Trends of hepatitis B notification rates in Guangzhou, China, from 2006 to 2020: An epidemiological study

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Abstract

Background: Although the prevalence of hepatitis B in Guangzhou, China, is high, the epidemiological trends have not been well-documented. We analysed the data of newly reported hepatitis B cases in Guangzhou from 2006–2020, to explore the epidemiological trend and provide a scientific basis for the prevention and development of control measures.

Methods: Information on the population and new cases of hepatitis B in Guangzhou from 2006–2020 was obtained from the China Information System for Disease Control and Prevention, which was used to calculate the annual notification rates of hepatitis B by gender, age group (0–9; 10–19; 20–59; ≥60), and location (urban or rural). The joinpoint regression analysis was used to analyse the time trends and calculate the average annual percentage change (AAPC) and annual percentage change (APC) for each identified trend line segment.

Results: From 2006 to 2020, 361,909 new cases of hepatitis B were cumulatively reported. The average annual reporting rate was 189.64/100,000, and after a sharp increase from 2006–2008 (APC: 29.99%; 95% confidence interval [CI]: 12.14% to 50.67%), the notification rate showed a long-term downward trend from 2008–2018 (APC: -7.55%; 95% CI: -8.68% to -6.40%), with an average annual decrease of 1.27% (AAPC: -1.27%; 95% CI: -3.77% to 1.28%). Males had a significantly higher notification rate than females; however, the gender ratio decreased from a maximum of 2.53 in 2006 to a minimum of 1.54 in 2020. A downward trend in notification rate in urban areas and an upward trend in rural areas was observed, with an increase in the rural/urban ratio from 0.41 in 2006 to 1.57 in 2020. The notification rate for all age groups showed a downward trend year by year, except for the group ≥60 years, for whom it started to decrease from 2015.

Conclusions: Although the overall notification rate of hepatitis B in Guangzhou was decreasing year by year, it was still high. Especially in rural areas, the notification rate has been increasing in recent years, and effective measures should be taken to control hepatitis B infection in Guangzhou.

Background

Hepatitis B is caused by infection with the hepatitis B virus (HBV) and has become a major global public health problem[1, 2]. The latest data from the World Health Organization (WHO) showed that there are 296 million people were living with chronic hepatitis B (CHB), and hepatitis B resulted in an estimated 820,000 deaths worldwide in 2019[3]. Several studies have shown that the prevalence of hepatitis B varies by geographical region, with infection rates less than 2% in the United States and Western Europe, 2–8% in the Mediterranean and South America, and up to 20% in Asia and Africa[4–6]. In addition, significant gender, age, race, and urban-rural differences in HBV infection have been frequently reported, although these reports are not entirely consistent[5, 7, 8]. For example, a meta-analysis of Chinese populations showed that the prevalence of HBV infection was higher in males than in females and in rural than in urban areas[7], but an Iranian study confirmed that it was higher in the cities[8].

HBV is highly contagious and transmitted primarily via the perinatal and percutaneous routes and sexual exposure as well as by close person-to-person contact, presumably by open cuts and sores[9]. HBV is highly resistant, surviving up to 30 days at room temperature on dry surfaces[10]. Individuals with CHB infection are at an increased risk of developing HBV-related liver diseases, such as liver cirrhosis and hepatocellular carcinoma (HCC)[11, 12]. Studies have shown that 15–40% of people with CHB infection develop cirrhosis, HCC, or liver failure, and 25% die prematurely from these complications[9, 13–15].

In China, the national epidemiological survey reported that the positive rate of hepatitis B surface antigen (HBsAg) in the Chinese population was 7.20% in 2006. However, the positivity rate in Guangdong Province was 11.10% during the same period, which was much higher than the national average[16]. Guangzhou is the capital of Guangdong province, located in the south of China, with a resident population of 18.7 million in 2020, a developed economy and frequent movement of people, and the most recent large-scale population-based epidemiological survey of hepatitis B in 2018 showed that the rate of HBsAg positivity in the Guangzhou population was 12.45%[17], higher than the national rate and the provincial rate in 2006[16, 18]. Unfortunately, few studies have been reported in recent years on the changing trends of new cases of hepatitis B in Guangzhou.

This study aimed to describe the trend of the reported HBV infection rate in Guangzhou from 2006 to 2020, to provide a reference for the government to develop strategies and measures for the prevention of hepatitis B infection.

Methods

Data sources

Information on the number of hepatitis B infection cases and population, by gender, age, and location, was obtained from the China Information System for Disease Control and Prevention (CISDCP). The CISDCP system, which was introduced elsewhere, is a web-based infectious disease reporting system that was established in 2004, and it created a standardized case reporting form for collecting demographic and diagnostic information for each case afflicted by reportable diseases[19–21]. Clinically diagnosed and laboratory confirmed cases with the onset date from January 1, 2006, to December 31, 2020, and the current address in Guangzhou were screened as the study population.

All cases were divided by age into four groups comprised of children aged 0–9 years, adolescents aged 10–19 years, adults aged 20–59 years, and elderly aged ≥ 60 years. Based on socio-economic development, Zengcheng and Conghua districts were classified as rural areas, and the other nine districts, such as Yuexiu and Liwan, were classified as urban areas. Notification rates were calculated per 100,000 persons.

Statistical analysis

First, we used Excel for data collection; R software (version 4.1.1) was used for data cleaning and descriptive statistics, such as hepatitis B notification rate, notification rate ratio of male to female and rural to urban areas, etc., for all age groups during the study period. Second, joinpoint regression analysis software (version 4.9.0.0. March 2021; Statistical research and applications branch, National Cancer Institute) was used to examine the trends in the notification rates of hepatitis B infection for the whole population and subgroup populations during the study period. A maximum of two joinpoints were allowed based on the number of data points. The Grid Search method and Monte Carlo permutation tests were performed to identify the best-fitting combination of line segments and joinpoints. The average annual percentage change (AAPC) and associated 95% confidence interval (CI) were calculated to measure the direction and magnitude of trends over the full range of periods. We also calculated the annual percentage change (APC) and 95% CIs of each line segment. A 2-sided $p < 0.05$ was considered statistically significant.

Results

Overall trend of hepatitis B notification rate in the whole population

From 2006 to 2020, 361,909 new hepatitis B cases were reported cumulatively in Guangzhou. Among them, 68.70% were males, the median age was 37 years (28–51 years), and the average annual notification rate was 189.64 per 100,000 persons, with an average annual decrease of 1.27% (AAPC: -1.27%; 95% CI: -3.77–1.28%). Joinpoint regression analysis showed three periods with two joinpoints in 2008 and 2018. The notification rate increased sharply since 2006, peaked at 283.76 per 100,000 in 2008 (APC: 29.99%; 95% CI: 12.14–50.67%), And then began to decline year by year to 120.62 per 100,000 in 2018 (APC: -7.55%; 95% CI: -8.68% to -6.40%). After 2018, there was an upward trend (APC: 4.13%; 95% CI: -9.93–20.37%) but with no statistical significance (Table 1; Fig. 1a).

Table 1
Notification rate of hepatitis B in Guangzhou, 2006–2020 (1 per 100,000)

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Overall	158.78	249.88	283.76	269.16	254.55	218.10	204.24	207.45	180.55	172.52	154.11	154.93	120.62	144.
Gender														
Male	226.68	354.43	391.60	373.31	353.98	285.90	270.77	267.16	234.30	213.84	200.00	197.43	152.09	172.
Female	89.54	140.88	171.35	160.62	151.34	143.89	131.33	140.78	121.99	123.69	104.01	108.11	85.95	109.
Male/Female	2.53	2.52	2.29	2.32	2.34	1.99	2.06	1.90	1.92	1.73	1.92	1.83	1.77	1.58
Location														
Rural	72.11	119.61	146.72	153.60	141.47	109.29	116.20	138.58	124.74	133.10	135.88	162.22	161.64	169.
Urban	177.59	278.29	308.02	289.72	274.82	238.49	220.91	220.62	191.22	180.06	157.59	153.54	114.01	140.
Rural/Urban	0.41	0.43	0.48	0.53	0.51	0.46	0.53	0.63	0.65	0.74	0.86	1.06	1.42	1.21
Age group														
0–9 y	22.15	30.26	26.14	23.52	18.45	23.56	13.85	15.59	14.98	18.09	9.97	8.72	7.63	6.15
10–19 y	98.20	133.22	126.57	107.03	84.88	71.93	70.98	67.16	53.29	42.00	31.82	26.55	20.82	29.7
20–59 y	214.48	342.86	396.81	377.53	357.56	268.40	236.50	240.47	207.98	194.81	175.40	179.76	140.55	165.
≥ 60 y	123.92	209.64	248.49	244.25	254.05	231.92	264.80	271.36	241.68	271.52	236.00	230.97	174.95	194.

Trends Of Hepatitis B Notification Rate In The Subgroups

Overall, males had a significantly higher notification rate than females, but this gap showed a downward trend year by year. The gender ratio (male/female) decreased from a maximum of 2.53 in 2006 to a minimum of 1.54 in 2020 (Fig. 2a). Before 2017, the notification rate of hepatitis B in rural areas was lower than that in urban areas; however, after 2017, the notification rate in rural areas had exceeded that in urban areas, and the gap had gradually widened. The rural to urban ratio increased from a minimum of 0.41 in 2006 to a maximum of 1.57 in 2020 (Fig. 2b).

Trends in the gender-specific notification rate of hepatitis B are depicted in Fig. 1b. For males, the notification rate of hepatitis B declined from 226.68 per 100,000 in 2006 to 168.93 per 100,000 in 2020, with an AAPC of -3.58% (AAPC: -3.58%; 95% CI: -6.50% to -0.56%). Specifically, it increased sharply from 2006 to 2008 before a steady decline from 2008. The highest and the lowest values were observed in 2008 (391.60 per 100,000) and 2018 (152.09 per 100,000), respectively. For females, the trend of hepatitis B notification rate was generally consistent with the overall notification rate. Two joinpoints were detected in 2008 and 2018, where the notification rate showed an increasing trend from 2006 to 2008, with an average annual increase of 34.78% (95% CI: 12.08–62.09%), and a decreasing trend from 2008 to 2018, with an average annual decrease of 5.70% (95% CI: -7.06% to -4.32%). The trend after 2018 was not statistically significant (APC: 7.63%; 95% CI: -8.43–26.49%).

Figure 1c showed the trends of hepatitis B notification rates in both rural and urban areas. From 2006 to 2020, the notification rate in rural areas showed an overall increasing trend, with an average annual increase of 6.71% (95% CI: 3.75–9.76%); in urban areas, there was an overall decreasing trend, with an

average annual decrease of 3.43% (95% CI: -6.40% to -0.32%). Specifically, joinpoint regression analysis showed a significant upward trend in both rural and urban notification rates before 2008, with APCs of 43.38% (95% CI: 1.05 to 103.43) and 27.09% (95% CI: 0.25–61.11%), respectively. After 2008, the notification rate in urban areas showed a decreasing trend year by year, with an APC of -7.72% (95% CI: -8.95% to -6.42%); however, after a brief decreasing trend with no statistical significance from 2008 to 2012 (APC: -7.94%; 95% CI: -20.71–6.88%), the notification rate in rural areas began to increase year by year again, with an APC of 6.71% (95% CI: 3.75–9.76%).

Trends in the age-specific notification rate of hepatitis B are depicted in Fig. 1d. Joinpoint regression analysis showed that no joinpoints were detected for children in the ≤ 9 years age group, and the notification rate of hepatitis B showed a decreasing trend year by year, with an average annual decrease of 10.20% (95% CI: -13.04% to -7.26%); one joinpoint was identified for adolescents in the 10–19 years age group, and the notification rate showed a short-term increase from 2006 to 2008 (APC = 8.50%; 95% CI: -12.85–35.07%), followed by a long-term decreasing trend from 2008, with an average annual decrease of 14.32% (95% CI: -16.42% to -12.17%) in this group. Both the 20–59 years and the ≥ 60 years age groups identified two joinpoints in 2008 and 2015, corresponding to the APCs of 33.71, -11.05, and − 3.08 and 34.67, 0.44, and − 7.29 for the three periods, respectively. The notification rate of hepatitis B in the 20–59 years age group decreased by an average of 11.05% per year from 2008 to 2015 (APC: -11.05%; 95% CI: -15.09% to -6.82%), and in the ≥ 60 years age group, the notification rate decreased by an average of 7.29% per year from 2015 to 2020 (APC: -7.29%; 95% CI: -14.21% to -1.87%). Trends in other periods were not statistically significant in both age groups.

Discussion

Liver disease caused by HBV infection has resulted in a huge disease burden worldwide, and CHB infection is particularly prevalent in Asia, specifically in China[22–25]. In 2016, the WHO approved the first global health sector strategy for viral hepatitis, with the goal of eliminating viral hepatitis as a major public health threat by 2030 (reducing new infections by 90% and mortality by 65%)[23].

This study shows that the notification rate for new hepatitis B cases in Guangzhou decreased from 158.78 per 100,000 in 2006 to 141.73 per 100,000 in 2020, with an average annual decrease of 1.27%. Although the overall decreasing trend was not statistically significant, joinpoint regression analysis showed that the notification rate showed a short sharp increase from 2006 to 2008, followed by a long-term decrease at an average annual rate of 7.55% from 2008 to 2018 with a statistical significance, and a random fluctuation from 2018 to 2020. The period of rising notification rate from 2006 to 2008 may be because the CISDCP system completed in 2004 was still in the early stage of construction, and the functions of the system and the reporting requirements for medical institutions were not yet perfect. A similar situation emerged when Wang et al. used data from the CISDCP system to analyse the trends in notification and mortality of tuberculosis in China from 2004 to 2019[26]. After 2008, there was a long-term downward trend in the notification rate of hepatitis B in Guangzhou, which can probably be attributed to a series of interventions and the introduction of relevant policies by the Chinese government. The Chinese government has made great efforts to prevent HBV infection. In 1992, a recombinant vaccine was licensed and introduced nationwide for a fee, requiring one dose of hepatitis B vaccine for all births and two additional doses during infancy, with the goal of interrupting perinatal HBV transmission and providing lifelong HBV protection for new-borns. In 2002, China included the hepatitis B vaccine in its Expanded Program on Immunization (EPI), vaccinating free of cost for children aged under 14 years. In addition, from 2009 to 2011, a catch-up campaign was launched for children younger than 15 years, which succeeded in vaccinating nearly 68 million children[25, 27]. With the unremitting efforts of the government and although the notification rate of hepatitis B in Guangzhou has decreased significantly, the rate of 141.73 per 100,000 in 2020 is still significantly higher than some developed western countries, such as the United States, the European Union (EU) countries[28, 29], and Asian countries, including Japan and South Korea[30, 31], and also higher than the national average of 69.05 per 100,000 in 2014[32]. Guangzhou is still under tremendous pressure to achieve the 2030 target set by the WHO.

This study shows a long-term decreasing trend in the notification rates in both gender from 2008 (except for females from 2018 to 2020), except for an increasing trend from 2006 to 2008, possibly because of CISDCP system imperfections. The prevalence is significantly higher in males than in females, although this gender difference has decreased from 2.53 times in 2006 to 1.54 times in 2020, which is consistent with the reports from EU/European Economic Area countries in 2018[29]. The reasons for observing this trend are as follows: studies have shown that the variant oestrogen receptors were expressed more in male than in female HCC patients, leading to speculation that oestrogen may play a role in the protection and defence against HBV infection[33]; secondly, China has implemented universal free mandatory hepatitis B vaccination, thus generating universal resistance in both men and women, which further reduced the gender difference in HBV infection rates.

In addition, this study also found that, except for a significant increase in the notification rate of hepatitis B in both urban and rural areas from 2006 to 2008, which may be because of CISDCP system imperfections, the notification rate in urban areas has been declining at an average annual rate of 7.72% since 2008. However, rural areas showed a brief decline from 2008 to 2012, after which it began to increase at an annual rate of 6.71%. The decline in urban morbidity may be attributed to the benefits of a series of government interventions and policies, such as the EPI, vaccine catch-up campaign, etc. The long-term upward trend in rural areas since 2012 may be attributed to the increasing degree of urban-rural integration with the development of China's economy, which has significantly improved the level of medical care, medical resources, and the convenience of medical care for residents in rural areas; and the gradually increasing living standards, literacy, and awareness of medical care among rural residents. The combination of these factors has contributed to the increase in the diagnostic rate of hepatitis B in rural areas and the rate of medical consultation among the residents, ultimately leading to a yearly increase in the notification rate of hepatitis B. The notification rate of hepatitis B in rural areas exceeded that in urban areas for the first time in 2017, and the gap widened year by year, reaching 1.57 times the rate in urban areas by 2020, which is inconsistent with the significantly higher incidence of acute hepatitis B in urban areas than in rural areas reported in Poland and Norway[34, 35]. Possible explanations are that the incidence of hepatitis B in these countries is low and many of the new cases are immigrants, who mostly live in urban areas[35, 36].

There was an overall decreasing trend in the ≤ 9 years and 10–19 years age groups, and a decreasing trend after 2008 in the 20–59 years age group, except for a spike in the incidence from 2006 to 2008, possibly because of CISDCP system imperfections. This may be primarily due to China's vaccination policy and

the improvement of medical care, which effectively blocked mother-to-child transmission of hepatitis B. In the group aged ≥ 60 years, after a plateau period from 2008 to 2015, the notification rate of hepatitis B began to decline year by year, for which we cannot give a scientific explanation, and further studies are needed.

Our analysis had several strengths. First, with the continuous improvement of the CISDCP system and the increasingly standardized implementation of infectious disease reporting requirements by medical institutions, the CISDCP system includes almost all new cases of hepatitis B. A study showed that the overall underreporting rate of infectious diseases in Guangzhou is 1.17%, and the total underreporting rate of infectious diseases of category B to which hepatitis B belongs is 0.36%, which would be even lower if only the incidence of hepatitis B is calculated[37]. Second, we included up to 15 years of data in the analysis, which will greatly increase our ability to detect trends in change, and the results will be more consistent. The study also has several limitations. First, from 2006 to 2008, the notification rate for HBV infection showed a sharp increase, which we speculate to be an artefact caused by the inaccuracy of data at the early stage of the system rather than a real trend of change. Second, although the underreporting rate of the CISDCP system was low, the consultation rate of hepatitis B patients was not available. It can be speculated from the yearly increased notification rate in rural areas that there may still be numerous undiagnosed patients without symptoms in rural areas and that the new incidence of hepatitis B may actually be much higher than the notification of this study.

Conclusions

The overall notification rate of hepatitis B in Guangzhou is decreasing year by year; however, there is an increasing trend in rural areas in recent years. Effective measures should be taken to control hepatitis B infection in Guangzhou, especially in rural areas.

Abbreviations

HBV
Hepatitis B virus
CHB
Chronic hepatitis B
HCC
Hepatocellular carcinoma
HBsAg
Hepatitis B surface antigen
WHO
World Health Organization
CISDCP
China Information System for Disease Control and Prevention
AAPC
Average annual percentage change
APC
annual percentage change
CI
Confidence interval
EPI
Expanded Program on Immunization
EU, European Union.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethical Committee of Guangzhou Center for Disease Control and Prevention. As no personal information was collected in the study, the requirement of informed consent was waived by the Ethical Committee of Guangzhou Center for Disease Control and Prevention. In this study all applied methods were carried out in accordance with relevant guidelines and regulations.

Consent for publication

Not applicable.

Availability of data and material

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

YL is the Principal Investigator for the study and oversaw all aspects of data collection and analysis. WL wrote the first draft of the paper. All authors contributed to study design and conduct of the study and contributed to the final manuscript. All authors have read and approved the final manuscript.

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Figures

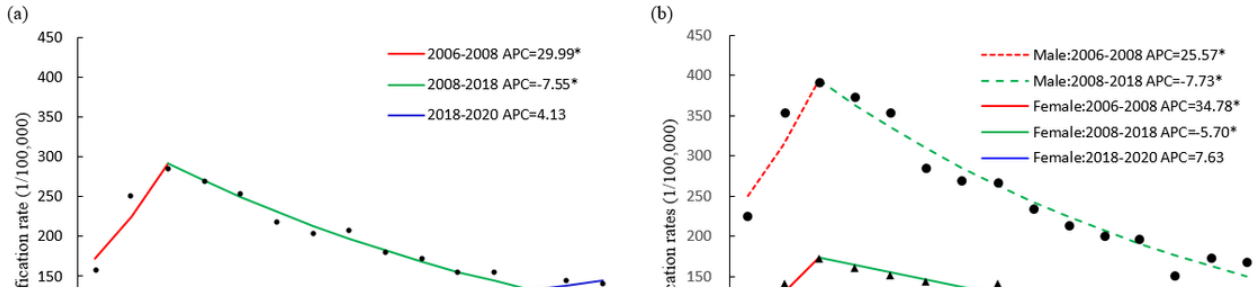

Figure 1

Joinpoint model estimates in Guangzhou during 2006–2020. (a) Trend in the overall notification rate. (b) Trends in the notification rate by gender. (c) Trends in the notification rate by location. (d) Trends in the notification rate by age group.

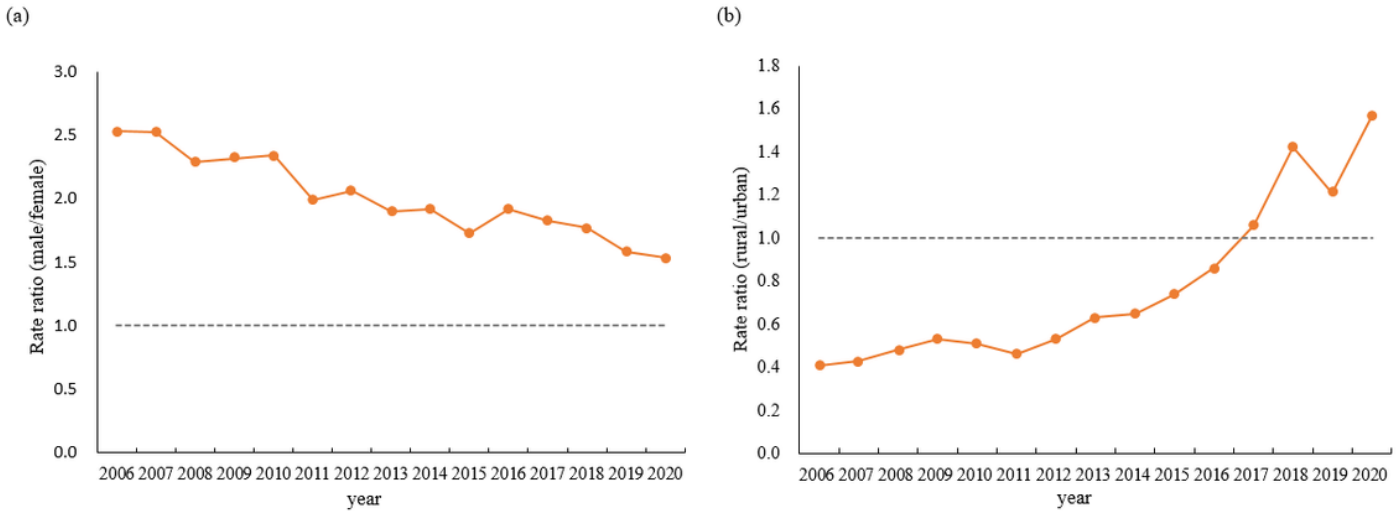

Figure 2

Trends in the notification rate of gender ratio and location ratio. (a) Trend of the gender ratio. (b) Trend of the location ratio.