basic characteristics of the study participants are presented as mean ± S.D. for continuous variables and as numbers with percentages for categorical variables. Chi-square tests and Student's *t* tests were used to compare values of categorical variables and continuous variables, respectively. Changes in hospitalization rates between 2002 and 2013 were determined with simple regression analysis. A 2-tailed p value <0.05 was considered to be statistically significant. All analyses were performed using SPSS version 18.0 for Windows (SPSS, Chicago, IL).

Results

Non-infectious liver disease-related admission rate during the study period

A total of 188,902 subjects with liver diseases were hospitalized in the liver unit at Beijing 302 hospital during the study period. Of these, the total admission rate secondary to ALD, NAFLD, AILD, and DILI was 10.7% (Table 1). ALD was the leading cause of inpatient hospitalization among 4 non-infectious liver diseases, accounting for 3.9% of total admissions. For those with DILI, the most commonly used medications leading to liver injury were Chinese herbal medicine (47.6%), antibiotics (13.9%), analgesic/antipyretic [acetaminophen] (12.7%), and anti-tuberculosis agents (5.5%).

Baseline demographic characteristics of ALD, NAFLD, AILD, and DILI among hospitalized patients

The gender distribution among 4 non-infectious liver diseases is shown in Fig. 1A. The majority of patients with ALD and NAFLD were male (98% and 75%, respectively). In contrast, patients with DILI and AILD were predominantly female (60% and 84%, respectively).

The mean age at presentation and the age distribution of 4 non-infectious liver diseases are shown in Fig. 1B–F. Thirty-seven percent of patients with ALD were between 40 and 49 years old, and this was statistically significant when compared to other age groups. For NAFLD, ~20%–25% of subjects were between 20 and 49 years old, with the highest prevalence being among those who were 30–39 years old (25%). Hospitalization due to NAFLD was significantly decreased in those who were older than 60 years old. The majority of patients with DILI were between 30 and 59 years old (~20%–25%). Subjects with AILD were older compared to subjects with the other three non-infectious liver diseases (peak prevalence at 33.7% for patients 50–59 years old). The prevalence of AILD in patients between 60 and 69 years old was 20.2%, which was significantly higher than that of ALD (9.7%), NAFLD (3.5%), and DILI (9.7%) in this age group ($p < 0.05$).

Table 1
The inpatient admission and mortality rate of ALD, NAFLD, AILD, and DILI during the study period.

Non-infectious liver diseases	Number of cases	Percentage of total hospitalized patients with liver diseases[a]	Deaths during hospitalization	Mortality rate (%)[b]
Alcoholic liver disease	7422	3.9%	117	1.6%
Autoimmune liver disease	6538	3.4%	30	0.45%
Drug-induced liver injury	5077	2.7%	37	0.73%
Non-alcoholic fatty liver disease	1341	0.7%	0	0%
Total	20,378	10.7%	184	0.90%

[a] Total hospitalized patients with liver diseases during the study period ($N = 188,902$).
[b] Mortality rate was calculated based on the number of deaths relative to total number of cases of each etiology.