

Acute Hepatitis B — China, 2005–2019

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ABSTRACT

Introduction: Hepatitis B is a major public health threat in China. Detailed subtyping of acute hepatitis B (AHB) has been reported to China's National Notifiable Disease Reporting System (NNDRS) since 2005. We divided the years since NNDRS reporting started into three stages: a “primary stage” (2005–2008), a “catch-up stage” (2009–2012), and an “AHB surveillance pilot stage” (2013–2019). We evaluated characteristics of AHB and progress towards AHB control in these three stages.

Methods: We obtained data on cases reported to NNDRS between January 1, 2005 and December 31, 2019 and compared the annual incidence of reported AHB in each of the three stages by region, age, and gender.

Results: The incidence of reported AHB declined from 7.52 per 100,000 in 2005 to 3.21 per 100,000 in 2019 — a decrease of 57.31%. The annual incidences of AHB in the primary stage, the catch-up stage, and the AHB surveillance pilot stage were 7.45 per 100,000, 5.78 per 100,000, and 4.26 per 100,000, respectively; 7 provincial-level administrative divisions (PLADs) had an annual incidence of more than 10 per 100,000 in the primary stage, 5 PLADs in the catch-up stage, and 1 in the AHB surveillance pilot stage. The group aged 20–29 years old had the highest annual rate of reported AHB in the primary stage (14.35 per 100,000) and in the catch-up stage (10.42 per 100,000), and the group aged 30–39 years old had the highest annual rate in the surveillance pilot stage (5.89 per 100,000). AHB affected males and females in all age groups.

Conclusions and Implications for Public Health Practice: The incidence of AHB had decreased significantly since the start of the NNDRS reporting in 2005, but additional action is needed to eliminate AHB in China. Hepatitis B vaccine (HepB) coverage in adults should be increased to reduce new AHB cases among people over 20 years old, epidemiological investigations of AHB cases should be conducted to identify risk factors for infection, and prevention of mother-to-child transmission needs to be strengthened.

INTRODUCTION

Hepatitis B is a major public health threat in China as China has over 30% of the hepatitis B surface antigen (HBsAg)-positive individuals in the world (1). In 2018, 12% of the global burden of liver cancer was among men in China (2). The combined incidence of acute and chronic hepatitis B increased from 75.57 per 100,000 in 2005 to 89.00 per 100,000 in 2007, and subsequently decreased to 68.74 per 100,000 in 2016 (3). However, the epidemiological characteristics of acute hepatitis B (AHB) are not clearly known, and the morbidity of AHB may reflect recent infections and impact of hepatitis B vaccination.

Hepatitis B cases have been reported to China's National Notifiable Disease Reporting System (NNDRS) since 1990, and detailed subtyping (acute and chronic) of cases has been available since 2005. The hepatitis B vaccine (HepB) was included into the Expanded Program on Immunization in 2002; a HepB catch-up campaign was conducted among children under 15 years of age during 2009–2011 to increase HepB coverage of adolescents; and an AHB surveillance pilot project was started in 2013 to improve the accuracy of AHB NNDRS reporting by standardizing diagnostic and reporting procedures and promoting IgM anti-HBc testing to help distinguish acute hepatitis B from flare-ups of chronic hepatitis B. For this study, we divide prevention and control of AHB into three stages: a “primary stage” (2005–2008), a “catch-up stage” (2009–2012), and an “AHB surveillance pilot stage” (2013–2019).

We obtained reported AHB case-based data from the NNDRS and analyzed the epidemiological characteristics of AHB and assessed progress towards AHB control in China.

METHODS

We obtained AHB case and incidence data reported to the NNDRS between January 1, 2005 and December 31, 2019. The NNDRS is a national, hospital-based, passive surveillance system that includes

all county and township hospitals. In 2004, China revised NNDRS by establishing a web based, real-time, data sharing surveillance platform. Data included in this study were from the mainland of China.

We compared the reported annual incidences of AHB in the three stages by geographical region and age and gender of patients. AHB cases were divided into 9 age groups: <9 years, 10–19, 20–29, 30–39, 40–49, 50–59, 60–69, 70–79, and ≥80 years old. We analyzed characteristics and morbidity of AHB by stage, age, and gender using Microsoft Excel (version 2007); we determined the spatial distribution of AHB reports with ArcGIS (version 10.4; Esri Institute).

RESULTS

The reported incidence of AHB in China declined from 7.52 per 100,000 in 2005 to 3.21 per 100,000 in 2019 (Mean=5.52), a 57.31% decrease. The annual number of reported cases in the primary, catch-up, and AHB surveillance pilot stages were 97,755, 77,520, and 58,396, respectively, and the annual incidences of AHB in the three stages were 7.45, 5.78, and 4.26 per 100,000. The annual incidence in the AHB surveillance pilot stage was 42.82% and 26.30% less than in the primary and catch-up stages. (Figure 1)

In the primary stage, there were 7 provincial-level administrative divisions (PLADs) with annual incidences over 10 per 100,000: Guangxi Zhuang Autonomous Region (22.18 per 100,000), Hainan Province (16.22), Gansu Province (14.97), Ningxia Hui Autonomous Region (14.12), Fujian Province (12.15), Inner Mongolia Autonomous Region (10.77), and Guizhou Province (10.30). In the catch-up stage, there were 5 PLADs with annual incidences over 10

per 100,000: Guangxi (21.72), Fujian (19.13), Hainan (12.12), Shanxi Province (10.92), and Xinjiang Uyghur Autonomous Region (10.39). In the AHB surveillance pilot stage, 1 PLAD had an annual incidence over 10 per 100,000: Guangxi at 14.72 per 100,000. (Figure 2)

During the primary stage, the 3 age groups with the highest annual incidence of reported AHB were aged 20–29 years old (14.35 per 100,000), 30–39 years old (9.75), and 40–49 years old (7.49). During the catch-up stage, the 3 age groups with the highest annual incidences were aged 20–29 years old (10.42 per 100,000), 30–39 years old (7.87) and 40–49 years old (6.41). In the AHB surveillance pilot stage, the 3 age groups with the highest annual incidence were aged 30–39 years old (5.89 per 100,000), 20–29 years old (5.77), and 50–99 years old (5.26). (Figure 3)

Compared with the primary stage, the 2 age groups with the largest decreases in annual incidence in the catch-up stage were aged 10–19 years old (a 52.29% decrease) and 0–9 years old (a 48.58% decrease). Compared with the catch-up stage, the 2 age groups with the largest decreases were aged 10–19 years old (a 55.02% decrease) and 20–29 years old (a 44.67% decrease). (Figure 3)

AHB affected males and females in all age groups. In the primary stage, there were 67,657 reported annual AHB cases among males (10.06 per 100,000 population) and 30,095 reported annual cases among females (2.29 per 100,000). In the catch-up stage, there were 52,223 reported annual AHB cases among males (7.60 per 100,000) and 25,297 reported annual cases among females (1.89 per 100,000). In the AHB surveillance pilot stage, there were 37,598 reported annual AHB cases among males (5.36 per 100,000)

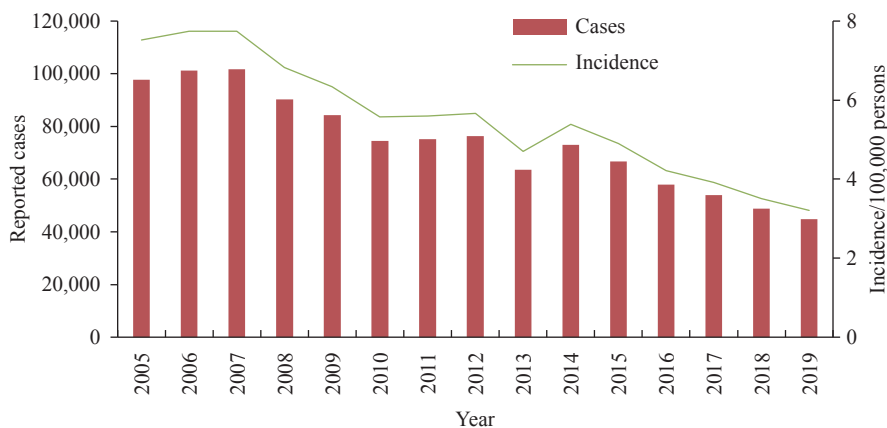


FIGURE 1. Reported cases and incidence of acute hepatitis B (AHB), in China, 2005–2019.

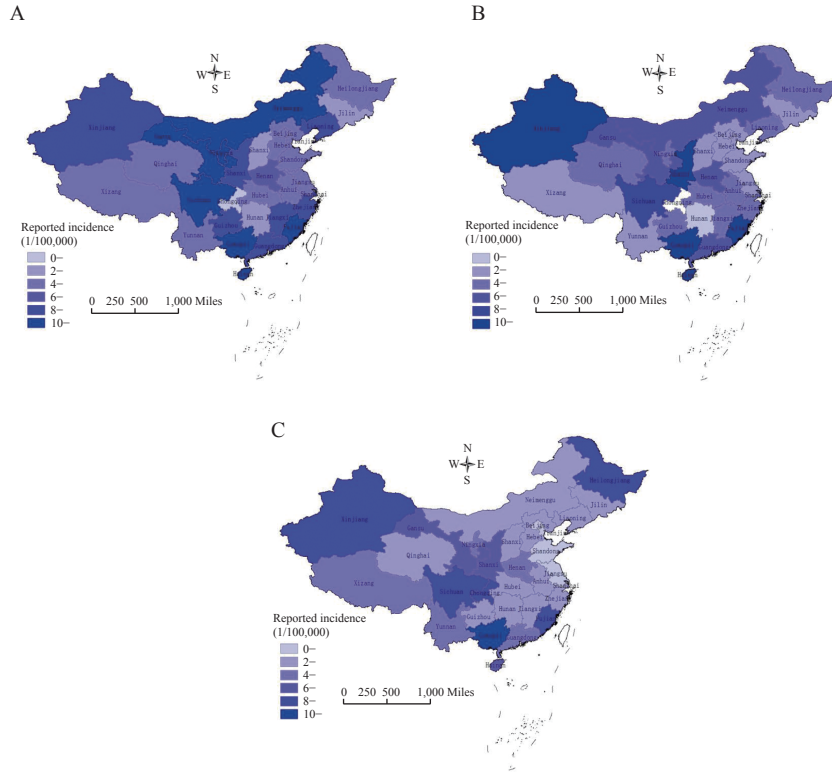


FIGURE 2. Geographical distribution of the reported acute hepatitis B (AHB) in China, 2005–2019. (A) Primary stage. (B) Catch-up stage. (C) Acute hepatitis B (AHB) surveillance pilot stage.

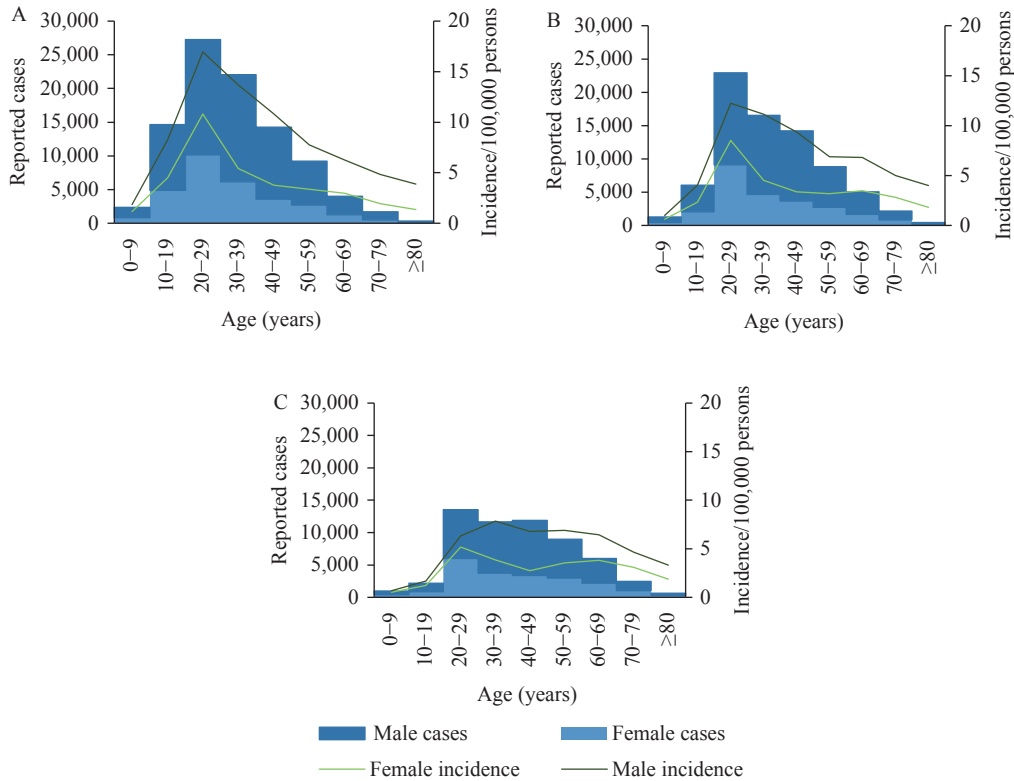


FIGURE 3. Age-specific and gender-specific cases and incidence of acute hepatitis B (AHB) in three stages in China, 2005–2019. (A) Primary stage. (B) Catch-up stage. (C) Acute hepatitis B (AHB) surveillance pilot stage.

and 20,797 reported annual cases among females (1.52 per 100,000). (Figure 3)

DISCUSSION

The World Health Organization (WHO)'s global health sector strategy on viral hepatitis (4) aimed to eliminate viral hepatitis as a major public health threat by 2030, specifically targeting reduction of the incidence of new hepatitis B infections. In China, coverage of HepB among newborns had consistently been over 95% since 2009 (5), and chronic hepatitis B caused by early childhood infections has been effectively controlled. China has continued to take measures to decrease the incidence of AHB. Our study showed that the annual reported incidences in the catch-up stage and AHB pilot stage were 20.69% and 40.26% lower than those in the primary stage.

In the catch-up stage (2009–2011), China conducted a HepB catch-up campaign for children <15 years of age who were born during 1994–2001. This campaign reached approximately 68 million children. As a result, the largest decrease in AHB was among those under 20 years of age during the catch-up stage — a decrease of 50.34% compared with the primary stage. In the AHB surveillance pilot stage, standardized diagnostic and reporting procedures for clinicians, based on national diagnostic criteria, were promoted to improve the accuracy of AHB reports from 200 sentinel counties. At the same time, AHB surveillance guidance encouraged hospitals to use IgM anti-HBc testing to help distinguish acute from chronic hepatitis B (6–8). These efforts led to a 26.30% decrease in AHB incidence compared with the catch-up stage.

Guangxi had the highest AHB incidence among all PLADs during all three stages, although incidence decreased over time. Several factors likely contributed to Guangxi's high incidence: first, sero-epidemiological studies conducted in 2006 (9) and 2014 (10) showed that the HBsAg prevalence in Guangxi was more than 8% higher than other PLADs; second, the HBsAg prevalence among women of childbearing age was approximately 10% in Guangxi, which may have led to infection of the spouses through sexual transmission without effective protection measures (11); and third, sexual transmission (12) and dental treatment in private clinics may also be contributing factors (13).

This study had strengths and limitations. A strength was that this study was the first to analyze the characteristics of AHB cases reported from all 31 PLADs of mainland China. Our study was limited by

variation in laboratory capacity in reporting hospitals as not all hospitals conducted IgM anti-HBc testing. Diagnosis of AHB should be based on positive IgM anti-HBc and HBsAg tests along with symptoms related to hepatitis B. However, IgM anti-HBc was present in approximately 10%–15% (14–16) of patients with chronic hepatitis B — especially in CHB with an acute flare-up. Therefore, the reported AHB incidence was higher than the true incidence. Another limitation was that differences in the diagnostic ability of each PLAD for AHB affected the reported incidence in each PLAD.

In summary, the incidence of AHB cases decreased significantly since 2005. Although much progress has been made in AHB control, creative work remains to be done in China. First, HepB coverage should be increased among adults to reduce AHB among people over 20 years old. Second, epidemiological investigations of reported AHB cases need to be conducted to identify risk factors for infection and develop effective strategies for prevention. Finally, a post-vaccination serological testing (PVST) recommendation for HBV-exposed newborns is crucial for the prevention of vertical transmission of hepatitis B virus.

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REFERENCES

1. The Polaris Observatory Collaborators. Global prevalence, treatment, and prevention of hepatitis B virus infection in 2016: a modelling study. *Lancet Gastroenterol Hepatol* 2018;3(6):383–403. [http://dx.doi.org/10.1016/S2468-1253\(18\)30056-6](http://dx.doi.org/10.1016/S2468-1253(18)30056-6).
2. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: Cancer J Clin*

- 2018;68(6):394 – 424. <http://dx.doi.org/10.3322/caac.21492>.
3. Zhang Q, Miao N, Zheng H, Sun XJ, Yin ZD, Wang FZ. Incidence by age and region of hepatitis B reported in China from 2005 to 2016. *Chin J Vaccin Immun* 2018; 24(2): 121-6. <http://d.wanfangdata.com.cn/periodical/zgjhmy201802001>. (In Chinese).
 4. WHO. Global health sector strategy on viral hepatitis 2016-2021. <http://www.who.int/hepatitis/strategy2016-2021/ghss-hep/en/>.
 5. Cui FQ, Shen LP, Li L, Wang HQ, Wang FZ, Bi SL, et al. Prevention of chronic hepatitis B after 3 decades of escalating vaccination policy, China. *Emerg Infect Dis* 2017;23(5):765 – 72. <http://dx.doi.org/10.3201/eid2305.161477>.
 6. World Health Organization. Hepatitis B: WHO Fact Sheet, July 2020. <https://www.who.int/en/news-room/fact-sheets/detail/hepatitis-b>. [2020-07-02].
 7. Centers for Disease Control and Prevention. Hepatitis B: CDC Fact Sheet, June 2016. <https://www.cdc.gov/hepatitis/HBV/PDFs/HepBGeneralFactSheet.pdf>. [2020-07-02].
 8. Ministry of Health of the People's Republic of China. WS 299-2008 Diagnostic criteria for viral hepatitis B. Beijing: People's Medical Publishing House, 2009. <http://www.csres.com/detail/197791.html>. (In Chinese).
 9. National Health Commission of the People's Republic of China, Chinese Center for Disease Control and Prevention. The national report of hepatitis B serosurvey of people in China in 2006. Beijing: People's Medical Publishing House. 2011; p. 1 – 77. <https://www.wl.cn/6898778>. (In Chinese).
 10. National Health Commission of the People's Republic of China, Chinese Center for Disease Control and Prevention. The national report of hepatitis B serosurvey of people aged 1–29 years in China in 2014. Beijing: People's Medical Publishing House. 2018; p. 1 – 154. <https://item.jd.com/12536387.html>. (In Chinese).
 11. Qin QH, Xie XH, Zhang H, Yao H, Wang Q, Wei P, et al. Monitoring and analysis on maternal HIV, syphilis and hepatitis B serologic testing in Guangxi, 2011–2016. *Chin J Health Educ* 2018;34(1):10 – 3. <http://dx.doi.org/10.16168/j.cnki.issn.1002-9982.2018.01.003>. (In Chinese).
 12. Wang FZ, Chi PP, Bi SL, Wang F, Zhang S, Zheng H, et al. Study on the risk of spouse infection with hepatitis b virus in patients with acute hepatitis B. *Chin J Prev Med* 2014;48(8):736 – 7. <http://dx.doi.org/10.3760/cma.j.issn.0253-9624.2014.08.017>. (In Chinese).
 13. Wu WS, Zhao Y, Chen J, Li C, He HY. Incidence trend of acute hepatitis B and related risk factors in Tianjin. *Dis Surveill* 2014;29(9): 729 – 32. <http://dx.doi.org/10.3784/j.issn.1003-9961.2014.09.015>. (In Chinese).
 14. Han YN, Tang Q, Zhu W, Zhang XQ, You LY. Clinical, biochemical, immunological and virological profiles of, and differential diagnosis between, patients with acute hepatitis B and chronic hepatitis B with acute flare. *J Gastroenterol Hepatol* 2008;23(11):1728 – 33. <http://dx.doi.org/10.1111/j.1440-1746.2008.05600.x>.
 15. Dao DY, Hynan LS, Yuan HJ, Sanders C, Balko J, Attar N, et al. Two distinct subtypes of hepatitis B virus-related acute liver failure are separable by quantitative serum immunoglobulin M anti-hepatitis B core antibody and hepatitis B virus DNA levels. *Hepatology* 2012;55(3):676 – 84. <http://dx.doi.org/10.1002/hep.24732>.
 16. Rodella A, Galli C, Terlenghi L, Perandin F, Bonfanti C, Manca N. Quantitative analysis of HBsAg, IgM anti-HBc and anti-HBc avidity in acute and chronic hepatitis B. *J Clin Virol* 2006;37(3):206 – 12. <http://dx.doi.org/10.1016/j.jcv.2006.06.011>.