Regional and Age Epidemiological Analysis of Hepatitis A Viral in China, 2004-2017

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Research Article

Abstract

Background: To describe the prevalence features, including age, regions, morbidity and mortality of hepatitis A viral in China from 2004 to 2017 by searching the China Public Health Sciences Data Center with the keyword "Hepatitis A virus (HAV)".

Methods: In this study, HAV morbidity and mortality data were retrieved from China Public Health Science Data Center (CPHSD) using HAV as a keyword. HAV infection data from 2004 to 2017, HAV cases and HAV-related deaths were retrieved from 31 regions in China, except Taiwan, Hong Kong and Macau. SPSS 18 is used for statistical analysis. GraphPad Prism 5 is used to draw line graphs and histograms. Microsoft PowerPoint 2016 and Adobe Illustrator CS 6 are used for drawing geographically distributed China maps.

Results: From 2004 to 2017, the rates of hepatitis A viral morbidity and mortality in China were keeping decrease annually (7.1997 and 3.0772 in 2004; 2.6430 and 0.2997 in 2010; 1.3679 and 0.2899 in 2017, respectively, 1/100,000) ($p<0.001$). The HAV infection rate of children (0-10 years old) was higher than that of the elderly (>50 years old) ($p<0.001$). The geographical distribution of HAV prevalence showed significant regional differences which showed that hepatitis A patients were more prevalent in Sichuan and Xinjiang provinces (averaged number >4,000/ year). HAV-related death does not differ much between regions (averaged number 0~2.1/ year)

Conclusions: Our analysis of viral hepatitis A prevalence features over past 14 years suggests that the incidence and mortality of HAV are decreased annually in China.

Introduction

HAV (Hepatitis A virus), one of the world's most common infected virus, is a plus-strand RNA virus, belonging to the Picornaviruses family of Hepatoviruses. HAV was discovered by Feinslone *et al.* (1973) in the feces of patients at the acute stage by immunoelectron microscopy.[1] HAV is spherical with a diameter of about 27 nm. The capsid of HAV has a 20-hedral symmetrical structure and is composed of 60 shell particles. Shell particles are composed of four kinds of peptides, VP1, VP2, VP3 and VP4.[2] HAV can cause symptomatic or asymptomatic infections in humans.

HAV infection is acquired primarily through the faecal-oral route, including close person-to-person contact and ingestion of food or water contaminated by the faeces of an infected person.[3] In rare cases, HAV infection may also be transmitted by receiving blood products from an infected blood donor.[4, 5] According to the prevalence of HAV, it can be divided into high, medium, low and very low HAV endemic areas. In highly epidemiological areas, most people are infected with HAV in early childhood. The first exposure of adults in low-prevalence areas to HAV is usually due to travel and living in areas with high prevalence of HAV, or engaging in risky behaviours, such as contact with infected persons, male-to-male sex (MSM), or the use of illicit drugs.[5–7]

With the widespread vaccination of HAV vaccine worldwide and the improvement of sanitary conditions, the epidemic areas of HAV show a trend of epidemiological decline, and the prevalence of HAV has been effectively controlled.[8, 9] In the past 20 years, HAV vaccination and lifestyle changes have both contributed to a rapid decline in HAV risk in China. Lifestyle changes are likely to have the biggest effect on reducing HAV risk in regions with the fastest GDP growth.[9] Reports from 2004 to 2009 show that most HAV cases in China are concentrated in Henan, Sichuan, Yunnan, Guizhou, Xinjiang and Gansu provinces. The number of HAV cases in those six provinces accounted for 44%~51% of the total cases in China during the investigation time. Nearly 30% of cases are children younger than 15 years of age.[10] HAV public health emergencies are mainly concentrated in primary and secondary schools, and the cases are mainly in school students.[11] The influence of regional and age differences on the clinical epidemiology of HAV was significant.[7]

The aim of this study is to investigate the incidence and mortality of HAV in China from 2004 to 2017, and to analyze the regional and age characteristics of patients with hepatitis A, so as to provide additional guidance for the government and improve the awareness of prevention and control of HAV in China.

Methods

HAV cases is an infectious disease of liver inflammation caused by HAV infection. Clinical fatigue, loss of appetite, hepatomegaly and abnormal liver function are the main manifestations. Some cases showed jaundice, mainly acute hepatitis. In addition, asymptomatic infection is more common. HAV related death is defined as all deaths from clinical diseases caused by viral hepatitis A, such as liver failure, hepatic encephalopathy, hepatorenal syndrome, and infection.

In this study, HAV morbidity and mortality data were retrieved from China Public Health Science Data Center (CPHSD) using HAV as a keyword[12]. HAV infection data from 2004 to 2017, HAV cases and HAV-related deaths were retrieved from 31 regions in China, except Taiwan, Hong Kong and Macau. The morbidity and mortality of HAV reported by CPHSD is equal to infectious diseases/population ×100,000; Deaths/population ×100,000. Grouping analysis by age and region was conducted to investigate differences in the prevalence of HAV.

The corresponding data expressed as "mean (standard deviation, SD)", "mean (standard error, SE)" or percentage learn as appropriate. For normally distributed continuous variables, student's t-test and one-way ANCOVA were performed to analyze the differences. The p value < 0.05 is considered a statistically significant difference. SPSS 18 is used for statistical analysis. GraphPad Prism 5 is used to draw line graphs and histograms. Microsoft PowerPoint 2016 and Adobe Illustrator CS 6 are used for drawing geographically distributed China maps.

Results

HAV in China

This study retrospectively analyzed HAV data published by the Chinese government (2004–2017). It was found that both the incidence of HAV (1/100,000) and HAV-related death (1/100,000) showed a decreasing trend year by year (Fig. 1)., which show that the incidence of HAV and HAV-related death were 7.1997 and 3.0772 in 2004, 2.6430 and 0.2997 in 2010, and 1.3679 and 0.2899 in 2017 (Fig. 1, Table 1). The results of linear regression analysis show good consistency ($r^2 > 0.719$, $p < 0.05$). In addition, from 2004 to 2017, there were 614,857 cases of HAV "43,918(24,184)" and 231 deaths due to HAV-related death "16.5(14.2)".

Figure 1. (A) The incidence of HAV cases (1/100,000) in Chinese populations, 2004–2017.(B) The incidence of HAV-related death (1/100,000) in Chinese populations, 2004–2017.

Table 1
The data of HAV cases, HAV-related death in China, 2004 to 2017.

Year	HAV cases		HAV-related death	
	Number	Morbidity (1/100,000)	Number	Morbidity (1/100,000)
2004	93587	7.1997	40	3.0772
2005	73349	5.6428	43	3.3080
2006	68667	5.2515	37	2.8297
2007	77135	5.8681	29	2.2062
2008	56052	4.2422	10	0.7568
2009	43841	3.3012	21	1.5813
2010	35277	2.6430	4	0.2997
2011	31456	2.3459	13	0.9695
2012	24453	1.8149	5	0.3711
2013	22244	1.6428	2	0.1477
2014	25969	1.9163	8	0.5903
2015	22667	1.6637	10	0.7340
2016	21285	1.5528	5	0.3648
2017	18875	1.3679	4	0.2899

Regional Difference Of Hav Prevalence

The study included 31 regions in China. We mapped histogram and geographical distribution to show regional differences in HAV incidence / HAV-related death (Fig. 2). According to the data on the number of HAV cases, the top three provinces with the highest number of HAV cases are Sichuan, Xinjiang and Yunnan, of which Sichuan and Xinjiang have an average number (year) of more than 4,000 (Fig. 2A, 2B). The average number (year) by regional distribution of HAV-related death in 31 regions is between 0-2.1. It does not differ much between regions. Among them, Guizhou means is 2.07, which is relatively the highest (Fig. 2C, 2D). In Beijing, the incidence of HAV decreased from 0.2093 in January 2004 to 0.0552 in January 2017 ($p < 0.05$). The reduction rate was also observed in regions with the highest HAV cases, such as Xinjiang and Sichuan provinces ($p < 0.05$).

(A) (B) The average number (year) by regional distribution of HAV cases; (C) (D) The average number (year) by regional distribution of HAV-related death. The coordinate numbers on the X axis of the Histogram (A) (C) represent different regions: 1-Beijing, 2-Tianjin, 3-Hebei, 4-Shanxi, 5-Inner Mongolia, 6-Liaoning, 7-Jilin, 8-Heilongjiang, 9-Shanghai, 10-Jiangsu, 11-Zhejiang, 12-Anhui, 13-Fujian, 14-Jiangxi, 15-Shandong, 16-Henan, 17-Hubei, 18-Hunan, 19-Guangdong, 20-Guangxi, 21-Hainan, 22-Chongqing, 23-Sichuan, 24-Guizhou, 25-Yunnan, 26-Tibet, 27-Shaanxi, 28-Gansu, 29-Qinghai, 30-Ningxia, 31-Xinjiang.

Age Differences Of Hav Prevalence

To investigate the age difference in HAV prevalence, we first divided the cases into three categories: 0–20 years old, 20–50 years old and > 50 years old. It was found that the number of HAV cases have the highest trend in 20–50 years old group, which was significantly higher than the > 50 years old group ($p < 0.05$). The number of HAV-related death cases have the highest trend in the > 50 years old group, and it was significantly higher than that of 0–20 years old group ($p < 0.05$) (Fig. 3).

To further investigate the relationship between age and morbidity and mortality, we divided cases aged 0–80 years into several age ranges on a 10-year scale. The results showed that the incidence of HAV decreased with the increase of age. Among them, the HAV cases of patients aged 0–10 years old group was the highest, which was significantly higher than that in 50–60 years old group, 60–70 years old group,70–80 years old group, and > 80 years old group ($p < 0.05$). The number of HAV-related death cases was highest in the 40–50 years old group and lowest in the 20–30 years old group. The difference in number of HAV-related death cases was significantly between the 40–50 years old group and the 20–30 years old group. In addition, although the incidence of HAV case was significantly higher in the 70–80 years old group than in > 80 years old group ($p < 0.05$), but there was no significant difference in number of HAV-related death between the two group ($p < 0.5$) (Fig. 4).

(A) HAV cases in Chinese populations, 2004–2017; (B) HAV-related death in Chinese populations, 2004–2017; (C) The percent distribution of HAV cases and HAV-related death.

(A) HAV cases in Chinese populations, 2004–2017; (B) HAV-related death in Chinese populations, 2004–2017.

Discussion

Based on the analysis of publicly available data from CPHSD, the annual prevalence of HAV and HAV-related death rates in China have been decreasing. Morbidity and mortality vary by region and by age group. The morbidity rate was the highest among children and adolescents, and the mortality rate was the highest among middle-aged and elderly people (40–50 years old group). The highest morbidity rate was found in Sichuan and Xinjiang provinces. Although the incidence of hepatitis A is decreasing year by year (Fig. 1) (Table 1). However, due to China's vast territory, regional economic development is uneven. And it can be found from Fig. 2 that the areas with high HAV incidence are mainly concentrated in the west, while the population in the west of China is much smaller than that in the southeast. Relatively poor economic conditions and sanitary conditions may be one of the reasons for the high incidence of HAV in the western region (Sichuan, Xinjiang, Yunnan etc.).

The prevalence of HAV, especially in developing countries, remains a great challenge for the world's public health authorities[6].But, in this study, the year-on-year decrease in the prevalence of HAV and HAV-related mortality indicates that China's prevention and control measures have played a positive role. It is known that the prevalence of HAV is closely related to economic conditions and hygiene habits. For more than 10 years, with the development of China's economy, health and medical conditions have gradually improved, residents' awareness of disease prevention has increased, and the promotion of hepatitis A vaccine. These are probably the reasons why the fatality rate and infection rate in China have been declining year by year.

HAV is the most common pathogen that causes acute liver disease worldwide. In 2010, there were 1.4 million cases of hepatitis A and 27,731 deaths worldwide. [13]The incidence of HAV widely between countries, with high prevalence in developing countries. It is also related to the quality of local sanitation, the quality of drinking water sanitation and socio-economic factors. In endemic areas, the severity of the disease is closely related to age. HAV infection mainly occurs in early childhood and, although mostly asymptomatic, can lead to illness and death in some cases. Symptomatic disease often occurs in older infected children and infected adults.[14] For developed areas, due to health, medical care, high economic level, low prevalence. However, herd immunity is low and outbreaks are often reported.[15]

HAV often causes symptomatic hepatitis in adults and asymptomatic subclinical infection in children. The incubation period for HAV is about 28 days. The clinical presentation usually occurs after the incubation period with sudden onset. Signs and symptoms of infection include nausea, vomiting, diarrhea, dark urine, jaundice, fever, headache, weight loss, abdominal pain, and loss of desire to smoke or drink alcohol. The likelihood of symptoms increases with age. Most children under the age of 6 have no symptoms. Jaundice can occur in more than 70 percent of older children and adults infected with HAV. Enlargement of the liver and spleen may occur. Acute illness from HAV infection usually lasts no more than two months. The clinical symptoms of HAV overlap with many other gastrointestinal and febrile symptoms, making it difficult to differentiate from other types of acute viral hepatitis.[16, 17]

Water-borne HAV infections are mainly due to drinking water contaminated by adjacent septic tanks or swimming in water contaminated with sewage.[18, 19] Food transmission mainly occurs when the faeces of HAV carriers are transferred to food during food preparation, or when the food plants are contaminated by the faeces of HAV carriers during harvesting or processing. Another modality of the faecal-oral route is extensive and close personal contact between the carrier and the vulnerable person. For example, MSM, in closed institutions such as schools and day-care attendance centers are susceptible to HAV by sharing items.[20, 21]

Therefore, the fecal-oral transmission of HAV can be effectively reduced in terms of daily diet, such as heating food and water to 85 degrees Celsius or above for one minute, avoiding contact with and eating uncooked food and natural water.[22, 23] In addition, prevention of vulnerable populations and children through active or passive immunization is the most important approach. Passive immunity: immunoglobulin. It can be used for pre-exposure prophylaxis or, in some cases, post-exposure prophylaxis. And according to the dose of different, in different time has a protective effect.[24] Active immunization: Vaccines. The approval and widespread use of the 1990s HAV vaccine has paved the way for the prevention of this disease. The initial focus was on immunizing children in high prevalence areas and certain other high-risk groups.[25, 26] In 2006, the Centers for Disease Control and Prevention (CDC) made a major change, recommending HAV vaccination for all children between 12 and 23 months of age. [27] In China, HAV vaccine has become one of the main vaccines for children and was included in the Expanded Immunization Vaccine for Children in May 2008.

As a developing country with a population of 1.4 billion, China faces great challenges in dealing with the spread of HAV. In 1988, an outbreak of hepatitis A sickened nearly 300,000 people in Shanghai, China, by eating raw clams, a popular delicacy that had been consumed by the city's residents in the month before the outbreak began[28]. With the improvement of economic level and the improvement of residents' environmental hygiene, as well as the widespread vaccination of HAV vaccine throughout the country, the reported incidence of hepatitis A decreased from > 50/100,000 in 1990 to 1.55/100,000 in 2017.[9] Our study found that the incidence of HAV was regional and age specific, and the highest incidence of HAV was found in Xinjiang and Sichuan. The incidence is manifested by age in children, adolescents are vulnerable to infection transmission. The number of death cases showed a relatively high trend in the 40–50 years old group, which was significantly higher than the 20–30 years old group.

There are some limitations in this study. The coverage of data collection is not high enough to cover the entire HAV-infected population in China, and the lack of access to HAV epidemiological data in Taiwan, Hong Kong and Macau may lead to bias in this study. Also, the public data studies here are incomplete, making it impossible to analyze other risk factors such as race, occupation, residential environment and blood donation. This study focuses on regional and age differences in HAV in mainland China and concludes that HAV has regional and age characteristics. Regional attention needs to be paid to the spread of HAV in Sichuan and Xinjiang. Attention needs to be paid to transmission among children and adolescents. The public should be aware that more effective prevention strategies should be implemented to reduce and prevent the incidence of HAV/hepatitis A disease.

Conclusions

This study analyzed the epidemiological characteristics of HAV. The incidence and mortality of HAV are decreasing year by year. The incidence of HAV varies by region and age. In terms of region, the higher incidence of HAV was found in Xinjiang and Sichuan (averaged number > 4,000/ year). HAV-related death does not differ much between regions (averaged number 0 ~ 2.1/ year). In terms of age, children and adolescents are vulnerable to transmission. The HAV cases of patients aged 0–10 years old group was the highest. And the number of HAV cases has a downward trend with age. The number of HAV-related death cases showed a relatively high trend in the 40–50 years old group, which was significantly higher than the 20–30 years old group. The results may provide basic data for preventing and controlling the spread of HAV. Regional attention should be paid to the spread of HAV in Xinjiang and Sichuan. Attention needs to be paid to transmission among children and adolescents.

Abbreviations

CPHSD
China Public Health Science Data Center
CDC
Centers for Disease Control and Prevention
HAV
Hepatitis A virus
MSM
male-to-male sex

Declarations

Availability of data and materials: In this study, HAV morbidity and mortality data were retrieved from China Public Health Science Data Center (CPHSD) using HAV as a keyword [12]. HAV infection data from 2004 to 2017, HAV cases and HAV-related deaths were retrieved from 31 regions in China, except Taiwan, Hong Kong and Macau.

Authors' contributions: Yan Xu designed the study, implemented the research plan, collected and analyzed the data, and wrote the first manuscript. Ruiti Tang also participated in the research project, analyzing and interpreting the data. Weiming Li also participated in the design of this research and revised the manuscript. All authors participated in the discussion, reviewed and edited the manuscript, and approved the final manuscript.

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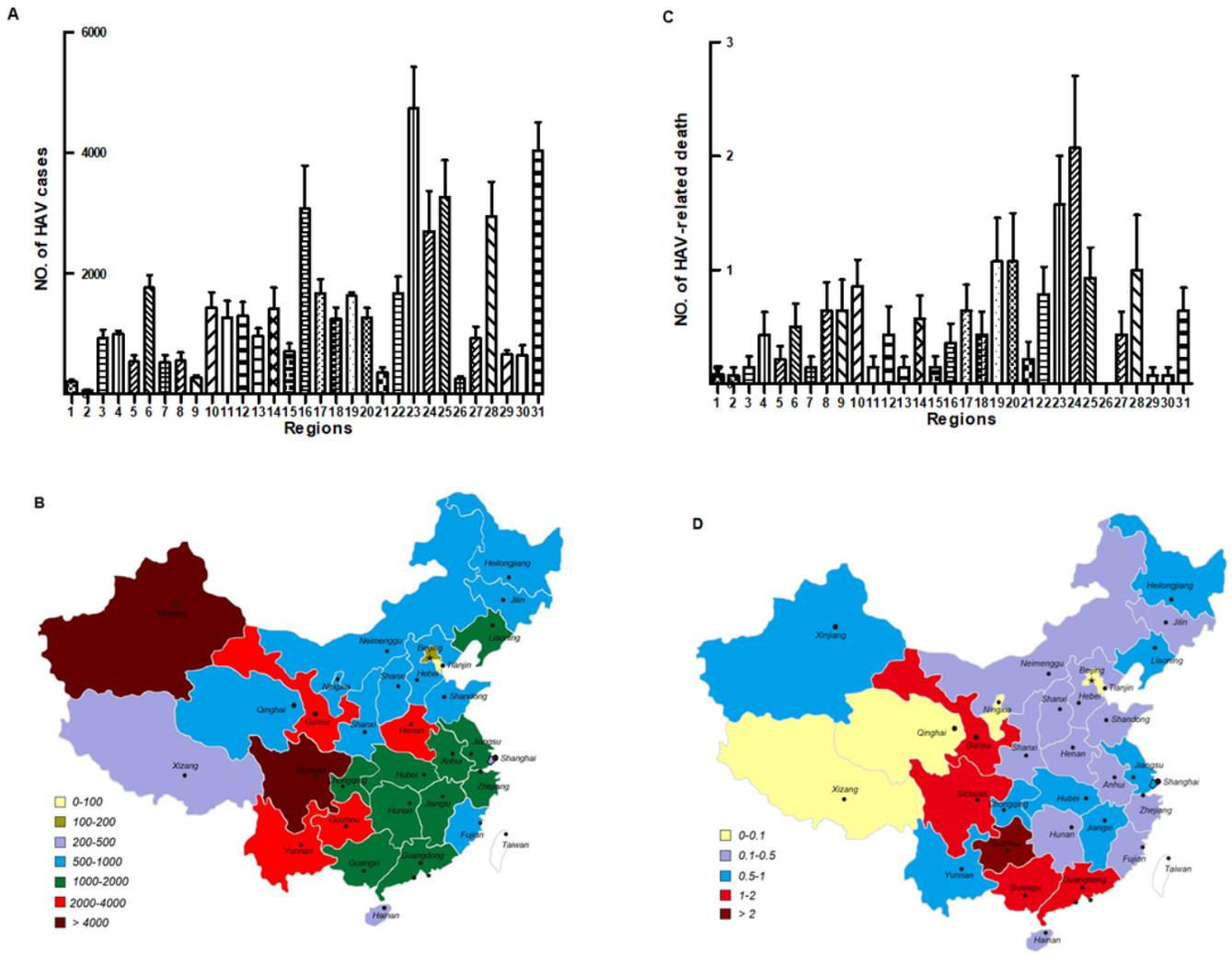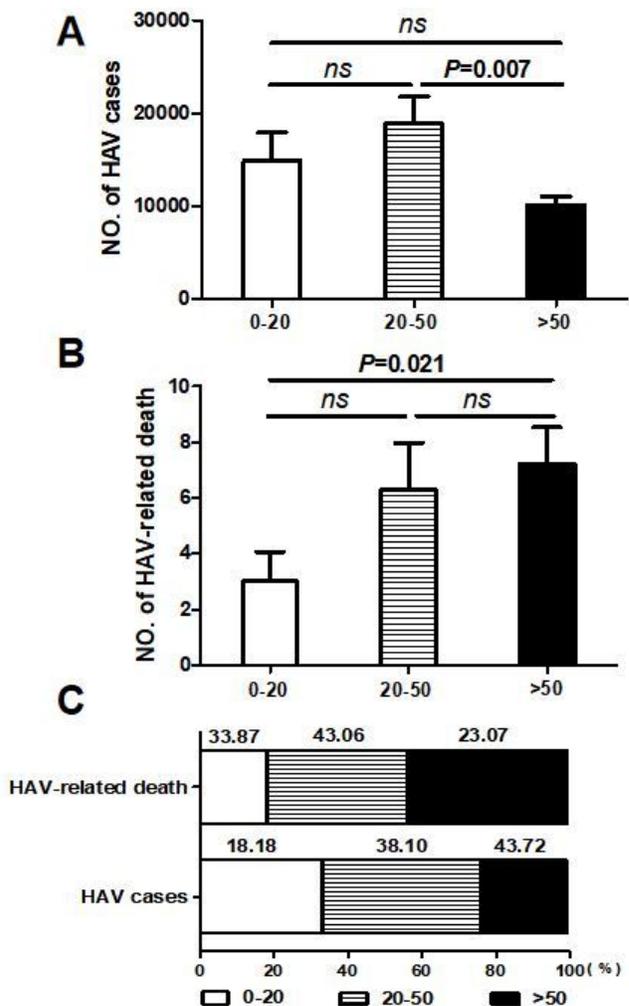
Figures

Figure 1.
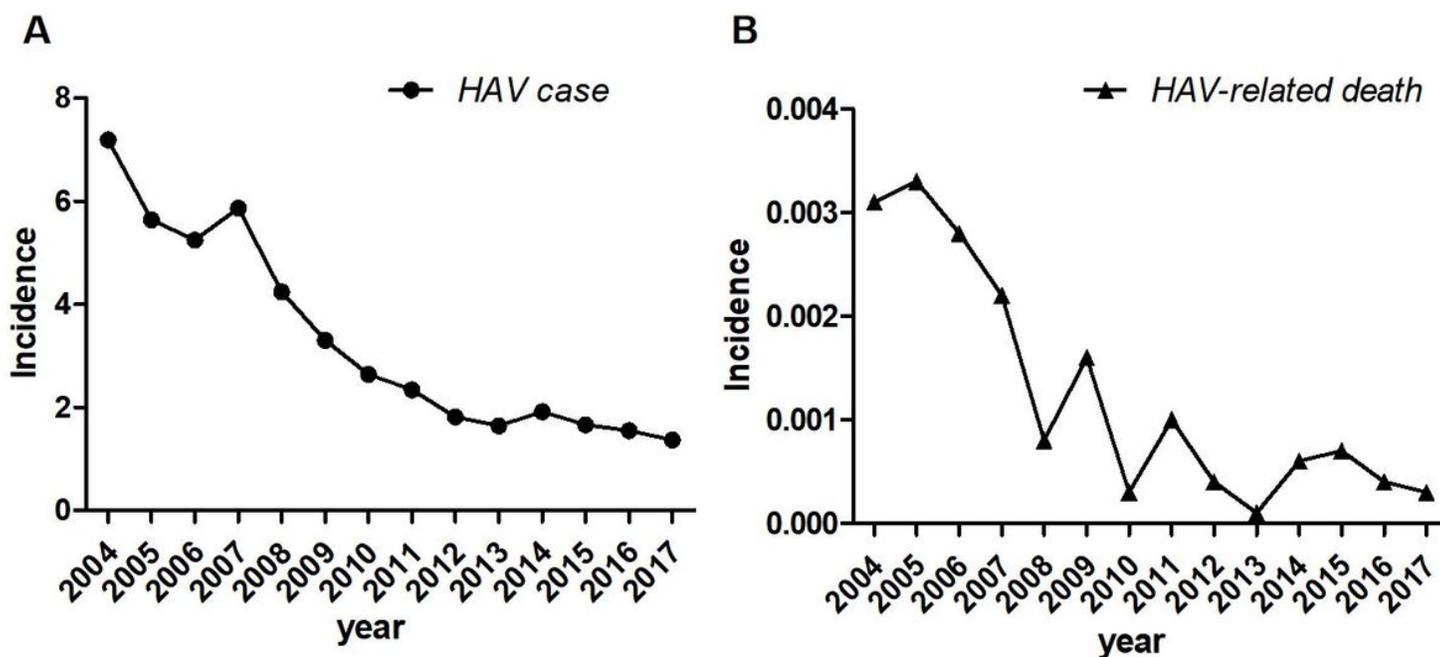
Figure 1

(A) The incidence of HAV cases (1/100,000) in Chinese populations, 2004–2017. (B) The incidence of HAV-related death (1/100,000) in Chinese populations, 2004–2017.

Figure 2

The average number (year) by regional distribution of HAV cases and HAV-related death in Chinese populations, 2004–2017 (A) (B) The average number (year) by regional distribution of HAV cases; (C) (D) The average number (year) by regional distribution of HAV-related death. The coordinate numbers on the X axis of the Histogram (A) (C) represent different regions: 1-Beijing, 2-Tianjin, 3-Hebei, 4-Shanxi, 5-Inner Mongolia, 6-Liaoning, 7-Jilin, 8-Heilongjiang, 9-Shanghai, 10-Jiangsu, 11-Zhejiang, 12-Anhui, 13-Fujian, 14-Jiangxi, 15-Shandong, 16-Henan, 17-Hubei, 18-Hunan, 19-Guangdong, 20-Guangxi, 21-Hainan, 22-Chongqing, 23-Sichuan, 24-Guizhou, 25-Yunnan, 26-Tibet, 27-Shaanxi, 28-Gansu, 29-Qinghai, 30-Ningxia, 31-Xinjiang.
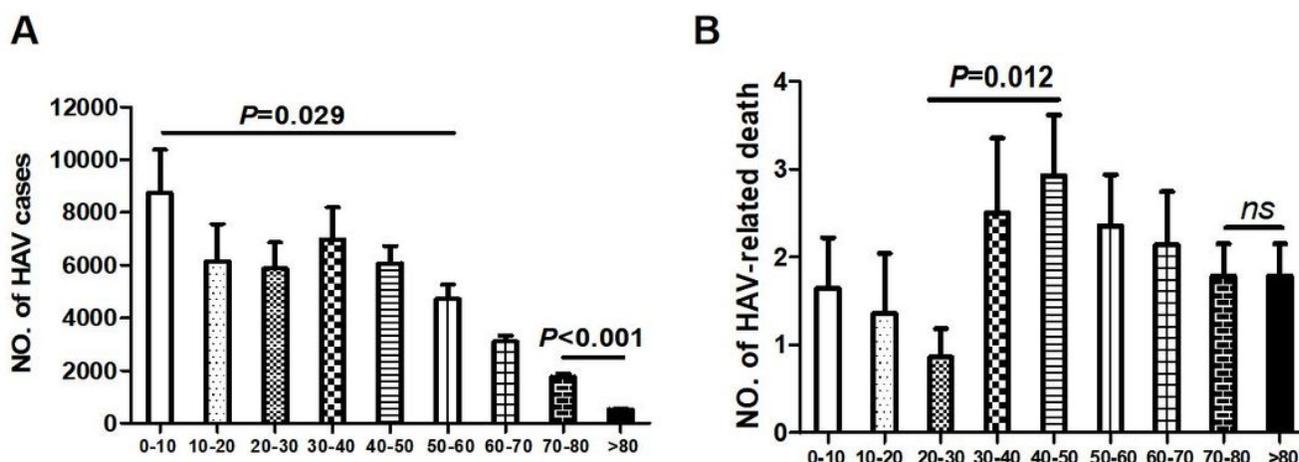
Figure 3

Figure 3

The averaged number (year) by age difference of HAV cases and HAV-related death in Chinese populations, 2004–2017 (A) HAV cases in Chinese populations, 2004–2017; (B) HAV-related death in Chinese populations, 2004–2017; (C) The percent distribution of HAV cases and HAV-related death.

Figure 4

Figure 4

The averaged number (year) by age difference of HAV cases and HAV-related death in Chinese populations, 2004–2017 (A) HAV cases in Chinese populations, 2004–2017; (B) HAV-related death in Chinese populations, 2004–2017.

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